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LEGAL IMPLICATIONS OF CLINICAL INVESTIGATION

by HOWARD N. MORSE*

I. INTRODUCTION

There is an increasing concern among the members of the medical profession with legal rights, obligations, and limitations affecting clinical investigation. This is understandable in light of the virtual explosion of clinical investigation within medical science.

Clinical investigation is the systematic collection, evaluation, and reporting, by or under the supervision of physicians, of data about other human beings for the purpose of advancing scientific medical knowledge. It thus includes neither investigation relating to animals (even though such investigation may also advance scientific medical knowledge), investigation of human beings for purposes unrelated to medical science, nor the trial of unproven procedures in the treatment of patients unless this is also a part of a systematic program of clinical investigation. Nevertheless, clinical investigation need not occur within the physician-patient relationship which arises when a person seeks and a physician undertakes to furnish medical diagnosis or treatment. For example, a person who volunteers as a subject of clinical investigation does not have a physician-patient relationship with a physician who does not undertake to furnish him any medical benefit.

II. RULES OF LIABILITY

The determination of the legal rights, obligations, and limitations involved in clinical investigation is complicated by the fact that special law in this field is virtually nonexistent. The sources of legal rules, constitutions, statutes, judicial decisions, and administrative decisions, rules, and regulations provide with few exceptions, no special legal rules for clinical investigation.

This does not mean, however, that clinical investigation is above the law. There are general rules of law that do apply, and they certainly

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will be applied by the courts if litigation arises. The most significant of these general rules are those relating to compensation for personal injury. Although it cannot be known with exactness how the courts will adapt these general rules of liability to the unexplored field of clinical investigation, the probable application of the rules can be foreseen with sufficient reliability to provide a practical guide for physicians engaging in clinical investigation.

A. THE REQUIREMENT OF CONSENT

Perhaps the most important general rule of liability law to be considered is that relating to assault, that is, the rule that anyone who intentionally takes any action which affects the body or mind of another without the legally valid consent of that person is liable for damages, unless there is a specific legal justification for that action.¹ To be an effective defense against such liability, consent must be both voluntary and informed.²

1. *Informed Consent*

Consent is not "informed" if the physician withholds information as to either the risk involved in the treatment (or, if treatment is not had, the nature of the treatment) or the results that may be reasonably expected, that is, the possibilities of successful treatment.³ These rules of law should apply to clinical investigation situations, where the therapy involved usually follows medically accepted, rather than unproven, procedures.

As long as he is motivated by concern for his patient, the physician may freely use his position of confidence and trust and his powers of persuasion in urging his patient to agree to medically indicated treatment.⁴ In exceptional circumstances recognized by standard medical practice, the physician may even withhold information from the patient which would otherwise be necessary in order to obtain an informed

1. See, e.g., *Lowry v. Standard Oil Co.*, 63 Cal. App. 2d 1, 146 P.2d 57 (1944); *O'Brien v. Howell*, 92 So. 2d 608 (Fla. 1957); *Blankenship v. State*, 130 Miss. 725, 95 So. 81 (1923); *Mendenhall v. State*, 18 Okla. Crim. 441, 196 P. 736 (1921). As to consent, see *Vanvactor v. State*, 113 Ind. 276, 15 N.E. 341 (1888); *Taylor v. State*, 214 Md. 156, 133 A.2d 414 (1957). But see *Wright v. Starr*, 42 Nev. 441, 179 P. 877 (1919).

2. See, e.g., *Guarro v. United States*, 237 F.2d 578 (D.C. App. 1956).

3. See, e.g., *Salgo v. Leland Stanford Jr. University Board of Trustees*, 154 Cal. App. 2d 560, 317 P.2d 170 (1957); *Natanson v. Kline*, 186 Kan. 393, 350 P.2d 1093 (1960).

4. *Hunt v. Bradshaw*, 242 N.C. 517, 88 S.E.2d 762 (1955).

consent.⁵ Obviously, in medical matters the physician and his patient are not equals. In the ordinary case, the patient is entitled to be informed about his condition, the nature of the treatment proposed and any unusual risks, and the results that may be anticipated.⁶ But in the final analysis he will usually rely upon the advice and judgment of his physician. If the information supplied is sufficient to serve as the basis for the patient's informed consent, the physician may freely urge the patient to submit to recommended treatment. What may be "acceptable persuasion" as applied to medical treatment may be "undue influence," however, when applied to clinical investigation outside of the physician-patient relationship.

Generally, physicians may be said to have a duty to inform. They must explain a proposed procedure or therapy in lay terms so that the patient has the opportunity to ask questions and come to a reasonable understanding of the decision he is to make.⁷ In the normal course of treatment, the physician is expected (1) to explain his diagnosis and prognosis,⁸ (2) to describe in nontechnical terms the procedure or therapy he proposes and explain any unusual hazard or risk of complications that may be inherent in such procedure or therapy,⁹ and (3) to explain the results that may be reasonably anticipated, particularly if the prospect for improving the patient's condition is limited.¹⁰ This does not mean, however, that the physician must discuss with his patient remote possibilities of disaster if satisfactory results are normally achieved uneventfully.¹¹

Medicine is both a science and an art, requiring the exercise of technical skills within the framework of the personal relationship between the physician and his patient. In the practice of his art, the physician can inspire the confidence and tranquility of his patient

5. *Watson v. Clutt*, 262 N.C. 153, 136 S.E.2d 617 (1964); *Roberts v. Wood*, 206 F. Supp. 579 (D.C. Ala. 1962); *Grosjean v. Spencer*, 140 N.W. 2d 139 (Iowa 1966); *Ball v. Mallinkrodt Chemical Works*, 381 S.W.2d 563 (Tenn. 1964); *Aiken v. Clary*, 396 S.W.2d 668 (Mo. 1965); *Fischer v. Wilmington General Hospital*, 51 Del. 554, 149 A.2d 749 (1959); *Hatcher v. Black*, (a) Eddy, J. P.: *Professional Negligence*, London: Stevens & Sons, Ltd. (1955). (b) Case Report, 2 BRITISH MEDICAL JOURNAL 105-106 (July 10, 1954).

6. *Natanson v. Kline*, *supra* note 3.

7. *Mohr v. Williams*, 95 Minn. 261, 194 N.W. 12 (1905); *Block v. McVay*, 80 S.D. 469, 126 N.W.2d 808 (1964).

8. *Hunter v. Burroughs*, 123 Va. 113, 96 S.E. 360 (1918); *Rogers v. Lumbermen's Mutual Casualty Company*, 119 So.2d 649 (La. App. 1960).

9. *Fritz v. Horsfall*, 163 P.2d 148 (Wash. 1945).

10. *Mitchell v. Robinson*, 334 S.W.2d 11, 19 (Mo. 1960); *Bolam v. Friern Hospital* (1957) 2 All E.R. 118.

11. *Bang v. Charles T. Miller Hospital*, 251 Minn. 427, 88 N.W.2d 186 (1958).

even under discouraging circumstances. Compliance with the legal requirements for informed consent need not keep the physician from being compassionate in his patient relationships. His tone and manner may freely express encouragement or a note of optimism for which a basis exists in the patient's circumstances.

The need for an informed consent does not require a departure from common sense standards of medical practice. Actually, the physician's obligation has been judicially interpreted as a duty to follow the standard of medical practice prevailing among reputable physicians in the community as to the extent and kind of information given to patients under similar circumstances.¹² It is customary for the conscientious physician not only to inform but also to employ an element of persuasion if this is in the best interest of the patient, such as where the advantages of treatment clearly outweigh its risks. But where there is a close or unknown balance between the possible benefits and hazards of an inherently risky procedure, the physician's influence should be so tempered as to give the patient greater responsibility in making his own decision.

Following standard medical practice means also that in exceptional circumstances the patient need not be given the details about his condition or proposed treatment.¹³ For example, it may be medically desirable and customary to withhold distressing information from a critically ill cancer patient, or to avoid a frank explanation of proposed treatment where the patient is so emotionally upset or disturbed that such an explanation would cause him to decline clearly advisable treatment. Under these circumstances, the physician should discuss the situation fully with a member of the patient's immediate family or, if there is none, with a friend who is concerned about the patient's well-being and informed regarding his personal affairs.¹⁴ This exception cannot be supported, however, simply on the possibility that information necessary to permit an informed consent might cause the patient to reject recommended treatment on an entirely rational basis.¹⁵ If this justification were acceptable, it would practically dispense with the need for informed consent and deprive the patient of the right which the courts are seeking

12. *Wells v. McGehee*, 39 So.2d 196 (La. App. 1949); *Luka v. Lowrie*, 171 Mich. 122, 136 N.W. 1106 (1912); *Ollet v. Pittsburgh, Cincinnati, Chicago and St. Louis Railway Company*, 201 Pa. St. 361, 50 Atl. 1010 (1902); *Jackovich v. Yocum*, 212 Iowa 914, 237 N.W. 444 (1931).

13. *Kennedy v. Parrott*, 243 N.C. 355, 90 S.E.2d 754 (1956).

14. *Natanson v. Kline*, *supra* note 3.

15. *Id.*

to protect, that is, the freedom to choose or decline treatment for whatever reason the patient may have.

The duty to disclose is limited to those disclosures which a reasonable chemical investigator would make under the same or similar circumstances. How he may best discharge his obligation to the subject in this difficult situation involves primarily a question of medical judgment. His choice of one of several plausible courses should not be called into question if it appears, all circumstances considered, that he was motivated only by the best interests of both the subject and medical science, and that he proceeded as competent investigators would have done in a similar situation.

The fundamental distinction between negligence and assault and battery is that the former is unintentional and the latter intentional. Thus where a subject consents to undergo clinical investigation, but the nature, consequences, and risks of the investigation are not properly explained to him, he may have a cause of action for assault. And where a subject does give informed consent to undergo investigation, but is injured as a result of lack of due care by the investigator, he has a cause of action for negligence.

The clinical investigator is under a duty to inform the subject generally of the possible collateral hazards. He violates that duty and subjects himself to liability, if he withholds from the subject any facts which are necessary to form the basis of an intelligent consent to the proposed investigation. Likewise, the investigator may not minimize the known dangers of an investigation in order to induce the subject's consent.¹⁶ The greater and more numerous risks, the greater the understanding thereof that the courts will require.¹⁷

"Caveat emptor"—let the buyer beware—still has much vitality in business matters today, but it has no place in the law of the business of medicine. Although in one sense the patient may be regarded as a buyer of medical services, the courts place a great deal of responsibility upon the physician because of the position of confidence and trust which he occupies in relation to patients.¹⁸ He is expected to explain his treatment, anticipated results, and unusual risks, and at the same time to dedicate himself to his patient's benefit. This becomes a legal tightrope when

16. *Mitchell v. Robinson*, *supra* note 10.

17. McCoid, A.H., *Reappraisal of Liability for Unauthorized Medical Treatment*, 41 MINN. LAW REV. 381, 427 (1957).

18. *Yeates v. Harms*, 193 Kan. 320, 393 P.2d 982 (1964); *Valentine v. Kaiser Foundation Hospitals*, 15 Cal. Rptr. 26 (1961); *Woods v. Brumlop*, 71 N.M. 221, 377 P.2d 520 (1962).

a frank explanation of hazards may serve to so upset an emotional patient that he will choose the greater risk of declining treatment. The courts, recognizing the physician's dilemma in such situations, have stated that he should conduct himself according to the standard prevailing among other reputable practitioners.¹⁹ If the circumstances in particular cases justify a lesser explanation of hazards in the interest of the patient, then it would follow that experimentation with a human subject would require a more thorough and objective explanation of risks than is normally required in medical treatment.

The question of how much information a physician must furnish to a patient in order to avoid legal liability is somewhat confused because it arises out of two separate and distinct legal obligations. One is the necessity to obtain valid consent. The other requires the physician to act with the highest degree of good faith to protect the best interests of the patient. Both obligations apply to clinical investigation within the physician-patient relationship; but the second obligation does not apply to clinical investigation outside of that relationship.

Thus it appears that the clinical investigator must always give the minimum amount of information necessary to obtain valid consent. The exception which permits the withholding of information for the benefit of the patient does not apply in the clinical investigation situation. On the other hand, where sufficient information has been given in order to obtain valid consent, it would not appear that liability would arise from a failure to give additional information to an investigative subject who is not a patient.

Consent by the patient must also be "voluntary." For instance, consent is obviously lacking if a surgeon through error operates on the wrong person, or amputates the wrong limb, or performs elective surgery upon a patient who is informed only that he is to be examined for purposes of diagnosis.²⁰ Voluntary consent presupposes that the individual was supplied with sufficient information to enable him to make a knowledgeable choice. Consent given in ignorance is not in any realistic sense voluntary. However, consent cannot be deemed voluntary simply because it was not obtained under force or duress.²¹

19. See, e.g., *Baldor v. Rogers*, 81 So.2d 658 (Fla. 1954); *Sinz v. Owens*, 33 Cal.2d 749, 205 P.2d 3 (1949).

20. *Fischer v. Wilmington General Hospital*, *supra* note 5; *Govin v. Hunter*, 374 P.2d 421 (Wyo. 1962); *Patrick v. Sedwick*, 391 P.2d 453 (Alaska 1964).

21. *Steele v. Woods*, 327 S.W.2d 187 (Mo. 1959).

2. *Voluntary Consent*

Although laymen are not ordinarily capable of the same understanding about proposed medical treatment or experimentation as are physicians, they are not completely ignorant about medical procedures and treatment. Considerable public interest and knowledge about medicine is gained from newspapers, magazines, and ordinary schooling. There is more common knowledge about medicine, its successes, and its failures than ever before. The courts have recognized that laymen are capable of understanding in general terms such matters as the results that may be reasonably expected from treatment and the degree of risk to life or health that may be involved.²² On the other hand, the courts have laid down the rule that an individual cannot be deemed to have voluntarily consented to treatment about which he knows little or nothing.²³ "Voluntary" consent is thus closely related to "informed" consent. But there is voluntary consent when there is freedom to choose with understanding; that is, voluntary consent arises out of an unrestricted freedom to choose and a reasonable understanding of the choices available.²⁴

3. *Constructive Consent*

In emergencies, where the patient is unconscious or irrational and there is no other person available who is legally authorized to approve treatment, "constructive" consent may be implied from the circumstances.²⁵ The physician's authority to proceed with treatment is based upon the presumption that the patient would have consented to treatment necessary to protect his life or health if he had been able to do so.²⁶ This is an exception to the physician's legal duty to obtain consent prior to treatment.

4. *Capacity to Consent*

The validity of consent also depends upon the legal capacity or authority of the person who gives the consent. It is generally recognized that infants or persons suffering from general mental incompetence are

22. *Mitchell v. Robinson*, *supra* note 10.

23. *Hunt v. Bradshaw*, *supra* note 4; *Patrick v. Sedwick*, *supra* note 20.

24. *Salgo v. Leland Stanford Jr. University University Board of Trustees*, *supra* note 3.

25. Regan, L. J., *Doctor and Patient and the Law* 41 (3rd Ed. 1956).

26. Moritz, A. R. and Stetler, C. J., *Handbook of Legal Medicine* 151 (2nd Ed. 1964).

not legally capable of giving consent on any subject.²⁷ Competence to give consent is not necessarily an all or nothing situation. Some persons may be legally capable of giving consent for some purposes, but not for all.²⁸ To whatever extent a person is incapable of giving consent, the law grants to some other person the authority to act for him, at least for limited purposes.²⁹

If the subject has been committed to a mental institution or certified as laboring under a legally recognized mental aberration and is therefore (to use the Illinois designation for the purpose of illustration) a legally insane person, a sexually dangerous person (a criminal sexual psychopathic person), a criminal mentally incompetent person, a person in need of mental treatment, or a mentally retarded person, then, of course, consent could not be obtained for the subject.³⁰ In such a situation consent should be obtained from *both* parties in loco parentis—the individual and the institution. If the subject is married, the individual would be the spouse.³¹ If the subject is unmarried, the individual would be the closest next of kin.³² For the ascertainment of the closest of kin, a good “rule of thumb” to follow is the order of priorities contained in the particular state’s law of descent and distribution.

The consent of the individual is of a higher nature and, consequently, of more importance than the consent of the institution. This is so because, from a legal point of view, the subject-individual relationship is analogous to the concept of possession, whereas the subject-institution relationship is analogous to the lesser concept of custody.³³ Again analogously, and again from a legalistic standpoint, the seat of the subject-individual relationship is akin to the concept of domicile, whereas the seat of the subject-institution relationship is akin to the concept of residence. Therefore, the ostensibly informed consent of the individual would be subjected to an even greater degree of legal scrutiny than the purported informed consent of the institution.

If the subject has not been committed or certified to be laboring under a legally recognized mental disability, his consent, of course, must be first obtained. If the subject is a prisoner, three consents should be

27. *Zoski v. Gaines*, 271 Mich. 1, 260 N.W. 99 (1935).

28. *Lacey v. Laird*, 166 Ohio St. 12, 139 N.W.2d 25 (1956).

29. *Crippen v. Pulliam*, 61 Wash.2d 725, 380 P.2d 475 (1963).

30. *Farber v. Olkon*, 246 P.2d 710 (Cal. App. 1952), *aff’d* 40 Cal.2d 503, 254 P.2d 520 (1953).

31. *Lester v. Aetna Casualty and Surety Company*, 240 F.2d 676 (5th Cir. 1957).

32. *Farber v. Olkon*, *supra* note 30.

33. *Crippen v. Pulliam*, *supra* note 29.

obtained—from the prisoner, his spouse (otherwise, his nearest of kin), and the institution.

The courts made it clear that a child is not the property of its parents and may not be dealt with without regard for his best interests.³⁴ In a number of cases, for example, the courts have intervened to order medically indicated blood transfusions over the objection of the child's parents.³⁵

If a parent or guardian agrees to a minor's participation in clinical investigation outside of the physician-patient relationship that is not hazardous in terms of life, health, pain, or suffering, and if injury does not occur, the likelihood of legal problems is remote. Here, the issue of legal consent is, more or less, academic. Where the possibility of danger to the minor's life or health is not remote, the legal issue of consent cannot be brushed aside so easily.

A parent or guardian has an obligation to act in the child's best interests and for his benefit.³⁶ Accordingly, consent can be given on behalf of the child for medically indicated treatment.³⁷ The parental responsibility may be violated, though, if a parent or guardian exposes the child to unnecessary danger.³⁸ Consequently, the parent's consent to the use of a child for clinical investigation that is not medically indicated for the benefit of the child may be of doubtful validity as a defense against a liability claim. Illness or injury may justify appropriate but unproven therapy if other procedures are unsatisfactory. But clinical investigation not for the purpose of treating the child cannot be assumed to be for the child's benefit simply because the child might later have the "satisfaction" or "reward" of participating in medical progress.

Although a number of courts have said that a minor who has reached the age of sufficient understanding (the so-called age of discretion) can consent to medically indicated treatment,³⁹ it is questionable whether the courts would take the same position with respect to his participation in clinical investigation. It is likely that a court would regard submission

34. See, e.g., *Pierce v. Jeffries*, 103 W.Va. 410, 139 S.E. 651 (1927); *Denton v. James*, 107 Kan. 729, 193 P. 307 (1920).

35. *State v. Perricone*, 37 N.J. 463, 181 A.2d 751 (1962).

36. Rubenstein, I. H., *A Treatise on Contemporary Religious Jurisprudence* 43, 44 (1948).

37. *People v. Pierson*, 176 N.Y. 201, 68 N.E. 243 (1903).

38. *Owens v. State*, 6 Okl. Cr. 110, 116 P. 345 (1911); *Mitchell v. Davis*, 205 S.W.2d 812 (Tex. Cr. 1947).

39. *Gulf and Ship Island Railroad v. Sullivan*, 155 Miss. 1, 119 So. 501 (1928); *Lacey v. Laird*, *supra* note 28; *Sullivan v. Montgomery*, 279 N.Y.S. 575 (1935).

to clinical treatment as a reasonable area for the decision of a mature minor, and that doubt concerning capacity to consent would be resolved in favor of the child acting for his own benefit.

The courts generally allow minors to make their own decisions in business and property matters only when such freedom is consistent with their own well-being and public policy.⁴⁰ Inasmuch as the courts give greater protection to life and health than to property rights,⁴¹ they may ordinarily be expected to regard voluntary participation in clinical investigation involving hazard as a privilege reserved only for adults.

One medical authority in England has said: "It is clearly within the competence of a parent or guardian of a child to give permission for procedures intended to benefit that child when he is not old or intelligent enough to be able himself to give a valid consent. In the strict view of the law parents and guardians of minors cannot give consent on their behalf to any procedures which are of no particular benefit to them and which may carry some risk of harm. The reality of any purported consent which may have been obtained is a question of fact, and as with an adult the evidence would, if necessary, have to show that irrespective of age the person concerned fully understood the implications to himself of the procedures to which he was consenting. In the case of children and young persons the question whether purported consent was true consent would in each case depend upon facts such as age, intelligence, situation, and character of the subject, and the nature of the investigation."⁴²

The general rule concerning consent in respect to a surgical operation on a child was stated in 1941 by the United States Court of Appeals for the District of Columbia in *Bonner v. Moran*.⁴³ It probably has equal application to consent in respect to a child's participation in clinical investigation. The rule was stated as follows:

"In deference to common experience, there is general recognition of the fact that many persons by reason of their youth are incapable of intelligent decision, as the result of which public policy demands legal protection of their personal as well as their property rights. Hence it is not at all surprising that, generally speaking, the rule has been

40. *Carolina Telephone and Telegraph Company, Inc. v. Johnson* 168 F.2d 489 (4th Cir. 1948).

41. *Application of Sacer Realty Corporation*, 73 N.Y.S.2d 211 (1947).

42. "Responsibility in Investigations on Human Subjects—Statement by Medical Research Council," *BRITISH MEDICAL JOURNAL*, 178, 179 (July, 1964).

43. 75 U.S. App. D.C. 156, 126 F.2d 121 (1941).

considered to be that a surgeon has no legal right to operate upon a child without the consent of his parents or guardian. There are, of course, exceptions to the rule. One of them is in cases of emergency, when obviously an operation is necessary . . . others perhaps in cases in which the child has been emancipated, or where the parents are so remote as to make impracticable the obtaining of their consent in time to accomplish proper results. And where the child is close to maturity, it has been held that the surgeon may be justified in accepting his consent. But in all such cases the basic consideration is whether the proposed operation is for the benefit of the child and is done with a purpose of saving his life or limb.⁴⁴

Outside of the physician-patient relationship, it is clear that persons lacking capacity to consent should not be used for clinical investigation merely because they are convenient or available. It is recognized, however, that in some instances the advancement of medical science would be impossible without the use of persons of this class as investigative subjects. Some kinds of clinical investigation of children's diseases cannot be accomplished without using children as subjects. Similarly, necessary research on mental retardation might be impossible without the participation of mentally retarded subjects. It seems unlikely that public policy would entirely foreclose clinical investigation in these fields outside of the physician-patient relationship. There would, of course, never be any justification for the use of subjects who lack capacity to consent if the data sought could be obtained by using mentally competent adult subjects. It is also doubtful that it would ever be justifiable to subject children to the same degree of risks as would be permissible in the case of mentally competent adult subjects or of patients for whom possible benefits might offset the risks.

It is likely that some mechanism will eventually be developed to provide authorization for the participation of subjects who lack the capacity to consent in clinical investigation outside of the physician-patient relationship, under appropriate limitations and with adequate safeguards. At present, however, there is no recognized procedure for establishing a defense against liability for unauthorized investigation of this type. The clinical investigator can minimize the legal risk by limiting the use of such subjects to situations in which there is the strongest scientific justification and the minimum of risk of injury.

44. 75 U.S. App. D.C. 156, 126 F.2d 121, 122, 123 (1941).

B. THE DUTY TO EXERCISE REASONABLE CARE

Another important principle of law is the general rule that a person is liable for damages when his negligence has caused injury to the person or property of another.⁴⁵ Negligence is the failure to conform to the standard of reasonable care.⁴⁶ In the physician-patient relationship the physician is expected to possess and exercise that degree of skill and care ordinarily possessed and exercised by physicians in good standing in similar circumstances.⁴⁷ This standard applies where clinical investigation is conducted within the physician-patient relationship. Where it is conducted outside of that relationship, it is likely that the applicable standard would be that of the reasonable and prudent clinical investigator; the investigator would be required to possess and exercise that degree of skill and care that is ordinarily possessed and exercised by clinical investigators under similar circumstances. In neither case would liability arise unless a failure to conform to the respective standards was the proximate cause of injury to the patient or the subject.⁴⁸

In clinical investigation, negligence may consist of errors in procedure or technique, as it would in other forms of activity. It may also consist, however, of exposure of the patient or subject to unnecessary or unwarranted risks of failure to provide adequate safeguards by departing from the respective standards of care.

There are many judicial decisions on the issue of professional negligence in the physician-patient relationship.⁴⁹ These would apply gen-

45. See, e.g., *Stone v. Proctor*, 259 N.C. 633, 131 S.E.2d 297 (1963). *Standard Oil Company v. Southern Pacific Company*, 268 U.S. 146 (1925); *Turlington v. Tampa Electric Company*, 62 Fla. 398, 56 So. 696 (1911); *Patten v. Bartlett*, 111 Me. 409, 89 Atl. 375 (1914); *West Virginia Central and Pittsburg Railway Company v. State*, 96 Md. 652, 54 Atl. 669 (1903); *Loso v. Lancaster County*, 77 Neb. 466, 109 N.W. 752 (1906).

46. Shearman, Thomas G. and Redfield, Amasa A., *A Treatise on the Law of Negligence* 7 (1941).

47. Cusumano, Charles L., *Malpractice Law Dissected for Quick Grasping* 35 (1962).

48. 3 Shearman, Thomas G. and Redfield, Amasa A., *A Treatise on the Law of Negligence* 1527, 1528 (1941).

49. *Goodwin v. Hertzberg*, 201 F.2d 204 (D.C. Cir. 1952) (perforation of woman's urethra in performance of operation); *Lawrence v. Nutter*, 203 F.2d 540 (4th Cir. 1953) (failure of physician to administer gas gangrene antitoxin); *Moore v. Belt*, 34 Cal.2d 525, 212 P.2d 509 (1950) (cause of infection of urinary passages resulting from genito-urinary examination); *Nielsen v. Milligan*, 100 Cal App.2d 40, 222 P.2d 916 (1950) (failure to check infection when it first developed); *Huffman v. Lindquist*, 37 Cal.2d 465, 234 P.2d 34 (1951) (nonsurgical treatment of brain injury); *Merkle v. Kegerreis*, 350 Ill. App. 103, 112 N.E.2d 175 (1953) (negligence of roentgenologist in removing plantar

erally, of course, to clinical investigation within that relationship. None of them relate specifically to clinical investigation as defined herein, either within or without the physician-patient relationship.

Usually, clinical investigation involves departures from generally accepted procedures for diagnosis or therapy. Not every instance of departure from such generally accepted procedures constitutes clinical investigation, however. To achieve that status, the departure must be a part of a systematic program for the advancement of scientific medical knowledge. The cultist practitioner who has a mistaken and scientifically unsupported belief in the efficacy of a special procedure is not engaged in clinical investigation when he applies that procedure to a patient. The conscientious physician who tries an unproved but promising therapy solely for the benefit of his patient, without engaging in any systematic collection of data is likewise not engaged in clinical investigation. A few cases involving these types of departures from accepted forms of therapy have reached the courts.⁵⁰ Some of the opinions contain references to clinical investigation and appear to convey the impression that such investigation can be carried on only at the risk of the investigator. The context of these decisions makes it doubtful, however, that this impression was intended. In any event, it is highly unlikely that courts would take such an extreme position today.

The significance of the case law in this area should nevertheless be examined and evaluated. In *Carpenter v. Blake*⁵¹ in 1871 the Supreme Court of New York declared:

"It is incumbent on surgeons to treat such an injury to conform to the system thus established; and if they depart from it, they do it at their peril. Before the new practice can be used to shield the surgeon from the charge of malpractice, it must appear that the cases in which it was tested were substantially the same as those treated by (other authorities) and that the treatment thus resorted to has been successful in so many instances as to establish satisfactorily the propriety and safety of adopting it."

wart from ball of foot); *Stickleman v. Synhorst*, 243 Iowa 872, 52 N.W.2d 504 (1952) (negligence in injecting oil into patient's trachea in lung mapping process causing excessive loss of blood); *Bradshaw v. Wilson*, 87 Ohio App. 319, 94 N.E.2d 706 (1950) (failure of orthopedic surgeon to properly reduce fracture of arm); *Frederickson v. Maw*, 119 Utah 385, 227 P.2d 772 (1951) (negligence of physician leaving part of surgical sponge in wound); *Madis v. Stellwagen*, 38 Wash.2d 1,227 P.2d 445 (1951) (failure to remove needle in eye operation).

50. *Hunter v. Burroughs*, *supra* note 8. *Natanson v. Kline*, *supra* note 6.

51. 60 Barb. (N.Y.) 488 (1871), *rev'd on other grounds*, 50 N.Y. 696 (1872).

The first sentence indicates a strong disposition on the part of the jurists to carry over the stultifying effect of a strict adherence to *stare decisis* to their medical brethren. The second sentence represents a classic example of circular reasoning by the judiciary. How can a new practice have been successful in prior instances unless it is used initially? How can a surgeon acquire experience in administering a new treatment without inaugurating such treatment? The second sentence overlooks the obvious fact that some human being somewhere must necessarily be the first one upon whom a medical technique is tried or to whom a new medicine is administered. A literal compliance with the second sentence would stifle to the point of stymieing medical innovation and consequent advancement. Clearly, in *Carpenter* the trial of an unproven procedure was confused with a failure to adhere to the community standard.

In *Langford v. Kosterlitz*⁵² in 1930 the District Court of Appeal of California ruled that subjecting a patient to unproven therapy without disclosure and consent is contrary to the custom of physicians, and thus constitutes negligence even though there was no technical error in the actual performance of the procedure. It is apparent that by 1930 there was an absolute judicial insistence on informed consent as a condition precedent to unproven procedures.

In *Fortner v. Koch*⁵³ in 1935 the Supreme Court of Michigan declared: "If the general practice of medicine and surgery is to progress, there must be a certain amount of experimentation carried on; but such experimentation must be done with the knowledge and consent of the patient or those responsible for him and must not vary too radically from the accepted methods of practice." *Fortner* is of special significance for here the court was not merely condoning but was actually encouraging the trial of unproven procedures. The first phrase of the quoted sentence should be considered and treated as a judicial policy statement. The last phrase of the quoted sentence contains three important points. The first of these repeats the insistence of *Langford* on informed consent as a prerequisite to such procedures. The second point raises the very significant and difficult problem, to be discussed and analyzed later in this paper, of whether one *in loco parentis* to a subject may give effective consent for the administration of an unproven procedure and, if so, under what legal disability must the subject be laboring and what must the *loco parentis* relationship be.

52. 107 Cal. App. 175, 290 P. 80 (1930).

53. 272 Mich. 273, 261 N.W. 762 (1935).

The third point projects the element of extent into the picture, that is, how far may the unproven procedure vary from the traditional methods—what, in short, is the degree of tolerance.

Similar misapprehension is sometimes created by extrajudicial statements on medical experiments. An example is the following statement by Claude Bernard:

“As far as direct applicability to medical practice is concerned, it is quite certain that experiments made on man are always the most conclusive. No one has ever denied it. First, have we a right to perform experiments and vivisections on man? Physicians make therapeutic experiments daily on their patients, and surgeons perform vivisections daily on their subjects. Experiments, then, may be performed on man, but within what limits? It is our duty and our right to perform an experiment on man whenever it can save his life, cure him, or gain him some personal benefit. The principle of medical and surgical morality, therefore, consists in never performing on man an experiment which might be harmful to him to any extent, even though the result might be highly advantageous to science, i.e., to the health of others. But performing experiments and operations exclusively from the point of view of the patient's own advantage does not prevent their turning out profitably to science.”⁵⁴

In actual litigation, the standard for protection from liability will undoubtedly be what the court or the jury believes to be the prevailing standard of reasonable care. A prevailing practice of following an inadequate standard of care will not necessarily afford a defense for liability is always tested by whether or not there was a failure to exercise reasonable care.

Research institutions have established high standards for clinical investigation, both within and without the physician-patient relationship. Other means of investigation are always exhausted before investigation with human beings is attempted. Subjects and patients are kept under close and frequent observation, and the investigation is terminated whenever adverse effects are detected. Research is conducted by teams of physicians and scientists who represent a wide spectrum of skills and who are trained in clinical investigation. Unless the physician in private practice can match the skill, care, and safeguards

54. Bernard, Claude, cited by Bean, William B., M.D.: “Testament of Duty: Some Strictures on Moral Responsibilities in Clinical Research,” *Journal of Laboratory and Clinical Medicine*, 3-9 (January, 1952).

provided in research institutions, he may be in a precarious position of legal liability if he attempts a radical form of unproven therapy. The skilled practicing physician is not necessarily a capable clinical investigator at all levels of investigation. No physician should undertake investigation beyond his level of competence.

III. STANDARDS DERIVED FROM COLLATERAL SOURCES

Specific legal authority concerning the details of what clinical investigators should or should not do to avoid liability is not available. Certain collateral sources which may offer some guidance in judging what is proper conduct are available, however.

A. THE FEDERAL FOOD, DRUG AND COSMETIC ACT

One possible source is section 505 of the Federal Food, Drug and Cosmetic Act.⁵⁵ It prohibits the introduction of any new drug into interstate commerce unless it is first accepted as safe and effective by the Food and Drug Administration. Regulations must be promulgated exempting from this prohibition "drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs," and such regulations must "provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drug, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will 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 interest of such human beings."

The Food and Drug Administration has issued a Statement of Policy,⁵⁶ interpreting these provisions of the statute, as follows:

(a) Section 505 (i) of the act provides that regulations on use of investigational new drugs on human beings shall impose the condition that investigators "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 interest of such human

55. 21 U.S.C.A., sec. 355 (1961).

56. 21 C.F.R. 130.36 (1966).

beings." (b) This means that the consent of such human beings (or the consent of their representatives) to whom investigational drugs are administered primarily for the accumulation of scientific knowledge, for such purposes as studying drug behavior, body processes, or the course of a disease, must be obtained in all cases and, in all but exceptional cases, the consent of patients under treatment with investigational drugs must be obtained. (c) "Under treatment" applies when the administration of the investigational drug for either diagnostic or therapeutic purposes constitutes responsible medical judgment, taking into account the availability of other remedies or drugs and the individual circumstances pertaining to the person to whom the investigational drug is to be administered. (d) "Exceptional cases," as used in paragraph (b) of this section, which exceptions are to be strictly applied, are cases where it is not feasible to obtain the patient's consent or the consent of his representative, or where, as a matter of professional judgment exercised in the best interest of a particular patient under the investigator's care, it would be contrary to that patient's welfare to obtain his consent. (e) "Patient" means a person under treatment. (f) "Not feasible" is limited to cases where the investigator is not capable of obtaining consent because of inability to communicate with the patient or his representative; for example, where the patient is in a coma or is otherwise incapable of giving informed consent, his representative cannot be reached, and it is imperative to administer the drug without delay. (g) "Contrary to the best interests of such human beings" applies when the communication of information to obtain consent would seriously affect the patient's disease status 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. (h) "Consent" or "informed consent" means that the person involved has legal capacity to give consent, is so situated as to be able to exercise free power of choice, and is provided with a fair explanation of all material information concerning the administration of the investigational drug, or his possible use as a control, as to enable him to make an understanding decision as to his willingness to receive said investigational drug. This latter element requires that before the acceptance of an affirmative decision by such person the investigator should make known to him the nature, duration, and purpose of the administration of said investigational drug; the method and means by which it is to be administered; all inconveniences and hazards reasonably to be expected, including the fact, where applicable, that the person may be used as a control; the existence of alternative forms of therapy, if any; and the effects upon his health or person that may possibly come from the administration

of the investigational drug. Said patient's consent shall be obtained in writing by the investigator.

It should be noted that the statute and policy statement technically relate only to the introduction into interstate commerce of a new drug intended solely for investigational use. In form, at least, it is a legal limitation on manufacturers or others who would introduce a drug into interstate commerce, not a limitation on clinical investigators. It has no application to clinical investigation of drugs not introduced into interstate commerce or to clinical investigation not related to drugs. It does not directly impose any duty on clinical investigators, although it has the effect of barring clinical investigation involving a new drug for introduction into interstate commerce where the investigators have not given the required information or obtained the required consent.

It is obvious, however, that the primary if not the only reason why Congress included these provisions in the statute was to protect those human beings who participate in clinical investigation of drugs either within or without the physician-patient relationship. For that reason, the statutory provisions and the policy statement tend to establish minimum standards for clinical investigators. These standards would not necessarily apply in litigation concerning legal liability, but they do furnish some guide to the standards that might be applied.

Other statutory provisions which have a bearing on clinical investigation are found in state statutes which permit prisoners to volunteer for medical research. In Iowa, the prisoner must volunteer in writing and may withdraw his consent at any time.⁵⁷ In Virginia, prisoners are permitted to participate in medical research under regulations prescribed by the State Board of Prisons.⁵⁸

B. INSISTENCE ON WRITTEN INFORMED CONSENT BY HOSPITAL ADMINISTRATORS

Collateral guidance may also be obtained from some court decisions not related to liability. One arose out of a cancer research program in a private hospital in New York.⁵⁹ A substance derived from cancer cells was injected into chronically ill patients, who were told that they would receive a harmless substance which might cause a

57. IOWA CODE ANN., sec. 246-47 (1946).

58. VA. CODE ANN., 53-57.1 (1950).

59. *Hyman v. Jewish Chronic Disease Hospital*, 21 A.D.2d 495, 251 N.Y.S.2d 818 (1964), reversed 15 N.Y.2d 317, 258 N.Y.S.2d 397, 206 N.E.2d 338 (1965).

slight discomfort. Only oral consent had been obtained. Litigation arose out of the efforts of one member of the hospital's board of directors to get information from the hospital records concerning this program.

In this 1964 case, *Hyman v. Jewish Chronic Disease Hospital*,⁶⁰ the Appellate Division of the Supreme Court of New York stated:

"The Hospital's future policy will be in accordance with petitioner's contention that experiments such as the one here involved should be done only with the patient's written consent after the patient has been properly informed. On September 7, 1963, the Hospital's Grievance Committee approved the experiment. On September 30, 1963, its board of directors approved its Grievance Committee's report. On January 27, 1964, the Hospital's Research Committee approved continuance of the cancer immunization studies, but only upon the written, informed consents of the patients. Here we have judicial insistence not only on informed consent but on "*written, informed*" consent, the court stating "that experiments should be done only with the patient's written consent after the patient has been properly informed."

Hyman was reversed on appeal by the Court of Appeals of New York,⁶¹ but on a ground unrelated to the propriety of clinical investigation. Stemming from this litigation, as the Court of Appeals pointed out, the board of directors "merely enacted rules of the hospital (which) now require that written and informed consents of the patients be obtained before experiment."

C. ETHICAL STANDARDS DEVELOPED BY THE MEDICAL PROFESSION

Also of some assistance in delineating reasonable standards for clinical investigation are certain ethical standards which have been developed by the medical profession.

1. *Nuremberg Code*

The most important of these perhaps is the so-called "Nuremberg Code."⁶² Early in 1946 the Allied Military Tribunal was preparing for

60. 21 A.D.2d 495, 499, 251 N.Y.S.2d 818, 822 (1964).

61. 15 N.Y.2d 317, 258 N.Y.S.2d 397, 399, 206 N.E.2d 338, 339 (1965).

62. U.S. GOVERNMENT PRINTING OFFICE, 2 UNITED STATES V. BRANDT, ET AL., TRIALS OF WAR CRIMINALS BEFORE NUREMBERG MILITARY TRIBUNALS, OCTOBER, 1946-APRIL, 1949, 194 (1950).

the trials of twenty-three Nazi physicians and scientists charged with demoniacal and diabolical experiments on political prisoners. At the requests of the Secretary of State and the Secretary of War, the American Medical Association appointed Dr. Andrew C. Ivy, to serve as an advisor to the prosecuting attorneys on the ethics of medical research. Dr. Ivy, with the assistance of other physicians drafted an outline of ten principles of ethics governing the use of human subjects in medical research. These principles, with slight amendment, were presented during the trials by General Telford Taylor as the cornerstone of the allied case against the Nazi physicians. The opinions of the Military Tribunal adopted these principles as a ten-point judicial summary of the expert medical testimony presented principally by the prosecution.

The ten points of the Nuremberg Code are as follows:

1. The voluntary consent of the human subject is absolutely essential.
2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiments should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

The phrase "voluntary consent" in Point No. 1 of the Nuremberg Code means informed consent as well. This can be determined from the elaborate definition of voluntary consent which accompanied Point No. 1:

"This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment. The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity."⁶³

In respect to Point No. 2 of the Nuremberg Code, it may be dangerous to suggest that an experiment which might otherwise be unjustifiable is justified because it is for the common good. Any clinical investigator can claim that what he is doing is for the good of society. Certainly an increased risk must never be accepted simply because the project is believed to be of great importance or value to the community. More important considerations than the possible value of a clinical investigation are:

- (1) whether it is well conceived and planned,

63. U.S. GOVERNMENT PRINTING OFFICE, 2 UNITED STATES V. BRANDT, ET AL., TRIALS OF WAR CRIMINALS BEFORE NUREMBERG MILITARY TRIBUNALS, OCTOBER, 1946-APRIL, 1949, 194 (1950).

- (2) whether thought has gone into the framing of hypotheses to be tested,
- (3) whether the experiment is designed to answer the questions posed,
- (4) whether the same information could be equally well obtained by experiments on laboratory animals, and
- (5) whether the clinician has the skill and knowledge necessary to conduct the investigation properly.

In connection with Point No. 9 of the Nuremberg Code, it is interesting to note that Barney G. Glaser and Anselm L. Strauss, in their *Awareness of Dying*, make the following observation:

"A basic principle in clinical research is that a subject should be allowed to withdraw when he feels that continuation is mentally and physically impossible, however, this rule is often not the operating criteria for deciding on a withdrawal. It is easy enough to say that the patient in his distraught condition is not mentally capable of deciding whether he is mentally and physically capable of continuing. It must, therefore, be decided for him (!) by family or the doctor, and thus the patient loses this apparent control."⁶⁴

It is apparent that the Nuremberg Code has an unusual status—it was drafted primarily for the purpose of a war crime trial, yet it was intended to be a statement of ethical principles for clinical investigation. There is no doubt that anyone in the United States who engaged in experiments similar to those disclosed in the Nuremberg trial would be convicted under existing criminal laws, that is, there would be no need to refer to the code. It should be noted, however, that in the Nuremberg trial in no instance was the guilt of an accused based *solely* upon a failure to give sufficient information to the experimental subject in obtaining his consent.

2. *Principles of Medical Ethics*

The significance attached to the Nuremberg Code was reflected in a report of the Judicial Council adopted by the House of Delegates of the American Medical Association in December of 1946.⁶⁵ According

64. Glaser, B. G. and Strauss, A. L., *AWARENESS OF DYING* 192 (1965).

65. The proceedings of the San Francisco, 1946, session of the House of Delegates of the American Medical Association contain a resolution presented by Robertson Ward, M.D., of California, directing the appropriate committee or council of AMA to review, clarify, and recommend to the next session of the House such revisions in the Principles

to this report, in order to conform to the Principles of Medical Ethics of the AMA, the following requirements for clinical investigations on human beings must be satisfied:

1. The *voluntary* consent of the person on whom the experiment is to be performed must be obtained;

of Medical Ethics as may be found necessary and advisable. The Judicial Council sat as a reference committee to consider this resolution and recommended its approval and requested that it be permitted to include its findings in its annual report to the House at the Annual Session in 1947.

The proceedings of the Chicago, 1946, session of the House of Delegates reflect that R. L. Sensenich, M.D., Chairman of the Board of Trustees, submitted the following report:

"The Department of State of the federal government several months ago requested the American Medical Association to suggest the name of an outstanding medical investigator to represent the United States on an inter-allied commission to study the medical experiments on human beings carried on by the Nazi government during the war. The Board of Trustees selected Dr. A. C. Ivy of Chicago as the representative. Dr. Ivy went to Europe and on his return submitted a report to the government and a copy to the Board of Trustees. The Board referred the report to the Judicial Council, and it is expected that the Council will report to the House of Delegates its conclusions and recommendations."

E. R. Conniffe, M.D., Chairman of the Judicial Council, presented the following report of the Council:

"This supplementary report concerns the report made by Dr. A. C. Ivy, who was sent to Europe as a representative of the United States Government to review the war crimes of a medical nature committed by the Germans, which report was referred to the Executive Committee of the Board of Trustees, which in turn referred the matter to the Judicial Council."

"The Council finds that the experiments described in Dr. Ivy's report are absolutely opposed to the Principles of Medical Ethics of the American Medical Association and are to be condemned. In order to conform to the ethics of the American Medical Association, three requirements must be satisfied: (1) the voluntary consent of the person on whom the experiment is to be performed; (2) the danger of each experiment must be previously investigated by animal experimentation; and (3) the experiment must be performed under proper medical protection and management."

This report was referred to the Reference Committee on Miscellaneous Business.

The report of the Reference Committee on Miscellaneous Business contains the following statement:

"Your Reference Committee finds that the experiments described in Doctor Ivy's report are opposed to the Principles of Medical Ethics of the American Medical Association, which have three basic requirements: 1. The voluntary consent of the individual on whom the experiment is to be performed must be obtained; 2. The danger of each experiment must be previously investigated by animal experimentation, and 3. The experiment must be performed under proper medical protection and management."

When this section of the Reference Committee report was presented, it was carried after an amendment suggested by Edward P. Flood, M.D., and seconded by James C. Sargent, M.D., was withdrawn following discussion by Holman Taylor, M.D., and Morris Fishbein, M.D.

2. The danger of each experiment must have been investigated previously by means of animal experimentation; and
3. The experiment must be performed under proper medical protection and management.

3. *Declaration of Helsinki*

Another set of widely recognized ethical standards is the "Declaration of Helsinki,"⁶⁶ which is set forth below:

Recommendations Guiding Doctors in Clinical Research

INTRODUCTION

It is the mission of the doctor to safeguard the health of the people. His knowledge and conscience are dedicated to the fulfillment of this mission.

The Declaration of Geneva of The World Medical Association binds the doctor with the words: "The health of my patient will be my first consideration" and the International Code of Medical Ethics which declares that "Any act or advice which could weaken physical or mental resistance of a human being may be used only in his interest."

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, The World Medical Association has prepared the following recommendations as a guide to each doctor in clinical research. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Doctors are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

In the field of clinical research a fundamental distinction must be recognized between clinical research in which the aim is essentially therapeutic for a patient, and the clinical research, the essential object of which is purely scientific and without therapeutic value to the person subjected to the research.

66. This declaration as a project code of ethics on human experimentation drawn up by the World Medical Association was published in the British Medical Journal, October 27, 1962. The original project of this was in English. A revised version was accepted as the final project at the meeting of the World Medical Association in Helsinki in June, 1964. The original of the project was in French.

I. BASIC PRINCIPLES

1. Clinical research must conform to the moral and scientific principles that justify medical research and should be based on laboratory and animal experiments or other scientifically established facts.

2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

II. CLINICAL RESEARCH COMBINED WITH PROFESSIONAL CARE

1. In the treatment of the sick person, the doctor must be free to use a new therapeutic measure, if in his judgment it offers hope of saving life, reestablishing health, or alleviating suffering.

If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient has been given a full explanation. In case of legal incapacity, consent should also be procured from the legal guardian; in case of physical incapacity the permission of the legal guardian replaces that of the patient.

2. The doctor can combine clinical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that clinical research is justified by its therapeutic value for the patient.

III. NON-THERAPEUTIC CLINICAL RESEARCH

1. In the purely scientific application of clinical research carried out on a human being, it is the duty of the doctor to remain the protector of the life and health of that person on whom clinical research is being carried out.

2. The nature, the purpose and the risk of clinical research must be explained to the subject by the doctor.

3a. Clinical research on a human being cannot be undertaken with-

out his free consent after he has been informed; if he is legally incompetent, the consent of the legal guardian should be procured.

3b. The subject of clinical research should be in such a mental, physical and legal state as to be able to exercise fully his power of choice.

3c. Consent should, as a rule, be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject even after consent is obtained.

4a. The investigator must respect the right of each individual to safeguard his personal integrity, especially if the subject is in a dependent relationship to the investigator.

4b. At any time during the course of clinical research the subject or his guardian should be free to withdraw permission for research to be continued.

The investigator or the investigating team should discontinue the research if in his or their judgment, it may, if continued, be harmful to the individual.

The "Declaration of Helsinki" was approved in 1966 by the American Medical Association, the American Federation for Clinical Research, the American Society for Clinical Investigation, the Central Society for Clinical Research, the American College of Physicians, the American College of Surgeons, the Society for Pediatric Research, and the American Academy of Pediatrics, with the following statement:

"We, the undersigned medical organizations, endorse the ethical principles set forth in the Declaration of Helsinki by the World Medical Association concerning human experimentation. These principles supplement the principles of medical ethics to which American physicians already subscribe."

IV. LAW DIVISION'S GUIDES

The Law Division of the American Medical Association has also issued some guides for physicians in connection with the use of drugs under clinical investigation. These guides are as follows:

Generally, drugs under clinical investigation should be administered only where: (1) the informed consent of the patient or his authorized representative has been obtained; (2) the physician is convinced of the reasonable accuracy of his diagnosis and, if necessary, has confirmed it by adequate consultation; and (3) existing methods of treatment have proven unsatisfactory. The voluntary participation of the patient

will not excuse a deviation from the physician's obligation to exercise his best skill in rendering the care required of a reasonable practitioner. Furthermore, the physician is advised to confine his clinical investigation of new drugs to those furnished by reputable sources who have supplied him with comprehensive written information concerning: (1) animal experimentation; (2) previous clinical investigations, if any; (3) recommended dosages; (4) contra-indications; (5) possible side-effects to be watched for, and (6) the safety and possible usefulness of the drug, from existing data.⁶⁷

The Law Division has drafted model consent forms for experimental procedure or treatment⁶⁸ and for treatment with drugs under clinical investigation.⁶⁹ These forms are widely used in the medical profession.

67. AMA LAW DEPARTMENT, MEDICOLEGAL FORMS WITH LEGAL ANALYSIS, 37, footnote 29 (1961).

68. *Id.* Form 28 reads as follows:

A.M.
P.M.

Date _____ Time _____

I authorize the performance upon _____
(myself or name
_____ of the following procedure or
of patient)
treatment: _____

(State nature of procedure or treatment)

The nature and purpose of the procedure or treatment, possible alternative methods of treatment, the risks involved, and the possibility of complications have been explained to me. I fully understand that the procedure or treatment to be performed is experimental and unproven by medical experience, and that the consequences are unpredictable.

Signed _____

(Patient or person authorized to consent for patient)

Witness _____

69. *Id.* Form 29 reads as follows:

A.M.
P.M.

Date _____ Time _____

I authorized Dr. _____, the
attending physician, to treat _____
(name of patient)
with the drug presently identified as _____
for the following condition: _____

(Describe symptoms of disease to be treated)

It has been explained to me that the safety and usefulness of the drug in the treatment of patients for the above condition are now being investigated and that the manufacturer or distributor has supplied the drug for the purpose of providing further evidence of its safety and usefulness.

I voluntarily consent to treatment with the drug and release the attending physician from liability for any results that may occur.

Signed _____

(Patient or person authorized to consent for patient)

Witness _____

The foregoing ethical standards provide some guidance for the clinical investigators and for the attorneys who are called upon to guide them. Clearly, these ethical standards are not the last word. Questions concerning the interpretation or application of the existing standards will surely arise. Other questions which are not specifically answered may require the adoption of new ethical guides.

The body authorized to decide questions of medical ethics for physicians is the Judicial Council of the American Medical Association. Since the volume of clinical investigation is increasing and since the ethics of such investigation is being discussed with increasing frequency, the Judicial Council can be expected to issue from time to time, statements and rulings supplementing and clarifying the standards established by the Principles of Medical Ethics and the "Helsinki Declaration."

V. CONCLUSION

At present, the law does not provide detailed specific rules concerning the rights, obligations, and limitations of clinical investigation. It is doubtful, however, whether it would ever be desirable for these rules to be established by statute. Statutory rules lack the flexibility that is necessary for reasonable adaptation to rapidly changing circumstances such as exist in the field of clinical investigation. The development and adaptation of rules on a case by case basis would appear to be preferable, even though this process always leaves areas of uncertainty.

At the threshold of this legal process, which is the point at which clinical investigation stands today, many specific legal questions are undecided. But a practical guide for conduct is afforded by the general rules of law and the ethical standards which have been developed. The conscientious clinical investigator can, in these circumstances, carry on with the kinds of investigation which are essential for the advancement of medical science and at the same time protect the rights and interests of his patients and subjects.