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THE BURGEONING LAW OF MEDICAL EXPERIMENTATION INVOLVING HUMAN SUBJECTS

by L. EDWARD BRYANT, JR.*

INTRODUCTION

Many Illinois physicians and health care institutions, primarily hospitals, are today directly involved in research projects which utilize human subjects. Some of these projects are formal, externally funded studies concerning hundreds or even thousands of patients or subjects; other projects may be isolated and informal. Some programs are aimed to help treat patients with specific problems; others do not in any way help the human subject involved. Although numerous studies present substantial risks of injury to the subjects, nearly all of these projects are considered by someone to be essential in saving lives, preventing disease or materially advancing the cause of medical science.

Until fairly recently medical investigation involving human subjects in Illinois and throughout the world was free from governmental and administrative regulation. Recent developments on both the state and federal level, however, require the attorney advising a hospital or any institution engaged in medical research to acquaint himself with the sudden proliferation of legal authority in the field.

The purpose of this article¹ is to advise Illinois attorneys and other interested parties on the status of the law presently appli-

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1. This article is being published in two parts since the final regulations of the U.S. Department of Health, Education and Welfare (DHEW) on the subject of protection for special categories of human subjects were not available when this issue went to press.

Part I, which appears in this issue, treats medical investigation involving human subjects and emphasizes the general rules and procedures applicable in Illinois hospitals.

Part II will consider the DHEW regulations, not presently in final form, relating to special categories of human subjects. Emphasis will be given to the peculiar procedures which will be required whenever human investigation involves minors, incompetents or the mentally infirm, prisoners, pregnant women or the unborn.

cable to medical experimentation involving human subjects in Illinois hospitals. Developing trends in the law will be considered; detailed instructions and forms for hospital use are included to assure compliance with present law.² The practitioner must recognize that the absence of precedent in this field may result in subsequent modifications, both substantive and procedural, in the existing authority. The opportunity exists for health care providers and their attorneys to contribute constructively to the formulation of any future changes.

BACKGROUND

Medical investigation, as used in this article, means any medical procedure, treatment or other activity which constitutes a departure from the accepted standards of medical procedures, insofar as the particular human patient or subject is concerned.³ Liability for damages proximately caused by an unreasonable departure from the accepted medical standard is the fundamental basis of recovery in the typical medical malpractice action.⁴ The early controversies involving health care providers who experimented with their patients, even in a good faith effort to help the patients, were predictably resolved by reference to traditional negligence theory.⁵

Formal attempts to place medical experimentation in a somewhat different legal context are often considered to have begun with the formulation of the Nuremberg Code in 1947.⁶ The "Declaration of Helsinki," adopted first by the World Medical Association in 1964,⁷ and the American Medical Association's "Ethical

2. Permission is granted to attorneys to use any part or all of the forms contained herein.

3. U.S. DEP'T OF HEALTH, EDUCATION AND WELFARE, *THE INSTITUTIONAL GUIDE TO DHEW POLICY ON PROTECTION OF HUMAN SUBJECTS 2* (1971).

4. W. PROSSER, *HANDBOOK OF THE LAW OF TORTS* § 32, pp. 162-63 (4th ed. 1971).

5. Ladimer, *Social Responsibility in Clinical Investigation*, *MED. SCI.*, Oct. 1967, at 33.

"It seems as if Mr. Baker wanted to try an experiment with this new instrument.

... [T]his was the first experiment made with this new instrument; and if it was, it was a rash action, and he who acts rashly acts ignorantly" Slater v. Baker, 95 Eng. Rep. 860, 862-63 (K.B. 1767). Compare the statement in Karp v. Cooley, 493 F.2d 408, 423-24 (5th Cir. 1974): "[A]n action for [human] experimentation must be measured by traditional malpractice evidentiary standards."

6. Beecher, *Council on Drugs: Experimentation in Man (Report to the Council)*, 169 J.A.M.A. 461, 472-74 (1959); Fletcher, *Human Experimentation: Ethics in the Consent Situation*, 32 *LAW & CONTEMP. PROB.* 620, 621 (1967).

7. World Medical Association, *Declaration of Helsinki: Recommendations Guiding Doctors in Clinical Research*, 197 J.A.M.A., Sept. 12, 1966, at 32.

Guidelines for Clinical Investigation," approved in 1966,⁸ are two of the more important declarations of professional organizations on this subject. Most other important national and international medical organizations have adopted similar policy positions as well.⁹

In the 1950's and the 1960's, many learned commentators considered the social, ethical, legal and medical rationale for placing human investigation in a special context.¹⁰ Most of these commentaries raised, but did not resolve, the complex question of how the rights of human investigation subjects were to be protected. These efforts resulted in few effective programs by governmental agencies or others to regulate medical studies involving human subjects.

While self-regulation by the medical profession has been considered by many health care professionals as the ideal method of assuring adequate protection to human investigation subjects,¹¹ self-scrutiny has not prevented some outrageous examples of violation of commonly accepted ethical standards.¹²

8. American Medical Association, *Ethical Guidelines for Clinical Investigation* (1966).

9. See, e.g., Medical Research Council, *Responsibility in Investigations on Human Subjects*, 2 BRIT. MED. J. 178 (1964); American Psychological Association, *Ethical Standards of Psychologists*, 14 AM. PSYCHOL. 279 (1959). See also U.S. DEP'T OF HEALTH, EDUCATION AND WELFARE, *supra* note 3, at 23. It is interesting to note that the American Association of University Professors has not taken any formal position concerning the standards to be used in research involving human subjects. The American Association of University Professors, AAUP POLICY DOCUMENTS AND REPORTS (1973 ed.).

10. Alexander, *Limitations of Experimentation on Human Beings with Special Reference to Psychiatric Patients*, 27 DIS. NERV. SYS. 61 (Supp. 1966); Beecher, *Consent in Clinical Experimentation: Myth and Reality*, 195 J.A.M.A. 34 (1966); Beecher, *Ethics and Clinical Research*, 274 NEW ENG. J. MED. 1354 (1966); BEECHER, *RESEARCH AND THE INDIVIDUAL* (Little, Brown & Co., 1970); Beecher, *Some Guiding Principles for Clinical Investigation*, 195 J.A.M.A. 1135 (1966); DeBakey, *Medical Research and the Golden Rule*, 203 J.A.M.A. 574 (1968); Fletcher, *Human Experimentation: Ethics in the Consent Situation*, 32 LAW & CONTEMP. PROB. 620 (1967); Freund, *Ethical Problems in Human Experimentation*, 273 NEW ENG. J. MED. 687 (1965); Guttentag, *The Problem of Experimentation on Human Beings: The Physician's Point of View*, 117 SCIENCE 207 (1953); Ladimer, *Ethical and Legal Aspects of Medical Research on Human Beings*, 3 J. PUB. LAW 467 (1954); Ladimer, *Human Experimentation, Medicolegal Aspects*, 257 NEW ENG. J. MED. 18 (1957); LADIMER & NEWMAN, *CLINICAL INVESTIGATION IN MEDICINE* (1963); Ladimer, *Social Responsibility in Clinical Investigation*, MED. SCI., Oct. 1967, at 33; Medical Research Council, *Responsibility in Investigations on Human Subjects*, 2 BRIT. MED. J. 179 (1964); Mulford, *Experimentation on Human Beings*, 20 STAN. L. REV. 99 (1967); Sessoms, *What Hospitals Should Know About Investigational Drugs: Guiding Principles in Medical Research Involving Humans*, 32 HOSPITALS 44 (1958); Welt, *Reflections on the Problems of Human Experimentation*, 25 CONN. MED. 75 (1961); Wolfensberger, *Ethical Issues in Research with Human Subjects*, 155 SCIENCE 47 (1967).

11. DeBakey, *supra* note 10, at 134.

12. Mitford, *Experiments Behind Bars*, ATLANTIC MONTHLY, Jan. 1973, at 64. Dr. H.K. Beecher has documented 22 cases in which the rights of patients or experimental subjects were abused by medical researchers.

The range of workable solutions has also been limited by the fact that the state courts alone are unable to protect adequately the rights of human investigation subjects. The reasons for this are that human investigation is still considered by some courts as simple medical malpractice,¹³ and there is little uniform decisional authority on the subject.¹⁴ Furthermore, the malpractice lawsuit in such instances is often too costly and time-consuming to afford a practical and effective remedy for the human investigation subject. Most state legal digests include no references whatever to this subject as a particular field for study or specialization.

The net result is that federal agencies with jurisdiction over related matters have promulgated regulations to assure protection of human investigation subjects;¹⁵ in addition, both state and federal legislators have begun to propose a plethora of laws to further assure such protection.¹⁶ This article is written at a time when the only definite conclusion is that substantial changes are likely in the future. The directions in which these developments will proceed deserve legal study and evaluation.

INVESTIGATIONAL NEW DRUGS

Congress has the power to enact legislation delegating authority to appropriate agencies to promulgate regulations under the Commerce Clause of the United States Constitution. The initial regulatory restrictions applicable to human investigation in Illinois hospitals were issued by the Federal Food and Drug Ad-

BEECHER, RESEARCH AND THE INDIVIDUAL (Little Brown & Co., 1970), ch. 1.

13. Perlman, *Human Experimentation*, 2 J. LEGAL MED., Jan.-Feb., 1974, at 40. See, e.g., the statement in *Karp v. Cooley*, 493 F.2d 408 (5th Cir. 1974), note 5 *supra*.

14. *Brinkley v. Hassig*, 83 F.2d 351 (10th Cir. 1936); *Fiorentino v. Wenger*, 26 App. Div. 2d 693, 272 N.Y.S.2d 557 (1966) (Sup. Ct. App. Div.); *Saron v. New York*, 24 App. Div. 2d 771, 263 N.Y.S.2d 591 (1965); *Hyman v. Jewish Chronic Disease Hosp.*, 42 Misc. 2d 427, 248 N.Y.S.2d 245 (Sup. Ct. 1964), *rev'd per curiam*, 21 App. Div. 2d 495, 251 N.Y.S.2d 818, *rev'd*, 15 N.Y.2d 317, 206 N.E.2d 338, 258 N.Y.S.2d 397 (1965); *Fortner v. Koch*, 272 Mich. 273, 261 N.W. 762 (1935).

15. U.S. Food and Drug Administration, 21 C.F.R. § 312.1 *et seq.*, 39 Fed. Reg. 11712 (1974) (New Drugs for Investigational Use), formerly 21 C.F.R. § 130.3 *et seq.* (1971); U.S. Dep't of Health, Education and Welfare, 45 C.F.R. § 46.1 *et seq.*, 39 Fed. Reg. 18914 (1974) (Protection of Human Subjects) and 39 Fed. Reg. 30648 (1974) (proposed regulations treating special categories of human subjects). The regulations concerning protection of human subjects have not yet been published in the *Code of Federal Regulations*. Reference to C.F.R. is made to aid the reader in locating a specific regulation in the *Federal Register*.

16. United States Senators Javits (R.-N.Y.), Kennedy (D.-Mass.) and Humphrey (D.-Minn.) have introduced comprehensive federal legislation on the subject. In Illinois Senate Bill 1670, entitled the "Illinois Clinical Research Act," was tabled in the House on July 2, 1974, after passage in the Senate on June 24. Notes 66-82 *infra* and accompanying text.

ministration (FDA),¹⁷ pursuant to the Federal Food, Drug and Cosmetic Act,¹⁸ and apply to all Illinois institutions utilizing investigational new drugs. Their purpose is to assure that all investigational new drugs used in human investigation studies in connection with any "research facility" be supervised and approved by an institutional review committee.¹⁹ The members of this committee must represent a broad spectrum of backgrounds:

The membership must be comprised of sufficient members of varying background, that is, lawyers, clergymen, or laymen as well as scientists, to assure complete and adequate review of the research project. The membership must possess not only broad competence to comprehend the nature of the project, but also other competencies necessary to judge the acceptability of the project or activity in terms of institutional regulations, relevant law, standards of professional practice, and community acceptance.²⁰

The Illinois legislature has also acted with respect to investigational new drugs. In 1973, the Illinois Food, Drug and Cosmetic Act²¹ was amended to require a filing with the Illinois Department of Health before any investigational new drug may be used in human beings or animals.²² This Act became effective on October 1, 1973.

17. 21 C.F.R. § 312.1 *et seq.*, 39 Fed. Reg. 11712 (1974), *formerly* 21 C.F.R. § 130.3 *et seq.* (1971).

18. 21 U.S.C. § 355 (Supp. II, 1972), § 371(a) (1970).

19. Hereinafter, sometimes referred to as the IRC.

20. 21 C.F.R. § 312.1(a) (2), 39 Fed. Reg. 11712, 11713 (1974), *formerly* 21 C.F.R. § 130.3(a) (2) (1971).

21. ILL. REV. STAT. ch. 56½, § 517 (1973).

22. Section 517 of Chapter 56½ provides as follows:

(a) No person shall sell, deliver, offer for sale, hold for sale or give away any new drug unless (1) an application with respect thereto has been approved and the approval has not been withdrawn under [21 U.S.C. § 355 (Supp. II, 1972)] and been withdrawn under Section 505 of the Federal Act and (2) a copy of the letter of approval or approvability issued by the Federal Food and Drug Administration is on file with the Director, if the product is manufactured in the State of Illinois.

(b) No person shall use in human beings or animals a new drug limited to investigational use unless the person has (1) filed with the Federal Food and Drug Administration a completed and signed application "Notice of claimed investigational exemption for a new drug" in accordance with [21 C.F.R. §§ 312.1, 312.9, 39 Fed. Reg. 11712-18 (1974), *formerly* 21 C.F.R. §§ 130.3, 130.39 (1971)] and the exemption has not been terminated and (2) filed with the Director, if any portion of the human or animal investigation is conducted in the State of Illinois, a form including but not limited to the following information: (a) name of person conducting the investigation; (b) type of drugs or chemicals used; (c) subjects (human or animal) of investigation; (d) location of investigation; and (e) purpose and expected results of investigation; such form shall be prescribed and furnished by the Department; and (3) the drug shall be plainly labeled in compliance with [21 U.S.C. §§ 355, 357 (Supp. II, 1972)].

(c) This Section shall not apply:

(1) to any drug which is not a new drug as defined in [21 U.S.C. § 301 *et seq.* (1970)]; or

(2) to any drug which is licensed under [42 U.S.C. § 201 *et seq.* (1970)] or under [21 U.S.C. § 151 *et seq.* (1970)]; or

Appendix A contains a copy of the form recently released by the Division of Food and Drugs of the Illinois Department of Public Health for complying with this enactment. It is suggested that the form be revised in at least the following particulars:

1. The filing form should be dated, since the filing is required to be made prior to the investigation;
2. In addition to the "sponsor" (which it is assumed means the sponsoring institution), it would be desirable to identify the funding source;
3. The principal investigator should also be identified, since that is required by the statute;
4. Since some principal investigators or institutions will deal contemporaneously with two or more studies involving the same drugs, the exact title of the study (and perhaps the institution's file number) should be included;
5. The category of subjects, whether human or animal, should be specified as required by the statute;
6. The location of the investigation will not always be that of the sponsoring institution. This should be given separately as required by the statute;
7. The form should state that the filing is being made pursuant to Section 517(b) of Chapter 56½ of the Illinois Revised Statutes.

In addition, care should be exercised to use the precise terminology of the principal investigator in describing the "purpose and expected results of the investigation" (the statutory phrase), so as to avoid any attempt to "soften" or otherwise misrepresent the investigation through the filing. Virtually all Illinois hospitals are likely to be affected to some extent by this enactment and are at present probably not in compliance with its provisions.

PROTECTION OF HUMAN SUBJECTS

Federal Regulations

The many new miracle drugs have not solved all the complications of illness and injury in our society. In addition to the anticoagulant drug, a cardiologist, for example, may find that his patient needs an electronic device to stimulate heartbeat, a plastic valve or aorta, or even a heart transplant. Each of these techniques of treatment either now involve, or have involved, some form of experimentation with human subjects.

Recognizing that human investigation is thus broader than the use of new drugs, in 1971 the United States Department of

(3) to any drug which is subject to [ILL. REV. STAT. ch. 56½, § 515 (1973)].

Health, Education and Welfare (DHEW) published "The Institutional Guide to DHEW Policy on Protection of Human Subjects," setting forth in detail its regulatory interpretation of earlier general policy statements made in DHEW Grant Administration Manual, Ch. 1-40, pertaining to protection of human subjects.²³ While this publication is soon to be revised in accordance with the regulations hereinafter discussed, it is presently the best single layman's summary of policy and rationale as applied by the DHEW and the National Institutes of Health to human investigation.

In October of 1973, the Secretary of DHEW published proposed general regulations for the protection of human subjects on authority of 5 U.S.C. § 301.²⁴ These regulations were published in final form on May 30, 1974,²⁵ along with a worthwhile evaluation of the responses which had been received to the initial proposals. They became effective on July 1, 1974.

These regulations formalize protective procedures similar to those originally required by the Food and Drug Administration; they apply to all DHEW grants and contracts supporting activities in which human subjects may be at risk.²⁶ "Risk," as defined in the regulations, becomes the measuring stick by which the protective provisions are applied. Thus, clinical or investigational research is covered by the regulations when a human subject

may be exposed to the possibility of injury including physical, psychological, or social injury as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.²⁷

The application of these regulations is considerably broadened by the inclusion of "psychological" and "social" harm, even though undefined, and by the fact that the injury need only be *possible* as opposed to probable or likely.

1. Procedural Requirements

Every institution²⁸ receiving DHEW support under a grant or contract involving subjects at risk must submit a written as-

23. U.S. DEPT OF HEALTH, EDUCATION AND WELFARE, *supra* note 3.

24. 38 Fed. Reg. 27882 (1973).

25. 45 C.F.R. § 46.1 *et seq.*, 39 Fed. Reg. 18914 (1974).

26. *Id.* § 46.2(b), 39 Fed. Reg. 18917.

27. *Id.* § 46.3(b), 39 Fed. Reg. 18917.

28. The regulations define an "organization" to be "any public or private institution or agency (including Federal, State, and local government agencies)." 45 C.F.R. § 46.3(a), 39 Fed. Reg. 18917 (1974).

assurance to DHEW for approval. The assurance must contain a statement that the institution will comply with the relevant regulations published by DHEW. The assurance must also contain the guidelines to be used in implementing the initial and continuing review of all supported activities. Further, the assurance must identify the committee to be charged with this responsibility and describe its review procedures.²⁹

The regulations denote two types of assurances which may be given by institutions: general and special.³⁰ The difference between the two relates primarily to the frequency with which the institution is engaged in such matters. A general assurance institution has a significant number of concurrent DHEW projects or activities involving human subjects, while the special assurance institution has only a "single activity or project."³¹ Organizational requirements for special assurance institutions are less cumbersome,³² but the functional responsibilities are the same. This article, including the accompanying forms, describes the requirements of a general assurance institution. In order to ensure conscientious compliance with the regulations, it is suggested that a special assurance institution may be well advised to adopt the same degree of formality as that required for a general assurance institution.³³

In addition to being charged with primary responsibility over all supported activities, the institution must assume specific executive functions, including the development and promulgation of policy and the continuing indoctrination of its personnel.³⁴ The purposes of these requirements are to provide guidelines by which future research techniques may be properly evaluated and to ensure the maintenance of a professional staff adequately trained for compliance with the regulations.

While the regulations assign overall responsibility to the institution for the protection of the rights and welfare of subjects

29. *Id.* § 46.4, 39 Fed. Reg. 18917.

30. *Id.* § 46.5, 39 Fed. Reg. 18917.

31. *Id.*

32. Compare the minimum requirements for general and special assurances. *Id.* §§ 46.6, 46.7, 39 Fed. Reg. 18918.

33. The ultimate decision as to whether an institution shall be a general assurance or a special assurance institution apparently rests with DHEW. The author is aware of one hospital which has set up an IRC with by-laws providing that the intent was to become a general assurance institution. Upon submission of the forms and the first reviewed proposal to DHEW, the hospital received a letter to the effect that it was a special assurance institution.

Attachments A and B to U.S. DEP'T OF HEALTH, EDUCATION AND WELFARE, note 3 *supra*, at 18-20, provide examples of statements of assurance, both general and special, which will need revision to comply with the final regulations.

34. 45 C.F.R. § 46.18, 39 Fed. Reg. 18920 (1974).

at risk,³⁵ the implementation of procedures designed to review and approve these projects or activities is vested in the institutional review committee.³⁶ While an IRC's approval of an investigation may for various reasons be overruled by the institution, IRC disapprovals, restrictions, or conditions cannot be rescinded or removed by the institution.³⁷ The membership, quorum and basic procedures for the IRC are set forth in detail.³⁸ The regulations provide, for example, that the IRC shall not consist entirely of persons who are "officers, employees or agents of, or are otherwise associated with" the institution.³⁹ They also require multi-disciplinary review of all proposals. Thus, the committee must be composed of individuals with "varying backgrounds."⁴⁰ The regulations emphasize this requirement by prohibiting the committee from being composed of only members from a single professional group.⁴¹

The function of the IRC is that of *prior* review of a research proposal, and not evaluation of completed research results (except insofar as the committee is involved in periodic review of a continuing project), regardless of whether the hospital or research facility is a general assurance or special assurance institution.⁴² "Unless the Secretary [of DHEW] otherwise provides," all proposals to which the regulations apply by institutions having approved general assurances "must be given review and, when found to involve subject [sic] at risk, approval, prior to submission to DHEW."⁴³

In fact, the Secretary has already agreed to two exceptions to this rule of prior review and approval. The first is in the nature of a grandfather clause which was revealed in the comments published on May 30, 1974, with the DHEW regulations. It amounts to a thirty-day extension to institutions having approved general assurances on July 1, 1974, but this exception will only exist until July 1, 1975.⁴⁴ The other exception is one spe-

35. *Id.* § 46.2(a), 39 Fed. Reg. 18917.

36. The institution must also supply the IRC with "appropriate administrative assistance and support" necessary for the performance of its functions. *Id.* § 46.18, 39 Fed. Reg. 18920.

37. *Id.*, 39 Fed. Reg. 18920. The regulations contain an ambiguity in this respect, in that committee disapprovals may be rescinded or removed "by action of a committee described in the assurance approved by DHEW." Since the regulations generally imply the creation of one committee, it is doubtful whether an institution could set up several committees with concurrent jurisdiction, able to review the actions of one another. To countenance such a procedure would place form over substance.

38. *Id.* § 46.6, 39 Fed. Reg. 18918.

39. *Id.* § 46.6(b)(4), 39 Fed. Reg. 18918.

40. *Id.* § 46.6(b)(1), 39 Fed. Reg. 18918.

41. *Id.* § 46.6(b)(5), 39 Fed. Reg. 18918.

42. *Id.* §§ 46.11, 46.12, 39 Fed. Reg. 18919.

43. *Id.* § 46.11(a), 39 Fed. Reg. 18919.

44. 39 Fed. Reg. 18915-16 (1974).

cifically granted in the regulations⁴⁵ and serves only to vitiate in a specific fact situation the regulation providing that premature filings (*i.e.* those final requests filed without prior IRC approval) will be returned to the institution without DHEW action.⁴⁶ If the filing occurs during the thirty-day delay period for FDA rulings on investigational new drugs,⁴⁷ the use of the drug is not yet finally assured to the institution. In this case, the institution must file a later statement with DHEW confirming the FDA ruling.

Appendix B contains a suggested model set of by-laws for an institutional review committee operating within a general assurance institution. These sample by-laws are annotated where appropriate and are submitted as being adequate for Illinois hospitals under the present laws and regulations.

Since the DHEW regulations charge the IRC with safeguarding the rights and welfare of human subjects who are at risk, its first responsibility is to determine in each human investigation setting whether the human subjects involved are at risk. Each application or protocol reviewed must be certified on this central question.⁴⁸ Appendix C contains a suggested form which may be used by the principal investigator in providing the IRC with the information necessary to determine whether the subjects are at risk and whether the proposal should be approved.

If the IRC determines that the subjects are at risk, the committee is charged with four additional general responsibilities:

- (a) to determine that the risks to an individual are outweighed by the potential benefits to him and by the importance of the knowledge to be gained;
- (b) to determine that the rights and welfare of the subjects involved are adequately protected;
- (c) to determine that legally effective informed consent is to be obtained by methods that are adequate and appropriate; and,
- (d) to conduct continuing review of the research activity at timely intervals.⁴⁹

Once the IRC has approved a specific proposal, it is suggested that the form contained in Appendix D be utilized as a means of combining the necessary certification as to risk with notification to the principal investigator.

45. 45 C.F.R. § 46.17, 39 Fed. Reg. 18920 (1974).

46. *Id.* § 46.11(b), 39 Fed. Reg. 18919.

47. 21 C.F.R. § 312.1, 39 Fed. Reg. 11712 (1974), *formerly* 21 C.F.R. § 130.3(a)(2) (1973).

48. 45 C.F.R. § 46.11, 39 Fed. Reg. 18919 (1974).

49. *Id.* § 46.2(b)(1)-(4), 39 Fed. Reg. 18917).

Special procedures are included in the regulations to cover proposed studies in which human subjects will not be involved,⁵⁰ and those projects which lack definite plans for the involvement of human subjects but will eventually require them.⁵¹

Almost hidden in the DHEW regulations is a provision which states:

No grant or contract involving human subjects at risk shall be made to an individual unless he is affiliated with or sponsored by an organization which can and does assume responsibility for the subjects involved.⁵²

Thus, physicians and medical groups engaged in human investigational studies, which are not affiliated with or sponsored by an organization assuming responsibility for the human subjects involved, cannot receive DHEW funding. Generally, it is the institution and not the individual researcher which applies for federal funds. Since the federal regulations require *all* human investigational studies to be conducted through an institution which has an IRC,⁵³ it is possible that institutional review committees might be asked to assume responsibility for physicians or medical groups with which they are not otherwise formally affiliated, in order to accommodate the unaffiliated professional. This type of relationship should be viewed with caution because of the court-initiated trend toward vicarious liability in some medical fields,⁵⁴ with Illinois courts leading the nation in holding hospitals liable for the acts of physicians having a less tenuous connection than that of an employee.⁵⁵

2. Informed Consent

The attorney representing a hospital or research facility sponsoring human investigation studies should also concentrate on the procedures by which the IRC assures that legally effective informed consent is obtained from each human subject. 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."⁵⁶ Thus, uninformed "consent" will not be legally effective. The basic elements of information necessary to obtain informed consent are:

50. *Id.* § 46.13, 39 Fed. Reg. 18919.

51. *Id.* § 46.14, 39 Fed. Reg. 18919.

52. *Id.* § 46.2(c), 39 Fed. Reg. 18917.

53. *Id.* § 46.2(a), 39 Fed. Reg. 18917.

54. *Cunningham v. MacNeal Memorial Hosp.*, 47 Ill. 2d 443, 266 N.E.2d 897, 45 A.L.R.3d 1353 (1970).

55. *Darling v. Charleston Community Memorial Hosp.*, 33 Ill. 2d 326, 211 N.E.2d 253 (1965), *cert. denied*, 383 U.S. 946 (1966).

56. 45 C.F.R. § 46.3(c), 39 Fed. Reg. 18917 (1974).

- (a) a fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;
- (b) a description of the attendant discomforts and risks reasonably to be expected;
- (c) a description of any benefits reasonably to be expected;
- (d) a disclosure of any appropriate alternative procedures that might be advantageous for the subject;
- (e) an offer to answer any inquiries concerning the procedures; and,
- (f) an instruction that the subject is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject.⁵⁷

The informed consent must be documented and may not include any exculpatory language "through which the subject is made to waive, or to appear to waive, any of his legal rights, including any release of the organization or its agents from liability for negligence."⁵⁸ This requirement departs radically from generally accepted standards for consent to medical treatment, where the hospital, the physician and the attorney representing them have long used consent forms which release or hold harmless those who provide health care.⁵⁹

Although the DHEW regulations permit a "short-form" written consent,⁶⁰ the wise course for the hospital attorney will be to rely almost exclusively on the well-documented written consent procedure, which the federal regulations assume will be the rule and not the exception.⁶¹

The Special Consent Form set forth in Appendix E fulfills all the requirements for obtaining and documenting informed consent under the DHEW or FDA regulations. This form may be modified in special cases, but none of the elements referred to above in the DHEW definition of informed consent should be omitted. Any further modification of the method by which informed consent is obtained should be discouraged. If, however, resort to the ordinary procedure "would surely invalidate objectives of considerable immediate importance,"⁶² to the investigation, the use of an approved short-form procedure for obtaining informed consent should be thoroughly documented.⁶³

57. *Id.* § 46.3(c)(1)-(6), 39 Fed. Reg. 18917.

58. *Id.* § 46.9, 39 Fed. Reg. 18918.

59. *See, e.g.*, the numerous illustrative consent forms in American Medical Assoc. Law Dep't, *MEDICAL LEGAL FORMS WITH LEGAL ANALYSIS*. Copyright © 1961.

60. 45 C.F.R. § 46.10(b), 39 Fed. Reg. 18919 (1974).

61. *Id.* § 46.10(a), 39 Fed. Reg. 18918.

62. *Id.* § 46.10(c), 39 Fed. Reg. 18919.

63. In such event, the IRC must also establish that the risk to the subject is minimal, and that any reasonable alternatives for attaining

Attorneys are often asked by hospital administrators and physicians for advice concerning who should witness consent forms to medical treatment. The question is particularly pertinent in the context of human investigation, as oftentimes relatives will claim that it was the "experimentation" which caused the untimely departure of a loved one. Part of the documentation of informed consent is the confirmation by a disinterested party that the subject actually gave his consent to participate in the study. It is recommended that institutional review committees formulate guidelines on this subject, similar to those set forth in Appendix F, to assist the professionals who will be obtaining the consent of the subject.

3. Sanctions

What happens if the DHEW regulations are ignored or compliance is not total? If the hospital attorney is not asked to assist in complying with the regulations, he or she may be asked to contest a DHEW termination of funding support. The Secretary of DHEW is empowered to enforce the regulations through the following provision:

If, in the judgment of the Secretary an organization has failed materially to comply with the terms of this policy with respect to a particular DHEW grant or contract, he may require that said grant or contract be terminated or suspended in the manner prescribed in applicable grant or procurement regulations.⁶⁴

The Secretary may also consider any prior history of noncompliance in evaluating applications for funds.⁶⁵ The power to suspend or terminate research funds thus gives the Secretary of DHEW a formidable sanction to ensure adequate compliance with the federal regulations by all institutions engaged in federally-supported activities.

Proposed Illinois Legislation

Because the federal regulations relating to human investigational studies apply only to activities supported under grants and contracts from federal agencies or under their direct supervision, House Bill 751, entitled the "Illinois Clinical Research Act," and modified as Senate Bill 1670, has been proposed in the General Assembly.⁶⁶ The bill would not apply in all cases where the fed-

these objectives would be less advantageous to the subjects. *Id.*, 39 Fed. Reg. 18919.

64. *Id.* § 46.21 (a), 39 Fed. Reg. 18920.

65. *Id.* § 46.21 (b), 39 Fed. Reg. 18920.

66. H.B. 751 passed the House on May 24, 1973. The bill was introduced on June 17, 1974, in the Senate as S.B. 1670. After passage in the Senate on June 24, S.B. 1670 was tabled in the House on July 2. The bill would be effective six months after becoming a law.

eral regulations apply because of the limited definition of "clinical research." That term is defined as:

any systematic clinical investigation involving human subjects following a formal protocol designed to study (1) normal physiologic processes in man, (2) the nature of human disease, or (3) the effectiveness of treatment programs, including any administration of investigational new drugs, and (4) excluding statistical studies of medical audit programs.⁶⁷

The drafters have made no attempt to correspond the legislation to the DHEW regulations, or to relate the precautions to any type of risk on the part of human subjects. For example, the DHEW regulations include those studies involving "social injury," a term which is not coextensive with "clinical research." Furthermore, the bill does not distinguish between varying degrees of risk, as is done in the federal regulations.

Senate Bill 1670 would allow "clinical research" only if:

- (a) that research has been initially approved and is subject to continuing review by a Research Review Committee, and
- (b) the Principal Investigator is a physician licensed to practice medicine in all its branches, or a licensed dentist, or a qualified health scientist with appropriate education for those projects involving his or her area of speciality,⁶⁸ and
- (c) there is compliance with all applicable rules and regulations

Unless the bill is enacted by December 31, 1974, at the conclusion of the 78th General Assembly, it will have to be reintroduced at the following session.

67. Some interesting questions might be raised concerning this definition:

- a) What if the investigation is not systematic?
- b) What if the protocol is non-existent? What form must the protocol take?
- c) The Act would arguably not apply unless the investigation follows "a formal protocol." This language, which was inserted into S.B. 1670, would have the opposite effect from that intended since it would exclude the "informal" research.

An earlier version of the bill omitted any reference to "a formal protocol." The effect would broaden the application of the Act to include *all* clinical research in Illinois. On the other hand, S.B. 1670 would apply primarily to organized research institutions, such as drug companies, universities, and hospitals, but arguably would not apply to private physicians engaged in informal research.

- d) How are studies of *abnormal* physiologic processes treated?

The language raises more questions than it answers.

68. An earlier version of the bill would have limited the Act by requiring all principal investigators to be licensed physicians or dentists. The addition of "qualified health scientist with appropriate education" creates a subjective test which may be abused. The bill does not state what agency will determine whether a particular principal investigator is "qualified" or has "appropriate education." Since the Act does not define "qualified health scientist," the standards by which an agency is to make such a determination are unclear. However, the failure to provide a clear definition of "qualified health scientist" is not as significant as the meaning of "clinical research." The latter term will create more exceptions to the federal regulations than the definition of principal investigator. See note 67 *supra*.

of the United States Department of Health, Education and Welfare.⁶⁹

Thus, the bill would adopt and apply the federal procedures to non-federally funded medical research in Illinois falling within the meaning of clinical research. Further, the bill would apply to all clinical research in Illinois regardless of the source of funding.

The bill provides for quarterly informational filings to the Illinois Department of Health by institutional review committees listing all pending and approved projects. There need be no filing, however, where one is already being made pursuant to the Illinois statute on investigational new drugs.⁷⁰ Likewise, the bill would not apply

to the practice of medicine or dentistry by any one licensed under the Medical Practice Act or the [Dental Practice Act] in which disease in a particular, individual patient is investigated and treatment initiated solely with the view of preventing, arresting, or curing the disease in that patient.⁷¹

This provision could produce confusion for institutional review committees, since it could be interpreted to exclude those procedures which fall somewhere in between clinical research and the practice of medicine. The line separating the two categories is not so clear, for example, in the case of acupuncture and organ transplantation, both of which arguably fit under either category. If Senate Bill 1670 were enacted into law, this ambiguity would be best resolved at the institutional level by applying uniformly the federal standards pertaining to subjects at risk⁷² and by having the IRC assert review jurisdiction over all cases where the procedure goes beyond accepted methods and is not an isolated, individual case of treatment.⁷³

Particularly significant to the hospital attorney is the likelihood that persons serving on institutional review committees will want to know whether they might be held liable for approving in good faith an investigative study which has untoward results. Physicians are protected by statute in such circumstances in the absence of willful or wanton misconduct,⁷⁴ but persons other than physicians are not presently afforded similar protection. There is a need to have this question resolved by statute in Illinois. Accordingly, it is suggested that as a minimum standard Senate Bill 1670 be amended to include the following provision:

69. S.B. 1670, § 5(a)-(c).

70. *Id.* § 8. Notes 21-22 *supra* and accompanying text.

71. *Id.* § 3.

72. 45 C.F.R. §§ 46.2(b), 46.3(b), 39 Fed. Reg. 18917 (1974).

73. *Id.* § 46.3(b), 39 Fed. Reg. 18917.

74. ILL. REV. STAT. ch. 91, § 2b (1973).

Except in cases involving willful and wanton misconduct, no person who in good faith serves as a member of a research review committee shall be liable for civil damages as a result of his acts, omissions or decisions in connection with his duties on the committee.

Most research of the type contemplated by the DHEW regulations and the proposed Illinois legislation is conducted by, and usually on the premises of, the larger health care institutions, universities or drug companies. By adopting in blanket form the DHEW regulations the Illinois legislation would require that human investigational studies will not originate in, be conducted in, and be totally evaluated in the office of the physician. It is unclear whether such studies have occurred frequently in private offices, although it is known that some members of the organized medical societies in Illinois have objected to the legislation on the grounds that it would make physicians interested in research more dependent upon hospitals or universities.

The sponsoring institution need not be a hospital, a university or a drug company. The passage of Senate Bill 1670 would require that the sponsoring institution be "an organization which can and does assume responsibility for the subjects involved" in the investigational activities.⁷⁵ While internally-funded studies would never require a filing with or approval by DHEW, the sponsoring organization and its IRC would have to be capable of receiving DHEW approval in all respects in order to qualify under Senate Bill 1670.⁷⁶

By adopting the federal regulations, Senate Bill 1670 would arguably require review and approval before the proposed research may be initiated, even though no application to DHEW for funding may be involved. It is recommended that the by-laws of the IRC make this point clear.⁷⁷ Senate Bill 1670 would also require after-the-fact quarterly filings by all Illinois institutional review committees containing the following information:

- (a) the name of the person conducting the research,
- (b) the title and purpose of the research, and
- (c) the location of the investigation; provided, however, that no filing would be required for clinical research for which a separate filing is required under Section 17 of the Illinois Food, Drug and Cosmetic Act.⁷⁸

While these filings would be public documents, the records of each IRC would not be treated similarly. Senate Bill 1670 recognizes the private nature of such records by forbidding the re-

75. 45 C.F.R. § 46.2(c), 39 Fed. Reg. 18917 (1974).

76. Note 67 *supra* and accompanying text.

77. See Appendix B, § 5.1.

78. S.B. 1670, § 8. Note 22 *supra*.

lease of privileged or confidential trade secrets, commercial or financial information (for example, a description of a drug company's research), and personnel and medical or similar files, "the disclosure of which would constitute an unwarranted invasion of personal privacy."⁷⁹

To the extent that clinical research in Illinois is not conducted in accordance with Senate Bill 1670, it could be "declared a nuisance inimical to the public health."⁸⁰ The Illinois Department of Public Health, the Attorney General, the local State's Attorney, or any "resident citizen" of Illinois could maintain an action to enjoin such conduct in the Illinois courts. Violation of an injunction would be punishable as contempt of court.⁸¹

The passage of Senate Bill 1670 would allow medical or dental clinics and societies, health maintenance organizations,⁸² and any other profit or non-profit organization to lawfully sponsor clinical research in Illinois, provided the organization complies with the DHEW regulations (and, where applicable, the FDA regulations and Section 17 of the Illinois Food, Drug and Cosmetic Act).

CONCLUSION

The laws applicable to human investigation in Illinois hospitals are already numerous and complex. The finalized DHEW regulations, coupled with the enactment of Senate Bill 1670, would not necessarily resolve all the problems, but would constitute a significant step forward. Hospitals and their attorneys need to familiarize themselves with the rules now in effect and the forms necessary to comply with those rules, to assure that human subjects involved in medical investigations are adequately protected, and to make sure that inadvertent noncompliance does not expose the hospitals to malpractice claims or to loss of research funds.

79. *Id.*

80. *Id.* § 9.

81. *Id.*

82. A health maintenance organization is a pre-paid health services program which emphasizes preventive care. This would ordinarily mean an Illinois Voluntary Health Services Plans Corporation, incorporated under ILL. REV. STAT. ch. 32, § 595 *et seq.* (1973), except for the exemptions allowed in § 597. The Illinois legislature has recently passed and sent to the Governor for signature a Health Maintenance Organization Act which would still require adherence to chapter 32, § 595 *et seq.*

APPENDIX A

INVESTIGATIONAL NEW DRUG APPLICATION*

TO: Division of Food and Drugs
Illinois Department of Public Health
535 West Jefferson Street
Springfield, IL 62761

NAME OF SPONSOR:

ADDRESS:

Best descriptive name of drug:

Name and address of each supplier:

Dosage and route of administration:

Intended results of investigation?

Investigators must file with the Food and Drug Administration form FD-1571 "Notice of Claimed Investigational Exemption for a New Drug" within 30 days of use of an investigational new drug in human subjects.

Applicant

PER _____
(Responsible Official or Agent)

* The primary concern of the Division of Food and Drugs of the Illinois Department of Public Health is that approval has been granted by the federal FDA and not withdrawn before research is undertaken in Illinois. Letter from the Chief of the Division of Food and Drugs of the Illinois Department of Public Health to the author, August 16, 1974.

APPENDIX B

BLACKACRE MEMORIAL HOSPITAL —

BYLAWS OF THE HUMAN INVESTIGATION COMMITTEE

ARTICLE I

NAME

§1.1 The name of the committee shall be the Human Investigation Committee of Blackacre Memorial Hospital (the "Hospital" herein).

Annotation: There is nothing magical about the term "human investigation committee;" it is not required by law in this form, but fits well into the functional scheme of names of committees usually adopted by the medical staff of a hospital. The applicable federal and state laws refer to the committee as the "review committee" or the "research review committee." 45 C.F.R. § 46.1 *et seq.*, 39 Fed. Reg. 18917 (1974); S.B. 1670, § 4.03. The name of the hospital or other institution (e.g. a university) should be included whether or not the committee is recognized in the medical staff bylaws, since the DHEW regulations make it clear that the committee is part "of the organization." 45 C.F.R. § 46.2, 39 Fed. Reg. 18917 (1974).

ARTICLE II

PURPOSE AND SCOPE

§2.1 The purposes of the committee shall be to safeguard the rights and welfare of human subjects involved in Hospital-related investigational activities and studies, to review such activities to determine that the rights and welfare of subjects involved are adequately protected, to assure that the risks to an individual are outweighed by the potential benefits to him and by the importance of the knowledge to be gained, to require that legally effective informed consent is obtained by methods that are adequate and appropriate, and to do all other actions necessary and proper at the Hospital through its various divisions and certain affiliated organizations for the protection of subjects of investigational studies, regardless of the source of funding for such studies.

Annotation: See 45 C.F.R. § 46.2, 39 Fed. Reg. 18917 (1974).

While the DHEW regulations apply only to human investigation activities "supported by DHEW grants or contracts," § 5 of S.B. 1670 would apply to clinical research in Illinois without regard to the source of funding. If S.B. 1670 is not enacted into law the phrase "regardless of the source of funding for such studies" would not be required.

§2.2 The committee's responsibility shall extend to all component parts of the Hospital's human investigative activities, including, but not limited to, inpatient care, outpatient care, the emergency room, and any teaching or research efforts. However, the committee's responsibility shall not include individual, emer-

gency, or other isolated patient care cases which are not otherwise part of an ongoing study involving other human subjects.

Annotation: Admittedly the jurisdiction granted to the committee by this section goes beyond the Illinois statutory definition of clinical research and applies without regard to the source of funding. S.B. 1670, § 5. This broad scope is recommended to assure that the committee is utilized uniformly within the hospital. The exclusionary language at the end of the section is designed to allow for freedom on the part of the treating physician in certain circumstances which would otherwise "handcuff" the conscientious review committee.

§2.3 Subject to the provisions of Article VI, the committee's responsibility for review and assurance shall extend to all circumstances involving any studies or investigations in which the Hospital or a member of its professional staff is a participant.

Annotation: If the institution is an educational one as well as a health care center the words "faculty or" should be inserted before "professional staff."

§2.4 It is anticipated that the committee will qualify as a general assurance institutional review committee for the protection of human subjects within the meaning of 45 Code of Federal Regulations (C.F.R.) § 46.6, 39 Fed. Reg. 18918 (1974), as promulgated by the U.S. Department of Health, Education and Welfare (DHEW).

Annotation: 45 C.F.R. § 46.5(a), 39 Fed. Reg. 18917-18 (1974), provides that this assurance format will be required by DHEW for organizations "having a significant number of concurrent DHEW-supported projects or activities involving human subjects." If a hospital does not have such a number of activities, the special assurance procedure is applicable. 45 C.F.R. § 46.5(b), 39 Fed. Reg. 18918 (1974). Illinois law allows either by adopting the federal standard. S.B. 1670, § 5(c). Because the field of law is developing so rapidly, it is recommended that the general assurance procedure be utilized so that an institution committee is able to keep abreast of changes.

ARTICLE III

MEMBERSHIP

§3.1 The committee shall be composed of not less than five (5) members with varying backgrounds and representing various professional groups (including, for example, medical, law, religious, nursing, pharmaceutical, and hospital administration) in order to assure complete and objective review of investigational projects and activities commonly conducted at the Hospital, at least one of whom shall be a person who is not an officer, employee, or agent of, or otherwise associated with the Hospital.

Annotation: 45 C.F.R. § 46.6, 39 Fed. Reg. 18918 (1974). It is not clear what "otherwise associated with" the hospital means or who this language in the DHEW regulations would exclude. It is arguable that the independent attorney for

a hospital is a person who is "associated with" the institution, although it seems clear that his responsibility is to remain an objective critic of the institution. Experience shows that a pharmacist, a nurse, and a hospital administrator are valuable participants on such a committee as well as the physician, the clergyman and the attorney. The comments published with the regulations conclude that this requirement "is an essential protection against the development of insular or parochial committee attitudes, that it assists in maintaining community contacts, and would augment the credibility of the committee's independent role." 39 Fed. Reg. 18915 (1974). This would appear to reflect the DHEW desire to have consumers or community representatives on review committees.

§3.2 Members shall be appointed for a term of one year by the President of the Hospital or his designee at the time of annual committee appointments, except that vacancies may be filled at any time, and additional members may be added at any time.

Annotation: Having committee members reappointed annually is recommended to clear out those who do not participate fully. Having appointments made by the chief executive or his designee will assure expediency in keeping the review committee personnel as professional as possible.

§3.3 The chairman of the Committee shall also be appointed by the President of the Hospital or his designee, for such term as shall be mutually agreed upon between them, as shall a first vice-chairman and a second vice-chairman, to serve as acting chairman, in that order, in the event the chairman may not be present or may not be eligible to act by virtue of section 3.4.

Annotation: A strong chairman is a prerequisite to a strong and effective review committee.

§3.4 No member of the committee shall be involved in either the initial or continuing review of an activity in which he has a professional responsibility, except to provide information requested by the committee.

Annotation: 45 C.F.R. § 46.6(b)(3), 39 Fed. Reg. 18918 (1974). Conflicts of interest are sometimes difficult to assess. They obviously include situations where the principal or co-investigator is on the committee. Is there a conflict if the committee member is, for example, chairman of the department in which the research will be conducted? The wise committee member will abstain in all cases where there is even the appearance of a conflict of interest.

§3.5 Committee members shall be identified to all appropriate governmental or other agencies by name, occupation or position, and by other pertinent indications of experience and competence in areas pertinent to the areas of review such as earned degrees, board certification and licensure. Employment by, or other relationship to the Hospital shall be identified. Changes in committee membership shall be reported to DHEW or other agencies from time to time where appropriate or required.

Annotation: 45 C.F.R. § 46.6(b)(2), 39 Fed. Reg. 18918 (1974).

§3.6 The President of the Hospital shall appoint as many ex-officio, non-voting members of the committee as (s)he deems desirable for the efficient operation of the committee, to serve at the pleasure of the President. Ex-officio members may, at the President's discretion, serve as chairman or vice-chairman of the committee.

Annotation: The non-voting status of ex-officio committee members should be specified for clarity. Persons likely to have frequent conflicts of interest should serve as ex-officio members if necessary to the committee's function.

ARTICLE IV

MEETINGS

§4.1 The committee shall meet at least quarterly or more frequently at the call of the chairman. Written minutes shall be kept of all formal committee activities and distributed to committee members and other appropriate individuals designated by the Chairman.

Annotation: 45 C.F.R. § 46.19, 39 Fed. Reg. 18920 (1974).

The frequency of the committee meetings should depend upon the volume of applications or proposals for review.

§4.2 Meetings will be conducted in accordance with Roberts Rules of Order (revised). A quorum of the committee will consist of no less than sixty percent (60%) of the then current membership for approval of any applications for review and fifty percent (50%) of the then current membership for taking any other action, including adoption and amendment of these by-laws and committee statements on policy and procedure. No quorum will consist entirely of members of one professional or lay group.

Annotation: 45 C.F.R. § 46.6(b)(5) & (6), 39 Fed. Reg. 18918 (1974). A workable percentage should be selected as the quorum.

§4.3 Minutes of committee meetings and other written evidence of committee assurances and determinations will be retained in accordance with the requirements of all applicable federal or state laws or regulations. Proposals and all supporting documents submitted to, or generated by, the committee shall likewise be retained as provided by law, and in no event for less than three (3) years following termination of the affected research activity, subject to the terms and conditions of grant and contract awards.

Annotation: 45 C.F.R. § 46.19, 39 Fed. Reg. 18920 (1974).

§4.4 The committee may, consistent with its obligations hereunder, conduct its business by mail, by telephone, or by separate individual review of proposals where deemed advisable by the chairman without the necessity of a formal meeting. In the case of the circulation of proposals to individual members of the committee, provision shall be made for circulation to all commit-

tee members and for distribution of the relevant committee comments to all other members.

Annotation: Under Roberts Rules of Order these procedures are not available unless authorized expressly in the by-laws.

ARTICLE V

COMMITTEE PROCEDURES AND RECORDS

§5.1 The committee shall, prior to the onset of any investigational study involving human subjects, determine the acceptability of all proposals seeking to use human investigation affecting the Hospital in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. In so doing the Committee may from time to time adopt policy statements on the general subject of human investigation which it believes reflect standards to which the committee should be committed.

Annotation: 45 C.F.R. §§ 46.6(a), 46.6(b) (1), 46.11(a), 39 Fed. Reg. 18918-19 (1974).

§5.2 The committee shall first determine whether the human subjects involved in any study are at risk or not. Each application shall be certified on this point. All studies of body tissues, fluids or parts which are removed or drawn as part of another, non-experimental procedure which, by itself, does not depart from the application of those established and accepted methods necessary to meet the patient's needs shall automatically be certified as not involving human subjects at risk.

Annotation: 45 C.F.R. § 46.11, 39 Fed. Reg. 18919 (1974).

The certification called for in this section requires affirmative committee action, except in the fact situation specified. An example of the automatic no-risk certification would be laboratory analysis of blood samples for a research project when the blood was drawn in the first place routinely and for purposes other than the study.

§5.3 The committee shall determine that the rights and welfare of the subjects involved are adequately protected, that risks to an individual are outweighed by the potential benefits to him and by the importance of the knowledge to be gained, that legally effective informed consent is to be obtained by methods that are adequate and appropriate, and that the conduct of the activity will be reviewed at timely intervals.

Annotation: 45 C.F.R. § 46.2(b), 39 Fed. Reg. 18917 (1974).

§5.4 All signed consent forms utilized by an investigator hereunder shall be retained by the investigator and delivered to the Hospital when and as provided by the committee.

Annotation: 45 C.F.R. § 46.19, 39 Fed. Reg. 18920 (1974).

§5.5 The committee shall establish a procedure for continuing review of the approved projects in keeping with the above determinations. Continuing review shall be no less frequent than annual. The committee has a legal obligation to and reserves its right to review the progress of all continuing studies approved

by it for the purpose of safeguarding the rights of human subjects.

Annotation: 45 C.F.R. § 46.6(c), 39 Fed. Reg. 18918 (1974).

§5.6 Except as otherwise provided by law, information in the records or possession of the Hospital acquired in connection with an activity under the committee's jurisdiction, which information refers to, or can be identified with a particular subject, shall not be disclosed except: (a) with the consent of the subject or his legally authorized representative, or (b) as may be necessary for the Secretary of DHEW pursuant to law.

Annotation: 45 C.F.R. § 46.19(b), 39 Fed. Reg. 18920 (1974).

§5.7 The committee shall establish procedures (a) to provide advice and counsel to investigators with regard to the committee's actions, (b) to insure prompt reporting to the committee of proposed changes in an activity and of unanticipated problems involving risk to subjects or others, and (c) to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labeled drugs, or to medical devices, are promptly reported to DHEW.

Annotation: 45 C.F.R. § 46.6(d), 39 Fed. Reg. 18918 (1974).

§5.8 The committee may prescribe conditions under which any investigative activity may be conducted, may recommend modifications, and may determine the nature and frequency of interim review procedures to insure continued provision of safeguards of the subjects. The conditions may not be removed except by the committee or DHEW.

Annotation: 45 C.F.R. § 46.18, 39 Fed. Reg. 18920 (1974).

§5.9 Favorable recommendations of the committee are always subject to further review, modification or rejection by the administration, or medical staff of the Hospital. Unfavorable rulings by the committee may not be overruled by the Hospital.

Annotation: 45 C.F.R. § 46.18, 39 Fed. Reg. 18920 (1974).

Educational institutions should insert the word "faculty" following the word "administration."

§5.10 Informed consent to be legally effective, shall include: (a) a fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental; (b) a description of any attendant discomforts and risks reasonably to be expected; (c) a description of any benefits reasonably to be expected; (d) a disclosure of any appropriate alternative procedures that might be advantageous for the subject; (e) an offer to answer any inquiries concerning the procedures; and, (f) 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. The committee shall assure that informed consent is both obtained pursuant to law and adequately documented and shall prescribe recommended forms for such documentation, which shall not include any exculpatory language in favor of the Hospital or the investigator.

Annotation: 45 C.F.R. §§ 46.3(c), 46.9, 46.10, 39 Fed. Reg. 18917-18 (1974).

§5.11 The committee shall adopt a procedure for considering separately any investigational studies dealing only with animals or those lacking definite plans for human subjects and for approving the same upon such criteria as are required by law.

Annotation: 45 C.F.R. §§ 46.13, 46.14, 39 Fed. Reg. 18919 (1974).

§5.12 The committee shall, wherever required by law, and may wherever desirable, require or recommend the appointment at the Hospital of standing or special committees or subcommittees for the protection of special groups of subjects, such as minors, incompetents, prisoners, pregnant subjects and the unborn; the committee may also, subject to prior Hospital clearance on budgetary grounds where applicable, appoint or retain one or more experts in any field to answer questions pertaining to any pending proposal for review.

Annotation: DHEW has published proposed regulations to cover procedures relating to special categories of human subjects. These were published at 38 Fed. Reg. 31738 (1973) and have not yet been finalized.

§5.13 The Hospital shall, where applicable, submit to DHEW, for its review, approval and official acceptance, an assurance of its compliance with the above stated responsibilities and shall also provide with each proposal involving human subjects a certification that it has been reviewed in accordance with that assurance.

Annotation: 45 C.F.R. §§ 46.4, 46.11(b), 46.15, 39 Fed. Reg. 18917-19 (1974).

§5.14 The committee shall publish its procedures and forms and shall make the same available generally to all members of the administration, and medical staff of the Hospital.

Annotation: 45 C.F.R. § 46.6(c)-(d), 39 Fed. Reg. 18918 (1974). Educational institutions should insert the word "faculty" following the word "administration." See also 45 C.F.R. § 46.18, 39 Fed. Reg. 18920 (1974), which requires "continuing indoctrination of personnel" by the institution.

§5.15 Material revisions in the implementation of policies and procedures of the committee shall be reported from time to time to DHEW for approval.

Annotation: 45 C.F.R. § 46.4, 39 Fed. Reg. 18917 (1974).

ARTICLE VI

AFFILIATED INSTITUTIONS

§6.1 Health care, educational or research institutions formally affiliated with the Hospital are encouraged to form and utilize their own institutional review committees. Where they have not done so, however, they may elect, with the express writ-

ten consent of the Hospital, to utilize the committee as an institutional review committee for the purposes and with the procedures provided for in these by-laws.

Annotation: The DHEW regulations provide that "No grant or contract involving human subjects at risk shall be made to an individual unless he is affiliated with or sponsored by an organization which can and does assume responsibility for the subjects involved." 45 C.F.R. § 46.2(c), 39 Fed. Reg. 18917 (1974). An investigator may be affiliated with both a hospital and another institution not having a review committee established, and the risk of professional liability may be so low that the hospital would be willing to "sponsor" the research under the aegis of its committee. While perhaps necessary at times, these situations should probably be avoided customarily. The proposed Illinois legislation increases the importance of this provision by adopting the federal procedures, meaning that a sponsoring institution is necessary for all clinical research in Illinois. S.B. 1670, §§ 4.03,5.

ARTICLE VII

ACCEPTANCE OF GOVERNMENTAL STANDARDS

§7.1 These by-laws acknowledge and incorporate by reference all existing regulations issued by the DHEW, the U.S. Food and Drug Administration, and the Illinois Department of Public Health pertaining to protection of human subjects in investigational studies. Wherever possible, these by-laws shall be construed consistently with any such regulations.

Annotation: This provision helps resolve any ambiguities which might grow out of the working rules or practices of the committee. If inconsistencies develop between the State and Federal regulations, the Federal rules would generally control.

ARTICLE VIII

AMENDMENT

§8.1 These by-laws may be amended by a simple majority vote at any meeting of the committee of which the members have been given at least one week's written notice and at which a quorum is present.

Annotation: These by-laws should be fairly easy to amend so that procedural problems and changes in the laws may be handled effectively. Roberts Rules of Order require more restrictive amendatory provisions unless they are expressly included in the by laws.

FORM HOSP-HIC 001

Adopted _____

Last Revised _____

HIC File No. _____

APPENDIX C

BLACKACRE MEMORIAL HOSPITAL —
HUMAN INVESTIGATION COMMITTEE

APPLICATION FOR COMMITTEE REVIEW AND APPROVAL

SUBJECT: Hospital-affiliated Clinical Research and Investiga-
tion Involving Human Subjects

INSTRUCTIONS:

All investigators in studies involving human beings as investigative subjects, regardless of the source of funding, must provide the following information for review and approval by the Hospital's Human Investigation Committee. Please submit—copies of this completed application, signed by the Principal Investigator and the Department Chairman, to the Research Affairs Office with any relevant grant applications.

Before completing this application the investigator should review the by-laws and all policy and procedure statements of the Human Investigation Committee. *Do not answer questions below by referring to attachments alone.*

The Committee is charged by federal and state law with this review on behalf of the Hospital and on behalf of the human subjects, and the Committee may request any additional information it deems necessary before acting on an application.

PRINCIPAL INVESTIGATOR:

DEPARTMENT:

TITLE OF PROJECT:

SOURCE OF FUNDS:

PROJECT PERIOD:

Starting date _____ Ending date _____

1. What kinds of patients or subjects are involved in this study and how are they to be selected?
2. How do you plan to obtain informed consent? How is the consent to be documented? (Please refer to the current suggested Committee special consent form for reference and attach a copy of the form to be used, whether or not modified from the Committee's form.)
3. Outline the potential diagnostic and/or therapeutic benefit to the patient if the study is clinical research combined with professional care. If there is no benefit to the subject please so state.
4. Outline the scientific benefit of the study.
5. Outline any potential hazards to patients, including knowledge of toxicities of any agents to be used. Describe the protective steps to be taken to guard against injury to the subjects.
6. (For protocols involving drugs only) Give below the new

drug number (s) issue by the U.S. Food and Drug Administration and describe the current FDA status of each drug or substance to be used.

7. State all special protective measures which are being taken to protect the rights of subjects who are minors (under age 18), incompetents or the mentally infirm, prisoners, pregnant women or the unborn. If the study will not include any such subjects, please so state.

Dated _____, 197__

Principal Investigator

Department Chairman

Institutional Official

FORM HOSP-HIC 002

Last Revised _____

HIC File No. _____

APPENDIX D

BLACKACRE MEMORIAL HOSPITAL —
HUMAN INVESTIGATION COMMITTEENOTICE OF APPROVAL OF APPLICATION AND
COMMITTEE CERTIFICATION AS TO RISK

Principal Investigator _____

Title of Project _____

Source of Funds _____

The above application for approval of investigations involving human subjects has been reviewed by the Human Investigation Committee. It is approved as appropriate upon a finding that:

1. The risks to the subject, if any (see below), are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;
2. The rights and welfare of all subjects will be adequately protected;
3. Legally effective informed consent will be obtained by adequate and appropriate methods;
4. The conduct of the investigation will be reviewed at timely intervals.

In conducting the study, the principal investigator has the individual responsibility to comply with the Human Investigation Committee's by-laws and procedures and to adhere to the statements of policy which have been adopted by the Committee.

APPROVAL IS GRANTED FOR ONE YEAR from the date of certification of risk below. Projects extending beyond one year from that date and involving risk must be resubmitted annually to the Committee. Any protocol changes in an investigation during its course must receive prior approval of the Committee.

The signatures of the Committee members below signify their approval of the application; approval by 60% of the members is necessary for Committee approval.

In addition, the Committee is required to certify as to whether or not subjects in this study are at risk, that being defined as exposure to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

Each member voting shall indicate "yes" or "no" on whether he or she believes that the subjects are at risk. A single members' finding of risk will cause certification as to risk, and an

APPENDIX E

BLACKACRE MEMORIAL HOSPITAL

This *sample* is intended as a guide in the preparation of a consent form for application to individual research projects. A comparable consent form must be submitted with each protocol prior to review by the Human Investigation Committee.

SPECIAL CONSENT FORM

I, _____, an adult [or: legal guardian of _____, a minor], have been invited to participate in a study of _____ under the direction of Dr. _____, in which I voluntarily consent to participate.

- a. The implications of my voluntary participation in this medical investigation, its nature, duration and purpose, the methods and means by which it is to be conducted, and the inconvenience and hazards which may be expected have been thoroughly explained to me by _____
- b. I have read and I understand all written materials which have been provided to me further describing the study and its potential risks and benefits to me.
- c. I have been given an opportunity to ask any questions I wish concerning this procedure and all such questions have been answered to my complete satisfaction. I understand that my participation in this study can be terminated at any time upon my request.

Volunteer's signature

Date

(_____)

Relationship

I was present during the explanation referred to above, as well as the Volunteer's opportunity for questions, and hereby witness his (her) consent to participate in the study.

Witness' signature

Date

[Attach to this form any written explanation of the study which is to be given to each subject.]

FORM HOSP-HIC 003

Last Revised _____

APPENDIX F

BLACKACRE MEMORIAL HOSPITAL — HUMAN INVESTIGATION COMMITTEE

RECOMMENDATIONS TO INVESTIGATORS CONCERNING WITNESSES TO SPECIAL CONSENT FORMS

Each subject in a study reviewed by the Human Investigation Committee must give his or her consent to participate in the study. Only truly informed consent, in which the subject is aware of the risks and voluntarily assumes them, is legally effective. To document informed consent the Committee requires the subject's signature on a written special consent form, prototypes of which may be obtained from the Committee: and, to evidence the authenticity of the signature, each such special consent form requires a witness. Signed consent forms must be retained by the principal investigator in any study.

Although virtually any adult might properly witness the signature of a subject, the following are factors which affect the selection of a witness for consent to human investigation:

- (a) If a controversy concerning a subject should develop into actual or threatened legal action and consent is drawn in issue, the witness must be available to testify; therefore, it is important to use witnesses who can be located easily and whose whereabouts will be known despite changes in residence.
- (b) The witness should be a competent adult who can understand and articulate the basic concepts of informed consent.
- (c) Witnessing a signature under circumstances surrounding a human investigation study should not be taken lightly; a witness should be someone who will conscientiously listen to the reactions of the subject as the study is being explained and who will make sure the subject asks the questions which may be bothering him or her.
- (d) A witness who is too closely related to the subject may tend to side unreasonably with the subject in the event of a controversy.
- (e) A witness who is too closely related to the study or the investigator may be accused of not being objective enough in witnessing a subject's consent.
- (f) The best witness in a legal controversy is usually one whose objectivity can be demonstrated, whose attention to detail is thorough, and whose profession and background is likely to evoke respect.

For these reasons, and to assure maximum protection to the subjects, the Hospital, and the investigating professionals, the Human Investigation Committee recommends that, whenever feasible, members of the following categories be utilized as witnesses to informed consent in connection with studies involving human investigation:

1. Medical staff (other than investigators) and interns
2. Nursing staff and paramedicals
3. Religious advisors
4. Social Service staff
5. Hospital administrative staff

Inability to utilize witnesses from these categories will not of itself invalidate informed consent or result in disapproval of the study by the Human Investigation Committee. If an investigator has a question on this general issue, the Committee would be happy to help resolve it.

COMMITTEE ON HUMAN INVESTIGATION

Chairman

FORM HOSP-HIC 004

Last Revised _____

