Appendix to

Report and Recommendations Institutional Review Boards

The National Commission
for the Protection of
Human Subjects
of Biomedical and
Behavioral Research

LeRoy Walters

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This Appendix contains the papers, reports and certain other materials that were reviewed by the Commission during its deliberations on the performance of Institutional Review Boards.

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A SURVEY OF INSTITUTIONAL REVIEW BOARDS AND RESEARCH INVOLVING HUMAN SUBJECTS

A Report to the National Commission
for the Protection of Human Subjects
of Biomedical and Behavioral Research

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Introductory Summary

The data presented in this report describe the performance of institutional review boards (IRB's) and the nature of research involving human subjects that passed through these boards at 61 institutions during the period of July 1, 1974 to June 30, 1975. Close to 3,900 persons were interviewed about their experiences with this research and with the review process. Slightly more than 2,000 of these persons were research investigators; over 800 were members of review boards or persons especially knowledgeable about the boards in our sample; and close to 1,000 were subjects or their proxies. Appendices provide a detailed statement about the way this sample of institutions and respondents were drawn.

Outline of the Report

This report is divided into seventeen sections. The first describes the types of research involving human subjects conducted in a variety of institutional settings such as universities, medical schools, and hospitals. The second section concerns the selection of subjects, the number of subjects per project, how they were approached, and the reasons for their selection. The third, fourth and fifth sections focus on the consent process, proxy consent, and consent forms, respectively. The data presented in these sections are based on interviews with investigators (or the persons responsible for obtaining consent) and on content and readability analyses of consent forms. The sixth section presents data on the organization and characteristics of review boards. Most of the data discussed in this section were provided by a "key person" -- usually the individual who signed the general assurance or the chairperson of the review committee--who was especially knowledgeable about the character of the board.

Sections seven to fifteen concern the performance of institutional review boards. In section seven, we describe how we measured some aspects of IRB performance and we present some information about the range of variation among boards in our sample with respect to each aspect. The eighth section examines the relationships among aspects of performance: are boards that obtain a high score on one aspect of performance likely also to obtain a high score on others--or are there trade-offs such that achieving a high level on one implies sacrificing on another? The ninth section examines the possible connection between the amount and type of research reviewed by the boards (i.e., whether it is primarily biomedical or behavioral) and the performance of the boards. The tenth section considers the level of effort of boards--the time members spend, the number of meetings they attend, the number of proposals they examine--and how this effort relates to performance. The eleventh section examines review board practices and procedures (such as screening out proposals that do not require review) and their relationship to aspects of performance. The twelfth examines the composition of boards with respect to the sex, minority status, education, and professional heterogeneity of members and also considers the participativeness of boards--the extent to which members share influence in board discussions--as possible correlates of the boards' performance. The thirteenth section presents information about how attitudes of investigators and board members regarding research practices and the purpose of the review process relate to aspects of performance. The fourteenth considers how the amount of experience that researchers have had with review boards might affect their treatment of human subjects. For example, do researchers who have served on a board and who previously have submitted proposals to a board use more complete and readable consent forms?

The fifteenth section explores two questions concerning risk -- how risk (and benefit) as estimated by investigators is distributed among different categories of subjects and whether IRB's which review more risky research differ from other IRB's in their performance. Section sixteen presents data provided by a nonrepresentative sample of subjects and proxies concerning their experiences with research. The final section includes comments and suggestions regarding the conduct and review of research offered by investigators, review board members, and subjects. A set of tables and three appendices (on field procedures, sampling, and consent form readability measures) supplement this report.

Summary of Findings

Research involving human subjects was reviewed by institutional review boards at a variety of institutions. Medical schools (and universities that share review committees with medical schools) accounted for 59 percent of this research, while universities (with IRB's separate from those for medical schools) and hospitals accounted for 18 percent and 15 percent, respectively. The remaining projects were conducted at research institutions, dental and nursing schools, and institutions for the mentally infirm. Approximately 60 percent of the research conducted in all types of institutions combined was primarily biomedical. Slightly more than 30 percent of the research was primarily behavioral, and the remaining projects involved secondary analysis.

Patients served as subjects in approximately two-thirds of all research and most subjects were selected because of a specific disease, condition, or characteristic, according to investigators. Close to half of the research was either designed or expected (with a medium or high probability) to benefit

subjects directly. Such "beneficial" research was more likely than "non-beneficial" research to include patients while the latter research was more likely to involve students or staff. Beneficial research tended also to be relatively more risky and investigators doing such research were not as certain as those doing non-beneficial research that they knew all of the risks to subjects. Nonetheless, few researchers reported that they found the actual risks of the research exceeding their expectations. Provisions for treating subjects who might suffer harmful effects were also more likely in beneficial projects than in non-beneficial ones. Actual harm to subjects attributable to research was very rare, according to investigators.

Review committees required changes in procedures for obtaining consent in 24 percent of the projects, according to investigators. Written consent was obtained in 78 percent of the projects and oral consent was obtained in an additional 10 percent. Investigators generally reported that they requested the participation of subjects, but they recommended participation in 35 percent of the beneficial projects and in seven percent of the projects where benefit was not probable. Very few subjects were paid for their participation, and the amount of payment was in general very small. Relatively few prospective subjects found the decision to participate difficult, according to investigators, although this decision appeared to be somewhat more difficult in beneficial than in other projects. Furthermore, the likelihood of some subjects declining to participate was slightly greater in beneficial than in non-beneficial research.

Proxy consent was used in 27 percent of the studies--somewhat more frequently in hospitals (38 percent) than in other places, and in beneficial projects (35 percent) than in projects where benefit was not probable. Age of subject was the main criterion for the decision to use proxy consent. Most proxies were parents or other relatives; courts and institutional representatives served as proxies only very rarely. Subjects for whom proxy consent was used

were sometimes reluctant to participate, and in these cases the subject did not participate or an attempt was made to persuade the subject to participate.

Consent forms were used in about 80 percent of the research projects involving human participants. The purpose and procedures of the research were mentioned in most forms and risks were mentioned in forms for most, but not all, projects that investigators indicated entailed some risk. Consent forms were in general at a difficult reading level for the average layperson, but this difficulty was not attributable entirely to the use of medical or technical terminology. The complexity of sentence structure along with word length (non-technical as well as technical) affected the readability of these forms adversely. Nor was comprehensiveness a cause of difficulty; the more complete forms were neither more nor less difficult to read than the less complete forms. Furthermore, we did not see evidence that review boards affected the readability or the comprehensiveness of consent forms, although boards did request modifications in these forms.

Most members of review boards were scientists, but about 30 percent of the members did not identify themselves as behavioral or biomedical scientists. This group included administrators, lawyers, nurses, members of the clergy, and others. Biomedical scientists, behavioral scientists, and members of these other groups differed somewhat from one another in the concerns they expressed. For example, compared to biomedical scientists, behavioral scientists and other members placed relatively more emphasis on informed consent procedures and issues of privacy and confidentiality than on contributions to scientific knowledge. Furthermore, biomedical scientists felt that they were more influential and active on the board than were the other members.

Data provided by the board members and by the principal investigators who submitted proposals to the boards were used to measure various aspects

of the performance of the IRB's in our sample. These aspects of performance concerned the extent to which each board was (or appeared to be) comprehensive in its discussions of proposals, had procedures to monitor the progress of research, made modifications in proposals to improve the protection of the rights and welfare of subjects, approved readable and complete consent forms, and was viewed positively by board members and researchers and was judged by them to be doing a good job.

Some boards may have been outstanding in the sense that they "scored" high on all of the aspects of performance that we measured, but in general a board that was high on one aspect was not necessarily high on others. For example, we found no correlation between the evaluation of a board by its members and by the investigators whose research it reviewed. A few aspects of performance, however, seemed to "hang together." For example, the frequency with which a board made modifications in the consent procedures proposed by an investigator showed a positive relationship to the completeness of the investigator's consent forms. The most complete forms tended to be submitted to and approved by the IRB's which made the most modifications ($r = .43$).[1] But some aspects of performance appeared to be related negatively to one another. For example, investigators were less likely to say that the review procedure protects subjects where boards frequently requested additional information from them regarding their proposals ($r = -.35$).

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[1]We shall follow the practice of showing in parentheses the magnitude of the correlation that defines the relationship discussed in the text. Ordinarily we follow the convention of considering as statistically significant, and therefore worth reporting, correlations that occur at the .05 level of confidence. Correlations as large as this are likely to be found no more than five times out of 100 by chance. The size of the correlation that meets this criterion depends on the number of cases in the group being analyzed and in most of our analyses this minimum value is .23. We note, however, that these correlations are based on weighted data and must be interpreted cautiously.

The nature of research reviewed by boards appeared to be an especially important correlate of performance. Boards whose work load included a large proportion of biomedical research tended to rank high on many (although not all) criteria of performance. For example, they made slightly more modifications regarding consent ($r = .23$) and risk ($r = .29$) in proposals, they more often monitored projects ($r = .35$), and their discussions were relatively comprehensive ($r = .24$). On the other hand, they were more likely to approve research in which no provisions have been made to protect the confidentiality of the data ($r = -.46$) and to approve less readable ($r = -.38$), though more complete ($r = .40$), consent forms.

Boards varied widely in the amount of time and effort they devoted to the review process. Some boards spent less than ten member-hours on each proposal while others spent as much as 250 member-hours. And those that spent relatively more time tended to make more modifications in consent procedures ($r = .30$) and with regard to reducing risk and discomfort to subjects ($r = .48$).

Boards also differed in the types of procedures they used to review proposals. The procedures a board used and the frequency with which it employed them appeared to be related to some aspects of performance. For example, boards that more frequently assigned proposals to individuals and/or subcommittees made a greater variety of modifications in the proposals they reviewed ($r = .27$). Boards that approved proposals which were subjected to a second review made more modifications concerning risk ($r = .36$) and scientific design ($r = .40$) than did other boards, but they appeared to be less likely to monitor the research as it was actually conducted ($r = -.51$).

We did not find that the percent of women or minority persons on a board was associated with the board's performance; but several small correlations

indicate that where boards included persons who had only a bachelor's degree (or less), modifications suggested by the boards were more varied (r = .28) and consent forms tended to be more complete (r = .29) but no more readable.

Boards that were participative (in the sense that members shared influence) tended to be smaller (r = .52) and to have a lower work load (r = .38) than less participative ones, but the participative boards did not appear to be generally more active than the latter. At the same time, researchers who submitted proposals to participative boards were not as likely to have a high opinion of them (r = -.37).

Divisive disagreements did not occur often among members of boards, but where such disagreements did occur, members were likely to say that the review process impedes research (r = .24), does not protect subjects (r = .29) and that the board may not learn about harm to subjects that may occur (r = .34). In these situations, investigators themselves were less likely to have a favorable attitude toward the board (r = -.40) and to feel that the board protects the rights and welfare of subjects (r = -.26). On the other hand, IRB's characterized by some disagreement among members made slightly more frequent modifications concerning consent procedures (r = .31) and made a greater variety of modofications in proposals (r = .26).

Approximately one out of four investigators served on or was currently serving on a review committee. Investigators who had such experience and those who had prior formal contact with the board through the submission of proposals were a little less likely to have had their projects modified by the board. These differences between researchers may be attributable to their experience with the board and the review process, but may also be due to other factors such as greater experience conducting research.

We attempted to answer two general questions about risk to subjects. Does risk fall disproportionately on special groups or classes of persons? Do boards that review projects that are relatively high in risk differ in their performance from other boards? In response to the first question, we did not find that children, women, minority or low income persons were more likely than others to participate in projects that were above average in risk. Nor were they less likely than others to participate in projects that were intended to benefit the subject.

In response to the second question, we found that, in some settings, boards that reviewed relatively risky research performed differently than did other boards. For example, the discussion of proposals was likely to be more comprehensive in the higher risk boards and the rate of modification of research proposals suggested by these boards was likely to be greater. But this correspondence between risk and performance did not occur in all settings. This finding indirectly suggests that some IRB's may not be distinguishing between no risk research and research with risk, and may not be allocating their energies in accordance with the riskiness of the projects they review. It is possible that they are putting too much into projects that entail little or no risk, or that they are putting too little into relatively risky projects. In either case, improvement in the effectiveness of the process might be achieved by a redirection of their energies.

Data from subjects provide some general information about the performance of boards, but these data must be interpreted cautiously since we did not have a representative sample of subjects and proxies. Most subjects or proxies whom we interviewed recalled giving consent for participation, but ten percent of them said that they did not understand that they were to be involved in "research." The majority, however, felt that they were given clear,

sufficient, and accurate information about the project in which they participated. The single most prevalent reason for subjects' participation was the expectation of medical, psychological or educational benefits. Almost all of the respondents (98 percent) felt that participation was voluntary; most reported positively on the experience; and two-thirds felt that they (or the subject) benefited directly. Thirteen percent, however, said that they experienced unexpected difficulties. About 70 percent said that they would be very willing to participate in a similar study again.

The existing review process was viewed more favorably than unfavorably by most research investigators and review committee members. However, a substantial minority, particularly of the investigators, felt that the procedure is an unwarranted intrusion on the investigator's autonomy, that the committee gets into inappropriate areas, that it makes judgements it is not qualified to make, and that it has impeded research. The problem most frequently indicated by board members (from a list of ten problems) was getting members together for meetings. Between a fourth and a third of the members indicated problems due to the need for rapid action in order to meet deadlines imposed by funding agencies, the lack of precise DHEW guidelines, and the time spent unnecessarily reviewing research with little risk.

Subjects and proxies offered a number of comments and suggestions, including the desirability (expressed by 19 percent) for additional information about the research and the need (expressed by 11 percent) for more carefulness or courtesy on the part of the researchers in their treatment of subjects.

Methodological Note

The data of this report are based on interviews with approximately 3,900 respondents. The data are "weighted" according to the sampling design outlined in Appendix II.

The data concern 80 boards in a variety of institutions. The boards differ from one another in size, work load, and type of research reviewed, as well as in the aspects of performance and other characteristics that we are exploring. We have employed in some of our analyses correlational techniques that define the extent to which the above characteristics covary and we introduce "controls" in most of the correlational analyses of Sections VIII through XV so that we might understand the covariation between characteristics of the boards and an aspect of performance independently of the effect of, for example, the size of the board, the type of research it reviews (i.e., the percentage of its research that is biomedical) and its work load. Because our sample is very heterogeneous, including boards from medical schools, hospitals, universities, and other institutions, we have attempted in these sections to seek relationships that might be general to all types of institutions. In fact, the relationship between two variables may be different in one type of institutional setting, like hospitals and medical schools, than in another. We illustrate this difference in Section XV. Possibly because of the importance of conditions like these, the magnitude of relationships based on our entire sample are often not very great.

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I. Research Reviewed by IRB's (Tables I.1-I.5)

Research projects which involved human subjects and which were approved by Institutional Review Boards (IRB's) were conducted in various types of institutions. Medical Schools and universities that share a board with medical schools accounted for 59 percent of this research. Hospitals and universities (with IRB's separate from medical schools) accounted for 15 and 18 percent, respectively. The remaining 8 percent was conducted at "other" institutions including biomedical research institutions, dental and nursing schools, and institutions for the mentally infirm.

Approximately 60 percent of the research projects approved by IRB's were primarily biomedical, most frequently entailing the administration of drugs or the clinical evaluation of bodily fluids or tissues (Tables I.1 and I.2). Most of this biomedical research was reviewed at medical schools (75 percent) and hospitals (18 percent) (Table I.3). Behavioral research, on the other hand, accounted for approximately 30 percent of the research involving human subjects (Table I.1). About a fifth of this behavioral research entailed the study of an intervention of some kind, such as social or psychological therapy, behavior modification, or educational innovations. The behavioral research which did not involve such interventions entailed primarily interviews or questionnaires, psychological or educational testing, or behavioral observation. Secondary analyses represented the remaining small fraction (about 6 percent) of the research. Some of these studies involved the evaluation of bodily fluids or tissues obtained for other purposes or new analyses of data that had been collected previously.

As illustrated in Table I.2, more than half of all the studies reviewed by IRB's involved either the administration of drugs or the clinical evaluation of bodily fluids or tissues. Based on the reports of the investigators, almost half of the drug studies were done under an

Investigational New Drug Application (INDA) from the FDA. Relatively few identified these as Phase I or Phase II studies, but about a quarter indicated that they did not know whether their projects fit any of the FDA categories (Table I.4). In about 40 percent of the studies, the drug(s) reportedly would have been administered even if the subjects had not been participating in the research.

Studies of bodily fluids included, in over 90 percent of the cases, the examination of blood. Forty percent involved the analysis of urine, which was almost always freely voided. Investigators reported that the procedures used to obtain these fluids would have been employed in about half of the cases even if the research had not been conducted.

The biomedical and behavioral studies reviewed by IRB's were based on various research designs and methodologies. One or another of several research design features like blind methods, randomization, cross-over designs, and placebo administration occurred in close to half of the studies (Table I.5).

II. Research Subjects (Tables II.1-II.10)

Investigators were asked about the number of subjects they had planned to use in their projects. Because a substantial number of investigators failed to answer this question, only rough estimates of the average number of subjects per project are possible here. The median number of subjects is about 107 for projects reviewed by IRB's at universities, 37 for projects at medical schools and hospitals, and 48 for projects at other institutions (Table II.1).

Characteristics of research subjects. Patients served as research subjects in 76 percent of the projects reviewed by IRB's at medical schools, in 86 percent of the projects in hospitals, in 66 percent of the projects in other institutions, and in only 17 percent of the projects in universities. University projects most frequently involved college students (37 percent) as research subjects (Tables II.2 and II.3).

Subjects in almost half of the projects at medical schools or hospitals were the investigator's own patients, and almost as many were referrals from other physicians or professionals. Investigators in all settings commonly indicated that their subjects were "from an institutional population to which the investigator has professional ties," but it seems likely that different definitions of "institution" were being used (Tables II.4 and II.5).

In a large majority of projects, investigators reported that subjects were selected on the basis of a specific condition or characteristic (Table II.6 and II.7). This was true for more than 85 percent of the projects conducted at medical schools, hospitals, and other institutions, and for about 70 percent of the projects at universities. The particular criteria used were different for projects conducted at universities compared with projects at other types of institutions (Tables II.8 and II.9). The presence of a specific disease

or medical condition was used as a selection criterion for 20 percent of university projects, for 81 percent of medical school projects, for 87 percent of hospital projects, and for 72 percent of projects at other institutions. The presence of a behavioral problem was used to select subjects in 4 percent of university projects, about 1 percent of medical school and hospital projects, and 7 percent of projects at other institutions. Demographic characteristics, such as age and educational situation, were used as selection criteria for 69 percent of university projects, 18 percent of medical school projects, 12 percent of hospital projects, and 25 percent of projects at other institutions.

Review committee emphasis on subject selection. Subject selection was not an area of major IRB involvement, according to investigators. By and large, IRB's accepted investigators' plans for subject selection (data not shown). Changes were required in only 3 percent of the projects, usually by limiting or restricting the sample in some way (Table II.10).

III. Informed Consent (Tables III.1-III.17)

Consent procedures. Persons knowledgeable about the functioning of the review boards at the sample institutions provided information on such issues as the boards' policies regarding informed consent. Forty-six percent of these "key" persons indicated that their boards did not require written consent in some types of studies, for example, studies involving blood and urine samples, secondary analyses, and questionnaire administration. The degree of risk was reported to be the most frequent criterion that determined whether oral or written consent was necessary in a particular study.

Ninety-six percent of the committees required that investigators submit consent forms to them for approval--when such consent forms were used. The majority of the IRB's reported that most consent forms were written specifically for the study for which they were used. Less frequently used were standard consent forms that contained either no information specific to the study or into which some degree of information specific to the study had been inserted. The presence of a third party as a witness to the consent process was always required by 44 percent of the boards. Sixty-two percent of them never required that a person not connected with the research be available to answer subjects' questions.

Review committees required changes in the procedures for obtaining consent in 24 percent of the projects, according to principal investigators. In addition, changes were made in 12 percent of the projects as the result of informal conversations between committee members and investigators prior to their review. Changes were required most frequently (30 percent) in projects reviewed at hospitals, though variations among institution types were not striking. Many of these changes pertained to the explanatory materials to be presented to subjects (Table III.1). Biomedical projects

more than other types tended to elicit a recommendation for change.

Written and oral consent. Written consent was obtained in 78 percent of the projects, some of which also included oral consent. Oral consent alone was obtained in an additional 10 percent of the projects. Consent was not obtained in 12 percent of the projects (Table III.2). The major reasons cited for not obtaining consent included: (1) the return of questionnaires implied consent; (2) only routine treatments or procedures were being used; and (3) only existing records or data gathered for other purposes were being used. The largest proportion of the projects (36 percent) in which no consent was obtained involved analysis of data that had been obtained for some other purpose (data not shown). Consent, especially written consent, was obtained in beneficial projects more often than in non-beneficial ones (Table III.3). Investigators from 82 percent of the projects said that they had provided an oral explanation of the study to subjects and/or their proxies (Table III.4).

The consent process: who obtains consent? Principal investigators had either exclusive responsibility or shared responsibility (with a member of their staff) for obtaining consent in the majority (70 percent) of the projects (Table III.5), and this frequency was greater for beneficial than non-beneficial projects (Table III.6). The others who obtained consent were most frequently on the study staff, but in some projects a person not on the study staff performed this activity. A professional colleague of the principal investigator or a resident or research fellow in medicine, either on or off the study staff, was the most frequent other person to obtain consent. Less frequent were nurses, research assistants, students, and technical assistants (Table III.7).

Aside from the person who obtained consent and the subject and/or the

proxy, other people were usually present in half the projects when consent was sought (Table III.8). Other persons were present more often in beneficial than in non-beneficial research (Table III.9). The other persons present tended most often to be nurses or family members of subjects.

Gaining the participation of research subjects. We analyzed the relationship between the purpose of the research projects and the points that were emphasized by investigators when seeking consent. Among beneficial projects, direct benefit to subjects was emphasized most frequently (67 percent) by investigators when they were seeking consent, although benefits to other individuals in the future or to scientific knowledge were also mentioned in about half the projects. Among non-beneficial projects, emphasis was placed about as often on scientific knowledge as it was on benefits to other individuals in the future (Table III.10). Direct benefit to subjects was emphasized in only 19 percent of the non-beneficial projects.

When obtaining consent, principal investigators generally reported that they requested the participation of subjects. Investigators, however, recommended participation in 35 percent of the projects where benefit was likely and in 7 percent of the projects where direct benefits to subjects were not probable (Table III.11).

Investigators in 15 percent of the projects reported that they withheld some information from subjects. Information was withheld most frequently (29 percent) in projects conducted at universities and least frequently (12 percent) in projects conducted at medical schools (Table III.12). Information was withheld from subjects as frequently in non-beneficial projects as in beneficial projects (Table III.13). The information not divulged most often pertained to the purpose or specific procedures of the research and on the medication or treatment being used in the study. Reasons for this withholding

of information were primarily that the subject would not understand all of the information or that the information would result in biased data.

In a few projects reviewed at universities and institutions other than medical schools or hospitals, subjects were told things that were not true concerning the purpose of the study or the specific procedures to be used in it (Table III.14). According to the investigators, subjects were told these things to avoid biasing the data.

In the vast majority of projects, investigators did not pay subjects for their participation. In the projects where subjects were paid, the amount was small, frequently $1-$5 (Table III.15). Payments occurred more often in non-beneficial than in beneficial projects.

Many investigators felt that the decision to participate in the study was not difficult for subjects or proxies. Difficulty in making such a decision was reported more often for beneficial than for non-beneficial projects (Table III.16). Subjects declined to participate in beneficial projects more often (48 percent) than in non-beneficial projects (38 percent). Within those projects where some subjects declined to participate, the average percentage of those declining was small and about the same for beneficial and non-beneficial projects (Table III.17).

IV. Informed Consent through the Use of Proxies (Tables IV.1-IV.9)

Proxy consent was used in 27 percent of the studies. The greatest frequency of proxy consent occurred in projects reviewed at hospitals, including children's hospitals (38 percent); projects reviewed at universities had the least frequent (24 percent) use of proxy consent (Table IV.1). Proxy consent was somewhat more likely to be used in beneficial projects than in non-beneficial ones (Table IV.2), and instances of proxy consent occurred most often in behavioral intervention projects.

In projects involving proxy consent, the most frequent criterion (21 percent) for determining whether to use it was the subject's age.[1] The subject's intellect and the degree of illness were cited less frequently as criteria for the use of proxy consent (Table IV.3). Degree of illness was used as a criterion more often in beneficial than in non-beneficial projects (Table IV.4).

Parents, relatives, and legal guardians of the subjects were the most frequently used proxies. Courts served as proxies for 2 percent of projects from universities and 4 percent of projects from institutions other than medical schools or hospitals. Institutional representatives or the subject's physician served as proxies in very rare instances (Table IV.5). Approval for participation was obtained from the subject's physician in a majority of cases when the subject was the patient of someone other than the principal investigator on the project.

A large majority of the investigators reported that subjects for whom proxy consent had been obtained were rarely or never reluctant to participate.

[1]The median age above which no proxy consent was obtained was 18 years. The median age below which consent was not obtained from the subject in addition to the proxy was 12 years.

In only 3 percent of the projects did investigators report otherwise (Table IV.6). Subjects were slightly more likely to be reluctant in beneficial than in non-beneficial projects (Table IV.7). Most of the investigators reported that when instances of such reluctance occurred, either the subject did not participate or an attempt was made to persuade the subject. Investigators rarely reported that subjects were given no choice but to participate.

Most investigators reported that proxy consent protected subjects "very well" or "fairly well." Only 12 percent of the investigators reported otherwise (Table IV.8). Investigators from institutions other than universities, medical schools, or hospitals indicated most often (21 percent) that proxy consent did not provide adequate protection for subjects. The main explanations given for the inadequacy of proxy consent were: (1) where proxy consent is used, subjects may not be able to decide themselves whether or not they wish to participate in the research; (2) the proxy may not be able to understand the research; and (3) the proxy may not care about protecting the rights of the subject (Table IV.9).

V. Consent Forms (Tables V.1-V.15)

About 80 percent of the research involving human subjects used written consent forms (See Table III.2). Most were developed specifically for each study, but some were based on a standardized format provided by the institution (Table V.1). Three-quarters of all forms totaled less than 300 words, and these are designated as "short" forms in our analyses (Table V.2). In most projects, subjects/proxies were not given a copy of the form to keep (Table V.3).

Content of consent forms. Consent forms contained information about a variety of topics. To increase comparability of consent forms, we constructed an index of completeness which considers six aspects of informed consent outlined in The Institutional Guide to DHEW Policy on Protection of Human Subjects.[1] This index represents the extent to which a consent form covers each of the following: (1) the purpose of the research, (2) procedures involved, (3) the risks, (4) the benefits, (5) a statement that subjects are free to withdraw from the research, and (6) an invitation to subjects to ask questions about participation. (See Table V.4 and the accompanying explanation for more information about this index.)

According to this index, 18 percent of all forms were complete or nearly complete (Table V.4). Less than 10 percent of the forms from universities and other institutions were this complete, while 21 percent of the hospital and medical school forms were complete or nearly so. Some elements, particularly research procedures, received more coverage than others (Table V.5). Approximately 70 percent of the forms mentioned risk, although in

[1] U.S. Department of Health, Education, and Welfare. The institutional guide to DHEW policy on protection of human subjects. (DHEW Publication No. (NIH)72-102) Washington, D.C.: U.S. Government Printing Office, 1971.

some cases this mention was very brief. Some of the elements not mentioned in consent forms were covered in the investigator's description of oral explanations given to subjects (Table V.6). Investigators reported that in their oral explanations they mentioned freedom to withdraw and invited subjects to ask questions in about 20 percent of the projects in which these elements were not mentioned in the consent forms. Of the projects which did not mention risk in either consent forms or oral explanations, 70 percent were described by investigators as entailing at least a minimal degree of risk (data not shown).

It would be appropriate that alternative treatments be mentioned in consent forms for projects designed primarily to benefit subjects; however, this occurred only rarely (Table V.7). Similarly, consent forms from projects described by investigators as including an experimental element might be expected to mention this element. About 60 percent of the consent forms from experimental projects, however, did not identify the experimental nature of the project through the use of words such as "experiment," "research," or "investigation" (Table V.8).

We compared the descriptions investigators gave us of their research with the consent forms and oral explanations they gave subjects on a number of points (Table V. 9). In close to two-thirds of the projects in which a possible breach of confidentiality was indicated by investigators, this possibility was mentioned in either their consent forms or explanations to subjects/proxies. Investigators for about two-thirds of those projects that were expected to benefit subjects described benefits in their consent forms or explanations to subjects/proxies. Investigators in about one-third of the projects that were <u>not</u> expected to benefit subjects (or that had a very low probability of benefit) described benefits to subjects in their consent

forms or explanations. Eighteen percent of the projects in which subjects were assigned to one of several treatments or procedures under study or comparison mentioned this assignment in their consent forms or explanations. In 13 percent of the projects in which some information was to be withheld from subjects, this was mentioned. The frequency with which other topics of interest appeared in consent forms is shown in Table V.10.

Readability of consent forms. We used the Flesch technique to assess the readability of consent forms. This is a statistical formula developed for the objective measurement of readability and comprehension difficulty. The "reading ease score" for a selected reading passage is based on word length, i.e., the average number of syllables per 100 words, and sentence length, i.e., the average number of words per sentence. We selected the Flesch formula over others primarily because of its validity and its general applicability to technical material (see Appendix III.) The following statements illustrate a "fairly difficult" (one level easier than "difficult") and a "very difficult" (one level harder than "difficult") text as measured by the Flesch scale:

Example 1: Radioactive substance stays on a part of the drug, and a chemist can look for this trace of radioactivity in the urine, stools, and blood. In this way we can find out whether a drug is absorbed (taken up by the body), how it is digested or metabolized (handled by the body), and how it is excreted.

Reading ease = fairly difficult

Example 2: In our studies on the effect of ethandrolone[1] on the body and to the appearance and disappearance of ethandrolone after oral doses, there is the opportunity to study norethandrolone indirectly. A direct study of this major metabolite (40%-60% conversion in the body) thus may be accomplished by oral administration.

Reading ease = very difficult

[1]The name of the drug was changed.

We coded short consent forms for overall readability, while the readability for long forms was coded separately with respect to three content areas: purpose, procedures, and risks. Tables V.11 to V.14 summarize our analyses and show that consent forms were difficult to read. For the short forms and all three content areas of the long forms, the majority were at least "difficult" to read, requiring some college education. Medical and technical terms appeared infrequently, comprising well below five percent of all words in consent forms, and thus were too rare to explain entirely the difficult reading level of many forms. Nonetheless, most of these terms that did appear were in the more difficult forms. They were typically found at points critical to understanding the consent form, and very few forms provided lay explanations of their medical and technical terms (Table V.15).

We found no clear relationship between readability of consent forms and their completeness. The more complete forms were neither more nor less difficult to read than the less complete forms. However, in universities and hospitals, the reading level of risk explanations appeared to be slightly more difficult for projects that investigators estimated to entail relatively high risk than for those estimated to entail relatively low risk.

Effect of review boards on consent forms. We compared pre- and post-review versions of consent forms matched by project and found no difference, on the average, between these versions in either readability or completeness. This was the case whether or not the review boards had requested that changes be made and whether or not informal discussions had taken place. Furthermore, we found no difference between those pre-review forms for which a modification was requested and those for which no modification was requested. Apparently, the less readable and complete forms, as defined by our measures, were not any more likely to elicit a request for modification than were the relatively readable and complete forms.

VI. Institutional Review Boards: Composition, Structure, and Activities (Tables VI.1-VI.48)

This section presents data on the organization, composition, and characteristics of review boards and information about the members of these boards. Most of the data discussed in this section pertain to current review committees and were provided by a "key person"--usually the individual who signed the general assurance or the chairperson of each review committee. In addition, this section also includes some information from board members about their own views and experiences during the year ending in July 1975.

Review board composition. Practically all of the review boards serving medical schools, hospitals, and other institutions included at least one member who had conducted biomedical research (Table VI.1). Similarly, all boards in universities and institutions for the mentally infirm included one or more persons who had conducted behavioral research. Nearly 90 percent of all the boards had members who were administrators at their respective institutions. University committees were the most likely to include administrators. The percentage of boards which included members of the legal profession varied widely among the five sets of institutions. More than 90 percent of all the hospital boards and boards in other institutions included a member of the legal profession. Only one-third of the boards in institutions for the mentally infirm included such members.

Approximately three-quarters of the boards in other institutions had "community representatives" as members, according to the key persons; nearly all of the boards in medical schools, hospitals, universities, and institutions for the mentally infirm included such members. Ninety percent of all committees included at least one female member and minority groups were represented on half of the boards. Tables VI.2 to VI.4 show the educational

background, professional status, and institutional employment of minority board members.

The experiences and views of review board members. In order to examine the experiences, interests, and attitudes of review board members, we compared three groups of members: (1) biomedical scientists (50 percent); (2) behavioral and social scientists (21 percent); and (3) others (30 percent). (The composition of these categories is presented in Table VI.5.) More than three-fourths of all board members reported that they had been asked to serve; fewer than five percent said that they had sought membership (Table VI.6). A very small percentage of the members--22 respondents from 10 different review boards--reported receiving financial compensation specifically for serving on the committee. Behavioral and social scientists were less likely than other board members to be ex-officio members of review boards.

Members learned what was expected of them most often through written instructions such as the DHEW regulations (mentioned by more than two-thirds of the members), followed by oral instructions (mentioned by almost half), experience on the review board (mentioned by less than one-third), and through their own professional experience and reading (Table VI.7). Less than five percent cited attendance at special seminars, workshops, or symposia as a factor in learning the functions of a review board member.

There was little difference among types of board members in attendance at meetings,[1] with more than 90 percent in all categories indicating that they attended all or most meetings (data not shown). Almost half said that they had been assigned to report to the board on specific proposals, with biomedical scientists somewhat more likely than others to report having been

[1] Since most of the data in this section pertain to committee meetings, data from members of boards which did not meet are excluded. These constituted fewer than five percent of the review board members interviewed.

given this responsibility (Table VI.8). Of those who were assigned proposals, biomedical scientists reported being assigned more proposals (a median of eight in the previous year) than the behavioral scientists (six) or other board members (three)(data not shown). Biomedical scientists were also more likely to report that they had been assigned particular types of proposals (Table VI.9).

Almost half of the board members reported that investigators had on some occasion consulted with them before submitting a proposal for review. Biomedical and behavioral scientists reported such consultation more frequently than other members (Table VI.10).

Most members reported that they had on occasion discussed proposals with other members outside of committee meetings (Table VI.11). There was a clear tendency for consultation to occur within categories, so that, for example, biomedical scientists tended to consult with other biomedical scientists (Table VI.12).

The biomedical scientists were more likely than others to describe themselves as more active (Table VI.13) and influential (Table VI.14) on the committee than the "average" member.

Two-thirds of the board members indicated that there were aspects of proposals which they themselves were more likely than other members to raise for discussion (Table VI.15), and there were differences among members on the issues so raised (Table VI.16). For example, medical issues and risk ranked relatively high on the list for biomedical scientists; informed consent and scientific merit ranked high for behavioral and social scientists; while informed consent, consent forms, and the issues of privacy and confidentiality ranked relatively high for the other members. Overall, these responses suggest that a diversity of membership on review boards

brings with it a diversity of concerns.

The majority of members also indicated that there were issues about which they felt they were "expected to comment because of [their] particular expertise or point of view" (Table VI.17). Aside from comments about particular types of research (i.e., medical, psychological, or social), the most striking difference among types of members concerned informed consent, where non-scientists felt they were particularly expected to comment.

Another view of the board members' concerns comes from their responses to questions about the degree of emphasis they placed on six elements when reviewing proposals (Table VI.18). Overall, they placed the greatest emphasis on informed consent, followed by balance of risks and benefits, privacy and confidentiality, appropriateness of subject selection, contribution to scientific knowledge, and, finally, scientific design. However, there were again variations among types of members, with biomedical scientists more interested in contribution to scientific knowledge and research design and less interested in privacy and confidentiality than other groups. Behavioral and social scientists were less concerned about the selection of subjects than were the other members. Overall, biomedical researchers reported placing heavier emphasis on more elements than did the other types of members.

When asked to choose between two descriptions of the review board's purpose--to protect human subjects <u>or</u> to balance the need for protecting subjects with the need to develop new knowledge--there was a tendency for biomedical scientists to choose the latter and non-scientists the former (Table VI.19). On a related question, one-third of the review board members agreed with the statement, "Review committee members vary widely on how they view the purpose of the committee," although almost 95 percent agreed that

"there is usually consensus among members about what factors should be given most weight in reviewing proposed research" (data not shown).

Biomedical members were more likely than others to report that they had requested that the review board seek additional information from investigators (Table VI.20), and they were also more likely than others to initiate a request for modifications in proposed research (Table VI.21). A substantial majority of the board members said that such requests were always or often responded to (Tables VI.22 and VI.23). However, 14 percent reported that their review boards had in the past approved at least one proposal which, in their opinion, should not have been approved (data not shown).

Nonetheless, there was little feeling expressed that minority views are stifled. Almost all (96 percent) review board members agreed with the statement, "All viewpoints expressed by members are considered in committee decisions;" more than 85 percent disagreed with the statement, "Differences of opinion among committee members often go unresolved;" and 98 percent agreed that "All members are encouraged to offer their opinions when proposals are reviewed." There was little difference among types of review board members in their responses to these items. Overall, almost 90 percent agreed with the statement, "I am satisfied with what I have been able to accomplish as a member of this committee" (data not shown).

To briefly summarize this section, non-scientists felt generally less active on review committees and perceived themselves to be less influential than other members. Nevertheless, they brought different concerns to review committees and felt that their views were heard.

Breadth of research coverage. Some of the IRB's in our sample excluded certain types of studies from review (Table VI.24). About 15 percent of the boards in both universities and other institutions omitted research funded

by sources other than DHEW. All boards in medical schools, hospitals, and institutions for the mentally infirm reviewed non-DHEW as well as DHEW research. Similarly, more boards in universities and other institutions excluded unfunded research from their purview than did boards in the other three categories. About one-third of the university boards did not review research which involved no risk to subjects; medical schools, hospitals, and institutions for the mentally infirm did not make this exclusion. Research conducted by graduate or medical students was reviewed in almost all institutions where such research occurred. Twenty percent of the boards serving institutions where undergraduates conducted research did not review these studies. In particular, half of the university boards did not cover undergraduate research. Additionally, a small percentage of the university boards did not review research conducted in their physical education departments or law schools (Table VI.25).

At least some of the research reviewed by more than half of the boards had been previously reviewed by another committee (See Table VI.24). The proportion of boards which encountered previously reviewed research ranged from one-third among boards in other institutions to over three-quarters among boards in medical schools, hospitals, and institutions for the mentally infirm.

Staff assistance. Most boards received some secretarial assistance (84 percent) and some boards had administrative assistance (34 percent), but only 3 percent of the committees had legal assistance (Table VI.26). Part-time support staff was more common than full-time staff. Fewer boards in institutions for the mentally infirm had staff assistance than other boards.

Committee meetings. A very small percentage of the boards reported that members commented on proposals by mail rather than during meetings (Table VI.27). Over four-fifths of the boards reported that principal

investigators, at least occasionally, attended meetings at which their proposals were discussed (Table VI.28). The frequency with which investigators attended these meetings varied among the types of institutions; investigators attended meetings least frequently at universities and medical schools. More than half of all the boards reported that meetings were open to non-members (Table VI.29).

Information about proposals. Over half the boards required that investigators use standard forms to describe their research (Table VI.30). Nearly all of the others either provided forms for optional use or made available other information regarding what should be included in proposals. University boards were most likely to require the use of a standard form, while boards from other institutions were the least likely to provide either standardized forms or written instructions to the investigators.

Decision making procedures. About half of the review boards took formal votes on all proposals. Members reached consensus about proposals without a formal vote most often on university boards (Table VI.31). When formal voting did occur, about half of all the boards always or often relied on a "voice" vote, although another quarter never voted by voice. Roll call votes (or a show of hands) were used with about the same frequency as voice votes. Very few committees (about four percent) ever used a secret voting procedure; only one committee reported that members "often" voted secretly.

Twenty-four percent of the boards in our sample required a unanimous vote to approve a proposal. Research proposals which met with majority approval were accepted as satisfactory by two-thirds of the boards (Table VI.32). University boards required unanimous approval more often than other boards, and medical schools were least likely to require unanimity.

Screening and intensive reviewing of proposals. Almost two-thirds of

the boards used some type of procedure to screen out proposals "which do not need committee attention," including research using existing records, no risk or low risk projects, and research which does not involve human participants (Table VI.33). Committees in hospitals and medical schools, in particular, were likely to use screening mechanisms.

Over half of all the boards assigned proposals to individual members for special or intensive review (Table VI.34). These assignments were usually made as an initial review step or to provide the committee with an expert opinion. Nearly 95 percent of the medical school boards made such assignments. Individual reviewers were never reported to make decisions for the committee regarding a proposal's acceptability.

Approximately 25 percent of the boards delegated some responsibility to subcommittees, a third of which were permanent. Proposals were assigned to subcommittees for basically the same reasons that they were assigned to individuals (Table VI.35). Most of these subcommittees were expected to present a summary or make a recommendation to the larger group; fewer than one out of five subcommittees were empowered to make final decisions (Table VI.36).

Secondary review and appeal procedures. Proposals approved by one-fifth of all the IRB's were routinely subjected to further review (Table VI.37). Proposals approved by another four percent of the boards were reviewed again under some circumstances, such as when work space or funding was requested. Reviews beyond that of the IRB occurred most commonly in institutions for the mentally infirm and in other institutions. The secondary reviewers frequently had the authority to reject proposals approved by a board (Table VI.38), though less than five percent of the IRB's reported instances of such reversals during the past year. Respondents from those boards whose

project approvals were reviewed by a second committee did not think that the later review influenced their board in any way.

Proposals rejected by some review boards (13 percent) were automatically reviewed a second time (Table VI.39). This review was usually, but not always, conducted by a different committee. Boards in institutions for the mentally infirm were most likely (and medical schools and university boards were least likely) to follow this practice.

Almost half of the boards in our sample allowed investigators to appeal a decision (Table VI.40). The group or individual to whom appeal was to be made varied widely among institutions--appeals might be made to various individuals and groups, including, in some cases, the board which originally rejected the proposal. Half of those committees which had had decisions appealed within the past year had a rejection reversed by a subsequent review.

Committee involvement after initial review. Most boards approved some projects with the requirement that they be reviewed again after a period of between one month and three years, but usually after one year (Table VI.41). Hospital review committees were most likely (and committees serving institutions for the mentally infirm were least likely) to review proposals with the understanding that the project would be reviewed again.

When an ongoing project was resubmitted for review, four out of five boards required that "additional information" be provided concerning the general progress of the research, changes in the protocol, tentative results, funding information, the number of active subjects and refusals, and consent forms and/or subject-related problems.

Only half of the review boards were reported to have either a formal or an informal policy with regard to investigators reporting accidental injuries to subjects (Table VI.42). Two-thirds of the hospital boards had such

policies as did one-third of the university boards. The policy of most of these committees was that the investigator report the injury to the board; relatively few committees automatically required that a project be discontinued or reviewed again under these circumstances. Forty percent of the boards had a policy for treatment of or compensation for subject injuries (Table VI.43). Substantial differences appeared among institutional types, with medical schools and universities the most likely and hospitals the least likely to have provided for this contingency.

Committee observation of projects. One-third of the boards were reported to have designated members or representatives at some time to "observe the manner in which a project is conducted" (Table VI.44). Slightly more boards within institutions for the mentally infirm and hospitals observed ongoing projects than did boards in the other types of institutions. One out of five boards observed projects on a routine basis; the others that observed projects did so only under certain circumstances, such as when there was a particular risk, when children were involved, or when there had been past problems. Ongoing projects were also monitored through progress reports (mentioned by 15 percent), reviews of data (11 percent), and informal sources of information (7 percent)(data not shown).

Unreviewed research. Over 80 percent of all the respondents felt that it was either likely or certain that their boards would learn of the existence of any research that had not been reviewed or that was being conducted substantially differently from the way it was approved. Respondents from universities felt less confident than other respondents that their committees would be aware of such research projects. One-quarter of the boards had in the previous year become aware of the conduct of such research. When cases of illicit research were identified, committees normally intervened to require

review and or reported it to an authority of the institution.

Review board actions. Data provided by principal investigators indicated that between one-third and one-half of the proposals which were eventually activated had been modified in some way by the boards (Table VI.45). Most such modifications occurred in the formal review process, though an additional five percent of all the projects were modified as a result of informal discussions between the investigators and committee members. (Information about types of changes made are reported elsewhere in this report.) There was little variation among types of institutions in the rates of modification of proposals by review committees.

Some problems faced by the boards. Data provided by review committee members suggests that their boards faced a variety of minor or somewhat serious problems (Table VI.46). The need for rapid action because of funding agency deadlines was seen as a minor problem for half of the boards. The frequency of changes in DHEW policies and regulations was a minor problem for some boards (54 percent) but no problem for others (37 percent). The lack of precise DHEW guidelines regarding specific procedures or types of research was more of a problem for university boards than for other boards. Members of half of the university committees felt that this imprecision was at least a somewhat serious problem.

Disagreements among board members about the purpose of the committee apparently was not a problem for two out of three boards. Similarly, disagreements between the committee and investigators about the purpose of the board was a minor problem for only one-third of the committees. In general, board members did not see investigator antagonism toward the committee as being a problem.

The volume of work that had to be accomplished presented difficulties

for many committees. This seemed to be particularly true for medical school review boards where work load was identified as a very or somewhat serious problem by half of the boards. The problem faced by the greatest number of boards, however, was getting members together for meetings. While this was a problem for all types of boards, getting members together was particularly difficult in the other institutions.

Data regarding the problems faced by IRB's are presented in a different format in Table VI.47. In this table, data are provided on the percent of individual board members (with biomedical, behavioral, and other backgrounds) who perceived problems in the various areas discussed above. Furthermore, data regarding two additional problem areas are included: (1) the amount of committee time spent reviewing research which was essentially without risk, and (2) disagreement or uncertainty among review committee members about the meaning or interpretation of basic concepts such as "informed consent," "human subjects," "risk," "benefit," and "continuing review." Approximately one-fourth of the committee members felt that the amount of time spent on research without risk was at least a somewhat serious problem. While relatively few board members reported that disagreement or uncertainty regarding basic concepts was a problem, one out of five members with a biomedical background did perceive this to be at least a somewhat serious problem.

Finally, only five percent of the IRB members felt that some departments or types of research were treated unfairly by the board (data not shown). This kind of problem was mentioned, by members with various backgrounds, mainly in regard to psychological or social research; research in psychiatry and in nursing also was mentioned several times.

Seeking clarification from DHEW and NIH. Two-thirds of the boards have tried to get clarification or advice from either DHEW or NIH regarding

regulations or issues which they have faced. More than half of those boards that requested assistance received the clarification or advice they needed (Table VI.48). A significant number of boards, however, indicated that they received a response that was inadequate or no response at all.

VII. Measuring the Performance of Review Boards (Tables VII.1-VII.2)

This and the following sections focus on the performance of IRB's. There is little agreement regarding the criteria on which the performance of these boards should be measured. While various criteria can be suggested, no single measure of performance is likely to be entirely adequate. This report therefore considers multiple criteria including the extent to which the IRB: (1) is comprehensive in its discussion of proposals, (2) has procedures to monitor the progress of research, (3) makes modifications in proposals to improve the protection of the rights and welfare of human subjects, (4) approves readable and complete consent forms, (5) is evaluated favorably by IRB members, and (6) is viewed positively by investigators. These six aspects of IRB performance are described in this section.

Impact on proposals. The first aspect of IRB performance concerns the impact that boards have on proposals submitted for review. Our measures are based on principal investigators' reports of whether IRB's made the following types of modifications in their proposals:

1. modifications in regard to how consent would be obtained from subjects
2. modifications to reduce risk, discomfort, or inconvenience to subjects
3. modifications to protect the confidentiality of data or the privacy of subjects
4. modifications in scientific design
5. modifications in the proposed selection of subjects
6. any other modifications.

Our first measure of board impact is based on the percentage of proposals submitted to each IRB that were modified in one or more of these six ways. A second measure is an index of variety of modifications, based on a count

of the number of different types of modifications made at each institution. In addition, we measured (1) the percentage of proposals modified as a result of informal discussion with board members prior to submission of the proposals and (2) the percentage of proposals about which the board requested more information from the investigator.

Although over half of all the proposals submitted to IRB's were modified in some way, the average board made only two or three different types of modifications. Requests for more information and for modifications in the way consent was to be obtained occurred most frequently (31 percent and 24 percent, respectively). IRB's made other types of modifications in fewer than five percent of the proposals.

There is great variation among IRB's in the percent of proposals which they modified. Modifications in every proposal were reported in 14 percent of the boards, while 22 percent of the boards modified one-third or less of the proposals reviewed. Boards also vary in the variety of modifications they made. Only one type of modification was reported at 19 percent of the boards, while 7 percent of the boards made all six types. The median number of types of modifications made by boards was 2.5.

Research practices. Our analysis includes several research practices that have relevance to the protection of subjects in most research:

1. the percentage of projects in which investigators reportedly made provisions to protect the confidentiality of subjects

2. the percentage of projects in which investigators reported giving subjects an oral explanation as part of the consent process

3. the completeness of consent forms (see Section V)

4. the readability of consent forms (see Section V)

The percent of projects per institution in which no measures were taken

to protect the confidentiality of subjects ranges from 1 percent to 54 percent, with an average of 12 percent. The percentage of projects per institution in which subjects received an oral explanation ranges from 40 percent to 100 percent and averages 91 percent.

IRB members' evaluations of the review procedure. We created the following indices based on the responses of board members:

1. IRB members' judgements about how well the review procedure protects the rights and welfare of subjects

2. IRB members' judgements about the extent to which the review procedure impedes research at the institution

3. an overall evaluation which adds to the above items judgements about possible effects of the review process on the quality of research and the autonomy of researchers.

IRB members' evaluations of IRB's are mostly very favorable; nonetheless, there is some variation. For instance, 82 percent of the review board members felt that the review procedure protects subjects to a large extent, while 15 percent felt it protects subjects only to some extent.

Investigators' evaluations of the review procedure. The same indices developed for member evaluations were also computed for principal investigators' judgements regarding the review process. In addition, we developed an index based on their responses regarding the extent to which consent requirements and the review procedure impede their own research.

Although investigators' evaluations also tend to be favorable, they are less positive than IRB members' evaluations (Table VII.1). For example, 73 percent of the investigators indicated that the review procedure protects subjects to a large extent, while 25 percent felt it protects subjects only to some extent. Virtually all investigators agreed that their review boards run with reasonable efficiency, at least to some extent, and more than two-thirds saw the process as improving the quality of scientific research.

Investigators' views of the review process are not wholly positive, however. A substantial minority of them agreed with statements that the procedure is an unwarranted intrusion on the investigator's autonomy, the committee gets into inappropriate areas, it makes judgements it is not qualified to make, and it has impeded research. While committee members and investigators both have favorable attitudes, it is apparent on most of these items that attitudes of review committee members are slightly more positive than those of investigators. Among investigators, behavioral researchers expressed the least favorable attitudes toward review committees (Table VII.2). Nevertheless, when we discuss differences between boards in evaluations by investigators and board members, it should be remembered that we are generally differentiating between favorable and very favorable evaluations, rather than favorable and unfavorable ones.

Special consent requirements. We created an index of special requirements concerning the obtaining of consent based on the frequency with which the boards required that (1) some interval be left between the time a subject is told about the research and the time it begins, (2) a third person be present to witness the consent process, and (3) a person not connected with the research be available to answer the subjects' questions.

Six boards reported that they always require each of the above procedures. However, most of the boards (80 percent) seldom or never require (1) that an interval be left between the time a subject is told about the research and the time participation begins and (2) that a person not connected with the research be available to answer subjects' questions. On the other hand, 47 percent of the boards reported that they always or often require that a third person be present to witness the consent process, and an additional 20 percent sometimes require it.

Monitoring practices. IRBs' responsibilities do not end with the approval of projects.[1] For this reason, our analysis included a monitoring index based on IRB members' reports of the frequency with which their IRB's (1) received copies of final reports, (2) received copies of interim (progress) reports, and (3) met with investigators to discuss the progress of projects.

Some boards always engaged in these monitoring procedures while others never did. Sixty percent of the boards seldom or never received copies of final reports, 47 percent seldom or never received copies of interim reports, and 73 percent seldom or never met with investigators to discuss the progress of projects.

IRBs' awareness of problems. Ideally, the review board should be aware of any harm to subjects or problems that might lead to harm. Our measure of the boards' awareness of such problems was based upon members' assessment of the likelihood that their boards would learn of (1) harm to subjects, (2) on-going research that had not been reviewed, and (3) discrepancies between research as it was approved and as it was actually conducted. We combined all responses from each IRB into an index concerning its awareness of problems, as estimated by members.

Members of 70 percent of the IRB's reported that they would be very likely to find out about harm to subjects (if it occurred), 23 percent reported that it would not be very likely that they would find out, and 2 percent reported that it would not be at all likely. Members of 14 percent of the IRB's said they would be certain to find out about research conducted differently from the way it was approved, 64 percent said that they would be likely to find out, and 16 percent said that they would be very unlikely or

[1] U.S. Department of Health, Education, and Welfare, op. cit., pp. 8-9.

not at all likely to find out. Twenty-four percent of the review boards reported that they would be likely to know about unreviewed research being conducted, 27 percent reported that they would be somewhat likely to know, and 39 percent reported that they would be unlikely to know.

Comprehensiveness of discussion. We asked IRB members about the frequency with which various issues are raised for discussion. We then created an index of comprehensiveness by combining the responses of the members of each IRB regarding:

1. the comprehensiveness of their IRB's discussions concerning consent.
2. the comprehensiveness of their IRB's discussions concerning risk and benefit to human subjects
3. the comprehensiveness of their IRB's discussions concerning the scientific quality of the research.

The scores on this index could range from "1" (very comprehensive discussions--these issues are raised often and on all or most proposals) to "4" (not at all comprehensive--these issues are never raised at all on any proposals). The average score for all boards was 1.86, signifying that boards have, for the most part, fairly comprehensive discussions. Only 2.8 percent of the boards had scores greater than 2.5, indicating that practically all of the IRB's discuss these issues on at least some of their proposals.

VIII. Relationships among the Dimensions of Performance (no tables)

This section focuses on the relationships between the aspects of IRB performance which were measured for this study. Different patterns of relationships would imply different conclusions. For example, if the same boards tend to rank high on many of these dimensions, we could view each of our indices as measuring a different aspect of a generalized high quality review process. Our data would then reflect the overall quality of review of each IRB. On the other hand, if boards that rank high on some dimensions rank low on others, we would view each of our indices as measuring different aspects of board performance. Our data would then reflect the trade-offs that may inhere within the IRB approach to the protection of human subjects.

The data do not conform closely to either model, showing no consistent pattern of relationship among the various aspects of performance. Almost 80 percent of the indices we employed showed no relationship to each other. Slightly over half of the remaining relationships turn out positive, with the other half negative. Thus, there appears to be no general tendency for boards high on one aspect of performance to be high on others.

We did find that the frequency with which a board made modifications in the consent procedures proposed by investigators shows a positive relationship to the completeness of the investigators' consent forms. The most complete forms tend to be found at institutions where IRB's require consent modifications in a relatively large proportion of the projects reviewed ($r = .43$). However, the consent forms submitted to these IRB's were also more complete <u>before</u> they were formally reviewed by the boards ($r = .45$). Although we found no evidence of improvement in the completeness (or readability) of consent forms as a result of IRB review, the present results suggest that IRB's which frequently modify consent procedures may have a less direct, but

still important, impact on consent forms (See Section XIV).

Though the frequency of modifications of proposals by IRB's shows no consistent pattern of relationship with other dimensions of performance, there is one notable exception to this general finding. Review boards which make the most common types of modifications tend to receive lower evaluations from investigators. At institutions where IRB's made relatively frequent modifications concerning consent, investigators were less likely to feel that IRB's protect the rights and welfare of subjects "to a great extent" ($r = -.33$). Similarly, IRB's which frequently made requests for more information received less positive evaluations by investigators ($r = -.39$). These findings suggest that there may be a trade-off between IRB activity and investigator acceptance, particularly when investigators do not see a link between IRB requests and the protection of subjects. Investigators' evaluations tend to be unrelated or slightly negatively related to the other dimensions of performance.

The lack of a consistent pattern of relationships among the various dimensions of performance suggests a degree of independence among the various facets of the IRBs' functioning. This means that no inference can be drawn that any of our measures provides an adequate, overall measure of IRB quality. On the other hand, clear trade-offs, such as the one described above, occur infrequently.

IX. Effect of Type of Research, Work Load, and Size of IRB (no tables)

We consider in this section the size and work load of IRB's and the type of research they review. Research type, in terms of the percent of projects which are biomedical rather than behavioral, differs widely among institutions. As illustrated in Table I.1, this percentage is very high in medical schools and hospitals and very low in universities.

The percentage of biomedical research reviewed by boards appears to be related to many of the dimensions of IRB performance. As the percentage of biomedical research reviewed by an IRB increases, so does the variety of the modifications it makes ($r = .24$) and the frequency of modifications concerning risk ($r = .29$) and consent ($r = .23$). (Such modifications may seem less relevant to boards that review predominantly behavioral projects.) Boards reviewing a high percentage of biomedical proposals more frequently monitor the conduct of research in their institutions ($r = .35$) and, probably as a result, their members believe that they are more likely to become aware of harmful effects to subjects and discrepancies between research as approved and as conducted ($r = .49$). These boards generally hold more comprehensive discussions ($r = .24$) and more frequently have special requirements concerning the obtaining of consent, such as the presence of a third party ($r = .25$). However, they are no more likely than other boards to request additional information from investigators ($r = .00$) or to make modifications concerning the protection of confidentiality ($r = .04$), scientific design ($r = .00$), or subject selection ($r = .06$).

Projects approved by boards that review predominantly biomedical studies were less often reported to have measures to protect the confidentiality of subjects ($r = -.46$). This may be due to the fact that many of the subjects are patients and research is tied to treatment for which standard record

keeping procedures exist. Furthermore, while consent forms in research approved by largely biomedical boards tend to be more complete ($r = .40$), they are less readable ($r = -.38$).

IRB members' attitudes toward the review process appear similar in boards with high and low proportions of biomedical research. Principal investigators' attitudes toward the review process become slightly more favorable as the percentage of biomedical research reviewed by IRB's increases ($r = .25$).

IRBs' work load (the number of proposals that they receive for review) is related to a few of the performance dimensions. Boards with larger work loads make a greater variety of modifications than those with smaller work loads ($r = .60$). However, as work load increases, IRB's are no more likely to request additional information or to make consent, confidentiality, scientific design, or subject selection modifications; and they are slightly <u>less</u> likely to make modifications regarding risk ($r = -.29$). Investigators whose projects are reviewed by boards with larger work loads tend to submit and use more complete consent forms ($r = .32$). However, members of these boards are less likely to feel that they would become aware of problems in the conduct of research ($r = -.46$), such as the differences between research as approved and as conducted. This seems important because investigators and board members on IRB's with large work loads are more likely to feel that in some instances subjects may be exposed to additional risk as a result of discrepancies between research as approved and as conducted ($r = .28$).

Boards with larger work loads tend to have more members ($r = .46$), but board size itself bears no relationship to any performance dimension once type of research and work load are statistically controlled.

X. Effort (Tables X.1-X.3)

The amount of time and effort devoted to review committee activities varies considerably among the boards in our sample. Table X.1 shows that while these boards hold (on the average) ten meetings a year, some of them hold as few as two and others as many as fifty. Similarly, the average length of the meetings held by these boards ranges from one to four hours. The total number of meeting-hours, computed by multiplying the number of times the board met by the average length of these meetings, ranges from 3 to 135 hours. The size of the review boards in our sample also varies considerably, ranging from 5 to 55 members. (The average number of members across all boards is 14.) Calculations based on the size of IRB's and the frequency and length of their meetings show that the total number of member-hours spent in committee meetings ranges from a minimum of 27 hours to a maximum of 2,310 hours a year. The average number of committee member-hours spent in meetings is about 290 hours (which is equivalent to, for example, a ten-member board holding 29 one-hour meetings).

Data provided by board members indicate that their committee responsibilities involve time commitments beyond attending meetings. On the average, members reported spending a total of 55.2 hours a year attending meetings, reading proposals, and discussing research projects with investigators. Members of one committee spent an average of 404 hours a year on review activities; at the other extreme, members of another board spent less than 20 hours each performing these activities. Combining these figures with the membership data indicates that review committee activities consume, on the average, 760 member-hours each year. As illustrated in Table X.1, however, the time invested by members of some boards is substantially greater than that invested by others.

The boards in our sample reviewed an average of 43 proposals during the one-year period on which this report focuses. Table X.1 shows that this work load varies widely among boards, with some reviewing only one proposal and others reviewing more than 300 proposals over the one-year period. (These work load figures are based on records maintained by the review boards and exclude any "renewal" proposals reviewed during the year.) Considering the number of new projects reviewed by these boards, we estimate that the average board spent ten member-hours per proposal in meetings (Table X.2). Some boards spent less than one member-hour on each proposal while others--particularly those which reviewed few proposals--spent up to 50 member-hours in meetings on each project. The total number of member-hours per proposal (including time in and out of meetings) averaged 38 hours. This ranged from a minimum of 3.9 member-hours to a maximum of 270 member-hours per proposal.

The number of member-hours spent on each proposal is negatively related to the number of proposals reviewed by the boards ($r = -.32$). Boards that review only a few proposals spend a disproportionately large amount of time on each project. This may be due either to the limited experience of these boards with the review process or to the inefficiencies inherent in spreading the "fixed costs" of maintaining a committee over a very small number of proposals. The type of research being reviewed is not strongly associated with effort. Boards that review mainly biomedical (as opposed to behavioral) projects tend to spend slightly more time on the review process, but this trend is not statistically significant.

We examined the data to see whether effort is associated with various "outcomes" of the review process, such as the number of projects modified by the boards. Three different measures of time and effort were used in this analysis. The first--the adjusted level of effort per proposal--is based

on the total amount of time spent by the members of each board in meetings and on review committee activities outside of meetings. This measure represents the number of member-hours spent on each proposal, "corrected" for the indirect effects of work load (which, if small, might otherwise inflate the figure).[1] The second is the total member-hours in committee meetings per proposal. The data concerning this measure, which does not make the above adjustment for work load, are presented in Table X.2. The third is based on the average member attendance at board meetings. While members of some boards attend all the meetings of their committees, members of other boards reported that they attend only "some" or "most" of these meetings. Member attendance decreases slightly as the number of meeting-hours per proposal increases ($r = -.27$); this attendance measure, therefore, may be related to criteria of IRB performance in different ways than are the other, more "objective" measures of effort.

Table X.3 presents the correlations between the three measures of effort and the frequency of various types of modifications in proposals made by the boards. A positive correlation in this table indicates that a high level of effort is associated with a "high" rate of project modification. (Certain types of modifications--risk, confidentiality, and subject selection--are rare and even a high rate represents a small number of modifications.) The table shows that member attendance is positively related to the frequency with which boards request additional information from investigators. Additionally, as member attendance increases, boards more frequently require modifications

[1]This adjustment was made because of the above mentioned negative relationship between the number of proposals reviewed and the time spent on each proposal. This adjusted measure, therefore, reflects the "actual" time devoted to each proposal by excluding the fixed-time costs involved in maintaining a committee.

in the scientific design of the research proposals they review. The more objective measures of effort are positively related to modifications regarding risk, consent procedures, and confidentiality. For example, as members spend more hours in meetings on each proposal, they more frequently modify projects to protect subjects' confidentiality. (The frequency of these consent, risk, and confidentiality modifications is negatively related to members' attendance.) Boards that spend more member-hours in meetings more frequently receive proposals that already have been modified as a result of informal discussions between investigators and committee members. It appears that IRB's characterized by a high level of member effort in meetings are also characterized by a high level of informal effort outside the meetings. However, high effort committees make fewer different types of modifications than boards which devote less time to each proposal.

These findings suggest two trends. First, review boards characterized by significant time contributions on the part of their members take more action, particularly in terms of requiring modifications in consent. They tend to focus on particular types of modifications and are more likely to change a proposal than are low effort boards. Second, review boards characterized by high member attendance are not likely to require modifications which are directly related to the protection of human subjects. These IRB's tend to request additional information from investigators and to require modifications in the scientific designs of the proposed studies. Members of these committees are less likely to spend large amounts of time in committee meetings or to reject proposals during committee meetings.

Research investigators tend to have different reactions to these two types of boards. On the one hand, investigators feel that boards characterized by high member attendance get into inappropriate areas and make

judgements they are not qualified to make ($r = -.30$). Investigators see these boards as protecting human subjects, even though they require fewer modifications relevant to consent, risk, and confidentiality. On the other hand, investigators do not necessarily view the boards which spend the most time reviewing each proposal as those that most effectively protect human subjects ($r = -.22$), despite the fact that these boards more frequently make consent, risk, and confidentiality modifications. These high effort boards review many low risk proposals ($r = -.38$) and may be modifying projects with little or no risk as well as those with higher risk. Research investigators, particularly those conducting the low risk studies, may feel that the modifications required in such proposals do not increase the protection afforded subjects.

XI. Review Board Procedures and Performance (no tables)

As described in section VI, IRB's differ in terms of the procedures they use to carry out or facilitate the review process. Some boards, for example, have procedures for screening out proposals which do not need committee attention; other boards fully review all proposals submitted to them. Similarly, many boards assign proposals to subcommittees or individual members for special review while others do not. Boards also differ in terms of voting procedures (i.e., unanimity vs. majority rule), their practices regarding the attendance of investigators at committee meetings, and the availability of secretarial and administrative assistance. In addition, proposals approved by some boards are subject to further review while those approved by other boards are not. This section focuses on the way in which these IRB procedures and practices are related to such factors as work load and to certain outcomes of the review process.

Screening of proposals. More than 60 percent of the boards in our sample use some kind of procedure to screen out proposals which do not need committee attention. In most cases, this screening is the responsibility of the chairperson, acting individually or in cooperation with others. While these procedures are usually employed to screen out projects that do not directly involve human subjects, a few boards also screen out projects which are based on routine clinical procedures, involve no risk, and/or fall outside the jurisdiction of the committee. Screening procedures are more likely to be used by boards which review predominantly biomedical, as opposed to behavioral, proposals ($r = .37$). We found a slight positive, but statistically non-significant, relationship between the number of proposals reviewed by the boards and the presence of screening mechanisms ($r = .14$); this correlation probably would

be higher if the work load figures included those proposals which already had been screened out. Thus, screening mechanisms may be used most by boards that receive a large number of proposals as a means of reducing their work load. However, this reduced work load apparently is not associated with an increase in the amount of time spent on the remaining proposals. Controlling for the type of research reviewed, the amount of time spent on proposals is negatively related to the presence of screening mechanisms ($r = -.23$).

A higher percentage of the projects reviewed by boards with screening procedures involved risk than those reviewed by boards without such procedures ($r = .26$). This observed relationship may itself be an effect of the screening procedures if boards screened out no risk or low risk proposals. Screening does not seem to be related--either positively or negatively--to many aspects of review board performance. In general, we did not find that screening is associated with the number of proposals modified by boards, investigators' or review board members' attitudes toward the committees, or the quality of consent forms. However, investigators are less likely to see boards which screen out proposals as impeding their own research ($r = -.25$).

Special reviews by subcommittees or individual members. The majority of the boards in our sample assign at least some proposals to subcommittees or individual members for special review. Subcommittee and individual assignments are more likely to be made by boards with heavy work loads ($r = .26$). However, the frequency with which these assignments are made does not seem to be associated with any decrease in the number of member-hours spent on each proposal ($r = .03$). While boards reviewing behavioral as well as those reviewing biomedical research use subcommittees equally, those reviewing primarily biomedical projects are more likely to assign proposals to individual members for special review ($r = .24$).

Boards that assign a relatively high proportion of their proposals to individuals and/or subcommittees make a relatively large variety of modifications (r = .36) and the frequency with which they modify consent procedures is also relatively great (r = .28). The use of these special assignments, however, is not related--either positively or negatively--to the frequency of modifications regarding risk, scientific design, or confidentiality. Though special assignments generally are not associated with either board members' or principal investigators' attitudes toward the committee, they do seem to be positively related to investigators' evaluations of the soundness of committee decisions (r = .27).

Voting procedures. Approximately 20 percent of the boards in our sample require a unanimous vote to approve proposals.[1] Boards requiring unanimity differ from other boards in two respects. First, they generally review only a small number of proposals. While the average board reviews more than 40 proposals per year, those requiring unanimous voting review an average of only 14 proposals. This may suggest that IRB's with heavy loads have less time to resolve differences of opinion. Second, boards requiring unanimous voting are slightly smaller than other boards: they average 12 members while majority voting boards average 15 members. In view of these differences and the small number of boards that require unanimous decisions, it is not possible to compare meaningfully these boards to others to assess the implications of unanimity vs. majority rule.

Attendance of investigators at meetings. Many IRB's ask or allow at least some investigators to attend the meetings at which their proposals are discussed. The presence of investigators at meetings implies neither more

[1] An additional 22 percent reported that they always achieve unanimity, even though it is not a formal requirement, and 56 percent reported that their decisions to approve proposals are often unanimous.

nor less effort on the part of board members (r = .00). Nevertheless, members of boards whose meetings are attended by investigators feel that they more comprehensively discuss such issues as the protection of human subjects (r = .32), informed consent (r = .34), and the scientific quality of the studies being proposed (r = .31).

Boards characterized by relatively high attendance of investigators less frequently make formal requests for additional information (r = -.23). Though they are not more likely to make modifications involving consent, risk, confidentiality, or subject selection, they tend to make more modifications in the scientific design of proposed research (r = .31). Additionally, these boards more frequently maintain contact with investigators regarding their research projects (r = .32). Though the attendance of investigators does not generally imply more favorable attitudes of members or researchers toward the boards, infrequent attendance is related to the extent that investigators feel that the board impedes research and gets into inappropriate areas (r = .28).

Staff assistance. Approximately 80 percent of the review boards receive some secretarial assistance and one-third of the boards have administrative assistance. In the majority of cases, this support staff works part-time rather than full-time. Boards with administrative assistance often have secretarial assistance as well (r = .51) and as the number of proposals reviewed by boards increases, the amount of secretarial and/or administrative assistance also increases (r = .29). Boards reviewing biomedical research and those reviewing behavioral research are equally likely to have support staff, but those serving institutions for the mentally infirm have less staff assistance than others.

Though staff support may facilitate the review process, we do not find that the availability of secretarial and/or administrative assistance is associated with special procedures which potentially could improve the performance of boards. For example, the amount of secretarial/administrative assistance is not associated--positively or negatively--with the availability to board members of proposals ($r = -.05$), summaries of proposals ($r = -.07$), or consent forms ($r = .02$) prior to meetings. Similarly, staff assistance does not appear to be related to the frequency of "routine" contacts between board members and investigators after proposals had been approved ($r = -.17$).

Review subsequent to IRB approval. It was noted in Section VI that the proposals approved by one-fifth of all the boards are routinely subjected to further review. Members of these boards do not think that the later review influences their boards in any way. While our analyses generally support this assumption, they show that these boards do, in fact, differ from others in two important respects. First, the reviews conducted by these committees are somewhat "scientific" in orientation. Boards whose projects are subject to further review make more modifications in the scientific design ($r = .40$) and the risk ($r = .36$) of the projects they approve, but are no more likely than other boards to make other modifications. In addition, these boards are more likely than others to discuss comprehensively the scientific quality and design of the proposed research ($r = .35$). Second, the committees whose approvals are subjected to further review are less likely than others to monitor the research being conducted in their institutions ($r = -.51$). These boards have relatively few contacts with researchers after approving their proposals and are less likely to receive copies of interim and final reports.

XII. Membership Composition and Participation (no tables)

In this section we consider the extent to which boards employ participative decision-making practices and include persons from a variety of academic and demographic backgrounds. Because these practices are consistent with the prevailing democratic values of our society, they have been recommended as appropriate principles for structuring review boards. Furthermore, many proponents assert that these practices, particularly participative decision making, can lead to improved organizational performance, including better decisions. A board that includes members from diverse groups such as lawyers, the clergy, women, and minorities should in principle be more effective in representing the interests of subjects, along with others, in the research enterprise. This at least seems to be a hypothesis worth exploring. We therefore examined whether heterogeneous boards and participative boards behave differently, in terms of our criteria of IRB performance, than boards that are relatively homogeneous and less participative.

Membership composition. We have four measures of membership composition, three of which concern demographic characteristics and one of which concerns academic and occupational background. The three demographic measures consist of (1) the percent of female board members, (2) the percent of black and other minority board members, and (3) the percent of board members with a bachelor's degree or less. As for academic and occupational background, we ascertained whether or not the following types of persons are members of each board: (1) biomedical researchers, (2) behavioral researchers, (3) those with full-time administrative positions in the institution, (4) those with legal backgrounds, and (5) community representatives. Each board received a score based on the number of categories that were present. While these scores could range

from "1" to "5," the boards in our sample actually range from "3" to "5."

The results of our analysis indicate that percent of female members and percent of minority members have no relationship to the criteria of performance we measured. Having members of both sexes and from minority groups may be desirable in and of itself, but it has no apparent effect on IRB performance, at least as measured in this study.

The percent of committee members with a bachelor's degree or less does have a slight relationship to some of our measures of performance. First, consent forms (both as submitted and as approved) are likely to be more complete where boards include a relatively high percent of such persons ($r = .29$). The forms approved by these boards, however, are not more readable ($r = -.11$). Second, these boards make a greater variety of modifications in the projects reviewed than do boards that are less heterogeneous with respect to education ($r = .28$). Third, it is possible that this type of heterogeneity may have a negative consequence since principal investigators who submit proposals to these boards indicate, more than do other investigators, that the boards impede research in their institutions ($r = -.25$).

Heterogeneity of occupational and professional background also shows relationships to our measures of performance, but not in the direction or of the magnitude one might expect. For example, relatively heterogeneous boards were less likely to seek additional information from principal investigators ($r = -.24$) and to make a large variety of modifications ($r = -.29$). Furthermore, consent forms used by these investigators were somewhat less complete ($r = -.32$) and investigators were less likely to have measures to protect the confidentiality of their subjects ($r = -.35$). In addition, heterogeneous boards (in comparison to less heterogeneous boards) did not discuss proposals more comprehensively, require consent forms to be more readable, or make

suggestions for the modification of consent forms more frequently. On the positive side, investigators associated with the more heterogeneous boards had more favorable attitudes toward them (r = .24). However, this may be due to the fact that these boards appear to be less active in a number of respects. The reasons why heterogeneous boards seem less active are unclear. It may be possible that scientist members assume that community representatives, lawyers, and administrators on the board will take responsibility for certain issues and that the scientist members, therefore, need not concern themselves with these issues. Thus, if these outside members do not raise questions on proposals, scientist members feel they need not be raised. However, this is merely speculation and only further study can reveal if this does, in fact, occur.

Participation. Participation implies that all members in a group, rather than just a few, exert influence. We asked board members how much they agreed with the following statement: "the views of some members carry much more weight in committee decisions." Boards on which members disagreed with this statement are considered to be relatively participative. We also asked each member to estimate the percent of discussions about proposals in which he or she personally participated and the percent of discussions in which he or she raised issues. The responses to these three questions were combined to form an index of participation.

In general, participative boards tend to be small (r = -.52), to have a light work load (r = -.38), and to be concerned with behavioral rather than biomedical projects (r = -.40). Furthermore, their membership is less heterogeneous with respect to professional background (r = -.25), indicating that there may be a trade-off between such heterogeneity and participation. On

the other hand, we did not find that participative boards put more effort into each proposal than did the less participative boards--contrary to what some proponents of participation might predict. Nor did we find that members of participative boards hold more favorable attitudes, engage in more comprehensive discussions, or make more frequent modifications of proposals. However, we did find that principal investigators submitting proposals to participative boards have somewhat less favorable attitudes toward them than do investigators who submit to other boards. The former researchers are more likely than the latter to report that the boards do not protect subjects ($r = -.31$), that they impede research ($r = -.31$), and that they perform poorly ($r = -.37$) in general. This does not occur because participative boards are more active or demanding, for there is no relationship between participation and the number of modifications of proposals that the boards require or the amount of monitoring they do.

XIII. Board Performance and Orientation of Review Board Members (Tables XIII.1-XIII.2)

In this section we examine whether attitudes held by IRB members and disagreements among members are associated with IRB performance. In particular, we focus on attitudes about the acceptability of investigators paying subjects and withholding information from them, attitudes about the purpose of the review procedure, and disagreements over the meaning of terms used in discussions.

Restrictiveness toward payment to subjects and withholding information. We measured review board members' attitudes toward:

1. the acceptability of researchers withholding information from subjects under two conditions: (a) where the information might adversely affect the validity of the research and (b) where, in the judgement of the researcher, the information might be harmful to the subject

2. the permissibility of paying subjects to induce them to participate in a research project or to compensate them for risk or for inconvenience.

We found that IRB members' attitudes toward payment and withholding information are related to some aspects of IRB performance, though not strongly. Boards composed of members with relatively restrictive attitudes more frequently reported having comprehensive discussions of protection of human subjects ($r = .23$), making modifications in consent procedures ($r = .27$), and monitoring research ($r = .28$). Boards composed of members with relatively restrictive attitudes are also characterized by more favorable member attitudes toward the functioning of the review procedure ($r = .39$). An exception to this pattern is the finding that boards composed of members with less restrictive attitudes toward withholding information are more likely to request additional information from investigators ($r = -.30$).

Attitudes about the purpose of the review process. IRB members' orientations toward the purpose of the review process (Table XIII.1) are associated with several aspects of board performance in a way that may be surprising. Boards with a relatively large proportion of members who believe that the board's purpose is "to protect human subjects," rather than "to balance the need for protecting subjects with the need for developing new knowledge," tend to:

1. report that they discuss proposals less comprehensively ($r = -.29$)
2. approve more proposals which have no provisions to protect subjects' confidentiality ($r = .34$)
3. monitor research less ($r = -.29$)
4. less frequently require that special procedures be used in obtaining consent ($r = -.23$)
5. have members who evaluate the review procedure less positively ($r = -.23$).

On the other hand, these boards:

1. made more requests for additional information from investigators concerning proposals ($r = .24$)
2. had investigators more frequently report that the review process does not impede research ($r = .34$).

These findings provide some evidence that emphasis by board members on the protection of subjects to the exclusion of concern for developing knowledge may not be conducive to IRB performance.

Disagreements among IRB members. We also asked board members about the extent to which problems developed over disagreements concerning the purpose of the board and the meaning of basic terms such as "risk" and "informed consent." The results, displayed in Table XIII.2, show that such disagreements present serious problems to only a few IRB's but create minor problems for the majority. Our analysis indicates that members of boards with more disagreements tend to have less favorable attitudes toward the overall

functioning of the review procedure (r = -.53). More specifically, members of such review boards more often indicate that the review process impedes research at the institution (r = .24) and does not protect subjects (r = -.29). In boards characterized by disagreement, members indicate less certainty that they would learn about problems in the conduct of research, such as harm to subjects or discrepancies between research as reviewed and as conducted (r = -.34). We also found that certain research practices are less adequate where the board is characterized by disagreement. Fewer investigators reported that they provide oral explanations to subjects (r = -.29) and fewer reported taking measures to protect the confidentiality of subjects (r = -.24). Investigators have less favorable general attitudes toward such boards (r = -.40) and less frequently indicated that their boards protect the rights and welfare of subjects (r = -.26).

On the other hand, IRB's characterized by some disagreement tend to make more frequent modifications concerning consent procedures (r = .31) and to make a greater variety of modifications in proposals (r = .26). While basic disagreements may not be completely dysfunctional, they are associated with a number of negative consequences and seem to be a source of some strain for IRB members, as reflected in their evaluations of the review procedure.

XIV. The Educational Effects of Review Boards (Tables XIV.1-XIV.2)

In assessing the impact of review boards, this report has emphasized such aspects of IRB performance as the number of proposals modified and the extent to which boards monitor research. Review boards, however, may protect human subjects in other ways which are less direct and more subtle. It is possible, for example, that the mere presence of these boards affects the way investigators select subjects, obtain consent, and balance risk with benefit. Similarly, review boards may have an educational effect and, over time, may disseminate information, establish norms, and provide guidelines regarding the participation of human subjects in research. While this study was not designed to ascertain the presence or absence of these indirect effects of review boards, the data can be analyzed to determine whether or not they are at least consistent with the hypothesized effects. More specifically, investigators who have served on IRB's can be compared to those who have not in terms of the adequacy of their consent forms and the extent to which their projects were modified by review boards. Similarly, the experiences of investigators who have had many projects reviewed by boards in the past can be compared to the experiences of those who have had few or no previous projects reviewed. If the amount of previous contact with IRB's is related to more complete consent forms and fewer modifications, the data would be consistent with the hypothesized educational effects of review boards. However, this would not confirm the presence of such effects since these findings could be the result of other forces (e.g., the investigators merely having greater experience with the research process).

Approximately one out of every four investigators interviewed had served or was currently serving on a review committee. Table XIV.1 compares these investigators to those who had never served on a board. These two groups do

not differ much in terms of the frequency with which they informally discussed their research plans with board members (prior to submitting their proposals) or the frequency with which the boards formally requested that they provide more information about their proposals. However, the investigators who had not held membership on boards were somewhat more likely to have had the project about which they were being interviewed modified by the board. In addition, the consent forms used by these investigators were somewhat less comprehensive than those used by the investigators who had review board experience. Approximately 48 percent of the forms used by investigators who had served on review boards were relatively complete; this figure is 44 percent for those who had not served on boards.

Table XIV.2 compares three groups of investigators: those who had not had any projects reviewed by a committee prior to the one about which they were interviewed; those who had submitted one, two, or three prior proposals; and those who had submitted four or more proposals to a review committee. (Less than half of the projects included in this sample were conducted by researchers who had previously submitted four or more proposals.) Investigators with extensive prior experience with research and the review process were less likely to have had their current projects modified by the board; those who had never submitted proposals in the past reported more modifications as well as more requests by the boards for additional information. Similarly, those with little or no previous experience were more likely to have discussed their proposals informally with review committee members and to have modified their proposals as a result of these discussions. Furthermore, the consent forms used by the relatively inexperienced researchers are less comprehensive than those used by their more experienced counterparts. Only 31 percent of the investigators with no previous proposals used relatively complete consent

forms; this figure is 46 percent for those with between one and three previous proposals and 50 percent for those with four or more previous proposals.

Some of these findings are consistent with the hypothesis that review boards have an educational effect. The more experienced investigators, possibly as a result of their previous contacts with review boards, may have submitted proposals which were more consistent with the boards' standards and less in need of modifications. However, the differences between these groups of researchers do not necessarily confirm the presence of an educational effect. It is possible, for example, that review boards are more lenient towards researchers who have extensive prior experience with research and/or the review process. In contrast to those with less experience, these researchers may have higher status in their organizations, be afforded greater autonomy in carrying out their research, and/or know how to "get around" the review process. In addition, the fact that these investigators used relatively complete consent forms may be a result of their experience with the research process as well as the review process. Our data suggest, however, that review boards which frequently modify consent procedures tend to receive relatively complete forms from investigators submitting proposals ($r = .46$), and this finding may lend some support to the educational effect hypothesis.

XV. Risks and Benefits of Research (Tables XV.1-XV.24)

Beneficial vs. non-beneficial research. Projects were classified according to their expected benefit to the research subjects. A project was considered "beneficial" if it met either of two criteria. The first concerned the primary purpose of the research. If an investigator reported that his/her project was primarily intended to benefit the subject directly, that project was classified as beneficial. The second criterion concerned the probability of benefits to subjects. If an investigator reported a medium or high probability that subjects would receive some medical benefit, some psychological benefit, or help with their disease or problem, that project was also classified as beneficial.

Some investigators reported that the primary purpose of their research was something other than that of directly benefiting subjects but that, nevertheless, there was a low probability of some medical, psychological, or other benefit to the subjects. Because little or no benefit to subjects was expected, these projects were classified as non-beneficial. About 17 percent of the investigators, however, did not answer the questions about benefits, in part because the questions were asked in the self-administered questionnaire, which had a somewhat lower return rate than the personal interview. Hence, the tables regarding beneficial and non-beneficial research show a substantial amount of missing data.

According to investigators, 45 percent of all projects were expected to benefit subjects in some way, while 37 percent were not expected to benefit subjects (Table XV.1). Assuming that the 18 percent of the projects which are unclassifiable due to a lack of relevant information are similar to those which have been classified, the percentage of beneficial projects comes to 55 and that of non-beneficial projects to 45 percent. In any event, the proportion

of beneficial projects is somewhat greater than that of non-beneficial projects.

Among those projects which involved biomedical research, 52 percent were classified as beneficial (Table XV.1). Projects where the primary intervention was the administration of a drug, the administration of a vaccine, or the use of a therapeutic or diagnostic device were expected to benefit subjects more often than were other projects (Table XV.2). Some benefit was expected for subjects participating in 57 percent of the projects using behavioral interventions. Thirty-three percent of the other behavioral projects and 15 percent of the secondary analysis projects were beneficial, according to investigators. Among these two types of research, the studies most likely to be considered beneficial involved testing and interviews. Projects involving retrospective data review usually were not expected to benefit the subjects.

About half the projects reviewed at medical schools, hospitals, and other institutions (e.g., institutions for the mentally infirm) were expected to benefit their subjects, while 61 percent of the university projects were not expected to benefit subjects (Table XV.3). Patients served as research subjects in three-fourths of the beneficial projects and over half of the non-beneficial projects. Other kinds of subjects, e.g., persons from the general population and persons with a specific characteristic, participated in 26 percent of the beneficial projects and 43 percent of the non-beneficial projects (Table XV.4).

Risks and benefits of research expected to benefit subjects. Each investigator was asked about the probability of the occurrence of different types of risks and benefits to subjects "in terms of [their] understanding of the risks and benefits at the time the study began." Two-thirds of the

investigators whose research was expected to benefit subjects estimated that there was at least a medium probability of medical benefit occurring (Table XV.5). There was a medium or high probability of psychological benefit for almost half the projects. For about one-fourth of these beneficial projects, investigators reported that there was at least a low probability of minor medical or psychological risks. More serious medical and psychological risks, as well as risks concerning any breach of confidentiality, were seen as much less probable.

Risks and benefits of research not expected to benefit subjects. Consistent with out definition, none of the investigators conducting "non-beneficial" projects reported a medium or high probability of benefits, but about 15 percent of these projects were reported to have a low or very low probability of some medical or psychological benefit to the subjects (Table XV.6). The probability of medical and psychological complications occurring in these non-beneficial projects was also quite low. There was no more than a low probability of minor psychological stress for about 40 percent of these projects and no more than a low probability of minor medical complications for about one-fourth of the projects. More serious risks or risks associated with confidentiality were reported as even less likely to occur.

Tables XV.5 and XV.6 suggest that research involving a relatively high probability of benefit to subjects entails a concomitant slightly higher probability of risk to subjects than does research which is not expected to provide benefits. For example, some degree of minor medical complications is expected in about 59 percent of the beneficial projects and in 27 percent of the non-beneficial projects. This positive relationship between risks and benefits within projects is illustrated in another way in Table XV.7. Medical and psychological complications are considered together in this table and,

thus, the projects in the "no risk" row involve no possibility of either medical or psychological complications. Only 16 percent of the beneficial projects entail no risk according to investigators, while 40 percent of the non-beneficial projects involve no risk. In addition, Table XV.8 shows that projects which entail some medical risk are more likely than projects without such risk to involve medical benefits to subjects. Similarly, projects with some risk of psychological complications are more likely than projects without such risk to involve psychological benefit to subjects (Table XV.9).

Investigators' present assessments of risks and benefits. Most investigators reported that the risks and benefits which actually occurred in their research corresponded to their initial estimates of those risks and benefits (Tables XV.10 and XV.11). Almost all investigators reported that they had been at least fairly certain that they knew all the risks to subjects before involving them in their studies (Table XV.12). Very few investigators considered the risks involved in their research as outweighing the benefits to subjects. This was true of their assessments of the balance of risks and benefits both before and after subjects became actively involved (Tables XV.13 and XV.14).

Injuries or harm as a consequence of research and provisions for compensating injured subjects. Investigators were asked how many subjects had experienced harmful effects due to the research that were not predictable as an integral part of the relevant therapy or procedure. For the vast majority of projects, there were no such harmful effects. However, in three percent of the projects some harm did occur to an average of two subjects. These effects generally were considered trivial or only temporarily disabling. Three investigators reported fatal effects; in each of two projects one subject died and in one project three subjects died. Each of these projects

involved cancer research and in two of the projects at least some subjects were in a terminal stage at the time of their participation in the research.

Slightly more than half the investigators from projects expected to benefit subjects reported that there were provisions for treating subjects in the event of harmful effects (Table XV.15). Only 28 percent of the non-beneficial projects reported such treatment provisions. More than half the investigators conducting non-beneficial projects considered the question of whether they provided such treatment "not applicable;" presumably they saw their research as not entailing risk of harm. Investigators reported provisions for financial compensation to subjects in case of harmful effects for about half of the beneficial projects and one-third of the non-beneficial projects.

Breach of confidentiality. Most investigators reported having some procedure to protect the confidentiality of their subjects. The procedures mentioned most often included: separating the names of subjects from the data, limiting access to data, using mechanical means such as locking up project material, and not mentioning names of subjects in publications.

The chairperson of each board (or the individual who signed the assurance) was asked if his/her committee had approved any proposals with the explicit understanding that particular procedures for protecting confidentiality be used. According to these respondents, 60 percent of the committees approved proposals which gathered data anonymously. Seventy percent of the committees approved proposals where identifying information was stored separately from the data and 37 percent of the committees approved proposals where identifying information would be destroyed at a specified time. Other procedures the committees approved included limiting access to the data and using code numbers rather than names.

Risk of a breach of confidentiality was noted primarily by behavioral researchers and was not related to other types of risk. Investigators reported more than a very low risk of embarrassment (due to a breach of confidentiality) in only four percent of the projects; and actual problems of this type were reported in only four of about 2,000 projects. The remainder of this section will therefore focus on medical and psychological risks.

Type of research and risk. In order to assess the degree of risk associated with each project, we combined responses to five questions about the likelihood of medical and psychological complications. Weights were attached to the risks so that "serious complications" were weighted twice as heavily as "minor complications," and "fatal complications" were weighted three times as heavily. In addition, the risk measure used with each project reflects the probability of occurrence of the harm, as well as the severity. In the following pages, we refer to projects that are above average and below average in risk as measured by this index. Since a large number of projects reportedly involve no risk, those with above average risk include many that have a rather low level of risk.[1]

The distribution of risks and benefits by type of research (i.e., biomedical, behavioral intervention, other behavioral, and secondary analysis) appear in Tables XV.16 to XV.19. Table XV.20 presents, for each more specific type of research, the percent of projects entailing above average risk, the percent expected to benefit subjects, and the percent in which investigators estimated risk to outweigh benefit to subjects. The last two columns show the percent of projects in which investigators reported the actual occurrence of harmful effects and the percent of projects which had provisions for

[1]Projects that we describe as having above average risk are technically those falling above the median of risk for all projects. Since some cases are on the median, only 45 percent of the total sample falls above it.

treating subjects who experienced complications.

Drug research, surgery, the use of diagnostic and therapeutic devices, and social and psychological therapy come out relatively high on benefit, risk, and treatment availability and (with the exception of social and psychological therapy) actual harm. Table XV.21 shows this pattern from another perspective--as risk increases so do benefit, harmful complications, and provisions for treatment. These tables show the correspondence of risk scores with complications, availability of treatment, and/or the objectively measured types of research, and so provide some indication that the scale provides a reasonable measure of risk.

The risk associated with specific research procedures can be seen in more detail in Table XV.22. (The risk associated with each of these procedures may not be entirely due to the procedure itself, because investigators' estimates of risk pertain to projects which may employ several procedures. The presentation of the risk associated with some procedures will be artificially high when they are used in conjunction with other procedures that are, in fact, relatively risky.) Some of the rarer types of research procedures, such as extracorporeal circulation or cardiac catheterization, often appear to involve above average risk and, more than any other types of procedures, may entail risk that outweighs benefit to subjects. Among those procedures that occur more frequently (at least 75 times in our sample), drug administration, the use of anesthetics, measurement of electrical activity (such as EEG and ECG), and the use of X-rays and radioisotopes involve above average risk and sometimes have risk that exceeds benefit to subjects, in the opinion of the investigators.

Characteristics of subjects. Table XV.23 examines projects that draw substantial percentages of subjects from various demographic groups. Projects

in which investigators report relatively high proportions of (1) males, (2) persons between 41 and 64 years of age, or (3) high or middle income persons are more likely than other projects to be above average in risk. All of these projects, except those which involve predominantly middle-income persons as subjects, are also more likely than others to entail risk that outweighs benefit to subjects (although the percent of cases in which risk outweighs benefit is small). On the other hand, projects involving large percentages of minorities and children under 18 (excluding newborns) are less likely to entail above average risk.

Projects involving substantial proportions of children or older people tend to be beneficial to subjects more often than those drawing more heavily on 19 to 40 year olds. Furthermore, the latter projects are more likely than others to have risk that outweighs benefit to subjects.

Review board treatment of projects differing in risk. In protecting subjects from harm, IRB's might be expected to react differently to projects involving risk than they do to those with very little or no risk. One might expect that when boards review research above average in risk they would:

1. spend more time considering the proposals
2. discuss the proposals more thoroughly
3. make more modifications, especially with respect to risk
4. monitor the progress of the studies more carefully
5. more frequently report that they would learn about problems that might lead to harm
6. more frequently require that investigators give an oral explanation to their subjects
7. more frequently insure that consent forms are complete and readable.

The data as a whole, however, do not show a correspondence between the degree of risk associated with projects that pass through a review board and

the above actions by the board. Because we did not find a correspondence where we had reason to expect one, we supplemented our index of risk with a second one that eliminated very low probabilities of minor psychological or medical risks. Thus, while these minor risks might raise the score of risk defined by our first index, they do not affect the score of the second index. We thought that this might be a more sensitive indicator of "real" risk and therefore used it to examine the relationship between risk and each of the above activities. With minor exceptions, however, the pattern of results obtained through the use of this index is like the pattern which emerged when using the first index.

We therefore tried several additional analyses. We surmised that because relatively risky projects are also likely to be beneficial, boards might be inclined to expedite their approval and not monitor them on the grounds that they will benefit subjects. But an analysis that takes benefit into account did not support this interpretation.

We then divided our sample of institutions into two groups: one including medical schools and hospitals, the other including universities and other institutions. This distinction yields a result that does indicate the expected correspondence between level of risk and activities of the board in some institutions, if not in others.

Table XV.24 shows correlations separately for the two sets of institutions. An asterisk indicates that we estimate the correlation to have some statistical significance.[1]

[1]In order to simplify the table, we present only those activities that yield correlations that meet or that come very close to meeting our usual criterion of statistical significance in one or another of the two subsets of institutions. This criterion is a correlation of .30 which is at the five percent level of confidence for the number of cases within our subsets of institutions. The table thus refers to 13 activities out of 24 which we investigated in this analysis. The 11 excluded activities do not show a relationship with risk in either subset.

In medical schools and hospitals, boards that review projects with relatively high risk react differently to proposals than do boards in these institutions reviewing less risky research. Furthermore, the way in which these boards react to proposals appears to be predictable from the assumption that boards that review relatively risky research should exercise more care than boards that review less risky research. The result in universities and other institutions, however, does not fit this assumption well.

For example, in medical schools and hospitals, boards that reviewed relatively risky research were more likely than other boards to:

1. engage in comprehensive discussion of proposals concerning consent ($r = .36$) and the selection of subjects ($r = .27$)

2. request modification concerning consent ($r = .37$), confidentiality ($r = .27$), research design ($r = .47$), and other aspects of the proposal ($r = .37$)

3. review and approve research in which investigators report that they give subjects an oral explanation ($r = .43$).

The data concerning the readability of consent forms, however, represents a substantial contradiction to the assumption that boards reviewing relatively risky research would exercise more care than those reviewing less risky research. In fact, the consent forms approved by the former boards appear less readable than those that passed through the latter ($r = -.51$). We also found the forms approved by higher risk boards to be no more complete ($r = .13$). It is conceivable that oral explanations to subjects, which were reported more frequently for research passing through these higher risk boards ($r = .45$), compensate for the relatively poor readability of the written consent forms.

The association between average risk and board performance appears to be less substantial and less consistent in universities and other institutions than it is in medical schools and hospitals, perhaps because the former is a heterogeneous set of institutions. In these settings, boards that reviewed

relatively risky research appear to be less likely than other boards to have comprehensive discussions (r = -.41), including discussions concerning the selection of subjects (r = -.29) and scientific design of research (r = -.49). But they were more likely to require that researchers modify their proposals with respect to provisions for protecting the confidentiality of subjects (r = .43).

Risk and attitudes of researchers. In general, investigators appear reasonably supportive of the review process; most agree that the decisions of their boards are sound and that the review procedure protects subjects. Investigators associated with boards reviewing relatively risky reserach, however, differ in their attitudes toward the board from those investigators who are associated with boards that review low risk research. The correlations presented in Table XV.25 illustrate these differences. In medical schools and hospitals, investigators who submitted proposals to boards reviewing relatively risky research were less likely than those who submitted to other boards to express favorable attitudes toward the board (r = -.58), to say that the decisions of the board are sound (r = -.32), and to believe that the review procedure protects subjects (r = -.38). In universities and other institutions, investigators who submitted proposals to high risk boards were also less likely to say that the decisions of the board are sound (r = -.47).

Conclusions concerning risk and board performance. IRB members invest substantial effort in review work, as we have seen in an earlier section. Furthermore, this effort results in modifications of proposals and has other effects on the conduct of research. Thus, one might expect, in principle, that the impact of review boards might be increased and their performance improved by increasing the effort that members put into the review process. However, boards that review relatively risky projects do not, on the average,

invest more (or less) time in the review of these projects than do boards that review less risky projects. While we do not have a measure of the effort spent on each project that a board reviews, the lack of relationship between the average risk of projects reviewed by a board and the average effort spent by the board suggests that proposals may not be distinguished form one another within each board on the basis of risk for purposes of allocating effort to their review. We do find, for example, that very few boards have procedures for screening out projects that entail little or no risk (see Table VI.33).

It might be assumed, therefore, that IRB effort is not being allocated according to the degree of risk associated with a project, even though the more risky projects may deserve more attention from reviewers than less risky projects. If this assumption is correct, then improvement in the effectiveness of the review process might be achieved by reallocating the effort of board members in accordance with the riskiness of the projects being reviewed, rather than by increasing the already substantial effort that members are putting into the process. Tables XV.20 and XV.22 indicate that it may be possible to estimate the level of risk associated with specific types of research procedures and suggest that more detailed estimates could be developed. The availability of information concerning risk typically associated with types of research procedures may be helpful to review boards in making preliminary estimates of the risk associated with the proposals they receive and in allocating their effort accordingly.

XVI. Subjects' and Proxies' Perceptions of Research (no tables)

Some of the principal investigators who were interviewed for this report agreed to contact their subjects or proxies on our behalf. Subjects and proxies were asked, by these investigators, to return a form to us if they were willing to participate in our study (see Appendices Ih and Ii). This procedure enabled us to interview 809 subjects and 153 proxies. This sample does not represent, in any statistical sense, the larger population of research participants and/or their proxies. Some institutions did not allow us access to subjects. Additionally, some of the subjects who were contacted by investigators chose not to be interviewed. For these reasons, and because the interviews often took place months after the subjects' participation in the research, the data presented here should be treated cautiously.[1]

The consent process. Most of our respondents understood, before their participation began, that they were to be involved in "research" and remembered giving consent for their (or the subject's) participation. Eighty percent of the respondents remembered signing a consent form; fewer than four percent did not recall giving either written or oral consent.[2] Either these subjects (and proxies) did not remember signing a form or perhaps they did not realize that a form they had signed was designed to obtain their permission to serve as research subjects. Approximately 10 percent of the respondents said that they did not understand before their participation actually began that they were to be involved in "research."

The majority of our respondents felt that they personally were provided with clear, sufficient, and accurate information about the research project in which they participated. (Approximately a third of the proxies, however,

[1]The results presented in this section are based on unweighted data.

[2]Only subjects who had signed consent forms were included in our sample.

indicated that the researchers did not explain the study to the subject and that the subject did not have a very good understanding of what was to happen.) Eighty-three percent of the subjects and proxies reported that someone connected with the study talked with them and told them what was going to be done. The great majority of respondents felt that the information they were given was clear (93 percent) and accurate (94 percent). Those who saw the information as being less than clear cited a general lack of detail or a lack of clarity regarding the purpose of the research, the procedures to be followed, or the risks and side effects. Fourteen percent of the respondents said that they were given less information about the research than they wanted.

Seventy percent of the subjects and proxies in our sample reported that they asked the researchers questions about the study or about the subjects' participation in the study. These questions most frequently focused on the procedures to be followed, the purpose of the research, and the risks, discomforts, and side effects which might be experienced by subjects. Questions concerning benefits, the availability of the results of the study, and the characteristics of the drugs to be used were also reported. Almost all of the respondents (97 percent) felt that the researchers were willing to answer any questions they might have.

The decisions to participate in the research. The subjects and proxies we interviewed apparently had few problems deciding whether or not they (or the person for whom they gave consent) should participate in the research. Most of the respondents said the decision was "not at all" difficult and only eight percent said that it was a "somewhat" or "very difficult" decision. Consistent with this finding, subjects and proxies cited many reasons in favor of participating in the research and very few reasons for not participating. One out of every four respondents said that the main reason they agreed to

participate was that the research could benefit them medically, psychologically, or educationally. The second most important reason for participating was to help other people with similar conditions, to help science, or to help people in general. Third, financial reimbursement was mentioned by some respondents (17 percent) as the most important reason for getting involved in the research. Less than five percent said that free care, more personal care, or faster admission (e.g., into a hospital) was their most important reason.

Only 14 percent of the respondents cited reasons for not participating in the research. Considerations against participating included the time and inconvenience involved, the unpleasant procedures, and the expectation of psychological or medical complications. When specifically asked whether they expected any risk of harmful effects, 64 percent responded negatively. Those subjects and proxies who saw at least a very slight possibility of harmful effects mentioned minor physical discomforts, side effects and allergic reactions, internal damage, and/or psychological complications. In many cases, these harmful effects were expected because the subjects had been told about the risks of the research or the nature of the drugs or procedures to be used. In some cases, subjects expected risk on the basis of their own knowledge or information provided by other people (not on the research staff). Only four respondents said they expected some risk because they mistrusted research or the investigators, and only three people assumed that risk must be involved simply because they were asked to sign something.

Almost all of the respondents (98 percent) felt that participation was voluntary. Only 19 individuals said that participation was not voluntary or that they were not sure that they were free to refuse. One young respondent said, "My mother made the decision for me;" and another said, "My mother and doctor made me." Other respondents cited situational or research-related

factors which made participation seem less than voluntary: "The medicine was just given to me to take;" "I was afraid that if I didn't take what they offered they wouldn't do anything for me;" and "They fed all kids the same thing unless we brought our own food to the day care center."

Subjects' experiences. The subjects and proxies generally reported that their experiences with the research projects were positive. Thirteen percent, however, said that they had experienced difficulties which they had not expected. In about 40 percent of these cases, the unexpected problems were minor or temporary discomforts. Other respondents reported unexpected side effects (e.g., from drugs or procedures) or unpleasant psychological complications. Some subjects mentioned other, more serious, difficulties which they felt were related to their participation in the project: "miscarriage," "loss of sex drive," "arthritis got worse," "a lot of trouble with menstrual periods," and "pain is worse--I can't stand or sit." Other difficulties reported by subjects could be classified as minor inconveniences or problems which were clearly unrelated to the research. (For example, unrelated medical problems were brought to the subject's attention by the researchers in the course of the study.) Two subjects mentioned inadequate follow-up procedures: "Their follow-up on subjects was too soon to detect subsequent ovulation problems" and "It was difficult to get [psychological] help from the people in the study after the session ended."

Two-thirds of the respondents felt that they, or the person for whom they gave consent, benefited as a result of participating in the research. Most frequently mentioned was some type of direct benefit relevant to the subject's condition or disease. Educational benefits also were cited by a large number of subjects. Other benefits mentioned by the respondents, in descending order of occurrence, include: financial reimbursement; the satisfaction of helping

(e.g., other people, science, the particular study); subsequent advantages in health care (e.g., check-ups, preventive benefits); participating in an interesting or enriching experience; gaining access to procedures or treatments which seemed superior to the alternatives; and gaining a better understanding of one's condition or disease. Other types of benefits, such as receiving better care or more personal attention, were mentioned less frequently.

All subjects were asked, "Was the actual experience of participating in the research better than you expected, about what you expected, or worse than you expected?" One out of four subjects said that the experience was better and only seven percent felt that it was worse than they had expected. Finally, the subjects and proxies were asked if they would be willing to participate in a similar study again. Over 70 percent said that they would be very willing, 21 percent somewhat willing, four percent not very willing, and three percent not at all willing. Many of those who were less than willing mentioned the time and travel involved, the unpleasant procedures, or the side effects. Other respondents said that their decision to participate in another study would depend on the nature of the research or its benefits to subjects.

XVII. Investigators', IRB members' and Subjects' Views (Tables XVII.1-XVII.12)

In this section data are presented on investigators' and IRB members' opinions regarding the use of such research practices as deception and the payment of subjects. Also, the opinions of IRB members as to whether certain research procedures require review and consent are reported. Finally, the comments of investigators, subjects, and board members regarding research and the review process are summarized.

Investigators' and review committee members' opinions regarding research practices. A list of eleven possibly controversial research procedures was presented to investigators and review committee members for their judgement on whether the procedure "should not be done," "may be done in some circumstances," or "should not be done." These items pertained to topics such as compensation, withholding information, research involving children, high risk research, and the secondary use of information. Review board members were consistently more likely than researchers to say things "should not be done" (Table XVII.1). For example, 40 percent of the review board members said that "giving compensation commensurate with risk" should not be done, compared to 23 percent of the investigators. The data in this table suggest some possible areas for conflict between review boards and investigators.

Biomedical scientists' attitudes were more restrictive than those of behavioral scientists, both as review committee members (Table VII.2) and as research investigators (Table XVII.3). For example, 27 percent of the biomedical researchers felt that information about the design or purpose of the research should not be withheld from subjects (when disclosure might affect the validity of measurement); only seven percent of the behavioral researchers said that this should not be done. (Such findings may reflect the different implications of withholding information in biomedical vs.

behavioral studies as well as, or rather than, differences in the restrictiveness of biomedical vs. behavioral researchers.)

These data on acceptability of selected research practices have some other interesting features. The data illustrate, for example, investigators' and IRB members' doubts about the use of compensation to "induce" participation and about withholding information from subjects. They also show a willingness on the part of some respondents to interpose a third party into a "therapeutic relationship" when therapeutic and experimental decisions could become "improperly entangled," to allow research on children which has "no benefit and minimal risk," and to allow important "high risk" research of no benefit to subjects providing there is informed consent. Additionally, there apparently is a willingness among respondents to allow the secondary use of data to which no identification is attached but strong reaction against one researcher giving another the name of subjects.

On many of these items there is a marked lack of consensus among investigators and among review board members in that a substantial percentage indicated a practice should be done <u>and</u> a substantial percentage felt the practice should not be done. (The percentages of people who felt a practice may be done in some circumstances are not shown in the tables.) There is, however, at least a small positive relationship between the attitudes of review board members at an institution and the attitudes of investigators at the same institution with regard to both withholding information ($r = .50$) and payment ($r = .33$). This means that at institutions where review board members hold relatively restrictive attitudes toward payment and withholding information (i.e., feel that subjects should not be paid and information should not be withheld), investigators also tend to be relatively restrictive (in comparison with investigators at other institutions). Still, review

board members appear to be more restrictive than investigators regarding these issues.

IRB members' opinions regarding the need for review and consent. All board members in the sample were asked whether a series of hypothetical research procedures should come under formal review, whether they should be disclosed to subjects, and whether written consent should be obtained from subjects. Board members with biomedical, behavioral, and other backgrounds were asked to provide opinions regarding a biomedical case study involving the obtaining of bodily fluids and tissue, a study based on the secondary analysis of data, and a behavioral project involving interviews. Additionally, board members who had conducted biomedical research projects were asked about two biomedical procedures which might be classified as medical research or medical practice, depending on one's perspective, and about the secondary analysis of bodily tissue.

The opinions of board members are summarized in Tables XVII.4 to XVII.9. Various conclusions are suggested by these data, and five broad generalizations are noted here. First, there was much disagreement among board members as to whether certain procedures should be formally reviewed and as to whether consent should be obtained. Second, with the exception of secondary analysis studies, members generally were more likely to report that consent should be obtained than they were to report that the project should be reviewed. Third, as compared to members with biomedical backgrounds, behavioral members were more likely to feel that the procedures should be reviewed and that consent should be obtained. Fourth, more than half of the members felt that written consent should not be obtained by researchers carrying out at least some of the hypothetical procedures described in the tables. Fifth, many board members distinguished among the procedures in terms of the need for formal

review and consent. With some degree of consistency, certain procedures were more likely than others to be viewed as requiring formal review and consent.

IRB members' comments and suggestions. Review committee members were asked for suggestions for "modifications or improvements in the federal regulations governing human subjects review procedures." Sixty-two percent of the committee members responded to this question. The responses fall into five major categories (Table XVII.10).

The first concerns "bureaucratic problems" such as the complicated nature of the review process and the adverse effects of the process in slowing and preventing research. Bureaucratic problems were mentioned by 9 percent of the committee members at universities and medical schools, 18 percent of those at hospitals, and 13 percent of those at other institutions. Remarks on the complicated nature of the process and its concomitant "unnecessary forms," "maze of paperwork," "petty regulations," "red tape," and "bureaucracy" were prevalent and many appeals were made "to simplify the God damned thing" and "to cut back on the work load." One respondent claimed that two full-time persons had to be hired to deal with the committee's paperwork and another described some more serious consequences:

> If we're over-burdened with minutia or harassed, we find ways of circumventing. You see the whole thrust of our function can be lost if you over-regulate.

A few board members offered suggestions for dealing with these complications, including making guidelines general rather than restrictive, reducing redundancy by having only one committee review the protocol, postponing review until after the proposal is funded, and having a few persons rather than the entire committee make judgements on the protocol. One board member advised:

> Keep regulations as brief and concise as possible, because the work of investigation, the work of the professional involved, is hampered by the multitude of paperwork and the complexity of the regulations, and the duplications. For instance, in human investigation we try to check to make sure that this protocol is not a duplication of something somebody else has done that really has no point to it. I would question this investigation we are doing here. I wonder if it is necessary for the Congress to check the checkers checking. How far do you carry this thing? . . . I'm not saying no regulations, not at all. But someplace we are putting national resources into counterproductive measures or super-development.

Another large group of respondents focused upon the adverse effects these bureaucratic problems were having upon the conduct of research. Thus, one rather irate board member remarked:

> The 'cure' is far more damaging to advances in human research than the 'abuses' it was supposed to correct. Saying so, openly, is like being against motherhood and has made me very unpopular, but is the truth as far as I see it. Maddeningly, I have no supporting data, because I'm not allowed to take from the files any rejected or 'amended to death' protocols, so my charges must be vague. The cost of this unnecessary policing of scientists and the imposition of typists and administrators and lawyers on the scientists could have advanced science by twenty years instead of preventing it in the past five years.

Others felt that particular types of research were being impeded by the regulations, including fetal research, epidemiological research entailing the use of medical records, psychological research involving deception, and research involving autistic children, the mentally ill, pregnant women, newborns, and children.

The second set of concerns, very much related to the first, reflects the feeling that parts of the review process should be abolished. These concerns and related suggestions were mentioned by 10 percent of the board members from universities, 11 percent of those from medical schools, 12 precent of those from hospitals, 8 percent of those from other institutions, and 10 percent of the board members overall. Many of the committee members making such suggestions focused on differentiating between high and low risk

research, proposing that review of innocuous research be simplified or eliminated. One respondent summed this up well by stating:

> Many projects don't need review, unless there is a significant risk to the subject. It would eliminate half of our workload. Federal agencies are concerned that they have to cover every alternative and that's not possible.

Others do not advocate eliminating review entirely for low risk research but, rather, forming a special subcommittee to deal with this separately or conducting this review at the department level. Some of these individuals have stated that they made such suggestions to HEW but have received no support from them. Thus one remarked:

> There should be some set-up for a policy we advocated in our assurance form which was refused. Our committee decided to advocate a policy of having a subcommittee review and pass on low risk projects, but HEW did not concur, so now we have to hear every proposal no matter how low risk.

Many feel that having to spend so much time on innocuous research is detracting from the more important committee functions of dealing with high risk research and performing "the educational work we'd like to do and should be doing with our colleagues." In addition, as one board member remarked, "This leads to de facto deception--a lot of research not being reviewed by anyone." Another smaller group of persons desired that informed consent and review for research involving blood, tissue, and urine from other interventions be eliminated and that rules be interpreted more leniently. One person, wishing to eliminate informed consent for these by-products, commented:

> Suppose there is blood that would be discarded once a small amount is taken for the procedure. An investigator wants some blood to study something. He now must get informed consent to use that blood. Personally, I find that ludicrous. The individual would certainly remain unknown. You have to tell the patient, 'We are going to do a research study,' which immediately elicits fear into certain individuals, and I think that is unnecessary. I suggest that in situations where an investigator is just looking at blood drawn for other procedures, or where tissue biopsy is obtained for diagnostic purposes and that tissue is now available

> for research, that informed consent is unnecessary provided the name of the patient is not disclosed. That would save time and and anxiety of the patient.

A third set of comments concerns the structure or authority of the committee. Comments regarding these issues were made by 10 percent of the board members from universities, 10 percent of those from medical schools, 14 percent of those from hospitals, 9 percent of those from other institutions, and 11 percent of the board members overall. Many of these committee members felt that more authority should be given to the local review board. One member commented:

> The horse got out of the barn twenty years ago, but he's safely in now. We should have less stringent regulations and more autonomy. The requests of our committee to HEW are all to give us leeway and use our judgement.

Another offered the suggestion:

> As much as possible, I think individual committees should have as much discretion as possible. I would be very unhappy if there were a large number of restrictive regulations we had to follow.

Other board members were concerned with the composition of the committee and the way it is selected. One person wanted "a member from pharmaceutical science or pharmacology" and another wished to see "more participation from subjects on the committee." Another board member thought there were many problems inherent in lay and community involvement:

> I found that the benefit of having a wide segment of the population was offset by the difficulty in getting attendance and getting sufficient medical expertise. If it were up to me, I would have preferred a group of conscientious doctors with the help of administrators and a lawyer. The mere fact that one is a physician does not make him more subject to ignore the rights of the individual. All doctors are not bad!

Thus, board members were not in agreement regarding the types of changes in composition that were necessary.

A fourth set of suggestions and comments concerns the need for more

information and increased communication. Comments regarding these issues were made by 27 percent of the board members from universities, 28 percent of those from medical schools, 26 percent of those from hospitals, 19 percent of those from other institutions, and 25 percent overall. Many of these comments concerned the need for more or better guidelines in general. Many committee members felt that the present guidelines and regulations are unclear, ambiguous, imprecise, unspecific, complicated, and inconsistent. One member complained that "because of the complicated guidelines, there are loop holes that can be used by large research institutions" and the fact that regulations constantly change caused another to remark:

> The regulations should be spelled out and stuck to for a period of time instead of changing all the time. Our biggest problem is that they are continually changing the system. If specific guidelines could be established and spelled out to the institutions, these could be adhered to. We're never sure we've kept up to date with the specific requirements.

Other smaller groups of individuals wanted more clarification and definition of specific topics. The more commonly mentioned topics included risk and deception, children and fetal research, the informed consent requirements, and the circumstances in which informed consent must be obtained. Thus, one committee member remarked:

> There is an essential need for a realistic definition of risk and this issue is of particular importance for behavioral research. It's been discussed at many levels in many places.

Another suggested that the federal government "take another look at the very stringent curtailment of research which involves a fetus or abortus." More clarification was desired on "the use of records and subjects' consent regarding the use of records" and one member stated, "I would like to see age of consent for children."

The fifth category of suggestions concerns protecting human subjects to

a greater extent than is presently done. Such suggestions were made by 8 percent of the respondents in universities, 14 percent of those in medical schools, 6 percent of those in hospitals, 9 percent of those in other institutions, and 10 percent overall. This category consisted mainly of suggestions that review committees do more follow-up after review to see that proposed procedures are actually implemented. One respondent described this problem well by stating:

> I don't know that federal regulations have any statement about review of an ongoing study. We must have reports from a principal investigator once a year for ongoing studies. It is done by the honor system. There is no monitoring. What is to prevent the principal investigator from complying with all the requirements of HEW on paper and then doing what he wishes? There is no mechanism for knowing about that other than some problem of a subject complaining and I don't know of that happening.

Others felt that such a post hoc review procedure was needed but that their committees did not have time to implement such a procedure. Some wanted federal guidelines for such a monitoring process while one respondent hoped that the institutions themselves would develop their own system:

> There should be, perhaps, a way of feeding back information to the committee and I don't know if that has to be federally mandated. But as a first step, there should be a request from the federal government to the institution to develop means by which they can follow up research that they approved. I don't think that's effectively done at the institutions I'm familiar with.

Investigators' comments and suggestions. Principal investigators were asked a somwhat different question than the one asked of the board members. The investigators were asked to give their suggestions for improvement "in the human subjects review procedures--either in the federal regulations or in their application by review committees." Sixty-three percent of the investigators offered comments and suggestions on the review process as they experienced it.

Comments of the principal investigators fall into the same five categories

as those of review committee members (Talbe XVII.11). Remarks related to the first category, "bureaucratic problems," mainly concerned the time consuming and complicated nature of the review process and the adverse effects of the process in impeding the progress of scientific research. Bureaucratic problems were mentioned by 21 percent of the investigators in universities, 26 percent of those from medical schools, 15 percent of those from hospitals, 32 percent of those from other institutions, and 24 percent overall. Some complained that the process was much too slow and one investigator suggested that "they should have more pre-screening so that it wouldn't take too long. Have review by own discipline." Similar to the board members, investigators expounded upon the "glut of paper work," "excessive red tape," and the "needless bureaucracy." One respondent felt that this could be reduced if review were postponed until after funding:

> I don't think that a review should be done at grant application time because this involves a lot of extra work and the majority of grants are turned down, but rather be approved at the time of funding. This will avoid a lot of needless bureaucracy on grants that are never funded.

Instead of simply describing bureaucratic problems, other investigators chose to concentrate upon their adverse effects upon scientific investigation. Thus, one respondent stated:

> I feel that the committee may make decisions on some projects which may set a precedent which they are either unaware of or, if they were, they might want to reconsider (e.g., the rule of information--that you shouldn't gather information without that person's consent). If this were strictly applied, it would stop most of the research in this department.

Another complained:

> I feel very strongly about this. As it is applied here, the review process is largely a bureaucratic roadblock to doing research. By that I mean the vast majority of requested corrections--and there are always corrections on every research project--are semantic, grammatic, or typographic, which only delays the ultimate approval which in my experience has been

> uniformly given. Therefore, the initiation of research is delayed. This particular project doesn't show it, but I have one here that had four typographical errors which were requested to be changed, which means a waiting time of another week or two while you retype 16 copies or pages.

Somewhat related to the first set of comments, the second set entails the idea that parts of the review process should be abolished. These comments were mentioned by 20 percent of the investigators from universities, 18 percent of those from medical schools, 13 percent of those from hospitals, 12 percent of those from other institutions, and 17 percent overall. Similar to the board members, many of the investigators had in mind a system for differentiating between high and low risk research that would allow review on innocuous research to be simplified or eliminated. One such person suggested:

> I guess the only thing I'd like to see somehow is more concentration on studies that involve more risk. Ninety-five percent of the studies we look at are psychological studies which don't involve risks and to some extent, because you have to look all through these, perhaps some that really do require more of a searching analysis don't get enough time from the medical committee. There are very few studies in the behavioral studies --maybe six out of 25 or 30--that really involve risks. I do feel they are innocuous. I don't feel a university committee should have to go through them. I feel it's unworkable that all studies involving subjects have to go through the committee. It's an unnecessary burden that all studies get the same scrutiny when so many do not involve risk of any kind.

Other smaller groups of investigators wanted more leniency in the application of rules or the elimination of review on research involving by-products of another intervention, such as blood, tissue, or urine. One researcher felt his secondary analysis research was hampered by the consent procedure:

> In cases where there's no risk to patients and it's tissues that would be discarded and confidentially maintained, I don't think a consent form is really necessary. If necessary, a modified simple consent form could be used. I lose samples because the surgeon doesn't want to be bothered with all the forms and paperwork. I'm using lens capsules from cataracts which would normally be thrown away.

Others thought that having to sign a consent form for such things alarmed or

confused subjects.

The third group of opinions concerned the need for change in the structure or authority of the review committee. Such comments were made by 7 percent of the investigators from universities, 11 percent of those from medical schools, 15 percent of those from hospitals, 9 percent of those from other institutions, and 11 percent overall. What many of the investigators had in mind were changes in the composition of the committee and the way it is selected. Similar to the board members, however, the investigators disagreed on the types of changes that would be desirable. A few wanted more lay involvement:

> My only comment is that there should be a representative of people on the committee, representing all the various phases of medicine including consumers and people of the community.

Others were opposed to lay involvement, often because they felt lay individuals do not possess adequate knowledge:

> I object to lay persons sitting in judgement of a complex, scientific system. I also object to the heavy weight they place on them--a priest, a minister, etc.. I find it impossible to believe that they can make a judgement. I also object to the jury system. I object to writing up something a lay person is going to pass judgement on. I don't know why in hell a priest has to sit there and pass judgement.

There were other complaints that lay persons did not attend meetings:

> I suspect the original concept of having effective participation by lay people, non-medical people, is not being realized here and a lot of other places. Lay people are appointed to the committee, but their enthusiasm wanes and you end up presenting to your colleagues.

There was even an individual who felt that many of his colleagues had no business judging his proposal:

> We also need more expertise on the review committees. I've had dentists and pharmacists reviewing my very technical radiation therapy protocols who can hardly spell cancer, let alone understand anything about X-ray therapy.

In order to solve problems of lack of expertise on the committee, a somewhat smaller group of investigators proposed getting help from consultants for a period of time. One such person felt that "there ought to be either on the committee or consultant to the committee an expert for every type of research."

The fourth group of comments concerns the need for more information and increased communication. Eighteen percent of the investigators from universities, 11 percent from medical schools, 7 percent from hospitals, 19 percent from other institutions, and 12 percent overall made comments about communication and information. Many of the investigators wanted more personal interaction between the researcher and the committee. One individual commented:

> I think that perhaps it may be helpful if the individual investigator were to present his application or proposal to the committee directly rather than have him just go by mail, so that he could defend it in person. I think that it may tend to make an individual think a little more clearly about his proposal.

In addition to making the investigator think more clearly about his/her proposal, such a system could give the committee members a clearer picture of the research as well. Thus, one stated:

> It would be helpful, when modifications and/or changes are suggested or requested by the IRB, that the proponent of the study be given a chance to have face-to-face direct sessions with the committee to discuss these changes because they may affect detrimentally what he is really intending to do. I've had one situation like that already myself and have heard of others. There is a good possibility that the way the proposal was written and what the proponent really meant might not be clear to them really.

Other smaller groups of respondents wanted more general information and guidelines about review or more guidelines on informed consent. One investigator wanted to see:

> the wider dissemination and increased ease of obtaining data referable to federal regulations governing human investigation. What I mean is as a member of a staff of this hospital, someone should hit you on the head with a set of regulations or tell you where they are before you start working here, so you know.

Another felt that this could be partially accomplished in the following way:

> I would suggest that NIH prepare a booklet available to investigators with a statement of policy and specific examples of how to write a consent form and it should also have some specific recommendations of how institutional review committees inform applicant investigators and have improved forms and guidelines for investigators.

Problems with the existing informed consent procedure were described by another:

> Arbitrary decisions about what does or does not constitute informed consent are made without consultation with those committees which must implement procedures for attaining informed consent.

The last group of comments concerns the need for more adequate protection for subjects. These comments were mentioned by 10 percent of the investigators from universities, 7 percent of those from medical schools, 8 percent of those from hospitals, 10 percent of those from other institutions, and 8 percent all together. Some of these comments were general and suggested that committees should be more stringent and keep a "closer watch over projects." Other comments were more specific and related to particular aspects of review board functioning. One respondent said:

> We never are asked how we plan to safeguard confidentiality and this has surprised me. It seems like they might ask some questions about it.

Other investigators wished to see more follow-up of projects to ascertain that what is proposed is actually carried out. One person described this problem well by stating:

> I don't really know how often people agree on one thing and do another. As things are now, there's really no enforcement. It's fairly voluntary and depends on the honor system and I think most people are running scared and don't want to be caught out on a limb if a problem arises with a subject, but I think certain things could be done in an effort to check up. Review committees could periodically look back and ask for investigations of bad problems. I do shudder at the idea of another bureaucracy, but the fact is the committee does serve as a brake and I must confess it never occurred to me that written consent was needed with all the subjects.

Another investigator suggested an alternative procedure for following up projects:

> Someone from the review committee should have unscheduled visits during the duration of the studies so that outside scrutiny is always a possibility. This would cut down on day-to-day abuses.

Subjects' and proxies' comments and suggestions. Thirty-eight percent of the subjects and proxies responded to a question asking for suggestions regarding how researchers might "improve the way they do studies involving human beings." The suggestions offered by these respondents fall into three categories (Table XVII.12). The first concerns requests for various types of additional information (19 percent). Many of these comments were general. For example, one respondent remarked, "People could explain research more," and another stated that researchers should "give participants as much knowledge as they want." One respondent complained, "I am a physician. They could have given me more information. My education is equal to theirs. They treated me like an idiot." Another common request was for information on the results of they study. One subject stated that "it would have been nice to have gotten a letter explaining the results," and another expressed the opinion that "volunteers deserve to know results." A smaller number of subjects desired to have more or better information on specific topics such as benefits, risk, and procedures. One respondent, wanting more information on risks, stated, "They should warn people more emphatically about the possibilities of unforeseen side effects." Another subject wanted more information on procedures and suggested that researchers "should make very clear the length of the study and what is involved."

A second category of suggestions (11 percent) concerns the experimenters' conduct of the research. Some felt that experimenters should be more efficient and better organized. One such person stated, "Some equipment was in poor

repair which wasted time. They should check it beforehand." Others suggested that experimenters perform procedures more carefully and humanely, one such person remarking, "have good blood-takers that don't poke around." Another group expressed a desire for experimenters to be more courteous and kind when dealing with subjects. Thus, one person felt that researchers should "treat me like a person! Remember who you're dealing with. It is bad enough to be ill." In a similar fashion, another suggested that "they could talk to patients and get their perspective. I felt like a number in the hospital. I think people should always be treated as individuals." A smaller group of subjects suggested that researchers keep the subjects in mind by making the location and scheduling more convenient.

A third category of suggestions (three percent) concerns improving the risk/benefit ratio by increasing types of care, service, and financial benefits or by reducing risks through testing more thoroughly before the experiment. One person suggested that researchers "increase the financial end of it; some studies are underpaid." Another remarked that studies "should be for the benefit of the subject--not for someone's thesis."

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Table I.1

General Types of Research Conducted in Different Institutions
(Percent of Projects)*

Type of Research	Type of Institution				
	Universities** (N=474)	Medical Schools*** (N=1191)	Hospitals**** (N=214)	Other***** (N=160)	All (N=2039)
Biomedical	13%	77%	74%	44%	63%
Behavioral intervention	13	3	6	14	6
Behavioral	71	13	15	37	25
Secondary analysis	3	7	5	5	6
Total	100%	100%	100%	100%	100%

*Excludes cases for which relevant information is unavailable. The data of this and subsequent tables are weighted.

**Including IRB's at universities only if the IRB's are separate from those of the medical school.

***Including IRB's at universities that share an IRB with a medical school.

****Including children's hospitals.

*****Including biomedical research institutions, schools of nursing and dentistry, and institutions for the mentally infirm.

Table I.2

The Primary Intervention or Procedure in Each Study

	Percent of Projects* (N=2039)
Biomedical	
Clinical evaluation of bodily tissues or fluids	25%
Administration of drug, chemical agent or blood	28
Administration of vaccines, blood products	2
Perinatal care	-**
Surgical (includes oral)	1
Exchange of bodily fluids	-
Use of diagnostic and/or therapeutic devices	6
Dental care	-
Other	-
Behavioral Intervention	
Educational intervention	2
Modification of an organization or service delivery system	1
Social psychological therapy	1
Behavior modification	2
Other	1
Behavioral (other)	
Interviews-questionnaires	11
Psychological or educational testing	6
Behavioral observation	6
Interviews with patient (e.g., medical histories)	2
Secondary Analysis	
Retrospective review of data	1
Retrospective review of data (medical)	2
Third party evaluation of bodily parts or fluids	3
Total	100%

*Projects in the sample for which information is unavailable are not included in this table.

**A dash indicates more than 0 percent but less than .5 percent.

Table I.3

Types of Institutions Conducting Research
(Percent of Projects)*

Type of Institution	Type of Research: Biomedical (N=1264)	Behavioral Intervention (N=547)	Behavioral (Other) (N=136)	Secondary Analysis (N=92)	All (N=2039)
Universities	3%	37%	49%	10%	18%
Medical schools	73	30	30	71	59
Hospitals	18	14	9	12	15
Other	6	19	12	7	8
Total	100%	100%	100%	100%	100%

*Excludes cases for which relevant information is unavailable.

Table I.4

Is this a Phase I, II, III or IV test?

	Percent of Projects (N=2110)
Phase I	2%
Phase II	4
Phase III	6
Phase IV	2
None of these	4
Don't know	7
No answer	5
Inappropriate*	70
Total	100%

*Includes other than drug administration research.

Table I.5

The following is a list of some methods which you may be using for your study--please check as many as apply.
(Percent of Projects)*

	Type of Institution				
	Universities (N=445)	Medical Schools (N=1025)	Hospitals (N=175)	Other (N=140)	All (N=1785)
Single-blind method (i.e., subject does not know which study technique is being used)	12%	8%	6%	10%	9%
Double-blind method (i.e., neither subject nor experimenter knows which study technique is being used)	6	13	15	10	12
Different treatment or procedures assigned by random method	22	17	18	13	18
Cross-over design (treatment or procedures switched between groups during the study)	4	8	2	13	7
Placebo administration	1	8	4	10	6
None of the above	56	49	44	55	50

*Totals need not add to 100% since respondents could check more than one method. Use of methods of secondary analysis, which some respondents checked, are reported in Table I.1.

Table II.1

Numbers of Subjects per Project: Type of Institution
(Percent of Projects)*

Number of Subjects	Type of Institution: Universities (N=140)	Medical Schools (N=529)	Hospitals (N= 99)	Other (N= 66)	All (N=844)
1-2	1%	1%	2%	2%	1%
3-5	1	1	0	2	1
6-10	6	11	10	14	10
11-20	9	16	18	8	14
21-30	7	15	13	12	13
31-50	7	17	19	13	16
51-75	6	5	8	2	6
76-100	11	13	14	13	13
101-150	14	4	1	-	5
151-200	5	4	1	5	4
201-300	4	4	5	4	4
301-500	16	3	6	5	5
501-1000	6	1	1	9	3
1001-2000	3	2	1	6	2
More than 2000	4	3	1	5	3
Total	100%	100%	100%	100%	100%

*This table excludes cases for which relevant responses are unavailable.

Table II.2

What kinds of subjects were selected for your study?: Type of Institution
(Percent of Projects)*

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Patients	17%	76%	86%	66%	67%
Patients (including adults and children)	15%	72%	80%	64%	63%
Former patients	1	1	1	1	1
Persons with specific medical condition**	1	3	5	1	3
Staff	19	5	2	15	8
Project staff	1	-	0	1	1
Other professional staff	6	2	-	5	2
Other institutional staff	12	3	2	9	5
Students	38	7	1	7	11
Medical, health students	1	2	-	3	1
Other college students	37	5	1	4	10
Other	55	32	15	42	33
General population	14	15	7	22	14
Persons with specific characteristic	17	8	3	17	9
Children under 18	15	6	4	1	6
Prisoners	-	-	0	0	-
Miscellaneous	9	3	1	2	4

* Totals may add to more than 100% since respondents could check more than one kind of subject.

**Not ascertained whether these persons were patients at the time of the research.

Table II.3

What kinds of subjects were selected for your study?: Type of Research
(Percent of Projects)*

	Type of Research				
	Biomedical (N=1272)	Behavioral Intervention (N=136)	Behavioral (Other) (N=552)	Secondary Analysis (N= 92)	All (N=2052)
Patients	79%	52%	38%	62%	67%
Patients (including adults and children)	76%	47%	35%	54%	63%
Former patients	-	2	1	2	1
Persons with specific medical condition**	3	3	2	6	3
Staff	6	10	12	2	8
Project staff	1	0	-	0	1
Other professional staff	2	4	4	0	2
Other institutional staff	3	6	8	2	5
Students	7	18	22	5	11
Medical, health students	2	3	1	0	1
Other college students	5	15	21	5	10
Other	23	56	54	51	33
General population	12	16	15	23	14
Persons with specific characteristic	5	14	20	12	9
Children under 18	4	18	12	7	6
Prisoners	-	1	0	0	-
Miscellaneous	2	7	7	9	4

* Totals may add to more than 100% since respondents could check more than one kind of subject.

**Not ascertained whether these persons were patients at the time of the research.

Table II.4

Which of the following sources are used to obtain subjects for this study?: Type of Institution (Percent of Projects)*

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
From among own patients	6%	44%	43%	29%	36%
Referrals by other physicians, professionals	7	39	43	25	33
Referrals by other subjects	12	11	9	11	11
Information from records	18	13	10	15	14
Institutional population via professional access	55	37	35	51	40
Advertisement or notice	15	6	3	6	7
Other source	25	10	5	16	11
General population	4%	1%	0%	9%	2%
Friends, relatives	1	1	0	-	-
Formal groups, organizations	12	3	3	2	4
Blood samples	0	2	1	-	1
Other sources	8	3	1	5	4

*Totals may add to more than 100% since respondents could mention more than one subject source

Table II.5

Which of the following sources are used to obtain subjects for this study?: Type of Research (Percent of Projects)*

	Type of Research				
	Biomedical (N=1272)	Behavioral Intervention (N=136)	Behavioral (Other) (N=552)	Secondary Analysis (N=92)	All (N=2052)
From among own patients	48%	16%	14%	15%	36%
Referrals by other physicians, professionals	45	18	10	9	33
Referrals by other subjects	13	8	8	3	11
Information from records	9	12	19	41	14
Institutional population via professional access	36	56	50	39	40
Advertisement or notice	7	6	10	1	7
Other source	8	15	24	8	11
General population	1%	1%	4%	0%	2%
Friends, relatives	–	0	1	0	–
Formal groups, organizations	2	7	12	1	4
Blood samples	2	0	0	4	1
Other sources	3	7	7	3	4

*Totals may add to more than 100% since respondents could mention more than one subject source.

Table II.6

Reasons for Selection of Subjects: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Subjects selected because of specific condition	69%	87%	92%	84%	85%
Some subjects selected because of specific condition	2	1	0	2	1
Subjects selected because of absence of specific condition	4	3	5	2	3
Selection not related to either presence or absence of specific condition	25	9	3	12	11
Total	100%	100%	100%	100%	100%

Table II.7

Reasons for Selection of Subjects: Type of Research
(Percent of Projects)

	Type of Research				
	Biomedical (N=1272)	Behavioral Intervention (N=136)	Behavioral (Other) (N=552)	Secondary Analysis (N=92)	All (N=2052)
Subjects selected because of specific condition	88%	82%	78%	77%	85%
Some subjects selected because of sepcific condition	1	1	1	1	1
Subjects selected because of absence of specific condition	3	3	3	5	3
Selection not related to either presence or absence of specific condition	8	14	18	17	11
Total	100%	100%	100%	100%	100%

Table II.8

Conditions Used as Basis for Subject Selection: Type of Institution
(Percent of Projects)*

Disease or medical condition	Type of Institution: Universities (N= 479)	Medical Schools (N= 1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Infective and parasitic diseases	20%	81%	87%	72%	71%
Neoplasms	1%	4%	3%	0%	3%
Endocrine, nutritional, metabolic diseases	1	13	23	13	13
Atavitaminoses & other nutritional deficiencies	1	5	5	7	5
Disease of nervous system and sense organs	3	5	5	4	5
Disease of the circulatory system	1	11	5	2	8
Disease of the respiratory system	-	3	3	-	2
Disease of the digestive system	-	5	8	1	4
Disease of the genitourinary system	1	7	7	-	5
Complications of pregnancy, childbirth	-	1	3	0	1
Disease of the musculoskeletal system and connective tissue	0	1	1	2	1
Congential anomalies	1	5	2	0	3
Symptoms and ill-defined conditions	1	1	1	0	1
Disease of the blood and blood forming organs	1	2	1	1	1
Certain causes of perinatal morbidity and mortality	-	3	-	3	2
Nature of injuries	1	1	1	0	1
Mental disorders	-	1	1	0	1
Medical characteristics	5	4	9	36	8
	3	9	9	3	7

(continued)

(Table II.8 continued)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Behavioral problem	4%	-%	2%	7%	2%
Educational problem	1%	0%	-%	-%	-%
Legal problem	1	0	1	1	1
Personal adjustment problem	2	-	1	5	1
Other behavioral problem	-	-	-	1	-
Demographic characteristic	69	18	12	25	26
Age	11	5	5	6	6
Sex	5	3	3	5	4
Race	4	1	-	0	1
Genetic or kinship ties	1	1	1	2	1
Height/weight	1	1	0	0	-
Income	2	1	0	0	-
Social class	1	1	0	0	1
Vocational and educational criteria	27	2	0	8	6
Life/family situation	7	2	2	2	3
Personal characteristic	6	1	1	1	2
Geographic location	2	-	0	0	1
Match on demographic characteristics	0	-	0	0	-
Other demographic characteristic	2	-	0	1	1
Other characteristic	3	1	2	1	2

*Totals may add to more than 100% since respondents could make multiple mentions.

Table II.9

Conditions Used as Basis for Subject Selection: Type of Research
(Percent of Projects)*

	Type of Research				
	Biomedical (N=1272)	Behavioral Intervention (N=136)	Behavioral (Other) (N=552)	Secondary Analysis (N=92)	All (N=2052)
Disease or medical condition	87%	58%	36%	63%	71%
Infective and parasitic diseases	4%	2%	1%	4%	3%
Neoplasms	18	2	2	12	13
Endocrine, nutritional, metabolic disease	7	3	1	1	5
Atavitaminoses & other nutritional deficiencies	6	4	1	6	5
Disease of nervous system and sense organs	9	5	3	3	7
Disease of the circulatory system	3	2	-	1	2
Disease of the digestive system	7	-	-	3	4
Disease of the respiratory system	7	1	1	2	5
Disease of the genitourinary system	1	1	2	2	1
Complications of pregnancy, childbirth	2	0	0	0	1
Disease of the musculoskeletal system and connective tissue	5	4	-	1	3
Congential anomalies	1	1	1	0	1
Symptoms and ill-defined conditions	1	1	1	-	1
Disease of the blood and blood forming organs	2	0	1	-	2
Certain causes of perinatal morbidity and mortality	2	0	1	1	1
Nature of injuries	1	-	-	1	1
Mental disorders	5	23	13	8	8
Medical characteristics	6	9	8	18	8

(Table III.9 continued)

Table II.9 (continued)

	Type of Research				
	Biomedical (N=1272)	Behavioral Intervention (N=136)	Behavioral (Other) (N=552)	Secondary Analysis (N= 92)	All (N=2052)
Behavioral problem	-%	11%	4%	2%	2%
Educational problem	0%	2%	1%	-%	1%
Legal problem	0	-	1	0	-
Personal adjustment problem	-	9	2	0	1
Other behavioral problem	0	0	-	2	-
Demographic characteristic	11	33	65	23	26
Age	4	7	13	2	6
Sex	3	2	5	5	4
Race	1	1	3	2	1
Genetic or kinship ties	1	1	2	0	1
Height/weight	-	0	1	0	-
Income	-	0	1	5	1
Social class	0	-	2	1	-
Vocational and educational criteria	1	16	22	1	7
Life/family situation	-	2	9	1	3
Personal characteristic	1	4	4	0	2
Geographic location	0	0	2	4	1
Match on demographic characteristics	-	0	0	0	-
Other demographic characteristic	-	0	1	2	-
Other characteristic		6	3	4	2

*Totals may add to more than 100% since respondents could make multiple mentions.

Table II.10

Did the review committee require you to make modifications in the proposed selection of subjects for your study? If yes, what changes? (Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Changes required	-%	3%	5%	4%	3%
Exclusion of some subject categories on the bases of risk	-%	1%	-%	0%	1%
Change due to considerations of equity	0	-	-	0	-
More subjects	0	0	0	0	0
Fewer subjects	0	-	0	1	-
Limit sample	0	2	4	3	2
Other changes	-	-	1	0	-
No changes required	99	96	94	94	96
Don't know	1	1	1	2	1
Total	100%	100%	100%	100%	100%

Table III.1

Modifications by Review Committee Regarding Informed Consent: Type of Institution
(Percent of Projects)

Did the review committee require that you make modifications in your study in regard to how consent would be obtained from subjects?	Type of Institution: Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Yes, change required*	20%	26%	30%	14%	24%
Required written (rather than oral) consent	5%	2%	-%	2%	2%
Required addition of material to be disclosed	7	9	13	5	9
Required simplification of material to be disclosed	2	6	4	1	5
Required other changes in material to be disclosed	3	9	9	4	7
Required change in setting in which consent obtained	0	0	0	-	0
Required change in timing of obtaining consent	-	0	0	1	-
Required change in who obtains consent	-	-	0	0	-
Required presence of witnesses when consent obtained	0	-	1	0	-
Required proxy consent	-	-	1	0	-
Required subject as well as proxy consent	1	-	0	0	-
Required consent info be put in subject file	-	0	2	0	-
Other changes	2	1	2	1	2
No, no change required	79	72	67	81	74
No information	1	2	3	5	2
Total	100%	100%	100%	100%	100%

*Percentages in the offset columns represent distributions among those projects where the "yes" response was checked. More than one of the offset responses could be checked in any project.

Table III.2

Type of Consent Obtained: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
In this study, is either oral or written consent obtained from subjects or someone acting for subjects?					
Yes, oral	24%	7%	8%	8%	10%
Yes, written	38	52	52	59	50
Yes, both	21	31	27	25	28
No consent obtained/needed*	17	10	13	7	12
Return of questionnaire implies consent	8%	1%	1%	-%	2%
Have sign-up sheet	-	0	0	0	-
Participation voluntary--no further specification	3	-	0	1	1
Anonymous/confidential research	1	-	-	-	-
Research involves necessary treatment/procedure	0	-	-	-	-
Subject's own physician determines participation	0	0	0	0	0
Research involves routine treatment procedures	1	2	3	-	2
Only existing records used	1	1	1	1	1

Table III.2 (continued)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
No consent obtained/needed (cont.)					
Materials from previous research being used	-%	4%	5%	1%	3%
Consent obtained elsewhere	-	1	1	1	1
Participation requested/recommended by someone other than research staff	1	-	0	0	-
Not required by review committee	-	1	1	2	1
Investigator says "no risk/harm involved for subjects"	2	1	-	1	-
Other	2	1	3	2	2
No Information	-%	0%	0%	1%	-%
Total	100%	100%	100%	100%	100%

*Percentages in the offset columns represent distributions among those projects where the "no" response was checked. More than one of the offset responses could be checked in any project.

Table III.3

Type of Consent Obtained: Expected Benefit
(Percent of Projects)

	Expected Benefit to Subjects			
	Beneficial (N=902)		Non-beneficial (N= 822)	
In this study, is either oral or written consent obtained from subjects or someone acting for subjects?				
Yes, oral	7%		14%	
Yes, written	55		41	
Yes, both	29		26	
No consent obtained/needed*	7		17	
Return of questionnaire implies consent		1%		3%
Have sign-up sheet		0		-
Participation voluntary--no further specification		-		1
Anonymous/confidential research		0		1
Research involves necessary treatment/ procedure		-		-
Subject's own physician determines participation		0		0
Research involves routine treatment procedures		2		2
Only existing records used		1		2
Materials from previous research being used		1		4
Consent obtained elsewhere		-		1
Participation requested/recommended by someone other than research staff		-		-
Not required by review committee		1		2
Investigator says "no risk/harm involved for subjects"		-		2
Other		1		2
No Information	2		2	
Total	100%		100%	

*Percentages in the offset columns represent distributions among those projects where the "no" response was checked. More than one of the offset responses could be checked.

Table III.4

Oral Explanation of Study: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N= 479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Are subjects (or proxies) given an oral explanation of the study?					
Yes	72%	83%	84%	76%	81%
Yes, but oral explanation only of consent form	0	1	0	0	1
No	8	2	1	7	3
Question inappropriate*	17	10	13	8	11
No information	3	4	2	9	4
Total	100%	100%	100%	100%	100%

*Asked only in those studies where consent was obtained

Table III.5

Who Obtains Consent: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Who obtains consent?					
Investigator usually obtains consent	40%	38%	29%	30%	36%
Investigator shares consent responsibility	25	35	40	28	34
Others usually obtain consent	18	17	18	35	19
Question inappropriate*	17	10	13	7	11
No information	-	-	0	-	-
Total	100%	100%	100%	100%	100%

*Question asked only in those studies where consent was obtained.

Table III.6

Who Obtains Consent: Expected Benefit
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N= 902)	Non-beneficial (N=822)
Who obtains consent?		
Investigator usually obtains consent	37%	32%
Investigator shares consent responsibility	38	28
Others usually obtain consent	16	21
Question inappropriate*	9	19
No information	-	-
Total	100%	100%

*Question asked only in those studies where consent was obtained.

Table III.7

Others Who Obtain Consent: Type of Institution
(Percent of Projects)*

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Study Staff					
Professional colleague	12%	31%	36%	31%	29%
Resident or research fellow in medicine	2	16	16	1	12
Intern/medical student/dental student	1	1	1	1	1
Graduate student	14	3	4	6	5
Nurse/physical therapist	1	7	7	3	6
Technician/dental assistant/physician's assistant	-	3	5	5	3
Research assistant/students	15	7	7	9	8
Interviewer	5	2	1	9	3
Other	2	1	4	3	1
Social worker/counselor	1%	-%	4%	0%	1%
Secretary/receptionist	1	1	0	0	-
Elementary/secondary school staff	-	-	-	0	-
Other	-	-	0	3	-

Table III.7 (continued)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Staff (not on study)					
Professional colleague	3%	3%	4%	4%	4%
Resident or research fellow in medicine	-	2	4	-	2
Intern/medical student/dental student	0	-	1	0	-
Graduate student	1	-	0	1	-
Nurse/physical therapist	1	1	2	2	1
Technician/dental assistant/physician's assistant	0	1	0	1	-
Research assistant/students	0	-	0	0	-
Interviewer	1	-	-	4	1
Other	4	1	1	3	2
Social worker/counselor	1	-	0	2	-
Secretary/receptionist	-	0	0	-	-
Elementary/secondary school staff	1	1	-	0	1
Other	2	-	1	1	1
Question inappropriate**	57	43	43	40	45
No information	-	1	2	2	1

*Percentages may add to more than 100% since more than one response could be checked.

**Question asked only in those studies where consent was obtianed, and where others shared in responsibility for obtaining consent.

Table III.8

Who Else is Present When Consent Obtained: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Aside from yourself and the subject (and/or proxy), is anyone else usually present when consent is sought?					
Yes*	34%	59%	58%	46%	54%
Family member	8%	21%	26%	14%	19%
Physician or dentist	2	19	21	13	16
Nurse	2	27	38	18	24
Research assistant	12	18	16	15	17
Other**	20	13	6	20	13
No	42	23	21	32	27
Question inappropriate***	19	13	17	10	14
No information	5	5	4	12	5
Total	100%	100%	100%	100%	100%

*Percentages in the offset columns represent distributions among those projects where the "yes" response was checked. More than one of the offset responses could be checked in any project.

**The others who were present when consent was sought included institution staff, secretaries, ward assistants, or anyone who was available at the time.

***Question asked only in those studies where consent was obtained, and where the investigator has already obtained consent from some subjects.

Table III.9

Who Else is Present When Consent Obtained: Expected Benefit
(Percent of Projects)

	Expected Benefit to Subjects			
	Beneficial (N=902)		Non-beneficial (N=822)	
Aside from yourself and the subject (and/or proxy), is anyone else usually present when consent is sought?				
Yes*	61%		42%	
Family member		24%		12%
Physician or dentist		20		11
Nurse		30		15
Research assistant		17		14
Other**		12		15
No	24		31	
Question inappropriate***	12		21	
No information	3		6	
Total	100%		100%	

*Percentages in the offset columns represent distributions among those projects where the "yes" response was checked. More than one of the offset responses could be checked in any project.

**The others who were present when consent was sought included institution staff, secretaries, ward assistants, or anyone who was available at the time.

***Question asked only in those studies where consent was obtained, and where the investigator has already obtained consent form some subjects.

Table III.10

Emphasis in Description of Study: Expected Benefit to Subjects
(Percent of Projects)*

Are any of the following emphasized when you described this study to a prospective subject or proxy?	Expected Benefit to Subjects: Beneficial (N=902)	Expected Benefit to Subjects: Non-beneficial (N=822)
Direct benefit to subject	67%	19%
Benefit to other individuals in the future	62	49
Benefit to scientific knowledge	51	50
Something else	10	8
No direct benefit to subject	2%	1%
Emphasized risks, hazards	4	1
Other (unspecified)	4	6
Question inappropriate**	14	25
No information	2	5

*Percentages may add to more than 100% since more than one response could be checked.

**Question asked only in those studies where consent was obtained where the investigator had already obtained consent from some subjects, and where an oral explanation of the study was given to subjects.

Table III.11

Participation Request or Recommendation: Expected Benefit to Subjects
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
When you are obtaining consent, is participation in this study presented to subjects (or proxies) as your request, your recommendation, or both?		
Request	42%	58%
Recommendation	15	2
Both	20	5
Neither	7	5
Question inappropriate*	14	25
No information	2	5
Total	100%	100%

*Question asked only in those studies where consent was obtained where the investigator had already obtained consent from some subjects, and where an oral explanation of the study was given to subjects.

Table III.12

Information Not Divulged to Subjects: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
In some research the design of the study requires that certain information not be divulged to subjects. Is that the case in this study?					
Yes, certain information not divulged*	29%	12%	13%	16%	15%
Existence of study	-%	-%	1%	1%	1%
Purpose of study	16	2	4	5	5
Purpose of specific procedures	15	2	5	6	5
Existence of confederate	1	-	0	0	-
Tape recording/filming/photographing	-	-	0	0	-
Possible benefits to subjects	1	-	2	2	1
Possible risks or discomforts to subjects	-	-	0	1	-
Medication or treatment being used	1	6	5	5	5
Other	6	3	4	4	4
No, not required by study design or all information divulged	71	87	86	83	84
No information	-	1	1	1	1
Total	100%	100%	100%	100%	100%

*Percentages in the offset columns represent distributions among those projects where the "yes" response was checked. More than one of the offset responses could be checked in any project.

Table III.13

Information Not Divulged to Subjects: Expected Benefit
(Percent of Projects)

	Expected Benefit to Subjects			
	Beneficial (N= 902)		Non-beneficial (N=822)	
In some research the design of the study requires that certain information not be divulged to subjects. Is that the case in this study?				
Yes, certain information not divulged*	17%		15%	
Existence of study		1%		1%
Purpose of study		3		7
Purpose of specific procedures		4		6
Existence of confederate		–		0
Tape recording/filming/photographing		–		–
Possible benefits to subjects		2		–
Possible risks or discomforts to subjects		–		–
Medication or treatment being used		9		2
Other		4		5
No, not required by study design or all information divulged	80		82	
No information	3		3	
Total	100%		100%	

*Percentages in the offset columns represent distributions among those projects where the "yes" response was checked. More than one of the offset responses could be checked in any project.

Table III.14

Subjects Told Things Not True: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
For purposes of your study is it necessary to tell some subjects some things which are not true?					
Yes, necessary to tell things not true*	7%	-%	-%	3%	2%
Existence of study	0%	0%	0%	0%	0%
Purpose of study	3	0	0	1	1
Purpose of specific procedures	4	0	0	1	1
Existence of confederate	1	0	-	0	-
Tape recording/filming/photographing	-	0	0	1	-
Possible benefits to subjects	0	0	0	0	0
Possible risks or discomforts to subjects	-	0	0	0	0
Medication or treatment being used	-	-	0	0	-
Other	1	-	-	1	-
No, not necessary	92	99	98	96	97
No information	1	1	2	1	1
Total	100%	100%	100%	100%	100%

*Percentages in the offset columns represent distributions among those projects where the "yes" response was checked. More than one of the offset responses could be checked in any project.

Table III.15

Payment for Participation: Expected Benefit to Subjects
(Percent of Projects)

	Expected Benefit to Subjects			
	Beneficial (N= 902)		Non-beneficial (N=822)	
Are subjects paid? If so, what is the average payment?				
All subjects paid	4%		13%	
Some subjects paid	3		7	
Average payment				
$1-5		1%		5%
$6-10		1		4
$11-15		1		1
$16-20		-		2
$21-25		1		1
$26-50		1		2
$51-75		-		1
$76-100		1		1
$101-150		-		-
$151-200		0		2
$201-300		-		-
More than $300		0		--
Other payment (e.g., dollars per hour)		-		1
No subjects paid	92		76	
No information	1		4	
Total	100%		100%	

Table III.16

Difficulty in Deciding to Participate: Expected Benefit to Subjects
(Percent of Projects)

How difficult for prospective subjects is the decision to participate?	Expected Benefit to Subjects: Beneficial (N= 902)	Expected Benefit to Subjects: Non-beneficial (N= 822)
Very difficult	2%	-%
Somewhat difficult	11	5
Not very difficult	29	22
Not at all difficult	40	44
Question inappropriate*	12	21
No information	6	8
Total	100%	100%

* Question asked only in those studies where consent was obtained where the investigator had already obtained consent from some subjects, and where an oral explanation of the study was given to subjects.

Table III.17

People Decline to Participate: Expected Benefit to Subjects
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Have any people declined to participate in this study after having been given information about it?		
Yes, some declined	48%	38%
Average percentage declining within a project*	(11)	(14)
No, none declined	35	32
Question inappropriate**	12	21
No information	5	9
Total	100%	100%

*"What percentage would you estimate have declined to participate?"

** Question asked only in those studies where consent was obtained where the investigator had already obtained consent from some subjects, and where an oral explanation of the study was given to subjects.

Table IV.1

Instances of Proxy Consent: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Are there instances in this study in which proxy consent is involved?					
Yes	24%	25%	38%	29%	27%
Not so far, but probablv will be later	0	—	1	0	—
No	56	61	46	54	57
Question inappropriate*	17	10	13	7	12
No information	3	4	2	10	4
Total	100%	100%	100%	100%	100%

* Question asked only in those studies where consent was obtained.

Table IV.2

Instances of Proxy Consent: Expected Benefit
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Are there instances in this study in which proxy consent is involved?		
Yes	35%	18%
Not so far, but probably will be later	—	—
No	54	58
Question inappropriate*	9	19
No information	2	5
Total	100%	100%

* Question asked only in those studies where consent was obtained.

Table IV.3

Circumstances Under Which Proxy Consent Used: Type of Institution
(Percent of Projects)*

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Under what circumstances has proxy consent been obtained?					
Age	20%	20%	27%	14%	21%
Intellect	2	2	8	5	3
Degree of illness	1	3	7	9	4
Other	1	1	1	2	1
Question inappropriate**	74	72	62	64	70
No information	4	4	4	12	4

* Percentages may add to more than 100% since more than one response could be checked.
** Question asked only in those studies where proxy consent was established, and where the investigator had already obtained consent from some subjects.

Table IV.4

Circumstances Under Which Proxy Consent Used: Expected Benefit
(Percent of Projects)*

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Under what circumstances has proxy consent been obtained?		
Age	26%	14%
Intellect	4	3
Degree of illness	6	2
Other	1	1
Question inappropriate**	65	79
No information	3	5

* Percentages may add to more than 100% since more than one response could be checked.

** Question asked only in those studies where proxy consent was obtained, and where the investigator had already obtained consent from some subjects.

Table IV.5

Who Acts as Proxy: Type of Institution
(Percent of Projects)*

Who is asked to give proxy consent for subjects in your study?	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Parent or other relatives	21%	24%	35%	21%	25%
Legal guardian	6	5	16	11	8
Subjects' own physician	—	—	2	1	1
Institutional representative	1	0	1	—	—
Courts	2	—	—	3	1
Someone else	—	0	0	0	0
Question inappropriate**	74	72	62	64	70
No information	3	3	2	11	4

* Percentages may add to more than 100% since more than one response could be checked.
** Question asked only in those studies where proxy consent was obtained, and where the investigator had already obtained consent from some subjects.

Table IV.6

Subjects Reluctant to Participate: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
In this study, how often do instances arise in which subjects for whom proxy consent has been obtained are reluctant to participate?					
Often	0%	1%	3%	2%	1%
Sometimes	2	2	2	2	2
Rarely	4	2	4	6	3
Never	15	17	19	14	17
Question inappropriate*	74	72	62	64	70
No information	5	6	10	12	7
Total	100%	100%	100%	100%	100%

* Question asked only in those studies where proxy consent was obtained, and where the investigator had already obtained consent from some subjects.

Table IV.7

Subjects Reluctant to Participate: Expected Benefit
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
In this study, how often do instances arise in which subjects for whom proxy consent has been obtained are reluctant to participate?		
Often	2	—
Sometimes	3	1
Rarely	4	2
Never	20	12
Question inappropriate*	65	79
No information	6	6
Total	100	100

* Question asked only in those studies where proxy consent was obtained, and where the investigator had already obtained consent from some subjects.

Table IV.8

Proxy Consent Protection for Subject: Type of Institution
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Recognizing that it is necessary to use proxy consent in some circumstances, from your general experience, do you feel that proxy consent protects the interests of subjects very well, fairly well, not very well, or not at all?					
Very well	20%	28%	36%	21%	28%
Fairly well	27	27	17	23	25
Not very well	8	8	10	14	9
Not at all	2	3	3	7	3
Question inappropriate*	17	10	13	7	11
No information	26	24	21	28	24
Total	100%	100%	100%	100%	100%

* Question asked only in those studies where consent was obtained.

Table IV.9

Proxy Consent Inadequate Protection: Type of Institution
(Percent of Projects)*

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
In what ways or in what situations may proxy consent not adequately protect subjects?					
Subjects do not know they are involved in research	0%	—%	0%	0%	—%
Subjects are not given complete information	4	3	1	4	3
Subjects not told about risks/hazards	—	1	0	0	—
Subjects have no choice about participating	7	5	9	8	6
Subject's right to privacy is violated	—	—	0	1	—
Subjects are incapable of giving consent	1	1	3	1	1
Where children are involved	1	2	—	0	1
Proxy not adequately informed about research	6	4	1	3	3
Proxy not adequately informed about risks/hazards	—	1	—	1	1
Proxy may not care about/want to protect subject	6	7	3	5	6
When proxy incapable of understanding research	4	4	7	12	5

Table IV.9 (continued)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
When proxy is a representative of the institution in which the research is done	—%	—%	—%	0%	—%
When proxy feels under obligation to the institution	—	0	0	0	0
When proxy does not want to assume responsibility for subject	—	1	0	0	—
When proxy believes some good could come from subject's condition	0	0	0	0	0
When proxy has something to gain from subject's participation	1	1	—	2	1
Other conflicts of interest of proxy	2	1	1	1	1
When research dangerous/potentially harmful	2	1	2	2	2
Oppose proxy consent in general	2	3	1	1	2
Think consent, in general, no guarantee	0	1	0	—	—
Other	1	2	2	—	2
Question inappropriate**	60	59	68	47	60
No information	9	13	10	21	12

* Percentages may add to more than 100% since more than one response could be checked.
** Question asked only in those studies were consent was obtained, and where investigator did not feel that proxy consent protected subjects very well.

Table V.1

Types of Consent Forms Used: Type of Institution*
(Percent of Projects)

Type of Form	Type of Institution: Universities (N=183)	Medical Schools (N=789)	Hospitals (N=133)	Other (N=110)	All (N=1215)
Institutional standard form with no details included about the particular study	10%	9%	14%	8%	10%
Institutional standard form which included details about the particular study	5	21	22	21	19
Original form	82	63	59	66	65
Not differentiable as to standard or original**	3	7	5	5	6
No information	-***	0	0	0	-
Total	100%	100%	100%	100%	100%

*Table based on those projects for which consent forms were available.

**These forms typically included details about the specific study, though in a form and format which suggested thy may have been written on a standardized blank form.

***Less than 1 percent.

Table V.2

Distribution of Long and Short Consent Forms: Type of Institutions*
(Percent of Projects)

Length of Form	Type of Institution				
	Universities (N=183)	Medical Schools (N=789)	Hospitals (N=133)	Other (N=110)	All (N=1215)
Short (less than 300 words)	85%	71%	80%	83%	75%
Long (more than 300 words)	15	29	20	17	25
No information	0	0	0	0	0
Total	100%	100%	100%	100%	100%

*Table based on those projects for which consent form were available.

Table V. 3

Are subjects given a copy of the consent form to keep?: Type of Institution*
(Percent of Projects)

	Type of Institution				
	Universities (N=183)	Medical Schools (N=789)	Hospitals (N=133)	Other (N=110)	All (N=1215)
Yes	16%	9%	10%	14%	10%
Upon request	7	14	25	14	15
No	71	71	59	62	69
No information	6	6	6	10	6
Total	100%	100%	100%	100%	100%

*Table based on those projects for which consent forms were available.

Table V. 4

Index of Consent Form Completeness: Type of Institution*
(Percent of Projects)

Degree of Completeness **	Type of Institution: Universities (N=183)	Medical Schools (N=789)	Hospitals (N=133)	Other (N=110)	All (N=1215)
1 Complete or nearly complete	6%	21%	21%	8%	18%
2	13	25	18	30	23
3	30	19	26	18	22
4	21	18	13	24	18
5	14	10	18	11	11
6 Totally or nearly incomplete	13	4	3	5	5
No information	3	3	1	4	3
Total	100%	100%	100%	100%	100%

*Table based on those projects for which consent forms were available.

**This index is based upon six items: descriptions of (1) purpose of the research, (2) the procedures involved, (3) the risks, (4) the benefits; and the presence of statements indicating that (5) participation is voluntary or that subjects could withdraw without prejudice and that (6) subjects and proxies might ask questions about participation. A consent form in the most complete category, for example, would contain at least four detailed descriptions and two brief mentions of these six elements. A form in the least complete category could include no complete descriptions and no more than one brief mention of any of these elements. See the following page for more information about the coding schemes used in the index.

The coding of consent forms for completeness. Four of the six components comprising the consent form completeness index were scored for degree of mention as follows:

0 no mention

1 unspecific certified statement

2 brief mention

3 detailed description

The components concerning two elements ("Questions" and "Withdrawal") were coded somewhat differently, as will be described below.

A certified statement indicates that the subject or proxy acknowledges having been informed regarding an issue such as the purpose of the research or the risks of participation. Certified statements may include reference to specific details of the issue or they may be "unspecific," simply indicating that the subject or proxy has been informed. Unspecific certified statements were coded 1; those with specific information about the issues were coded for the degree of detail presented.

Purpose. The extent to which the form contains a description of the purpose of the study and whether or not it contains an unspecific certified statement of purpose is coded as degree of "Purpose."

Procedures. The content relating to procedures was coded in the same way as that of purpose.

Benefits. "Benefits" is coded on the basis of the extent to which the form contains statements discussing the probability of medical benefit to the subject and statements discussing general benefits to the subject. Statements of the nature of benefits or lack thereof are regarded as detailed descriptions.

Risks. The extent to which the form contains statements regarding severity of risk is coded as "Risk." Also included in this code are statements pertaining to psychological, medical, and minor risks and discomforts and unspecific certified statements of risk. The most detailed discussion among these items defines the code value assigned.

Subject Withdrawal. Coded in "Subject Withdrawal" is the extent to which the form contains statements to the effect that participation is voluntary or that the subject is free to withdraw without prejudice. For this element, a certified statement was assigned a value of 2 (rather than 1) because such a statement implicitly involves a brief description.

Questions. This component was coded either 0 or 3, corresponding to the absence or presence of an invitation to ask questions.

Index of consent form completeness. A summary measure combining the six elements described above was constructed by averaging the six scores. In cases where more than two scores were unascertainable, the index for that consent form received a score of "no information."

Table V. 5

Components of Index of Consent Form Completeness: Type of Institution*
(Percent of Projects)

	Type of Institution																	
	Universities (N=183)						Medical Schools (N=789)						Hospitals (N=133)					
	No Mention	Unspecific Certified Statement**	Brief Mention	Detailed Description	No Information	Total	No Mention	Unspecific Certified Statement**	Brief Mention	Detailed Description	No Information	Total	No Mention	Unspecific Certified Statement**	Brief Mention	Detailed Description	No Information	Total
Purpose	31%	6	54	8	1	100%	22%	7	62	8	1	100%	18%	8	61	13	0	100%
Procedures	16%	5	58	20	1	100%	9%	6	54	30	1	100%	6%	9	63	22	0	100%
Benefits	74%	7	7	11	1	100%	41%	18	15	25	1	100%	40%	18	10	32	0	100%
Risks***	66%	5	11	15	3	100%	25%	11	22	38	4	100%	19%	17	19	42	3	100%
Withdrawal	17%	0	54	28	1	100%	20%	0	45	34	1	100%	37%	0	35	28	0	100%
Questions****	44%			56	0	100%	38%			61	1	100%	47%			53	0	100%

*Table based on those projects for which consent forms were available.
**For example, "I certify that I have been informed about the purpose, procedures, and risks of this study."
***Of those projects which made no mention of risk in either the written consent form or the oral consent information statement, about seventy percent were characterized by investigators on our questionnaire as entailing at least a very low probability of minor harm to the subject.
****Coded dichotomously: either provided statement inviting questions or did not.

Table V. 5 (continued)

Type of Institution

Component	Other (N=110) No Mention	Unspecific Certified Statement**	Brief Mention	Detailed Description	No Information	Total	All (N=1215) No Mention	Unspecific Certified Statement**	Brief Mention	Detailed Description	No Information	Total
Purpose	25%	14	52	8	1	100%	23%	8	59	9	1	100%
Procedures	13%	5	58	23	1	100%	10%	6	56	27	1	100%
Benefits	42%	7	19	31	1	100%	45%	15	14	25	1	100%
Risks***	37%	6	15	39	3	100%	30%	11	20	36	3	100%
Withdrawal	14%	0	65	18	3	100%	22%	0	47	30	1	100%
Questions****	57%			42	1	100%	42%			57	1	100%

*Table based on those projects for which consent forms were available.

**For example, "I certify that I have been informed about the purpose, procedures, and risks of this study."

***Of those projects which made no mention of risk in either the written consent form or the oral consent information statement, about seventy percent were characterized by investigators on our questionnaire as entailing at least a very low probability of minor harm to the subject.

****Coded dichotomously: either provided statement inviting questions or did not.

Table V. 6

Oral Mention to Subject of Elements Not Mentioned in the Written Form: Type of Institution
(Percent of Projects)

Element not mentioned in consent form	Universities					Medical Schools					Hospitals				
	N	Mentioned	Not Mentioned	No Information*	Total	N	Mentioned	Not Mentioned	No Information*	Total	N	Mentioned	Not Mentioned	No Information*	Total
Purpose	(53)	46%	41	13	100%	(163)	58%	36	6	100%	(25)	65%	35	0	100%
Procedures	(24)	39%	45	16	100%	(47)	59%	33	8	100%	(9)	80%	20	0	100%
Benefits	(125)	7%	81	12	100%	(289)	23%	71	6	100%	(50)	38%	61	1	100%
Risks	(107)	2%	45	53	100%	(168)	23%	70	7	100%	(23)	27%	70	3	100%
Withdrawal	(31)	8%	76	16	100%	(114)	14%	77	9	100%	(43)	23%	75	2	100%
Ask Questions	(69)	24%	63	13	100%	(253)	12%	83	5	100%	(55)	24%	74	2	100%

*This category included projects in which there was no oral statement as well as those projects for which oral mention of the elements could not be ascertained.

Table V.6 (continued)

Element not mentioned in consent form	Other N	Other Mentioned	Other Not Mentioned	Other No Information*	Other Total	All N	All Mentioned	All Not Mentioned	All No Information*	All Total
Purpose	(30)	43%	44	13	100%	(262)	55%	38	7	100%
Procedures	(9)	63%	19	18	100%	(92)	57%	33	10	100%
Benefits	(49)	21%	63	16	100%	(513)	22%	71	7	100%
Risks	(43)	31%	61	8	100%	(341)	19%	72	9	100%
Withdrawal	(19)	16%	52	32	100%	(207)	16%	75	9	100%
Ask Questions	(66)	9%	70	21	100%	(112)	16%	77	7	100%

*This category included projects in which there was no oral statement as well as those projects for which oral mention of the elements could not be ascertained.

Table V.7

Mention in Consent Form of Availability of Alternative Procedures:
Type of Institution
(Percent of Forms)*

Mention of Alternatives	Type of Institution				
	Universities (N=42)	Medical Schools (N=388)	Hospitals (N= 80)	Other (N= 44)	All (N=554)
No Mention	98%	74%	82%	94%	79%
Alternatives exist	0	15	10	6	12
Alternatives offered	0	7	3	0	5
No alternatives	0	3	5	0	3
No information	2	1	0	0	1
Total	100%	100%	100%	100%	100%

*This table is based on 554 consent forms from projects described (by the investigator) as intending to benefit subjects. Sixty-four percent of these projects made no mention in their consent form or oral statement of alternative procedures or treatments available to subjects.

Table V.8

Mention in Consent Form of Experimental Nature of the Research:
Type of Institution
(Percent of Forms)*

Mention of Experimental Nature of Project	Type of Institution: Universities (N=8)	Medical Schools (N=252)	Hospitals (N= 56)	Other (N= 30)	All (N=346)
No Mention	50%	57%	71%	77%	62%
Brief Mention	50	32	21	18	28
Experimental elements identified	0	11	8	0	9
No information	0	-	0	5	1
Total	100%	100%	100%	100%	100%

*This table is based on 346 consent forms from projects described as experimental in nature. Fifty-one percent of these projects made no mention of the project's experimental nature in either their consent form or oral statement.

Table V.9

Mention of Project Characteristics
in Consent Form or in Oral Explanation
(Percent of Projects)

Investigator reported in interview that:	% Mentioned	% Not Mentioned	No Information	Total
Project entailed risk of breach of confidentiality (N= 256)	63%	37	0	100%
Subjects were assigned to different treatments or procedures (N= 831)	18%	82	-	100%
Project involved the use of placeboes (N= 99)	61%	39	0	100%
Information about research was withheld from subject (N=188)	13%	86	1	100%
Project should benefit subject (N=601)	64%	36	-	100%
Project should not benefit subject (N=444) [This now shows the percentage of forms or explanations that indicate benefits]	35%	65	-	100%

Table V.10

Mention of Elements Not Covered by Completeness Analyses
(Percent of Forms)
(N=1215)

Element	% Mentioned	% Not Mentioned	No Information	Total
Expected duration of participation	27%	72	1	100%
Mention of review committee approval	5%	94	1	100%
Agreement of participation included	88%	12	-	100%
Discuss voluntary nature of participation	43%	57	-	100%
Mention injuries will be treated	3%	96	1	100%
Mention harm will be compensated	-%	99	1	100%
Investigator or institution released from responsibility for harm incurred	1%	98	1	100%
Project contact information (phone number) included	12%	87	1	100%
Provision to contact subject for future research	1%	98	1	100%
Provision to allow future use of data	7%	92	1	100%
Results will be made available to subject	6%	93	1	100%

Table V.11

Readability of Short Consent Forms: Type of Institution and Overall
(Percent of Projects)*

	Readability								
	Very Easy (Comics)	Easy (Pulp fiction)	Fairly Easy (Slick fiction)	Standard (Time)	Fairly Difficult (Atlantic)	Difficult (Scholarly, academic)	Very Difficult (Scientific, professional)	No Information	Total
All Projects (N= 908)	-%	-	1	6	16	57	19	1	100%
Universities (N=155)	0%	-	2	14	23	48	13	-	100%
Medical Schools (N=557)	0%	-	-	5	17	57	20	1	100%
Hospitals (N=105)	0%	0	-	8	5	60	27	0	100%
Other (N= 91)	1%	0	2	3	18	61	13	2	100%

*Table based on those projects for which consent forms were available.

Table V.12

Readability of Long Consent Forms-Purpose Area: Type of Institution and Overall
(Percent of Projects)*

	Readability								
	Very Easy (Comics)	Easy (Pulp fiction)	Fairly Easy (Slick fiction)	Standard (Time)	Fairly Difficult (Atlantic)	Difficult (Scholarly, academic)	Very Difficult (Scientific, professional)	No Information	Total
All projects (N= 307)	0%	-	2	2	8	36	42	10	100%
Universities (N=28)	0%	0	0	10	11	23	32	24	100%
Medical schools (N=232)	0%	-	1	2	9	33	46	9	100%
Hospitals (N= 28)	0%	0	9	1	1	60	25	4	100%
Other (N= 19)	0%	0	8	0	9	27	44	12	100%

*Table based on those projects for which consent forms were available.

Table V.13

Readability of Long Consent Forms-Procedures Area: Type of Institution and Overall
(Percent of Projects)*

	Readability								
	Very Easy (Comics)	Easy (Pulp fiction)	Fairly Easy (Slick fiction)	Standard (Time)	Fairly Difficult (Atlantic)	Difficult (Scholarly, academic)	Very Difficult (Scientific, professional)	No Information	Total
All projects (N=307)	0%	-	2	11	23	43	21	0	100%
Universities (N= 23)	0%	0	10	18	7	47	18	0	100%
Medical schools (N=232)	0%	0	1	8	23	46	22	0	100%
Hospitals (N=28)	0%	2	1	17	21	44	16	0	100%
Other (N= 19)	0%	0	8	11	47	6	28	0	100%

*Table based on those projects for which consent forms were available.

Table V.14

Readability of Long Consent Forms-Risks Area: Type of Institution and Overall (Percent of Projects)*

	Readability								
	Very Easy (Comics)	Easy (Pulp fiction)	Fairly Easy (Slick fiction)	Standard (Time)	Fairly Difficult (Atlantic)	Difficult (Scholarly, academic)	Very Difficult (Scientific, professional)	No Information	Total
All projects (N= 307)	1%	1	1	5	16	42	21	14	100%
Universities (N= 28)	0%	0	0	3	6	19	15	57	100%
Medical schools (N=232)	0%	-	1	5	16	49	21	8	100%
Hospitals (N= 28)	5%	1	0	5	24	33	20	12	100%
Other (N= 19)	0%	0	8	6	6	26	23	31	100%

*Table based on those projects for which consent forms were available.

Table V.15

The Percentage of Medical and Technical Terms
Accompanied by Lay Explanations in Consent Forms
(Percent of Projects)
(N=1215)*

	Percentage of terms accompanied by a lay explanation					
	0 - 10%	10.1-35%	35.1-60%	60.1-85%	No Information	Total
Medical terms	76%	1	1	-	22	100%
Technical terms	81%	1	1	1	16	100%

*Table based on projects for which consent forms were available.

Table VI.1

Percent of Committees Including Members with Each Characteristic: Type of Institution
(Percent of Boards)*

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
Does your committee include members who are (have):						
Done biomedical research	74%	98%	100%	77%	100%	89%
Done behavioral research	99	73	80	100	76	89
Administrators	96	91	85	92	69	88
Legal professionals	70	91	60	31	94	69
Community representatives	94	100	99	92	73	93
Non-institutional members	85	100	89	92	92	94
Male	100	100	100	100	100	100
Female	75	100	77	100	99	88
Black	12	45	33	27	5	30
Any minority	22	50	56	54	17	48

*Percentages may add to more than 100% since more than one response could be checked. Percentages are calculated excluding those respondents who chose not to state whether or not their committee had members in one of these categories. These figures represent the percent of boards including members with each characteristic, not the percent of members in each board having each characteristic.

Table VI.2

Minority Group Members of Review Committees:
What degree do you hold?

Degree	Race: Black (N=33)	Race: Other Minority (N=16)
M.D.; D.D.S.; D.D.; D.V.M.	28.7%	70.3%
Ph.D.; Ed.D.; J.D.; LL.D.	26.5	28.4
M.S.; M.A.; M.S.W.; M.B.A.	20.2	0.0
B.A.; B.S.; R.N.	19.0	1.3
A.A.	2.3	0.0
No information	2.3	0.0
Total	100.0%	100.0%

Table VI.3

Minority Group Members of Review Committees:
What is your field of training or discipline?

Discipline	Race: Black (N=33)	Race: Other Minority (N=16)
Hospital administration	2.5%	0.0%
Dentistry	0.0	2.9
Biological science	12.7	18.8
Behavioral science	3.2	0.0
Law	12.7	0.0
Theology/religion	8.7	0.0
Education/educational administration	10.5	0.0
Business administration	0.0	4.8
Social work	0.7	4.8
Nursing	3.6	0.0
Health-related discipline	17.4	0.0
Medicine (speciality not ascertained)	0.7	1.2
Internal medicine	2.2	6.1
Obstetrics/gynecology; neonatology	0.0	27.4
Pathology	0.0	20.0
Pediatrics	13.3	0.0
Radiology	4.8	0.0
Surgery	7.0	14.0
Total	100.0%	100.0%

Table VI.4

Review Committee Members, by Race:
Are you employed by the institution to
which this review committee belongs?

Employed by institution?	Black (N=33)	Other Minority (N=16)	White (N=761)
Yes	71%	79%	85%
No	29	14	15
No information	0	7	0
Total	100%	100%	100%

Table VI.5

Primary Field of Training of Review Board Members Interviewed
(Number of Members)*

Biomedical Scientists		Behavioral and Social Scientists		Other	
Medicine		Anthropology	4	Administration	25
Anesthesiology	8	Economics	3	Law	50
Internal Medicine	68	Education	28	Religion	27
Neurology	7	Political Science	7	Philosophy/Ethics	3
Nuclear Medicine	6	Psychology	65	Other Liberal Arts	11
Ob/Gyn	10	Sociology	23	Business Administration	28
Opthamology	7	Other	2	Social Work	17
Pathology	28			Nursing	35
Pediatrics	39			Other Health-related	20
Psychiatry	38			Statistics	2
Radiology	10			Physical Science	7
Surgery	40			Other	3
Urology	6				
Other	22				
Dentistry	11				
Biological Science	100				

*These figures, unlike any others in this report, are unweighted. They are provided to describe the persons from whom data was obtained, but should not be interpreted as describing the population from which they were drawn. At the time this was prepared, data on the field of training was not available for 77 review board members who were interviewed.

Table VI.6

How Individuals Became Review Committee Members
(Percent of Members)

	Field of Training		
	Biomedical Sciences (N=382)	Behavioral and Social Sciences (N=136)	Other (N=224)
Ex-officio	20%	9%	23%
Sought membership	3	4	2
Were asked to serve	76	87	74
Elected	-	0	1
Other	-	0	-
Total	100%	100%	100%

Table VI.7

How did you learn about what was expected of you in your role as a review committee member?
(Percent of Members)*

	Field of Training		
	Biomedical Sciences (N=384)	Behavioral and Social Sciences (N=138)	Other (N=228)
Briefed by committee member	45%	47%	49%
Written instruction	64	85	70
Through experience on the committee	35	25	31
Attendance at workshops, seminars, etc.	2	2	5
Prior professional and research experience	21	8	9

*Percentages add to more than 100% since more than one response could be given.

Table VI.8

Were you asked to report to the review committee on any proposals?
(Percent of Members)

	Field of Training		
	Biomedical Sciences (N=349)	Behavioral and Social Sciences (N=122)	Other (N=216)
Yes	48%	41%	40%
No	52	59	60
Total	100%	100%	100%

Table VI.9

Were any particular types of proposals assigned to you?*
(Percent of Members)

	Field of Training		
	Biomedical Sciences (N=198)	Behavioral and Social Sciences (N= 56)	Other (N= 96)
Yes	65%	51%	53%
No	35	49	47
Total	100%	100%	100%

*Table includes only those who were asked to report to the review board on any proposals.

Table VI.10

Before submitting proposals for review, did investigators ever consult with you personally about ethical issues or committee requirements? (Percent of Members)

	Field of Training		
	Biomedical Sciences (N=355)	Behavioral and Social Sciences (N=124)	Other (N=219)
Yes	48%	54%	33%
No	52	46	67
Total	100%	100%	100%

Table VI.11

How often did you discuss proposals with other committee members outside of committee meetings--often, sometimes, seldom, or never?
(Percent of Members)

	Field of Training		
	Biomedical Sciences (N=356)	Behavioral and Social Sciences (N=124)	Other (N=218)
Often	14%	4%	10%
Sometimes	27	21	19
Seldom	43	54	43
Never	16	20	28
Total	100%	100%	100%

Table VI.12

What is the field of training or discipline of the committee member with whom you most often had these informal discussions?*
(Percent of Members)

	Field of Training of Respondent		
	Biomedical Sciences (N=130)	Behavioral and Social Sciences (N= 25)	Other (N= 66)
Field of Training of Person with Whom Consulted			
Biomedical sciences	80%	19%	37%
Behavioral and social sciences	5	42	20
Other	15	39	43
Total	100%	100%	100%

*Table includes only those who were asked, and responded to, this item.

Table VI.13

Compared to the average committee member, would you say you were much more active in committee discussions, more active, about as active, somewhat less active, or much less active?
(Percent of Members)

	Field of Training		
	Biomedical Sciences (N=347)	Behavioral and Social Sciences (N=122)	Other (N=216)
More active than average	51%	47%	20%
About as active or less active than average	49	53	80
Total	100%	100%	100%

Table VI.14

Overall, how would you assess your own influence on committee decisions?
(Percent of Members)

	Field of Training		
Response Categories	Biomedical Sciences (N=345)	Behavioral and Social Sciences (N=119)	Other (N=212)
More than average influence	47%	35%	23%
About average influence	43	56	64
Less than average influence	10	9	13
Total	100%	100%	100%

Table VI.15

During the committee review, were there any aspects of research proposals that you were more likely than most other members to raise for committee discussion?
(Percent of Members)

	Field of Training		
	Biomedical Sciences (N=352)	Behavioral and Social Sciences (N=124)	Other (N=218)
Yes	70%	56%	66%
No	30	44	34
Total	100%	100%	100%

Table VI.16

Are there aspects of research proposals that you are more likely than other members to raise for committee discussion?*
(Percent of Members)

	Field of Training		
	Biomedical Sciences (N=241)	Behavioral and Social Sciences (N=71)	Other (N=137)
Risk	16%	9%	5%
Consent forms	5	6	12
Other aspects of informed consent	8	19	17
Privacy, confidentiality	6	9	11
Special subject groups--e.g., pregnant women, children, institutionalized, comatose	4	8	7
Deception; withholding information	0	2	0
Scientific merit or importance/quality of research design	6	12	1
Necessity, appropriateness of procedures, techniques, methodologies	10	1	10
Equity in subject selection	0	2	0
Criteria for subject selection	1	1	-
Medical matters	33	8	7
Psychological matters	2	6	2
Social science matters	-	4	6
Protect reputation or liability of institution or investigator	0	0	2
Legal matters	-	2	7
Scope of responsibility of IRB	1	-	1
Other	8	11	12
Total	100%	100%	100%

*Table includes only members who indicated that they are more likely than other members to raise particular aspects for discussion, and it includes only one response per respondent.

Table VI.17

Were there any aspects of research proposals on which you thought you were expected to comment because of your particular expertise or point of view? (Percent of Members)*

	Field of Training		
	Biomedical Sciences (N=349)	Behavioral and Social Sciences (N=121)	Other (N=205)
No	27%	44%	33%
Yes			
Risk	7	4	2
Consent and consent forms	2	2	20
Privacy, confidentiality	1	1	2
Special subject groups	2	4	3
Scientific merit and quality	2	1	1
Necessity and appropriateness of procedures	4	5	5
Equity in subject selection	0	1	0
Medical matters	46	4	9
Psychological matters	3	8	1
Social science matters	1	17	1
Legal matters	-	0	7
Financial, budget, personnel, etc.	-	1	5
Other	5	8	11
Total	100%	100%	100%

Table VI.18

How much emphasis did you, yourself, place on each of the following when you reviewed new proposals? (Percent of members giving heavy emphasis* to each aspect)

	Field of Training		
	Biomedical Sciences (N=350)**	Behavioral and Social Sciences (N=120)**	Other (N=215)**
Contribution to scientific knowledge	47%	31%	31%
Balance of risks and benefits	97	86	87
Issues of privacy and confidentiality	71	87	87
Informed consent procedures	87	92	94
Scientific design of the research	47	25	16
Whether subjects are chosen appropriately	64	46	54

*Includes respondents checking categories 4 and 5 on a 5-point scale ranging from (1) little or no emphasis to (5) great deal of emphasis.

**Actual numbers on which percentages calculated vary slightly due to non-response.

Table VI.19

Which of the following descriptions of the review committee's purpose comes closest to your view?
(Percent of Members)

	Field of Training		
	Biomedical Sciences (N=351)	Behavioral and Social Sciences (N=123)	Other (N=219)
The purpose is to protect human subjects	47%	54%	60%
The purpose is to balance the need for protecting human subjects with the need to develop new knowledge	52	46	39
Both, other, don't know	1	0	-
Total	100%	100%	100%

Table VI.20

How often did you personally initiate a request that the committee seek additional information about a proposal from an investigator? (Percent of Members)

	Field of Training		
	Biomedical Sciences (N=384)	Behavioral and Social Sciences (N=138)	Other (N=228)
Often	12%	6%	5%
Sometimes	49	41	36
Seldom	28	32	37
Never	11	21	22
Total	100%	100%	100%

Table VI.21

How often did you personally initiate a request that modifications be made in proposed research? (Percent of Members)

	Field of Training		
	Biomedical Sciences (N=381)	Behavioral and Social Sciences (N=138)	Other (N=228)
Often	6%	5%	2%
Sometimes	44	27	25
Seldom	31	34	29
Never	19	34	44
Total	100%	100%	100%

Table VI.22

When you personally desired additional information, how often did the committee actually seek that information from an investigator?* (Percent of Members)

	Field of Training		
	Biomedical Sciences (N=343)	Behavioral and Social Sciences (N=107)	Other (N=179)
Always	79%	81%	72%
Often	17	14	17
Sometimes	3	1	5
Seldom	0	3	3
Never	0	1	1
Don't know	1	0	2
Total	100%	100%	100%

*Table includes only those who reported actually requesting that more information be sought.

Table VI.23

When you personally felt that a modification should be made, how often did the committee require that the investigator actually make the modification? (Percent of Members)*

	Field of Training		
	Biomedical Sciences (N=320)	Behavioral and Social Sciences (N= 94)	Other (N=140)
Always	47%	46%	53%
Often	35	40	33
Sometimes	14	11	12
Seldom	2	0	1
Never	0	2	0
Dont' know	2	1	1
Total	100%	100%	100%

*Table includes only those who reported that they had requested modifications be made.

Table VI.24

Types of Research Reviewed: Type of Institution
(Percent of Review Boards)*

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
Is each of the following categories of research included or excluded from the purview of your committee--either by policy or in practice?						
Non-HEW funded research	76%	100%	100%	100%	85%	92%
Unfunded research	68	100	97	100	69	87
No-risk research	61	95	97	100	85	86
Graduate or medical student research	90	100	100	100	100	97
Undergraduate student research	51	86	92	100	97	80
Previously reviewed research	46	80	99	100	34	61

*Percentages are percentages of boards including each sort of research. Percentages may add to more than 100% since more than one response could be checked. Percentages omit boards reporting that they have no contact with a particular type of research.

Table VI.25

University Review Committees:
What types of research are not reviewed?
(N=43)

Are research projects from the following departments subject to the review procedure?	Departments		
	Law	Journalism	Physical Education
Yes, reviewed	43.9%	41.9%	70.8%
Not reviewed	8.3	0.5	4.6
No such department at university	22.2	23.2	1.9
Don't know	19.3	28.1	16.3
No information	6.3	6.3	6.3
Total	100.0%	100.0%	100.0%

Table VI.26

Staff Assistance
(Percent of Boards)

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
Does your committee have any administrative or clerical assistance?						
Yes	85%	92%	99%	69%	79%	86%
Secretarial assistance						
Full-time	19	35	13	15	0	17
Part-time	65	53	88	62	64	67
Administrative assistance						
Full-time	14	11	12	15	15	13
Part-time	32	24	17	23	1	21
Legal assistance						
Full-time	0	0	0	0	0	0
Part-time	0	0	3	0	0	0
No	15	8	1	31	21	14
Total	100%	100%	100%	100%	100%	100%

*Percentages in offset columns may add to more than 100% since more than one response could be checked.

Table VI.27

Mechanisms for Committee Deliberations: Type of Institution
(Percent of Boards)

	Type of Institution					
	Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N= 11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
Do members discuss proposals at meetings of the committee, do they comment by mail, or what?						
Meetings	90%	58%	99%	84%	63%	81%
Mail	1	0	0	8	0	2
Meetings and phone or mail	9	42	1	8	37	17
Total	100%	100%	100%	100%	100%	100%

Table VI.28

Attendance of Principle Investigators: Type of Institutions
(Percent of Boards)

	Type of Institution					
	Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N= 11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
Do investigators attend the meetings at which their proposals are discussed?						
Always	17%	9%	34%	53%	37%	28%
Often	0	0	30	8	38	14
Sometimes	33	51	6	8	15	23
Seldom	8	40	9	15	10	16
Never	41	0	17	8	0	16
Committee does not meet	1	0	0	8	0	2
No information	0	0	4	0	0	1
Total	100%	100%	100%	100%	100%	100%

Table VI.29

Openness to Non-members: Type of Institution
(Percent of Boards)

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
Are committee meetings open to non members?						
Yes	36%	75%	42%	54%	86%	56%
No	51	25	43	38	0	34
Committee does not meet	1	0	0	8	0	2
No information	12	0	15	0	14	8
Total	100%	100%	100%	100%	100%	100%

Table VI.30

Availability of Information to Investigators Concerning Proposal Content
(Percent of Boards)

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
Do investigators have available to them written material which describes the information which their proposal should include or standard forms on which to describe their proposals?						
Standard forms required	75%	53%	36%	61%	37%	54%
Standard forms available but optional	7	9	24	8	0	10
Written instruction available	18	34	40	23	26	28
Neither standard forms nor written instructions available	0	4	0	8	37	8
Total	100%	100%	100%	100%	100%	100%

Table VI.31

Consensus without Formal Vote
(Percent of Boards)

How often is consensus reached concerning a proposal without a formal vote?	Type of Institution: Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N= 75)
Always	41%	1%	1%	8%	0%	12%
Often	24	33	28	38	42	32
Sometimes	0	0	3	0	0	1
Seldom	0	4	0	0	13	3
Never	35	62	68	54	45	52
Total	100%	100%	100%	100%	100%	100%

Table VI.32

Criterion for Proposal Approval
(Percent of Boards)

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
What vote is required to approve a proposal?						
No votes taken	6%	0%	0%	8%	0%	3%
Unanimous	48	1	22	15	27	24
Majority	40	86	78	77	54	66
Other	0	8	0	0	3	2
No information	6	5	0	0	16	5
Total	100%	100%	100%	100%	100%	100%

Table VI.33

Screening of Proposals: Type of Institution
(Percent of Boards)*

	Type of Institution					
	Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N= 11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
Does your committee use any kind of procedure to screen out proposals which do not need committee attention?						
Yes	34%	86%	87%	46%	56%	62%
Those not using human subjects	24	43	49	15	43	35
Training grants	1	10	0	0	0	2
Minor modifications of existing protocals	0	1	0	0	0	0
Routine clinical procedures	0	10	12	15	6	8
Those obviously against Federal guidelines; too risky; too poorly designed	0	5	0	0	0	1
Low or no risk	9	7	0	0	0	4
Those outside committee jurisdiction	2	9	12	8	13	8
Other	0	1	6	8	0	3
No	66	14	13	54	44	38
Total	100%	100%	100%	100%	100%	100%

*Percentages in offset columns may add to more than 100% since more than one response could be checked.

Table VI.34

Special Assignment of Proposals for Review: Individuals
(Percent of Boards)*

	Type of Institution					
	Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N= 11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
Why are proposals assigned to individual boards members for intensive review?						
Initial review	18%	47%	12%	8%	0%	19%
Determine risks and benefits	0	4	1	0	28	4
Emergency situations	0	0	0	0	0	0
Expert review	17	42	43	31	27	33
Objective reviews (by non-institutional members)	1	1	0	0	0	-
Special issues	8	5	1	15	0	6
Determine value of full committee review	0	0	0	0	0	0
Other	0	0	3	0	0	1
No such assignments are made	58	6	41	46	48	41

*Percentages may add to more than 100% since respondents might indicate more than one reason for proposal assignment.

Table VI.35

Special Assignment of Proposals for Review: Subcommittees
(Percent of Boards)*

Why are proposals assigned to subcommittees for intensive review?	Type of Institution: Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
Initial review	9%	21%	0%	8%	13%	10%
Determine risks and benefits	0	0	4	0	0	0
Emergency situation	1	12	0	0	0	2
Expert review	11	20	16	8	1	12
Objective reviews (by non-institutional members)	0	4	0	0	0	1
Special issues	8	12	14	0	0	7
Determine value of full committee review	0	0	0	0	0	0
No such assignments made	72	47	72	85	86	72

*Percentages may add to more than 100% since respondents might indicate more than one reason or proposal assignment.

Table VI.36

Impact of Subcommittees
(Percent of Boards)

	Type of Institution					
	Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
In general, what actions are subcommittees expected to take on each proposal?						
Make a final decision	9%	0%	0%	0%	13%	4%
Make a recommendation	18	45	28	8	1	21
Present a summary	1	8	0	8	0	3
No subcommittees exist	72	47	72	84	86	72
Total	100%	100%	100%	100%	100%	100%

Table VI.37

Further Review of Approved Proposals
(Percent of Boards)

When your committee approves a proposal, is its decision subject to any further review within the institution?	Type of Institution: Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
Yes, automatically	9%	5%	24%	39%	36%	21%
Yes, under some circumstances	1	1	9	8	0	4
No	90	94	67	46	51	73
No information	0	0	0	7	13	2
Total	100%	100%	100%	100%	100%	100%

Table VI.38

Power of Later Reviewers
(Percent of Boards)

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
May the later reviewers reject a proposal or only request reconsideration?						
May reject	1%	6%	1%	54%	17%	14%
Request reconsideration only	9	0	22	0	13	9
No further review given	90	94	67	46	64	74
Don't know	0	0	1	0	6	1
No information	0	0	9	0	0	2
Total	100%	100%	100%	100%	100%	100%

Table VI.39

Further Review of Rejected Proposals
(Percent of Boards)

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N= 11)	Institutions for Mentally Infirm (N= 13)	Other (N= 13)	All (N= 75)
If the review committee decides to reject a proposal, is this decision automatically subject to further review?						
Yes, automatically	13%	5%	16%	15%	15%	13%
Yes, if a minority rejects	0	0	0	8	0	1
No	71	95	84	69	79	80
No information	16	0	0	8	6	6
Total	100%	100%	100%	100%	100%	100%

Table VI.40

Investigator Appeal
(Percent of Boards)

	Type of Institution					
	Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
Can an investigator appeal a review board decision?						
Yes	58%	38%	43%	62%	37%	48%
No	36	62	57	38	48	48
Don't know	6	0	0	0	15	4
Total	100%	100%	100%	100%	100%	100%

Table VI.41

Agreements for Periodically Repeated Review
(Percent of Boards)

How many proposals has your committee reviewed during the past year with the understanding that the project would be reviewed again after a specified period of time?	Type of Institution					
	Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
All	47%	47%	63%	23%	50%	47%
Most	0	11	11	8	0	7
Some	3	22	0	8	13	8
Few	22	15	23	15	3	17
None	28	0	3	46	34	21
Total	100%	100%	100%	100%	100%	100%

Table VI.42

Committee Policy Regarding Reporting of Subject Injuries
(Percent of Boards)*

	Type of Institution					
	Universities (N= 17)	Medical Schools (N= 21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
Does your committee have any policy or practice with regard to investigators reporting injuries or harm to subjects as a result of research?						
Policy exists	32%	51%	63%	54%	36%	47%
Report incident	32	48	44	54	31	31
Discontinue project	0	0	1	8	0	2
review project again	0	0	0	0	5	1
No policy exists	68	33	26	46	49	45
No information	0	16	11	0	15	8
Total	100%	100%	100%	100%	100%	100%

*Percentages in offset columns may add to more than 100% since respondents could indicate more than one answer.

Table VI.43

Institution Policy Concerning Treatment or Compensation for Injuries
(Percent of Boards)*

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N=13)	All (N=75)
Does your institution have any policy regarding the treatment of or compensation for injuries suffered by subjects in research?						
Institution policy exists	52%	53%	14%	38%	60%	43%
Institute provides (or pays for) all necessary treatment	18	39	14	31	35	26
Institute is insured	18	14	0	8	38	14
Investigator must be insured	2	0	0	0	15	4
Other policy	1	0	0	0	0	-
No institution policy exists	25	17	56	54	22	35
Don't know	27	30	30	8	18	22
No information	1	0	0	0	0	-
Total	100%	100%	100%	100%	100%	100%

*Percentages in offset columns need not add to 100% since respondent might make more than one response.

Table VI.44

Observation of Ongoing Projects

(Percent of Boards)

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N=11)	Institutions for Mentally Infirm (N=13)	Other (N= 13)	All (N= 75)
Has your committee ever designated members or other representatives to observe the manner in which a research project is being conducted?						
No	75%	65%	49%	54%	74%	63%
Yes, routinely	17	0	33	23	26	20
Yes, under certain circumstances	8	35	18	23	0	17
Total	100%	100%	100%	100%	100%	100%

Table VI.45

Review Board Action on Research Proposals
(Percent of Projects)

Type of Institution	Projects Modified by Board	Projects Modified Informally*	Projects for Which Board Sought More Information**	Projects not Modified in Any Way	No Information	Total
Universities (N=136)	30%	7	16	45	2	100%
Medical schools (N=475)	33%	8	10	44	5	100%
Hospitals (N=105)	45%	4	10	37	4	100%
Institutions for mentally infirm (N=31)	35%	7	9	43	6	100%
Other (N=34)	29%	4	3	49	15	100%

*Includes projects not modified by formal board action, but which were modified as a result of informal discussions with IRB members.

**Includes projects not modified by either formal actions or informal discussion, but for which the IRB requested information beyond that originally provided by the investigator. In some cases this can be equivalent to the IRB requiring modifications in the project.

Table VI.46

Problems Faced by Review Boards
(Percent of Boards)
(N=75)

	Very Serious Problem	Somewhat Serious Problem	Minor Problem	No Problem	No Information	Total
The need for rapid action because of funding agency deadlines	4%	16	51	27	2	100%
The frequency of changes in DHEW policy or regulations	1%	7	54	37	1	100%
The lack of precise DHEW guidelines regarding specific procedures or types of research	2%	17	60	21	-	100%
Disagreements among members about the purpose of the committee	0%	7	20	68	5	100%
Disagreements between the review committee and investigators about the purpose of the committee	0%	1	32	59	8	100%
Antagonism of the investigators toward the committee	1%	3	16	69	11	100%
The volume of work that had to be accomplished by the committee	5%	20	38	29	8	100%
Getting members together for meetings	4%	34	37	24	1	100%

Table VI.47

Considering the operation of this committee, please indicate whether each of the following was a very serious problem, a somewhat serious problem, a minor problem, or no problem at all. (Percent of Review Board Members Indicating Each Factor Is a Somewhat or Very Serious Problem)

	Field of Training			
	Biomedical Sciences (N=375)*	Behavioral and Social Sciences (N=135)*	Other (N=220)*	All (N=730)
The need for rapid action because of funding agency deadlines, how serious a problem was this?	34%	37%	32%	34%
The frequency of changes in DHEW policy or regulations?	32	23	24	28
The lack of precise guidelines in DHEW regarding specific procedures or types of research?	32	40	28	32
Disagreements among the members about the purpose of the committee?	12	12	12	12
Disagreements between the review committee and investigators about the purpose of the committee?	16	11	13	14
Antagonism of investigators toward the committee?	9	7	10	9
The volume of work that had to be accomplished by the committee?	38	28	38	36
Getting members together for meetings?	44	44	44	44
The amount of committee time spent reviewing research which was essentially without risk?	26	26	16	23
Disagreement or uncertainty among review committee members about the meaning or interpretation of basic concepts such as "informed consent," "human subjects," "risk," "benefit," "continuing review?"	10	21	10	13

*Numbers on which each percentage is based vary slightly due to non-response.

Table VI.48

Review Board Requests for Clarification Regarding Regulations
(Percent of Boards)

	Type of Institution					
	Universities (N=17)	Medical Schools (N=21)	Hospitals (N= 11)	Institutions for Mentally Infirm (N= 13)	Other (N= 13)	All (N= 75)
When you have requested clarification or advice from HEW or NIH regarding regulations or issues faced, have you gotten the help you needed?						
Yes	44%	31%	39%	23%	57%	39%
Yes, but not satisfied with help	7	16	6	0	0	6
Not yet	6	0	0	0	5	2
No	26	33	32	0	6	21
No requests have been made	17	20	23	77	32	32
Total	100%	100%	100%	100%	100%	100%

Table VII.1

Attitudes of Investigators and Review Committee Members Toward the Review Procedure and Committees

	Percent Agreeing With Each Statement	
	Review Board Members (N=725)*	Research Investigators (N=1515)*
The human subjects review procedure has protected the rights and welfare of human subjects--at least to some extent.	99%	98%
The review procedure has improved the quality of scientific research done at this institution--at least to some extent.	73	67
The review procedure runs with reasonable efficiency--at least to some extent.	98	95
The review procedure is an unwarranted intrusion on an investigator's autonomy--at least to some extent.	11	28
The review committee gets into areas which are not appropriate to its function --at least to some extent.	32	48
The review committee makes judgments that it is not qualified to make--at least to some extent.	24	43
The review procedure has impeded the progress of research done at this institution--at least to some extent.	26	45

*N's are approximate since non-response varied from item to item.

Table VII.2

Attitudes of Different Types of Investigators and Review Committee Members Toward the Review Procedure and Committees

	Percent Agreeing With Each Statement					
	Review Board Members			Research Investigators		
	Biomedical Sciences (N=370)*	Behavioral & Social Sci. (N=135)*	Other Other (N=220)*	Biomedical Sciences (N=940)*	Behavioral & Social Sci. (N=395)	Other (N=180)
The human subjects review procedure has protected the rights and welfare of human subjects--at least to some extent.	99%	99%	99%	99%	96%	98%
The review procedure has improved the quality of scientific research done at this institution--at least to some extent.	78	62	70	69	55	83
The review procedure runs with reasonable efficiency--at least to some extent.	99	96	99	96	94	94
The review procedure is an unwarranted intrusion on an investigator's autonomy--at least to some extent.	13	11	6	25	38	23
The review committee gets into areas which are not appropriate to its function --at least to some extent.	39	24	27	50	49	39
The review committee makes judgments that it is not qualified to make--at least to some extent.	28	21	20	43	49	25
The review procedure has impeded the progress of research done at this institution--at least to some extent.	26	30	22	43	54	36

*N's are approximate since non-response varied from item to item.

Table X.1

Review Board Effort

	Minimum	Maximum	Average
Number of meetings/year	2 meetings	51 meetings	9.7 meetings
Length of average meeting	1 hour	4 hours	1.8 hours
Total meeting hours/year	3 hours	135 hours	16.8 hours
Number of members	5 members	55 members	13.8 members
Total member-hours spent in committee meetings each year	27 hours	2,310 hours	290.5 hours
Hours spent on committee work per year (average number)[1]	17 hours	404 hours	55.2 hours
Total member-hours spent on committee work per year (by board)	120 hours	5,085 hours	760 hours
New proposals reviewed (year)	1 proposal	357 proposals	43.3 proposals

[1] Members were asked, "Approximately how many hours do you devote to review committee activities during an average month?" Their responses were averaged for each review board and multiplied by 10 (assuming a ten-month working year for IRBs) to derive these yearly averages.

Table X.2

Review Board Effort per Proposal

	Minimum	Maximum	Average
Meetings per proposal	.014 meetings	3 meetings	.6 meetings
Meeting hours per proposal	.06 hours	4 hours	.85 hours
Member-hours in committee meetings per proposal	.7 hours	52 hours	10 hours
Member-hours spent on committee work per proposal	3.9 hours	270 hours	38.1 hours

Table X.3

Review Board Effort and Rate of Modifications

Type of Modification	Adjusted Level of Effort per Proposal (correlation)	Member-hours in Meetings per Proposal (correlation)	Member Attendance (correlation)
Additional information requested	-.08	-.04	.23*
Consent procedure modification	.30*	.51*	-.39*
Risk modification	.48*	.17	-.18
Confidentiality modification	-.08	.73*	-.33*
Scientific design modification	-.09	.01	.23*
Subject selection modification	-.14	-.11	.09
Informal modification	.05	.36*	.12
Modification variety	-.38*	-.20	-.06
Proposals rejected**	-.28*	-.45*	.02
Percent proposals rejected***	.06	.07	-.28

*Statistically significant at the .05 level.

**Based on IRB members' reports that proposals were rejected.

***Based on the reports of investigators whose proposals were rejected.

Table XIII.1

View of Purpose of the Review Committee: Field of Training
(Percent of Members)

	Field of Training				
	Biomedical Sciences (N=479)	Behavioral Sciences (N=165)	Philosophy/ Ethics/Religion (N=31)	Law (N=51)	Other (N=75)
Which of the following descriptions of the review committee's purpose comes closest to your view?					
The purpose is to protect human subjects	48%	57%	57%	61%	63%
The purpose is to balance the need for protecting human subjects with the need to develop new knowledge	52	43	43	39	37
Total	100%	100%	100%	100%	100%

Table XIII.2

Problem of Disagreement among Members Concerning Purpose of Committee and Meaning of Terms (Percent of Review Committees)(N=88)

	Very Serious Problem	Somewhat Serious Problem	Minor Problem	No Problem	Total
How serious a problem was disagreement among the members about the purpose of the committee?	0%	5%	58%	37%	100%
How serious a problem was disagreement or uncertainty among members about the meaning or interpretation of basic concepts such as "informed consent," "human subjects," "risk," "benefit," "continuing review"?	0	3	77	20	100

Table XIV.1

Review Board Actions on Proposals and Investigators' Experience as Board Members (Percent of Investigators)

Actions	Have Served on Human Subjects Review Committee	Have Not Served on Human Subjects Review Committee
Had informal discussions with board members	25%	28%
Informal discussions led to modifications	15	14
Committee requested additional information	31	32
Current project modified by board:		
Consent procedures	18	26
Risk	6	4
Confidentiality	1	4
Scientific design	3	3
Subject selection	4	3

Table XIV.2

Review Board Actions on Proposals and Investigators' Experience with Research (Percent of Investigators)

Actions	No Previous Proposals	1-3 Previous Proposals	4 or More Previous Proposals
Had informal discussions with board members	35%	33%	20%
Informal discussions led to modifications	17	17	11
Committee requested additional information	36	30	31
Current project modified by board:			
Consent procedures	26	23	22
Risk	5	4	4
Confidentiality	7	2	2
Scientific design	3	4	2
Subject selection	2	5	3

Table XV.1

Distribution of Beneficial/Non-Beneficial Projects: Type of Research*
(Percent of Projects)

	Type of Research				
	Biomedical (N=1272)	Behavioral Intervention (N=136)	Behavioral (Other) (N=552)	Secondary Analysis (N=92)	All (N=2052)
Beneficial	52%	57%	33%	15%	45%
Non-beneficial	31	27	51	64	37
No information	17	16	16	21	18
Total	100%	100%	100%	100%	100%

*Based on data provided by the investigators.

Table XV.2

Primary Intervention or Procedure of Study: Expected Benefit to Subjects
(Percent of Projects)

	N*	Beneficial	Non-beneficial	No Information	Total
Biomedical					
Clinical evaluation of bodily tissues or fluids	(602)	31%	51	18	100%
Administration of drug, chemical agent	(623)	66%	16	18	100%
Administration of vaccines, blood products	(37)	63%	14	23	100%
Surgical procedures	(41)	58%	22	20	100%
Bodily fluid exchange	(3)	64%	0	36	100%
Use of diagnostic, therapeutic device, technique	(130)	68%	22	10	100%
Perinatal care	(3)	39%	61	0	100%
Dental care	(11)	44%	38	18	100%
Other medical interventions or procedures	(18)	32%	51	17	100%

Table XV.2 (continued)

	N*	Beneficial	Non-beneficial	No Information	Total
Behavioral Intervention					
Educational intervention	(48)	54%	18	28	100%
Modification of an organization or a service delivery system	(25)	63%	30	7	100%
Behavior modification or experimentation	(35)	50%	42	8	100%
Social psychological therapy	(21)	73%	8	19	100%
Behavioral (other)					
Interviews-questionnaires	(267)	28%	55	17	100%
Psychological or educational testing	(136)	40%	46	14	100%
Behavioral observation	(153)	29%	49	22	100%
Interviews with patient (e.g., medical histories)	(35)	54%	44	2	100%
Secondary Analysis					
Retrospective review of data	(20)	1%	98	1	100%
Retrospective review of data (medical)	(32)	39%	57	4	100%
Third party evaluation of bodily parts or fluids	(57)	8%	52	40	100%

*N's are unweighted; percentages are weighted.

Table XV.3

Distribution of Beneficial/Non-Beneficial Projects:
Type of Institution*
(Percent of Projects)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Beneficial	23%	50%	53%	51%	46
Non-beneficial	61	34	29	35	38
No information	16	16	18	14	16
Total	100%	100%	100%	100%	100%

*Based on data provided by investigators

Table XV.4

What kinds of subjects were selected for your study?:
Expected Benefit to Subjects
(Percent of Projects) *

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Patients	78%	53%
Patients (including adults and children)	75%	48%
Former patients	1	1
Persons with specific medical condition **	2	4
Staff	3	12
Project staff	-	1
Other professional staff	1	4
Other institutional staff	2	7
Students	4	18
Medical, health students	-	2
Other college students	4	16
Other	26	43
General population	12	14
Persons with specific characteristic	6	13
Children under 18	6	9
Prisoners	-	-
Miscellaneous	2	7

* Totals may add to more than 100% since respondents could check more than one kind of subject.

**Not ascertained whether these persons were patients at the time of the research.

Table XV.5

Probability of Risks and Benefits to Subjects: Research Expected to Benefit Subjects*
(Percent of Projects)(N=902)

	** None	Very Low	Low	Medium	High	Unknown	No Information	Total
Medical benefits	19%	3	4	35	32	5	2	100%
Psychological benefits	37%	4	4	28	18	5	4	100%
Other benefits	80%	1	1	5	12	1		100%
Minor psychological stress	30%	33	16	7	2	2	-	100%
Serious psychological stress	72%	15	2	0	-	1	-	100%
Minor medical complications	39%	34	14	8	3	2	-	100%
Serious medical complications	61%	27	6	3	1	2	-	100%
Fatal complications	73%	22	3	1	-	1	-	100%
Embarrassment (breach of confidentiality)	78%	18	2	1	1	-	-	100%
Legal risk (breach of confidentiality)	88%	9	1	-	-	1	1	100%
Other risks	94%	3	2	1	-	-		100%

*Based on data provided by the investigators.

**The "none" category includes projects where the investigator saw the risk or benefit as "not applicable" to his/her research.

Table XV.6

Probability of Risks and Benefits to Subjects: Research Not Expected to Benefit Subjects*
(Percent of Projects) (N=822)

	None	Very Low	Low	Medium	High	Unknown	No Information	Total
Medical benefits	81%	3	8	0	0	3	0	100%
Psychological benefits	80%	9	6	0	0	5	0	100%
Other benefits	97%	1	1	0	0	1		100%
Minor psychological stress	58%	29	8	3	1	1	-	100%
Serious psychological stress	93%	5	1	0	0	1	-	100%
Minor medical complications	72%	23	3	1	-	-	1	100%
Serious medical complications	87%	12	1	-	0	-	-	100%
Fatal complications	93%	7	0	-	0	-	-	100%
Embarrassment (breach of confidentiality)	81%	14	4	-	1	0	-	100%
Legal risk (breach of confidentiality)	91%	6	2	0	0	1	-	100%
Other risks	96%	2	1	-	-	1		100%

*Based on data provided by the investigators.

Table XV.7

Probability of Risk: Research Expected to Benefit Subjects vs. Research Not Expected to Benefit Subjects (Percent of Projects)

	Non-beneficial Research (N=822)	Beneficial Research (N=904)	All Research (N=1726)
No risk	40%	16%	27%
Very low risk of minor complications	27	23	25
At least a low risk of minor complications and/or a very low risk of serious complications	33	61	48
Total	100%	100%	100%

Table XV.8

Investigators' Estimates of Medical Benefit and Risk
(Percent of Projects)

	Some Medical Risk	No Medical Risk	Total
Projects with some medical benefit (N=915)	68%	32	100%
Projects with no medical benefit (N=1080)	19%	81	100%

Table XV.9

Investigators' Estimates of Psychological Benefit and Risk
(Percent of Projects)

	Some Psychological Risk	No Psychological Risk	Total
Projects with some psychological benefit (N=746)	74%	26	100%
Projects with no psychological benefit (N=1201)	37%	63	100%

Table XV.10

From what you have learned in this study, which of the following best describes your present assessment of benefits to subjects as compared to your expectations when the research began?*
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Much more benefit than expected	7%	2%
Somewhat more benefits than expected	14	6
Benefits as expected	53	45
Somewhat less benefit than expected	4	1
Much less benefit than expected	2	1
Assessment cannot be made	14	26
No information	6	19
Total	100%	100%

*Based on data provided by the investigators

Table XV.11

From what you have learned in this study which of the following best describe your present assessment of risks to subjects as compared to your expectations when the research began?*
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Much more risk than expected	-%	0%
Somewhat more risk than expected	2	1
Risk as expected	63	67
Somewhat less risk than expected	9	4
Much less risk than expected	9	3
Unable to assess	9	11
No information	8	14
Total	100%	100%

*Based on data provided by the investigators.

Table XV.12

Before involving subjects in this study,
how certain were you that you knew all of the risks to subjects?*
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Very certain	49%	72%
Fairly certain	44	22
Not very certain	4	-
Not at all certain	1	-
No information	2	6
Total	100%	100%

*Based on data provided by the investigators.

Table XV.13

Before you began involving subjects in this study, which one of the following statements best describe your assessment of the balance of risk and benefits to the average subject?* (aside from any financial benefit) (Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Much more risk than benefit	2%	2%
Somewhat more risk than benefit	--	4
Equal risk and benefit	4	4
Somewhat more benefit than risk	13	6
Much more benefit than risk	68	12
No risk or benefit	8	58
Assessment cannot be made	2	3
No information	3	11
Total	100%	100%

*Based on data provided by the investigators.

Table XV.14

How would you assess the balance of risks and benefits to subjects at the present time?*
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Much more risk than benefit	2%	2%
Somewhat more risk than benefit	2	4
Equal risk and benefit	3	4
Somewhat more benefit than risk	13	6
Much more benefit than risk	65	13
No risk or benefit	7	57
Assessment cannot be made	3	3
No information	5	11
Total	100%	100%

*Based on data provided by the investigators.

Table XV.15

Is there any provision for giving treatment to subjects if they suffer any harmful effect due to this research?*
(Percent of Projects)

	Expected Benefit to Subjects	
	Beneficial (N=902)	Non-beneficial (N=822)
Yes	54%	28%
No	6	13
Don't know	2	2
Question considered inapplicable by respondent	38	57
Total	100%	100%

*Based on data provided by the investigators.

Table XV.16

Probability of Risks and Benefits to Subjects: Biomedical Research*
(Percent of Projects) (N=1272)

	None	Very Low	Low	Medium	High	Unknown	Not Applicable	Total
Medical benefits	28%	5	6	22	21	5	13	100%
Psychological benefits	55%	5	4	11	6	4	15	100%
Other benefits	88%	1	1	3	6	1		100%
Minor psychological stress	43%	27	11	4	2	1	12	100%
Serious psychological stress	76%	10	1	0	-	1	12	100%
Minor medical complications	32%	36	11	6	2	1	12	100%
Serious medical complications	54%	26	5	2	-	1	12	100%
Fatal complications	65%	20	2	1	-	-	12	100%
Embarrassment (breach of confidentiality)	78%	9	1	-	-	-	12	100%
Legal risk (breach of confidentiality)	81%	5	-	0	0	1	13	100%
Other risks	96%	3	1	-	-	-		100%

*Based on data provided by the investigators.

Table XV.17

Probability of Risks and Benefits to Subjects: Behavioral Intervention Research*
(Percent of Projects)(N=136)

	None	Very Low	Low	Medium	High	Unknown	No Information	Total
Medical benefits	61%	3	4	12	8	3	9	100%
Psychological benefits	33%	4	5	13	30	5	10	100%
Other benefits	71%	2	1	8	14	4		100%
Minor psychological stress	39%	33	15	4	2	-	7	100%
Serious psychological stress	82%	10	1	0	0	-	7	100%
Minor medical complications	77%	11	1	5	0	0	7	100%
Serious medical complications	91%	3	0	0	0	0	6	100%
Fatal complications	92%	1	0	0	0	-	7	100%
Embarrassment (breach of confidentiality)	66%	22	3	1	1	0	7	100%
Legal risk (breach of confidentiality)	80%	8	4	-	1	-	7	100%
Other risks	89%	4	-	6	-	1		100%

*Based on data provided by the investigators.

Table XV.18

Probability of Risks and Benefits to Subjects: Other Behavioral Research*
(Percent of Projects)(N=522)

	None	Very Low	Low	Medium	High	Unknown	No Information	Total
Medical benefits	81%	5	1	4	1	1	7	100%
Psychological benefits	47%	8	6	17	10	6	6	100%
Other benefits	79%	1	1	6	11	2		100%
Minor psychological stress	44%	33	10	7	-	2	4	100%
Serious psychological stress	84%	9	1	0	0	1	5	100%
Minor medical complications	91%	3	1	0	-	-	5	100%
Serious medical complications	94%	1	-	-	0	-	5	100%
Fatal complications	94%	1	-	0	0	-	5	100%
Embarrassment (breach of confidentiality)	59%	29	5	1	2	0	4	100%
Legal risk (breach of confidentiality)	81%	11	3	-	-	1	4	100%
Other risks	96%	2	2	-	-	0		100%

*Based on data provided by the investigators.

Table XV.19

Probability of Risks and Benefits to Subjects: Secondary Analysis Research*
(Percent of Projects)(N=92)

	None	Very Low	Low	Medium	High	Unknown	No Information	Total
Medical benefits	65%	-	4	6	2	6	17	100%
Psychological benefits	74%	-	0	4	-	5	17	100%
Other benefits	93%	0	1	1	4	1		100%
Minor psychological stress	80%	2	1	0	0	0	17	100%
Serious psychological stress	82%	1	0	0	0	0	17	100%
Minor medical complications	75%	8	0	0	0	0	17	100%
Serious medical complications	77%	6	0	0	0	0	17	100%
Fatal complications	82%	1	0	0	0	0	17	100%
Embarrassment (breach of confidentiality)	64%	11	8	-	0	0	17	100%
Legal risk (breach of confidentiality)	70%	9	4	-	0	0	17	100%
Other risks	96%	-	4	0	0	0		100%

*Based on data provided by the investigators.

Table XV.20

Risk and Benefit of Different Types of Research
(Percent of Projects)

Research Type	Above Average in Risk	Expected to Benefit Subjects	Risk Greater than Benefit to Subjects	Harmful Effects Occurred	Treatment for Harmful Effects Reported Available
Biomedical					
Drug administration (N=658)	76%	82%	6%	7%	61%
Blood or blood product administration (N=37)	56	81	0	6	39
Surgical procedures (N=41)	57	72	11	2	36
Use of diagnostic or therapeutic devices (N=136)	53	72	0	5	44
Bodily fluid exchange (N=5)	50	100	0	0	48
Clinical evaluation of bodily parts or fluids (N=619)	44	40	5	3	41
Perinatal care[1] (N=3)	39	39	0	0	39
Interviews with patients (N=35)	29	47	0	0	16
Other medical procedures (N=18)	26	43	6	0	45
Dental care (N=11)	11	53	0	0	29
Review of existing data (N=33)	7	32	6	0	6
Third party evaluation of bodily parts or fluids (N=59)	5	15	0	2	7

[1]Percentages do not correspond to number of cases because of weighting procedures.

Table XV.20 (continued)

Research Type	Above Average in Risk	Expected to Benefit Subjects	Risk Greater than Benefit to Subjects	Harmful Effects Occurred	Treatment for Harmful Effects Reported Available
Behavioral					
Social or psychological therapy (N=21)	58%	90%	4%	0%	42%
Behavioral modification or experimentation (N=35)	44	56	0	4	27
Other behavioral research (N=12)	28	38	0	0	5
Modification of organization or service delivery system (N=25)	25	69	0	0	21
Behavioral observation (N=155)	25	37	1	2	8
Research on educational innovation (N=50)	22	73	0	0	8
Interviews and/or questionnaires (N=271)	22	34	3	0	13
Psychological or educational testing (N=140)	21	47	1	0	16
Review of existing data (N=20)	2	2	0	0	0

Table XV.21

Risk, Benefit, and Treatment for Harmful Effects
(Percent of Projects)

Relative Risk Level*	Expected to Benefit Subjects	Harmful Effects Reported	Treatment Reported Available
No risk (N=710)	34%	0%	14%
Very low risk (N=446)	52	1	31
Low risk (N=459)	63	3	52
Moderate risk (N=483)	80 **	12	81

*Projects in the sample were broken into quartiles on the basis of the scores which represent the combined probability and severity of medical and psychological risks. The projects in the moderate risk group, therefore, entail moderate risk relative to the other projects; many of these projects involve risks which might be assessed as "low" on an absolute scale by an objective observer.

**About one hundred research projects in the sample were classified as moderate risk/low benefit studies. While some of the projects in this group may have entailed risks which outweighed benefits to subjects, it appears that some of them did not have an "unfavorable" risk/benefit ratio. On the one hand, about one out of four investigators conducting these projects reported, in response to a questionnaire item, that they expected their research to involve more risk than benefit to subjects. Furthermore, IRB's were more likely to formally modify these projects (about half were modified) than other projects in the sample. And in 40 percent of these projects, at least some of the subjects were paid for participating. On the other hand, some of these projects may have entailed relatively little risk or benefit from an objective perspective. Certain investigators where highly conservative or conscientious in answering the questions concerning the risks and benefits of their research; they may have reported more risk and less benefit than would have an outside observer. Many of these investigators, in responding to a subsequent question concerning the balance of risks and benefits to subjects, reported that their projects entailed no significant risks or benefits.

The types of subjects participating in these moderate risk/low benefit projects included: Patients (50%); general population, volunteers (23%); students, college-level (10%); children (6%); and prisoners (3%). A small percentage of these projects involved persons with specific conditions (not patients) and members of the project staff. The majority of the projects with moderate risk and low benefit fell into the following categories: Clinical evaluation of bodily fluids or parts (48%); drug administration (37%); interviews/questionnaires (6%); surgery (3%); and diagnostic and therapeutic devices (3%). The other projects in this group involved behavioral observation, social/psychological therapy, and the administration of blood products. In many of these projects, the same procedures would have been used with the subjects even if they were not participating in the research. (For example, the same substance would have been used in 40% of the drug studies even if the subjects were not participating in the study.)

Table XV.22

Risk Associated with Different Research Procedures

Research Procedure	Number of Projects in Which Procedure Used	Percent of Projects: Above Average in Risk	Percent of Projects: Risk Greater than Benefit to Subjects
Extracorporeal circulation	6	83%	30%
Radiotherapeutic techniques	39	82	2
Cardiac catheterization	29	81	15
Ultrasound	65	80	5
X-ray use	283	77	6
Drug administration	628	76	5
Isotope administration	148	75	7
Measurement of electrical activity of the body	270	74	9
Examination of internal structures, not using natural orifices	51	71	2
Non-invasive measurement of bodily activity	472	69	8
Administration of electricity	21	68	18
Dietary manipulation	130	67	6
Anesthetic administration	96	67	9
Physical therapy	55	63	2
Examination of internal structures, using natural orifices	136	61	5
Obtaining bodily fluids	874	61	5
Obtaining tissue	210	59	2
Obtaining medical history	944	59	2
Social or psychological therapy	76	56	2
Surgery	117	53	1
Administration of other energy forms	45	52	2
Counseling or advising	203	51	2
Obstetrical care	39	48	4

Table XV.22 (continued)

Research Procedure	Number of Projects in Which Procedure Used	Percent of Projects: Above Average in Risk	Percent of Projects: Risk Greater than Benefit to Subjects
Reproductive biology	52	47%	6%
Review of existing data	961	47	4
Other procedure	219	47	5
Interviews	674	46	4
Dental care	38	43	4
Kidney dialysis	19	43	0
Psychological or educational testing	315	38	3
Behavioral observation or experimentation	430	38	3
Questionnaire	505	34	4
Laser use	9	31	0
Exchange transfusion	8	31	8
Research on educational innovation	104	30	1
Modification of organization or delivery system	85	28	2
Prosthetic devices	32	28	0

Note: Several procedures may be used in any single project.

Table XV.23

Risk and Characteristics of Subjects

Category	Number of Projects	Percent of Projects: Above Average Risk	Percent of Projects: Expected to Benefit Subjects	Percent of Projects: Risk Greater than Benefit to Subjects
Sex				
Projects with more than 75% male subjects	528	54%	56%	6%
Projects with fewer than 75% male subjects	1285	43	55	3
Projects with more than 75% female subjects	306	46	59	3
Projects with fewer than 75% female subjects	1404	44	56	3
Minorities				
Projects with more than 25% minority subjects	529	47	60	3
Projects with fewer than 25% minority subjects	1277	49	56	4
Income				
Projects with more than 25% high income subjects	226	47	57	5
Projects with fewer than 25% high income subjects	1363	49	59	4
Projects with more than 25% middle income subjects	1230	50	60	3
Projects with fewer than 25% middle income subjects	357	45	52	6
Projects with more than 25% low income subjects	921	49	62	4
Projects with fewer than 25% low income subjects	668	49	55	4

Table XV.23 (continued)

Category	Number of Projects	Percent of Projects: Above Average Risk	Percent of Projects: Expected to Benefit Subjects	Percent of Projects: Risk Greater than Benefit to Subjects
Age				
Projects with more than 25% newborns	81	46%	68%	0%
Projects with fewer than 25% newborns	1911	46	55	4
Projects with more than 25% 3 mo. to 6 yr. old subjects	156	46	62	1
Projects with fewer than 25% 3 mo. to 6 yr. old subjects	1832	46	55	4
Projects with more than 25% 7-12 yr. old subjects	182	44	58	1
Projects with fewer than 25% 7-12 yr. old subjects	1806	47	56	4
Projects with more than 25% 13-18 yr. old subjects	196	40	55	1
Projects with fewer than 25% 13-18 yr. old subjects	1785	48	56	4
Projects with more than 25% 19-40 yr. old subjects	1193	47	51	5
Projects with fewer than 25% 19-40 yr. old subjects	766	47	65	2
Projects with more than 25% 41-64 yr. old subjects	773	52	63	3
Projects with fewer than 25% 41-64 yr. old subjects	1191	44	51	4
Projects with more than 25% 65+ yr. old subjects	230	50	71	2
Projects with fewer than 25% 65+ yr. old subjects	1744	46	54	4
Mentally Infirm				
Projects with more than 25% mentally infirm subjects	192	36	55	3
Projects with fewer than 25% mentally infirm subjects	1544	48	62	3

Table XV.24

Correlations between Average Risk of Projects and Actions of the Review Board

	Institutions	
	Universities and Other	Medical Schools and Hospitals
Comprehensive discussion concerning:		
Consent	-.24	.36*
Selection of subjects	-.29*	.27*
Quality of research	-.49*	-.16
Overall	-.41*	-.17
Board requested from investigator:		
Modifications concerning consent	.09	.37*
Modifications concerning confidentiality	.55*	.27*
Modifications concerning research design	-.18	.47*
Other modifications	-.03	.37*
Investigators give oral explanation to subjects	.11	.43*
Subjects keep a consent form	-.30*	.22
Consent form readability	.03	-.51*
Approved proposals subject to further review	-.35*	.21
Screen out some proposals	.23	.56*

*A correlation of .30 is significant at the .05 level. We have noted correlations that are close to or above .30. The index of risk employed in this table is the second of the two described above and, thus, does not define research involving only very low probabilities of minor psychological and/or medical complications as research with risk.

Table XV.25

Riskiness of Research that Passes through a Board and the Attitudes of Investigators toward the Board

	Institutions	
	Universities and Other	Medical Schools and Hospitals
Investigator's attitude is favorable in general	-.02	-.58*
Investigator says decisions of board are sound	-.47*	-.32*
Investigator says review protects subjects	.28*	-.38*

*A correlation of .30 is significant at the .05 level. We have noted correlations that are close to or above .30. The index of risk employed in this table is the second of the two described above.

Table XVII.1

Acceptability to Review Board Members and Investigators of Selected Research Practices

	% Indicating Practice "should be done"*		% Indicating Practice "should not be done"*	
	Review Board Members (N=740)**	Research Investigators (N=1660)**	Review Board Members (N=740)**	Research Investigators (N=1660)**
1. Giving compensation to subjects for time spent in research not intended to benefit them directly	21%	29%	8%	7%
2. Giving compensation commensurate with the degree of risk to subjects	21	33	40	23
3. Giving compensation to subjects for the purpose of inducing participation	5	11	37	26
4. Withholding from subjects information about the design or purpose of research when disclosure might affect the validity of measurements	15	23	33	21
5. In research not intended to benefit subjects and with negligible risk, withholding from subjects the fact that they are subjects to prevent measurement bias	14	14	45	39
6. Withholding information about an experimental intervention from a subject when the subject is the patient of a physician/researcher who decides that withholding the information is in the patient's best interest	11	11	45	41
7. When there is an existing therapeutic relationship between a subject and investigator, the introduction of a third party to assure that therapeutic and experimental decisions do not become improperly entangled	46	43	9	6
8. The use of children as subjects of research having no benefit and minimal risk	22	24	16	11
9. High risk research of considerable importance in which there is no direct benefit to subjects but they are fully informed and capable of giving consent	27	30	12	10
10. The use by one researcher of data gathered by another researcher and to which no identification of subjects is attached	50	48	9	5
11. The giving by one researcher to a second researcher the names of subjects in a completed project without the subjects' consent so that they may be followed up in a second project	2	3	78	65

*Not shown are the percentages indicating that each practice "may be done in some circumstances." Such percentages can be obtained by subtraction using the data in the table.

**N's are approximate since non-response varied from item to item.

Table XVII.2

Acceptability of Selected Research Practices: Review Board Members

	% Indicating Practice "should be done"*			% Indicating Practice "should not be done"*		
	Biomedical Science (N=380)**	Behavioral Science (N=135)**	Other (N=225)**	Biomedical Science (N=380)**	Behavioral Science (N=135)**	Other (N=225)**
1. Giving compensation to subjects for time spent in research not intended to benefit them directly	23%	19%	19%	7%	4%	11%
2. Giving compensation commensurate with the degree of risk to subjects	20	26	21	45	24	40
3. Giving compensation to subjects for the purpose of inducing participation	6	3	5	40	22	44
4. Withholding from subjects information about the design or purpose of research when disclosure might affect the validity of measurements	12	25	12	38	17	34
5. In research not intended to benefit subjects and with negligible risk, withholding from subjects the fact that they are subjects to prevent measurement bias	13	22	10	48	27	50
6. Withholding information about an experimental intervention from a subject when the subject is the patient of a physician/researcher who decides that withholding the information is in the patient's best interest	11	8	13	46	43	42
7. When there is an existing therapeutic relationship between a subject and investigator, the introduction of a third party to assure that therapeutic and experimental decisions do not become improperly entangled	47	42	45	10	6	8
8. The use of children as subjects of research having no benefit and minimal risk	45	34	16	15	14	21
9. High risk research of considerable importance in which there is no direct benefit to subjects but they are fully informed and capable of giving consent	24	38	23	15	8	9
10. The use by one researcher of data gathered by another researcher and to which no identification of subjects is attached	45	56	52	10	10	6
11. The giving by one researcher to a second researcher the names of subjects in a completed project without the subjects' consent so that they may be followed up in a second project	3	-	2	71	81	87

*Not shown are the percentages indicating that each practice "may be done in some circumstances." Such percentages can be obtained by subtraction using the data in the table.

**N's are approximate since non-response varied from item to item.

Table XVII.3

Acceptability of Selected Research Practices: Research Investigators

	% Indicating Practice "should be done"*			% Indicating Practice "should not be done"*		
	Biomedical Science (N=1040)**	Behavioral Science (N=430)**	Other (N=190)**	Biomedical Science (N=1040)**	Behavioral Science (N=430)**	Other (N=190)**
1. Giving compensation to subjects for time spent in research not intended to benefit them directly	29%	33%	23%	7%	4%	8%
2. Giving compensation commensurate with the degree of risk to subjects	27	50	39	28	9	16
3. Giving compensation to subjects for the purpose of inducing participation	11	14	2	29	11	38
4. Withholding from subjects information about the design or purpose of research when disclosure might affect the validity of measurements	21	25	33	27	7	18
5. In research not intended to benefit subjects and with negligible risk, withholding from subjects the fact that they are subjects to prevent measurement bias	12	17	21	45	25	29
6. Withholding information about an experimental intervention from a subject when the subject is the patient of a physician/researcher who decides that withholding the information is in the patient's best interest	12	9	13	41	44	43
7. When there is an existing therapeutic relationship between a subject and investigator, the introduction of a third party to assure that therapeutic and experimental decisions do not become improperly entangled	41	48	50	8	3	6
8. The use of children as subjects of research having no benefit and minimal risk	19	40	20	14	4	11
9. High risk research of considerable importance in which there is no direct benefit to subjects but they are fully informed and capable of giving consent	27	35	34	11	5	9
10. The use by one researcher of data gathered by another researcher and to which no identification of subjects is attached	47	54	41	7	2	6
11. The giving by one researcher to a second researcher the names of subjects in a completed project without the subjects' consent so that they may be followed up in a second project	3	2	2	63	66	77

*Not shown are the percentages indicating that each practice "may be done in some circumstances." Such percentages can be obtained by subtraction using the data in the table.

**N's are approximate since non-response varied from item to item.

Table XVII.4

Review Committee Members' Judgements Regarding a Hypothetical Project: A Biomedical Case Study

A physician has been treating a particular patient for several years. He decides that a case report should be prepared for publication. Since there will be no benefit to the patient, cost will be borne by the physician.

A. To prepare this report, it will be necessary to collect a new urine sample (freely voided) for analysis.

	Biomedical Members (N=380)	Behavioral Members (N=135)	Other Members (N=225)
In this situation, do you feel that the approval of the human subjects review committee should be obtained?			
Yes	21%	42%	39%
No	79	58	61
Should the physician disclose the fact that the new urine sample is for research purposes and obtain the patient's consent?			
Yes	70	85	78
No	30	15	22
Should written consent be obtained?			
Yes	22	45	44
No	78	55	56

B. Suppose the physician determines that an additional blood sample is needed.

Do you feel that the approval of the human subjects review committee should be obtained?			
Yes	41	59	70
No	59	41	30
Should the physician disclose the fact that the blood sample is for research purposes and obtain the patient's consent?			
Yes	90	94	92
No	10	6	8

Table XVII.4 (continued)

	Biomedical Members (N=380)	Behavioral Members (N=135)	Other Members (N=225)
Should written consent be obtained?			
Yes	44%	68%	71%
No	56	32	29
C. Suppose the physician determines that an additional set of X-rays is needed.			
Do you feel that the approval of the human subjects review committee should be obtained?			
Yes	50	72	78
No	50	28	22
Should the physician disclose the fact that the X-rays are for research purposes and obtain the patient's consent?			
Yes	92	97	95
No	8	3	5
Should written consent be obtained?			
Yes	55	79	82
No	45	21	18
D. Suppose the physician determines a biopsy of an internal organ is needed.			
Do you feel that the approval of the human subjects review committee is needed?			
Yes	90	92	89
No	10	8	11
Should the physician disclose the fact that the biopsy is for research purposes and obtain the patient's consent?			
Yes	99	98	96
No	1	2	4
Should written consent be obtained?			
Yes	97	93	94
No	3	7	6

Table XVII.5

Review Committee Members' Judgements Regarding a Hypothetical Project: Secondary Analysis of Data

A researcher wishes to examine patient or student records to ascertain the frequency with which something occurs in different types of individuals. No names will be recorded.

	Biomedical Members (N=380)	Behavioral Members (N=135)	Other Members (N=225)
Should this be brought before a human subjects review committee?			
Yes	50%	63%	63%
No	50	37	37
Should the researcher obtain the consent of the patients or students?			
Yes	44	49	53
No	55	51	47
Should written consent be obtained?			
Yes	35	42	47
No	65	58	53

Table XVII.6

Review Committee Members' Judgements Regarding a Hypothetical Project: A Case Study with Interviewing

A researcher is doing a paper on the development of institutional policy in which he wishes to interview administrators in the institution.

	Biomedical Members (N=380)	Behavioral Members (N=135)	Other Members (N=225)
Should this be brought before a human subjects review committee?			
Yes	25%	43%	33%
No	75	57	67
Should the researcher obtain the consent of the administrators?			
Yes	82	89	81
No	18	11	18
Should written consent be obtained?			
Yes	30	47	37
No	70	53	63

Table XVII.7

Review Committee Members' Judgements Regarding a Hypothetical Project: Biomedical Research vs. Practice

A physician at this institution has a patient with a right colon fecal impaction which has not responded to various enema treatment regimens. He has previously observed that Hypaque, a contrast medium approved by the FDA for use in diagnostic X-ray studies of the gastrointestinal tract, acts as an osmotic agent and pulls water into the intestine. He believes that this action might free the impaction, and therefore decides to administer Hypaque to his patient for this purpose, as an enema.

	Review Board Members Who Have Conducted Biomedical Research* (N=312)
In your view, should this activity be considered as research and brought before a human subjects review committee?	
Yes	42%
No	58
Do you feel that the activity mentioned in the example should be treated as a research procedure with regard to the informed consent of patients?	
Yes	57
No	43
Should written consent be obtained?	
Yes	47
No	53

*This series of questions was asked only of those respondents who have conducted biomedical research studies. These respondents are primarily those who have previously been classified as biomedical members (279), along with 9 behavioral members and 24 "other" members.

Table XVII.8

Review Committee Members' Judgements Regarding a Hypothetical Project: Secondary Analysis of Bodily Tissue

A physician wishes to conduct research on material removed at surgery from patients whose surgery involved no experimental interventions. This research is not intended to benefit the patients.

	Review Board Members Who Have Conducted Biomedical Research (N=316)
Should this research be brought before a human subjects review committee?	
Yes	54%
No	46
Should the physician obtain the consent of patients to use these materials for research purposes?	
Yes	43
No	57
Should written consent be obtained?	
Yes	35
No	65

Table XVII.9

Review Committee Members' Judgements Regarding a Hypothetical Project: Biomedical Research vs. Practice (Surgery)

A surgeon believes that new support technologies make possible a surgical procedure which has not previously been feasible. The surgeon and the patient's private physician determine that the risk/benefit ratio is acceptable and that the surgery is in the patient's interest.

	Review Board Members Who Have Conducted Biomedical Research (N=312)
Should this be brought before a human subjects review committee?	
Yes	66%
No	34
Should this be treated as a research procedure with regard to the informed consent of the patient, with disclosure to the patient that the procedure has not previously been feasible?	
Yes	89
No	11
Should written consent be obtained?	
Yes	84
No	16

Table XVII.10

Suggestions for Improvement: Review Committee Members
(Percent of Projects)*

	Type of Institution				
	Universities (N=155)	Medical Schools (N=260)	Hospitals (N=116)	Other (N=199)	All (N=736)
No suggestions	39%	34%	38%	42%	38%
Comments regarding "bureaucratic problems" with review process and their negative consequences for research	9	9	18	13	12
Speed up the process; takes too long now	-%	-%	-%	2%	1%
Simplify; too complicated; too much to do	4	5	13	7	7
Review procedures are having adverse effects on research, slow it, prevent it, etc.	5	3	7	4	5
Less emphasis on details; more on human subject protection	0	-	-	1	-
Rules should be consistent across boards; avoid multiple reviews by having a consistent procedure	0	1	-	1	1
Review committees are overly protective, extreme in concern for subjects	-	0	0	-	-
Timing and scheduling of review causes problems	2	-	-	-	1

Table XVII.10 (continued)

	Type of Institution				
	Universities (N=155)	Medical Schools (N=260)	Hospitals (N=116)	Other (N=199)	All (N=736)
Parts of review process should be abolished	10%	11%	12%	8%	10%
Be less rigid/more lenient in application of rules and procedures	1%	3%	5%	2%	3%
Review subject use only, don't review study design and purpose. Should not control research beyond human subject treatment; committee gets into areas and decisions not appropriate to its purpose	1	2	-	0	1
Eliminate reviews on previously approved studies, don't review renewals or continuations of projects	0	1	-	0	-
Do not review studies using materials from previously approved research or materials which would be available even if there were no research	0	1	-	2	1
Differentiate; more caution when risk/intervention involved; less severe/rigid for more innocuous research; no review for innocuous research	8	5	6	3	5
Eliminate reviews on standard research practices	0	1	0	-	-
Eliminate written/informed consent in some circumstances (for example participant observation and cases where results would be biased)	1	0	0	1	-

Table XVII.10 (continued)

	Type of Institution				
	Universities (N=155)	Medical Schools (N=260)	Hospitals (N=116)	Other (N=199)	All (N=736)
Stress privacy and confidentiality for subjects	1%	2%	-%	1%	1%
Simplify consent forms for subject	0	0	-	1	-
Insure that all or more research is reviewed	1	1	0	0	-
Physician/patient treatment with experimental procedures and substances should be reviewed	0	-	0	0	-
Miscellaneous and other suggestions	8%	6%	4%	3%	5%

*Totals will add to more than 100 percent because investigators could make more than one mention

Table XVII.10 (continued)

	Type of Institution				
	Universities (N=155)	Medical Schools (N=260)	Hospitals (N=116)	Other (N=199)	All (N=736)
Should be opportunity for interaction between the researcher and the committee	0%	0%	0%	-%	-%
Need special guidelines on children, fetal research	1	5	4	2	3
Need special guidelines on pregnant women	1	1	0	0	-
Need special guidelines on prisoners	0	1	-	1	1
Need special guidelines on mental patients, the mentally retarded and the mentally incompetent	-	-	-	-	-
Need special guidelines on social science research	-	0	0	0	-
Training sessions should be provided for the committee members	3	1	1	0	1
Do more to protect human subjects--be stricter	8%	14%	6%	9%	10%
Do job more carefully/be tougher; more strict review	0%	1%	-%	-%	-%
Do more follow-up after review to see that proposed procedures are implemented	6	11	5	7	7

Table XVII.10 (continued)

	Type of Institution				
	Universities (N=155)	Medical Schools (N=260)	Hospitals (N=116)	Other (N=199)	All (N=736)
Give more information to researchers and committees; improve communications between committees and researchers; define, clarify and set guidelines	27%	28%	26%	19%	25%
Need more or better guidelines in general	14%	14%	4%	13%	11%
Define "informed consent," tell investigators more clearly/specifically what needs to be done to meet "informed consent" requirement; provide sample consent forms	3	1	12	1	4
Decide/clarify when written consent must be obtained	2	6	2	1	3
Decide/define what research must be reviewed; define "human subject" for review purposes	3	2	2	1	2
Define/clarify liability and responsibility	-	1	0	1	1
Define/clarify risks and deception	8	4	7	2	5
Define/clarify proxy consent	-	1	0	-	-
Review committees should disseminate information on what they want/action they've taken and why the action was taken	-	-	-	0	-

Table XVII.10 (continued)

	Type of Institution				
	Universities (N=155)	Medical Schools (N=260)	Hospitals (N=116)	Other (N=199)	All (N=736)
Change structure and/or authority of review process or review committee	10%	10%	14%	9%	11%
Get help or consultants if the review committee is not able to understand or handle aspects of some proposals	0%	1%	0%	-%	-%
Change or improve the composition of the committee; get different kinds of people; use a different selection process	3	2	5	4	3
Give more authority to local boards	2	5	9	4	5
The committee is too political	0	-	0	0	-
Monitor the review committee for thoroughness, fairness, efficiency	2	0	0	1	1
Abolish the committee, certify investigators, and let them decide	2	1	0	0	1
Funding of committee work--federal government/grant/overhead institutions should provide funds for committee operation	2	1	-	-	1

Table XVII.11

Suggestions for Improvement: Principal Investigators
(Percent of Projects)*

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
No suggestions	34%	37%	41%	29%	37%
Comments regarding "bureaucratic problems" with review process and their negative consequences for research	21	26	15	32	24
Speed up the process; takes too long now	9	9	3	14	9
Simplify; too complicated; too much to do	4	6	6	6	6
Review procedures are having adverse effects on research; slow it; prevent it; etc.	6	9	4	5	7
Less emphasis on details; more on human subject protection	2	1	1	1	1
Rules should be consistent across boards; avoid multiple reviews by having a consistent procedure	1	2	2	4	2
Review committees are overly protective, extreme in concern for subjects	1	2	2	2	2
Timing and scheduling of review causes problems	1	1	0	-	1
New, stricter regulations on privacy are causing or will cause problems	-	1	1	6	1
Parts of review process should be abolished	20	18	13	12	17
Be less rigid/more lenient in application of rules and procedures	2	4	2	4	3

Table XVII.11 (continued)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Review subject use only; don't review study design and purpose. Should not control research beyond human subject treatment; committee gets into areas and decisions not appropriate to its purpose	1	-	2	0	1
Eliminate reviews on previously approved studies; don't review renewals or continuations of projects	-	1	-	0	1
Do not review studies using materials from previously approved research or materials which would be available even if there were no research	1	6	4	-	4
Differentiate; more caution when risk/intervention involved, less severe/rigid for more innocuous research; no review for innocuous research	14	7	4	7	7
Eliminate reviews on standard research practices	-	2	-	0	1
Be less rigid with research on patients with life threatening conditions and terminally ill patients	0	-	-	-	-
Eliminate written/informed consent in some circumstances (for example, participant observation and cases where results would be biased)	3	1	2	1	2
Change structure and/or authority of review process or review committee	7	11	15	9	11

Table XVII.11 (continued)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Get help or consultants if the review committee is not able to understand or handle aspects of some proposals	1	3	3	4	3
Change or improve the composition of the committee; get different kinds of people; use a different selection process	3	5	11	4	6
Give more authority to local boards	-	1	2	1	1
The committee is too political	-	1	1	1	1
Monitor the review committee for thoroughness, fairness, efficiency	1	1	-	1	1
Have outside authority to which to appeal review committee decision	-	-	2	0	-
Abolish the committee; certify investigators, and let them decide	2	1	-	1	1
Funding of committee work--federal government/ grant/overhead institutions should provide funds for committee operation	0	-	0	0	-
Give more information to researchers; improve communications between committees and researchers; define, clarify, and set guidelines	18	11	7	19	12
Need more guidelines in general	7	2	-	7	3
Define "informed consent;" tell investigators more clearly/specifically what needs to be done to meet "informed consent" requirement; provide sample consent forms	1	2	2	5	2

Table XVII.11 (continued)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Decide/clarify when written consent must be obtained	1	1	-	-	1
Decide/define what research must be reviewed; define "human subject" for review purposes	1	-	0	2	1
Define/clarify liability and responsibility	-	-	-	0	-
Define/clarify risks and deception	2	-	-	2	1
Define/clarify proxy consent	-	-	-	1	-
Review committees should disseminate information on what they want/action they've taken and why the action was taken	5	2	-	1	2
Should be opportunity for interaction between the researcher and the committee	2	3	4	3	3
Need special guidelines on children, fetal research	2	1	-	-	1
Need special guidelines on social science research	2	-	0	0	-
Training sessions should be provided for the committee members	0	-	0	0	-
Do more to protect human subjects--be stricter	10	7	8	10	8
Do job more carefully/be tougher; more strict review	2	2	3	-	2
Do more follow-up after review to see that proposed procedures are implemented	4	3	3	3	3

Table XVII.11 (continued)

	Type of Institution				
	Universities (N=479)	Medical Schools (N=1203)	Hospitals (N=214)	Other (N=161)	All (N=2057)
Stress privacy and confidentiality	1	1	-	1	1
Simplify consent forms for subjects	1	1	-	-	-
Insure that all or more research is reviewed	2	1	1	2	1
Physician/patient treatment should be reviewed	1	-	2	1	1
Require that more information be given to subjects	1	-	1	3	1
Miscellaneous and other suggestions	7	5	8	8	6

*Totals will add to more than 100% since investigators could make more than one mention.

Table XVII.12

Suggestions for Improvement: Subjects and Proxies

	Percent of Subjects/Proxies* (N=962)
No suggestions	62%
Increase benefits and reduce risks; improve risk/benefit ratio	3
Increase benefits to subjects--financial	1
Increase benefits ot subjects--care/services	-
Increase benefits to subjects--general	1
Reduce risks; test more thoroughly before human experimentation	1
More and better information to subjects	19
More, better, or simpler explanation of benefits	1
More, better, or simpler explanation of risks or side effects	3
More, better, or simpler explanation of procedures	3
More, better, or simpler information given--general or other areas	11
Give information on results to subjects and/or proxies	6
Explain less	-
More informed consent; use consent forms; given subjects a copy of consent form	-
Tell subjects that participation is voluntary; allow them to quit anytime	-
Give subjects written as well as oral information	-
Conduct of research	11
Perform procedures more carefully, more humanely	3
Perform procedures more efficiently, be better organized	4
Choose sample better; sample all economic groups	-
Be more courteous and kind in dealing with subjects; take more time with subjects	3
Make it more convenient; more convenient location or scheduling	1
Improve the survey or questionnaire; word questions better; conduct it in person rather than by mail	-
Debrief subjects; let them know whether they are taking the placebo or drug	-
Miscellaneous and other	9
Do more research; make it avaiable to more people; publicize it more	1
Other	9

*Totals will add to more than 100% because investigators could make more than one mention.

Appendix I

Procedures

Contacting Institutions

The Commission staff provided a complete list of all general assurances along with the name of the person who had signed that assurance for each institution. In November 1975, after the sample was drawn (see Appendix II), we called the office of the persons who had signed the assurances at the sampled institutions in order to inform them of our planned study and to learn whom we should contact within the institutions to obtain formal agreement permitting us to proceed with our study. Letters describing our research plans and requesting cooperation were sent to each of these persons (usually the president, dean, or chairperson of the review board). Most of the institutions contacted agreed to participate in the research. We then identified all the review boards under each assurance in the sample, the names of all members of each board, and the titles of research projects that were reviewed by each board between July 1, 1974 and June 30, 1975, along with the names of the principal investigators of these projects. (These dates were used because of the importance of obtaining a sample of projects which had actually begun and in which subjects had already participated.) At many institutions we obtained copies of the consent forms that were initially submitted to the boards in connection with those projects. Appendix Ia presents the form on which we recorded the information that was obtained at this stage.

Contacting Researchers

Interviewers from our staff called the principal investigators of each project to obtain preliminary information. Most of this information pertained to several criteria that defined a project's eligibility for our

research. Investigators were asked, for example, whether their projects were actually conducted and whether they involved human subjects. The form employed in this brief telephone interview is presented in Appendix Ib.

Some principal investigators had been informed through institutional channels, prior to our telephone call, about our intention to contact them, but others had not been informed and several of the latter persons objected to the unanticipated call from us. We therefore modified our procedure at an early stage by writing an introductory letter to investigators briefly describing our research and indicating our intention to call (Appendix Ic).

The brief telephone conversations with investigators provided information essential to the planning of interviews, including: (a) whether projects met the criteria of eligibility and (b) the identities of the persons most knowledgeable about the projects. A letter indicating that an interviewer would call to request an interview was then sent to the most knowledgeable person for each project which met the eligibility criteria. The letter briefly described our purpose and procedures, indicated that the investigator's participation was voluntary, and offered assurance that the names of neither respondents nor institutions would be revealed in any reports (Appendix Id).

Each principal investigator was asked to provide information through a face-to-face interview as well as through a self-administered questionnaire. Where possible, the interviewer asked the respondent to complete the self-administered form immediately after the interview--while the interviewer waited.[1] The response rate for this self-administered aspect of the survey is somewhat smaller than that for the personal interview. In addition, each investigator was asked for a copy of the consent form that was actually employed in the research. Thus, for many projects we received both a copy of

[1] If the self-administered form was left to be completed at a later time, the chances that it would be completed diminished.

the form originally submitted to the IRB and the form actually used in the research.

Contacting Review Board Members

Letters were sent to persons who served on each of the review boards as of May 30, 1975 (Appendix Ie). The May 30, 1975 date was chosen to enable us to interview individuals who were members of IRB's when our sample of projects was reviewed. Letters also were sent to one "key" person associated with each board who was expected to be able to provide information about the structure of the current board (Appendix If). Additionally, a special letter was sent to those persons who were expected to be able to provide information about both the earlier period and the current one (Appendix Ig). Each of these various letters was followed by a phone call from one of our interviewers, who requested an appointment for an interview.

Contacting Subjects of Research

We approached subjects and proxies through principal investigators who agreed to write to their subjects and proxies on our behalf, asking them to return a form if they were willing to be contacted by us. It was only through the forms that were returned that we learned the names of subjects (Appendix Ih) and proxies (Appendix Ii). Some institutions did not allow this access to subjects, and some investigators were unable (since they did not have the names and/or addresses of their subjects) or unwilling (for example, some had guaranteed no further contact) to contact subjects for us. We were able, nonetheless, to reach and to interview by phone approximately 1,000 subjects or their proxies from over 200 different studies.

Confidentiality

We assured persons at each of the research sites that our reports, whether written or oral, would not include the names of institutions or persons

associated with these institutions. Additionally, a letter from the Executive Director of the National Commission expressing the Commission's concern for confidentiality was forwarded by us to each of the participating institutions (Appendix Ij).

The purpose of our study and interviews was to understand the procedures employed in protecting human subjects and the attitudes and perceptions of persons who play a role in the research process. It was not our purpose to expose, positively or negatively, particular individuals or institutions. Persons who contributed to our study--investigators, members of review boards, subjects, and officials from many institutions--demonstrated trust through their participation; and we followed a number of procedures to honor that trust by protecting the confidentiality of the data. Some of these were procedures normally employed in studies conducted by the Institute for Social Research; others were special to this project. The standard procedures regarding confidentiality included instructing each interviewer on the importance of maintaining the confidentiality of the data they were collecting, consistent with a long-standing policy of the Survey Research Center. (See Appendices Ik and Il for a copy of the Center's statement of professional ethics with which each interviewer is familiar and a copy of a pledge of confidentiality signed by each interviewer.)

A number of additional steps were taken to protect the confidentiality of respondents. First, the cover sheet used by the interviewer to identify and locate the designated respondent was removed from the questionnaire as soon as it arrived at the Center. The cover sheet was then filed separately in a locked cabinet. Some information from the cover sheet and the project information form was coded, including action taken by the review board in regard to the project. However, no names were coded or entered into the data files. The cover sheet and project information forms were then destroyed.

Second, names of persons, institutions, and drugs and certain items of demographic information about respondents were physically cut out of completed questionnaires and destroyed. Some of these items of information, such as age or title of respondent, were coded into relatively broad categories.

Third, the sample books and numerical logging materials used in accounting for sample projects were kept in a locked vault after normal working hours. The control clerk assigned to the study had a list of persons who were allowed access to these books. The names of principal investigators and the names of their projects have now been physically cut out of the sample books and destroyed. Before the final report or any data tapes are released from the Survey Research Center, the sample books will be destroyed.

Fourth, the consent forms and the first two pages of each questionnaire, which contain descriptions of the projects, were stored in Canada. The identifying numbers that connect the data in the tapes with specific questionnaires were scrambled. Additionally, the address labels prepared for all respondents (for the purpose of sending them copies of a summary report) were stored in Canada.

Appendix I a

Sheet ___ of ___

P453533
Study of Institutional Review Boards

Survey Research Center
Institute for Social Research
The University of Michigan

Name of Institution: _____

Review Board for: _____ 1. IRB No. _____

Source of Information: _____

2. SRC I.D. _____
3. Assurance No. _____

4. PROJECT LISTING SHEET

Project Title (a)	Principal Investigator (b)	IRB Proj. No. (if any) (c)	Date of First Review (d)	Project Activated (e)		SRC Proj. No. (f)	✓ Selections (g)
				Yes	No	1	
				Yes	No	2	
				Yes	No	3	
				Yes	No	4	
				Yes	No	5	
				Yes	No	6	
				Yes	No	7	
				Yes	No	8	
				Yes	No	9	
				Yes	No	0	

Form: IRB #3

SAMPLE COPY

P453533
Study of Institutional Review Boards

Sheet ___ of ___

Survey Research Center
Institute for Social Research
The University of Michigan
SRC I.D. _____
Assurance No._____

Name of Institution: _____

Review Board for: _____ IRB No. _____

Source of Information: _____

May 30, 1975 REVIEW BOARD MEMBERS - LISTING SHEET

(a) Member No.	(b) Board Members' Names	(c) Phone Number	(d) Term of Office	(e) Member of This Institution? Yes	No
1					
2					
3					
4					
5					
6					
7					
8					
9					
0					

SAMPLE COPY

Form: IRB #2

Sheet ___ of ___

(3) For the time periods (below), please request:

Jan. 1, 1974 - June 30, 1974	July 1, 1974 - Dec. 31, 1974	Jan. 1, 1975 - June 30, 1975
a) Number of new projects reviewed	a) Number of new projects reviewed	a) Number of new projects reviewed
_____ number	_____ number	_____ number
b) Of new projects reviewed during this time period, no. activated	b) Of new projects reviewed during this time period, no. activated	b) Of new projects reviewed during this time period, no. activated
_____ number	_____ number	_____ number

(4) What is the system used to review documents (project proposals)? Is the review conducted by subcommittees of this board, which in turn presents recommendations to the entire board? Or, is each document reviewed by every board member?

Form: IRB #2

P453533 Appendix Ib
Study of Institutional Review Boards

1. Interviewer's Label

SAMPLE COPY

Survey Research Center
Institute for Social Research
The University of Michigan

2. SRC I.D. _____

3. Assurance No. _____

4. IRB No. _____

PROJECT INFORMATION FORM

5. PROJECT TITLE _____

_____

6. IRB PROJECT IDENTIFICATION NO. (column c of Project Listing Sheet) _____

7. SRC SAMPLE PROJECT NUMBER (column f of Project Listing Sheet) _____

8. PRINCIPAL INVESTIGATORS

NAME	TELEPHONE	OFFICE ADDRESS	CHECK INFORMANT FOR THIS FORM

9. WAS THIS PROJECT EVER ACTIVATED, THAT IS, DID THE PROPOSED RESEARCH EVER OCCUR?

YES → NO → GO TO Q. 14

10. DID THE RESEARCH INVOLVE HUMAN SUBJECTS?

YES → NO →

11. DID THE RESEARCH UTILIZE RECORDS ON HUMAN SUBJECTS?

YES → NO →

Form: IRB #4

12. ARE/WERE PRISONERS USED IN THIS PROJECT?

YES NO

13. WHO IS THE MOST KNOWLEDGEABLE PERSON ABOUT ALL ASPECTS OF THIS RESEARCH?

_____ NAME

13a. WHAT IS THE RANK OR POSITION OF (NAME) ON THIS PROJECT (CO-INVESTIGATOR, RESEARCH ASSISTANT, NURSE, ETC.)

_____

14. IF PERSON NOT INCLUDED IN LIST OF PRINCIPAL INVESTIGATORS ON PAGE 1, ASK FOR PHONE NUMBER.

_____ PHONE NUMBER

Form: IRB #4

15. WHAT IS YOUR RANK OR POSITION? (e.g. Chairman of the Department, Associate Professor etc.)

RANK OR POSITION _____

16. FROM WHICH DEPARTMENT IS/WAS THE PROPOSAL (item 5 on the first page of this form) SUBMITTED? (e.g. Surgery, Medicine, Sociology etc.)

DEPARTMENT _____

17. WHAT WAS THE FIRST REVIEW COMMITTEE ACTION ON YOUR PROPOSAL? WAS IT .....

- ☐ 1. APPROVED WITHOUT QUALIFICATIONS
- ☐ 2. APPROVED WITH QUALIFICATIONS
- ☐ 3. RETURNED TO INVESTIGATOR FOR INFORMATION OR MODIFICATIONS
- ☐ 4. TABLED OR NO ACTION TAKEN
- ☐ 5. REJECTED

18. WAS THERE A SEPARATE OR FINAL REVIEW?

[1. YES] [5. NO] → Go to Q. 19

18a. WHAT WAS THE ACTION AT THAT TIME? WAS THE PROPOSAL .....

- ☐ 1. APPROVED WITHOUT QUALIFICATIONS
- ☐ 2. APPROVED WITH QUALIFICATIONS
- ☐ 3. RETURNED TO INVESTIGATOR FOR INFORMATION OR MODIFICATIONS
- ☐ 4. TABLED OR NO ACTION TAKEN
- ☐ 5. REJECTED

19. WAS THIS PROPOSAL REVIEWED BY ANY HUMAN SUBJECTS REVIEW COMMITTEE OTHER THAN THE REVIEW COMMITTEE FOR (NAME)?

[1. YES] [5. NO] → Go to Q. 20

19a. WHAT HUMAN SUBJECTS REVIEW COMMITTEES WERE THOSE?

REVIEW BOARD FOR:	19b. WITH WHAT ORGANIZATION IS THAT BOARD AFFILIATED?	19c. WHEN WAS THE PROPOSAL REVIEWED BY THIS BOARD?
1. _____	_____	MO _____ YR _____
2. _____	_____	MO _____ YR _____
3. _____	_____	MO _____ YR _____
4. _____	_____	MO _____ YR _____

20. (If project was not activated) I HAVE A FEW QUESTIONS ABOUT THE REVIEW PROCEDURE. DID THE HUMAN SUBJECTS REVIEW BOARD REQUEST ANY MODIFICATIONS IN THE PROPOSAL AS IT WAS FIRST SUBMITTED?

1. YES

5. NO → 20a. DID THE REVIEW COMMITTEE REQUEST ANY ADDITIONAL INFORMATION?

1. YES 5. NO

GO TO Q.21

20b. WHAT KINDS OF MODIFICATIONS? _____

_____

_____

_____

21. IS ONE OF THE REASONS THE PROJECT IS NOT ACTIVE BECAUSE OF PROBLEMS WITH THE REVIEW BOARD OR THE REVIEW PROCEDURE?

1. YES 5. NO

22. DO YOU HAVE ANY SUGGESTIONS FOR MODIFICATIONS OR IMPROVEMENTS IN THE HUMAN SUBJECTS REVIEW PROCEDURES--EITHER IN THE FEDERAL REGULATIONS OR IN THEIR APPLICATION?

_____

_____

_____

_____

_____

Appendix Ic

ISR

SURVEY RESEARCH CENTER / INSTITUTE FOR SOCIAL RESEARCH / THE UNIVERSITY OF MICHIGAN / ANN ARBOR, MICHIGAN 48106

[First letter to principal investigators--prior to initial phone call]

The Survey Research Center of The University of Michigan is conducting a study on the participation of human subjects in research projects. The study is being done at the request of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Your institution is in our sample and the chairperson of the review committee has made it possible for us to collect the initial data we need concerning the number of new projects reviewed between July 1, 1974 and June 30, 1975 and the name of these projects. Although you may already be aware of our study, we wanted to give you further information and explain our proposed procedures.

The impetus for this study arises from the Commissioners' need for systematic information about the consequences of federal policies for protection of human subjects. Review committees set up under DHEW guidelines have been in existence for almost ten years and there has been no national evaluation of their efficacy in protecting human subjects or examination of whether or not this kind of regulatory procedure impedes needed research or places unintended burdens on researchers.

A packet of detailed information about this study has been sent to the office noted on the enclosed form. It contains a current summary of the study design attached to a copy of the original proposal, an outline of procedures to maintain confidentiality, and copies of our sampling forms. We welcome your perusal of these materials or, if you wish, we would be glad to send the packet directly to you.

Our interviewer will be calling you to ask a few questions about the project or projects listed on the enclosed form. She will be asking whether each project was activated, whether it involved human subjects directly or records of data previously collected, and the action taken by the review committee in response to your project proposal(s). This very brief (2-3 minutes) phone contact will provide the information needed to determine which projects from your institution are to be included in our sample. If your project "falls into" our sample we may be in touch with you again--by letter--to request an appointment for an interview.

Although we would be most appreciative of your help with our study, your participation is, of course, completely voluntary. We think you will find the study interesting and we hope you will feel as we do that research on this topic is both timely and of great social importance. If you have any questions about the purpose or objectives of the study, please do not hesitate to call me collect at (313) 764-8390.

Sincerely,

Arnold S. Tannenbaum

Arnold S. Tannenbaum
Program Director

SURVEY RESEARCH CENTER

INSTITUTE FOR SOCIAL RESEARCH / THE UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN 48106

The name of the interviewer who will call:

_____

The name of the project(s) we will be asking about:

_____

_____

_____

_____

_____

_____

A packet of materials containing a current summary of the study design attached to a copy of the original proposal, an outline of our procedures to maintain confidentiality and copies of our sampling forms has been sent to your institution in care of the office of:

_____

ISR

Appendix I d

SURVEY RESEARCH CENTER / INSTITUTE FOR SOCIAL RESEARCH / THE UNIVERSITY OF MICHIGAN / ANN ARBOR, MICHIGAN 48106

[Second letter to principal investigators--prior to request for interview]

The Survey Research Center of The University of Michigan is conducting a study on the participation of human subjects in research projects. The study is being done at the request of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

As you may already be aware, your institution is in our sample and the chairperson of the review committee has made it possible for us to collect the initial data we needed concerning the number of new projects reviewed between July 1, 1974 and June 30, 1975 and the name of these projects. We are writing to you at this time to request an interview concerning the project identified on the enclosed card.

The interview is divided into two parts -- a short in-person interview and a self-administered questionnaire. We estimate that the combination of interview and questionnaire will take approximately 60 minutes and we hope you will be able to find the time in your schedule to help with this research effort. We will be asking about the content area of your study, the subject consent procedure, and your general experience with and opinions about the review process. The interview is, of course, completely voluntary and if, by chance, there should be any questions you would rather not answer the interviewer will simply proceed to the next question.

Our interviewers are all trained members of our permanent field staff. They fully understand that all information they obtain in the conduct of this study is confidential and they are pledged to protect confidentiality. The Survey Research Center guarantees that your name, the name of your project and the name of your institution will not be entered in the computerized data file used in the analysis of our findings. Our reports, which will be statistical in nature, are intended to assist the Commission in making policy recommendations. There will be nothing in the reports which would in anyway serve to identify investigators, projects or institutions.

Our interviewer will be calling you in the near future to inquire about a convenient time for the interview and she will be glad to answer any further questions you may have. We think you will find the interview interesting, and we would like to assure you that your individual contribution is of the utmost importance.

Sincerely,

Arnold S. Tannenbaum
Program Director

P.453533

II

ISR

Appendix Ie

Letter to Review Board Members

SURVEY RESEARCH CENTER / INSTITUTE FOR SOCIAL RESEARCH / THE UNIVERSITY OF MICHIGAN / ANN ARBOR, MICHIGAN 48106

The Survey Research Center of The University of Michigan is conducting a study on the participation of human subjects in research. The study is being done at the request of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

As you may already be aware, your institution is in our sample and we have been collecting data on the new proposals which were reviewed during the period July 1, 1974 - June 30, 1975. We would now like to conduct an interview with you as a review committee member and with all other members who were on the committee as of May 30, 1975.

The interview concerns review committee procedures and the attitudes of committee members toward human subjects research and the review process. We anticipate that these personal interviews will take about an hour and we hope that you will be able to find the time in your schedule to help us with this research effort. The interview is, of course, completely voluntary. If there should be any questions that you would rather not answer, the interviewer will simply proceed to the next question.

Our interviewers are all trained members of our permanent field staff. They fully understand that all information they obtain in the conduct of this study is confidential and they are pledged to protect confidentiality. The Survey Research Center guarantees that your name and the name of your institution will not be entered in the computerized data file used in the analysis of our findings. Our reports, which will be statistical in nature, are intended to assist the Commission in making policy recommendations. There will be nothing in the reports which would in any way serve to identify review committee members or institutions.

Our interviewer will be calling you in the near future to inquire about a convenient time for the interview and will be glad to answer any further questions you may have. We think you will find the interview interesting, and we would like to assure you that your individual contribution is of the utmost importance.

Sincerely,

Arnold S. Tannenbaum

Arnold S. Tannenbaum
Program Director

P. 453533 - RB

Appendix I f

ISR

Letter to "Key Person" Familiar with Present Board Structure

SURVEY RESEARCH CENTER / INSTITUTE FOR SOCIAL RESEARCH / THE UNIVERSITY OF MICHIGAN / ANN ARBOR, MICHIGAN 48106

The Survey Research Center of The University of Michigan is conducting a study on the participation of human subjects in research. The study is being done at the request of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

As you may already be aware, your institution is in our sample and we have been collecting data on the new proposals which were reviewed during the period July 1, 1974 - June 30, 1975. We would now like to conduct an interview with you about the structure of the current review board.

The interview deals with the number and kind of projects reviewed by the committee and the structure under which the committee operates. We anticipate that this personal interview will take about an hour and we hope that you will be able to find the time in your schedule to help us with this research effort. The interview is, of course, completely voluntary. If there should be any questions that you would rather not answer, the interviewer will simply proceed to the next question.

Our interviewers are all trained members of our permanent field staff. They fully understand that all information they obtain in the conduct of this study is confidential and they are pledged to protect confidentiality. The Survey Research Center guarantees that your name and the name of your institution will not be entered in the computerized data file used in the analysis of our findings. Our reports, which will be statistical in nature, are intended to assist the Commission in making policy recommendations. There will be nothing in the reports which would in any way serve to identify you or your institution.

Our interviewer will be calling you in the near future to inquire about a convenient time for the interview and will be glad to answer any further questions you may have. We think you will find the interview interesting, and we would like to assure you that your individual contribution is of the utmost importance.

Sincerely,

Arnold S. Tannenbaum
Program Director

AST:pv

P. 453533 - KP

Appendix Ig

Letter to Review Board Members Who Were Also Knowledgeable about the Present Structure of the Board

ISR

SURVEY RESEARCH CENTER / INSTITUTE FOR SOCIAL RESEARCH / THE UNIVERSITY OF MICHIGAN / ANN ARBOR, MICHIGAN 48106

The Survey Research Center of The University of Michigan is conducting a study on the participation of human subjects in research. The study is being done at the request of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

As you may already be aware, your institution is in our sample and we have been collecting data on the new proposals which were reviewed during the period July 1, 1974 - June 30, 1975. We would now like to conduct two interviews with you--one concerns the procedures and attitudes of committee members toward the review process during our sample time period and the other concerns the number and kind of projects reviewed and the structure of the current board. We would very much like to obtain your perceptions of the review process from the standpoint of both perspectives.

We anticipate that each interview will take about an hour and we hope that you will be able to find the time in your schedule to help us with this research effort. The interviews are, of course, completely voluntary. If there should be any questions that you would rather not answer, the interviewer will simply proceed to the next question.

Our interviewers are all trained members of our permanent field staff. They fully understand that all information they obtain in the conduct of this study is confidential and they are pledged to protect confidentiality. The Survey Research Center guarantees that your name and the name of your institution will not be entered in the computerized data file used in the analysis of our findings. Our reports, which will be statistical in nature, are intended to assist the Commission in making policy recommendations. There will be nothing in the reports which would in any way serve to identify you or your institution.

Our interviewer will be calling you in the near future to inquire about a convenient time for the interviews and will be glad to answer any further questions you may have. We think you will find the interviews interesting, and we would like to assure you that your individual contribution is of the utmost importance.

Sincerely,

Arnold S. Tannenbaum
Program Director

AST:pv

P. 453533 - KP/RB

Appendix Ih

Letter to Subjects

SRC

SURVEY RESEARCH CENTER

In 1974 the U. S. Congress created the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. The University of Michigan is now doing a study for this commission. They wish to talk to people who have had experience in research and I am writing on their behalf to people who have participated in my research to request an interview.

The interview will take approximately 10 minutes and will be done by telephone at a time convenient for you. The questions will be about your experience in my research. The interviews are being conducted by the staff of the Survey Research Center of The University of Michigan. The information you provide will be kept in strict confidence by the Survey Research Center and will not be identified with your name in any report, even to me.

The interview is completely voluntary. If you are willing to be interviewed, please check "YES" and complete the form below. If you are not willing, check "NO." In either case, please return this letter to the Survey Research Center in the postage paid pre-addressed envelope enclosed.

Sincerely,

Project Identification Number:

☐☐☐☐

☐☐

☐☐☐☐

☐ **YES I WOULD LIKE TO PARTICIPATE**

Name: (please print) _____
(last) (first) (middle initial)

Home address: _____
(number/street/apt.)

_____
(city/state) (zip code)

Home telephone: _____ _____
(area code) (number)

Please indicate convenient times for the interviewer to phone:

	WEEK DAY(S)	SATURDAY	SUNDAY
HOURS	_____ AM / PM	_____ AM / PM	_____ AM / PM

☐ **NO I WOULD NOT LIKE TO PARTICIPATE (Please return this letter without entering the information above)**

INSTITUTE FOR SOCIAL RESEARCH
THE UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN 48106

Appendix II
Letter to Proxies

SURVEY RESEARCH CENTER

In 1974 the U.S. Congress created the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. The University of Michigan is now doing a study for this commission. They wish to talk to people who have had experience in research and I am writing on their behalf to people who have participated in my research to request an interview. Since you signed as proxy or guardian for a research subject in my project, you are receiving this request.

The interview will take approximately 10 minutes and will be done by telephone at a time convenient for you. The questions will be about your experience and the experience of the subject in my research. The interviews are being conducted by the staff of the Survey Research Center of The University of Michigan. The information you provide will be kept in strict confidence by the Survey Research Center and will not be identified with your name or the name of the subject in any report, even to me.

The interview is completely voluntary. If you are willing to be interviewed, please check "YES" and complete the form below. If you are not willing, check "NO." In either case, please return this letter to the Survey Research Center in the postage paid pre-addressed envelope enclosed.

Sincerely,

Project Identification Number:

☐☐☐☐

☐☐

☐☐☐☐

☐ YES I WOULD LIKE TO PARTICIPATE

Name of Subject: (please print) _____

Name of Proxy/Guardian: (please print)

_____
(last) (first) (middle initial)

Home address: _____
(number/street/apt.)

_____
(city/state) (zip code)

Home telephone: _____ _____
(area code) (number)

Please indicate convenient times for the interviewer to phone:

	WEEK DAY(S)	SATURDAY	SUNDAY
HOURS	_____ AM PM	_____ AM PM	_____ AM PM

☐ NO I WOULD NOT LIKE TO PARTICIPATE (Please return this letter without entering the information above)

INSTITUTE FOR SOCIAL RESEARCH
THE UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN 48106

Appendix Ij

National Commission for the Protection of Human Subjects
of Biomedical and Behavioral Research

Westwood Building, Room 125
5333 Westbard Avenue
Bethesda, Maryland 20016

March 5, 1976

Dr. Arnold Tannenbaum
Program Director
Survey Research Center
University of Michigan
Ann Arbor, Michigan 48104

Dear Dr. Tannenbaum:

There is a real possibility that harm may be done to the Institutional Review Board Study now underway by a report that has come to my attention of a complex discussion that took place at the Commission's February meeting. This is a matter of deep concern to me as the study you are doing is of great importance to the Commission. As a result of this report, some institutions may have gained a very distorted impression of the provisions for protecting confidentiality in the study. As you know, I cannot write to sample institutions directly because their identity is unknown to me, but I would like to do everything that I can to set the matter straight. Consequently I hope that you will see that this letter is distributed to the cooperating institutions.

First and categorically I would like to state that no data identifying individuals or institutions will be reported, or given to the Commission or made public. The Commission will not request nor has it any interest in data which identifies individuals or institutions.

The discussion at the meeting arose in response to two different concerns regarding the confidentiality issue. First was the question of whether the code could be broken on the final data tapes and identifications thereby revealed. While there may be no code that could not be broken the process is not necessarily a simple one. You probably know, better than I, how difficult it would be in this instance, but given the fact that a list of participant individuals and institutions would not be available and certainly is not on the data tape, any linkage would appear to be rather difficult.

The second question pertained to whether the Commission or even the Department of Health, Education and Welfare could protect data from a properly directed subpoena. It is not clear why someone would seek these data by subpoena, since the same information could be obtained by any court of proper jurisdiction by the same device and from the same people who participated in the study -- in that event, the information would be developed under oath. However the question was raised and the answer appears to be that no one can say with confidence that the Commission could protect data in its possession although an important protection is described in the statute which created the Commission.

Public Law 93-348, Section 204-C states:

The Commission will not disclose any information reported to or otherwise obtained by it in carrying out its duties which -

(1) identifies any individual who has been the subject of an activity studied and investigated by the Commission, or -

(2) which concerns any information which contains or relates to a trade secret or other matter referred to in Section 1905 of Title XVIII, of the United States Code.

Thus a statutory basis has been provided which reinforces our ability to maintain confidentiality. This brings us back to the very important matter of what information the Commission will come to possess as a result of this study. The only materials to be furnished to the Commission will be your reports and the data tapes from which all identifying information has been removed. This is stipulated in our contract with you. I further understand that material used at the time of interviewing which identifies individuals (e.g. cover sheets of questionnaires) are to be destroyed as soon as they have been coded. Thus no information identifying individuals will be available.

Your organization has built an outstanding reputation in social research over many years. A part of this reputation rests on your ability to guarantee and maintain confidentiality. I understand that this guarantee has remained unbroken during the thirty years you have been conducting research. It is clear that the reputation of both this Commission and the Survey Research Center would be adversely affected by violations of a pledge of confidentiality. It is in our mutual interest and essential that we maintain this trust.

Sincerely yours,

Charles U. Lowe, M.D.
Executive Director

Appendix I k

STATEMENT OF PROFESSIONAL ETHICS

All interviewers for the Survey Research Center are expected to understand that their professional activities are directed and regulated by the following statements of policy:

The Center undertakes a study only after it has been evaluated in terms of its importance to society and its contribution to scholarly knowledge. The Center does not conduct studies which are, in its opinion, trivial, of limited importance, or which would involve collecting information that could be more easily obtained by other means. The Center does not undertake secret research or conduct studies for the sole benefit of one individual, company or organization. The Center is a community of scholars whose findings are available to everyone. An effort is made to disseminate research results as widely as possible; this is done through books, journal and magazine articles, news releases, papers presented at professional meetings, and in the classroom.

The rights of human subjects is a matter of primary concern to the Center. All study procedures are reviewed to assure that the rights of individual respondents are protected at each stage of research. While it is the Center's policy to make study findings public, the utmost care is taken to see that no data are released that would permit any respondent to be identified. All information that connects a particular interview with a specific respondent is removed as soon as the interview is received at the Center; this information is maintained in special confidential files while the study is in progress, and is destroyed after the study closes. Interviews themselves are identified only by numbers.

The Center's strict precautions to protect the anonymity of respondents would be undermined if the interviewer does not treat information concerning respondents with equal regard. Center interviewers perform a professional function when they obtain information from individuals by means of the personal interview, and they are expected to maintain professional ethical standards of confidentiality regarding what they hear and observe in the respondent's home. All information about respondents gained during the conduct of research is privileged information, whether it concerns the interview itself or includes extraneous observations of the respondent's home, family, and activities.

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Appendix I1

SURVEY RESEARCH CENTER / INSTITUTE FOR SOCIAL RESEARCH / THE UNIVERSITY OF MICHIGAN / ANN ARBOR, MICHIGAN 48

PLEDGE OF CONFIDENTIALITY

The Survey Research Center of The University of Michigan promises respondents that data will be kept completely confidential; therefore, it is imperative that we all have the same understanding of "confidentiality." For this purpose the "Statement of Professional Ethics," outlining the obligations of the Ann Arbor office and interviewers in the field, has been included in the Interviewer's Manual, (page vii). Please read it carefully and then sign your name at the bottom of this sheet indicating that you understand and hereby pledge to uphold this policy of confidentiality.

After signing your name and the date, please return this sheet, with your application, to the supervisor.

We believe you may find it helpful to be able to tell respondents that you have pledged yourself to uphold the policy of confidentiality of the Center.

_____ Signature

_____ Date

3/9/73

Appendix II

The Sample Design for the Study of Institutional Review Boards

The initial proposal suggested a probability sample of 50 institutions having general assurances of compliance with the Department of Health, Education, and Welfare (DHEW) regulations on research involving human subjects. Within each sample institution, data were to be collected from Institutional Review Board committee records, from IRB members, from investigators conducting research involving human subjects, and from a sample of human subjects who had formally consented to participate in the selected research projects. From a list of institutions provided by the Commission a 20 percent sample of children's hospitals and institutions for the mentally infirm and a 10 percent sample of all other institutions was suggested; however, the final design was to be negotiable, subject to the approval of the Project Officer.

According to preliminary thinking, the following was desired from sample institutions:

a. Lists of proposals submitted to IRB's for one prior year

b. Interviews with all IRB members (as of May 30, 1975), estimated to average 12 to 16 per institution

c. Interviews on additional matters with one "key" person associated with each IRB

d. Interviews with a sample of principal investigators (average of approximately 100 per institution and a total of 5,000 for this study)

e. Interviews with subjects from a sample of projects (average of approximately 100 subjects per institution from around eight to ten different projects).

Data on children and the mentally infirm were desired not only from specialized institutions but also from other institutions which conducted research using these special classes as subjects. In the case of research

involving prisoners, a supplement to the institutional sample was anticipated. All of these considerations and others influenced the final sample design, which is a combination of several designs.

Assurances and Institutions: the Universe and the Sample

The study universe, as defined by the Commission, was a list of "institutions" by name and type. Twelve types were defined: (a) universities, (b) universities and medical schools operating under the same assurance, (c) universities which have medical schools with separate assurances, (d) medical schools at universities, (e) independent medical schools, (f) hospitals, (g) children's hospitals, (h) VA hospitals, (i) institutions for the mentally infirm, (j) biomedical research institutions, (k) other research institutions, (l) other institutions. For each institution, the list contained the general assurance number and the type and number of IRB's or committees. (A large majority of institutions was reported as having single review boards.) In addition, the list included, for some institutions, the number of projects and the dollar amount of NIH support.

Under the direction of the Project Officer, the list was edited, revised, and updated, with the following results:

a. The number of types was reduced from 12 to 11 by eliminating VA hospitals, which were the focus of a separate study, conducted by another research organization, for the Commission.

b. Institutions with a single assurance number were combined and, for sampling purposes, were regarded as one organization.

c. Institutions served jointly by one IRB were combined and, for sampling purposes, were regarded as one organization.

d. When either of the preceding combinations crossed institutional types, the combination was assigned to the type thought to be dominant.

As illustrated in Table AII1, there was almost complete consistency between the number of institutions and the number of assurances, 424 and 423,

Table AII.1

The Study Universe and the Sample by Institutional Type, Coterminous United States, 1974-1975

	Institutional Types	The Universe: Institutions No.	Institutions %	Assurances No.	Assurances %	NIH Support Millions of $	NIH Support %	Primary Units No.	Primary Units %	The Sample: Primary Units No.	Primary Units %
	1	2		3		4		5		6	
	All types	424	100.0	423	100.0	491.7	100.0	412	100.0	67	100.0
a	Universities	64	15.1	64	15.1	15.5	3.2	64	15.5	8	11.9
b	Universities and medical schools on same assurance	51	12.0	51	12.1	207.5	42.2	48	11.6	11	16.4
c	Universities which have medical school with separate assurance	36	8.5	36	8.5	5.9	1.2	36	8.7	5	7.5
d	Medical schools of universities	51	12.0	51	12.1	149.2	30.3	44	10.7	10	14.9
e	Independent medical schools	11	2.6	11	2.6	10.3	2.1	10	2.4	3	4.5
f	Hospitals	83	19.6	82	19.4	61.8	12.6	82	19.9	9	13.4
g	Children's hospitals	19	4.5	19	4.5	12.7	2.6	19	4.6	3	4.5
h	Institutions for the mentally infirm	37	8.7	37	8.7	1.0	.2	37	9.0	6	9.0
i	Biomedical research institutions	34	8.0	34	8.0	24.5	5.0	34	8.3	8	11.9
j	Other research institutions	18	4.3	18	4.3	.7	.1	18	4.4	2	3.0
k	Other institutions	20	4.7	20	4.7	2.7	.5	20	4.9	2	3.0

respectively; it therefore became convenient and not misleading to use the terms interchangeably. However, because one IRB in several cases served more than one assurance, the number of sampling units was 412. These modest clustering effects occurred in types b, d, e, and f only--types which involved medical schools and general hospitals.

The sample for this study included 67 primary units which were selected from the universe in consideration of such factors as institutional type and research volume. An institution with millions of dollars for research may affect many more human subjects than an institution with a few hundred dollars for research. Information was available about the amount of research support from NIH at each instutiton, but information on the total amount of research at each institution was unknown in terms of either number of projects or research dollars. In Table AII.1,columns 2 and 4, it can be seen that universities (type a) comprised 15 percent of the universe of institutions but received only three percent of NIH support, while universities and their medical schools (types b and d) comprised about 25 percent of the institutions and received nearly 75 percent of NIH support. Sampling the 412 primary units with equal probability directs the sample toward types of institutions that are relatively numerous (whether or not very much research is done at these institutions); sampling in proportion to NIH support concentrates the sample in types where a substantial amount of research is being done, such as types b and d, dominated by medical schools. Three design changes were proposed in order to meet better the several objectives of this research: (a) permit a sample size of about 60 (rather than 50) institutions; (b) use variable institution selection probabilities; and (c) accept a reduced sample of projects.

Although the "manipulation" of institution selection probabilities may

appear to lead to a distortion in the sample, compensations were introduced through appropriate weights and by variable sampling rates for projects within institutions. These manipulations of selection probabilities were undertaken for two reasons: (a) if institutions had been given equal selection probabilities, the resulting sample would have included predominately small institutions that carry out, collectively, only a relatively low volume of research; and (b) in order to conduct detailed analyses in certain types of institutions (e.g., institutions for the mentally infirm), we needed to build up the number of cases in those places.

The sample design steered a selection course between equal probability for the 412 units and probability in proportion to research volume. First, primary units that were thought to be unusual or unique in some way (a large volume of research, specialized research, or some other unusual characteristic) were assigned to the sample with certainty. Then, regarding institutional types as strata, a fixed sample size was allocated to each using the following criteria:

a. The minimum number of sample selection from a stratum must be two.

b. The number of sample selections from types b and d (those with the highest research volume) should be about twice the number that would be achieved if the sample were allocated in proportion to the number of primary units.

c. The number of sample units from type h, institutions for the mentally infirm, should be at least six.

The application of these criteria resulted in 11 certainty and 46 noncertainty selections.

Having allocated 46 selections to the 11 institutional types, two other stratification variables were introduced: geographic region and volume of research. For geographic control, the four well-known regions of the

coterminus United States were used: Northeast, Northcentral, South, and West (U.S. Bureau of the Census, 1970). Three classes of research volume were defined according to reported NIH support: high--$4,000,000 and more; medium--$500,000 to $3,999,999; and low--less than $500,000.

Within an institutional type, each unit in the low group was assigned a rating of "1;" medium units were rated "2;" and high units were rated "4." A basic rate of 1:x which would yield the allocated sample size was calculated. Then lows were sampled at the rate of 1:x, mediums at 2:x, and highs at 4:x. Expected sample sizes by volume rating and geographic location were added across institutional types and a controlled selection procedure (Goodman & Kish, 1950) was used to determine the number of primary selections to be made from each cell of the cross-tabulation (geographic location by volume within type). Within individual cells of the cross-tabulation, primary units had equal selection probabilities. As appropriate, some ordering by amount of reported NIH support was maintained; the low classes had additional stratification to distinguish between units with NIH support and those with none.

In the early stages of data collection, it became evident that projects were not as numerous as had been anticipated and that variability among institutions was higher than expected. A decision was therefore made to increase sampling rates for projects within sample institutions and to increase by 10 the number of low-volume sample institutions. (Since all projects were being included in the sample from low-volume institutions, the only way to increase that sample was to expand the sample of institutions.) The total sample was then 67 primary selections comprising 71 institutions or 71 assurances.

In the final sample of 56 noncertainty selections, there were 9 sample selections from primary units classed as high volume, 13 from the medium

volume class, and 34 from the low-volume class. Exclusive of certainty selections, 21 sample units are located in the Northeast, 11 in the North-central, 15 in the South, and 9 in the West.

Weighting for Unequal Selection Probabilities

Since primary units were assigned unequal selection probabilities, it was necessary to weight the data to compensate for the inequalities. In the analyses, institutions included with certainty were assigned a weight of 1; other institutions were assigned weights ranging from about 1:2 to 1:14. These institutional or assurance weights became factors in the calculation of weights for all sample data, whether they relate to institutions, IRB's and their members, projects and investigators, or subjects.

Institutional Participation in the Study

Of the 67 primary selections, nine, or 13.4 percent, were unable or unwilling to cooperate. As time and resources permitted, a substitute institution was chosen with characteristics (type, class, geographic region) as similar as possible to those of the nonparticipating institution. The substitution process was successful in three cases. Sample units with characteristics similar to the remaining six were weighted to compensate for those missing institutions.

Review committees. The sample design specified that all review boards and all IRB members at the sample institutions were to be included in the study. Therefore, a review committee, its members, and its key person (see Appendix I) had the same selection probability as the institution in which they were located. Among the 61 participating primary units, there were 88 IRB's with about 1,000 members and 88 key persons who were the chairpersons or individuals designated by chairpersons. Interviews were obtained from nearly 800 IRB members and from 77 key persons. Eight of the 11 key persons

who were not interviewed represented IRB's that had reviewed no projects during the relevant time period; consequently, neither the questionnaire nor the interview was appropriate. No adjustment for nonresponse was made beyond the adjustments for nonparticipation by designated sample institutions.

Projects and research investigators. As originally planned, within institutions projects were to be sampled at rates inversely proportional to the institution selection rates in order to equalize overall project selection rates. However, when it became evident that projects were less numerous than had been anticipated, the sample design was changed to the following:

a. Add 10 primary selections, two each from the low-volume class in institutional types a, c, d, f, and i. (Thus, the total primary selections were increased from 57 to 67.)

b. Within the certainty class of institutions, increase the sampling rate of projects to 1:2 (from a rate that might have been as low as 1:8 in some cases).

c. In all other institutions, accept all projects for the sample.

From each IRB we sought a list of projects first reviewed and approved during the period of July 1, 1974 through June 30, 1975. The project lists were then sent to the Ann Arbor office for review. Next, for each sample project, we sent to an SRC interviewer information to enable her to contact the investigator and to request further information necessary to classify the projects as eligible or ineligible for the study. The following criteria were applied to establish project eligibility:

the project was activated; AND

the project involved human subjects; OR

the project involved records of human subjects.

For each eligible project, appropriate forms were sent to an interviewer, who then attempted to make an appointment to interview the project investigator.

From the 88 participating IRB's, lists of about 4,150 sample projects

were obtained. Of these, approximately 2,880 were classified as eligible and around 2,210 interviews about the projects were obtained with investigators, a response rate of approximately 74 percent.

To adjust for nonresponse, a project weight was calculated for each IRB by dividing the number of eligible projects by the number of project interviews. The weight was then applied to interviews, thereby implying that interviews and non-interviews differ only by the presence or absence of the interview.

Subjects/proxies. During the course of the interview with a project investigator, information about human subject participation in the research was collected. Affirmative responses to the following questions were required before the number of subjects (including proxies) was requested:

a. Did human subjects participate in the research?

b. Was written consent obtained?

c. Is subject participation completed?

d. Are you [the project investigator] willing to contact subjects to request their participation in our study?

If all the responses were positive, then the number of subjects was requested; if any one of the responses was negative, no additional information was gathered.

With the preceding conditions, it is impossible to define the universe of subjects or to choose a probability sample of participants from that universe. Given that a project investigator was willing to contact subjects, there remained two stages of sampling: (a) the sampling of all projects with willing investigators and (b) the sampling of subjects within selected projects.

The sampling of projects took place in the Ann Arbor office, where sample institutions were assigned to one of three strata on the basis of project

selection probabilities. The subject sampling rates, varied to complement the project selection rates, were calculated to yield around 10 to 20 subjects per project and no more than 30.

Instructions for sampling subjects were sent to project investigators, who had the task of selecting the sample and mailing materials to the subjects. The chosen subjects/proxies were asked to mail a form to the Ann Arbor office, where a telephone interview was then attempted with each cooperating subject (see Appendix I).

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Appendix III

The Flesch Reading Ease Yardstick

Various techniques have been used to measure the "readability" of written materials. One such technique, the Flesh Reading Ease Yardstick, was used to estimate the readability of consent forms for this study of IRB's. Three issues regarding the use and appropriateness of this scale will be discussed here. They are: (1) our reasons for selecting this scale for assessing the readability of consent forms; (2) the validity of this measure; and (3) the possibility that the scale may not be sensitive enough to detect changes in consent forms.

The selection of the Flesch scale. We selected the Flesch scale (1948) for the readability analysis of consent forms largely on the basis of consultation and advice provided by reading specialists. Three factors were particularly important in choosing this scale over more than thirty alternative formulas. The first was that the validity of the Flesch scale has been fairly well established in terms of such criteria as comprehension and reading speed (Klare, 1956). Also, the Flesch scale has been found to provide an extremely high inter-rater reliability (England, Thomas, & Paterson, 1953; Haynes, Jenkins, & Walker, 1950). Though the formula promised to be somewhat more tedious and time consuming to use than others (Blumenfeld & Justice, 1975), the validity and reliability of the scale seemed to balance these costs.

Second, the Flesch scale seemed to be among the best available for estimating the readability of the particular documents we would be analyzing. We were advised that this scale would be better than many others for analyzing materials which might include many technical and medical terms and

which might vary widely in difficulty. While no readability scales are perfectly suited to behavioral and biomedical materials, the Flesch Yardstick has been frequently used to assess the readability of psychology textbooks (Gillen, 1973; Ogdon, 1954; Stevens & Stone, 1947) and other scientific material.

Third, the Flesch scale is the most widely used method of analyzing readability (Blumenfeld & Justice, 1975; Klare, 1956) and is most likely to be recognized by people familiar with problems of readability, comprehension, and recall. Given the national scope and potentially high visibility of the Institutional Review Board study, it seemed appropriate to use an established scale (the strenghts and weaknesses of which are well documented) rather than an experimental or unknown measure.

The validity of the scale. The Flesch Yardstick is accepted by many as being an adequate measure of readability or comprehensibility. The formula is based on the number of syllables per 100 words (wl) and the average number of words per sentence (sl): Reading Ease = 206.835 - .846 wl - 1.015 sl. The reading ease score thus considers both the complexity of the sentences and the abstractness of words (as approximated by the number of syllables). The formula is based on the McCall-Crabbs Standard Test Lessons in Reading (1926), which are among the most satisfactory criteria available. Flesch reported a .71 correlation between his scale and these tests of comprehension (1948). The scale also has been shown to be related to other comprehension tests, including the Ojemann Test (r = .82)(Klare, 1952; Ojemann, 1934). This latter criterion test focuses on health-related adult-level materials of potentially high interest to readers. Like other readability formulas, however, the Flesch Yardstick does not always correlate highly with measures of comprehension, learning, and retention. Correlations may be suppressed

when the reader is highly motivated, has an extensive background in the given topic, or has plenty of time to read the materials (Klare, 1963).

In addition to its correlations with reading comprehension tests (Dunlap, 1954; Peterson, 1956), the Flesch scale has been shown to be related to many other "criterion" variables. Early studies have shown that the scale is related to reading speed (Brown, 1952; Pitcher, 1953) and more recent studies have suggested that the reading ease of a paragraph, as measured by the Flesch formula, is related to the speed with which subsequent paragraphs are read (Rothkopf & Coatney, 1974). Reading ease is also related to readership, that is, the likelihood that the material actually will be read. Various studies have found that people are more likely to read materials that are rated easy or standard (rather than difficult) on the Flesch scale (Murphy, 1947; Swanson, 1948). In addition, the Flesch scale seems to be related to lay and expert judgements regarding the readability of materials; Jongsma (1972), for example, has found that Flesch scores correlate .60 with grade-level readability estimates of librarians. Finally, the Flesch scale has been shown to be highly related to many (but not all) alternative measures of readability. For example, Klare (1952) has found that the scale is strongly related to the Dale-Chall formula (1948), a highly accurate formula which considers the number of words in a passage which are outside a list of common words. However, Schlief and Wood (1974) did not find a significant relationship between the Flesch scale and the Cloze Readability Index (which involves replacing every few words in a piece of text with blanks and having the reader fill in the missing words).

On the whole, our review of the literature suggests that the use of the Flesch Yardstick should not be subject to serious criticism. One criticism that might be expected is a common one: yardsticks such as this one make

poor formulas for writing. They were not, however, intended for this purpose and the predictors of readability must be distinguished from the production of readable writing (Klare, 1956, 1971). While IRB's might be able to improve consent forms by reducing the length of sentences and the number of abstract words, many other factors would have to be considered to improve the readability and comprehensibility of these forms. A second, and more important, criticism is that the Flesch reading ease scale measures only one aspect of the quality of consent forms. This problem was anticipated and, consequently, we also analyzed consent forms in terms of other factors, including their "completeness," their mention of information particularly relevant to the specific study, their use of technical and/or medical terms, and their explanations of such terms.

The sensitivity of the Flesch scale. As noted in Section V of this report, consent forms finally approved by IRB's were not significantly more readable than those initially submitted to them. This kind of finding leads one to question whether or not the readability scale is sufficiently sensitive to detect such differences. While this finding may be an artifact of the instrument, three points lend some credence to it. First, the readability and understandability of consent forms are not emphasized in the current guidelines, and IRB's simply may not be focusing on this problem. Second, only five percent of the investigators reported to us that the boards required simplification of their consent forms and only seven percent reported that "other changes" (possibly related to reading ease) were required. Third, we found no evidence that IRB's received consultation on the production of readable consent forms; in the absence of such consultation, improved readability may be difficult to achieve even when it is "required."

It might, nevertheless, be argued that this negative finding is

artifactual. To explore this argument in an empirical and manageable manner, we will focus on a subset of the research projects in our sample: those projects which used "long" consent forms (300 words or more) and for which the forms submitted to the boards, as well as the forms approved by the boards, were made available to us for coding. More than 200 projects fall into this particular subsample. These forms did not change significantly in terms of their readability. The sections of these consent forms explaining the purpose of the research and the risks/discomforts associated with the research procedures remained at a difficult reading level (purpose: $t = -1.62$, $p = .11$; risk: $t = .85$, $p = .40$). The same finding holds even if we focus only on those projects for which the review boards required simplification, reformatting, or similar modifications of the consent forms (purpose: $t = -1.43$, $p = .16$; risk: $t = .89$, $p = .38$).

Either review boards are not succeeding in making consent forms more readable or the Flesch Yardstick is not successfully measuring these improvements. One way to explore the latter hypothesis is to see whether the formula can distinguish between the readability levels of different parts of consent forms. We purposely measured the reading level of those sections of consent forms which focus on "purpose" separately from those sections which focus on "risks and discomforts." (This was done because we expected that a discussion of the purpose of research may be more abstract, and thus less readable, than a statement concerning risks.) We found that within the "long" consent forms approved by IRB's, materials regarding purpose were significantly more difficult to read than the materials regarding risks ($t = -5.16$, $p = .0000$). The Flesch scale seems to be sufficiently sensitive to measure differences in readability within forms and, though the measurement of change may be more difficult, the formula should be responsive to differences between the forms submitted to

IRB's and the forms approved by IRB's.

We can also consider an independent measure of consent form comprehensibility to check on the sensitivity of the Flesch scale. All consent forms initially submitted to IRB's, as well as all forms finally approved by the boards, were coded as to the "percentage of technical and medical terms explained." Focusing on the same "long" forms described above, we found that forms submitted to IRB's did not differ significantly from the forms approved by IRB's with respect to the explanation of medical and technical terms. Few of these consent forms, as submitted to the IRB's, included lay explanations for more than ten percent of the medical/technical terms used; and about the same number of these forms, as approved by the boards, included such explanations. Furthermore, no improvements were found with respect to the percentages of medical terms explained, even if we limit this analysis to only those projects for which the boards required simplification of the consent forms. The percentages of technical terms explained in these modified forms increased slightly, but this increase was not significant ($\underline{t} = 1.0$, $p = .32$). These findings are consistent with those suggested by the readability analyses based on the Flesch formula.

In conclusion, these data, as well as past research on readability measures, fail to support the hypothesis that the Flesch Yardstick is too insensitive to measure the reading ease of consent forms. We note, however, that the literature on readability does not claim that this formula provides a perfect measure of comprehensibility.

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SUMMARY ANALYSES OF FEDERAL POLICIES AND PROCEDURES FOR THE PROTECTION OF HUMAN SUBJECTS (BY AGENCY)

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE (DHEW)

I. National Institutes of Health (NIH) and Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA)

NIH and ADAMHA conduct and support extensive biomedical and behavioral research.

Authority: P.L. 93-348 (1974); 45 CFR 46 revised as of April 1, 1967; DHEW Grants Administration Manual, Chapter 1-40.

Applicability: Section 474(a) of the National Research Act (P.L. 93-348) provides that the Secretary, DHEW, must require each institution applying for a grant or contract that will involve the conduct of biomedical or behavioral research with human subjects to establish an Institutional Review Board (IRB) "to review biomedical and behavioral research involving human subjects conducted at or sponsored by such entity in order to protect the rights of the human subjects of such research." It is unclear from the language of the Act whether the IRB thus established must review all research involving human subjects that is conducted under the auspices of such institutions, or whether it must review only such research supported by DHEW. The implementing regulations (45 CFR 46) apply only to research, development and related activities conducted or supported by DHEW; nevertheless, as a practical matter DHEW is now requiring grantees to assure that all research conducted under their auspices is reviewed by an IRB. The uncertainty surrounding the applicability of the review requirements is exacerbated by Section 46.121(b) of DHEW regulations (45 CFR 46) which provides that the Secretary may withhold research funds from any institution that fails materially to protect human subjects under its care "whether or not DHEW funds were involved." The result is that many institutions have required IRB review

for all their research involving human subjects as a matter of prudence.

Review Procedures: All research involving human subjects must be reviewed by an Institutional Review Board (IRB) having an approved general or special assurance on file at DHEW. Requirements for such an assurance include a statement of principles that will govern review of such research (e.g., Helsinki Code, Nuremberg Code), and a membership with sufficient diversity of background to enable review of research proposals with respect to applicable law, institutional regulations, standards of professional conduct and practice, and community attitudes. IRBs must consist of at least five members, none of whom may have an interest in the research under review. No IRB may consist entirely of officers, employees or agents of the institution, nor of members of a single professional group. Board members must be identified to DHEW by name, earned degrees, position or occupation, representative capacity, and other pertinent indications of experience. The institution must state the IRB's quorum requirements (which must be no less than a majority of total membership) as well as the procedures to be followed for initial and continuing review of proposals and activities, including procedures for notifying the board and DHEW of adverse reactions, changes in the research design, or unanticipated problems that may increase the risk to human subjects. The institution establishing the IRB must provide administrative assistance and support for the board's functions and for implementation of its recommendations.

In addition to reviewing applications for general or special assurances and certifying approval of IRB membership and procedures, NIH and ADAMHA require that proposals be reviewed by agency staff, scientific advisory committees (study sections) and interdisciplinary national advisory councils for scientific merit

and for further review of such considerations as risk to human subjects, adequacy of protection against those risks, potential benefits to the subjects and to others, and the importance of the knowledge to be gained. Some protocols are subject to review by a national Ethical Advisory Board and modification or waiver of specific requirements are permitted with approval of the Ethical Advisory Board following opportunity for public comment.

Review Standards: The IRB must review all research involving human subjects to determine whether subjects will be at risk. If so, the IRB must then determine that: (1) the risk to the subjects is outweighed by the sum of the benefit to the subjects and the importance of the knowledge to be gained; (2) the rights and welfare of subjects will be protected; (3) legally effective informed consent will be obtained by adequate and appropriate methods; and (4) adequate steps are taken to avoid unintentional involvement of pregnant women. The conduct of any activity involving risk to human subjects must be monitored by the IRB at timely intervals.

Consent Provisions: "'Informed consent' is defined as the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress or other form of constraint or coercion. The basic elements of information necessary to such consent include:

"(1) a fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;

"(2) a description of any attendant discomforts and risks reasonably to be expected;

"(3) a description of any benefits reasonably to be expected;

"(4) disclosure of any appropriate alternative procedures that might be advantageous for the subject;

"(5) an offer to answer any inquiries concerning the procedures; and

"(6) an instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject."

A consent form must be signed by each subject or a legally authorized representative; if part of the required information is conveyed orally (and omitted from the written form), the consent document must also be signed by an "auditor witness to the oral presentation." Written copies of the information disclosed must be filed with the IRB.

Special Subjects: Additional protections and special procedures are imposed for research involving fetuses, pregnant women or human *in vitro* fertilization, as well as for research involving investigational new drugs as required by the Food and Drug Administration.

Sanctions: No grant or contract involving human subjects will be awarded to an individual unless he or she is affiliated with an institution that "can and does assume responsibility for the subjects involved." The Secretary may terminate funds or withhold funds from grantees or contractors when either the institution or the principal investigator has failed materially to protect human subjects under their care (whether or not DHEW funds were involved).

II. DHEW Components other than NIH and ADAMHA

A. The following DHEW components require compliance with 45 CFR 46:

1. Office of Assistant Secretary for Planning and Evaluation

Authority: Letter (February 2, 1976) from Assistant Secretary for Planning and Evaluation (William A. Morrill).

2. Office of Human Development Services (includes: Administration on Aging; Administration for Children, Youth and Families; Administration for Handicapped Individuals; and Administration for Native Americans).

Authority: Letter (April 15, 1976) from Jane Lampmann, then Director, Office of Planning and Evaluation, OHD; Rehabilitation Services Manual, Section 4010.18.

3. Health Services Administration

a. Bureau of Community Health Services

Authority: Letter (January 23, 1976) from Edward D. Martin, M.D., Director. ("Every project involving human subjects must have an NIH general or special assurance clearance.")

b. Bureau of Medical Services

Authority: Division of Hospitals and Clinics Operations Manual C11.4.6, April 23, 1975. For further information contact Director, Bureau of Medical Services.

c. Indian Health Service

Authority: Indian Health Manual, TN No. 77.5, Part 1, Chapter 7, July 13, 1977.

B. The following components of DHEW deviate from 45 CFR 46:

1. Center for Disease Control (CDC)

Authority: Manual Guide - General Administration No. CDC-11, June 8, 1973; letter (February 6, 1976) from David J. Sencer, M.D., then Director, CDC.

Research conducted or supported by CDC, or performed on a collaborative basis by CDC employees with other institutions or agencies, is governed by the Manual Guide No. CDC-11, "Protection of the Individual as a Research Subject." This guide, in turn, requires compliance with the 1971 Institutional Guide to DHEW Policy on Protection of Human Subjects.

Although the informed consent provisions in the Institutional Guide to DHEW Policy are generally the same as those in DHEW regulations (45 CFR 46), the requirement for review by an Institutional Review Board (IRB) is not triggered unless the research investigator determines that the subjects in his or her research will be at risk. There is no mechanism for reviewing the decision of the investigator as to whether or not the subjects will be at risk and thus,

whether or not there is a need for IRB review. By contrast, under present DHEW regulations, the IRB must review all research involving human subjects, and it is the IRB that makes the threshold determination as to whether or not the subjects will be at risk. To the extent that the investigator of a project may not be sensitive to the risks which the research entails, the protection afforded by the present CDC manual will be less than that afforded by DHEW regulations (45 CFR 46) which provide that the initial determination as to whether or not subjects will be at risk will be made by an IRB.

Dr. Sencer indicated in his letter that CDC's policies will be updated "in the near future" to incorporate the provisions of 45 CFR 46; and the Commission has recently been informed by Dr. Bruce Dull, Assistant Director for Program, that CDC is awaiting the Secretary's regulatory response to the Commission's recommendations on research involving children, in order to incorporate those provisions into its revisions of the manual.

2. Education Division (includes: the National Institute of Education (NIE), the Office of Education (OE), and the National Center for Education Statistics).

   Authority: 45 CFR 100a.263; 45 CFR 1400; DHEW Procurement Rules, Title 41, Chapter 3, Subpart 3-4.55; DHEW Grants Administration Manual, Chapter 1-40, 1974; the General Education Provisions Act, 20 U.S.C. § 1221 *et seq*.

Section 1221e(3) of the General Education Provisions Act vests authority in the Commissioner of Education, the Director of the National Institute of Education (NIE), and the Assistant Secretary for Education to issue their own regulations. Consequently, it has been the position of the Education Division that it is not subject to the Department's regulations (45 CFR 46) unless and until specifically adopted by the Commissioner, OE, and the Director, NIE. This was recognized by the Secretary, DHEW, in his comments to the publication of 45 CFR 46 (Federal Register, May 30, 1974, p. 18917), although no such exemption appears in the regulations per se.

Research conducted or supported by the Education Division must comply with provisions of the DHEW Grants Administration Manual Chapter 1-40 and the DHEW Procurement Rules. These both require IRB review only when the investigator of a research project determines that the research involves subjects at risk. If the investigator does not believe his or her subjects will be at risk, none of the provisions for the protection of human subjects will be applied.

Section 1232 of the General Education Provisions Act requires parental consent for release of records or identifiable information of children in public schools, and suggests that the Commissioner of Education require parental involvement in the planning and conduct of programs supported by OE if he believes it would enhance the effectiveness of the program. Section 1232h requires that all

instructional materials to be used in connection with any research or experimental program be open to inspection by the parents or guardians of the children "engaged in such program or project."

3. Food and Drug Administration (FDA)

Authority: 21 CFR 310.102, 312.1(a)(2) 10C; FDA Compliance Program Guidance Manual, transmittal 77-39, March 15, 1977.

The regulations governing investigations of new drugs differ from 45 CFR 46 with respect to requirements for IRB review and for informed consent. FDA requires research protocols to be reviewed by an Institutional Review Committee (analagous to an IRB) only when the proposed subjects are institutionalized or when the investigator is "affiliated with an institution which agrees to assume responsibility for the study." For all other drug research, no such review is required.* Instead, the principle investigator must merely attest that the informed consent of all subjects will be obtained. (In 1975, FDA Commissioner Schmidt testified before the Senate Health Subcommittee that FDA was considering extending the committee review requirements to noninstitutionalized subjects, and we are informed that FDA is developing such proposed regulations, to be issued for public comment sometime early in 1978.)

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* FDA proposed similar provisions for the testing of medical devices, 41 Federal Register 35282, August 20, 1976.

In addition, section 505(i) of the Food, Drug and Cosmetic Act requires that investigators proposing to test investigational new drugs on human beings "obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings." Thus, under FDA regulations, consent need not be obtained if "the communication of information to obtain consent would seriously affect the patient's well-being and the physician has exercised a professional judgment that under the particular circumstances of this patient's case, the patient's best interests would suffer if consent were sought." 21 CFR 310.102(g). The regulations define "not feasible" as situations "wherein the investigator is not capable of obtaining consent because of inability to communicate with the patient or his representative, for example, the patient is in a coma or is otherwise incapable of giving consent, his representative cannot be reached, and it is imperative to administer the drug without delay." 21 CFR 310.102(f).

THE AMERICAN NATIONAL RED CROSS

The Red Cross conducts research related to its blood program. This may include studies of the motivation of volunteers or clinical trials necessary for the licensure of new products by FDA.

Authority: Blood Program Directive 4.380-1 (revised July 1975); "Special Exemption - Previously Collected Blood or Blood Products" (undated); letter (November 17, 1977) from George M. Elsey, President.

Applicability: The directive is applicable to all research studies involving human subjects or materials of human origin. Exception: Certain procedures found by the Red Cross Headquarters Committee for the Protection of Human Subjects not to involve risk may be exempt from local review requirements, provided "federal funds are not involved."* Procedures specifically exempted include the use of blood components derived from units of blood collected from Red Cross donors in the normal course of blood center activities; blood obtained from commercial sources; removal of up to fifty milliliters of additional whole blood subsequent to the donation of a unit of blood, through the same venipuncture; and blood collected previously in the course of routine clinical procedures, or another approved research project.

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* The Directive evidences some confusion regarding applicability of DHEW regulations: "DHEW requires that any research activity supported in whole or in part by federal funds and which involves human subjects . . . must be reviewed by a Human Protection Committee . . . . In studies involving federal funding, DHEW will require assurance of compliance with their regulations directly from the local review committee." (Blood Program Directive 4.38, p. 2). In fact, DHEW regulations apply only to institutions conducting research supported by the Department of Health, Education, and Welfare; they do not necessarily extend to research funded by other federal agencies. In his letter (November 21, 1977) to the Commission, the president of the Red Cross indicates that future directives will substitute "DHEW" for "federal funds."

Review Procedures: The Red Cross requires that local review boards be established in conformity with procedures set forth in the DHEW regulations (45 CFR 46) but permits alternative methods of fulfilling the requirement. Institutions or Red Cross Centers may either submit proposals for local review to an Institutional Review Board (IRB) with an approved assurance on file at DHEW or to an IRB with similar composition and duties. (In the latter case, the Red Cross instructs the regional center to establish an IRB in conformity with DHEW regulations, but no assurance is required and no procedures have been established by the Red Cross for initial review or monitoring for compliance.) Alternatively, research proposals from the Washington, D.C., metropolitan region may be submitted directly to the National Red Cross Committee for the Protection of Human Subjects for review. The Red Cross has an approved general assurance on file at DHEW, and its Committee therefore complies with DHEW regulations (45 CFR 46).

Each investigator must submit a form to the National Red Cross Headquarters indicating either that the protocol has been reviewed and approved by an Institutional Review Board or that review by the National Red Cross Committee for the Protection of Human Subjects is requested. The national committee obtains documentation of local review, when such is performed.

Review Standards: The Red Cross requires compliance with the review standards of DHEW regulations (45 CFR 46).

Consent Provisions: IRBs with approved DHEW assurances follow the DHEW regulations. Those not having approved DHEW assurances are given no formal guidance by the Red Cross regarding consent procedures except that when abnormalities are found in the course of conducting studies on blood obtained from

donors, the Red Cross is obliged to inform the donor of such abnormalities and to keep the information confidential "unless specifically released in writing by the donor or a legally appointed representative of the donor."

Sanctions: No specific provisions are made for sanctions in the case of noncompliance.

CIVIL SERVICE COMMISSION

The Civil Service Commission conducts research related to examining programs and personnel management.

Authority: There are no formal regulations or policies for the protection of human subjects in research conducted or supported by the Civil Service Commission.

In a letter to the National Commission for the Protection of Human Subjects (October 7, 1975), Robert E. Hampton, then Chairman of the Civil Service Commission, indicated that the staff of the Personnel Research and Development Center all have copies of the Ethical Principles in the Conduct of Research with Human Participants issued by the American Psychological Association in 1973, and are guided by those principles.

COMMISSION ON CIVIL RIGHTS

The Commission on Civil Rights conducts observational behavioral research.

Authority: There are no formal regulations or policies for the protection of human subjects in research conducted by the Commission on Civil Rights.

In a letter to the Commission (November 8, 1977), Louis Nunez, Deputy Staff Director, U.S. Commission on Civil Rights, indicated that behavioral research conducted by the Office of Research is guided by the ethical standards of the American Psychological Association as set forth in Ethical Principles in the Conduct of Research with Human Participants, 1973, and in Principle 9: Pursuit of Research Activity, Ethical Standards of Psychologists, January 1977.

CONSUMER PRODUCT SAFETY COMMISSION (CPSC)

The Consumer Product Safety Commission supports research to determine safety standards for consumer products.

Authority: 16 CFR 1028 (42 Federal Register 36819, July 18, 1977).

Applicability: The regulations apply to all grants or contracts or other agreements supporting research or related activities in which human subjects are involved. Exception: The regulations are not applicable to opinion surveys, questionnaires, or solicitation of information about past events.

Review Procedures: CPSC adopts the DHEW provisions (45 CFR 46) for establishment of Institutional Review Boards (IRBs). Grantees or contractors may utilize an IRB having an approved general assurance on file at DHEW or, alternatively, may submit an assurance directly to CPSC for approval, following the same procedures and requirements as those required by the DHEW regulations.

CPSC reviews applications to determine either that the applicant institution has an approved general assurance on file at DHEW or, alternatively, to ascertain compliance with requirements for an assurance negotiated directly with CPSC. In addition, CPSC submits proposals for further evaluation to such consultants and staff as it deems appropriate. Such evaluation may take into account, among other pertinent factors, the apparent risk to subjects, the adequacy of protection against risks, the potential benefits of the research to the subjects and to others, and the importance of the knowledge to be gained. CPSC may impose additional safeguards for the protection of human subjects (such as restrictions on the use of certain subjects or groups of subjects or the use of additional procedures for informed consent).

Review Standards: CPSC applies the review standards of the DHEW regulations, with the following addition: the IRB must determine that "a qualified psychologist, doctor of medicine, or other appropriate professional, having established emergency medical procedures, will oversee each test."

Consent Provisions: CPSC generally follows the consent provisions of the DHEW regulations.

Sanctions: CPSC may withhold or withdraw grant or contract funds if an investigator or institution fails materially to discharge its responsibility for the protection of the rights and welfare of human subjects.

DEPARTMENT OF AGRICULTURE

The Department of Agriculture conducts and supports biomedical and behavioral research related to human nutrition.

Authority: Administrative Memorandum No. 130-2 (November 26, 1976); and Administrative Memorandum 730 (November 26, 1976).

Applicability: Administrative Memorandum No. 130-2 applies to research conducted or supported by the Department of Agriculture and involving human subjects. It is specifically applicable to "economic, social and behavioral research that may involve varying degrees of discomfort, irritation, or harassment of persons or groups and to research in which rights of privacy of persons must be safeguarded" in addition to "biological science research." Administrative Memorandum No. 130-2 is applicable to all such research conducted or supported by the Department of Agriculture, and sets forth departmental review procedures and responsibilities. Administrative Memorandum 730 sets forth additional requirements for certain taste test and quality evaluation studies.

Review Procedures: The Department of Agriculture requires that IRBs be established in conformity with procedures set forth in the Institutional Guide to DHEW Policy on Protection of Human Subjects, but requires IRB review of all studies involving human subjects, thus bringing its policy in conformance with present DHEW regulations (45 CFR 46).* This requirement may be fulfilled by an

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* The major substantive difference between the Guide and the present regulations (45 CFR 46) is that the former applied only to research projects determined by the investigator to involve subjects at risk, whereas the latter applies to all research involving human subjects.

IRB having an approved general assurance on file with DHEW or, alternatively, by an IRB with similar composition and duties whose compliance with DHEW regulations is "ascertained" by the Department of Agriculture. (No procedures for doing so are provided.)

Documentation of IRB review and approval must be forwarded to the Human Studies Review Committee in the Agriculture Research Service which reviews all research proposals involving human subjects conducted or supported by the Department of Agriculture. No medical or biological research involving human subjects may be initiated without written approval of this committee. Approval of the committee is also required for taste tests and quality evaluation studies involving food additives or chemicals not "generally recognized as safe" by the FDA and for studies involving pesticides or other chemical residues for which the acceptable level has not yet been established. Exempt from review by the committee are consumer acceptance tests that require and receive prior approval by the FDA.

Review Standards: Review standards are those stated in the 1971 Guide to DHEW Policy on Protection of Human Subjects, with the following addition. Selection of persons or groups for study must be made "without regard to sex, race, color, religion, or national origin unless these characteristics are factors to be studied." Any investigation that includes such characteristics as factors for classification must be approved in writing by the director of the responsible agency.

Consent Provisions: The Agriculture Research Service adopts the consent provisions set forth in the Guide to DHEW Policy on Protection of Human Subjects.

Special Subjects: No pregnant or lactating women may be included in studies to evaluate the safety or nutritional qualities of foods or in taste tests involving food additives or chemicals that are not listed by FDA as "generally recognized as safe" or that involve residues of pesticides or other chemicals for which an acceptable level has not been established by FDA, the Environmental Protection Agency or the Animal and Plant Health Inspection Service. Children may participate in taste tests and quality evaluation studies only with the written approval of their parents.

Sanctions: No provisions are made for sanctions in the case of noncompliance.

DEPARTMENT OF COMMERCE

I. National Bureau of Standards

The Bureau of Standards conducts research related to product safety; environmental measurements and standards for air, water and noise pollution, and radiation safety; prosthetic devices; materials for dental research; mine safety; and lead paint poisoning control. Much of the research conducted by the Bureau of Standards is at the request of various regulatory agencies.

Authority: NBS Administrative Manual 3.01 Appendix A (February 2, 1976); NBS Policy Bulletin No. 12 (February 14, 1975).

Applicability: The policy applies to research conducted by the Bureau of Standards.

Review Procedures: A Human Research Ethics Committee, appointed by the Director of the Bureau of Standards, reviews all research proposals involving human subjects. Members include federal employees both from within the Bureau and from outside, with a broad range of expertise. Among the five members, there must be at least one medical doctor, one behavioral scientist, and one engineer or physical scientist. Two alternate members are appointed to serve in the absence of a regular member or in cases when a regular member cannot vote because of conflict of interest. "Line managers" in the divisions performing human research are excluded from membership. No individual may serve as a committee member where he or she is a principal investigator or is directly associated with the proposed research. The chairman of the committee may request advice or information from the Office of the Legal Advisor or other organizations within the Bureau of Standards. Recommendations for approval require con-

currence of three of the five committee members (or alternates serving in their place).

The Bureau of Standards' Human Research Ethics Committee is responsible for initial review and ongoing monitoring of all research. The committee may discuss proposed research with the principal investigator, negotiate modifications with the investigator, and recommend approval or disapproval of the research to the Director of the Bureau of Standards or his designee. The authority of the Director or his designee to approve or disapprove research may not be delegated to a member of the committee.

Review Standards: Review by the Human Research Ethics Committee is limited to concerns of an ethical nature; review for technical soundness is performed through other supervisory channels. The ethics review is designed to protect the physical and psychological well-being of subjects, to assure that Bureau of Standards' policies are observed, and to protect the Bureau against errors in ethical judgment that might result either in harm to subjects, law suits and adverse publicity. Subjects must be protected against an unreasonable degree of physical danger or psychological distress. Provisions must be made to protect personal privacy and maintain confidentiality of data. Such provisions include: limiting the information recorded about a subject to that which is essential, separating subjects' names from their data as soon as possible, destroying identifiable records as soon as possible, and using data only for the purpose described in the approved protocol. Adequate preparations must be made for treatment of injuries that may occur.

Consent Provisions: Subjects must be provided with all the information that is likely to influence their willingness to participate, as well as with

explanations of any other aspects about which they inquire. They must sign a form which explains the responsibilities of both subjects and investigators and which makes explicit the subjects' right to withdraw at any time "without incurring legal liability." Prospective subjects must be free from undue pressure, coercion or temptation by excessively high rewards of a monetary or any other nature. Data may not be used for any purpose other than that described to the subjects without their written consent.

If the "control of the expectations of subjects with respect to the purpose of the research, the design of the research, or the specific events which will occur during the course of the research" is necessary in order to obtain useful data and reach valid conclusions, such "control" is permissible provided the review committee determines that: (a) it is absolutely necessary to the success of the research; (b) the personal safety and dignity of the subjects are not compromised; (c) there is good reason to believe that it would be irrelevant to the subjects' decisions to participate in the research; and (d) the subjects are debriefed in a manner and at a time that is maximally compatible with their well-being and with the success of the research.

Special Subjects: If the proposed subjects are not legally, psychologically or intellectually capable of giving informed consent because of age or any other reason, the committee must ascertain whether it is appropriate to use such subjects and, if so, shall insure that lawful consent is obtained from the parent or legal guardian. In such cases, the committee must consult with the Bureau of Standards' Legal Advisor.

Sanctions: No provisions are made for sanctions in the case of noncompliance.

II. National Oceanic and Atmospheric Administration (NOAA)

NOAA conducts and supports research concerned with the physical and biological technology involved in deep sea diving and other underwater activities.

Authority: NOAA Diving Regulations, Appendix C in the NOAA Diving Manual (1975); letter to the Commission (November 14, 1977) from John M. Golden, Director of Personnel, Department of Commerce.

Applicability: The diving regulations apply to all diving projects conducted or supported by NOAA.

Review Procedures: There is no review of ethical acceptability of research; rather, NOAA undertakes comprehensive review of safety factors.

Review Standards: Review standards pertain to such safety considerations as the training of divers, their medical condition, and the adequacy of equipment and personnel to meet the demands of the project and to respond to emergencies.

Consent Provisions: "Each diver has the responsibility and privilege to refuse to dive if, in his judgment, conditions are unsafe or unfavorable; if at any specific time he feels he is not in proper physical or mental condition for diving; or if, by diving, he would violate the dictates of his training or these regulations. The conditions and reasons for refusing to dive may be required to be documented. If requested, the incident will be reviewed by the Unit Director with the Unit Diving Officer and diver, and appropriate action may be taken. Any action resulting from this review may be appealed to the NOAA Diving Safety Board."

Sanctions: Violation of any of the applicable regulations may result in suspension of a diver's certification.

NOTE: In his letter to the Commission, the Director of Personnel, Department of Commerce, stated:

> In future years there may be some use of human subjects in tests of decompression or in experimental excursions for saturation of great depths; NOAA officials are considering adoption or modification of HEW or NAVY Human Use Rules for such research efforts, depending on the circumstances of each project.

DEPARTMENT OF DEFENSE

I. Army

The Army conducts and supports extensive biomedical and behavioral research involving human subjects, including basic research and clinical investigations.

Authority: U.S. Army Regulation 70-25 (31 July 1974); U.S. Army Medical Research and Development Command Regulation 70-25 (15 September 1976); Army Regulation 40-7 (4 April 1975); Army Regulation 40-38 (amended 1 September 1975); Office of the Surgeon General Regulation 15-2 (1 March 1976); and Memorandum of Understanding Between the Food and Drug Administration (FDA) and the Department of Defense (39 Federal Register 41570, November 27, 1974).

Applicability: Army Regulation 70-25 is applicable world-wide to intramural research wherever human volunteers are used as subjects. Army Medical Research and Development Command Regulation 70-25 is applicable world-wide to all intramural research and to research supported by Army grants and contracts, regardless of Army appropriation source. Regulation 40-7 applies to the investigational use of drugs and the use of Schedule I controlled drug substances whether such use occurs intramurally or by grant or contract. The Memorandum of Understanding Between the Food and Drug Administration and the Department of Defense applies to clinical investigations involving drugs that are classified for reasons of national security, and waives the requirement to file a formal "Claim for Exemption" otherwise imposed by FDA.* Research conducted or supported

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* In an enclosure to a letter to the Commission (28 November 1977), Gerald P. Dinneen, Principal Deputy to the Under Secretary for Research and Engineering, reports that the waiver provision of the Memorandum of Understanding has never been invoked by the Department of Defense.

by Army Intelligence is governed by the directives of the Intelligence Community (see page 82).

Review Procedures: The Army adopts the review procedures set forth in the DHEW regulations (45 CFR 46). Medical centers, grantees or contractors may utilize an Institutional Review Board with an approved assurance on file at DHEW, or they may establish an IRB that complies with the provisions of DHEW regulations and submit assurance of such compliance to the Army. Committees established to review intramural research must include, whenever possible, at least one lawyer and one clergyman. Intramural research is reviewed by local committees prior to submission to the Human Use Review Office in Washington, just as extramural research is reviewed by IRBs.

A Human Use Review Office, under the direction of the Assistant Surgeon General for Research Development, is the central Army processing point for all extramural and intramural research involving human subjects. The staff includes two pharmacists and a biostatistician. Additional outside review and advice may be sought, including supervision of the review by a physician.

Local commanders and the Inspector General are responsible for determining compliance of medical hospitals with directives from the Surgeon General; yearly site visits by Headquarters personnel ensure compliance of research laboratories. Annual reports must be submitted to the Human Use Review Office.

All protocols (except those deemed to be of low risk by the Human Use Re-

view Office)* are reviewed by a Human Subject Review Board. This board is composed of the Assistant Surgeon General for Research and Development, or his designee; seven consultants (expert in medicine, surgery, pharmacy, behavioral science, preventive medicine, allied medical sciences, and infectious disease); a chaplain; an attorney; and two community representatives. The board's recommendations for approval or disapproval (including any dissenting opinions) are forwarded to the Surgeon General who makes the final decision regarding each protocol.

Although most of the intramural research involving human subjects is conducted either in Army hospitals or in Army research laboratories, the regulations are applicable to all components of the Army. The Surgeon General has encouraged all agencies to construe the language of the regulations broadly, to include, for example, tests of new uniforms, vehicles and other equipment. Tests from any Army component that may expose human subjects to risk are reviewed by the Human Use Review Office and are processed in the same manner as research conducted under the auspices of the Medical Research and Development Command.

Review Standards: The Army adopts the review standards of the DHEW regulations. In addition to meeting such standards, all studies conducted or supported by the Army must meet scientific standards including: (1) use of the minimum number of human subjects necessary to achieve the required results; (2) perfor-

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* Studies deemed to be of low risk include analysis of hair, nail clippings, or deciduous teeth; collection of external excretions; recording of data by physical sensors applied superficially (EEG, EKG); and collection of no more than 450 ml. of blood within a six week period from subjects who are over 18 years of age and not anemic.

mance of appropriate laboratory and animal studies prior to involving human subjects; (3) avoidance of all unnecessary physical and mental discomfort; (4) proper preparations and adequate facilities to handle any foreseeable injuries; and (5) appropriate qualifications of principal investigators and those assisting in the research.

Consent Provisions: Provisions governing informed consent are those of the DHEW regulations, supplemented as follows. Consent forms must be in non-technical language so that they can be clearly understood by a subject who has no particular familiarity with medical terminology. Consent procedures must be witnessed. Provisions must normally be made for debriefing subjects following their participation in research; this is mandatory for research involving deception. Additional provisions are made for consent to research involving special subjects, as described below.

Special Subjects: Special protections and restrictions apply to research involving children, prisoners,* the institutionalized mentally infirm and mentally disabled subjects, including: (1) limitation of research to projects that either will benefit the subjects directly or cannot be conducted on any other subject population; (2) requirement for consent of children and mentally incompetent subjects, in addition to the consent of a legal guardian, when such subjects are able to express an opinion regarding their participation in research; (3) adequate living conditions, employment opportunities and medical care in any prison proposed as a research site; and (4) a site visit by a senior medical

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* The Assistant Surgeon General for Research and Development has written the Commission (November 28, 1977) that by current policy, prisoners and others with restricted civil liberties are not regarded as acceptable subjects of research.

officer and a member of the Army's legal staff to any prison or mental institution proposed as a research site. Prisoners of war may not be used as research subjects under any circumstances.

Additional Provisions: The regulations provide that civilian or military volunteers may be treated for research-related injuries in Army medical facilities and that military personnel are eligible for workman's compensation.

Research conducted abroad must comply with Army regulations as well as with all laws and customs of the country in which the research will be conducted. If, in exceptional circumstances, the laws or customs of the country involved would render a particular provision of Army regulations unacceptable, a waiver may be granted by U.S. Army Medical Research and Development Command Headquarters following a site visit by a senior medical officer and a member of the legal staff.

Sanctions: No provision is made for sanctions in the case of noncompliance.

II. Navy

The Navy conducts and supports biomedical and behavioral research related to basic factors underlying health and disease, effects of environmental stress, methods for studying biological systems and for diagnosing, treating and preventing disease or injury, basic psychological functions, psychological response to stress, and group behavior.

A. Intramural Research

Authority: Secretary of the Navy Instruction 3900.39 (28 April 1969 under revision); Bureau of Medicine and Surgery Instructions 6000.4B (15 January 1975), 3900.3B (1 May 1969), and 3900.6 (2 April 1976); and

Memorandum of Understanding Between the Food and Drug Administration and the Department of Defense (39 Federal Register 41570, November 29, 1974).*

Applicability: Secretary of Navy Instruction 3900.39 applies to the use of human volunteers in research, development, test and evaluation activities. Bureau of Medicine Instruction 3900.3B applies to biomedical and behavioral research conducted by the Navy Bureau of Medicine and Surgery (intramural). Instruction 3900.6 applies to medical research "performed at BUMED-managed activities irrespective of the source of funding support" if such research entails risk to subjects as a result of their participation. Instruction 6000.4B applies to the intramural Clinical Investigation Program conducted at regional Navy medical centers with the exception of "those research proposals that are unique to the operational mission of the Navy and Marine Corps (militarily relevant), which may be approved and supported through the Director of Defense Research and Engineering." The Memorandum of Understanding Between the Food and Drug Administration and the Department of Defense applies to clinical investigations involving drugs that are classified for reasons of national security, and exempts such research from the filing of a formal "Claim for Exemption" with FDA.**

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* The documents reviewed refer to additional documents, copies of which were not provided: SECNAVINST 3900.32A (6 August 1968); ONRINST 3900.24A (19 Sept. 1968); MANMED Chapter 20; DOD Directive 6000.4 (7 April 1971); BUMEDINST 6320.31 series; BUMEDINST 6710.49D.

** Defense Department reports that this exemption provision has never been invoked.

Review Procedures: The Navy adopts the review procedures of DHEW regulations (45 CFR 46). Although Navy regulations refer to the 1971 Institutional Guide to DHEW Policy on Protection of Human Subjects, the review procedures required by the Navy are those of the current DHEW regulations. (The only substantive difference between the Guide and the regulations, on the matter of review procedures, is whether IRB review is required for all research involving human subjects, or only for research involving risk to human subjects. By requiring that all research involving human subjects be reviewed by an IRB, the Navy has adopted the standard of the current DHEW regulations.)

Clinical investigation studies are submitted from local medical departments, through the Regional Clinical Investigation Center, to the Director of Clinical Investigation, who serves under the Commanding Officer of the Naval Health Sciences Education and Training Command. Proposals must be reviewed for compliance with all applicable directives and approved by the Regional Clinical Investigation Center prior to submission (with a priority score) to the Health Sciences Education and Training Command for review, approval and funding. Annual progress reports are required, and changes in research personnel, objectives or funding requirements must be reported within a reasonable amount of time. Reports are also required when a project is terminated (explaining the reasons for termination) or when a project is completed.

Review Standards: The Navy adopts the review standards of the DHEW regulations. In addition to meeting such standards, all studies conducted or supported by the Navy must meet scientific standards including: (1) use

of the minimum number of human subjects necessary to achieve the required results; (2) performance of appropriate laboratory and animal studies prior to involving human subjects; (3) avoidance of all unnecessary physical and mental discomfort; (4) proper preparations and adequate facilities to handle any foreseeable injuries; and (5) appropriate qualifications of principal investigators and those assisting in the research. There must be no greater intrusion into the privacy of subjects than is absolutely necessary for the conduct of the study involved.

Consent Provisions: Provisions governing informed consent are those of the DHEW regulations, supplemented as follows. The subject must be made aware of the provisions of the Privacy Act of 1974 and an appropriate Privacy Act statement must be included in the consent form. In addition, consent forms must be signed by a witness who is not directly involved with the research.

Special Subjects: Prisoners, prisoners of war, or institutionalized mentally disabled persons may not be used as research subjects under any circumstances.

Additional Provisions: Medical or dental treatment, including hospitalization if necessary, must be provided to any subject who requires such treatment or hospitalization as a result of participation as soon as such need is recognized. The physician-in-charge must have consultants, available on short notice, who are competent to advise or assist with unexpected complications. Volunteers may not be included if they have any physical or mental disease that will make participation in the research more hazardous for them than for normal healthy persons.

Sanctions: There are no provisions for sanctions in the case of non-compliance.

B. Extramural Research

Authority: Code 600 Memorandum No. 97A (27 March 1974).

Applicability: The memorandum governs the use of human volunteer subjects in any contract with the Office of Naval Research.

Review Procedures: No provisions are made for the establishment of an Institutional Review Board or any comparable committee.

Review Standards: The contractor is responsible for ensuring that the research is conducted under the supervision of a qualified physician and that there are adequate safety equipment and medical facilities to protect the volunteer against the possibility of injury, disability or death. "Adequacy of the medical safety facilities, the supervision of the physician-in-charge, and of the consultants [must be] consistent with the standards of medical ethics as enunciated and practiced by the American Medical Association."

No procedures for implementing or monitoring the provisions of the memorandum are provided beyond insertion of the provisions in the contract.

Consent Provisions: The contractor is responsible for determining that the rights and welfare of subjects are adequately protected and that informed consent is "obtained by methods that are adequate and appropriate." The contractor is further responsible for assuring that volunteers are in-

formed of their right to withdraw or to withhold consent without prejudice, and that they are competent to give legally valid consent.

Additional Provisions: Contractors are responsible for ensuring that volunteers have no physical or mental disease that would make participation in research more hazardous for them than for normal volunteers.

Sanctions: There are no provisions for sanctions in the case of noncompliance.

III. Air Force

The Air Force conducts biomedical and behavioral research in Medical Service treatment and clinical investigation programs; it also conducts and supports research in the aerospace research and development program.

A. Clinical Investigation Program

Authority: Air Force Regulation 169-6 (4 November 1977); and Memorandum of Understanding Between the Department of Defense and the Food and Drug Administration (39 Federal Register 41570, November 29, 1974).

Applicability: These regulations apply to research involving the biological, behavioral or psychological study of persons, their bodies or their surroundings conducted by or in collaboration with Air Force Medical Service personnel. Applicability thus appears to be limited to intramural research. Such research is generally conducted in Air Force medical facilities and Air Force clinical research laboratories. Exceptions: (1) studies involving nonidentifiable data collection from medical records, passive observation, analysis of excreta, diagnostic, surgical, or autopsy

specimens; (2) treatment administered with the consent of the Director of Base Medical Services as a life-sustaining measure; and (3) the use of human volunteers in the Air Force Biotechnology Research, Development, Test and Evaluation Program (see Part B, below), provided the diagnostic and treatment procedures employed conform to accepted professional practice and all medications used are administered in a manner approved by the Food and Drug Administration. The Memorandum of Understanding Between the Food and Drug Administration and the Department of Defense applies to clinical investigations involving drugs that are classified for reasons of national security, and exempts such research from the filing of a formal "Claim for Exemption" to the FDA.*

Review Procedures: Review procedures are similar to those of DHEW regulations (45 CFR 46) with the following additions: Institutional Review Boards, chaired by a physician, must include at least three lay members, including at least one lawyer and one clergyman. A medical or dental officer (as appropriate) other than the investigator must be assigned responsibility for assuring proper conduct of the experiments and the professional care of volunteers. The physician or dental officer may terminate the study at any time.

The medical facility commander is responsible for establishing an Institutional Review Board (IRB), for approving or disapproving each proposal following the IRB's review, and for assuring compliance with appli-

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* Defense Department reports that this exemption provision has never been invoked.

cable Air Force regulations. He is also responsible for submitting approved proposals to the Air Force Surgeon General, and assuring that his approval is received before any investigation is initiated. He must submit progress reports to the Office of the Surgeon General every six months, and a final report of findings and conclusions upon completion or termination of each investigation.

A Clinical Investigation Committee, appointed by the Surgeon General, reviews and approves or disapproves all clinical research not involving the investigational use of drugs, and serves as the Review Board for proposals that do involve the investigational use of drugs. The Surgeon General makes final decisions regarding research involving the investigational use of drugs, and generally monitors the overall clinical investigation program of the Air Force.

Misadventures must be reported by the Director of Base Services directly to the Surgeon General. If the misadventure is serious, this must be reported by "electrical means" as quickly as possible, followed by a complete written narrative within 15 days.

Review Standards: Studies must meet the following standards: (1) safeguarding the rights and welfare of human subjects; (2) any risks to subjects outweighed by potential benefits in terms of medical advances; (3) use of the minimum number of volunteers consistent with the study objectives; (4) nature of the investigation must require participation of human subjects; (5) performance of preliminary tests with laboratory animals and human simulators, as far as possible; and (6) avoidance of unnecessary physical or mental discomfort.

Consent Provisions: Consent provisions generally follow the DHEW regulations (45 CFR 46) with the following additions. Consent forms must be signed by at least one witness as well as by the officer who advises the volunteer of possible consequences of participation in the research. The completed consent form must be filed in the volunteer's medical records.

Special Subjects: Minors and mentally disabled or institutionalized mentally infirm individuals may participate as subjects only if the nature of the research is such that no other subjects are suitable. Legally effective informed consent must be given by parents or a guardian, and the consent of a mentally disabled subject must also be obtained, when the subject is capable of comprehending what is proposed. Children should be given the right to refuse to participate "depending upon the circumstances" and, as they approach maturity, should be given an opportunity to consent, as well. It is recommended that the local Staff Judge Advocate be consulted regarding consent for the participation of children in research, since no hard and fast rules can be laid down. Prisoners may participate in research only if it concerns the diagnosis, treatment, prevention or etiology of the particular impairment with which the prisoner is afflicted, and there is a direct potential benefit to the prisoner.

Sanctions: There are no provisions for sanctions in the case of noncompliance.

B. Aerospace Research, Development, Test and Evaluation Studies Program

Authority: Air Force Regulation 169-xx (draft, has completed formal Air Staff coordination and is undergoing review by the Air Force Scientific Advisory Board).

Applicability: This draft regulation applies to both intramural and contract research and governs aerospace research, development, test and evaluation procedures in which human subjects are used and in which there is "inherent risk" of distress, pain, damage to health, physical or emotional injury, invasion of privacy, surrender of autonomy or death. Exceptions: (1) clinical, biomedical and behavioral research performed under the provisions of Air Force Regulation 169-6 (see Clinical Investigation Program, above); (2) research that involves exposure to occupational hazards such as encountered in flight training, jump training, handling of explosives; (3) human engineering portions of research involving only hazards encountered in normal military duty; and (4) experiments judged to be nonhazardous. To be judged nonhazardous, research must: (a) be conducted in a normal environment, free from safety hazards; (b) involve only the application of stimuli to the senses of sight, hearing, touch and smell at levels and durations commonly experienced and tolerated; and (c) involve neither unusual physical exertion nor application of unusual or harmful physical or chemical substances.

Review Procedures: The Air Force adopts the review procedures of DHEW regulations (45 CFR 46).

In addition, a Human Use Committee, established by the Surgeon General provides additional review of projects, as necessary, and reviews all applications for modification or waiver of regulatory requirements, and all reports of misadventures involving human subjects. This committee is composed of representatives of the staff offices of Research and Development, Personnel, the Surgeon General, the Judge Advocate General, the Inspector General and Chaplain. The Director of Professional Services, Office of the Surgeon General, serves as Chairman. He also reviews all proposals submitted by IRBs, determines whether review by the Air Force Human Use Committee is required, and notifies the Major Command of the organization submitting a proposal of its approval or disapproval.

Review Standards: The Air Force adopts the review standards of DHEW regulations. In addition to meeting such standards, all studies conducted or supported by the Air Force must meet scientific standards including: (1) use of the minimum number of human subjects necessary to achieve the required results; (2) performance of appropriate laboratory and animal studies prior to involving human subjects; (3) avoidance of all unnecessary physical and mental discomfort; (4) proper preparations and adequate facilities to handle any foreseeable injuries; and (5) appropriate qualifications of principal investigators and those assisting in the research. There must be no greater intrusion into the privacy of subjects than is absolutely necessary for the conduct of the study involved.

Consent Provisions: Generally, to give legally valid consent, subjects must be 21 years of age except in jurisdictions in which a lesser age is speci-

fied.* The Air Force adopts the consent provisions of DHEW regulations (45 CFR 46) with the following addition. Consent must be documented in writing by each volunteer in the presence of at least one witness who must also sign the consent form.

Special Subjects: "Participation of females as volunteer subjects is permitted only when there is reasonable assurance of no concomitant pregnancy which would place the fetus at risk and if methods adopted for contraception do not place the female subject at increased risk without complete disclosure to the female subject. Children, institutionalized mentally infirm persons, mentally disabled persons, and prisoners must not participate as human subjects in Department of the Air Force research projects."

Projects conducted outside the United States must comply with all laws and customs of the country in which the research will be conducted. In exceptional circumstances, when the laws or customs of the country indicate that certain provisions of the regulations would not be acceptable, special permission may be granted by the Surgeon General for a waiver. Only the Surgeon General may grant such a waiver.

Sanctions: No provision is made for sanctions in the case of non-compliance.

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* For active duty personnel participating in intramural studies, there is no minimum age requirement.

DEPARTMENT OF ENERGY (DOE)

(No description of research supported by DOE was provided.)

Authority: 10 CFR 745 (41 Federal Register 52434, November 30, 1976, as amended in 42 Federal Register 30492, June 15, 1977). (These regulations were issued by the Energy Research and Development Administration and continue in effect pursuant to Section 705(a) of the Department of Energy Organization Act. Authority: letter to the Commission (December 1, 1977) from James L. Liverman, Acting Assistant Secretary for Environment, DOE.)

Applicability: The regulations are applicable to Department of Energy (DOE) agreements including, but not limited to, contracts supporting research, development and related activities in which human subjects are involved. The regulations, therefore, apply only to extramural research. The requirements set forth in the regulations are applicable to research conducted outside the United States and its territories "to the maximum extent practicable as determined by the Administrator on a case-by-case basis, taking into account the relevant laws and practices of the foreign nation in which the activity will be conducted."

Review Procedures: DOE requires that IRBs be established in conformity with procedures set forth in DHEW regulations (45 CFR 46) but permits alternative methods of fulfilling the requirement. The DOE accepts an assurance approved by DHEW as documentation of such compliance, or alternatively, will negotiate an assurance directly with an institution receiving DOE support. DOE staff reviews assurances for general acceptability taking into account, among other pertinent factors, the adequacy of the proposed Institutional

Review Board in light of the anticipated scope of the applicant institution's activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution. No provision is made for agency review of individual research proposals.

Review Standards: DOE adopts the review standards set forth in DHEW regulations (45 CFR 46).

Consent Provisions: DOE adopts the consent provisions of DHEW regulations (45 CFR 46).

Sanctions: DOE adopts the sanctions of DHEW, namely, withholding or withdrawal of grant or contract funds if an investigator or institution fails materially to fulfill responsibilities for protection of human subjects.

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT (HUD)

The Department of Housing and Urban Development supports research involving human subjects in projects such as the Experimental Housing Allowance Program and programs related to reduction of the risk of lead poisoning.

Authority: There are no formal regulations or policies for the protection of human subjects in research supported by HUD. (Information was supplied in letters to the Commission by Charles J. Orlebeke (September 17, 1975), then Assistant Secretary for Policy Development and Research, and by Patricia M. Worthy (November 18, 1977), Deputy Assistant Secretary for Regulatory Functions.)

In her letter of November 18, 1977, the Deputy Assistant Secretary for Regulatory Affairs stated that HUD has "never sponsored any human subject or biomedical studies." It is clear, however, that projects such as the Experimental Housing Allowance Program constitute research with human subjects.

DEPARTMENT OF JUSTICE

I. Bureau of Prisons

The Bureau of Prisons conducts and supports research related to correctional programs.

Authority: Draft revision of Policy Statement 6110.1 (October 31, 1967), to be published in the Federal Register in Spring 1978; Policy Statement 37000.3 (June 10, 1977).

Applicability: The policy applies to "research activities undertaken by individuals or organizations either in or out of federal, state or local governments where the Bureau of Prisons assumes either a host or sponsorship role." No research involving medical experimentation or drug testing is permitted.

Review Procedures: Research proposals made at the institutional or regional level must be reviewed by a Research Committee prior to submission to the Bureau of Prisons Chief of Research. Suggested membership includes the warden or associate warden, research analyst, chief psychologist, a unit manager or department head, an inmate, a representative of the employees union and a representative of the community.

The Director of the Bureau of Prisons must approve all research projects. This authority may not be delegated. The Chief of Research sets the number and frequency of progress reports that will be required for each project, depending upon the nature of the research. At a minimum, reports must be submitted to the prison warden and forwarded to the Chief of Research of the Bureau of Prisons every six months.

Review Standards: Research proposals are reviewed for relevance to the mission and "collateral objectives" of the Bureau of Prisons, for potential benefits to mankind or advancement of knowledge, for professional standing of the investigator, and for assurance that the conduct of the research will not adversely affect Bureau of Prisons' programs or operations. Priority is given to projects holding promise for advancing knowledge and capability for treatment of offenders. The Bureau of Prisons is "guided by" the Nuremberg Code, and relies on the investigators to protect the "rights and lives" of subjects.

Consent Provisions: The Bureau of Prisons generally follows the consent provisions of DHEW regulations (45 CFR 46).

Additional Provisions: "Offering inmate incentives of a material nature seems inappropriate and are prohibited; however, soft drinks and snacks may be offered to subjects at the test setting."

Investigators must adhere to all requirements of the Privacy Act of 1974 and implementing regulations. They may not report information which can be used to identify an individual to any party other than to Bureau of Prisons research personnel without written consent of the subject. Further, no individual other than an employee of the Bureau of Prisons may have access to personally identifiable information without the written consent of the individual from whom the information was obtained, unless the information is already accessible to the general public.

Prospective investigators must also submit an assurance of compliance with the Civil Rights Act of 1964 and the appropriate regulations of the Department of Justice (28 CFR 42).

Sanctions: The Bureau of Prisons maintains the prerogative to suspend or terminate any project at any time if there is reason to believe that the project violates research policy or that continuation of the project will be detrimental to the inmate population or the functioning of the staff or program. Any suspected violations of law must be referred to the Office of General Counsel.

II. Law Enforcement Assistance Administration (LEAA)

> The Law Enforcement Assistance Administration supports research in crime prevention and in treatment of offenders through categorical grants to individual institutions and block grants to states.

Authority: There are no formal regulations or policies for the protection of human subjects in behavioral research; biomedical research is restricted by LEAA Guideline 6060.1A (June 18, 1974).

Applicability: Guideline 6060.1A applies to categorical grants funded through LEAA Central and regional offices, and block grants provided to states pursuant to the Omnibus Crime Control and Safe Streets Act of 1968.

Review Procedures: The Office of Administration must specifically approve in advance any medical research projects, after consultation with the Department of Health, Education, and Welfare.

Review Standards: LEAA funds may not be used to support (1) psychosurgery; (2) medical procedures which seek to modify behavior by aversion therapy, chemotherapy (except as part of routine clinical care) or physical therapy; or (3) projects involving medical research "except in limited types of programs generally

recognized and accepted as not involving physical or psychological risk to the patient, as specifically approved by the Office of Administration after consultation with and the advice of the Department of Health, Education, and Welfare." The guideline specifically does not prohibit programs of behavior modification involving environmental changes or social interaction.

Consent Provisions: There are no provisions governing informed consent.

Sanctions: There are no provisions for sanctions in the case of noncompliance.

DEPARTMENT OF STATE:

AGENCY FOR INTERNATIONAL DEVELOPMENT (A.I.D.)

The Agency for International Development supports research in a variety of fields including agriculture, rural and urban development, health, population, nutrition, education, economics, institutional and social development, and science technology.

Authority: Manual entitled Contract Program in Centrally Funded Research, issued by the Agency for International Development, January 1977.

Applicability: A.I.D. policy for the protection of human subjects applies to all grants, contracts or other awards for the support of research involving human subjects conducted both within and outside the United States.

Review Procedures: A.I.D. requires initial and continuing review and approval of each research project by "an appropriate committee of the applicant institution." A.I.D. reviews each institution's assurance for: (1) compliance with requirements for initial and continuing review, (2) adequacy of the institution's review committee structure, (3) its review procedures, and (4) the facilities and personnel available to protect the health and safety of human subjects. In addition, each institution must certify to A.I.D. for each proposal that its committee has reviewed and approved the proposed research. The Agency may submit research protocols involving human subjects to independent review by staff, consultants and advisory groups. Where applicable, A.I.D. also requires evidence of compliance with regulations of the Food and Drug Administration.

Review Standards: Review must assure that (a) the rights and welfare of the individuals involved are adequately protected, (b) the methods used to obtain informed consent are adequate and appropriate, and (c) the risks and the potential benefits of the investigation are assessed.

Consent Provisions: The consent procedures must be adequate and appropriate. For guidance A.I.D. refers to DHEW regulations (45 CFR 46).

Additional Provisions: Research conducted outside the United States must comply with all the above provisions and, in addition, conform to legal and other requirements governing human research in the country in which the research will be conducted. For guidance A.I.D. refers to DHEW regulations (45 CFR 46).

Sanctions: There are no provisions for sanctions in the case of noncompliance.

DEPARTMENT OF TRANSPORTATION (DOT)

Except as otherwise noted, information regarding DOT agencies was supplied to the Commission in a letter (November 24, 1975) from Admiral O.W. Siler, Commandant, U.S. Coast Guard, responding on behalf of all components in the Department of Transportation that conduct or support research involving human subjects. The information provided by Admiral Siler was amended (to reflect subsequent agency policies) in a letter (December 9, 1977) from Martin Convisser, Acting Assistant Secretary for Environment, Safety, and Consumer Affairs, DOT.

I. Office of the Secretary of Transportation

> Mr. Convisser reports that the Office of the Secretary is developing a Departmental order to provide uniform procedures for protecting human subjects of research conducted or supported by any component of the Department of Transportation.

II. Federal Aviation Administration (F.A.A.)

> The F.A.A. conducts and supports aeromedical research to study factors contributing to accidents, to establish aeromedical standards for airmen, to maintain fitness and performance of aviation personnel, and to improve the working procedures and environment of air traffic control personnel.

Authority: Order 9950.3A (December 6, 1974) - Medical Research Program Guide; letter to the Commission (July 25, 1975) from Stanley R. Mohler, then Chief, Aeromedical Applications Division, Office of Aviation Medicine. NOTE: A more comprehensive order governing research with human subjects is under development.

Applicability: Order 9950.3A applies to aeromedical research activities conducted intramurally under the auspices of the Civil Aeromedical Institute or supported by contract.

Review Procedures: The Office of Aviation Medicine reviews all research proposals for scientific merit, program and budget requirements, and to establish research priorities. All research must be approved by the Federal Air Surgeon, following technical review by the Research Task Review Panel which is composed of chiefs of various branches of the F.A.A. Aeromedical Division.

Review Standards: There is no provision for review relative to protection of human subjects. Dr. Mohler stated in his 1975 letter that: "We never undertake an experiment in which the likely outcome would be injury or death to a subject, and for each experiment with humans that would entail any kind of potential risk, a committee of scientists, including medical scientists, reviews the experiment. During the conduct of a potentially hazardous experiment, a physician is in the building on call, in case of a mishap."

III. Federal Highway Administration

> The Federal Highway Administration conducts and supports research to study reaction times, vehicular control responses, choice behaviors, and measures of alertness and performance.

Authority: There are no formal regulations or policies for the protection of human subjects in research conducted or supported by the Federal Highway Administration. (No biomedical research is conducted or supported.)

Staff investigations are performed principally by research psychologists "who are bound by the American Psychological Association's code of ethics for the conduct of experiments with human subjects," and work plans for contractor studies "are carefully reviewed to assure minimum risk to subjects of both traffic engineering studies and controlled experiments."

IV. National Highway Traffic Safety Administration (NHTSA)

> The Highway Traffic Safety Administration conducts biomedical and behavioral research on such topics as the effects of alcohol and other drugs on judgment and performance, methods to detect alcohol or drug ingestion, effects of stress on driving performance, factors in visibility, driver's education and training, and prevention of injuries during crashes.

Authority: NHTSA Order 700-1 (December 7, 1977); NHTSA Order 700-2 (September 7, 1976); and letter to the Commission (August 13, 1975) by Fred B. Benjamin, then Senior Research Physiologist, Office of Driver and Pedestrian Research.

Applicability: NHTSA Orders 700-1 and 700-2 are applicable to all intramural research and all contracts supporting research with human subjects.

Review Procedures: In any project involving human subjects, the contract technical manager (or, if intramural research, the investigator) is responsible for determining whether or not subjects will be at risk and, if so, for preparing a risk/benefit analysis. Such analysis must take into account: the extent of predictable risk, the extent of benefits to be derived from the program, the harm to society which might result from not conducting the proposed program, and "the ethics and standards which are acceptable to the societal segments having a stake in the human subjects experiments or the ethical guidelines to be established by the President's [sic] Commission for the Protection of Human Subjects of Biomedical and Behavioral Research." The approval of both the responsible Associate Administrator and the Chief Counsel is required for any project involving human subjects at risk, and review by the NHTSA Human Use Steering Panel may be requested by the Associate Administrator, prior to making his decision.

Once a contract proposal is approved by the Assistant Administrator and the Chief Counsel, it is referred to the contract technical manager and the Proposal Evaluation Committee for review of procedures for the protection of human subjects. Intramural research is reviewed by the NHTSA Human Use Steering Panel, which may also review contract proposals if requested by the Associate Administrator.

Review Standards: NHTSA adopts the review standards of DHEW regulations (45 CFR 46). In addition, review for the protection of human subjects includes consideration of whether subjects are given adequate physical and psychological evaluations or monitoring prior to their selection, during the experiments, and after completion of the research; whether there are trained medical personnel and adequate equipment for emergency treatment; whether risks are reduced as much as possible; whether there are alternate ways of obtaining the desired information; what the criteria are for selection of human subjects; whether compensation will be commensurate with the risk involved, but not so excessive as to constitute undue inducement; and whether there are adequate plans to ensure privacy and confidentiality according to the provisions of the Privacy Act of 1974.

Consent Provisions: NHTSA generally follows the consent provisions of DHEW regulations (45 CFR 46), with the following additions. It is suggested that subjects be given information regarding (1) medical compensation and/or liability insurance in force (together with any limits involved); (2) nature and extent of medical supervision and emergency procedures; and (3) reviews by the contractor's IRB.

Sanctions: No provisions are made for sanctions in the case of noncompliance.

V. Federal Railroad Administration

> The Federal Railroad Administration reports that it is supporting only one research project involving human subjects, a study on cab vigilance.

Authority: There are no formal regulations or policies for the protection of human subjects in research conducted or supported by the Federal Railroad Administration.

In one study (on cab vigilance) performed under contract at the Transportation Systems Center, the Federal Railroad Administration reports that certain professional guidelines (including DHEW regulations) "are used to insure the safety and privacy of the human subjects."

VI. U.S. Coast Guard

> The Coast Guard supports research relating to safety in both recreational and maritime vessels, emergency treatment for hypothermia, and the evaluation of safety procedures and equipment.

Authority: There are no formal regulations or policies for the protection of human subjects in research conducted or supported by the Coast Guard; however, the Coast Guard uses the provisions of DHEW regulations (45 CFR 46) as guidelines.

One contractor adheres to the policies of the American Psychological Association; volunteers are fully informed and must provide written consent prior to participation. No release from liability is contained in either the written or oral presentations.

DEPARTMENT OF THE TREASURY:

INTERNAL REVENUE SERVICE

The Internal Revenue Service conducts research related to personnel management, motivation and job performance, typically through questionnaire, interview and work-simulation methods.

Authority: There are no formal regulations or policies for the protection of human subjects in research conducted or supported by the Internal Revenue Service. (Information was supplied to the Commission in a letter (November 29, 1977) from Morris A. Simms, Director of Personnel, Department of the Treasury.)

Mr. Simms reports that personnel research follows the guidelines prescribed by the American Psychological Association in Ethical Principles in the Conduct of Research with Human Participants.

ENVIRONMENTAL PROTECTION AGENCY (EPA)

The Environmental Protection Agency conducts and supports research related to the effects of pollutants on human beings.

Authority: EPA Order 1000.17 (October 25, 1977); letter to the Commission (December 19, 1977) from Stephen J. Gage, Acting Administrator for Research and Development.

Applicability: Order 1000.17 applies to all intramural studies, grants, contracts, Public Law 480 projects, and other research with human subjects supported in whole or in part by EPA. Exceptions: Order 1000.17 does not apply to (1) opinion polls, questionnaires or the solicitation of information about past events; (2) the taking of blood, urine, mothers' milk, "nonviable fetus tissue" or human tissue samples; or (3) the conduct of any medical observations where such testing is not preceded or followed by purposeful exposure to chemicals, physical conditions or other environmental conditions being tested. EPA is developing orders to address (1) the acquisition of information and the collection of tissue or fluid samples (blood, urine and human milk) for use in epidemiologic studies, and (2) the conduct of research by industrial laboratories for the purpose of acquiring data required by EPA for product approval.

Review Procedures: EPA requires compliance with DHEW regulations (45 CFR 46) for the establishment of Institutional Review Boards, and further requires that grantees, contractors or other parties responsible for the conduct of research with human subjects have an approved general or special assurance on file at DHEW. Applications for an assurance may be made to DHEW through the EPA Deputy Administrator for Health and Ecological Effects.

Certification of IRB review and approval, and a description of the procedures to be used in obtaining informed consent (along with a copy of the consent form to be used), must be submitted to the EPA Deputy Assistant Administrator for Health and Ecological Effects for review and approval.

Review Standards: EPA requires compliance with the review standards of DHEW regulations (45 CFR 46). In addition, EPA will not support any research involving (1) risk of substantial or irreversible injury to a human subject, or (2) determining whether or not a substance is a carcinogen by testing on human subjects.

Consent Provisions: EPA requires compliance with the consent provisions of DHEW regulations (45 CFR 46) and with any subsequent modifications thereto.

Sanctions: The Deputy Assistant Administrator for Health and Ecological Effects may terminate a grant, contract or other agreement in the case of noncompliance with approved human testing procedures or if the Secretary, DHEW, withdraws his approval of the general or special assurance.

INTELLIGENCE COMMUNITY

The Intelligence Community has conducted and supported biomedical and behavioral research relating to the effects of drugs on behavior; methods for lie detection, stress detection and information gathering; hypnosis; motivation; effects of biologicals on human tissue; and methods of "surreptitious delivery" of biologicals.

NOTE: At the request of the National Foreign Intelligence Board, the Commission, in 1977, reviewed a draft directive governing research conducted or supported by components of the Intelligence Community. In a letter dated 23 December 1977, Walter Elder, Executive Secretary of the Board, reported that the directive reviewed by the Commission is undergoing substantial revision and is no longer current. He added that the newest draft, now undergoing review, "will adopt many of the provisions of the Department of Health, Education, and Welfare regulations (45 CFR 46), and will require agencies of the Intelligence Community to publish their own regulations." The revised directive should be available early in 1978. The following summary, based upon the 1977 draft, is included in this report for purposes of completeness and to indicate the general approach that is being taken by the Intelligence Community in this sensitive area.

Authority: Executive Order 11905 (18 February 1976); Draft Director of Central Intelligence Directive IC-77-4563 (17 May 1977); statement of Admiral Stansfield Turner, Director of Central Intelligence, before the Senate Select Committee on Intelligence (3 August 1977).

Applicability: The Executive Order applies to experimentation with drugs on human subjects conducted or supported by Intelligence Community agencies;

the draft Directive applies to all research conducted or supported by Intelligence Community agencies.

Review Procedures: In the draft directive, the Intelligence Community adopts the provisions of DHEW regulations (45 CFR 46), with the following addition. No more than half the members of an IRB may represent Intelligence Community organizations, even when all IRB members must have security clearance in order to review classified research.

Each component of the Intelligence Community must establish procedures to implement the directive. One requirement is the appointment of an "agency expert" who will be responsible for determining that Institutional Review Boards are established in compliance with the regulations, and who will also serve as the point of contact for subjects participating in intramural research. The resident expert must remain knowledgeable on matters pertaining to the protection of human subjects, and maintain contacts with the National Commission for the Protection of Human Subjects, the Department of Health, Education, and Welfare, and other appropriate federal agencies, soliciting guidance and consultation, as necessary, on specific proposals or general issues.

Review Standards: In the draft directive, the Intelligence Community adopts the review standards of DHEW regulations (45 CFR 46).

Consent Provisions: In the draft directive, the Intelligence Community adopts the provisions of DHEW regulations (45 CFR 46) with the following additions. Consent documents must be signed in the presence of a disinterested third party. In addition, when the research is of a classified nature, subjects may be required to sign an agreement not to disclose information regarding

the research to other members of the public, or they may be informed that the sponsor of the research prefers to remain anonymous. The subject must indicate willingness to participate under such conditions on the consent document. In no event, however, may security considerations "constitute a basis for contravening the informed consent requirements."

Special Subjects: When members of the military, U.S. government employees or employees of U.S. government contractors are enrolled as research subjects, "scrupulous attention shall be paid to ensure that no coercion is directed to the employee as a means of securing his or her participation. Data collected as a result of the employee participating in the research shall not be incorporated in subject's personal file." [Quotation from draft directive.]

Additional Provisions: In the draft directive, the Intelligence Community requires adherence not only to present DHEW regulations but also to any future DHEW regulations adopted pursuant to the recommendations of the National Commission for the Protection of Human Subjects.

Sanctions: Contract funds may be withdrawn in the case of noncompliance. No sanctions are provided in the case of noncompliance in research conducted within the Intelligence Community.

NATIONAL ACADEMY OF SCIENCES

The National Academy of Sciences occasionally conducts and supports biomedical and behavioral research involving human subjects. No description of such research was provided.

Authority: National Academy of Sciences Administrative Guide. (Additional information was supplied in a letter (September 25, 1975) by Philip Handler, President of the National Academy of Sciences.)

Applicability: The policy of the Academy is to require review by an IRB approved by DHEW for any research involving human subjects regardless of the potential source of support. This policy applies to all elements of the Academy complex (including the National Academy of Engineering, the Institute of Medicine, and the National Research Council).

Review Procedures: The Academy maintains an Institutional Review Board with an approved assurance on file at DHEW; thus the review procedures are those of DHEW regulations (45 CFR 46). The composition and procedures of the IRB are reviewed and approved by DHEW. All research proposals must be submitted to the President of the Academy with documentation of IRB review and approval.

Review Standards: Research is reviewed according to the provisions of DHEW regulations (45 CFR 46). The Academy specifically requires review of proposals involving the use of questionnaires, interviews, photographs, observations, taped records or stored data.

Consent Provisions: The IRB adheres to the consent provisions of DHEW regulations (45 CFR 46).

Sanctions: No sanctions in the case of noncompliance are provided by the Academy.

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION (NASA)

NASA conducts and supports biomedical and behavioral research in biotechnology, environmental biology, spacecraft simulation and medicine.

Authority: NASA Management Instruction 7100.8 (February 2, 1972); NASA Management Delegation AD 7100.9 (February 2, 1972); Ames Management Manual 7170-1 (as revised March 19, 1969); Ames Memorandum 74/200 (December 11, 1974); and Lyndon B. Johnson Space Center Management Instruction 7100.8A (March 29, 1977).

Applicability: NASA Management Instruction 7100.8 applies to "all human research conducted by NASA, by or under the direct supervision of a NASA officer or employee or an officer or employee detailed to NASA from another Government agency." It specifically does not apply to human research conducted under grant or contract or conducted "under a cooperative arrangement or agreement entered into by NASA and another Government agency, private entity, or non-Federal public entity." The Management Delegation empowers the Directors of each NASA field installation and, for NASA Headquarters, the NASA Director of Life Sciences, to authorize human research and to grant such waivers as are permitted under the NASA instructions. The Ames Management Manual applies NASA policy both to all human research conducted at the Ames Research Center Moffet Field, California, and, to all human research conducted for or on behalf of Ames by NASA contractors, subcontractors or grantees. The Lyndon B. Johnson Management Instruction applies to all human research conducted by, or under the direct supervision of officers or employees of the Johnson Space Center, Houston, Texas. It specifically does not apply to research conducted under

grant or contract or to research conducted under cooperative arrangement with government agencies or with private entities, but requires that grantees and contractors comply with the provisions of NASA general policy as set forth in NASA Management Instruction 7100.8.

Exceptions: Although neither of the two space centers make such exceptions, the NASA Management Instruction 7100.8 does not apply to research "as determined by the principal investigator,* that is (a) performed by or under the supervision of a physician (who may be the principal investigator) for the purpose of diagnosing, preventing, curing or alleviating disease in a particular human subject; (b) performed primarily for the human subject's benefit; and (c) recognized generally by the medical profession as proper." Nor does it apply to research involving no risk (as determined by the principal investigator)* or to (1) evaluative procedures authorized by the Civil Service Commission or by other government agencies to determine qualifications of job applicants or to determine the state of an employee's health; (2) research involving as subjects individuals who are specially trained for that occupation (e.g., using test pilots to evaluate air or space flight equipment); or (3) research involving NASA employees whose regular position description includes such tests or evaluative procedures.

Review Procedures: The NASA Office of Life Sciences neither conducts nor directly supports research involving human subjects. All such research is conducted under the auspices of the NASA field centers (primarily Ames and Johnson). Both Ames Research Center and the Johnson Space Center require (in their own

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* The investigator's determinations must be approved by "line management." (Letter dated November 16, 1977 from Robert A. Frosch, Administrator, NASA.)

management directives) that their intramural research be reviewed by a review board; they require only adherence to general NASA policy, however, for research that they support under contract. Thus it appears that the requirement for review by an Institutional Review Board applies only to intramural research conducted at one of the two research centers. The IRB at the Johnson center is chaired by the Deputy Director of Life Sciences and includes the heads of divisions of biomedical research, health services, safety, reliability, and quality assurance; and a representative of the Chief Counsel. Three ad hoc members may also be appointed by the Chairman. The composition of the review board at the Ames center as set forth in Ames Memorandum 74/200 includes six staff physicians or scientists and a personnel officer.

Research proposals must be approved by the installation's counsel's office, safety office and medical officer before being approved by the appropriate authorized NASA official (i.e., the Director of the Ames Research Center, the Deputy Director of Life Sciences at the Johnson Center, and the Director of Life Sciences at NASA Headquarters, respectively). At the Ames Center, the Director also signs each test participant's certification of medical acceptability forwarded by the physician conducting the medical examination. The authorized official must also be informed in the event of any injury, illness or disease that occurs to subjects, any change in the environment or in a subject's response that could lead to some medical disturbance, and any change in the research as described in the approved protocol.

Review Standards: Research involving human subjects is reviewed to determine that: (1) the importance of the research objective outweighs the risk to the subjects; (2) subjects will not be exposed unnecessarily to risk of

injury, discomfort or inconvenience; and (3) the subject or his representative will be compensated in the event the subject suffers loss, injury, illness, disease or death as a result of participating in the research. The review at the two research centers also assesses the scientific merit of the research, the competence of the investigators, and the adequacy of the facilities for the safe conduct of the research, and for treatment of injuries.

Consent Provisions: NASA consent provisions generally follow those of DHEW regulations (45 CFR 46), with the following modification. Subjects must be informed if, for any reason, withdrawal during the conduct of the research is not an option (because it would be "unwise, dangerous, or impossible"). In exceptional cases, waivers of the consent requirements may be granted by "the cognizant authorized NASA official" if such requirements are deemed "not to be necessary, for various reasons, to protect the subjects."

Special Subjects: The Ames Manual provides that no person who is a minor or who is without legal capacity to give his voluntary informed consent may be a subject of human research without the specific authorization, in writing, of the NASA Administrator. (No such provision appears in the other manuals.)

Additional Provisions: The Ames Research Center requires that all human subjects be examined by a physician, who has been informed of the nature of the proposed research, for a determination of fitness. Subjects must be re-examined at the conclusion of the research, and reports of the results of both the examinations must be forwarded to the Director of the research center.

Sanctions: There are no provisions for sanctions in the case of noncompliance.

NATIONAL SCIENCE FOUNDATION (NSF)

The National Science Foundation supports research involving human subjects primarily in the behavioral and social sciences and in education.

Authority: NSF Grant Policy Manual (October 1, 1977); letter (November 9, 1977) from Richard T. Louttit, Director, Division of Behavioral and Neural Sciences.

Applicability: The policy applies to research, development and related activities supported by NSF grants.

Review Procedures: NSF adopts DHEW provisions (45 CFR 46) for establishment of Institutional Review Boards (IRBs).

Review Standards: NSF grantees must comply with review standards of DHEW regulations (45 CFR 46)

Consent Provisions: NSF grantees must comply with the consent provisions set forth in DHEW regulations (45 CFR 46).

Special Subjects: NSF specifically applies its policy to research, development and related activities in which students are involved as subjects.

Sanctions: No provisions are made for sanctions in the case of noncompliance.

UNITED STATES INFORMATION AGENCY (USIA)

The agency supports media surveys and attitude research that is conducted abroad by contractors.

Authority: There are no formal regulations for the protection of human subjects of such research. (Information was supplied to the Commission in letters (September 29, 1975) by James Keogh, then Director, U.S. Information Agency, and (November 7, 1977) by Harold E. Engle, Acting Assistant Director, Office of Research.)

Mr. Engle writes that "it is the policy of USIA that in keeping with the need for objective results, contractors be required to assure the respondents their answers will be kept confidential."

VETERANS ADMINISTRATION (VA)

The Veterans Administration conducts biomedical and behavioral research in its hospitals, clinics and centers, and permits outside investigators to conduct such research at those facilities.

Authority: Veterans Administration Issue M-3, Chapter 1, Part 1, as modified by interim issue 10-75-8 (March 10, 1975); Circular 10-75-121 (June 19, 1975).

Applicability: The policy applies to the use of drugs and/or procedures for research purposes, including prosthetics research.

Review Procedures: The VA generally follows provisions in DHEW regulations (45 CFR 46) for establishment of Institutional Review Boards. Institutions already having established boards may utilize such boards providing the board conforms to, or exceeds, the requirements set forth by the VA.

The hospital or clinic director is responsible for assuring that the review board is free from undue pressures in discharging its obligations, and is also responsible for implementing the board's decisions. No recommendation of the review board may be modified or reversed, other than by the board itself. Any appeal must be made in writing to the Assistant Chief Medical Director for Research and Development with "sufficient detail and background to allow evaluation of the recommendation and its appeal."

Review Standards: The VA generally follows the review standards set forth in DHEW regulations (45 CFR 46).

Consent Provisions: The VA adopts the consent provisions of DHEW regulations (45 CFR 46) with the following additions. Subjects must sign each page of the information sheets in the consent form; but when the procedure is simple and the experiment is brief, several or all of the subjects may sign the same information sheets which are kept separate from the signed consent forms. The investigator may give subjects their own copies of the information sheets; but one copy of each sheet must be signed by the subject and retained by the investigator. In addition, investigators "must assure that the consent is given freely without threats, even by implication, without promises of unrealistic results, and without excessive material reward for participation."

Additional Provisions: "Experimental procedures must not be added surreptitiously to accepted clinical ones; so-called 'bootleg' or 'piggy-back' research is forbidden."

Sanctions: The Institutional Review Board must consider and recommend action in any instance in which it is claimed that a subject's rights were violated or the subject's safety unduly jeopardized during research. A written report of such findings and recommendations is forwarded to the hospital or clinic director who then decides what actions are necessary. Copies of the report, recommendations, and the director's decision are forwarded to the Assistant Chief Medical Director for Research and Development, to the administrative officer for research in the institution, and to the investigator.

SUMMARIES OF TESTIMONY AT IRB HEARINGS

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Diana Baumrind, Ph.D. (Psychologist, University of California at Berkeley) expressed concern over the present situation in which IRBs are responsible for interpreting ill-defined guidelines and tend to be overly restrictive of research. The vagueness of the guidelines leads to problems in three areas: the incentives that may properly be offered subjects to induce their participation and cooperation in research; secondary analyses that may not be covered in the original consent form; and the meaning of "social risk" to a group of which a subject is a member. Another problem area is the quality of IRB membership. The responsibilities of an IRB require that members have training and expertise in both scientific methodology and ethical philosophy. IRBs who lack this expertise often go beyond their competency by requiring changes in research design and by arbitrary resolutions of ethical disputes. Dr. Baumrind said that lay members particularly contribute to these problems and that IRBs tried to be protective of institutions rather than subjects. She expressed the need for clear delimitation of the functions of IRBs so that they do not move from subject protection to unwarranted intrusion into research design or even to censorship. She called for mechanisms to insure that the researcher is given due process, including access to an appeal procedure and to a complete record of IRB deliberations. She also called for uniform interpretation of DHEW regulations and noted that the elimination of review for secondary analyses of data would lessen the burdensome workload of IRBs. Finally, she recommended avoidance of paternalistic, patronizing treatment of subjects, and expressed the need for a distinction between persuasion and coercion of subjects.

Linda Beckman, Ph.D. (Psychologist, University of California Medical School, Los Angeles) described the review of a survey research project by the IRB at her institution. The Board decided that the act of sending an interviewer to a potential respondent's door, and sending an explanatory letter beforehand, constitutes harrassment and invasion of privacy. Dr. Beckman maintained that the act of asking subjects to participate in a survey does not constitute a risk, regardless of the method of contact used, although some risk may exist in situations where information about potential subjects might be transmitted unintentially to third parties. Another question raised by the IRB was whether husbands as well as wives should sign a consent form before the wives responded to questions about the husband. Dr. Beckman is concerned that different IRBs respond differently to survey research methodology. This variation in IRB response indicates the need for clearer federal guidelines for the protection of human subjects of social research. She recommended that at least a significant minority of review board members have expertise in the area of research that they are responsible for reviewing. If an institution has multiple IRBs, proposals should be referred to the IRB that has the appropriate expertise.

John A. Clausen, Ph.D. (Professor of Sociology, University of California, Berkeley) noted that the degree of risk and consequences of certain safeguards vary enormously in different types of research. He expressed particular concern about the effects of written consent requirements on the validity of social research that has minimal risk. In survey research involving systematic sampling techniques and personal

interviews of designated respondents, differential participation by various segments of the population leads to biased samples and possibly invalid conclusions. The requirement for signed consent forms may cause such results in survey research because individuals from different segments of the population, even if quite willing to be interviewed, vary in their willingness to sign a form presented by a stranger. Dr. Clausen, however, finds it appropriate to tell persons designated for interview in a given study what the study is about, how the data will be used, and how the confidentiality of the data will be maintained. He also pointed to the need for legal protection of the confidentiality of information provided to investigators by subjects.

Dale H. Cowan, M.D. (Chairman, Committee on Investigation in Humans, Cleveland Metropolitan General Hospital and Case Western Reserve University) addressed three issues. First, he argued that a requirement that IRBs review research activities on body fluid and tissues that are to be discarded creates a workload for investigators and IRBs that cannot be justified on the basis of providing safeguards to individuals or society. He stated that funding agencies (both federal and private) are now requiring copies of the committee approval and consent forms for such studies. Second, his committee has difficulty with the judgment, which must be forwarded to DHEW on form 596, of whether subjects are at risk in proposed research, particularly in studies which assess procedures or treatments already considered routine. The requirement that IRBs must certify that risk is either present or absent, with no gradations for degree of risk, would be even more of a problem if HEW

adopts a policy of denying funds for any project involving risk to children that is not beneficial to the individual subjects. As one of over 40 affilidated institutions in the Eastern Cooperative Oncology Group (ECOG), Dr. Cowan's institution participates in protocols designed to assess the effect of new drugs or new combinations of drugs in the treatment of cancers of every organ system. During the preparation of such protocols, they are reviewed and re-reviewed by numerous committees of the ECOG including a disease-oriented committee, a drug evaluation committee, a radiotherapy and immunotherapy committee where indicated, the statistical office of the ECOG, a committee consisting of the principle investigators from each institution, and the Executive Committee of the group. In addition, each protocol is reviewed by several branches of the National Cancer Institute. Finally, after this exhaustive evaluation, the protocols are presented to the entire membership for its consideration. In addition, Dr. Cowan reviews the information provided in the protocols to ascertain that the performance of the studies is ethically justified and that the recommended consent forms provide the necessary information in a manner understandable to the non-physician. Dr. Cowan said it is unrealistic to expect a local IRB to make an informed judgment on the ethical propriety of such projects. Even the physicians on the IRB do not feel qualified to render an informed judgment; those at the institution who are capable of such judgments are generally involved with the investigation. Outside consultation is often not feasible since the few potential outside consultants are often unable or unwilling to devote the time required to make an independent judgment. The problem is even worse at satellite institutions working under the aegis

of the parent institution. Dr. Cowan urged that these practical difficulties be recognized and that consideration be given to the development of procedures on a national level that would be acceptable to HEW and compatible with the concept of local control of research activities.

Ms. Jane Crisler and Wallace J. Gingerich, Ph.D. (Institutional Review Board, University of Wisconsin, Milwaukee) indicated that the IRB is a workable and effective mechanism, but needs clarification of the definition of a human subject (particularly in relation to teaching and training activities), requirements for informed consent, and the relationship of informed consent to other safeguards for subjects. Present regulations make it diffiult for IRBs to deal with evaluative research carried out in connection with various social service programs. Other problems include perceived infringements on academic freedom that may result from risk/benefit assessments by IRBs, costs associated with IRB activities, the need for more guidance from DHEW, and the need for flexible regulations in view of the wide variation in the types of research covered. Finally, they expressed the need for uniform requirements for all federal agencies. In a written statement included with their testimony, Ronald L. Heilman, Acting Director of the Management Research Center at the University of Wisconsin, Milwaukee, discussed the particular problems raised by the application of present regulations to survey research. The informed consent procedures developed for biomedical research seem inappropriate and may have a serious effect on the validity of survey research.

Clarence Dennis, M.D., Ph.D. (President, National Society for Medical Research, and Emeritus Professor, Downstate Medical Center, New York) recognized the need for Institutional Review Boards, and also stressed the need for the research experience in the education of medical practitioners. Dr. Dennis expressed the view that overly detailed informed consent requirements pose obstacles to the conduct of research and are of questionable use in protecting subjects. He opposed the informed consent requirement for studies on blood, surgical specimens, other tissues, X-rays, and records, when these have been obtained in the course of routine care. Dr. Dennis concluded by recommending that regulation of research be given thoughtful reconsideration to avoid retarding development of new medical knowledge and improvements in the delivery of medical care.

Carol A. Distasio, R.N., M.S. (Research Assistant Professor, University of Maryland, Baltimore) recounted her experience with the IRBs that reviewed her project, "A Multigenerational Study of Families of Opiate Addicts." Because the study involved several institutions, five IRBs reviewed the proposal. The time required for approval by each IRB ranged from 3 months up to 12 months. This was costly in time, money, case-finding and data collection, and interfered seriously with the projected research schedule. Among the benefits of IRB review were advice on the development of a system of double coding to increase the protection of confidentiality of the data, and advice regarding the availability of "Grants of Confidentiality" under the Federal Comprehensive Drug Abuse Prevention and Control Act of 1970, of which the investigator

had been unaware. She suggested that IRBs schedule enough meetings to review a proposal within a reasonable amount of time. Concerns and conflicts should be communicated directly to the investigator who should have an opportunity of appearing before the IRB and IRB membership should be racially and sexually representive of the community the institution serves.

Leon Gordis, M.D., Dr. P.H. (Committee on Human Volunteers, Johns Hopkins University School of Hygiene and Public Health) noted that the Commission had not heard directly from representative of schools of public health, in which research is inherently multidisciplinary and frequently has an international dimension. Dr. Gordis' committee supports the institutional review board system as the best mechanism for monitoring research activities and assuring that the rights of individuals and of society are protected. Dr. Gordis expressed the need for procedural flexibility in reviewing international research. For example, informed consent procedures must be adapted to the culture of the country in which the research will be performed. Another problem area is research on minors, particularly mature minors, and studies of families which contain young children. Distinctions must be made between the need for parental consent for serious research risks such as surgical procedures, versus the need for parental consent for mature minors for venipuncture, interview, or similar low risk research procedures. A third problem of particular importance to epidemiology is that of access to medical records. Dr. Gordis stressed that individually identifiable information is essential for conducting epidemiologic studies and that

such research would be virtually impossible to conduct if patient consent were required for access to medical records. Dr. Gordis recommended that for epidemiologic research IRBs review the investigator's statement that medical records must be used as sources of information and that individuals must be identified. The IRB should ensure that no unnecessary invasion of privacy will take place and that adequate safeguards will be provided for the confidential handling of data. A fourth problem area is confidentiality of research records. Dr. Gordis stated that the IRB should play a role in assuring that investigators have adequate procedures for physically protecting data from disclosure and strongly suggested the need for legislation to protect research data from subpoena. Finally, Dr. Gordis pointed to problems regarding the staffing and cost of IRBs, the need to compensate non-university members, the lack of clarity about whom non-university members should represent, and the question of whether committees composed of colleagues of investigators are able to enforce IRB decisions. In conclusion, however, he emphasized that the IRB provides the ideal mechanism for implementing most recommendations for protection of human subjects, that they are the least bureaucratic and most effective way of doing so, and that local review at the institution where the research is carried out is the best way of making many of the assessments and decisions necessitated by the Commission's recommendations.

Thomas R. Hendrix, M.D. (Professor of Medicine, Johns Hopkins University School of Medicine representing the Association of American Medical Colleges.) Dr. Hendrix stated that local IRB review of

research provides the best protection of human subjects and that a centralized review process would lose the most desirable features of the present system. IRBs are familiar with the strengths and weaknesses of investigators in their institutions, they are acquainted with the characteristics of the patient populations from which subjects are drawn, and they heighten the investigator's sensitivities to the issues of human experimentation by requiring an explanation of the risks and benefits of proposed research. They also assure that the consent form (a) is written in language that is readily understood by the subjects, (b) clearly explains the purpose and importance as well as risks and discomforts of the research, and (c) affirms that the subject is under no obligation to participate in the studies. He stated that the success of any system for the protection of human subjects in biomedical research can be measured by the experience of the subjects, whether they feel a part of the experiment and comfortable in the protection being given them and others involved in the research. Close personal monitoring of the interaction between investigator and subject provides the best assurance that human subjects are fully protected. IRBs, however, have not been adequately appreciated in the academic committee's in which they reside, and they are in need of additional administrative and fiscal support. Dr. Hendrix suggested developing educational programs to inform the institution and the public about the work of the IRB and to train other clinical investigators for future service on IRBs.

Jerry W. Higgins, Ph.D. (Department of Psychology, University of California, Santa Barbara) called attention to several problems faced by research psychologists in their relationship to IRBs. He questioned the need for informed consent in studies in which subjects are observed in their natural environment, in which their awareness of being studied would produce changes in the behavior under study, and in which there is no risk to subjects. He also pointed out that in some psychological research, a request to sign a consent form may conflict with assurances of confidentiality; he suggested that verbal consent should be sufficient in such studies, when there is no perceptible risk. He also suggested that in studies that have no risk and that involve institutional populations whose ability to give voluntary consent may be questioned, the consent of a responsible official, such as a school principal or hospital administrator, should be sufficient. Finally, without questioning the importance of protection of human subjects, Dr. Higgins argued that the integrity of legitimate, no-risk psychological research is especially vulnerable under the current regulatory system and needs protection as well.

Professor Howard Higman (Department of Sociology, University of Colorado, Boulder) testified that he had been asked by the Chancellor of the University of Colorado to attempt to adjudicate an impending conflict between faculty in the humanistic and social sciences and the Human Research Committee (HRC) which had issued a memorandum stating that "every experiment involving human subjects (including questionnaires, surveys, unobtrusive observation experiments, and the use of public

information) must be reviewed." A committee was formed for the "Reconciliation of Academic Freedom and Public Law 93-348." One subcommittee concluded that a basis exists for a test of the constitutionality of PL 93-348, particularly on First Amendment grounds. Another subcommittee collected reports of 36 individual conflicts between professors and the HRC, and concluded that the regulations do not fit certain research. The concept of informed consent is not relevant, for example, in observation and surveys, and some consent rules are inapplicable in studies of preliterate populations. They recommend that "human subject" be defined as "a person who is under the immediate control of and whose behavior is being modified by the commands of a research investigator." This would exclude research involving questionnaires and surveys, unobtrusive observations, and public records. While Professor Higman believes that certain problems are traceable to PL 93-348 and the DHEW Regulations, other problems have resulted from local interpretations. He concluded by saying that the Committee for Reconciliation of Academic Freedom and PL 93-348 did not find any situations at the University of Colorado that would warrant the stringent procedures of the HRC.

Julien I. E. Hoffman, M.D. (Professor of Pediatrics and Member of the Cardiovascular Research Institute, University of California, San Francisco) based his testimony on his experience as a member and chairperson of the University's Committee on Human Research. After noting the usefulness of IRBs in protecting subjects and improving the quality of research, he identified several problems with the current regulatory system. The review process sometimes lasts two to three months, which is a problem when the study involves the diagnosis or treatment of sick

people. Another problem is the tendency of IRBs to over-emphasize relatively minor risks on consent forms or to include information about standard tests with which subjects are familiar. The requirement for annual re-submissions of research projects is too inflexible; not all projects need such review. He suggested that full protocol and consent forms should not be required for minor studies done in the course of clinical diagnostic or therapeutic studies, as when residual blood in a syringe or a piece of fat removed in surgery is used for research purposes. Dr. Hoffman believes that changes dealing with these problems would produce greater compliance with the regulations. Dr. Hoffman expressed concern that present regulations do not require adequate monitoring of the conduct of research. He recommended a study to determine whether the monitoring of the conduct of research would justify the investment of people, time, and money that would be required. Dr. Hoffman also stated that different materials must be included and different formats used when the same proposal is submitted to a funding agency, an institutional clinical research center, and an IRB. While local administrative actions could help with this problem, he urged the Commission to recommend a uniform method of presentation of proposals. Finally, Dr. Hoffman suggested that there is a useful role for a national advisory board in establishing communication among IRBs, defining broad guidelines for common problems, and resolving conflicts between IRBs and funding agency review groups.

Walter T. Hughes, M.D. (Chairman, Clinical Trials Committee, St. Jude Children's Research Hospital) offered support for the IRB system as a means both to protect the rights of human subjects and to foster research

of high quality. The advantages of local review include increased awareness of opportunities for collaboration, a view of the relationship of a project to other projects at the institution, and the ability to request the appearance of an investigator before the IRB to discuss proposed research. Dr. Hughes advocated the need for guidelines, rather than rules and regulations, to serve as an operational basis for IRB deliberations. Efforts are needed at three levels to prepare IRB members and investigators for their roles as protectors of human rights and advocates for the advancement of health and welfare. First, there is a need for self-education through published materials. Second, IRBs need to develop detailed operating guidelines to deal with the research activities at their institutions. Third, guidance from the national level must be in terms understandable to all members of a multidisciplinary IRB. Regarding the issue of consent in research involving sick children, Dr. Hughes spoke of the need for the investigator/physician to work with the family to determine the information that will be disclosed to the child.

Ada Jacox, Ph.D., R.N. (Chairperson, Commission on Nursing Research, American Nurses Association, and Associate Dean for Research and Doctoral Programs Development, School of Nursing, University of Colorado). Dr. Jacox observed that as the number of nurses conducting clinical nursing research has grown, so have reports of difficulties in getting proposals approved by review committees. Some problems are due to more stringent policies regarding human subjects and are common to all health researchers. However, she believes that many problems are attributable to the way IRBs are constituted and the orientation of IRB members. The biomedical science

orientation of IRBs creates powerful pressure to encourage research designs that are experimental rather than non-experimental in nature. Furthermore, the traditional viewpoint that health and illness research means biomedical research and that clinical research is done only by physicians, creates many misunderstandings between nurse investigators and reviewers. When proposals are submitted that do not fall into the category of experimentally designed research and when they are focused primarily on the study of psychosocial behavior, the approval process often becomes extended and frequently the proposal is disapproved. A major part of this misunderstanding comes from the inherent differences between studying disease treatment and studying health care. An essentially biological view of illness does not adequately take into account the interaction between biological and behavioral science that is needed in the study of health care. Nursing research often involves the use of questionnaires, surveys, analyses of census and demographic data, psychological tests, and personality inventories which rarely involve physical risk but are essential to the proper understanding of health care facilities and the effect of their organizational structure.

Dr. Jacox recommended that the composition of all IRBs reflect adequately the various disciplines involved in the proposals under review. Nursing, with a unique methodology that usually involves more than one discipline, must be among those represented.

Paul Kay, Ph.D. (Chairman, Committee for the Protection of Human Subjects, University of California at Berkeley) testified against the

current regulatory requirement that the level of risk in every project be formally determined by the full IRB, arguing that this function should be decentralized. Current regulations seem to assume that a large proportion of proposals pose substantial risk, when in reality well over half of the IRB's time is spent on processing the 99% of submissions that pose zero or minimal risk to human beings. Dr. Kay recommended that institutions be allowed to set up a system of decentralized committees to (a) determine whether the level of risk is greater or less than minimal, and (b) administer the projects found to pose no more than minimal risk. Projects with more than minimal risk would be forwarded to the central IRB for review. Dr. Kay also expressed strong concern about a possible discrepancy between the intended effect and actual effect of written consent procedures. He contends that the act of signing one's name to an official, permission-granting document creates in the majority of subjects the belief that by so signing they have formally obligated themselves to participate. There are many reports of prospective subjects hesitating or refusing to sign consent forms, though willing to participate in an experiment, because they fear that the signature would entail some further obligation. Dr. Kay recommended that the Commission conduct systematic empirical research to investigate possible coercive effects arising from the use of consent forms.

Charles A. Kiesler, Ph.D. (Executive Officer, American Psychological Association) identified three areas that should be exempted from IRB review: the development of new teaching techniques by teachers, laboratory exercises conducted as course assignments, and most program evaluation

projects. IRBs should be concerned about whether subjects are given adequate information about research procedures and the potential risks and benefits of participation, and they should be concerned about whether subjects consent is voluntary. However, IRBs should not be concerned about whether the risks to subjects can be justified by the scientific merit of the research, because they are usually not qualified to make those judgments. He urged the creation of IRBs on the basis of general scientific discipline, with the addition of perspectives from other disciplines and non-scientist members of the community to ensure adequate review.

William Konnert, Ed.D. (Chairperson of Institutional Review Board, University of Tennessee, Knoxville) noted that a number of federal agencies are developing procedures and requirements for protection of human subjects and urged that these efforts be channeled into the development of one set of guidelines. Dr. Konnert identified a number of matters that should be clarified. These include the circumstances under which a researcher should have access to personal files; how IRBs should apply risk/benefit policy; and whether IRBs should become involved in research design; whether the return of questionnaires can be construed as informed consent if the questionnaire has been accompanied by a cover letter with the relevant information; and the degree to which confidentiality can be assured against subpoena. He also called attention to the cost of reviewing and monitoring of research, and suggested that when research involving federal funds is reviewed, a portion of the overhead funds received by the institution could be diverted to underwrite

IRB activities. However, Dr. Konnert estimated that 75-80% of the research conducted at his institution is not supported by outside funding. Furthermore, several agencies, e.g., FDA, state that IRBs have a responsibility to provide a local mechanism for day-to-day monitoring of the study to insure the safety of the subjects and to assure that the study is adhering to any conditions imposed upon the sponsor and investigators. For an IRB to carry out its responsibilities effectively, a staff of considerable size would be required. The federal government should consider financing such a staff.

Richard L. Landau, M.D. (Chairman, Clinical Investigation Committee, Division of Biological Sciences, University of Chicago) indicated general satisfaction among IRB members with the present system, which provides assurance to the public and a constant reminder to investigators that high ethical standards are to be observed. He urged a continuation of the autonomy of local boards and an avoidance by IRBs of the role of policeman. His suggestions included elimination of review and consent requirements for studies with negligible risk, such as studies on hospital charts or on urine, blood, or tissue removed for purposes other than the research; the elimination of written consent requirements, except for normal persons volunteering for biomedical research; that, for subjects who understand the conditions and voluntary nature of research, participation be considered to be prima facia evidence that subjects do not consider their privacy to be violated; that observation of everyday life not be considered an infringement on privacy; and that information about identifiable

subjects not be made publicly available. He also indicated that his IRB is seriously concerned with issues of scientific design, that payment to subjects to undergo risk is acceptable, that the effect of lay members on an IRB is through their presence, and that it is useful to include statisticians on IRBs. On Dr. Landau's IRB, only a primary reviewer, chosen from among physician members, is expected to read each protocol.

Darwyn E. Linder, Ph.D. (Department of Psychology, Arizona State University) raised three problems he has encountered as chairperson of an IRB. First, difficult matters of definition and policy arise from the requirement that IRBs review research not supported by DHEW. Guidance is needed as to whether the IRB should review the wide range of research, training, instructional, and demonstration activities that occur within the university. A second problem area is in the requirement that IRB review applications for training grants, which frequently do not describe specific research projects. The third problem is the question of legal liability of IRB members if a human subject is injured in an approved project. Concern about this question may affect both the judgments of IRBs and the willingness of individuals to serve as members.

Mortimer B. Lipsett, M.D. (Director of the Clinical Center, National Institutes of Health) criticized the current requirement that all research be reviewed, regardless of whether there is any risk. Research protocols are required not only for potentially

hazardous drug studies, but also for procedures as essentially harmless as withdrawal of small amounts of blood, collection of urine and feces, even the collection of nail clippings. Like their colleagues elsewhere, Clinical Center investigators have been spending many hours writing and reviewing protocols for such procedures as the collection of stools from newborns, dental plaque from normal volunteers, and urine samples for biochemical analysis. The situation at the Clinical Center is particularly critical since it is a 540 bed hospital and all patients admitted are participating in research protocols. Dr. Lipsett estimates that a senior investigator spends an average of 5-10 hours writing a protocol and another half hour for the initial screening and review. Committee review takes about an additional half hour on non-controversial protocols, and final review and approval another hour. The annual review of single protocols at the Clinical Center takes a minimum of one hour of time for both the senior scientist and the reviewer. The three-year review process takes as much as 10 hours per protocol. He said that the review of relatively risk-free research dilutes the effectiveness of committee review and contributes to a feeling of cynicism about the review process: therefore, he recommended that procedures presenting essentially no risk be reviewed in the course of ward rounds and other routine medical care supervision, and that IRB review be reserved for procedures presenting risk. Dr. Lipsett submitted a list of procedures generally regarded as safe, so long as data are not released in an individually identifiable fashion, and

recommended that they be exempt from IRB review. He also suggested that consent should be obtained for risk-free procedures through a generalized consent form signed at the time of admission to a research program.

Andre Malecot, Ph.D. (Chairman, Committee on Activities Involving Human Subjects, University of California, Santa Barbara) noted that the general principles of the Nuremberg Code, Declaration of Helsinki, and DHEW regulations are understood, accepted, and necessary; but he suggests that escalation of complex rules and regulations and the resulting paper work is increasingly costly to institutions and investigators. Dr. Malecot suggested that a uniform federal policy is needed for protection of human subjects, and that institutions should be required to submit only one assurance of compliance. IRBs should be continually informed of court decisions and legal opinions regarding use of human subjects. Dr. Malecot also indicated that vague or general regulations, even if intended to give IRBs discretion in individual cases, have tended to be interpreted by IRBs in a restrictive manner. He suggested that the Commission review current regulations to eliminate those not pertinent to protection of human subjects (e.g., the review of research using outdated blood from a blood bank) and those whose ambiguity may place unintended constraints upon researchers. Finally, he called for the government to assist institutions with the costs of administering governmental regulations for the protection of human subjects.

Hans O. Mauksch, Ph.D. (Executive Officer, American Sociological Association) indicated that sociologists are deeply committed to the intent underlying the activities of the Commission and the procedures which have been established to protect human subjects. However, Dr. Mauksch suggested that some IRBs may infringe on the proper conduct of scholarly inquiry, particularly with respect to the social sciences. The sociologist typically uses methodologies for which the term "subject" is not considered appropriate because those studied ("participants," "respondents," or "informants) do not usually enter a domain in which the researcher is dominant. Dr. Mauksch expressed particular concern about qualitative research methodologies, such as participant observation or unstructured interviewing, in which the specific items of inquiry cannot be specified for prior review. For these reasons, Dr. Mauksch urged that guidelines for and procedures of IRBs be sufficiently flexible for applicability to the wide range of methodologies used in research. Regarding risk, Dr. Mauksch pointed out that much social research involves no risk, and the risk that exists may lie more with the competence of the researcher than with the topic to be studied or the methodology to be used. Dr. Mauksch also noted that the researcher's efforts to protect subjects by maintaining confidentiality may come into conflict with the law if the subjects' identity is sought in a court action. Regarding informed consent, Dr. Mauksch noted that the procedures are not easily transferrable to all research situations; not all segments of society equally understand consent forms nor are they equally willing to sign a piece of paper, even if they are willing to be interviewed.

The result of consent requirements may be the introduction of serious, systematic biases in social research and result in erroneous conclusions in studies in which social stratification is a major factor. He also noted that the obtaining of a signature on a consent form may serve to reduce protection of subjects by transferring to a bureaucratized procedure the researcher's sense of professional, scientific, and ethical obligation to subjects. Regarding the composition and function of review boards, Dr. Mauksch indicated that IRBs sometimes have difficulty distinguishing between their mission and extraneous concerns, such as the substance, theory, and methodology of the research. This is a particular problem when an IRB is composed largely by members of one dominant profession as are medical school review boards. In such situations, Dr. Mauksch contends that the methodology, and the areas of inquiry that characterize sociological research are frequently misunderstood. Sociologists submitting research to an IRB in a medical school are often called on to defend their discipline rather than to demonstrate that the respondents in their research have been accorded proper protection. A researcher is entitled to have his or her research judged by a board where at least one member understands and is sympathetic to the methodology and the thrust of the proposed project. Dr. Mauksch also emphasized that IRBs should be free of local pressures. For example, a proposal which would result in a sizable grant may be viewed favorably by the IRB if the institution is eager to obtain funds. On the other hand, a study of a controversial issue -- and sociologists frequently study such issues -- may be viewed with disfavor because it is feared that some embarrassment to the institution might result.

William W. May, Ph.D. (Associate Dean, Graduate School, University of Southern California, representing the Los Angeles County-USC Medical Center Institutional Review Board), urged the Commission to define levels of risk, and recommend different levels of review structures for research involving (a) minimal risk, (b) standard procedures, and (c) significant risk. The minimal risk category would include such procedures as obtaining single cord blood samples at birth, studying blood pressure and urine flow by use of accepted techniques during treatment of shock, examining tissue removed during indicated surgical procedures, gathering epidemiologic data, and comparing the efficacy of accepted modes of therapy. The "standard procedures" category would apply to accepted treatment modalities which become "research" only in certain contexts, for example, when assigned randomly. The additional review and consent requirements that are presently required in this context may not be in the patient's interests. Dr. May said that their IRB assigns approved projects to categories for ongoing review according to the level of risk involved. In Category A, proposals are reviewed at intervals of six months or less with mandatory reporting to the IRB; in Category B, proposals are reviewed at intervals of 6 to 12 months, with optional reporting to the IRB; in Category C, annual reports are required on a standard form; in Category D, there is no requirement for ongoing reports.

Ms. Diana McCann (Director, Human Subjects Office, University of Washington, Seattle) noted that the present regulatory system has worked well and that the past ten years have seen remarkable changes in the protection of human subjects. She offered a number of suggestions based

on the experience of her institution, which reviews approximately 1,000 proposals for research involving human subjects every year and which just created its fifth IRB. Though the various problems she identifies may seem minor when taken separately, she contends that they add up to a serious problem of inefficient use of scarce resources. First, present regulations are too broad in requiring IRB review (and certification of such review) of projects in which subjects are not at risk. There should be local discretion regarding the need for IRB review of research involving anonymous questionnaires or the use of residual human materials (if the identity of patients is not provided to the researchers). Second, Ms. McCann discussed problems regarding the appointment and service of IRB members. She suggested changing the quorum requirement from a majority of members to a fixed number (three, since the minimum IRB size is five members) to assist IRBs who have difficulty assembling quorums during summer months. She suggested the need for flexibility in the community member requirement for both practical reasons (e.g., finding suitable people who can donote eight hours a month) and theoretical reasons (e.g., such persons do not add significant diversity to a large university IRB). She also believes that the NIH Office for Protection from Research Risks (OPRR) presently requires institutions to provide more information than it can use about membership and appointment procedures. She suggested an accreditation plan under which an institution would provide information necessary to receive accreditation, and then would not ordinarily have to provide more information during the accreditation period (five years). Third, she identified problems in the relationship of institutions to federal agencies. These include the submission of the certification form (HEW 596)

with each original and follow-up application (2,000 a year from the University of Washington); the duplication of efforts by IRBs and funding agency review panels; the occasional contract for which funding is contingent upon following research designs that are unacceptable to the IRB; the need for an appeals mechanism to mediate disagreements between IRBs and funding agencies; and the need for a unified federal approach toward protection of human subjects, rather than a proliferation of regulations from different agencies. Finally, Ms. McCann called attention to the need for a mechanism to compensate human subjects who suffer adverse effects from participation in research.

Harold T. Meryman, M.D. (Chairman, Committee for the Protection of Human Subjects, American National Red Cross) suggested that projects in which the only human use involves blood or blood products obtained from routine blood donors should be exempt from review; that multiple reviews of collaborative projects should be eliminated except those in which local monitoring is advisable; and that if no change has been made in protocol and no adverse reactions have occured among subjects the annual review of an ongoing project should not have to take place in a convened IRB meeting. Dr. Meryman also discussed problems arising in research involving collaborators in foreign countries. While it is essential that an IRB in the United States determine that the risks of a study are acceptable, serious problems result from the imposition on other countries of consent requirements appropriate to this country. A review board in each country should accept responsibility for protection of subjects' rights, consistent with the laws and customs of that

country. A foreign collaborator and his review board should outline proposed procedures for protecting the rights of subjects, and the cognizant IRB in this country should have the option of accepting those procedures, even if they differ from those required by DHEW regulations, so long as basic human rights are protected.

Mr. Allen C. Moore (Director of Research Administration, Case Western Reserve University) objected to section 46.113 of DHEW regulations (45 CFR 46) which requires that applications and proposals lacking definite plans for the involvement of human subjects be reviewed and approved. A system is needed to allow a project director, using a general institutional research grant, to make a commitment to furnish the IRB with specific protocols as they are developed. Dr. Moore also suggested eliminating HEW Form 596, the certification for protection of human subjects which accompanies the submission of research proposals to DHEW, because the form goes beyond the requirements of the regulations and the needs of the government; it includes information which is the primary concern of the IRB and thereby casts doubt on the validity of DHEW's acceptance of the general assurance. Dr. Moore would prefer a system of site-visit audits to assure the adequacy of an IRB rather than a practice of conducting subsequent reviews of proposals approved by IRBs.

Virginia Olesen, Ph.D. (Professor of Sociology, School of Nursing, University of California, San Francisco) discussed the concerns of sociologists and anthropologists who do qualitative social research or

field work, where the goal is to understand the pattern of meaning and relationships in a group rather than predicting or measuring; thus, the work is relatively unbounded in time and space. The social relationships between researchers and participants in field work differ from those of researchers and subjects in a medical experiment. These differences have implications for informed consent and for evaluating risks and benefits. Field work poses the possibility of greater information flow from the participant to the researcher, as well as greater risk because more personal information is known. But field work also has greater potential for participant control of the researcher, than does biomedical research. Consent in the field work setting is a continual process of dialogue between the field worker and participants, with participants having available all of the interpersonal strategies which are part of the human repetoire for controlling and sanctioning others. Dr. Olesen argues that there is a human paradigm of equality and reciprocity in the field work case which is not at issue in the biomedical situation, where researchers frequently are in powerful professional positions, or where the research situation is a brief one-way interaction with instructions flowing from the researcher to the subject. Participants in field work may risk embarassment, anxiety, or stress in interactions with the researcher, but they almost always have the chance to modulate the interaction. In some situations, however, the participant may not be able to exercise the controls normally used to deflect an annoying or intrusive interaction. Here Dr. Olesen noted the particular importance of sensitivity on the part of the field worker. The publication of field work may also involve some risk for

the group or category with whom the work was done. This may be difficult to anticipate, because social attitudes toward life styles sometimes change rapidly. Dr. Olesen believes that field workers writing for publication must take extreme care to protect participants, but that self-imposed voluntary standards are the best course. She called for the use of principles that are relevant to the research to which they are being applied, and for the inclusion of field workers on IRBs that review field work protocols.

Edward M. Opton, Jr. Ph.D. (Associate Dean of the Graduate School and Senior Research Psychologist, the Wright Institute) pointed out that the Commission's hearings will obtain highly selective information from representatives of the largest and best-managed research institutions. At non-elite institutions, state hospitals, and county welfare departments, cutting corners is standard operating procedure. He noted some unconventional features of the IRB system, e.g., the carrying out of national policy with localized membership and the potential of IRBs' judgments conflicting with the basic aims of the organization of which they are a part, and suggested that the Commission consider alternative models that more nearly resemble conventional administrative decision-making. He called for multi-level review, with local auditors to review the operation of research projects and outside reviewers to correct for any "cronyism" within an institution.

Ms. Gwen O'Sullivan (Executive Officer, Committee on Clinical Investigation, Children's Hospital Medical Center, Boston) questioned whether the purpose of the regulations is to protect human subjects or to protect

the federal establishment. DHEW's emphasis on Form 596, the form on which an IRB certifies that it has reviewed a project, is misplaced, she believes; and the requirement that all research (including no-risk projects) be reviewed in convened meetings of the IRBs prevents the development of efficient administrative procedures to reduce IRBs' workloads. She criticized the recent change by DHEW which requires certification to be submitted within 60 days, rather than the previous 90 days, after submission of proposals, and expressed fear that the resulting pressure of deadlines will result in only cursory reviews. Because IRBs also spend much time and effort reviewing proposals that ultimately are not funded, she recommended that the Commission review the present NIH policy of requiring IRB approval before an application goes to study section for review. She also called for standardization of rules among federal agencies. Ms. O'Sullivan stressed the importance of monitoring, and described the duties and activities of the Consent Committee at Children's Hospital. Whenever the IRB deems it necessary, a consent committee member will be present during the consent procedure to assist the patient in understanding and to answer questions. The Consent Committee also conducts telephone surveys of subjects recently involved in research projects to ask them questions about their participation (e.g., whether it is voluntary, whether they understood the explanation and written consent form, and whether they had any complaints). However, committee members have found it difficult to carry out the monitoring activities because all committee members have regular jobs. A reduction in recordkeeping requirements would increase the time available for this type of monitoring. Finally, Ms. O'Sullivan proposed a program of accreditation

for institutions that meet DHEW requirements for protection of human subjects and that have demonstrated their competence. Under the model she recommends, once organizations have demonstrated an ability to handle their affairs in a satisfactory and responsible manner, they would no longer have to report to DHEW on a continuing basis but would br site-visited periodically, at random. Such an accreditation system might give IRBs a higher priority at institutions and lead to provision of adequate funds and personnel.

Michael L. Parker, LL.B. (Adjunct Associate Professor of Health Policy, School of Medicine, University of California, San Francisco) believes that the existing system generally serves the interests of subjects and of science, yet it will be inadequate until there is a mechanism to assure that subjects have given consent and are generally satisfied with their participation in research. He suggested that every major research institution have a "research advisor" who would be responsible to the chief administrator of the institution and be available to subjects to respond to inquiries regarding research. Such a person could also act as an intermediary between subjects and investigators in resolving difficulties in communication. The funds for such a position could come from a small assessment of research grants and contracts. Mr. Parker also expressed dissatisfaction with the general quality of progress reports provided to the IRB by investigators. Finally, he supported the inclusion of lay members on IRBs, saying that they are able to understand explanations

of proposed research and that their questions often prompt the scientists to ask further questions regarding scientific design and risk of proposed research.

Paul Parkman, M.D. (U.S. Food and Drug Administration) described the FDA's current activities regarding Institutional Review Boards. Since 1971, the FDA has required institutional review of clinical research for drugs and biologics when the study involves institutionalized human subjects or when non-institutionalized human subjects are involved and an institution agrees to assume responsibility for the investigation. FDA currently has a task force to define the role of institutional review in human studies regulated by FDA, and to ensure that the role is adequately and reliably performed. A series of 75 inspections by the Bureau of Drugs showed that there were very serious deficiences under the existing system; and a new, randomized inspection program has been undertaken. The task force has recommended that FDA require its IRBs to conform to the DHEW regulations (45 CFR 46). Problem areas identified by Dr. Parkman include the need for administrative sanctions when an IRB has failed to comply with federal standards, the role of IRBs in the continuing review of studies, the possibility of exempting low-risk studies from IRB review (e.g., phase 3 drug studies on non-institutionalized subjects, unless the Commissioner determines there is sufficient risk to warrant IRB review), and the need to encourage adequate review when the institution involved is a commercial drug testing firm that has a vested interested in the research.

Alfred J. Perkins, Ph.D. (Institutional Review Board, University of Illinois at the Medical Center) cited the need for definitions of "risk," "subject," and "biomedical and behavioral research", and the need for a mechanism other than full IRB review for research on tissue, blood and other materials gathered for purposes unrelated to the research from individuals whose identity is not known by the investigator. Such review could be carried out by an IRB staff member who would refer questionable cases to the entire board. It is unnecessary to require full IRB review for behavioral research in which there is little or no risk. Dr. Perkins advocated greater flexibility regarding the conditions under which written consent could be waived. Concern was also expressed about the development of different requirements for different federal agencies. Finally, Dr. Perkins disagreed with the policy of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) that requires applicants to complete a form (ADM441) describing how subjects will be protected, said that if DHEW cannot rely on the work of an IRB, then the system should be abandoned. He suggested that site-visit audits of IRBs would be preferable to the re-examination in Washington of protocols reviewed by a local IRB.

William S. Robinson, M.D. (Professor of Medicine and Chairman, Medical Committee for the Protection of Human Subjects in Research, Stanford University) described in detail the policy

and procedures used by the two IRBs at Stanford. Their experience shows that IRBs that receive adequate institutional support can work well under the general guidelines provided by the present DHEW regulations. The regulations leave sufficient flexibility so that IRBs can design review procedures to meet local needs and make decisions about the quality of investigators, the institution's procedures for treatment of research subjects, and the degree of monitoring required by the research. More detailed regulations are not needed or desirable. Dr. Robinson recommends that IRBs should include approximately equal numbers of members with scientific and non-scientific backgrounds and that they should be selected by a responsible institutional official. Establishing more than one committee may produce better review by reducing workload and by permitting IRBs to focus on their own areas of expertise (e.g., behavioral or medical science). The size of the committee should be sufficient to permit one more than half of the membership to review each protocol in detail and include individuals from each constituency served by the committee. Dr. Robinson also called for agencies to provide funding for indirect costs in research awards that would be adequate to support IRB activities. Finally, Dr. Robinson stated that it should not be necessary for investigators to make their research ideas public prematurely in order to protect human subjects, and suggested statutory limitations on the information that IRBs can be required to make available to the public.

Professor Edward Rose (Department of Sociology, University of Colorado, Boulder) testified that as a result of interpretations of the National Research Act by DHEW and the University of Colorado, student researchers are vulnerable to sanctions while faculty members are not. A provision in the University of Colorado's General Assurance gives the Dean of the Graduate School power to reject any graduate student's research and thus withhold a degree, if the research does not conform to the policy to protect human subjects. Professor Rose sees a double standard being applied to faculty members and students, and believes that the implementation of the National Research Act by DHEW and the University of Colorado may have breached various Constitutional provisions. Professor Rose maintained that the DHEW regulations and IRB activities are inappropriate to the review of research in the fields of ethnography and sociolinguistics. He disagreed with the requirement for legally effective informed consent, because it is actually used to protect hospitals and universities against law suits. It would be better to require assurances to be written and signed by the investigator and presented to the subject or the informant as a binding document. Under the present circumstances, consent is something that a subject is asked to give up. Professor Rose recommended that, if sanctions are needed, the government should establish uniform sanctions for all institutions and all investigators.

John J. Sampson, M.D. (Chairman, Committee on the Protection of Human Subjects, Mount Zion Hospital and Medical Center, San Francisco) indicated that IRBs are uncertain about issues such as the adequacy of investigators' assurances to subjects regarding confidentiality, the assessment of potential psychological trauma in psychology and psychiatric research, and the proper levels of payment to subjects. The definition of the term "at risk," proper intervals for monitoring research, the distinction between research and demonstration projects, the need for review of educational activities and training grant applications, and the necessity of informed consent in studies based on hospital patient records should all be clarified.

Sandra Scarr, Ph.D. (Psychologist, University of Minnesota, representing the Board of Scientific Affairs of the American Psychological Association) recommended clarification of the standards IRBs should apply, establishment of appeal procedures for investigators, increases in federal research funding to cover the growing costs of federal regulations and elimination of restrictions on the participation of competent adults in research involving little or no risk, as long as fully informed consent is guarenteed. She also recommended the building of IRB case law through written records of IRB deliberations, removal of requirements that IRBs judge scientific merit of research proposals, and clarification of the definition of risk so that it will not be

interpreted to include risks to social categories of which subjects are members. She said that problems arise from the inclusion on IRBs of people who are unqualified to make scientific or ethical judgments on behalf of human subjects, particularly representatives of the community. She suggested that IRBs form panels of members whose research expertise is closely related to the proposals they are to evaluate. Finally, to reduce the work load and resulting difficulty of obtaining long-term service from IRB members, Dr. Scarr suggested (a) elimination of review of continuation grants, secondary analyses of previously collected data, and social surveys gathering anonymous data; and (b) establishment of broad guidelines for no-risk and low risk behavioral research and routine laboratory studies with established procedures, so that automatic approval may be given by IRB staff, if informed consent is assured.

Ms. Priscilla R. Schaff (Human Subjects Review Committee, Columbia University) discussed the experience of the IRB that serves all of Columbia University except the Health Sciences Division. The basic problem is that of dealing with research in the social and behavioral sciences and in disciplines that use their methods. Regulations and the various written instructions are strongly phrased in terms which do not clearly apply to behavioral research. The difficulty is not with the IRB, but with investigators who believe that the regulations apply only to biomedical research and who are troubled by the procedures with which they are asked

to comply. Ms. Schaff discussed various difficulties experienced by her IRB. First, there is difficulty in recruiting members. Membership entails much work and little or no credit; and there is a general lack of understanding among the faculty of the purposes of the IRB and the University's commitment to its activities. The membership is increasingly from junior faculty who can be ordered to volunteer. Second, the IRB has difficulty in completing reviews in a timely fashion. (Only proposals for which outside funding is being sought are reviewed; they have no way of identifying other projects.) Delays result from having to convince investigators that a proposal must be reviewed, inadequate preparation of protocols by investigators, difficulty in assembling a quorum of the IRB, and various delays in correspondence between the IRB and investigators. Third, in addition to the lack of understanding about the IRB, researchers sometimes are openly hostile. Fourth, the IRB has no sanctions it can apply to assure compliance except asking the Office of Projects and Grants to restrict funds at the beginning of a budget period. Fifth, good documentation is critical for the development of a body of law and precedent, but this is difficult to do without adequate staff.

Reagan Scurlock (Executive Director, Committee on Governmental Relations, representing the National Association of College and University Business Officers) opposed further regulation of IRBs

because of the need for flexibility in adapting review procedures to the existing communication and decision-making network of an institution. In addition, further regulation would distract from the exercise of sound and deliberate professional and lay judgment regarding the complex ethical issues involved in research involving human subjects. Mr. Scurlock pointed out that financial costs of reviewing research have escalated in recent years and he recommended that the federal government adopt the policy of full reimbursement of both the direct and indirect costs of federally sponsored research. He also expressed the need for a uniform policy of review for all federal agencies, and recommended that the Department of Health, Education,and Welfare assume the responsibility as the lead agency to avoid duplicative administrative effort and increased costs. Institutions would then be able to submit one General Assurance that would apply to all federally-sponsored research. Institutions conducting only one or two studies involving human subjects could apply for a Special Assurance, as provided in current regulations.

Robert R. Sears, Ph.D. (Psychologist, Stanford University, representing both the Society for Research in Child Development and the Division of Developmental Psychology of the American Psychological Association) stated that the IRB mechanism has been

excellent in protecting human subjects, and offered suggestions for improving its effectiveness. The work load for the IRB members could be reduced by (a) elimination of secondary data analysis from review, (b) development of guidelines and administrative procedures for eliminating the need for full IRB review of studies with little or no risk, and (c) the elimination of requirements for annual review of continuing, previously approved projects. He also identified as a problem the frequent changes of IRB membership. Dr. Sears recommended clarification of the authority and responsibility of IRBs, especially regarding aspects of research design that are irrelevant to the protection of human subjects. In weighing the potential benefits and importance of research that has some risk for subjects, he suggested the use of subcommittees of technically competent scientists who would evaluate the research and prepare a statement for the IRB's consideration. Finally, he cited the need for a formal appeal procedure for researchers whose proposals have been disapproved, ranging from appearances before IRBs to regional appeal boards established by DHEW.

Lynwood Smith, M.D. (Chairman, Human Studies Committee, Mayo Clinic and Foundation, Rochester, Minnesota) stated that the DHEW guidelines and regulations, and the activities of the Commission have made investigators and IRBs more conscious of ethical questions, of potential risks, and of community interest in medical

research. He believes that additional community representatives on the Mayo IRB has enriched the review process by bringing fresh perspectives and different values to the committee's discussions. Dr. Smith expressed concern that the subtle and difficult questions buried in scientific protocols are in danger of being overlooked as a result of the sheer magnitude of the paper-handling and information-disseminating process. The work load of the Mayo clinic's IRB has increased steadily over the past few years, and in 1976 it reviewed 258 new protocols and monitored 300 ongoing studies. The Board meets weekly in plenary session, and an executive committee meets in advance of each meeting to prepare the agenda. Each protocol and progress report is submitted, in full, to the entire IRB, and if the protocol has more than minimal risk, the investigator is invited to be present at the review. Dr. Smith presented data showing the great increase in man-hours expended on committee business and stressed the need to control the amount of paper work required. He also recommended that the Commission establish guidelines to discourage the fragmentation of regulatory authority among governmental entities; set IRB staffing and composition requirements that allow for differences in institutional interests, capacities, and purposes; and articulate policies on confidentiality of records to insure individual privacy without needlessly restricting research involving medical records or interfering with the physician-patient relationship. He further

suggested that the Commission determine whether "consent committees" or similar devices can be effective in ensuring free choice (or whether such committees would undermine patient confidence and rapport) and that existing and alternative monitoring activities be evaluated to determine their effectiveness. He urged the Commission to establish a forum for continuing, open discussion of these questions. Such a forum should have legitimacy and authority because it would include ethicists and philosophers as well as scientists, administrators, governmental officials, special interest groups, and ordinary citizens.

Robert Sprague, Ph.D. (Institutional Review Board, University of Illinois at Urbana-Champaign) stated that the risks of research are often inseparable from the risks of not doing research. To assist IRBs in protecting human subjects and to reduce costly, unnecessary review, he cited the need for clear delineation of which activities require review and the need for clear definitions of subjects, research, and risk. He suggested categories of activities that could be excluded from review without risk to subjects, including anonymous surveys, non-intervening observation of public behavior of unidentified subjects, use of secondary data when subjects are unidentified, use of taste panels to evaluate foods when subjects are adults and informed of the identity of the food to be involved, use of fluids, tissues and other human material gathered for purposes unrelated to the research from persons whose identity

is unknown to the investigator, and curriculum development and evaluation research using methods within a school's established practices. He also suggested alternatives to full IRB review, including delegation (under careful guidelines) of responsibility for determining risk, decentralization of some decisions when subjects are not at risk, and judicious use of staff, subcommittees, and primary and secondary reviewers. Dr. Sprague stated that problems arise in the application of present regulations to social science and education research, because the assessment of risk differs from biomedical research, the consent process and the balance of power between researcher and subject differ from biomedical research, and research using field work methodologies (e.g., participant observation) often has an evolving research design and takes place in remote sites. Alternative approaches for review are needed. Dr. Sprague also recommended elimination of Section 411 of the HEW Appropriation Act, which requires written consent for participation in any "experimental" project, program or course and written consent of parents for any participamt or subject under 18 years of age. Dr. Sprague also said that the participation of non-employees on IRBs has been valuable but that such individuals should not be viewed as any more representative of the community than other members of the IRB. He added that such individuals should receive compensation for time spent in IRB activities. Dr. Sprague also believes that IRBs should not be asked to make political or social policy decisions.

William C. Sturtevant, Ph.D. (Executive Board, American Anthropological Association) stated that present regulations and the operation of IRBs are inappropriate for ethnographic research; and that the application of the medical model tends to stifle ethnographic research, to invade scientific freedom, and to increase federal control over universities, without protecting subjects. The research techniques of ethnography are neither experimental nor manipulative, and carry no risk. The risks arise when the research is complete and they stem from the presentation and dissemination of results. Intervention to protect subjects here implies censorship of research results. The control of this type of risk is properly left to the professional ethics of anthropologists. Dr. Sturtevant stated that IRBs, particularly those weighted with clinicians, experimenters, and lawyers, and those at smaller institutions, have harmed ethnographic research by trying to impose consent requirements and concepts of research design that are inappropriate to ethnography. He offered several suggestions, including distinguishing between biomedical and behavioral research, on the one hand, and ethnography and other non-manipulative social science, on the other; he also urged the Commission to consider ethnography as a "setting" in its deliberations about the nature and definition of informed consent in various research settings. He further suggested that IRBs be limited to supervision of clinical or biomedical research, or alternatively, that the fields to which regulations apply be more carefully defined to exclude studies in linguistics,

folklore, ethnomusicology, oral history, and ethnography. He recommended that compliance with the ethical codes of the American Anthropological Association and the Society for Applied Anthropology be sufficient for such research.

Ms. JoAnn Weinberger (Research for Better Schools, Inc., Philadelphia, representing the Council for Educational Development and Research) testified about review procedures for educational research, which she defined as "the study of any aspect of the teaching and learning process or of the setting in which teaching and learning take place." She described the review procedure at Research for Better Schools (RBS) as an example of the process used to protect human subjects in educational research. The IRB consists of a lawyer, a school principal, a psychologist, and educational R & D specialist and a member of the RBS board of directors. The IRB is guided by the code of ethics of the American Psychological Association, since there is no appropriate code specifically for educational research; it is also concerned with the issues addressed in the Privacy Act, the Freedom of Information Act, and the Family Educational Rights and Privacy Act.

The Board's evaluation of risk involves consideration of the content and method of the research, whether the project involves individual subjects, schools, or school districts, the procedures for collecting and handling the data, and the way the data will be reported. The policy on consent requires RBS to obtain a

written informed consent for the use of a curriculum and/or teaching procedure in any formalized program that poses unusual and extended risk to the participants or that provides materials intended for purposes other than program evaluation and revision.

Ms. Weinberger stated that her IRB has not hindered educational research of good quality and has increased the awareness and sensitivity of investigators toward the protection of human subjects. To do this, however, it had to develop its own set of criteria for judging projects and its own definitions (e.g., of risk). She noted the financial limits within which an IRB must operate and the need for sufficient time for the review process. She argued that the need to review all proposals prior to funding was an unnecessary waste of resources and money and that federal agencies do not realize the time and dollar costs of the IRB process. Ms. Weinberger offered four recommendations. First, the medical model cannot be transferred in toto to educational research, particularly with respect to the term "subjects," the distinction between research and treatment, the definition of "risk," and the use of consent procedures. Second, educational researchers should be encouraged to develop a code of ethics appropriate for their research activities. Third, IRB members must be protected from personal liability through an insurance mechanism backed by the federal government. Fourth, educational constituents must be represented on the Commission and/or its staff in order to

formulate knowledgeable proposals. She noted that the treatment of human subjects in educational research also falls under regulations governing privacy and that research in school settings is carefully scrutinized by institutional officials such as superintendents.

Linda S. Wilson, Ph.D. (Associate Vice Chancellor for Research, University of Illinois at Urbana-Champaign, representing the Committee on Institutional Cooperation) stated that IRBs are a very appropriate and effective mechanism because of their adaptability to the structure of particular institutional settings, their proximity to investigators, the efficacy of continuing review, and their ability to foster a climate of cooperative compliance. Present composition requirements provide the proper blend of technical expertise and breadth of perspective beyond the university community; and institutional flexibility in decisions regarding staff and the openness of meetings, should be maintained. The IRB should not be used to make political or social policy decisions. The problem of heavy work load and the volume of unnecessary reviews could be alleviated by clarifying terms such as "risk," "subject," and "biomedical and behavioral research;" eliminating full IRB review for certain projects using human tissues, body fluids and other materials not gathered for research purposes; and delegating IRB responsibility for determination of risk under careful guidelines and IRB supervision. Problems arise from applying a biomedical

model for research to social science and educational research. Greater flexibility in the requirement of written informed consent and recognition that certain fields differ in the extent to which research plans can be precisely specified in advance would help solve these problems. Finally, Dr. Wilson noted the growing problem of differing regulations and review requirements eminating from various federal agencies, and stressed the need for an IRB to be able to follow a single set of regulations and procedures.

4

"The Institutional Review Board"

April 2, 1976

Robert J. Levine, M.D.

The institutional review board

April 1, 1976

Robert J. Levine

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The Commission is charged to consider: "Mechanisms for evaluating and monitoring the performance of Institutional Review Boards...and appropriate enforcement mechanisms for carrying out their decisions" (PL 93-348; 202 (B) (v). This paper does not address the issue of developing these sorts of mechanisms; rather, it provides some background information upon which such considerations might be based.

The first part is written primarily for the reader who has not--through service on an IRB--had the opportunity to become familiar with its usual activities and functions. There is an account of the history of the evolution of the IRB culminating in a summary of the most recent DHEW regulations defining minimal standards for its membership, procedures, and duties. This is followed by a brief survey of the sparse literature concerning IRB composition and functions, as well as the problems it faces and its shortcomings as perceived by various authors. It is apparent that not much is known about IRBs in general. A current study by the Commission is designed to develop some general information. This paper provides a detailed description of one IRB--the Human Investigation Committee (HIC) at Yale University School of Medicine--with the hope that much of what I say about its membership, procedures and problems will prove to be generally applicable.

The second part of the paper is addressed to various issues that might be considered in the formulation of future public policy on the membership and functions of IRBs. These issues are listed in the table of contents (cf, Title page). Most of them were raised by the Commission at its meeting in February, 1976 (cf, Transcript No. 15). Some additional issues are drawn from publications by commentators on the social control of research, by consultants who have prepared papers on various aspects of the Commission's mandate, and from existing or proposed federal regulation.

I shall now make some general statements of my biases on what the purposes and role of the IRB is (or should be) and what criteria should be applied for evaluating its performance. I agree with Walters (25 at p. 25) that there are "...four general requirements--adequate research design, favorable risk-benefit ratio, equitable subject selection, and informed consent--(which) are individually necessary and jointly sufficient to provide moral justification for any proposed..."research on humans. Further (25, at pp. 21-22): "...social control is a procedural rather than a substantive issue. Therefore, it is not in itself one of the necessary conditions for ethically-acceptable human research. Rather, it is a means for insuring, in so far as possible, that research is conducted in accordance with basic ethical principles. Thus, from an ethical perspective the primary criterion for judging the adequacy of any particular social control mechanism will be the extent to which the mechanism promotes..."; the four specified general requirements.

Of the various social control mechanisms that now exist to promote the values suggested in the preceding paragraph, the one that is most likely to have a consequential impact at the level at which research is actually conducted is the IRB. The IRB is a rather new invention; it is only 10 years since the first document was published in which its membership and functions were specified (cf, History). Subsequently, developing upon their own experience and in response to criticisms based upon studies of their function, IRBs have begun to learn how they might accomplish their functions with increasing effectiveness. The effectiveness of an IRB depends greatly on the degree of credibility it can establish not only within the institution in which it works but also within the community served by the institution and from which it might recruit research subjects. I shall refer repeatedly to various forces that can tend to undermine the authority of the IRB. Many sections of this paper will reflect my opinion that it is in the interests of all participants in the conduct, support, and regulation of research to foster--

within the community and the institution--an attitude of respect for the IRB and to resist any forces that might tend to erode its credibility.

In discussing one important function of the IRB--the assessment of risks and benefits--Barber (24, at pp. 10-11) wrote: "...even where difficulty and strain occur in the assessment process, they (assessments) are worthwhile just because the process of making assessments has value over and beyond the outcome or product of the process. Whether routine or difficult and causing strain, the process...is important in itself. The process is in itself "consciousness-raising"; it leads to higher ethical awareness. One hopes that the product, now or eventually, will also be better, but that happy condition we should not expect ourselves to guarantee. We should not expect, and certainly not require perfection of risk-benefit assessment in all cases from our biomedical or behavioral review groups. Perfection in all cases is for utopias and heavenly worlds. Moreover, we should inform the general public that we do not guarantee perfection of assessment product but only excellence in the process. We should inform them that we are prepared to defend scientific research assessment, when it is conscientiously and competently carried out by professional peer review groups, against all demands for utopian perfection of product." (emphasis in original).

I think this statement by Barber is equally applicable to review for adequacy of research design, equitable subject selection, and informed consent. The four general requirements specified by Walters are and should be the primary focus of IRB review. My views of the factors that should be considered by the IRB and the devices available to the IRB to meet these purposes have been summarized in previous papers (1-4).

History

Systematic review of research by committees having as their principal responsibility the protection or safeguarding of the rights and welfare of research subjects is a very recent development. While it is difficult to determine when the first such committee was established, it is not likely that it was over 20 years ago. Apparently the first committees were established in university medical centers and, for the first few years of their existence, functioned without much publicity. At first these committees were truly "peer review" groups in that they were composed of peers of the investigators. Subsequently, while membership on these committees has been diversified, the informal designation of peer review group has been maintained. Now, of course, it is unclear as to whose peers are involved.

The early history of the IRB was reviewed in detail by Curran (6). More recently, Veatch (16) has discussed the history of the IRB concentrating particicularly on the evolution of federal requirements for diversity of membership. Much of the following discussion is derived from these two papers; they may be consulted for some specific citations of government and other documents that I have omitted.

The first suggestion that a physician should consult with his peers before proceeding with research or innovation is generally attributed to Thomas Percival; it is contained in the following oft-quoted paragraph from his Medical Ethics (cited in 16, at p. 32):

"Whenever cases occur, attending with circumstances not heretofore observed, or in which the ordinary modes of practice have been attempted without success, it is for the public good, and in special degree advantageous for the poor (who, being the most numerous class of society, are the greatest

beneficiaries of the healing art) that new remedies and new methods of chirurgical treatment should be devised. But in the accomplishment of the salutary purpose, the gentlemen of the faculty should be scrupulously and conscientiously governed by sound reason, just analogy, or well authenticated facts. And no such trials should be instituted without a previous consultation of the physicians or surgeons according to the nature of the case."

It is of interest that the Nuremburg Code and the Declaration of Helsinki make no mention whatever of committee or peer review; these documents place all responsibility for experimental design, safeguarding the rights and welfare of subjects, and so on, on the investigators. In the revision of the Declaration of Helsinki at the 29th World Medical Assembly in Tokyo in 1975, committee review is mentioned:

I.2. "The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment and guidance."

The document is otherwise silent on the matter of committee review prior to the initiation of research. It is of interest that the authority of the committee is limited to "...consideration, comment and guidance."

Apparently, the first federal document requiring committee review was dated November 17, 1963 (16, at p. 32). This consisted of a set of guidelines entitled: "Group Consideration of Clinical Research Procedures Deviating from Accepted Medical Practice or Involving Unusual Hazard". These guidelines applied only to intramural research at the National Institutes of Health (NIH). However, earlier there were reports of committee activities in medical schools. In 1961, Welt reported on the results of a questionnaire he sent to each university department of medicine in the country (5, at p. 889). He received

responses from 66 departments; of these, 8 had procedural documents and 24 had committees to review human experimentation. There was a mixture of strong opinion as to whether there should be such procedural documents or committees. In 1962, a similar survey was conducted by the Law-Medicine Research Institute at Boston University (6, at p. 407). Of 52 departments of medicine responding, 9 institutions had procedural documents and 5 more indicated that they were in the process of developing such documents. Twenty-two departments had committees.

The first federal policy statement on protection of human subjects was that circulated over the signature of the Surgeon General of the United States Public Health Service on February 8, 1966. This specified that (6, at p. 436 et seq):

> "No new, renewal, or continuation research or research training grant in support of clinical research and investigation involving human beings shall be awarded by the Public Health Service unless the grantee has indicated in the application the manner in which the grantee institution will provide prior review of the judgment of the principal investigator or program director by a committee of his institutional associates. This review should assure an independent determination: (1) Of the rights and welfare of the individual or individuals involved, (2) of the appropriateness of the methods used to secure informed consent, and (3) of the risks and potential medical benefits of the investigation. A description of the committee of the associates who will provide the review should be included in the application."

On July 1, 1966, a revision of this policy statement extended the requirements for prior review of research involving human beings to all PHS grants. This revision also revoked the requirement of individual assurances of compliance and replaced it with a requirement for institution-wide assurance which could be used to cover all grant proposals eminating from a single institution. Institutions who wished to use this mechanism were requested to

file "general statements of assurance" of compliance with USPHS policies which were to include, among other things, a description of the review committee.

In a subsequent revision of the policy statement in December 1966, the grantee institution is informed that it is responsible for assuring that investigations are: "...in accordance with the laws of the community in which the investigations are conducted and for giving due consideration to pertinent ethical issues."

In 1968, NIH analyzed the activities of 10 per cent of the committees operating in institutions with general statements of assurance (6, at p. 443). Of 142 institutions thus examined, 73 per cent of the committees were limited in membership to immediate peer groups; ie, they were exclusively composed of scientists and physicians without the addition of theologians, lawyers, philosophers, or lay members. Interdisciplinary groups in which co-professionals of the investigator were in a minority were found in only 11 institutions. Twenty-six institutions had some representatives of other professions or laymen. Of these, 18 had lawyers on the committees, 16 had laymen and 1 had both lawyers and clergy.

Since 1966 there have been several revisions in USPHS policy which reflect evolving federal expectations regarding the composition and duties of IRBs. A revision of the guidelines dated May 1, 1969, suggested for the first time that a committee composed exclusively of biomedical scientists would be inadequate to perform the functions now expected of the committee. "...the committee must be composed of sufficient members of varying backgrounds to assure complete and adequate review...". Further, "...the membership should possess not only broad

scientific competence to comprehend the nature of the research, but also other competencies necessary in the judgment as to acceptability of the research in terms of institutional regulations, relevant law, standards of professional practice, and community acceptance." The requirements for filing general assurances now request specific information on each of the committee members including "...position, degrees, board certification, licensures, memberships, and other identifications of experience and competence."

On May 30, 1974, these policies and guidelines were revised and issued as DHEW regulations. The new language calling for differences in committee membership includes the following: The committee must be composed of not fewer than five persons and must include capacity to judge the proposal in terms of community attitudes. "The committee must therefore include persons whose primary concerns lie in these areas of legal, professional, and community acceptability rather than in the conduct of research, development, and service programs of the type supported by HEW." It is further required that no committee or quorum of a committee shall consist entirely of employees of the organization where the research will be conducted. Further, no committee or quorum of a committee shall be composed of a single professional or lay group.

The regulations promulgated on May 30, 1974, also contain new requirements for specific procedures and administrative responsibilities. These regulations were revised and republished as technical amendments in the Federal Register of May 13, 1975 (17). In view of the fact that some of the new regulations were susceptible to varying interpretations, a memorandum was

circulated on May 22, 1975 from the Director, Office for Protection from Research Risks, to grantee and contractor research officers responsible for implementing DHEW policies and regulations on protection of human subjects at institutions with general assurances (18). This memorandum states that while the general assurances "...will be substantially the same as those submitted in response to the 1971 DHEW policy issuance...some amendments and changes will be necessary..."; these are specified in the subsequent 6 pages.

The applicability (18) of the regulations is extended to "...research, development, and related activities. A related activity is one labelled other than research or development as, for instance, training, demonstration, improvement, or support, which nevertheless contains an r and d component."

"The definition of "subject at risk" has been changed to permit exclusion of projects which do not involve changes in the ordinary risks of daily life or in recognized occupational risks." Thus, it is made clear that DHEW is concerned with activities that present to subjects risks that are in excess of those that might be expected in the course of their usual activities. Accordingly, one might assume that activities that present no excess risk would not be covered by DHEW regulations including IRB review. However, as discussed earlier (3, at p. 75) de facto, NIH requires IRB review as well as full implementation of all requirements for any application for funds in which contact with humans is even mentioned.

The jurisdiction of the IRB is extended as follows (18):

"While DHEW regulations and reporting requirements must necessarily be framed in terms of DHEW grants and contracts, the National Research Act, as cited in the preamble to the technical amendments, requires that the board '...review biomedical and behavioral research involving human subjects conducted at or sponsored by (the institution) in order to protect the rights of human subjects.' The statement of compliance therefore refers to 'projects and activities' without limitation to DHEW projects and activities."

Thus, it appears, that all research activities conducted in an institution which has on file a general statement of assurance must be subject to IRB review and other protections prescribed in DHEW regulations.

Each institution must provide (17) "...a statement of principles which will govern the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects." OPRR elaborates (18) "... that DHEW regulations and policies are procedural and do not constitute an ethical code." Further, "...assurance implementation procedures should indicate how the appropriate codes are to be made conveniently available to institutional staff, board members, and investigators undertaking activities with human subjects. Board members should understand that the code(s) or principles do not supersede DHEW regulations or applicable law."

There are some additional requirements for IRB membership; statements of assurance must identify the representative capacities (if any) of members. It is further specified that (18) "...no board shall consist entirely of persons who are ...associated with the institution apart from their membership on the board. In addition, when the board is considering an activity that involves an investigational new drug, the Food and Drug Administration

regulations require that the quorum of the board include at least two members who are licensed to administer drugs and at least one member who is not so licensed."

To meet the requirement for an individual "not otherwise associated with the institution" the following sorts of people are excluded. Those who have continuing financial dependence on the institution such as immediate members of staff families, paid consultants, part-time employees, or persons on retainers. Various types of persons who are dependent upon the institution for facilities (eg, attending or visiting faculty), trainees, students, residents, or interns dependent on the institution for admission. The institution is permitted to appoint these "unassociated individuals" to the board to meet institutional requirements for purposes of insurability, to pay costs of attendance, or provide compensation for services. However, membership on the board shall be the only appointment or compensation received by members "not otherwise associated with the institution".

The revised regulations call for increasingly detailed descriptions of procedures to insure prompt reporting by investigators to the IRB and by the IRB to DHEW of proposed changes in activities, unanticipated problems and adverse reactions. Although the regulations require that all applications must be reviewed and approved by the IRB prior to their submission to DHEW, a notice in the Federal Register on May 20, 1975, made provisions for institutions to certify completion of review within 30 days if requested by DHEW in writing or in any event within 90 days following specified deadlines for receipt of grant or contract applications.

The IRB in the literature

I have been able to locate very few articles on IRB structure or activities. In this section I shall identify and comment briefly on those I have found; detailed comments on most of them are in other sections of this paper.

Several articles in Experimentation with Human Subjects (6-10,27) make reference to the review committees as they existed in the 1960s. These articles reflect the concerns of their authors as to the composition and duties of IRBs; some of these concerns are quite similar to those expressed more recently. Katz (5) assembled some of the early governmental and institutional policies on IRBs.

The books by Barber et al (11) and Gray (12) report the results of empirical studies on the structure, functions and effectiveness of IRBs. The studies upon which these books are based were conducted in 1969 and 1970 respectively; however, since they are the only two reports of extensive empirical studies available, the data they contain and their recommendations for changes in policy continue to be cited frequently by current authors.

In 1974, Marcy reported (14) the results of her study of the records of one IRB from 1970-1974; this study documents the progesssive increases in both the quantity and quality (as reflected in the finally approved protocols and consent forms) of the IRB's efforts. In 1975, Veatch (16) analyzed in detail the various functions that might be expected of an IRB and--based on this analysis--recommended substantial changes in its structure (cf, Proposals for modification of IRB structure). Also in 1975, Cowan (15) published a detailed description of the two IRBs at Case-Western Reserve University Medical Center; so far as I can determine, this is the only such description published by an IRB member since Melmon et al reported on the one at UCSF in 1970 (5, at pp. 898-900). The two committees described by Cowan are similar in many aspects of

membership and procedure to the HIC at Yale (infra). Also, Cowan's perceptions of some of the major problems confronted by IRBs are similar to those I shall discuss.

Finally, although no consultant to the Commission was asked to comment on IRBs, several (19-26) did offer specific comments, criticisms, and suggestions for change.

The Human Investigation Committee (HIC) at Yale University School of Medicine

Since there is very little in the literature describing in detail the activities of an IRB it might be useful to study the one with which I am most familiar. Parenthetically, this committee has already had much more than its share of public scrutiny. The guidelines for preparation of protocols it developed in 1968 were published (5, at pp. 891-892) as were its 1971 (5, at p. 892) and 1973 (13) guidelines for preparation of consent forms. It has also been subjected to a detailed analysis of its activities (14) as well as a study of the quality of informed consent in the conduct of research activities it had approved (12).

Membership on the HIC

Individuals are appointed to membership by the Dean from a list of candidates recommended by the Medical School Council. The Medical School Council is a governance group of elected representatives of various constituencies within the institution; there are six students, six non-tenured faculty, four tenured faculty, two departmental chairmen, and one or two representatives each of the clinical faculty, housestaff, and so on. Each year members of the medical school community are asked to nominate themselves for membership on various committees. From this list of volunteers the Council selects nominees for each open committee position. The ordinary procedure is that two individuals are recommended to the Dean for each position; of these two the Dean selects one. Thus, if four positions on a committee are open, the Dean is not presented with a list of eight from which he may select any four. Rather, he is presented with four pairs of candidates. Each of these pairs is presumed to have the qualifications required by the Committee.

The chairperson of the HIC keeps the council informed of its requirements for individuals with specific capabilities. If no person having the required capabilities volunteers, such persons may be recruited through the joint efforts of the Council and the HIC. No attempt is made to have all departments represented. Rather, when seeking scientific expertise, an attempt is made to have adequate representation in those research disciplines which present the greatest problems to the HIC. Thus, for example, a person having suitable expertise in Oncology might be appointed from any of the following departments: Medicine, Pediatrics, Surgery, Pharmacology, and so on.

The term of appointment to membership on the HIC is three years. A member may be asked to serve a second term if he represents an area of expertise not duplicated by others in the medical school community. Members have been asked to leave the committee before their terms are completed owing to either poor attendance at meetings or other manifestations of unwillingness or incapability to serve the committee adequately. I am not aware that anyone has been asked to resign owing to his holding of unpopular positions relevant to the purposes of the committee.

The committee currently consists of 25 persons of whom 14 are full-time medical school faculty; all of these 14 have M.D. degrees. This is rather unusual for the HIC; until 1975 there was invariably at least one Ph.D. basic scientist who had no M.D. The major responsibilities of these 14 are distributed as follows: Teaching of house staff and medical students, 14; patient care, 9; patient service functions other than clinical care, 3; active research

programs, 9; major administrative responsibilities, 4. Of these 14, 7 are tenured. The other 11 members of the committee are numbered 15-25; their roles are self-explanatory.

1) Chairperson: Associate Professor of Clinical Pediatrics with a special interest in child development. Research and consultation involves juvenile court and school system.
2) Professor of Medicine with special interest in Clinical Pharmacology.
3) Associate Professor of Medicine with special interest in Oncology.
4) Associate Professor of Anesthesiology with special interests in pediatric anesthesia and pulmonary function.
5) Associate Professor of Medicine with special interests in invasive cardiology and coronary care unit.
6) Assistant Professor of Pediatrics with special interest in Endocrinology; Director, Pediatric Clinical Research Center.
7) Professor of Epidemiology and Medicine with special interest in basic virology and epidemiologic field studies.
8) Professor of Surgery--ex-chairman, Department of Surgery; Director, Comprehensive Cancer Center.
9) Professor of Pathology and Laboratory Medicine.
10) Associate Professor of Diagnostic Radiology with special interest in radioisotopes.
11) Associate Professor of Pediatrics and Obstetrics/Gynecology; Director, Newborn Special Care Unit.
12) Assistant Professor of Obstetrics/Gynecology and Diagnostic Radiology with special interests in mechanisms of induced labor and ultrasound techniques.
13) Professor of Clinical Anesthesiology and Neurology with special interests in the mechanisms and control of pain.
14) Associate Professor of Psychiatry with special interest in the biology of behavioral disorders; Director, Psychiatric In-patient Service.
15) Associate Director, Yale New Haven Hospital.
16) Clinical pharmacist; Director, Drug Information Service, Yale New Haven Hospital.
17) A lawyer who is Grants and Contracts Administrator for the Medical School.
18) A lawyer who has a special interest in health law and, more specifically, in medical malpractice.
19) Consultant for Minority Affairs to the Medical School and Hospital.
20) Director of Community Affairs, Greater New Haven Chamber of Commerce.
21) Medical School Chaplain.
22-24) One medical student each from the second, third, and fourth year class.
25) One student from the School of Public Health.

Committee Meetings

The HIC holds its regular meetings twice each month. Occasionally, when there is an unusually high work-load, it may meet a third time in a month; this

is occasionally necessary in the months preceding DHEW deadlines for receipt of new or other competing grant applications. During the summer it ordinarily meets once each month. Each meeting lasts 2 to 3 hours. The purpose of these meetings is to review and to take action on specific protocols; these include new protocols and periodic review of and proposed amendments to approved protocols. In addition, special meetings are called as necessary to consider new policies or procedures.

The requirements for a quorum necessary to conduct business are in accord with DHEW regulations. The committee has two additional rules of procedure. The first has to do with voting. Approximately seven years ago the committee began to enlarge its membership so that various types of expertise and view points other than what might be reasonably expected of biomedical researchers and physicians would be represented systematically. Although the committee at that point rarely found occasion to vote on a substantive issue, it was assumed that votes might now become necessary. It was further recognized that it would never be possible to balance the various presumed vested interests without developing a committee that would be much too large to conduct meaningful business. That is to say that in order to have the necessary scientific expertise available, it would always be necessary to have scientists as the majority of the committee. Thus, the following rule of procedure for voting was developed. All scientists together have one vote. All students together have one vote. The clergyman has one vote. And so on. Subsequent experience indicates that the assumptions upon which this rule was based did not obtain.

Differences of opinion among committee members are virtually never determined by profession, discipline, or presumed constituency. The physician-investigator members of the committee are likely to be as diverse in their opinions as are the others. It is quite typical to find that on any given issue on which there are two possible (eg, yes or no) positions, those favoring the yes decision will include several scientists, some students, and several others while the opposition is likely to be composed of a similar mixture of members. It is further typical that such differences can be resolved through discussion, explanation, and/or compromise. In fact, the committee rarely votes on substantive issues. Voting is usually reserved for purposes of terminating trivial discussions. The committee always attempts to achieve consensus on substantive issues and almost invariably succeeds. My recollection is that the committee has voted on whether or not to approve a protocol less than once per year; I can recall no such occasion where more than two members voted contrary to the majority. Thus, even where it is necessary to resort to a vote the actions of the committee represent near consensus.

A second rule of procedure is concerned with tabling a protocol. Any member of the committee may move to table a protocol after its discussion has occupied more than 10 minutes. A motion to table must include a plan for subsequent action. There are only 3 possible plans for subsequent action:

1) The investigator may be called upon to supplement the information contained in the protocol. This plan is followed if the committee feels that the cause of its inability to reach a decision is lack of information. Ordinarily, when this plan is invoked, there is agreement among the members that if this information is made available it will be possible to make a definitive decision

at the next meeting. In this case, one member of the committee is assigned to inform the investigator exactly what information will be necessary and to see to it that this is made available to the committee prior to the meeting at which the protocol will be reconsidered.

2) The committee may agree that it has adequate information but there are still irreconcilable differences of opinion. In this case, a sub-committee is appointed for purposes of discussing the problems further and, if necessary, negotiating some compromise. The sub-committee is appointed by the chairperson; it ordinarily includes the most forceful exponents of the opposing points of view as well as one or two members who are most expert in the field of research being considered. If the committee finds it necessary to recommend revised procedures, it is expected to consult with the investigators to learn whether these procedures will be acceptable to him. After the sub-committee has completed its business it reports back to a meeting of the full committee which--based upon the sub-committee's report--almost always is able to achieve consensus.

3) The committee may feel that it does not have sufficient expertise to assess some aspects of the protocol. In this case, one or more members is appointed to find a suitable consultant and to make his views available to the full committee at a subsequent regular meeting.

4) Commonly, the impetus for tabling discussion of a protocol involves a combination of two or three of the above mentioned problems,

The discussion of each protocol at the meeting is initiated by one of two members who have been designated primary reviewers. For the past several years the primary reviewers have been designated by the chairperson based upon

their special interest or proficiency in the field of research or other types of specific problems presented by the protocol. It has been their responsibility to study the protocol in detail, to identify any flaws in form or substance that might preclude satisfactory review by the committee and to contact the investigator to supply any deficiencies in information or to modify the protocol or consent form to meet HIC standards. Recently, the HIC has revised its procedures; it now calls upon the investigator to select one primary reviewer to provide advice and consultation during the early phases of development of the protocol (infra). It is too early to assess the effects of this new procedure.

One of the primary reviewers initiates discussion of the protocol. This discussion is based on the assumption that all members of the committee have read the protocol; thus, their remarks are directed toward making specific recommendations for revision as necessary. The next speaker is the second primary reviewer. After he speaks discussion is opened to all members who might wish to make additional recommendations for modification. Members who know they will not be able to attend the meeting are requested to transmit written recommendations for revision to the chairperson; any such suggestions that are not made by those present at the meeting are read by the chairperson. The committee then determines which of these recommendations reflect the opinion of the full committee. These recommendations are transmitted to the investigator in the form of a memorandum from the chairperson. Some recommendations for action are designated mandatory; that is, the committee will not approve the protocol until these revisions are made. Some other recommendations are presented as suggestions the investigator might wish to consider. He may use

them if he agrees that they might improve his protocol. However, approval of the protocol is not contingent upon acceptance of this second type of suggestion.

At the meeting each protocol is classified in one of the following categories:

1) Approved: This means that no further action is required and the investigator may proceed with the research.

2) Approved contingent upon specific revisions: This means that the committee has identified certain problems in either the protocol or consent form and that it has sufficient information to understand what specific revisions will make the protocol acceptable. Thus, for example, a specific recommendation for revision might be the incorporation of a specified sentence in the consent form. The majority of protocols reviewed by the committee are classified in this category after initial review. Such protocols are revised by the investigator and returned to the chairperson. If the specified revisions are made the chairperson grants approval without further consulting the full committee.

3) Approval withheld pending major revision: Historically, this category became identified as it was because protocols entering into it required such extensive revision and/or discussion that it was not feasible to incorporate all requirements in a memorandum from the chairperson. Also in this category are protocols that for any of a variety of reasons the committee does not ever expect to approve.

4) Tabled: The protocols entering into this category are of the sort described above.

5) Disapproved: This is a category that is in theory available to the

committee. However, the committee virtually never labels a protocol disapproved. The way disapproval is accomplished de facto is that a protocol is entered into category 3 and requirements for revision are made that the investigator chooses--for any of a large variety of reasons--not to accept. At the end of each academic year a memorandum is sent to investigators who have protocols in category 3 and who have not taken any action that might lead to the development of an approvable protocol. The investigators are asked either to take such action or to withdraw the protocol from consideration. Thus, the ultimate disposition of these protocols is to place them in a category known as "withdrawn".

Some perspective on the frequency of use of these various categories may be provided by considering the following information (14): In the academic year 1972-1973, the HIC reviewed 145 new protocols. Of these, 24 were approved without change on first review and 16 were ultimately classified as withdrawn. The remainder were initially classified in categories 2, 3, or 4 and were ultimately approved.

Procedures for preparation and review of protocols

Each member of the faculty at Yale University School of Medicine is provided with a document entitled: "Guidelines for preparation of protocols for review by the Human Investigation Committee (HIC)". This contains detailed instructions for the preparation of protocols and consent forms. The investigator initiates the process by drafting a protocol and consent form. At that point he selects a primary reviewer:

"...whose field of expertise is closest to the designed research...if the HIC member who is asked to be primary reviewer is overburdened with requests or cannot give early consideration to the task, he or she or the chairman of the

HIC will be responsible for suggesting another member for this review. The reviewer will study the protocol and advise the investigator about revisions if necessary. The reviewer's suggestions are not binding, nor does this preliminary review insure immediate approval by the HIC, but it will promote more efficient use of the HIC to have obvious revisions made before the whole committee acts on a protocol."

After preliminary negotiations between the investigator and the primary reviewer results in a protocol suitable for the committee's consideration, the investigator presents the protocol to the chairmen of all departments involved in the research for their signatures. The purpose of the signature of the department chairman is to insure that each chairman is afforded an opportunity to keep aware of what research is being conducted in his department. Some departments have their own committees which review protocols before the chairman will sign them; this is not required by the School.

After signature by the department chairman a sufficient number (28) of copies are made and delivered to the HIC secretary. Those that are received 1 week prior to the next scheduled regular meeting are circulated to HIC members for consideration at that meeting. Those that are received later are circulated for consideration at the next subsequent meeting.

At the meeting the committee takes action on the protocol as specified above. Notification of the committee's action is transmitted to the investigator in the form of a memorandum from the chairperson. Further disposition of the protocol is contingent upon its initial categorization by the committee. Those that are placed in category 3 must be revised as indicated and presented once again to a full meeting of the committee. Thus, 28 copies of the revised protocol are necessary and they must be delivered to the HIC secretary at least one week in advance of the regular meeting at which they are to be reconsidered.

Information available for HIC review.

The information is presented to the HIC on standard forms; the forms have four sections.

I. Face Sheet. The face sheet includes the title of the project, the name(s) of investigator(s), telephone number and address of investigator responsible for correspondence, signatures of departmental chairman, and spaces for annotations of committee actions and the dates on which they are accomplished.

II. Description of study. Information is provided under the following headings:

A. A brief statement of the purpose of the study including the hypothesis to be tested.

B. A brief synopsis of the background information and data that provide the rationale for the research. The investigator is asked to provide sufficient information so that the rationale may be comprehensible without reference to other materials; however, references to the literature may be cited to provide interested reviewers with additional information. If it is proposed to use a new drug (or an old drug for a new purpose) its FDA status is to be provided.

C. The location of the study. Specific information is provided as to exactly which in-or out-patient facility, community, institution, and so on will be the location of various components of the research.

D. Duration of the project. In this section there is an estimate of how long it will take to complete the entire research project. In addition,

there is specified the period for which HIC approval is being requested. The HIC ordinarily will not approve projects for periods of greater than two years. Many funding agencies (eg, DHEW) require that periods of approval not exceed one year.

E. Experimental method. This section contains an orderly account of the proposed procedures as they directly affect the subject. To quote from the guidelines:

"There need not be a detailed account of experimental techniques that do not directly affect the human subject (ie, details of in vitro studies). Include number and estimated length of hospitalizations, length of time for various procedures and frequency of repetition, any manipulation which may cause discomfort or inconvenience, doses and routes of administration of drugs, amount of blood to be withdrawn and plans for follow-up. If there is a point at which study procedures would be discontinued, state how they will be identified. Include measures which will be taken to overcome side effects. If letters to subjects or intermediaries, questionnaires or rating scales are to be used, append copies."

F. Material inducements: This section provides a description of any inducements which will be offered to subjects in return for their participation; eg, direct payment, free hospitalization, medical care, medication, food , tests, and so on.

G. This is a section which is to be completed only if one of the Clinical Research Centers (CRC) are to be used for the study. In this case the following additional information is provided. An identification of which CRC is to be used; the approximate number of subjects to be admitted; an estimate of the length of stay for each subject; a statement as to why the research must be conducted in a CRC; and the names and telephone numbers of two responsible physicians.

The next section of the protocol is designed according to DHEW instructions for preparation of grants and contracts. When appropriate, this information is presented on standard continuation pages (provided by DHEW or other funding agencies) which may be included in the grant application and which will also suffice for HIC review. This information is required by the HIC whether or not the funding agency also requires it.

A. Subject population: This calls for a description of the prospective subject population and an explanation of the necessity for using such special groups as prisoners, children, the mentally disabled or groups whose ability to give voluntary informed consent may be in question.

B. A description of risks: The investigator is asked to provide a description of risks to either the subject or society in the following categories: Physical, psychological, social, economic, or legal. To the extent possible an estimate is provided of the probability and magnitude of each risk. In the event there are consequential risks, there is to be a description of alternative methods that might have been used and a statement as to why they were rejected.

C. Consent procedures. This section contains a description of the consent procedures to be followed including how, where, and by whom informed consent will be negotiated. The information to be included in the consent negotiations is presented in section IV (consent form).

D. Protection of subjects: In this section there is a description of the procedures (including confidentiality safeguards) for protection against or minimization of potential harms and an assessment of their probable effectiveness.

E. Analyze the risk-benefit ratio: In this section the investigator is asked to provide his view of the proportionality between the risks and potential benefits of the research. Parenthetically, it should be noted that this particular request for information presents a problem to many investigators. The HIC never called upon investigators to attempt this until it was required by NIH. The problems this presents have been discussed in detail in earlier papers (2,4).

IV. The consent form. The sorts of information called for by the HIC in the consent form have been discussed in detail in an earlier paper (3); that paper also detailed some of the more common variant forms that might be used for various types of studies.

If the investigator feels that it would be appropriate to negotiate consent orally and not document it in writing he is asked to request a waiver of the requirement for written documentation of consent. In this case he is asked to record on the consent form the information that will be provided to the prospective subject during the consent negotiations.

Procedures following initial approval of protocol

Periodic review: As noted above the HIC approves protocols for periods not exceeding two years. Many funding agencies including DHEW require review at one year intervals. When appropriate, the HIC may specify even shorter periods of approval. It is the responsibility of the investigator to initiate the process of periodic review. A form is provided by the HIC for this purpose. This form provides space for a brief summary of the experience of the preceding period (since approval) and a statement by the investigator as to any requests to modify the protocol or consent form based on that experience. Four copies of

this form are sent to the HIC chairperson. The request for reapproval is reviewed by each of the two original primary reviewers if they are still members of the HIC. If they are no longer members, a new primary reviewer is designated. The primary reviewers may find that there are no substantive changes in the protocol and, further, that there are no substantive changes in HIC policy that would influence the protocol. In that case they may recommend to the HIC that the protocol be reapproved without full review by the committee. Alternatively, if there are substantive changes in either the protocol or relevant HIC policy, they make this known to the investigator. In this case, review of the protocol proceeds as if it were a new project (supra).

Amendments to approved protocols: The procedures for requesting amendments to approved protocols are exactly the same as those for periodic review of approved protocols. Depending upon whether the proposed amendments are substantive, the review may be either by the primary reviewers or by the entire committee. As with periodic review, this judgment is made by the primary reviewers.

Reporting of adverse reactions: The HIC requires that any adverse reactions or other untoward incidents that develop in the course of conducting research according to approved protocols be reported immediately to the HIC chairperson. A form is provided for this report. Upon receipt of a report, the chairperson assigns a HIC member--usually one of the primary reviewers--to look into the situation and to report to the committee. If the reaction or incident is serious, the investigator may be requested to discontinue the study pending HIC review. It is the responsibility of the HIC to report such events to DHEW or any other funding agency that requires such reports. The form for reporting adverse reactions requests the name and address of individuals and agencies to whom such

notification must be sent.

Institutional endorsement: Many funding agencies including DHEW, require IRB approval of research involving human subjects before they will either review (DHEW) or fund (many other funding agencies) proposed research involving human subjects. Often, these agencies provide forms which must be signed by authorized persons to indicate that the necessary review and approval has been accomplished. The HIC policy is that only the chairperson and vice-chairperson may sign such forms. Further, these forms may be signed only after the investigator has signed a form indicating that there is no research involving human subjects described in the grant application that is not also described in protocols approved by the HIC. Specifically, it is requested that the investigator provide the title and number (if any) of the grant application as well as the title(s) and number(s) of protocols approved by the HIC. This policy is necessary because most grant applications are much too long to be considered in detail by the full committee. The HIC is only concerned with those parts of grant applications that have to do with human research subjects.

HIC records

Log book: Each new protocol received by the HIC is assigned a number. This number is placed on the face sheet of the protocol; it is also placed on each bit of communication or correspondence concerning that protocol. HIC numbers are assigned to protocols in the order of their receipt.

Immediately upon receipt of a protocol, the following bits of information about it are entered into the log book: HIC number; title of the protocol; name of the principal investigator; name of other investigator who is to receive correspondence (if other than the principal investigator); date of receipt;

names of two primary reviewers. Subsequently, the following information is entered in the log book: Date of approval; dates of approval of amendments or of periodic re-approval; date of withdrawal.

Protocol files: Each protocol has a file set up for it. These files are arranged by HIC protocol number. There are several sub-divisions in the filing system. New protocols are entered into a sub-division entitled protocols pending review. After they are reviewed they are entered into one of two other sub-divisions; viz, approved protocols or protocols pending revision. Those in the latter category are eventually entered into either of two subdivisions; viz, approved protocols or withdrawn. In each folder there is retained a copy of the original protocol, copies of all correspondence concerning the protocol, and a copy of the final form approved by the committee and endorsed by the chairperson.

Parenthetically, there is no administrative necessity for retaining the original protocol. However, these have been retained for research purposes for approximately the past six years. Their availability permits comparison with protocols that are finally approved by the committee for purposes of identifying the effects of HIC review.

Minutes: After each meeting of the HIC detailed minutes are sent to all members of the committee. These minutes contain the following information: Attendance; action taken on protocols listed by categories as detailed earlier; eg, approved, approved contingent upon specific revisions, and so on. Also included are the results of periodic review of previously approved protocols, con-

siderations of amendments, and so on. These minutes merely list by category the protocols by number, title, and name of principal investigator. A detailed account of the actions of the HIC on each protocol is reflected in the memoranda addressed by the chairperson to investigators which contain the specific recommendations and suggestions of the HIC as well as understandings reached in communications between the HIC and investigators.

Interim approval

In some situations it may be necessary for the investigator to secure approval to proceed with research prior to the next scheduled meeting of the HIC; the procedure for doing this is called interim approval. Interim approval is not granted except in situations which legitimately require prompt action. One such situation is presented by the unexpected availability of a patient with an unusual disease. Another is the development of an indication for an innovative therapy that has not been reviewed previously by the HIC. In each case the main justification for interim approval is in the interests of the patient. In the first case, awaiting full HIC approval may unduly prolong the patient's hospitalization. In the second case, the patient might be deprived of important therapy beyond the point at which it might be expected to be most efficacious.

The investigator may request interim approval by contacting the HIC chairperson, presenting the completed protocol along with a written request for interim approval including the reasons why it is urgent to begin the study before the next HIC meeting. The chairperson makes the decision to grant interim approval in consultation with at least one and usually two

HIC members. Interim approval usually provides authorization to proceed with one subject; the term of approval expires at the time of the next HIC meeting when the protocol is reviewed by the entire committee. Under no circumstances can interim approval be used for purposes of meeting a grant deadline; that is, the chairperson may never sign institutional endorsement forms based on approval by anything less than a full committee meeting.

Appeals.

A formal mechanism for hearing appeals from investigators of HIC decisions was established in March 1976; it has not yet been used. The group assigned responsibility for hearing appeals was appointed as a standing committee for a different purpose; ie, to coordinate the activities of the three IRBs at Yale University and to continually review and revise university-wide policy on safeguarding the rights and welfare of human research subjects. The members of this standing committee are the chairpersons of each of the three IRBs--the HIC and analogous committees in the School of Nursing and in the Faculty of Arts and Sciences. The latter committee reviews all research activities not covered by the first two. Prior to the establishment of this standing committee, university-wide policy was reviewed and revised from time to time by ad hoc groups assembled to respond either to issues perceived within the university or to new laws, regulations, and so on.

In the past 10 years there have been only 2 requests for appeal of a HIC decision. The most recent was in 1970. One appeal concerned the jurisdiction of the HIC; a faculty member felt that HIC review of research he planned to conduct while on sabbatical in another country was not necessary; the Provost

of the University ruled that it was; the research was reviewed and approved by the HIC.

The second request for appeal concerned a HIC decision that a surgeon was not qualified to conduct studies of the effects of a major tranquillizer without the collaboration of a psychiatrist. This problem was resolved when the departmental chairman indicated that he would not permit such studies in his department without such collaboration.

POLICY CONSIDERATIONS

This section of the paper is addressed to various issues that might be considered in the formulation of future public policy on the membership and functions of IRBs. In addition, there is a discussion of some problems confronted by IRBs and suggestions for their resolution. Most of the issues discussed in this section were raised by the Commission at its meeting in February, 1976 (cf, transcript No. 15). Some additional issues were drawn from publications by commentators on the social control of research, by consultants who have prepared papers on various aspects of the Commission's mandate, and from existing or proposed federal regulations.

Should IRB meetings be open to the public?

At present, meetings of some IRBs are open to the public and some are not. IRBs in some state universities may be obliged to be open to the public according to state freedom of information acts (FOIAs). Meetings of IRBs in some private universities and other institutions may or may not be open to the public according to local policy. The meetings of the HIC at Yale Medical School are, in fact, open in that any person who asks to observe a meeting is permitted to do so. However, the policy at Yale would certainly not meet FOIA standards. Although it is announced in the guidelines circulated to the faculty that regular meetings are held at a consistent time on the second and fourth Wednesday of each month, there is no public announcement of each meeting and no announcement whatever of special meetings or meetings of subcommittees. At most meetings there are no observers present. Over the years, observers have included graduate students in law, sociology, divinity, mis-

cellaneous other disciplines, various members of state government (executive and legislative branches), and reporters from television and newspapers. Observers are not permitted to participate in discussions or ask questions during the meetings.

I have found no discussion in the literature of the consequences of opening IRB meetings to the public. While there is much informal discussion of the potential grave consequences of opening such meetings, I have yet to hear of one of these consequences materializing.

There has been substantial discussion in the literature of opening the meetings of various other policy making and implementing groups to the public. The arguments against opening either meetings or the records of meetings at which research protocols are discussed tend to be similar regardless of which meetings or which records form the basis of the discussion. These arguments have been outlined in a recent article by Morgan, et al (28). Although they were discussing current requirements to open to the public research protocols submitted to DHEW for consideration for funding--as well as reports of their review by study sections--the arguments are analogous to those often presented against opening IRB meetings. The basic themes in the argument are as follows:

1) "The ideas of scientists are equivalent to "trade secrets" and therefore should be protected." The advancement of investigators on academic faculties has a tendency to be based heavily upon their abilities to develop important and novel ideas. Considerable weight is given to whether an individual is the first to demonstrate an important new principle. Thus academic faculties will usually resist any procedure that presents a threat of plagiariam.

It is not likely that one individual in an institution will plagiarize ideas presented to the IRB by another individual within that same institution. Once the first individual has presented his protocol to the IRB, it becomes known to a substantial number of colleagues--at least the IRB members--who originated the idea. Any other individual in the same institution who proceeded with the same research would first be obliged to submit the protocol to the same IRB. He would be informed immediately that the same research already was being conducted by another in that institution. On the other hand, if the proposal became widely disseminated--as through publication in national news media--the possibility of plagiarism in other institutions becomes more substantial.

2) "Preservation of confidentiality best serves the public interest by assisting in the protection of the quality of the peer review process." The major thrust of this argument is that the assembled members of the committee--feeling that they are speaking in confidence--are likely to be appropriately critical. The presence of "strangers" who might inappropriately repeat their remarks might reduce the desired candor and frankness of IRB members.

This potential problem merits serious consideration. However, in the early years of IRB development, the same sorts of anxieties were expressed when it was proposed to add students, lawyers, clergyman, and others to the committee. My own experience is that it has not so far inhibited the discussion of IRB members. However, a fundamental distinction must be made between the potential consequences of having individuals join the committee as members and having others visit infrequently. In the former case the individuals come to

know, trust, and respect each other. Additionally, each member has the opportunity to express his opinion and to expect a response. In the latter case, the visitors (outsiders) do not have a continuing relationship to the IRB. If, as at Yale, they are not invited to express themselves at the meeting, they might be more motivated to express themselves publicly.

3) "Premature disclosure of research protocols may infringe patent rights." In general, this argument does not appear to be applicable to considerations of IRB activities. It is quite extraordinary that any invention that might eventually be patented is not already patented before it is studied in humans.

4) "Premature disclosure of research protocols may lead to premature release of scientific hypotheses and discoveries and harm to the public." This seems to me to be the most important argument against opening IRB meetings. As discussed earlier, (2, at p. 31) investigators tend to be very optimistic in assessing the potential benefit of proposed research. All too often an investigator may say that if his research is "successful" it may lead to the development of a "cure" of a major disease. Whatever caution may be contained in the wording of the research protocol may be lost as it is reported in media addressed to the public. Thus, it may appear that we are on the verge of producing an important new "breakthrough" in the treatment of some major disease. At times, in fact, it has appeared that the breakthrough has already been accomplished.

In fairness to Morgan and his colleagues, I should point out that they were not discussing IRB meetings. In fact, they were quite careful to point

out that they were not recommending confidentiality of all protocols describing research to be done on human subjects. They recommended that those types of research activities involving human subjects that ought to be open to the public should be identified by the Commission as those categories of research that should be reviewed at the national level by the Ethical Advisory Board. They cited as their example the two categories of research on the fetus that were to be reviewed by the Ethical Advisory Board under all of the provisions of the FOIA and the Public Advisory Committee Act.

On the other hand, one could speculate that there might be some important benefits of opening IRB meetings to the public. First, IRBs performing under public scrutiny might become increasingly conscious of the necessity to perform well. This would be particularly true if they knew that any manifestations of poor performance might be made known publicly. Secondly, if it became generally knownthat IRBs were performing well, it might increase public confidence in the process through which the rights and welfare of research subjects are protected. For example, I have the strong impression that the General Assembly of the State of Connecticut chose against passing very restrictive legislation against some sorts of research--particularly research on the human fetus--based in large part upon favorable impressions they formed by observing IRB meetings and studying IRB functions.

Educational functions of the IRB

IRBs were not designed to have educational functions. However, in the course of performing their primary responsibilities they have developed a number of procedures which clearly have educational value. I shall review

some of these educational activities first from the perspective of who gets educated--IRB members; members of the university (or other institutional) community who are not IRB members; and the public. Then I shall consider how the existence of IRBs prompts some individuals to scholarly activity.

IRB members: In general, the greatest beneficiaries of the educational opportunities afforded by the existence of IRBs are their members. IRB members at Yale (and perhaps elsewhere) are selected on the bases of expressed interest in the functions of the Board as well as their possession of certain types of technical or other expertise. Membership on the IRB greatly broadens the perspective of each member. Since the range of activities of the IRB is very large, virtually no member has sufficient scope to be able to perform all of its functions even after several years of experience. The assumption shared by experienced members of Yale's HIC is that a new member--even a most diligent one--does not achieve his full potential of value to the HIC until he has been a member for approximately six months. Of course, those that are selected for scientific or legal expertise can be expected to provide adequate expert information in their field from the outset. Perhaps the last important competence to develop in new members is a sophisticated understanding of the full range of risks to society as well as some of the more subtle risks to individual research subjects (2, at pp. 5-29).

An attempt was made to document the fact that membership on the HIC educated the member. Specifically, it was hypothesized that one "outcome" of such education would be an enhanced ability to prepare a protocol that would receive IRB approval without recommendations for modification (14). It was found that

active and past HIC members achieved this objective with approximately the same frequency as individuals who had never been members. However, this study did not analyze whether the requirements for modification were major or minor. Further, there was no way to analyze the possibility that IRB members might impose more strict standards on each other for any of a variety of reasons; eg, a feeling that they must prove to themselves and to others that they were not showing favoritism.

Members of the university (or other institution) community who are not IRB members: Efforts on the part of the IRB to educate members of the institutional community have three components: Circulation of guidelines for preparation of protocols and consent forms; meetings with departments to discuss various aspects of regulations and so on; and direct communication with individuals in the course of review of specific protocols.

The HIC periodically (approximately once every 2 years) revises its guidelines for preparation of protocols and consent forms and circulates them to all faculty members. It was the assumption of HIC members that they could reduce their work-load by providing clear instructions and guidance. An attempt was made to document the efficacy of such educational activities (14). It was found that following the circulation of each revised set of guidelines, the percentage of protocols at first review without need for revision diminished; if the assumption that motivated the HIC to circulate the guidelines had been correct, the percentage would have increased. However, an examination of various specific attributes of "good" protocols and consent forms indicated that with time there was a steady increase in the quality of these instruments.

Thus, it was apparent that something was going on that had the effect of yielding higher quality protocols and consent forms with time. However, since the circulation of guidelines was associated with a decrease in the frequency with which protocols were approved at first review, it was speculated that the guidelines were probably read more carefully by HIC members than they were by anyone else. Therefore, HIC members were reminded to make necessary recommendations for revision more consistently.

At irregular intervals--usually early in the academic year--various departments in the medical school have meetings at which HIC members discuss new developments in HIC policies as well as the legal and regulatory framework within which the HIC works. Attendance at these meetings tends to be high and the discussions tend to be lively. No effort has been made to document the effects of these meetings.

Probably the most effective means of educating individual members of the university community is the communication that develops between HIC members and the individual investigator in the course of discussing a specific protocol. There are a number of obvious explanations for this. First, the discussion centers on concrete issues concerned with a specific protocol rather than the generalities usually discussed at larger meetings. The motivation of investigators to understand issues raised by their own protocols is high. Again, it is not possible to document the effect of such interchange on the education of investigators. However, as IRB members receive new protocols for review, it is very easy to identify those prepared by investigators who have submitted

previous protocols.

In the early years of the HIC, suggestions for modification of scientific design commonly were greeted with hostility. Investigators often responded with angry assertions that the turf of the HIC was ethics--not science. During the past 3-4 years such communications have been rare. In fact, the HIC chairperson has received a number of letters expressing appreciation for suggestions in the arena of scientific design.

The public: Some activities that might be considered as contributing to the education of the public and their elected and appointed representatives were presented in the discussion of whether IRB meetings should be open to the public. In addition, some members of Yale's HIC have appeared on television to describe HIC functions or have been interviewed by newspaper and magazine reporters. In general, audience feedback to the media has been quite satisfying. It is my impression that such communication tends to increase public confidence in and support of research activities involving human subjects. As far as I know there has been no systematic attempt to assess the effects of such communications. However, in response to one television program during which two HIC members were interviewed there were many unsolicited letters to the television station. Among the most frequent remarks were variations of the following theme: "I guess I always assumed that if you were admitted to the University Hospital you would be used for research. I did not know that the doctors had to ask you first and that you could refuse."

The presence of an IRB in a university stimulates various sorts of scholarly activity. For example, several publications have developed from ideas developed by HIC members in the course of performing HIC functions

(13,29,30) and the following represent studies of HIC function by non-members (12,14). Several other authors have reported that their work was stimulated by membership on an IRB (eg, 5,15,16,20,24).

Boundaries of IRB jurisdiction

The jurisdiction of the IRB is variously defined within institutions by virtue of two criteria. The first is based upon the intrinsic nature of the activity. Thus, research--which is reviewed by the IRB--is defined so as to clearly distinguish it from other sorts of activities conducted by professionals within the institution--eg, medical practice--which are not reviewed by the IRB. The second type of boundary is defined not by the nature of the activity but rather by the nature of its financing. Thus, in some institutions, IRB jurisdiction is limited to reviewing only those activities funded by agencies requiring such review.

The jurisdiction of the HIC at Yale is defined in its guidelines:

"It is required...that all research involving human subjects done on the premises of the medical center, or anywhere else by faculty, students, or employees of the Yale University School of Medicine or Yale-New Haven Hospital, be reviewed and approved by the HIC prior to its initiation. Research is defined as any manipulation of a human done for purposes of developing new information and which differs in any way from customary medical (or other professional) practice."

This definition is followed by several sentences which illustrate the sorts of deviations from customary practice that would tend to cause an activity to be considered research. The definition is deliberately overinclusive for two reasons. The definition was developed for the benefit of members of the medical center to provide guidance as to which of their activities ought to be reviewed by the HIC. While it is understood that innovative practices are not necessarily research, it is the intent of this definition to have them reviewed

by the HIC and, further, to have them conducted in association with research activities designed to test their relative safety and efficacy. The definition further reflects the attitude that when in doubt the investigator should consult the HIC. It is better for the HIC to make the determination prior to its initiation that an activity does not fall within its jurisdiction than to find during the conduct of an activity that it should have been reviewed.

The investigator is responsible for initiating communication with the HIC. The HIC does not conduct any systematic surveillance of the institution for purposes of detecting research activities that are being conducted without HIC approval. As I shall elaborate subsequently, systematic surveillance and other types of monitoring activities would probably undermine the effectiveness of the IRB without yielding much benefit. It is my impression that 5 or 6 years ago there was probably a substantial amount of research going on in Yale-New Haven Medical Center without HIC review; in most cases, proceeding without review was inadvertent while in some other cases there was deliberate evasion of HIC review.

In the past few years there has been a progressive decrease in the amount of unreviewed research activity; this decrease reflects a number of factors. First, members of the medical center community have become increasingly aware of what sorts of activities are to be reviewed by the HIC. A second, perhaps even more important factor is that with time most investigators in the institution have had experience with HIC review of their protocols. In general, the HIC is not viewed as hostile or obstructive; rather, it seems to be perceived as a committee that attempts to find ways to conduct legitimate research

without violating the rights or damaging the welfare of research subjects.

Yet it must be acknowledged that there will always be some investigators who might proceed with research without HIC approval. There are a variety of groups and individuals in the environment in which research is conducted who tend to detect unapproved activities and to refer investigators to the IRB. My impression that the prevalence of unreviewed activities is decreasing with time is based on the fact that the number of such referrals has been decreasing substantially. I shall now mention some of the groups and individuals who are located strategically to be aware of research activities and who have a tendency to bring them to IRB attention when appropriate.

Funding agencies: Virtually all agencies that fund research activities in medical centers require IRB approval. These include not only DHEW but also many other agencies of the Federal Government, private foundations, and industry. Most private foundations and industries have developed policies for the conduct of research that are very similar to DHEW regulations. In fact, the formalities of certifying that IRB review and approval have been appropriately accomplished tend to be even more complex with most drug companies than they are with the Federal Government. Thus, since almost all research conducted in medical centers is financed by outside agencies, the investigator who was not previously aware of the necessity for IRB approval will almost certainly learn of it at the stage of applying for funding.

Medical practice committee: In every accredited hospital there are various committees assigned the responsibility to monitor various aspects of medical practice within the hospital. In all hospitals there is at least a medical board and a tissue committee. In larger hospitals there may be large numbers of committees charged with highly specialized functions. There may be

separate committees for the diagnostic use of radioisotopes, therapeutic use of radioisotopes, utilization of in-patient facilities, utilization of out-patient facilities, and so on. Most hospitals will allow no drug to be administered unless it has passed through its own pharmacy. All of these groups are placed strategically to identify deviations from customary medical practice. In general, when they identify a deviation they may require that its continuation either be justified through documentation of its safety and efficacy or, if such documentation is not available, that it be referred to the IRB. Alternatively, they may require that it be discontinued.

Third Party Payment: Almost all in-patients and many out-patients have their medical bills paid either partially or in full by third parties; eg, Medicare, Medicaid, private insurance carriers, and so on. When these carriers receive a bill for services that representsa substantial departure from customary medical practice they are likely to question it. Third party payers are not likely to refer physicians to the IRB. Rather, they are likely to either refuse to pay or to refer serious problems to the medical board. As discussed above, the medical board, when appropriate, may refer the physician to the IRB.

PSRO: These agencies are designed to provide outside surveillance of medical practice activities. It is likely that when they detect substantial departures from customary medical practice they will make appropriate referrals.

Informal surveillance: Informal reporting is probably the most effective means through which the IRB becomes aware of research activities which either have not been approved or are being conducted in a manner inconsistent with

what has been approved. Almost every activity in a university hospital is subject to observation, discussion, and review by physicians, nurses, students of various sorts, and others. Many of these individuals may be considered as functioning as the IRBs informal monitoring system. When they become aware of a research activity which--in their view--is being conducted in a way that might not afford due protection of the rights and/or welfare of the subject, they are likely to either confront the investigator or contact a member of the IRB or both. The motivations of these informal monitors are quite various; motivations notwithstanding, the system does appear to be quite effective.

Publication: In those rare circumstances in which an investigator manages to complete a research project without IRB approval it is becoming increasingly likely that he will be sternly reminded of the fact that he should not have done so when he submits a report of his work for publication. In 1972 the Council of Biology Editors recommended that editors of journals adopt certain procedures to aid them in forming judgments on the ethical aspects of submitted manuscripts (31). The recommended policy states in part:

> "As a regular policy, the editor should require that the published report of any research on human beings should contain a statement that the institution's committee on ethics (or other responsible person or group) approved the description of the proposed research on a certain date. The author should be asked to supply, with the manuscript submitted for publication, a photocopy of the committee's statement of approval."

Subsequently, an increasing number of journals have been adopting this policy. As noted earlier, the 1975 revision of the Declaration of Helsinki calls for review of proposed research by an independent committee. This revision also contains the following new basic principle:

I. 8. "In publication of the results of his or her research, the doctor is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this declaration should not be accepted for publication."

My own view is that some such manuscripts should be published along with editorials in which the ethically questionable aspects of the activities are discussed; I have developed the rationale for this view elsewhere (31).

A second way in which the jurisdiction of the IRB may be defined is by virtue of who finances the research. Historically, when the development of IRBs was first required by USPHS policy in 1966, some institutions established committees charged with the responsibility for review only of USPHS funded research. Subsequently, the jurisdiction of these committees was extended to cover research sponsored by all agencies requiring such review. Committees in other institutions have been assigned responsibility for reviewing all research in those institutions regardless of its financing or sponsorship; eg, HIC at Yale has had this broad jurisdiction since its inception in 1961. As noted above, since the vast majority of research projects receive financial support from "outside" funding agencies and since nearly all funding agencies require IRB review of grant applications, the distinctions between these two types of jurisdiction determining policies are gradually disappearing. As also noted earlier, DHEW de facto requires IRB review of all research involving human subjects in institutions receiving any DHEW funds whether or not such funds are used to support any particular research project.

This is not to say that there is general agreement on the part of all concerned that all research should be reviewed by IRBs. In response to the recent extension of IRB jurisdiction through DHEW regulation, several individuals

and institutions protested that such extension was not only illegal--ie, it extended the authority of DHEW regulation beyond the agency's statutory authority--but also an inappropriate curtailment of academic freedom. It is of interest in this regard that the Commission--as it was developing its first draft of identification of the ethical principles which should underlie the conduct of research--addressed itself to the fact that there might be distinctions between ethical principles that might be developed and applied in different contexts (32, at pp. 6-7):

> "The proper balance to be struck between these different interests will vary from one situation to another, depending on the nature of the research, the context of the decision, and other factors. For instance: the question, 'What kinds of biomedical or behavioral research should be forbidden or restricted by law?', calls for a different balance of considerations from the question, 'What kinds of research are ethically acceptable for the purpose of receiving (or debarred on ethical grounds from receiving) financial support out of public funds?'; and both these questions differ in significant respects from the question, 'What kinds of research should properly-informed adult subjects be allowed to volunteer for of their own choice?'"

Thus, it might be appropriate for the federal government to tolerate the conduct of some sorts of research that it might not wish to sponsor and that among the bases for such distinctions might be ethical considerations.

My view is that all research involving human subjects should be reviewed by an IRB. It undermines the credibility of the IRB to limit its jurisdiction to review of research sponsored by funding agencies which require such review. It is tantamount to saying that the review process does not, in fact accomplish anything meaningful in the way of safeguarding the rights and welfare of human subjects; rather, it is merely an inconvenience to which investigators must subject themselves in order to secure financing of their research. Of interest in this regard is the finding of Barber et al (11, at p. 165) that as early as

1969 the great majority (240 of 282) of committees he studied reviewed all clinical investigation conducted within the institution. Further, he found, that in those institutions in which all clinical investigation was reviewed, 55 per cent of respondents said that the work of the committee was "very well received", while in those in which the committee reviewed less than all clinical research, only 38 per cent of respondents reported that the committee was "very well received."

My recommendation that the IRB should review all research is based primarily on my view that the review system contributes substantially to all aspects of the research enterprise. It contributes to the development of appropriate safeguards of the rights and welfare of research subjects, to the public acceptance of research involving humans, and to the scientific design of research. In order for the IRB to be effective in making its contributions it is essential that it maintain a high level of credibility. An IRB which has a high degree of credibility can do much to foster an attitude within the institution that is favorable toward respecting the rights and safeguarding the welfare of research subjects.

The IRB is largely guided by federal and other governmental policies, guidelines, and regulations. Members of the IRB in performing their educational functions (supra) can serve an important translator function. They can explain how these policies, guidelines, and regulations have their roots in important ethical principles and, therefore, should be respected. In fact, for several years it was a matter of some satisfaction in some institutions that their IRBs were routinely following procedures that seemed important before they were included in various guidelines and regulations. This phenomenon seemed to enhance confidence within institutions that these procedures made sense and, in

fact, should be followed whether or not they were required through regulation.

However, members of the IRB cannot create respect for guidelines and regulations which they do not themselves respect. To this end it is very important to avoid developing regulations which do not have reasonable bases. When this happens, IRBs begin to develop "double-standards". They apply one set of guidelines to research conducted or supported by DHEW and another set to otherwise identical research activities not supported by DHEW. Consequently, members of the institutional community begin to perceive that the IRB is obliged to impose on investigators the requirement that they follow certain procedures that even the IRB does not respect. The resultant destruction of the trusting relationship between the IRB and the institution in which it functions could have disasterous consequences. For further elaboration of these consequences in general the reader is referred to Baumrind (19, at p. 46 et seq), Cowan (15, at p. 554 et seq) and Ingelfinger (33). Holder and Levine focussed on the consequences of one particular ill-advised NIH policy--the requirement for documentation of informed consent to do research on specimens obtained at either surgery or autopsy (30, 3, at pp. 75-77). There are now several institutions at which different standards for negotiation for and documentation of informed consent to do research on such specimens are applied depending upon the source of funding.

The distinction that the Commission is beginning to develop is most important. This distinction should be expressed clearly in guidelines and regulations promulgated by DHEW. It should be made clear that there are some sorts of activities that the government does not wish to sponsor or finance. Some of these activities may be viewed as illegal; this view should be expressed

through legislation. On the other hand, some of these activities will not be viewed as illegal; they will be tolerated but not supported by the federal government. Clarification of such distinctions should have several good effects not the least of which would be to enable the IRB to maintain its credibility.

Monitoring by the IRB of activities in the institution

There have been suggestions from various sources that the IRB should develop systematic mechanisms for monitoring or surveillance of activities conducted in its institution. These have ranged from proposals that the IRB should consistently monitor all activities, that it should monitor all activities within certain categories of either high risk research or research on subjects having limited capacities to consent, to proposals that it ought to perform "spot-checks". The arguments in favor of surveillance activities are based mainly on the assertion that they will detect and correct two types of problems. First, monitoring might detect research that is being conducted without prior review and approval by the IRB. This, of course, could be achieved only if the IRB reviewed all activities in the institution--not only those that had been submitted to it for review. Secondly, monitoring might detect departure by the investigator from the procedures approved by the IRB. There is some evidence that departure from IRB approved procedures occurred with sufficient frequency to cause concern 5-7 years ago (11, 12). The Commission's IRB study should indicate the current magnitude of this problem. I have already discussed the bases for my belief that the magnitude of both problems now is small.

The principal arguments against monitoring activities are based on their expected costs--both economic and even more importantly, social. These concerns

were summarized in a position statement prepared by the American Federation for Clinical Research (34). I shall not dwell on the potential economic costs at this point. A matter of greater concern to me is the social cost. In several sections of this paper I have emphasized my view that much of the good that can be accomplished by the IRB is dependent upon the degree of credibility it can achieve within the institution. If it is perceived as a police force operating under what cannot be construed as anything other than assumptions of mistrust and bad faith, it is likely to sacrifice much of its current effectiveness.

I suggest that monitoring activities should not be required by regulation. Rather, it would be appropriate to identify some areas in which various sorts of monitoring activities might be of value to all concerned. It should then be the responsibility of the IRB to develop mechanisms for appropriate monitoring on a protocol by protocol--not category by category--basis.

The need for monitoring systems is most likely to arise from considerations of some aspects of risks and benefits and some aspects of the negotiations for and documentation of informed consent.

In considerations of risks and benefits, the investigator should be asked to provide adequate description of both in the protocol as described earlier (2). Also, the investigator should be asked to provide a detailed account of what steps will be taken to assure the early detection and, when appropriate, remediation of developing harms. In some sorts of research--particularly those presenting unknown risks of physical or psychological harm (4) it might be most difficult to anticipate the probability, magnitude or even the nature of the

harm. In some other sorts of research it might be difficult to predict the probability or magnitude of benefits. In such cases the IRB should limit its approval to studies on a specified small number of subjects. After these initial studies have been completed the IRB should review the accumulated experience and decide whether it should approve additional studies. In the event such a decision is made, based upon the early experience, it might be found advantageous to modify various aspects of the protocol; further, a more informative consent negotiation might be developed.

In the realm of monitoring risks for purposes of identifying developing harms and applying appropriate correctives, while the current system is generally adequate, in some cases it might be utilized more effectively. However, there is one exception; ie, there is one category of harm that might not be detected even with the most effective utilization of the existing system. That is the detection of harms that develop only after a long period of latency. The most conspicuous example of this sort of harm may be seen in those rare cases in which cancer is apparently induced through administration of a drug--the latent period often being 10-20 years. In some cases the situation may be complicated by the fact that it is not the research subject himself who develops the cancer; it is the progeny of the subject (eg, vaginal carcinoma in the daughters of women who received diethylstilbesterol during pregnancy). The problem is not limited to drugs (eg, the development of thyroid carcinoma years after irradiation of the thymus in children).

What are some of the problems in the existing system that would inhibit first, the determination that there was a serious adverse reaction with long latency, and secondly, which of those having been exposed developed the adverse reaction? Current FDA regulations require that investigators maintain their re-

cords for only 2 years following the termination of a study. Although many investigators keep records for longer periods of time, there is no way at present of being certain that they are kept sufficiently long for these purposes. This part of the problem could be resolved easily through requirements that records--at least names and addresses of individuals who participate in certain categories of biomedical research--be maintained for 20-30 years.

However, this alone would not solve the problem. We live in a highly mobile society. Research subjects move and may be lost to follow-up. Thus, when it becomes apparent that there is an adverse reaction with long latency, investigators may find it most difficult to locate those who might benefit from follow-up examination. Announcements in the public media are of limited effectiveness and produce their own harms. Not all persons who have been exposed see the announcements. Many persons who once were research subjects do not recall the name of the drug, device, and so on, to which they were exposed. In the aftermath of such public announcements, some physicians have reported that they were bombarded with multiple phone calls; in many cases they found it most difficult and, at times, impossible to determine whether these individuals were, in fact, exposed to the modality in question. I know of no way to solve this problem completely. Perhaps a contribution to its resolution could be made by providing each research subject with a durable record (perhaps a plastic coated card) of the details of his research participation that he might have to recall years later; eg, the name of the drug or other modality, dose, duration of administration, name of individual to contact for further details, and so on.

In many cases, in the interests of protecting the privacy and confidentiality of the research subject, the IRB requires that the investigator not reveal the name of research subjects to any person or agency. In fact, in some research projects dealing with particularly sensitive issues, the investigator is asked to use only code numbers to identify individuals in the project, to keep a securely locked file in which the code numbers may be linked to names or other unique identifying features, and to limit access to the linking file to the smallest possible number of responsible investigators. Study report forms provided to investigators by industrial sponsors (eg, drug companies) commonly contain a space for entry of individual subjects' initials and hospital record numbers; the IRB ordinarily requires that these bits of information not be provided on the form.

It is not only the subjects who change residence from time to time; investigators are also mobile. Thus, when an investigator moves, there may be no local person who can identify past research subjects. A partial solution to this problem might be provided by adopting the following policy. The IRB might offer to the investigator the service of retaining copies of codes which would identify past subjects. Provision should be made for breaking the codes only when necessary in the health interests of the subjects. Special problems would be presented when dealing with highly sensitive information as in cases where studies are done on use and abuse of illegal drugs. Of course, if this procedure were adopted, it would be necessary to inform the prospective subject that records were being kept by persons other than the investigator and his colleagues and the circumstances under which he might be identified by name.

Most proposals to impose on IRBs requirements for monitoring activities are addressed to issues in <u>informed consent</u>. In particular, these proposals are

oriented toward providing assurance that prospective subjects exhibit manifestations of satisfactory comprehension and autonomy. Some have proposed that this monitoring or surveillance be conducted during the process of negotiation for informed consent and that it be continued for the duration of the study--the continuation would be designed to continually update the relevant information presented to the subject and to ensure his continuing opportunity to withdraw. An example of this sort of informed consent monitoring is presented by the DHEW proposal to establish consent committees for research involving subjects having limited capacities to consent; this is described in detail in an earlier paper (3, at pp. 43-46).

Gray (12, at pp. 250 et seq)--based on his studies--feels that it is necessary to develop some "...regular monitoring procedure in which someone, probably a representative of the IRB, determines whether subjects knew they were in research, whether they understood the risks, benefits, and alternatives, and whether they felt free to refuse to participate." He feels that this might best be accomplished through an interview. For several reasons he does not propose that such an interview take place before the research actually begins:

> "The mechanics of arranging interviews between the time subjects give consent and the time their participation begins are forbidding. Such an arrangement would put the monitor in an awkward position and could make the researcher-subject relationship more difficult. Such a procedure is not necessary to achieve the goal of assuring that informed consent takes place." Rather, he suggests "...the less direct, but more efficient, procedure of interviewing randomly selected subjects after they have participated in research. Thus, the monitor would not be put into the position of having responsibility for <u>informing</u> subjects."

In earlier papers (3,4) I have outlined some of the devices that might be

used to enhance the process of negotiations for informed consent. I have also discussed some of the perils of inappropriate imposition of third party scrutinizers or witnesses to the consent negotiations as well as the perils of excessive attention to documentation of the consent process. Again, I suggest that the IRB should be aware of the various devices that are available to enhance the consent process and should make recommendations on a protocol by protocol basis as to when they might be offered as options and when they might be considered mandatory. Gray's objections to monitoring the process of consent prior to the initiation of research are in accord with some of my own (3). His suggestion that some subjects might be interviewed following the completion of a research project might be employed to advantage in some projects. In particular, it might be employed at the discretion of the IRB in cases where there was some cause for concern that negotiations for informed consent had not been conducted properly. Causes for concern may arise through any of the previously mentioned informal mechanisms for monitoring within the institution (cf, Boundaries of IRB jurisdiction).

The interface between the IRB and the federal government

Under this general rubric there are two categories of potential problems. The first is the generally harmful effect on IRB functions when it is called upon to implement ill-conceived regulations and policies. Examples of these problems were discussed in preceding sections. The second potential problem area is created by repeating some IRB functions at a national level.

It seems appropriate to review some sorts of research proposals at a national level for purposes of safeguarding the rights and welfare of human subjects. In an earlier paper, I discussed the sorts of activities that I

think merit such review (2, at pp. 54-55). In general, these are the sorts of activities that present what was classified in that paper as social risks to society; more particularly, those activities that might erode our concepts of personhood or our assumptions of trusting relationships with one another. Other types of activities that might appropriately be reviewed at a national level include those in which society is the subject and the risks to society are substantial and those in which the risks might be borne by subsequent generations.

Veatch (26, at p. 35) has classified all subjects in whom the capacity to consent is problematic as group II. In this group he includes children, formerly competent adults, prisoners, clinic patients, and subjects in experiments where consent would destroy the research (unseen observer and undisclosed purpose research). He suggests that such individuals should be used as research subjects only in cases in which research on other persons is impossible. He emphasizes that he means impossible, not merely inconvenient. He further suggests that review of all research involving group II subjects should be conducted at a national level by a national board charged with reviewing all protocols using the same criteria as local IRBs (26, at pp. 48-49). In an earlier paper (4) I have identified similar problems with some of these categories of subjects. With Veatch, I suggest that such persons are in general not suitable for research which present known or unknown risk--as opposed to inconvenience--when capable subjects will suffice. The approaches I have proposed to addressing such problems (4) seem to me to be less cumbersome and more specifically addressed to the problems peculiar to the protocols

and the populations.

The Commission has established something of a precedent in this regard. In its recommendations on research on the fetus--one type of group II subject--it did not propose that all protocols be reviewed at a national level; rather, it identified two categories of research in this population that seemed to present particularly difficult problems. I favor continuing to identify specific categories of research in specific categories of subjects for review at a national level based upon the expectation that these will present the most difficult problems. To the extent possible, I favor review at a national level on a category by category basis. I would attempt to minimize the necessity for review of individual protocols by the Ethical Advisory Board. Discrete categories should be identified within which protocol review is considered necessary. As these categories are developed, it would be most helpful to provide explanations as to why review at a national level on a protocol by protocol basis seems necessary. This would facilitate the efforts of IRBs to support, and when necessary, justify such necessities to the larger community of investigators.

My lack of argument with the necessity for review at a national level by the Ethical Advisory Board is based on the assumption that these boards will be constructed so as to be competent in such review. Also, I hope that they will be sufficiently prompt and responsive in their proceedings to maintain credibility within the academic community. The reasons for this are the same as those presented for the necessity of maintaining the credibility of the IRB. It is often stated that IRBs are either too slow (21) or too bureaucratic (19) or both. Yet, the delays and formalities about which in-

vestigators complain seem rather insignificant when compared with the average time necessary to secure authorization to proceed with a project from federal agencies such as FDA or NIH. Parenthetically, the fact that the establishment of Ethical Advisory Boards was formally mandated in regulations promulgated on August 8, 1975, and that as of March, 1976 they have not been established provides little basis for reassurance.

Weighed against the potential benefits of review at a national level, one potential harm must be acknowledged. If IRBs operate with the understanding that what they approve may be disapproved at a national level and, further, that what they disapprove will never even be seen at a national level, it seems reasonable to predict that they will become less stringent in their requirements. In close cases they may feel that there is no necessity for them to make a negative decision on grounds that the protocol ought to be given its day in court at the national level.

I do wish to express concern with the current practice by NIH and other study sections of review of research proposals for issues in the safeguarding of the rights and welfare of subjects. Study sections are composed exclusively of individuals selected on the basis of their scientific and technical expertise. They do not have the broader base of expertise and experience necessary to make decisions on issues other than those of scientific design. Additionally, they lack an awareness of the communities in which the research is to be conducted and what is and is not acceptable to those communities. IRB members commonly discuss difficult issues with the investigators and find that through clarification and compromise many apparent problems can be resolved; study sections

do not have this degree of access to investigators. Consequently, I urge that study sections refrain from making negative decisions on grant and contract applications based upon their perception of inadequacies in the safeguarding of the rights or welfare of subjects. If in the course of their deliberations it appears that they might have reservations in this regard, they should contact the IRB and, if necessary, the investigator in order to attempt to resolve such problems before making final decisions.

Communications between IRBs

Several authors have suggested that an important contribution could be made to the function of IRBs through the development of a vehicle for publication of their important decisions (6,9,15,27,35). The large majority of decisions are routine and require no publication. For these purposes, important decisions include those resulting from review of protocols which present difficult problems--which could or could not be resolved--and those in which novel procedures are introduced to achieve such ends as limitation of risks, enhancement of potential for deriving benefits, improvement of negotiations for informed consent, equitable distribution of either risks or benefits, and so on. It would be of no value merely to publish decisions; rather, what really would be of value would be careful analyses of the problems presented by a protocol, alternative possibilities for resolving the problems and which were selected and why. These publications would be analogous to the publications of judicial decisions; they would contribute to the development of something akin to a common law in this field. IRBs would not be constrained to adhere to published precedents. Yet, if one chose to depart from precedent, it should know that it has made such a choice and it should be prepared to justify its departure.

It is not the purpose of this proposal to establish uniform standards. Rather, it is intended to provide an improved basis for informed decision making by IRBs. While I believe it would be in the best interests of all concerned to develop this communication vehicle in the private sector, DHEW or some other federal agency should be encouraged to contribute to its support. Attempts to develop it as an official publication of a federal agency--eg, DHEW --would almost certainly tend to suppress submission of some of the most valuable decisions and analyses. This is because many IRB members--aware that DHEW has ever increasing regulatory responsibilities--will assume that DHEW is incapable of receiving a report just for its information without feeling an obligation to take action on it. That is to say, DHEW, in response to receiving a decision or an analysis that it was not certain it could justify to the public, would probably feel obliged to put a stop to the procedure pending an investigation or perhaps indefinitely. Also, as noted earlier, the federal government may begin to distinguish between activities it might wish to sponsor and those that it might merely wish to tolerate. Discussions of both types of activities are necessary.

Proposals for modification of IRB structure

Over the years there have been several proposals for modification of IRB structure. Some of these have to do with gradual evolution of IRB membership through addition of certain sorts of persons. Others have proposed drastic alterations in IRB structure or the creation of other groups to perform some of the functions that we now expect of the IRB. Those that have been expressed in DHEW regulation or proposed regulations were reviewed earlier in this paper (cf, History).

The most recent requirement through DHEW regulation is to appoint to the IRB a person--designated "community representative"--who has no affiliation with the institution other than IRB membership. This requirement has presented a problem to quite a number of IRBs. Many of them indicated that they had already met the spirit of this requirement through appointment of various sorts of individuals. For example, the HIC at Yale felt that it had met the spirit of this requirement through appointment of the individual designated "Consultant for Minority Affairs to the Medical School and the Hospital". However, because he is paid by the university to perform other functions as well, his appointment did not meet the "letter of the law". As noted elsewhere, pro forma procedures by the IRB designed to meet the letter--as opposed to the spirit--of the law can have a destructive effect.

Apparently, this requirement presented a problem to a sufficient number of institutions to provoke OPRR to publish the following in its monthly bulletin (36, at p. 4):

"Q. In selecting a 'community representative' should we be looking for a person who is knowledgeable of the community, perhaps in an academic sense, or for a community member who can give us a "gut reaction" to proposed research?

"A. Since a community representative should be able to represent the community to the Board, and Board to the community, he or she should, ideally, be knowledgeable on both sides, and able to relay the reactions to the Board, and able to explain the actual risks to the community. Social workers, nurses, and occasionally psychologists, and physicians working in community based clinics or other community service organizations often have these abilities particularly if they live in or come from the community being served. Community members who have had responsible positions in institutional auxillary units, or similar posts with such groups as the American Cancer Society, American Heart

Association, or local mental and physical disease oriented groups, in short, persons who are familiar with the needs and concerns of the people who are beneficiaries of research, as with those who are doers and subjects of research."

Barber et al (11, at pp. 196 et seq) proposed "...the invention of a new social role, that of informed outsider, a role that could more effectively represent the values and interests of all who have stakes in the proceedings of the review committees, not only the patient-subjects and future patients but the research profession itself." Several functions are specified for this "informed outsider".

Further: "A special professional school or a training program for this kind of role could be set up, a school in which the training communicated the several kinds of knowledge that we have indicated are necessary and in which various opportunities for 'case instruction' and apprenticeship experience were available. Such a school or program might be set up in close association with the law and medical schools of a given university."

Both the Barber proposal of the "informed outsider" and the DHEW requirement for the "community representative" are oriented toward the same objective. They both require people who are highly skilled in seeing all relevant sides of issues and responding to legitimate interests. It is my opinion that, over the past several years, this objective has been achieved to a large extent. Each IRB has developed certain of its members--eg, lawyers, social scientists, clergymen, minority representatives, and so on--to have these broad interdisciplinary skills. None of these individuals himself can provide the perspectives of all the communities from which potential subjects might be drawn. I rather doubt that it would be possible to accomplish this objective through appointment of individuals to the IRB. Therefore, as I have suggested earlier, when the perspective of the community is desired, the

community should be consulted (4).

Barber has also suggested that it might be advantageous to add social and behavioral scientists to committees primarily involved in the review of biomedical research (24, at p. 6). I agree. As I have attempted to demonstrate at several points in this series of papers there are many problems common to biomedical, behavioral, and social research. The perspectives of each type of researcher are often valuable to solve problems confronted by others. The HIC has found the availability of individuals involved in social and educational research of value in this regard; some examples drawn from HIC experience have been presented in earlier papers (1-4).

I shall now survey some of the more radical proposals for change in the review structure:

In an earlier paper, I discussed the proposal for establishment of consent committees to review research conducted on persons having "limited capacities to consent" (3, at pp. 43-46). I concluded that for now, there was no need to establish such committees and, further, that their functions could be accomplished where needed through other less cumbersome and costly mechanisms.

Gallant (21, at pp. 4 et seq) recommends the development of an Extraordinary Treatment Committee (ETC) which would consist of legal advisors, physicians, and statisticians not associated with the institution. It should be recalled that Gallant's suggestion is presented in the context of a suggestion that the charge to the Commission should not have been to consider the

boundaries between research and the accepted and routine practice of medicine but rather between the competent and incompetent practice of medicine. The main feature offered by his ETC is rapid responsiveness to situations in which--in the interests of the patient--rapid decisions are required. Accordingly, he would have individuals appointed to it who are experts in the various medical research specialties.

I have two objections to this proposal. First, it seems to me that the same degree of rapid responsiveness can be provided by the IRB. For example, I have described a device--interim approval--used by the HIC to respond to legitimate appeals for quick decisions. The IRBs at Case-Western Reserve have developed a similar mechanism (15, at p. 543).

Secondly, a major function he assigns to the ETC is to evaluate unusual approaches to therapy and if the "...technique were based only upon empirical observations in other medical reports and not upon statistically valid, controlled studies, it would then be the responsibility of the ETC to require that a controlled trial of the specific...technique be conducted, with the protocol approved by the local IRB, before the technique is utilized as a standard or routine treatment procedure." Thus, what he is proposing is not a replacement for the IRB, but rather a specialized committee which would assume the functions I have identified with the existing medical boards, tissue committees, PSROs, and so on.

Raisz (20, at p. 9 et seq) has proposed a drastic revision of the current approach to review of research protocols. His proposal is limited to review of research in which those taking the risks are different from those who might

benefit. In situations in which those who assume risk are also those who are likely to receive direct health benefits he seems to have no quarrel with current IRB structure and function. He refers to his proposed mechanism as one of "tripartite review". In the category for which he intends tripartite review he would divide the functions of assessing risks and assessing benefits. He suggests that:

"...the assessment of risk may involve different forms of expertise and certainly involves different societal considerations than the assessment of benefit. Second, the risk-benefit equation cannot be balanced internally by a single institutional review committee. The risks will be taken in one institution but the benefits will accrue outside it.

"In assessing the risks for a volunteer group in a Phase I trial one needs information from animal studies and an analysis of potential risks based on the experience of clinical pharmacologists whose special area of competence is adverse drug reactions. In addition, the volunteers need an advocate both to assure their general rights and to ascertain that there is no coercion. In assessing the benefits there should be input not only from those who are sponsoring the drug, but also from disinterested experts in the therapy of the disease or condition for which the drug is intended who can testify as to the degree of need for additional or new therapy and the likelihood that the therapy to be tested will fill that need. An additional advocate who represents the patient population at risk should have input.

"The final review must assess the material on risks and benefits coming from the different sources and attempt a balance. This should be carried out by a group which is not only broad in composition, but includes individuals who are independent of the institution where the initial research is carried out."

In an earlier paper (4) I suggested that one of the most difficult problems presented to the IRB is the one which Raisz identifies; viz, the case in which subjects are asked to assume substantial known or unknown risks with an expectation that the benefits--if any--will accrue to others. These problems led to my proposal for community consultation followed, when appropriate, by selection of subjects through a lottery.

Veatch (16) has also proposed a radical revision in the approach to local review of research protocols. A brief discussion of some of his conclusions are contained in the paper he prepared for the Commission (26, at pp. 26-28). After reviewing the various problems the IRB is expected to address he concludes that either of two solutions seems necessary (16, at pp. 39-40):

"First, the task of experimentation review could be turned over to a group more skilled in representing the community attitudes or the view of the reasonable person. At the moment, the most obvious candidate is the community hospital advisory board in institutions which have such boards. They have been elected or selected for their capacity to represent the lay person, the consumer of the hospital's services."

"Second, we might have to resort to dual committees. One would be made up of professionals charged with the professional tasks of determining scientific feasibility and also judging ethical acceptability from their perspective in terms of risks and benefits, informed consent, and the knowledge to be gained. We would not expect that committee to hand down judgments that reflect the reasonable person's standards, but they would provide for the introduction of the professional skills, including judgments of risks knowable only to one with the appropriate training. The second committee would be the community committee which...would make value judgments of the scientific worthiness as well as the more obvious ethical judgments."

Of the two potential solutions, he favors the latter. To support his view of the necessity for committees having representative or jury skills he draws most heavily on two arguments. The first is that--given the assumption that a major responsibility of the committee is to determine what constitutes appropriate informed consent--and given the fact that the concept of informed consent is evolving rapidly toward the "reasonable person" standard--the IRB is in a poor position to determine what a reasonable person might wish to know. Scientists and physicians have much different values and perspectives than the reasonable lay person. Secondly, another responsibility of the IRB is to determine what sorts of risks and benefits will be accepted according to community standards. In other words how will the community assess the risks and benefits according to their own values and standards. As Veatch observes:

"...the systematic value perspectives of the professional group: the use of scientific models, the love of rationality, and most important, the quest for knowledge and scientific progress--these values which all scientists ought to share--these in principle cannot be eliminated by the establishment of a

committee of those who hold these unique values. What is more, while the addition of other professional groups may eliminate the peculiar scientific value patterns, it almost certainly does not eliminate the wider constellation of values held by the educated, professional class as a whole."

I agree that both sorts of problems identified by Veatch exist and that they are important; I have discussed various facets of each in earlier papers (2-4). These problems present the greatest difficulties to decision makers as they are considering research characterized by known or unknown risk in which the benefits (if any) are likely to accrue to persons other than the research subject. The solutions I propose for these sorts of problems involve community consultation and consent and their variants as described earlier (4). The mechanisms I proposed have some important advantages over those of both Raisz and Veatch. First, as I have noted earlier, the classes of research for which they are necessary represent a small fraction of all research activities. Thus, it is unlikely that any single institution will require standing committees to deal with them. In contrast to standing committees, the ad hoc assemblies I have proposed are not likely to be used when they are not truly needed. In addition, the groups assembled to reflect community attitudes and to provide consultation on what information would constitute an appropriate basis for informed consent would not be a collection of generalists but rather groups specifically designed to reflect the interests and values of the community that would assume the risk and to whom the benefits might accrue.

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