

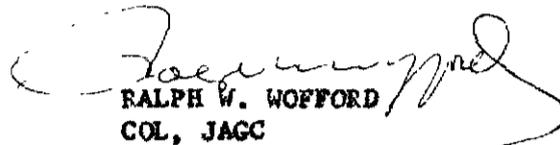
Proposed Publication of Article, "The Need for a Workable Concept of Informed Consent for Clinical Investigation"

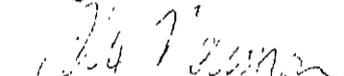
MEDJA
Ch, TLO

JA

9 Sep 1969
A. Naimon/35456/mw

1. Reference is made to your request for review of and comment on proposed publication of subject article.
2. This office does not object to publication of subject article, providing publication is accompanied by a disclaimer to the effect it represents only the views of the author and not that of the Army, or Army medical authorities.
3. Further review is recommended by D, Prof Svc, and Special Asst to TSG for Medical Statistics.


 RALPH W. WOFFORD
 COL, JAGC
 Judge Advocate


 ALEXANDER NAIMON
 Deputy Judge Advocate

401-02 Consents

WNRC: 30 DEC 94 Archives
 RG: 112
 Accession # 73-0014
 Box #3
 File Name: 401-02 Consents, 1969

DISPOSITION FORM

REFERENCE OR OFFICE SYMBOL

MEDTL-R

SUBJECT

Material for Review

TITLE: "The Need for a Workable Concept of Informed Consent for Clinical Investigation" By: Zimmerly, James O, M.D.

TO

Judge Advocate, OTSG
Room 2601

FROM

Chief, TLO, OTSG

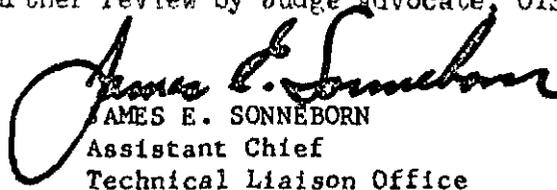
DATE

17 Jul 69/cs/62385

CMT 1

1. Reference: AR 360-5, 27 September 1967 and OTSG Regulation 360-1, 8 August 1966
2. Attached material is forwarded for: professional review
 security review
3. Constructive criticism is desirable to assist and encourage Army Medical Department personnel to contribute to professional literature. Your comments are desired by this office. In case detailed comments are applicable, they should be submitted on DA Form 1598, omitting OTSG staff identity.
4. A copy of this material is being or has been submitted to the following for review:
Medical R&D Command who recommends further review by Judge Advocate, OTSG

Incls a/s


JAMES E. SONNEBORN
Assistant Chief
Technical Liaison Office

TO Chief, TLO
Room 1743

FROM

DATE

CMT 2

Subject material reviewed and returned with the following comments:

- Presentation and/or publication recommended. NOT RECOMMENDED.
- All illustrations and/or figures considered necessary for full understanding of this article, and text cannot be shortened without seriously impairing its value.
- Further review is recommended by:
If agreeable to author and editor, the material should be should not be considered for public news release.
- No objection to publication on grounds of security.

(DUPLICATE FORM IS FOR REVIEWER'S FILE)

Signature

OTSG FL 262, 1 Jul 68

DA FORM 2496
1 FEB 62

REPLACES DD FORM 86, EXISTING SUPPLIES OF WHICH WILL BE ISSUED AND USED UNTIL 1 FEB 63 UNLESS SOONER EXHAUSTED. U.S. GOVERNMENT PRINTING OFFICE: 1963 O-707-974

The Need for a Workable Concept of
Informed Consent for Clinical Investigation

by

JAMES G. ZIMMERLY, M.D., J.D., M.P.H.

Division of Preventive Medicine
Walter Reed Army Institute of Research
Washington, D.C. 20012

Stefano Vivona

STEFANO VIVONA, COL, MC
Director
Div of Preventive Medicine

[Signature]

Editorial Board

1975

1975

Within the past few years the notion of "informed consent" has been a frequently discussed topic whenever physicians and lawyers meet. Some discussion of informed consent has appeared in most every leading medical and legal journal and no combined medico-legal forum has been complete without some discussion of the topic. One would hope that with all of the attention given to the subject, any problems would be readily resolved. But to my mind, the more the subject is discussed, the deeper and more painful the wound is becoming. The problem has reached the point where certain types of medical research are in danger of coming to a grinding halt.

The law relating to clinical investigation is just now beginning to develop. The courts have yet to consider the problems of informed consent to research procedures. Statutes are presently being considered by at least two states, partly because of the uncertainty of the case law. To date all that the researcher has to guide him are analogies drawn from cases involving consent to medical and surgical procedures, a few administrative regulations which do not deal with liability and the various medical codes of ethics.

Our thinking today as espoused in the various codes of medical ethics, still reflects the horror of the criminal medical experiments carried out in Germany during World War II. The first principle of permissible medical experiments, outlined in the Nuremberg Code states that:

"The voluntary consent of a human subject is absolutely essential. 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 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 an 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 the 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." ¹

As early as 1946, the House of Delegates of the American Medical Association agreed that experiments on human beings, in order to conform to the principle of medical ethics of the American Medical Association, must satisfy three requirements: (1) the voluntary consent must be obtained from the person on whom the experiment is to be performed; (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.

This set of guidelines was broad enough to allow medical research to proceed as it had been in the United States and was seemingly acceptable to everyone at the time. It very notably required consent of the subject but did not demand written consent.

Twenty years later, on November 30, 1966, the House of Delegates of the American Medical Association expanded their set of ethical guidelines.

¹ - The Nuremberg Code, United States v Karl Brandt et al, as printed in Law for the Physician by Carl Erwin Wasmuth, M.D., LLB, Lea and Febiger, Philadelphia, 1966, p 304.

The new guidelines contained the following provisions:

In clinical investigation primarily for treatment -

A. The physician must recognize that the physician-patient relationship exists and that he is expected to exercise his professional judgement and skill in the best interest of the patient.

B. Voluntary consent must be obtained from the patient, or from his legally authorized representative if the patient lacks the capacity to consent, following:

(a) disclosure that the physician plans to use an investigational drug or experimental procedure,

(b) a reasonable explanation of the nature of the drug or procedure to be used, risks to be expected, and possible therapeutic benefits,

(c) an offer to answer any inquiries concerning the drug or procedure, and,

(d) a disclosure of alternative drugs or procedures that may be available.

1. In exceptional circumstances and to the extent that disclosure of information concerning the nature of the drug or experimental procedure or risks would be expected to materially affect the health of the patient and would be detrimental to his best interests, such information may be withheld from the patient. In such circumstances such information shall be disclosed to a responsible relative or friend of the patient where possible.

2. Ordinarily, a consent should be in writing, except where the physician deems it necessary to rely upon consent in other than written form because of the physical or emotional state of the patient.

3. Where emergency treatment is necessary and the patient is incapable of giving consent and no one is available who has authority to act on his behalf, consent is assumed.

In clinical investigation primarily for the accumulation of scientific knowledge -

- A. Adequate safeguards must be provided for the welfare, safety and comfort of the subject.
- B. Consent, in writing, should be obtained from the subject, or from his legally authorized representative if the subject lacks the capacity to consent, following:
 - (a) a disclosure of the fact that an investigational drug or procedure is to be used,
 - (b) a reasonable explanation of the nature of the procedure to be used and risks to be expected, and
 - (c) an offer to answer any inquiries concerning the drug or procedure.
- C. Minors or mentally incompetent persons may be used as subjects only if:
 - (a) the nature of the investigation is such that mentally competent adults would not be suitable subjects.
 - (b) consent, in writing, is given by a legally authorized representative of the subject under circumstances in which an informed and prudent adult would reasonably be expected to volunteer himself or his child as a subject.
- D. No person may be used as a subject against his will.

This new code endorsed the ethical principles set forth in the 1964 Declaration of Helsinki of the World Medical Association, concerning human experimentation. The latest code recognized the difference between patients as the objects of clinical research, primarily for treatment or benefit, and subjects as the objects of clinical investigation, primarily for the accumulation of scientific knowledge. Written consent is required of the latter group in all cases.

The Federal Food, Drug, and Cosmetic Act, as well as the Kefauver-Harris amendments of 1962 dealing with drug testing, had not required written consent. On August 24, 1966, Dr. James L. Goddard, Commissioner of the Food and Drug Administration, issued a new statement of policy regarding consent for the use of investigational new drugs on humans.

The FDA's statement of policy declared:

Pursuant to the provisions of the Federal Food, Drug and Cosmetic Act (secs. 505(i), 701(a), 52 Stat. 1053, as amended, 1055; 21 U.S.C., 355(i), 371(a), and under the authority delegated to the Commissioner of Food and Drugs by the Secretary of Health, Education, and Welfare (21 CFR 2.120; 31 F.R. 3008), Part 130 is amended by adding thereto a new statement of policy, as follows:

130.37 Consent for use of investigational new drugs on humans; statement of policy.

(a) Section 505(i) of the act provides that regulations on use of investigation 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 judgement, contrary to the best interest of such human 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 purpose 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 judgement, 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 judgement 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 judgement 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.²

² Federal Register Doc 66-9407; Filed, August 29, 1966, 8:46 a.m.

The August 1966 ruling stirred up a flurry of opposition which ultimately led to the FDA's easing the requirement that investigators must obtain the written consent of patients who are being given experimental drugs.

Under the newest regulation, in Phase 3 investigations, the last step prior to general marketing of a drug, subject to FDA approval, physicians are given some latitude in determining whether written consent is obtained or whether oral consent will be all that is sought. The investigator is given the responsibility to determine when it is necessary or preferable to obtain consent in other than written form. The investigator can now take into consideration the physical and mental state of the patient, but a minimum of oral consent is required at all times. Written consent is still demanded in Phase 1 and Phase 2 investigations except in those few exceptional cases where written consent is not feasible or is contrary to the patient's best interests.

This is where the researcher stands today. He is at least morally bound by the FDA regulations and medical ethics.³ Obviously, neither

³ There is no statutory sanction against the researcher who violates the Food and Drug Administration Regulations on drug testing. This, of course, does not mean that the researcher is immune from civil suit for the consequences of his acts. It merely means that the regulations are aimed at the improper use of the drugs and could result in the drug not being marketable and the researcher being precluded from further clinical trials.

the FDA regulations nor the medical codes of ethics recognize those instances where any kind of consent would invalidate the study. The regulation was not meant to cover vaccine trials, although I don't mean to imply that vaccines are the only drugs which are hurt by such a regulation when it is applied inappropriately. Those exceptions where written consent need not be obtained under the FDA regulation apply only to instances where the patient is in a coma and cannot respond or where his well-being may be jeopardized by insisting on written consent. There is at present no exception which would allow use of a drug without consent in those cases where the subject's knowledge would invalidate the study.

Having considered the present status of informed consent in the United States, we might glance at the evolution of the concept in our law.

It is a basic principle in our society that every man has the fundamental right to the physical security and integrity of his body and that this right is inviolate. This is well known law and we need not labor the point nor build up an appearance of erudition in this paper with encyclopedic citations upon points which no one disputes.

The source of much of our law, the common law, has long recognized that one of the basic rights of all persons is the right to be free from the intentional touching of ones own body.

The 1905 case of *Mohr v Williams*⁴ is oft quoted as the leading United States case in the area of informed consent. This case serves to point

⁴ *Mohr v Williams*, 95 Minn 263, 104 N.W. 12 (1905)

out some of the reasons for today's critical problem. In the Mohr case the Supreme Court of Minnesota stated:

"Under a free government, at least, the free citizen's first and greatest right, which underlies all others - the right to the inviolability of his person; in other words, the right to himself - is the subject of universal acquiescence, and this right necessarily forbids a physician or surgeon, however, skillful or eminent, who has been asked to examine, diagnose, advise, and prescribe to violate, without permission, the bodily integrity of his patient by a major or capital operation, placing him under the anesthetic for that purpose, and operating upon him without his consent and knowledge. The patient must be the final arbiter as to whether he will take his chance with the operation, or take his chances of living without it. Such is the natural right of the individual, which the law recognizes as a legal one. Consent, therefore, of an individual, must be either expressly or impliedly given before a surgeon may have the right to operate."

Mohr v Williams involved the problem of consent to a surgical procedure. Most of the early cases considering consent problems were cases involving surgery. Our law, however, provides that consent to any medical treatment, surgical or nonsurgical, is required.⁵ There are marked differences between informed consent for surgery, informed consent for medical treatment and informed consent for medical research. But we have no case law to date which recognizes that differences do exist.⁶

5 Mims v Boland, 110 GA App 477, 138 S.E. 2d 902 (1964)

6 To further complicate the picture there is a difference between consent to a tested, proven and accepted procedure to cure a defect and consent to an experimental procedure to cure a defect. But the biggest problem lies in consent to being a human guinea pig where either no benefit or questionable benefit is expected. An example of the former would be injecting cancer cells into a healthy volunteer. An example of the latter would be giving an experimental vaccine to a volunteer.

Some of the differences exist because the legal obligation of the physician researcher varies with the status of the subject of the research. If the subject of the procedure is a patient, who consents to the procedure for his own expected benefit, it is probable that his informed consent would foreclose any liability based on lack of consent. But if the procedure is designed solely to increase medical knowledge, without the expectation of any benefit to the subject, his own informed consent may not be sufficient to bar any claims of his dependents if the subject is injured in the procedure and the injury interferes with the subject's duties to his dependents. In such a case the researcher may need the informed consent of everyone concerned.

Where the object of the experimental procedure is a patient who expects benefit from the procedure, it is not necessary to increase the danger of the procedure by unnecessarily alarming the patient. In this situation a lesser degree of information would be compatible with informed consent. On the other hand, where the object of the experimental procedure is a voluntary subject, expecting no benefit from the procedure, other than perhaps financial, complete disclosure of all known risks must be made in order to obtain an informed consent.

The cases were litigated and the ethical guidelines were composed with a mind toward clarifying the problem of informed consent for surgery. As a result they are more than inadequate. They are hampering other areas of medical progress! Their presence on the books, coupled with the absence of similar cases dealing with consent to research procedures, has

led lawyers to interpret the existing laws across the board to all forms of medicine and surgery. Physicians similarly have viewed the existing regulations and applied them to areas they were not meant to cover.

This is not to criticize physicians or their lawyer advisors. They have had good reason to "play it safe" in the light of today's suit prone society. This is especially true since a suit for assault and battery based on a failure to obtain informed consent is almost indefensible compared to the negligence suit where the defendant at least has a fighting chance.⁷

At the AMA National Medicolegal Symposium in Miami, Florida, in 1963, it was predicted that medical progress would suffer if our ideas of informed consent did not change. In my limited experience in clinical research, I have found the 1963 prediction to be very correct. If the problem were not ^{made} bad enough ^{to} merely misapply the law covering surgical consent to areas of medical research, it is compounded by the fact that there is no clear, uniform concept of informed consent even for surgery. The cases should have promoted a uniform rule in at least this one area!

⁷ A suit for assault and battery is less defensible because damages need not be proven by the plaintiff. Damages are presumed in assault and battery cases, but not in negligence actions. Even if a patient benefits from treatment he may be able to collect punitive damages.

Another difference between a negligence action and an assault and battery action is that different proof may be required. Furthermore, the physicians professional liability insurance contract usually excludes assault and battery. Also, the applicable statute of limitations may be longer for assault and battery actions than for negligence actions. The confusion between pure assault and battery and some medical malpractice cases is beyond the scope of this paper.

It has been suggested that informed consent is adequate when the patient understands (1) the nature of his condition, (2) the nature of the proposed treatment or procedure, (3) the alternatives to such course of action, (4) the risks involved in both the proposed and the alternative procedures, and (5) the relative chances of success or failure of the proposed and alternative procedures.

The criteria of some courts is not as reasonable as that of the above suggestion. It is impossible to adequately pre-inform by some courts standards and may not even be possible by the above suggested criteria. Very recent studies carried out by investigators in the Department of Psychiatry at the University of Wisconsin Medical School and by others at the University of Missouri School of Medicine indicate that our ideas of obtaining truly informed consent, by any criteria, are groundless. These studies indicate that no matter how intense the efforts are to make the nature of the procedures clear and comprehensible to the subjects, those who volunteer and sign the "informed consent" document have no more understanding of the threat to human life of the procedures than those who refuse to participate.⁸

Some courts have stated that the physicians obligation to obtain informed consent would be satisfied by the type of disclosure that a reasonable physician would make under like circumstances.⁹ The decision

⁸ Fellner, C. H. and Marshall, J.R., Twelve Kidney Donors, JAMA 206: 2703-7, 16 Dec 68.

.. Martin, D. C., Arnold, J.D., Zimmerman, T.F. and Richart, R.H. Human Subjects in Clinical Research - A Report of Three Studies, New England Journal of Medicine, 279:1426-31, 26 Dec 68.

⁹ Natanson v Kline, 350 P 2d 1093, Affirmed on rehearing, 354 P 2d 670 (Kansas 1960)

in the Nathanson case has been interpreted to mean "reasonable disclosure" and not "reasonable physician" by other courts.

What is a reasonable disclosure? In determining what to disclose can the physician take into consideration the patient's heart; his mental state; whether the risks are very great or merely remote possibilities; and whether disclosure of all the risks might jeopardize the proposed treatments' chance of success? A few cases have held that where the degree of risk is very minimal no warning need be given.¹⁰ But it is a lay decision whether "reasonable" disclosure was made and expert testimony from physicians is not required according to the views of one court.¹¹ I feel this aspect of the decision in the previous case is unsound. Certainly, a lay person is not competent to describe the procedure or discuss the probable consequences. In *Aiken v Clary*¹² the court rejected the dicta of the earlier Missouri case of *Mitchell v Robinson*. The court in the *Aiken* case distinguished the *Mitchell* case as a situation where the contention was held by the plaintiff that no disclosure was made. This was a fact question which the jury could handle without the aid of expert medical testimony, but the case is still subject to controversy. The language of the court was such that it could be interpreted to mean that

10 *Yeates v Harms*, 393 P 2d 982 (Kan 1964)

.. *Valentine v Kaiser Foundation Hospitals*, 15 Cal Rptr 26 (1961)

11 *Mitchell v Robinson*, 334 S.W. 2d 11, (Mo 1960)

12 *Aiken v Clary*, 396 S.W. 2d 668 (Mo 1965)

it is a jury question whether any disclosure was made at all, but also that the jury is permitted to resolve conflicts of lay testimony concerning whether in a given case it is negligent not to disclose. In *Govin v Hunter*¹³ the custom of the medical profession to warn had to be established by expert medical testimony. This seems to me to be the better view.

The more progressive courts have taken the enlightened view that the physician does not have to disclose every imaginative or speculative element that might go into making up the risk. In the *Patrick* case¹⁴, the court said "A doctor does not have to inform a patient of all the risks involved in an operation but may as is frequently done, tailor his warning to the particular patient." The requirements of other courts are too vague to characterize. As was stated previously, there is no uniform concept of how much disclosure is necessary to result in a consent being "informed."

Other courts have also recently recognized the therapeutic limitation of disclosure. In *Watson v Clutt*¹⁵ the court recognized that the physician's primary duty is to do (that what) is best for the patient and any conflict between this duty and that of a frightening disclosure ordinarily should be resolved in favor of the primary duty. In the same year another court in an adjoining state arrived at a similar conclusion. They recognized that explaining every conceivable risk could easily result in alarming a patient who is already unduly apprehensive and who may, as a result, refuse the

13 *Govin v Hunter*, 374 P2d 421 (Wyo 1962)

14 *Patrick v Sedwick*, 391 P 2d 453 (Alaska 1964)

15 *Watson v Clutt*, 136 S.E. 2d 617 (N.C. 1964)

treatment when there is in reality little risk. The court also recognized that the risk can actually be increased by reason of the psychological result of increased fear.

16

In the Govin case, cited previously, the court recognized that it is a matter of medical judgement how the physician discharges his obligations. But the distressing concept which pervades all of the cases to date, is that whatever discretion the physician uses, it must be consistent with the full disclosure necessary for an informed consent.

The crisis facing medical researchers today is that very often it is not possible to attempt to obtain any semblance of informed consent without jeopardizing the results of the study. This problem is more critical in some areas of medical research than in others. There is certainly more than one type of situation where obtaining informed consent is not practicable but if I can adequately illustrate one case my point will be made.

For purposes of illustration let us consider the hypothetical vaccine we will call Preparation K. The developers of Preparation K feel that it will wipe out the dreaded disease we will call the Singapore Krud. Preparation K has been exhaustively tested in laboratory animals and in the human developers of the drug and is believed to be free of untoward side effects. The Singapore Krud is characterized by headache, malaise, anorexia, low grade fever, loss of appetite and sometimes a mild, unproductive cough. The

16 Ball v Mallinkrodt Chemical Works et al, 381 S.W. 2d 563 (Tenn 1964)

.. Salgo v Leland Stanford, Jr University, Board of Trustees,
317 P 2d 170, 154 Cal App 2D 560 (1957)

.. Roberts v Weed, 206 F Supp 579 (Ala 1962)

symptom complex in adults resembles very closely the common cold.

It is hoped that Preparation K will be an effective vaccine because the Krud is a major killer of young children. The state health commissioner in the state of Backward is anxious to add this vaccine to the preschool immunizations because he expects the Krud to have a peak epidemic year in 1971.

The path leading to the eventual marketing of Preparation K has been an easy one to date. It has merely required many long years of research in the medical laboratory and huge sums of money. At this point the developers reach their first major stumbling block. Case law in the state of Backward demand that informed consent be given for all forms of medical treatment. Legal counsel for the state advises the researchers to closely adhere to the law because the citizens of the state are very suit conscious.

17

The researchers decide to scrap the entire vaccine because they know from their past experience in drug testing, that a statistically valid study designed to test the effectiveness of Preparation K could never be carried out in the state of Backward. Experienced public health workers are very much aware of the fact that disease reporting is markedly influenced by the subjects psychological frame of mind.

In order to perform their study the researchers would have to

17 In deciding whether to go ahead with the project the researchers were aware of the absolute liability placed on the vaccine manufacturer in the recent case of Timmerholm v Parke-Davis and Co., decided by the United States District Court for the Southern District of New York. A similar recent case was Davis v Wyeth Laboratories, Inc and American Home Products Corp, No 20, 995, United States Court of Appeals for the Ninth Circuit. (Petition of rehearing denied) It is doubtful that this liability can be waived by any form of disclaimer.

depend on the reported incidence of the disease since they don't have enough doctors to go around and examine everyone who develops a symptom which might be part of the Krud. If a sample population is given Preparation K, and in order to obtain informed consent are told that it is a vaccine designed to protect against the Singapore Krud, the reported incidence of Singapore Krud in the vaccinated population will be very low, tending to indicate that the vaccine is indeed effective. It will be a falsely low incidence simply because the vaccinees want the vaccine to be an effective one. Without consciously being aware of their motives they will pass off any minor symptoms of the Krud as merely being a slight cold. (Remember, many of the symptoms of the Krud and the common cold are identical).

Similarly, the group that is not vaccinated or is given a shot of sterile water (after being told that it is sterile water because of the informed consent requirement) will categorize many symptoms of the common cold as being the Krud and there will be a very high apparent incidence of the Krud in the control group. This also would inaccurately characterize the vaccine's effectiveness. For these reasons the researchers decide to abandon the project.

But the Mayor of the city of Retarded in the state of Backward wants to save the project and have his citizens immunized. He feels that the letter of the law can be complied with by seeking volunteers who will agree to take either the vaccine or a placebo. He feels that many of his citizens would volunteer for the project and would

agree to take whatever is given them, without their knowing whether they received the vaccine or water.

The Mayor's suggestion is unacceptable to the researchers for several reasons. In order to validly test the vaccine it is important that the study population be evenly distributed in the total population at risk, and that the natural spread of the disease not be interfered with during the course of the study. The Mayor cannot guarantee that the volunteers will be evenly distributed and equally at risk with the rest of the population. Most of the volunteers might come from the German section of the city. There may be none from the Chinese section of town. If the disease has a high attack rate in the Chinese sector and a low attack rate in the German sector during the course of the study all will have been wasted. There are many reasons why a disease might skip one segment of a population, and if that segment is the study group the researchers may as well have spent their time fishing.

Another reason why the mayor's suggestion is unacceptable is due to the very low incidence of the Krud in nonepidemic years. In order to conduct a statistically valid study, many thousands of subjects need to be included in the study group. Fewer subjects would be necessary if a high risk group could be immunized.

Children are a high risk group but minors can not give informed consent until they have reached their majority or some age close to their majority. The population of the city of Retarded is not large enough to support the study if minors are excluded. This reason alone is not enough to abandon the project, but it will take years instead of months to evaluate the vaccine under these conditions. It certainly will not be ready in time for the expected 1971 peak epidemic.

Ordinarily a medical procedure should not be performed on a minor without the consent of the minor's parent or legal guardian except in an emergency where the patient's life is endangered by the delay.¹⁸ One court has implied that legal effect should be given to the consent of minors where the minors are mature enough to comprehend the nature of the procedure and the risks involved.¹⁹ But the minors consent is not valid unless the procedure is intended to be of therapeutic benefit to him.²⁰

Additional problems arise with regard to whether or not valid consent can be given by emancipated minors. These problems exist because there is no clear uniformity among the states as to who is deemed a minor, or what constitutes emancipation, or the legal effect of emancipation on the giving of consent to medical treatment. It is possible that the consent of an 18-year old wife may be necessary in order to perform a medical procedure on her 20-year old husband in some states. As mentioned previously, if there is no expected benefit to the subject in a research procedure, it may be necessary to obtain the consent of even his dependent children.

In the case of medical experimentation rather than treatment it is of questionable legality to use children, even if the parent or guardian consents. It would certainly be advisable to obtain the consent of the minor as well as the parent if a child of more than tender years is going to be a clinical subject. By analogy, since a husband has no inherent

18 Zoski v Gaines, 217 Mich 1, 206 N.W. 99 (1935)
.. Jackovach v Yocom, 212 Iowa 914, 237 N.W. 444 (1931)
.. Tabor v Scobee, 254 S.W. 2d 474 (KY 1951)
19 Lacey v Laird, 166 Ohio 12, 139 N.E. 2d 25 (1956)
.. Bakker v Welsh, 144 Mich 632, 108 N.W. 94 (1906)
20 Bonner v Moran, 126 F 2d 121 (D.C. Cir., 1941)
.. Pratt v Davis, 224 Ill 300, 79 N.E. 562 (1906)

authority to consent to a dangerous operation on his wife without her consent, the same would probably hold true in the case of a minor of more than tender years. Parents have always had the obligation to act in the best interests of their children. Volunteering a child for participation in a research study is hardly in the best interests of the child unless the child is a patient and can reasonably expect some benefit from the procedure.

If there is to be progress and advancement in the practice of medicine, there must be controlled experimentation on humans. Experimental trials on patients by competent clinical groups are always necessary before drugs may safely be entrusted to the profession at large. Courts have never been blind to the fact that there is a necessary transition period from laboratory experiment to general human use of all new drugs. Indeed, the courts have helped construct safeguards to protect patients from becoming unbeknowning guinea pigs. The safeguard has been the requirement of informed consent. However, the courts responsibility is to not only be fair to the patient but also to be fair to the medical researcher. If not, the researcher is going to avoid the legal problems by the only route left available to him. It would be catastrophic if the better researchers all left the field.

Since there are at present no legal guidelines on how one may legally test these "unique" drugs and since I find it easy to criticize, I ought to end with my recommendations for improving the present situation.

To begin with it must be recognized that safeguarding the rights of patients cannot be simply secured by legislation requiring written informed consent. The studies mentioned in references 6 and 7 illustrate that our present concept of informed consent is probably illusory. Since our concept of written informed consent is in all probability groundless, there is no compelling reason to insist that written consent is any better than oral or implied consent. The two studies noted above show that written consent is anything but perfect. Certainly the mere signature on a standard consent form falls far short of the legal requirement of an informed consent, if informed consent is possible at all. If a patient can prove that the nature and risks of treatment were not fully explained to him, he may collect a nice award despite his signature on a blanket consent form. And, as previously noted, the actual written consent may increase the danger to the patient by reason of the increased apprehension occasioned by the attention given to the consent.

So my first recommendation is that "written consent" be lowered from the pedestal it now occupies and be given less attention by those individuals who draft the regulations which we all must live with. Their mistakes remain with us for many years, long after the draftsmen have departed.²¹

²¹ The State of Maryland is presently considering the drafting of a statute which will codify the requirements for informed consent within the state. This statute, if adopted, will most likely not be directed towards the problems of informed consent to research procedures. The risk exists, however, that the presence of such a statute will result in its being misapplied unless very carefully worded. The code could create more problems than it solves.

The next thing we need is some legal mechanism which would provide the necessary consent for those individuals who lack the capacity to consent (e.g. by minority or insanity) and in those cases where the validity of the experiment would be destroyed if the subjects were aware of all of the details of the study.

A step in the right direction would be to guarantee to parents or guardians, the legal authority to consent to their minor dependents participating in research procedures. This would not solve all of the problems of consent from minors because exigencies of the procedure may not always permit sufficient time to obtain consent. Or, it may be impractical to attempt to obtain consent for other reasons alluded to earlier. Or, consent may even be withheld by the parents, contrary to the best interests of the child.

Another legal mechanism can be provided by giving the authority to consent to a disinterested third party. This would necessitate that the third party be qualified to judge the relative merits of the research protocols. In cases where the scientific justification far outweighs the risk to the subject, the consent should be supplied. This third party might be, but does not have to be, the same committee that passes on and approves the protocol of an experiment and the qualifications of the researcher. There are some good reasons for having the committees distinct. Some hospitals already have medical staff committees for clinical research. This might be one of their additional functions. Or the state or local medical society might appoint an appropriate committee of experts with

the same legal authority. In federal government hospitals, the appropriate government agency might appoint a similar committee.

Selection of these committees ought to be delegated to responsible members of the medical community. The committee's function would be to evaluate the proposed research protocol and weigh the benefits to be gained by the proposed research against the risks to the proposed subjects. In cases where the scientific justification far outweighs the risk to the subjects, the committee should have the power to waive the necessity of consent of the subjects. The committee should only have this power, however, in those rare instances where the necessity of obtaining informed consent cannot be reasonably complied with, without adversely affecting the results of the research project. In those instances where informed consent is practicable, it should still be required. Certainly, if litigation were to arise, the researcher would be in a better position if his protocol had been evaluated and approved by a competent and impartial committee.

Ideally, the committee should be composed of physicians with broad experience in clinical medicine and research. However, the possibility of having lay members should not be overlooked. A lay member or two might temper the vested interest of the physician members. The physician members should have no interest in the specific research protocols being considered by the committee, but one cannot deny their interest in the advancement of medical knowledge. The responses of lay members would be primarily a result of their past experience with physicians and their

philosophy of life. They may be advantageous to some committees and detrimental to others. Proper evaluation of research protocols could result in being subjugated to personality struggles. Furthermore, the lay person may not be able to fully comprehend the significance of the experiment and the subjects may not want a lay person to decide what is best for them. On the other hand, they may prefer an all lay committee.

To get a committee such as I propose, to function properly without fear of civil suit in today's society, would be quite a project. It might be possible to protect such a committee by means of liability insurance and this would help. But to convince lawmakers that such a committee is needed, may well be a herculean task.

It may be easier to get the Food and Drug Administration, as well as responsible medical organizations, to recognize exceptions to their ethical requirements of informed consent. Following this, it might be possible to convince the courts, when litigation arises, that there are differences between informed consent to surgery and informed consent to research procedures. The next step would be to convince the courts that, in certain instances, consent of any kind is not practicable. We could then hope that the resultant new case law would not completely tie the hands of medical researchers.

Obviously, I recognize that guidelines are necessary to protect the interests of persons who find themselves the subjects of human experimentation. But I feel that the guidelines can be flexible and can promote the acquisition of new knowledge while at the same time protecting the patient's rights.

Our courts, as well as the draftsmen of statutes, must recognize that one cannot construct a rule that demands equal disclosure of risks to all patients, for all procedures, without hampering safe medical progress to some degree. Even I recognize that we need absolute, full disclosure where the procedure is purely experimental and of absolutely no possible value to the subject (e.g., injecting cancer cells into an apparently healthy person). But, in other circumstances, the medical researcher needs some leeway and a certain amount of discretion ought to be left with the researcher, subject to the approval of the third party review committee.

So long as the researcher does not use coercion or overstate the scientific case in order to obtain consent and so long as he is motivated only by the patient's best therapeutic interest, we ought not to stifle his progress needlessly. In many cases, the good faith of the investigator has been demonstrated by his subjecting himself to the new drug or procedure early in its development. I feel this is to be encouraged but is understandably not always possible. At any rate, the physician has always had the ultimate responsibility of safeguarding the rights and interests of the patients. I suggest we leave that responsibility where it is and now see to it that our courts and legislators become equally concerned with protecting the interests of medical researchers as well as mankind as a whole.