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THE IMPACT ON FETAL RESEARCH OF THE REPORT OF
THE NATIONAL COMMISSION FOR THE PROTEC-
TION OF HUMAN SUBJECTS OF BIOMEDICAL AND
BEHAVIORAL RESEARCH.

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An assessment of the impact upon fetal research of the Report and Recommendations (Report) of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research¹ depends, to some extent, upon one's perspective. This article will focus upon the impact of the Commission's Report as perceived by a physician-investigator.

In the past three years there has been a substantial decrease in the amount of fetal research performed in the United States. This decrease reflects the effects of multiple social and political forces that were operative before the Commission was convened and which continued during its deliberations and after its report was issued. A point by point comparison of the Commission's Report with previous expressions of national public policy indicates that the Report's overall impact should be to encourage the conduct of high quality fetal research. However, due to the aforementioned social and political factors, it is not yet clear whether the Report will have this effect. This article will examine these developments in detail.

Another area of difficulty involves the conceptual and semantic problems that undermine most efforts to discuss the law as it relates to research. This article will identify some of the semantic problems perpetuated by the Report and suggest an approach to the resolution of one — the spurious distinction between therapeutic and nontherapeutic research.

I. THE DECREASE IN FETAL RESEARCH —
IMPACT OF THE COMMISSION'S REPORT

A. *Decreased Research on and Involving the Fetus*

During the past three years there has been a substantial decrease in the amount of research done on the fetus. This is illustrated by re-

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1. NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, REPORT AND RECOMMENDATIONS: RESEARCH ON THE FETUS, (DHEW Pub. No. (OS) 76-127, 1975), also printed in 40 Fed. Reg. 33,530 (1975) (partially codified in 45 C.F.R. §§ 46.101-301 (1976)) [hereinafter cited as COMMISSION'S REPORT]. For the reader's convenience, chapters VIII and IX are reprinted herein at 300-24, and unless otherwise indicated, all citations to the *Commission's Report* refer to these pages.

viewing the experience of the National Institutes of Health (NIH).² In March, 1976, the Office for Protection from Research Risks (OPRR) at NIH reviewed all proposals to do fetal research received by NIH since July, 1974 — the date the National Research Act placed a moratorium on some sorts of fetal research.³ In twenty-one months, NIH had received only three proposals to do research on the fetus, each of which was for either renewal or continuation of ongoing research programs.⁴ All three would have been classified as therapeutic research as defined in the Commission's Report.⁵ In two of the proposals, the research maneuver was the use of ultrasound as an aid to determining fetal size. The third involved administration of blood transfusions to the fetus *in utero*. In the latter proposal, blood was to be administered only to fetuses who required it due to severe congenital anemia. Performance of this maneuver presented a risk of premature induction of labor, and if labor is induced before the fetus becomes viable a non-viable fetus is delivered which will certainly die.⁶ Thus, a risk of

2. Conversation with Dr. Donald T. Chalkley, Director of the Office for Protection from Research Risks (OPRR), National Institutes of Health (NIH) (December 13, 1976). During the course of this conversation, the author's impressions of the effects of various events on the quantity and quality of fetal research were supported.

3. Pub. L. No. 93-348, Title II, § 213, 88 Stat. 353 (1974). It should be noted that NIH distinguishes between research *on* the fetus and research *involving* the fetus. In the former category, a maneuver performed for research purposes actually touches the fetus. This touching might be through an instrument, administration of a drug, or the use of X-rays or ultrasound. Research involving the fetus is, in general, research in which the subjects are pregnant women and there is some cause to suspect that there might be some influence on the fetus. However, there is no direct touching of the fetus. For example, anything that alters the physiologic state of the mother might be viewed as having a potential effect on the fetus. Some types of research maneuvers which are classified as involving the fetus — *e.g.*, amniocentesis performed for research purposes — are substantially more likely to have an adverse effect on the fetus than are some classified as research on the fetus — *e.g.*, ultrasound done for purposes of determining fetal size (which presents no known risk either to the fetus or the mother).

4. NIH grants and contracts are ordinarily funded for one year terms. At the time an award is made there is also a statement of a period (usually three to five years) during which financial support — usually at approximately the same level — may be expected to continue. A *continuation* application is a request by an investigator to continue funding of a project for another year within the initially stated period of support. A *renewal* application is a request for a new period of support (usually three to five years) of an on-going project at the time the initial period is ending. A *new* application is a request to initiate a new project.

5. "Therapeutic research" is defined in the Report as "research designed to improve the health condition of the research subject by prophylactic, diagnostic or treatment methods that depart from standard medical practice but hold out a reasonable expectation of success." COMMISSION'S REPORT, *supra* note 1, at 40 Fed. Reg. 33,532 (1975).

6. The terms viable, nonviable, previable and death have carefully defined technical meanings. For a full elaboration of these and other terms useful in discussing the fetus at various stages of its development see Levine, *Viability and Death of the Human Fetus: Biologic Definitions*, 23 CLINICAL RESEARCH 211-16 (1975). Viability is a term applied to a fetus which, taking into account its present circumstances, is

this maneuver is the induction of an abortion. However, it was confidently estimated that the risks to the fetus of transfusion would be much smaller than the risks of not transfusing.

As of December 13, 1976, no new research grant or contract applications to do research on the fetus had been funded by NIH since the moratorium. There is no data as to how many proposals there were between March and December, 1976, but it has been estimated that the number is extremely low.⁷ In summary, since July, 1974, NIH has funded very little research on the fetus and has received very few proposals to do such research. Currently funded projects present either no known risk or, in one case, risks that are clearly outweighed by anticipated direct benefits to the fetus.

B. *Factors Contributing to the Decline in Fetal Research*

Many persons assume that the decline in the amount of fetal research is in some way connected with the activities of the Commission. Yet there have been so many events during the past four years that have influenced the climate in which research is done and the motivations of those who do the research that it is quite impossible to assess the impact of the Commission.⁸

Early in 1973, the United States Supreme Court in *Roe v. Wade*⁹ and *Doe v. Bolton*¹⁰ established the right of a pregnant woman to have

predictive of the likelihood that it will become an infant capable of maintaining life independently of the mother. Nonviability is a status which may exist *in utero* or *ex utero*. The diagnosis of nonviability is absolutely predictive of death. Previability describes the status of a presumed viable fetus *in utero* prior to the twentieth week of gestation. Spontaneous or induced delivery of a previable fetus will result in a fetus that will be classified as nonviable *ex utero*. Death is the total and permanent cessation of those biologic functions that, taken together, provide grounds for classifying a fetus (as a total integrated organism) alive. It is possible, indeed usual, for some organs, tissues, and cells to remain alive for varying periods of time after the total organism is dead.

Unfortunately, the definitions developed by the Commission provide no language which one might use to discuss the probability of a fetus' survival after spontaneous or induced delivery. See COMMISSION'S REPORT, *supra* note 1, at 40 Fed. Reg. 33,531-32 (1975).

7. Conversation with Dr. Donald T. Chalkley, *supra* note 2.

8. A chronology of some of the more important events that have recently influenced fetal research:

January 1973	Supreme Court: <i>Roe</i> and <i>Doe</i> decisions on abortion.
November 1973	DHEW proposed regulations on protection of subjects with "limited capacities to consent."
April 1974	Indictment of Dr. Sabath et al for "grave-robbing."
1974-1975	Development of state laws proscribing various categories of fetal research.
July 1974	National Research Act establishes Commission, moratorium on fetal research.
February 1975	Conviction of Dr. Edelin for manslaughter.
May 1975	Commission Report: <i>Research on the Fetus</i> .

9. 410 U.S. 113 (1973).

10. 410 U.S. 179 (1973).

an abortion during the first two trimesters of pregnancy for whatever reasons she and her doctor consider appropriate. It is generally assumed that these decisions greatly encourage fetal research because they increased the availability of fetuses upon which to do research. However, this is not the case. Even before 1973 there were many more fetuses available than researchers had the capacity to study. These fetuses became available through therapeutic abortions and spontaneous miscarriages. The effect of the *Roe* and *Doe* decisions was merely to increase an already excessive supply. This does not mean that there was a large amount of fetal research; rather, there were relatively few people having the appropriate training, interests, and expensive equipment necessary to do good fetal research.¹¹ However, the *Roe* and *Doe* decisions did have two effects: one which might eventually inhibit one type of fetal research, and the other which tends to facilitate one particularly important category of fetal research.

For some types of research on the fetus, *e.g.*, research done to determine the feasibility of transplanting fetal organs, it is essential to have relatively large, intact, living but nonviable fetuses as subjects. Because of the *Roe* and *Doe* decisions there has been a tendency to perform abortions much earlier in pregnancy, since the delays associated with certifying an abortion as "therapeutic" no longer exist. The trend toward a diminished availability of such fetuses began with the *Roe* and *Doe* decisions and was accelerated following the *Edelin* decision.¹² In 1976, fetal availability was approximately twenty-five percent of what it was prior to 1973.¹³ Some investigators have complained that the progress of their research which is dependent upon the availability of this type of fetus has, in fact, been delayed.

On the other hand, the *Roe* and *Doe* decisions facilitated the conduct of some very important fetal research of the sort that is or should be initiated shortly before an abortion procedure.¹⁴ Now

11. As a corollary, it is often stated that one reason to restrict or prohibit fetal research is that it would remove the motivations of researchers to encourage abortions so as to make more fetuses available for their research. This is clearly incorrect; there is no numerical deficiency that any researcher might wish to supply.

12. See notes 27-29 and accompanying text *infra*.

13. Conversation with Dr. Donald T. Chalkley, *supra* note 2.

14. There are two types of research, which if they are to be done at all, are most appropriately initiated shortly before an abortion procedure. The first is research in which the proposed objective cannot be achieved unless the fetus can be examined shortly after it is aborted. This most commonly entails administration of a drug to the mother before the abortion is begun and the examination, shortly after the abortion, of the tissues of the fetus to determine: 1) whether the drug has gotten into the tissues and 2) if so, what effects (either good or bad) it might have had. Development of rational drug therapy for the pregnant woman and for the fetus is dependent upon

healthy women can have abortions performed in clinics or hospitals according to a schedule around which the research can be planned rather than having illegal abortions of which investigators may not even be aware.

In 1973 and 1974, the Department of Health, Education and Welfare (HEW) proposed regulations to safeguard the rights and welfare of research subjects having "limited capacity to consent"; such persons — in the view of HEW — include the fetus, children, prisoners and the institutionalized mentally infirm.¹⁵ These proposals produced considerable concern and anxiety in the biomedical research community.¹⁶ In general there were several kinds of problems that were presented by the proposed regulations.¹⁷ First, they would have created

the performance of such research. For example, it would be absurd to attempt to treat an infection in the fetus with a drug that did not even penetrate the fetal tissue. It is highly uncommon for drugs to produce any harm to the fetus that could not be anticipated from the results of research done before such research on the fetus is performed. See Levine, *Appropriate Guidelines for the Selection of Human Subjects for Participation in Biomedical and Behavioral Research* 64-69 (February 2, 1976) (paper presented to the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Feb. 2, 1976) (on file at the offices of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Westwood Building, Room 125, 5333 Westbard Avenue, Bethesda, Maryland 20016). For an elaboration of the consequences of not proceeding with this sort of research, see Mirkin, *Impact of Public Policy on the Development of Drugs for Pregnant Women and Children*, 23 *CLINICAL RESEARCH* 233-37 (1975); Shirkey, *Therapeutic Orphans*, 72 *J. PEDIATRICS* 119 (1968).

The second type of research that it seems most appropriate to do in anticipation of abortion is that in which there is cause to suspect that some harm might befall the fetus as a consequence of the research. The sort of harm with which one is most commonly concerned is that a maneuver might induce premature labor. If this is done at a time when the fetus is previable, the delivered fetus will be nonviable and will die. Usually in the early stages of such research it is not known whether premature labor will be induced. However, during the early stages of experimentation with diagnostic instruments which penetrate the uterine cavity one may ordinarily assume that in some cases labor will be induced prematurely. Thus, in the early stages of development of such techniques as amniocentesis and fetoscopy, researchers have preferred to do this shortly before initiation of a procedure to terminate pregnancy. In the view of researchers, the greatest harm that might befall such a fetus is that its abortion might be induced an hour or perhaps a day earlier than it would otherwise. For a discussion of the consequences of not proceeding with this sort of research, see Mahoney, *Implications of Restrictions on Fetal Research for Biomedical Advance*, 23 *CLINICAL RESEARCH* 229-32 (1975).

15. For the first draft of the proposal, see 38 Fed. Reg. 31,738-49 (1973). This draft was revised and republished as a proposal. 39 Fed. Reg. 30,653-57 (1974).

16. The Department of Health, Education, and Welfare received 450 responses to its November 16, 1973 proposal of regulations. See 39 Fed. Reg. 30,648 (1974). For a detailed account of the problems perceived by the biomedical research community with these proposed regulations, see the position statements of the American Federation for Clinical Research, reprinted in 22 *CLINICAL RESEARCH* 135-38 (1974) and 23 *CLINICAL RESEARCH* 53-60 (1975).

17. See Levine, *Proposed Rules on Ethics of Human Experimentation: Tensions Between the Biomedical Research Community and the United States Federal Government*, in *SOCIAL RESEARCH IN CONFLICT WITH LAW AND ETHICS* 67-81 (P. Nejejski ed. 1976).

a formidable bureaucracy which probably would not have contributed materially to the avowed purpose of safeguarding the rights and welfare of human subjects. Further, in some cases they might have achieved results contrary to this purpose. Among the new bureaucratic structures that would have been created was the Ethical Advisory Board (EAB) which — because it would have reviewed all research on persons with limited capacities to consent — would have largely duplicated the efforts of the Institutional Review Board (IRB). There was also a proposal to establish Consent Committees to monitor the negotiations for informed consent between investigators and prospective subjects and, further, to monitor the ongoing research activity.¹⁸ In the view of some investigators, this proposal would have resulted in the overregulation of research, the trivialization of medical ethics, and the paper documentation of apparent — as opposed to actual — protection of the rights and welfare of human subjects.¹⁹ Rather than waste so much time and energy, many investigators diverted their energies to less tedious pursuits.

Second, the proposed regulations would have created various new bureaucratic structures and assigned new functions to existing ones. These changes seemed to reflect a prevailing climate of mistrust.²⁰ It did not seem to the biomedical research community that this assumption of mistrust had any legitimate support in actual experience.

Finally, some specific proposals to foreclose categories of research seemed particularly dangerous. For example, there was to be a uniform proscription of all research initiated prior to the procedure to terminate pregnancy.²¹ Even though these proposals were not final regulations many investigators behaved as if they were. Thus, shortly after publication of these proposals there was a sharp reduction in the amount of important research done in this category.

In July 1974, Congress passed the National Research Act which contained the “moratorium” on fetal research: “Until the Commission has made its recommendations . . . the Secretary may not conduct or support research . . . on a living human fetus, before or after the

18. See 39 Fed. Reg. 30,654 (1974).

19. See generally Ingelfinger, *The Unethical in Medical Ethics*, 83 ANNALS INTERNAL MED. 264-69 (1975). For a detailed analysis of the problems presented by one NIH policy, see Holder & Levine, *Informed Consent for Research on Specimens Obtained at Autopsy or Surgery: A Case Study in the Overprotection of Human Subjects*, 24 CLINICAL RESEARCH 68-77 (1976).

20. This sense of not being trusted by either the public or the government is reflected in the statements of hospital administrators and doctors as reported in the *New York Times* immediately following the arrest of four doctors for “grave robbing.”

See N.Y. Times, Apr. 19, 1974, at 42, col. 4; *id.* Apr. 20, 1974, at 1, col. 1; *id.* Apr. 21, 1974, § IV, at 11, col. 1; text accompanying notes 23 & 24 *infra*.

21. See 39 Fed. Reg. 30,654 (1974).

induced abortion of such fetus, unless such research is done for the purpose of assuring the survival of such fetus."²² Elsewhere in the legislation, the Commission was instructed to deliver its recommendations on fetal research within four months of its having been convened. Because of delays in convening the Commission and the time needed for the Commission to formulate its recommendations, the actual moratorium which the Commission recommended lifting, continued for approximately ten months.

It is difficult for those who are not involved in either the conduct or the administration of research to imagine the impact of a moratorium. It takes a long time to assemble a team of people having the expertise necessary to do sophisticated research. It also takes a long time to acquire ample space and adequate instruments to conduct this research. The personnel, space, and instruments may all be viewed as very valuable and quite scarce resources; if they are not employed for one purpose, they will generally be employed for another. During the ten month moratorium the personnel, space, and instruments that had previously been committed to doing fetal research were, in some cases, committed either to doing other sorts of research or to nonresearch purposes. At the end of the moratorium it became necessary for investigators to again begin seeking funding for research — *e.g.*, to pay the salaries of highly skilled technicians and other personnel — and to secure laboratory space commitments from institutional administrators who had assigned the space to other projects for which funding seemed more stable and secure. This moratorium had a particularly chilling effect. It was imposed at a time when the NIH was in the final stages of planning the programs which would have provided contracts for the development of such techniques as fetoscopy. The research community anticipated that these large contract programs would have provided a relatively stable source of support for ongoing activities. Several substantial research operations were dismantled, and those administrators and investigators who had been involved in them have been quite loathe to begin again.

In 1973, an article published in the *New England Journal of Medicine* reported on a research project which involved the administration of antibiotics to pregnant women shortly before initiation of therapeutic abortions and the subsequent examination of aborted fetuses.²³ The objective was to determine which of two antibiotics

22. Pub. L. No. 93-348, Title II, § 213, 88 Stat. 353 (1974).

23. Philipson, Sabath & Charles, *Transplacental Passage of Erythromycin and Clindamycin*, 228 *NEW ENG. J. MED.* 1219-21 (1973). This particular project is an example of the first type of research discussed in note 14 *supra* in which the proposed

concentrated most effectively in the fetus, with an aim toward predicting which might prove most useful in the treatment of such infectious diseases as syphilis. Since reports of similar studies of different drugs had been published previously in reputable medical journals, one would not have anticipated the ensuing legal consequences. Dr. Sabath and the other authors were indicted for "grave robbing,"²⁴ and they are still awaiting trial. Shortly thereafter, legislation was enacted in Massachusetts making this important category of research a felony,²⁵ several other states have since adopted similar laws.²⁶

While searching for the fetuses described by Sabath, representatives of the Boston prosecutor's office found a fetus that had been aborted by Dr. Kenneth Edelin.²⁷ Dr. Edelin was convicted of manslaughter on February 15, 1975.²⁸ This conviction was rendered in the face of conflicting evidence by eyewitnesses as to whether the fetus in question showed *any* of the "signs of life."²⁹ Most fetuses exhibiting less than all of the signs of life — *i.e.*, spontaneous muscle movement, respiration, heartbeats and pulsating umbilical cords — are nonviable; that is to say that they have no chance whatsoever of survival.³⁰ Yet, as a consequence of this highly publicized conviction, there is now a strong tendency to perform abortions using techniques that will guarantee that there will be no signs of life. These techniques, in general, render the aborted fetus useless for the kinds of research activities that require the availability of larger fetuses which are living and yet nonviable.³¹ The legal forces which diminished the availability of such fetuses beginning with the decisions in *Roe* and *Doe*, were greatly accelerated by the *Edelin* decision.³²

objective cannot be achieved unless the fetus can be examined shortly after it is aborted. The tendency of the *Roe* and *Doe* decisions to facilitate this type of research was substantially offset by the indictment of these authors.

24. N.Y. Times, Apr. 14, 1974, § IV, at 7, col. 1.

25. See MASS. GEN. LAWS ANN. ch. 112, § 12J (West) (Supp. 1976-77) (amended).

26. For a survey of state laws relating to fetal research, see Capron, *The Law Relating to Experimentation with the Fetus*, in NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, *Appendix to REPORT AND RECOMMENDATIONS: RESEARCH ON THE FETUS* (DHEW Pub. No. (OS) 76-128, 1975).

27. See Culliton, *Manslaughter: The Charge Against Edelin of Boston City Hospital*, 186 SCIENCE 327-30 (1974).

28. For a detailed account of the Edelin trial, see Culliton, *Edelin Trial: Jury Not Persuaded by Scientists for the Defense*, 187 SCIENCE 814-16 (1975).

29. *Id.*

30. For a discussion of the signs of life and their relative importance in determining the viability of a fetus *ex utero*, see Levine, *supra* note 5.

31. See text accompanying note 8 *supra*.

32. On December 17, 1976, the Massachusetts Supreme Judicial Court set aside the conviction of Dr. Edelin. *Commonwealth v. Edelin*, ___ Mass. ___, 359 N.E.2d 4

Thus, several events which antedated the Commission's Report tended to discourage fetal research. In the absence of some dramatic encouragement, it appears unlikely that there will be any substantial recovery in the level of activity of fetal research in the near future. Directors of some of the leading programs in obstetrics and gynecology have reported a sharp reduction in research interest on the part of physicians seeking training in their field.³³ Young physicians who are interested in doing research are being attracted to other medical specialties.

C. *Impact of the Commission's Report*

In order to analyze the impact of the Commission's Report, its recommendations will be compared with previous expressions of public policy made at a national level: the National Research Act³⁴ and the proposed HEW regulations on fetal research.³⁵ A detailed comparison of the Commission's recommendations with the second draft of the HEW proposed regulations reveal that in each case in which the former is at variance with the latter, the effect of the Commission's recommendations was to decrease the development of pointlessly cumbersome procedures and needlessly restrictive proscriptions. Rather than review all of these differences, this article will focus upon the issues identified as the items of gravest concern to the biomedical research community.³⁶

The HEW proposal called for the development of an Ethical Advisory Board to review "all applications or proposals for support of . . . biomedical research, development, and related activities involving: 1) the fetus *in utero*, 2) the abortus . . . 3) pregnant women, and 4) *in vitro* fertilization. In addition, these regulations are applicable to all such activities involving women who could become pregnant . . ." ³⁷ In short, the HEW proposed regulations called for a tremendous amount of duplication of the IRB's effort at a national level. By contrast, the Commission recommended approval by "a national

(1976). However, it seems unlikely that the trend of avoiding the abortion of fetuses that might show a sign of life will be reversed.

33. Conversation with Dr. Donald T. Chalkley, *supra* note 2.

34. Pub. L. No. 93-348, Title II, § 213, 88 Stat. 353 (1974). For a discussion of the impact of the moratorium on fetal research, see text accompanying note 23 *supra*. The Commission recommended that the moratorium on fetal research be lifted. COMMISSION'S REPORT, *supra* note 1, at 300-24. However, the effects of the 10 month moratorium are not likely to be quickly overcome.

35. 39 Fed. Reg. 30,653-57 (1974).

36. See text accompanying notes 16-21 *supra*.

37. 39 Fed. Reg. 30,653 (1974) (proposed section 46.304).

ethical review body" only for nontherapeutic research directed toward the fetus in anticipation of abortion and during the abortion procedure, and that directed toward the nonviable fetus *ex utero*.³⁸

Secondly, the Commission's recommendations did not support the HEW proposal³⁹ to establish Consent Committees for fetal research. Consequently, there is no mention of these committees in the final HEW regulations. In addition, the HEW proposal of an absolute proscription of nontherapeutic research in anticipation of abortion regardless of whether any risk is presented to the fetus⁴⁰ was not supported by the Commission. The Commission's recommendation number five instead provided that such research may be conducted or supported if it is done in accord with specified procedural safeguards.⁴¹

In conclusion, the Report of the Commission should be a source of encouragement to those who are interested in fetal research. When considered in its historical context it may be interpreted as an effort to restore a rational perspective. The Commission's recommendations contain no prohibition of any type of research that might be proposed by a responsible investigator. To resolve the most difficult problems, the Commission depends heavily upon the development of a procedural mechanism; a national ethical review body. However, in contrast to the HEW proposals, the recommendations do not overtax this procedural mechanism with the performance of meaningless tasks. Further, the Report does not attempt to anticipate all future research contingencies and to resolve them through the development of regulations. Rather, it provides a framework of guidelines within which the EAB and the IRB can be expected to function. However, owing to some of the circumstances beyond the control of the Commission, it may be a long time, if ever, before the full positive impact of its report is expressed.

38. COMMISSION'S REPORT, *supra* note 1, at 300-24. The Commission forwarded its recommendations to the Secretary of DHEW, in May, 1975 and the final regulations were published in the *Federal Register* on August 8, 1975. See 40 Fed. Reg. 33,526-30 (1975). The DHEW regulations called for the establishment of two Ethical Advisory Boards to review proposals to do fetal research in the three categories specified in the text. As of December, 1976 — 15 months later — no Ethical Advisory Boards have been established. Perhaps one of the factors contributing to the absence of proposals to do research in these categories is the fact that investigators who might wish to develop such proposals know that there is no mechanism in operation to review them.

39. 39 Fed. Reg. 30,653 (1974) (proposed section 46.305).

40. *Id.* (proposed section 46.306). As noted earlier, this is an extremely important class of research. See note 14 *supra*.

41. COMMISSION'S REPORT, *supra* note 1, at 312.

II. A CONCEPTUAL FLAW: THE SPURIOUS DISTINCTION BETWEEN THERAPEUTIC AND NONTHERAPEUTIC EXPERIMENTATION

Perhaps the greatest contribution the Commission could make to those who wish to participate intelligently in the formulation and implementation of public policy as it relates to research involving human subjects would be a clarification of the language used to discuss such research. If it were to do this, the Commission's favorable impact on the conduct of research would be greatly enhanced. Evidence that the Commission is beginning to accomplish this salutary objective will be discussed below.⁴² First, however, one serious conceptual flaw contained in the Report should be identified:⁴³ The definitions upon which the Commission's recommendations are based perpetuate the meaningless distinction between therapeutic and nontherapeutic research.⁴⁴ This is not merely a semantic problem; this spurious dichotomization leads us to reach wrong conclusions in our ethical analyses and, as an inevitable consequence, to develop inappropriate law.

It is not clear when this unfortunate distinction began to be made in discussions of the ethics and regulation of research. The Nuremberg Code makes no such distinction.⁴⁵ The Declaration of Helsinki in 1964 distinguished nontherapeutic clinical research from clinical research combined with professional care.⁴⁶ In the 1975 revision of this Declara-

42. See text accompanying notes 55-64 *infra*.

43. In fact, there is more than one problem with the definitions contained in the Commission's report. The Commission's report, for example, provides no language that can be used to discuss whether a living fetus *in utero* might be expected to survive after delivery. See note 6 *supra*.

44. COMMISSION'S REPORT, *supra* note 1, at 40 Fed. Reg. 33,532 (1975). The pertinent definitions are as follows:

"Research" refers to a systematic collection of data or observations in accordance with a designed protocol.

"Therapeutic research" refers to research designed to improve the health condition of the research subject by prophylactic, diagnostic or treatment methods that depart from standard medical practice but hold out a reasonable expectation of success.

"Nontherapeutic research" refers to research not designed to improve the health condition of the research subject.

Id. I shall not provide detailed comments on these definitions. Rather, it should suffice to ask the reader at this point to try to imagine a "... systematic collection of data or observations . . . designed to improve the health condition of a research subject." Actually, since most diagnostic activity involves a systematic collection of data or observations, it is possible to imagine some activity that would conform to the Commission's definition. However, even this does not work well. This is because the diagnostic activity one would have to imagine, ordinarily would not present a departure from standard medical practice. Moreover, it clearly was not the intent of the Commission to develop through these definitions the possibility of discussing ordinary diagnostic activities.

45. Nuremberg Code of Ethics, *reprinted in Appendix, supra* note 26, at 17-1 to 17-2.

46. Declaration of Helsinki (1964) (amended 1975), *reprinted in Appendix, supra* note 26, at 18-1 to 18-3.

tion, "medical research combined with professional care" is designated "clinical research" while "nontherapeutic biomedical research involving human subjects" is designated "non-clinical biomedical research."⁴⁷ Principles set forth to govern "clinical research" provide that, "[t]he doctor can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient."⁴⁸ This is to be contrasted with principles developed with respect to nonclinical research: "[t]he subjects should be volunteers — either healthy persons or patients for whom the experimental design is not related to the patient's illness."⁴⁹ It is beyond the scope of this article even to list all of the problems that derive from the use of this unfortunate distinction. For present purposes, discussion will be confined to the identification of only three such problems. These three are sufficiently serious that an awareness of them should force us to conclude that we must abandon this classification.

First, many types of research done by physicians on human subjects cannot be categorized either therapeutic or nontherapeutic. Consider, for example, the placebo-controlled, "double-blind" drug trial. Certainly the administration of a placebo for research purposes is not "justified by its potential diagnostic or therapeutic value for the patient."⁵⁰ Therefore, it is nontherapeutic. Thus, according to the Declaration of Helsinki, those who receive the placebo must be "either healthy persons or patients for whom the experimental design is not related to the patient's illness."⁵¹ This would be absurd.

Secondly, a strict interpretation of the Declaration of Helsinki would lead one to conclude that all rational research designed to explore the pathogenesis of a disease is to be forbidden. If such research cannot be justified by its potential diagnostic or therapeutic value for the patient, it must be considered nontherapeutic. Therefore, such research may be performed only upon healthy persons or patients not having the disease one wishes to investigate. Again, this would be absurd.

47. Helsinki Declaration (1975) (copies can be obtained from the World Medical Association, 1841 Broadway, New York, New York 10023).

48. *Id.* (Principle II.6). In recent years, we have seen the distinction between therapeutic and nontherapeutic research assume a central position in the papers of those who discuss the ethics or law of research involving human subjects. *See, e.g.*, C. FRIED, *MEDICAL EXPERIMENTATION* (1974); P. RAMSEY, *THE PATIENT AS A PERSON* (1970).

49. *Id.* (Principle III.2).

50. Helsinki Declaration (1975) (copies can be obtained from the World Medical Association, 1841 Broadway, New York, New York 10023).

51. *Id.*

Paul Ramsey provides us with a good example of how one can be lead to erroneous conclusions by assuming that there is a distinction between therapeutic and nontherapeutic research. He claims that the use of a nonconsenting subject is wrong whether or not there is risk, simply because it involves an "unconsented touching."⁵² This wrongful touching is rectified only when it is done for the good of the individual. Thus, based upon the assumption that therapeutic research is always done for the good of the individual subject, he concludes that proxy consent is permissible for therapeutic research.⁵³ He further concludes that nontherapeutic research on children is never justified because they cannot consent for themselves and the potential benefit to the subject that would validate proxy consent to therapeutic research is lacking.⁵⁴

In order to avoid these embarrassments we must abandon the distinction between therapeutic and nontherapeutic research. The Commission has begun to do this. In its later report, *Research Involving Prisoners*,⁵⁵ the terms therapeutic and nontherapeutic research are not used. The language used in this later report should provide much more suitable guidance to those who develop regulations, to IRB members, and to investigators. But before the Commission was able to clarify its use of terminology, it was necessary for it to begin to systematically address the general conceptual charges in its mandate.⁵⁶ If the Commission had had the opportunity to begin its general conceptual considerations before addressing the specific problems of research on the fetus, the terms therapeutic and nontherapeutic research might not have been perpetuated.

Subsequent to the publication of *Research on the Fetus*, the Commission drafted its definitions of research,⁵⁷ practice,⁵⁸ and a third class

52. P. RAMSEY, *supra* note 48, at 11.

53. *Id.* at 11-12.

54. *Id.* at 13.

55. NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, REPORT AND RECOMMENDATIONS: RESEARCH INVOLVING PRISONERS (DHEW Pub. No. (OS) 76-131, 1975).

56. In the National Research Act, the Commission is charged to "consider," among other things: "The boundaries between biomedical or behavioral research involving human subjects and the accepted and routine practice of medicine." Pub. L. No. 93-348, Title II, § 202(a)(1)(B)(i), 88 Stat. 349 (1974).

57. The term "research" is defined as follows:

Biomedical and behavioral research involving human subjects refers to a class of activities designed to develop or contribute to generalizable knowledge. By generalizable knowledge we mean theories, principles or relationships (or the accumulation of data on which they may be based) that can be corroborated by accepted scientific observation and inferences.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Boundaries Between Biomedical or Behavioral Research and Accepted and Routine Practice* (draft document, Feb. 24, 1976) (on file at the

of activities, innovative therapy, which definition is especially relevant here:

[O]ther uncertainties may be introduced by the application of novel procedures as, for example, when deviations from common practice in drug administration or in surgical, medical or behavioral therapies are tried in the course of rendering treatment. These activities may be designated innovative therapy, but they do not constitute research unless formally structured as a research project [T]here is concern that innovative therapies are being applied in an unsupervised way, as part of practice. It is our recommendation that significant innovations in therapy *should* be incorporated into a research project in order to establish their safety and efficacy while retaining the therapeutic objectives.⁵⁹

It is made clear in other parts of this draft statement that diagnostic and prophylactic maneuvers are included under this rubric.⁶⁰ Thus, a more descriptive title for this class of activities might be "innovative practices."

In subsequent discussion by the Commission, it has been made apparent that novelty is not the attribute that defines this class of practices; rather, it is the lack of suitable validation of the safety or efficacy of the practice.⁶¹ Therefore, it is proposed that the best designation for this class of activities is "nonvalidated practice." A practice might be nonvalidated because it is new; *i.e.*, it has not been tested sufficiently often or sufficiently well to permit a satisfactory prediction of its safety or efficacy in a patient population. An equally common way for a practice to merit the designation nonvalidated is when, in the course of its use in the practice of medicine, some legitimate question arises concerning previously held assumptions about its safety

offices of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Westwood Building, Room 125, 5333 Westbard Avenue, Bethesda, Maryland 20016).

58. The term "practice" is defined as follows:

[T]he practice of medicine or behavioral therapy refers to a class of activities designed solely to enhance the well-being of an individual. The customary standard for routine and accepted practice is a reasonable expectation of success. The absence of validation or precision on which to base such an expectation, however, does not in and of itself define the activity in question as research. Uncertainty is inherent in therapeutic practice because of the variability of physiological and behavioral human response. This kind of uncertainty is, itself, routine and accepted.

Id.

59. *Id.*

60. *Id.*

61. See transcripts of the recent meetings of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (on file at the offices of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Westwood Building, Room 125, 5333 Westbard Avenue, Bethesda, Maryland 20016).

and/or efficacy. The source of the problem might be that the practice was never validated adequately in the first place, that a question is raised of previously unknown serious toxicity, or that a new practice seems likely to be either more safe or more effective. At the time of the first substantial challenge to the validity of a previously accepted practice, continuing use of that practice should be considered non-validated. For purposes of developing ethical norms, guidelines, or regulations, all nonvalidated practices may be considered together. As the Commission has suggested in the case of innovative therapy, these practices should be conducted in the context of a research project designed to test their safety and efficacy; however, the research should not interfere with the basic therapeutic (or diagnostic or prophylactic) objectives.⁶²

When research is done to test the safety or efficacy of a non-validated practice, the relationship between the physician-investigator and patient-subject is more complex than in either a physician-patient or investigator-subject relationship. In order to determine whether it is justified to proceed with the total activity or with any of its component parts, it is necessary to analyze each of the component parts for what it really is. The employment of a nonvalidated practice is not in and of itself research, although it may be malpractice.⁶³

Nonvalidated practice has much more in common with validated practice than it has with research. The decision to use a nonvalidated diagnostic procedure or therapeutic modality should ordinarily be made in the same way one makes the decision to use a validated procedure. That is, of the various modalities or procedures available to accomplish the purpose agreed upon by the physician and patient, the physician chooses the one which seems most likely to achieve the shared objective and least likely to produce adverse effects. When deciding to use nonvalidated procedure, it makes sense to talk about alternatives, as is required by the HEW regulations on informed consent.⁶⁴ A choice between the various alternatives may be based

62. Research designed to test the safety and/or efficacy of nonvalidated practices includes those activities ordinarily referred to as therapeutic research. It also includes such nontherapeutic maneuvers as placebo administration, randomization, and so on.

63. I wish to reemphasize that nonvalidated practices should ordinarily be conducted in the context of a research project designed to test their safety and efficacy. The conduct of such activities should adhere to the standards established for research — most importantly, an Institutional Review Board should review proposals to proceed. The Institutional Review Board should determine whether there are compelling reasons to depart from other standards of research; *e.g.*, adherence to such standards would be to the detriment of the therapeutic objective. The employment of a non-validated practice without approval by an Institutional Review Board might appropriately — if not technically — be considered malpractice.

64. 45 C.F.R. 46.3(c) (4) (1975).

upon those factors that seem most important to the patient; *e.g.*, risk, benefit, inconvenience, and expense. In research, on the other hand, there are no alternatives between which one might choose. The only alternatives are to proceed with the research or not to proceed. In the complex activity which is commonly called therapeutic research, the components that would properly be called research are those designed to establish the safety and/or efficacy of the nonvalidated practice. These are virtually never done for the benefit of the individual patient or subject. They are always designed to contribute to generalizable knowledge. While research activities can always be rejected without jeopardy to the life or health of the patient, the nonvalidated practice often cannot. The requirement for an explication of alternatives — derived from the medical practice model — clearly is inapplicable to research.

III. SUMMARY AND CONCLUSIONS

In the past three years there has been a substantial decrease in the amount of fetal research performed in the United States. This decrease reflects the effects of multiple social and political forces that were operative before the Commission was convened and which continued during its deliberations. By the time the Commission was convened, the situation seemed quite dark to those who wished to conduct fetal research; it is most unlikely that the Commission could have made any recommendations that might have been more discouraging to them.

A detailed comparison of the Commission's Report with previous expressions of public policy made at a national level, however, indicates that, in general, the Commission recommended a decrease in the development of pointlessly cumbersome procedures and needlessly restrictive proscriptions. Thus, when considered in its historical context, the Report of the Commission may be viewed as an effort to restore a rational perspective to the development of public policy on fetal research.

Perhaps the greatest contribution the Commission could make to those who wish to participate intelligently in the formulation and implementation of public policy as it relates to research involving human subjects would be a clarification of the language used to discuss it. Some semantic and conceptual flaws that have become firmly entrenched in the language used to discuss research and its regulation are unfortunately incorporated in the Commission's Report on *Research on the Fetus*. Since the Commission issued that report, however, it

has begun to consider systematically the general conceptual charges in its mandate. This has begun to yield a clarification of the language we use to discuss research.⁶⁵ Consequently, the language used in the Commission's Report on *Research Involving Prisoners* should provide much more suitable guidance to those who develop regulations, to members of Institutional Review Boards, and to investigators.

65. See NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, REPORT AND RECOMMENDATIONS: RESEARCH INVOLVING PRISONERS (DHEW Pub. No. (OS) 76-131, 1976).