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# THE STABILITY OF THE DECISION TO SEEK INDUCED ABORTION

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## INTRODUCTION

This paper focuses on the stability of the decision to seek an induced abortion. Three areas are considered: (a) the available literature has been reviewed, and some previously unpublished data are presented, in a manner which sheds a little light on the frequency with which women change their mind about seeking induced abortion; (b) evidence suggesting possible characteristics of women who might be at higher risk of changing their mind about deciding to abort is reviewed; and (c) some psychological and situational factors which might contribute to a change in the decision to abort are examined.

In addition to attempting to collect and integrate currently available material in a manner which contributes to our knowledge of the problem of decision-making stability prior to seeking induced abortion, the reviewer has attempted to limit his observations to issues of particular pertinence to the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The review, therefore, has two further restrictions.

First, the literature published before 1970 has not been generally considered although in at least one case[1] the data presented were collected prior to that time. While there is some evidence from other countries to suggest that restrictive abortion laws have less than total impact in preventing women from seeking abortion[2-5] studies from Britain and the United States show a considerable increase in the number of women obtaining abortions following liberalization of abortion laws. In Britain, since the 1967 Abortion Act, the rate of abortion per 1000 resident women ages 15 to 44 has risen from 3.5 in 1968 to 10.0 in 1971.[6] In the United States approximately 200,000 legal abortions were performed in 1970, 745,400 in 1973 (a rate of 16.5 abortions per 1000 women aged 15 to 44) and it has been projected that in 1974, 892,000 legal abortions were performed.[7] These data also show that the United States Supreme Court Decision in 1973,[8] which liberalized abortion laws, did not have a particularly marked effect on what has been a steady annual increase in the rate of abortion, in the United States, since the late 1960s when several states enacted less restrictive abortion codes.

The second restriction in the current review is that only one aspect of the stability of the abortion decision--the change from a decision to abort to one in favor of delivery--has been considered. As we shall see below, decision making during unwanted pregnancy may include periods in which a woman continually revises and re-revises the options open to her. While a decision to deliver may later be changed to a decision to abort[9,10] (or regret that abortion can no longer, for medical reasons, be performed), this change in decision is not considered further in this paper.

## THE RATE AT WHICH WOMEN CHANGE THEIR MIND ABOUT ABORTION

In reviewing the available information on the rate at which women change their mind about abortion we will consider three aspects of the source of evidence: (1) the period in the individual's own decision making when the change in decision was ascertained, (2) the location--clinic, hospital, county and socio-legal conditions in effect when the data were collected, and (3) the nature of the statistic itself--including factors influencing the numerator and denominator which may effect the computed rate.

### The Period of Decision Making During Which Indecision May Occur

All women who experience pregnancy may consider the possibility of abortion and, therefore, are at risk of changing their decision from abortion to delivery. Nonetheless, it is clear that many women who become pregnant unequivocally wish for the pregnancy to lead to delivery and for them abortion is not a serious option. Other women, however, variously described as having an unwanted or unplanned pregnancy,[9] give abortion considerable consideration. It is convenient to examine the stability of the decision process, in these women, for two periods: (a) the time between suspecting pregnancy and making an appointment at an abortion facility, and (b) the time between visiting an abortion facility and actually having the abortion. While such a dichotomy helps us to examine the decision process on an empirical level, however, it does not necessarily conform with the psychological reality of the decision process itself.

Evidence from studies of the first period of decision making may be most useful in predicting the characteristics of women who will change their decision to abort after reaching the clinic, and in predicting the psychological and situational correlates of such a change. Decisions which occur after the abortion client has made personal contact with an abortion facility are of acute interest to the Commission since this is the time when a woman is most likely to be asked to participate in medical studies.

### The Time Between Suspicion of Pregnancy and Personal Contact at the Clinic

In a study carried out at Yale-New Haven Hospital and also at a private New York Clinic women who aborted were asked to retrospectively report how frequently they changed their mind about the decision to abort. Approximately one third of the respondents had changed their minds about the decision to abort at least once (Table 1).[11]

Table 1. Distribution of Variable-Indecision About Abortion and Association with Gestation Group*

| | New York | | New Haven | | | |
|---|---|---|---|---|---|---|
| | | | Black | | White | |
| Times changed mind about abortion | No. | Percent | No. | Percent | No. | Percent |
| Never | 197 | 62.3 | 74 | 71.8 | 126 | 72.0 |
| Once or twice | 83 | 26.3 | 17 | 16.5 | 35 | 20.0 |
| Many times/all the time | 36 | 11.4 | 12 | 11.7 | 14 | 8.0 |
| Gestation group (weeks) | Percent changed mind about abortion | No. | Percent changed mind about abortion | No. | Percent changed mind about abortion | No. |
| < 9 | 27.5 | 80 | 20.0 | 10 | 25.8 | 31 |
| 9-12 | 32.5 | 83 | 42.8 | 28 | 23.9 | 71 |
| 13-18 | 48.2 | 85 | 21.3 | 47 | 32.2 | 59 |
| > 18 | 40.0 | 75 | 27.9 | 18 | 35.7 | 14 |
| **p < 0.01 | $\gamma$ = .19** | | $\gamma$ = .15 | | $\gamma$ = .14 | |

*Source: Table is reprinted from Bracken.[11]

A less direct way of considering the frequency with which women may change their mind about the abortion is to examine the difficulty in making the decision. Women aborting at the State University Hospital in Syracuse, New York, between July 1970 and June 1971, were asked about their decision to abort and reported that it was: not difficult 56 percent; mildly difficult 20 percent; considerably difficult 24 percent. Similar results were found in the New Haven and New York Study[11] in which abortion clients were asked to rank, on a 7-point scale, whether their decision had been extremely easy (scored 1) or extremely difficult (scored 7). The mean scores for women aborting in both New Haven and New York were 3.3 indicating that almost half the women had experienced some difficulty in making their decision. In another New York study at Park East Hospital, carried out between December 1971 and April 1972, one-fourth of the women aborting found the decision "difficult to make."[13]

Another way of obtaining some estimate of the risk for a change in the decision to abort is to measure the degree of conflict during the decision

process. When this was done in the New Haven and New York studies mean levels of conflict of 2.5 were found (measured on a 7-point scale where 1 = low and 7 = high conflict).[11,14]

Yet another way of estimating the level of indecision during this period is to determine the number of women who make appointments at abortion facilities but fail to keep them. The results of a small, *ad hoc* survey designed to collect data on the frequency of missed appointments are shown in Table 2.

Inspection of Table 2 suggests that roughly 10 percent of appointments made for first trimester abortion are not kept. It would be wrong, however, to interpret this figure as anything other than a maximum estimate for women who have decided not to abort. It was mentioned at all clinics surveyed that an appointment might be missed because a woman had elected to abort at another clinic, or that the appointment was inconvenient and might be rescheduled (much, but probably not all, of duplicate scheduling was avoided in computing clinic statistics), or that the client found she was not pregnant, or had spontaneously aborted.

Table 2. Proportion of Women Failing to Keep Clinic Appointments for First Trimester Abortions

| Source | Year | Number of Women Making Appointments | Number of Women Missing Appointments | Percent Missed Appointments |
|---|---|---|---|---|
| Eastern Women's Center, New York[20] | Feb 1 to Aug 1, 1972 | 11,765 | 1,360 | 11.6 |
| Eastern Women's Center, New York[20] | 1973 | 9,830 | 1,493 | 15.2 |
| Nathanson[15] | Jul 1970 to Aug 1971 | 29,696 | 1,848 | 6.2 |
| Preterm, Boston[27] | Dec 1974 to Feb 1975 | 2,758 | 237 | 8.5 |
| Erie Medical Center, Buffalo, New York[28] | 1973 | 7,061 | 646 | 9.1 |
| | 1974 | 5,041 | 369 | 7.3 |

## Decision Changes Following Personal Contact with Abortion Facility

The essential information collected for this section is presented in Table 3. In order to determine the rate at which women change their decision to abort after making personal contact with the abortion clinic, an attempt has been made to standardize the rate as follows:

$$\text{Rate of women deciding to deliver after visiting abortion clinic} = \frac{\text{Number of women reported deciding to deliver}}{\text{Total number of women visiting clinic for abortion in same time period}} \times 100$$

The reported rates range from a low of 0.06 percent to 9.7 percent, a 162-fold difference! In order to weight the evidence in Table 3 we will review the sources of data in more detail in the following two sections.

## The Type of Abortion Facility from Which Rates were Obtained

The effect of different types of abortion facility on the rate at which women change their decision to abort is highlighted by contrasting the two facilities showing the extreme differences in rate. Grady Memorial Hospital, at the time of the study,[18] was a 1,100 bed hospital serving medically indigent people from Atlanta. In 1970, in order for a woman to obtain an abortion, three licensed physicians and two out of three members of a hospital committee had to agree that an abortion was necessary. This system continued in the hospital even after a Georgia Federal District Court had ruled, in July of 1970, that established specific indications for abortion were unconstitutional. During 1970, 341 women applied for abortion of whom 139 were found to be "ineligible" or withdrew before they could be presented to the abortion committee, 43 women who were presented were refused abortion and 134 women were aborted. The median time for the abortion work-up was reported to be 15 days. In this, rather formidable, institutional and psychosocial environment, 31 women were reported to have changed their decision to abort (Table 3).

Eastern Women's Center[20] is typical of many large clinics specializing in abortion and reproductive health found in the United States at the present time and a description of the routines for obtaining abortion at other clinics[15,22] could equally apply there. Most appointments are made by telephone after the abortion client has, in many cases, already been counseled by a family planning or other agency counselor. When the abortion patient visits the clinic she is examined, counseled and aborted on the same day. Counseling at free standing abortion clinics provides emotional support prior to, sometimes during, and often following the abortion.[23-26] In 1973, at Eastern Women's Center, 553 women were denied abortion because of advanced gestation, 3 women were found on medical examination to have medical contraindications, 7 women decided not to abort and 7,770 women had an abortion.

Table 3. Description of Studies Providing Rates for Women Who Decide Not to Abort After Personal Contact With Abortion Facility

| Source | Year of Data Collection | Stages in Referral for Abortion | | | Rates* |
|---|---|---|---|---|---|
| | | Patients Referred From | Patients Referred To | Time When Decision to Abort was Changed | |
| Newton et al.[16] | 1972 | General practitioners and family planning clinics | Abortion Counseling Clinic, King's College Hospital, London | After first contact with Abortion Clinic** | 26/1,173 (2.2%) |
| Bracken and Swigar[17] | 1970-1971 | Family planning clinics, referral agencies and physicians | Yale-New Haven Hospital, Connecticut | After first contact with Abortion Clinic** | 31/474 (6.6%) |
| Bracken[11] | 1972-1973 | Initial visit at Yale-New Haven Hospital Clinic | Yale-New Haven Clinic for abortion | Between initial visit and abortion– on same day for first trimester cases | 2/395 (0.5%) |
| Yale-New Haven Hospital[21] | Jan 1972 to May 1973 | Clinic visit for abortion | Abortion at same clinic | During the clinic visit | 30/3,887 (0.8%) |
| Baker and Freeman[18] | 1971 | Private physicians and direct application to hospital | Grady Memorial Hospital, Atlanta, Georgia | Between contact with abortion "coordinator" and abortion procedure | 33/341 (9.7%)† |
| British Pregnancy Advisory Service (BPAS)[19] | 1971 | BPAS counseling and approval for abortion | BPAS Clinic for abortion | Between consultation with 2 MDs who signed a certificate approving the abortion and the procedure | 248/16,088 (1.5%) |
| Preterm Boston[27] | Aug 1, 1973 to Dec 31, 1974 | Clinic visit for abortion | Abortion at same clinic | During the clinic visit | 31/10,858 (0.3%) |
| London Pregnancy Advisory Service (LPAS)†† | Probably 1969-1970 | Initial LPAS interview | LPAS Clinic for abortion | Between initial interview and abortion | 42/3,000 (1.4%) |
| Pare and Raven[1] | 1962-1968 | Psychiatric interview and recommended for abortion | St. Bartholomew's Hospital, London | Between psychiatric approval and abortion | 2/130 (1.5%) |
| Eastern Women's Center[20] | Feb 1 to Aug 1, 1972 | Clinic visit for abortion | Abortion at same clinic | During the clinic visit | 6/9,820§ (0.06%) |
| Eastern Women's Center[20] | 1973 | Clinic visit for abortion | Abortion at same clinic | During the clinic visit | 7/7,777§ (0.09%) |

*Number of women changing mind over total number of women referred for abortion. For some studies rates have been recomputed for the current report.

**It is unclear what proportion of those women who decided not to abort did so following a telephone appointment but before visiting the clinic versus those women who visited the clinic and then changed their mind.

†An additional two women were listed as "rejection of system" and nine as a "minor unwilling or unable to obtain (parental) consent." Inclusion of these women in the rate of those listed as "changed mind" increases it to 12.9%. At follow-up only 27 of the 44 women not "aborting" were found to be pregnant (see text for details).

††*These data were reported as evidence to the Committee on the Working of the Abortion Act.*[6]

§These data exclude women not aborted because of advanced gestation and other medical contraindications.

Several of the reported studies are from Britain[1,6,16,19] and these data show a more uniform rate for changes in decision which range from 1.4 percent to 2.2 percent. Even though abortions are performed under liberal laws in Britain a woman must have the consent of her physician before an abortion may be performed. Contact with the physician may be a relatively uniform institutional process which, in effect, filters out women who might otherwise be candidates for later changing their decision to abort. Moreover, this process may account for the similarity of the rates from the British data. In other respects, particularly their counseling and medical procedures, the larger scale British abortion facilities, the London[6] and British[19] Pregnancy Advisory Services, are not unlike free standing abortion clinics in the United States. One wonders, then, why the rates in changing the decision to abort are not more alike. For example, the lowest available rate from the United States, 0.06 percent, is 23 times lower than the lowest British rate of 1.4 percent. One explanation may be that data from the free standing facilities includes only women aborting in the first trimester whereas the British data included second trimester patients. The possible influence of gestation on changing the decision to abort will be discussed in a later section.

## Problems in Computing the Change in Decision Rate

The formula used to compute the rate for women who change their decision to abort has been presented above. It is, of course, essential in computing the rate to ensure that all the women in the numerator have also been listed in the denominator and this has been done in Table 3. In comparing rates from different abortion facilities one would like to be assured that criteria for entering the numerator are the same across studies, as are criteria for entering the denominator.

Typically, women are identified who have "changed their mind" or who are "having the baby." There has been no systematic attempt to adequately define what is meant by a change in the decision, indeed there is no specific study of the phenomenon of decision changes prior to abortion anywhere in the literature. Some of the data presented in this report have been culled from clinic statistics and one can have little assurance that correct criteria for collecting research data were completely followed. Other data have been determined from reports of methodology and sampling in studies which were essentially dealing with other research questions. Several studies[16,17] include an unknown proportion of women who changed their decision to abort prior to reaching the clinic among those women who did so after the clinic visit. In a sample from Yale-New Haven Hospital some women who changed their decision to abort before visiting the clinic are included[17] whereas these women are not included in service statistics from the same hospital which show a much lower rate[21] as does information from the sampling frame for another study at the same hospital.[11]

In one study[18] women who "rejected the system" and minors "unwilling or unable to obtain (parental) consent" were not included with those who "changed

their mind." One cannot be confident, however, that such women would not have been included in the numerator of other studies.

As we have seen, the characteristics of women entering the denominator, that is women referred for abortion, have been influenced by different social, legal and clinic policies. Women who are prescreened by physicians, excluded because of advanced gestational age, or disinclined to request abortion because of institutional policies, have been disproportionately excluded from some studies rather than others.

## CHARACTERISTICS OF WOMEN WHO MAY BE AT HIGHER RISK OF DECIDING NOT TO ABORT

Again it is useful to consider the period during which a woman might decide not to abort in two stages; the time between suspicion of pregnancy and contact at a clinic, and the period following personal contact at the clinic. There is no evidence in the literature, nor from clinical impression, that tells us which women have been more likely to change their decision to abort after making contact with the abortion facility. Nonetheless, it is possible to paint some picture, albeit an incomplete one, of women who are more likely to report, when they finally do obtain an abortion, that they went through a period of indecision. This evidence will be reviewed in the remainder of this section.

### Evidence From Studies of Delayed Decisions to Abort

Indecision,[11] increased conflict over the decision to abort[14] (Table 1), and delayed decisions to abort[11,13,29] have been shown to be related to abortion obtained in the second trimester. Women who have been shown to be significantly more likely to delay in seeking abortion, therefore, might also be similar to those who are more likely to change their decision to abort. There is a growing body of information on the phenomenon of delayed abortion[30] and only the major correlates of delay will be reported here.

Women delaying in seeking induced abortion have been generally found to be young,[13,17,31,32] single,[13,17,29,31-33] primigravidas,[13,29,32] and experiencing their first abortion.[34,35] Black women have been found to be later presenters for abortion,[13,17,31] as have women from lower socioeconomic groups,[32,33] those with lower levels of completed education,[17,32] and women who are unemployed.[13,17,32]

These observations should not suggest that the delay in seeking an abortion results entirely, or even principally, from changes in the decision to abort. Many of the women who delay in seeking abortion have been reported to at least be partially delayed because of institutional hurdles in obtaining abortion[13,17,29,33,36-38] or because of an unstable relationship with the partner[13,32,39] or parents.[40] Yet another contributor to delayed abortion has been reported to be delay in recognition of pregnancy[11,13,17,29,32,40,41] or denial of pregnancy.[14,40]

Evidence from Unpublished Data

In a study of the decision to seek induced abortion among samples of women in New York and New Haven[11] respondents were asked "How many times did you change your mind about having the abortion?" The responses have been shown in Table 1. Indecision over the decision to abort was used as a dependent variable (dichotomized as never changed mind versus changed mind once or more) in order to reanalyze data from the study to examine the correlates of indecision prior to the abortion.

When simple socioeconomic factors were considered, women who were younger, less well educated and nulliparas were significantly more likely to report indecision prior to abortion. In order to obtain a more complete picture of the socio-demographic and psychological milieu in which indecision occurs the New York data were analyzed using a stepwise multiple regression technique. The first step in the regression analysis selected the single variable with the greatest prediction on the dependent variable based on the simple correlations. The second independent variable put into the regression equation was that which provided the best prediction of the dependent variable in conjunction with the first variable. Only independent variables making a significant contribution (as measured by an F-test) when added to the other independent variables have been presented in Table 4.

Table 4. Stepwise Multiple Regression Analysis of Changes in the Decision to Abort by Selected Independent Variables, New York Sample (n = 345)

| Step | Variable* | B | s.e.B | F | R | $R^2$ | r |
|---|---|---|---|---|---|---|---|
| 1. | Difficulty in making the decision to abort | .1220 | .0246 | 24.70 | .622 | .387 | .622 |
| 2. | Initially rejected idea of abortion | .1148 | .0282 | 16.59 | .665 | .442 | .569 |
| 3. | Initially happy about pregnancy | .0860 | .0271 | 9.97 | .692 | .479 | .437 |
| 4. | Nonsupportive relationship with partner | .0829 | .0393 | 4.46 | .698 | .487 | .127 |
| 5. | More people know about abortion decision | .0527 | .0306 | 2.97 | .704 | .495 | .212 |
| 6. | Low ego resilience | .4544 | .2715 | 2.80 | .709 | .503 | .158 |

*Variables are described to indicate prediction of more frequent indecision over decision to abort.

The six independent variables first entering the regression equation were able to explain 50 percent of the variance in the dependent variable. None of the demographic measures entered the regression equation, indeed the most powerful variables predicting indecision are ones reflecting the woman's psychological reaction to the pregnancy and abortion, the level of support she is likely to receive from her partner, the influence of many people knowing about the abortion and the woman's ability to cope with conflict during the decision process as measured by her ego resilience.

This analysis suggests, then, that changes in the decision to abort prior to visiting the clinic are associated less with simple demographic variables and more with psychological attributes which are less easily measured. Thus any attempt to develop measures which would enable clinicians to improve their ability to identify women who might change their decision to abort would have to include factors operationalizing the kind of psychological parameters shown in Table 4.

The evidence presented above may be summarized as follows. There is fairly substantial agreement, in the literature, on the demographic characteristics of women who have delayed abortion procedures. There has been less success in identifying women who delay making decisions to abort independent of other factors which may cause delayed abortion. Furthermore, there is some evidence that delayed abortion is associated with indecision to abort and this will be discussed more thoroughly in the next section.

It is quite obvious that a good deal of further investigation is required to confirm the rather tenuous relationships which emerge out of the currently available research findings. Moreover, it is important to emphasize that there is nothing in the available literature to indicate that women who are indecisive about their abortion prior to reaching the clinic will also continue to be indecisive after visiting the clinic. It could be argued that women who are indecisive during the earlier stages of their decision to abort might be more likely to continue to be indecisive until the abortion is performed, and, indeed, even after the abortion.[12,42] Alternatively, women who pass through an indecisive period prior to visiting the clinic and then resolve the decisional conflicts may be least likely to change their decision to abort after visiting the clinic. There is evidence in the psychological literature for both points of view[43] and few, if any, clinical reports speak to the issue.

Possibly other parameters, such as the woman's ability to cope with conflict, her self-esteem, feelings of powerlessness, and so on, will be more important indicators of late changes in the decision to abort than will a simple measure of how indecisive a woman was during her pre-clinic decision making. In one study[14] women of low ego resilience delayed relatively less in seeking abortion when the decision was highly conflictful than women of higher ego resilience. One explanation of this unexpected finding is that women who are better able to cope with the distress of having to decide to abort (the high ego resilience group) delay with increased conflict because they use the time to resolve conflicting issues which may produce indecisiveness. Women who cannot cope with the conflict of decision making may have truncated their decision processes in order to avoid the stress and anxiety of decisional conflicts and thus they will not resolve their indecisiveness. Such women are much more likely to be prone to changing their abortion decision after arrival at the clinic and when

they are faced with new considerations in their decision for which they were not prepared. Some of the possible factors which may change the woman's decision at this stage are discussed below.

## PSYCHOLOGICAL AND SITUATIONAL FACTORS WHICH MIGHT CONTRIBUTE TO A CHANGE IN THE DECISION TO ABORT

Here we consider a number of factors which might contribute to a change in the decision to abort. In the previous section it was postulated that an important determinant of late changed decisions could be the failure to resolve conflicting issues (rather than simply the presence of conflict) in the earlier decision-making stages. When late changes in the decision to abort occur the full ramifications of the decision to abort may not have been thought through making the decision vulnerable to new (possibly, even trivial) pieces of information which change the decisional "balance sheet" in favor of the delivery option.

The concept of "balanced decision" hints at a psychosocial concept of decision making which has been more fully developed by Janis and Mann[44,45] and described in terms of decision making during unwanted pregnancy elsewhere.[30] It has been proposed that during the decision to abort a woman passes through five stages. She must (1) acknowledge that she is pregnant, (2) consider the options, abortion or delivery, which are open to her, (3) consider the advantages and disadvantages of abortion or delivery by scanning and weighing the pros and cons of each alternative, (4) commit herself to one particular option, and (5) adhere to the decision.

Stage 3, when the pros and cons of abortion are considered, is of particular relevance to the Commission's interest since the degree of effort put into considering all information pertinent to the decision at this stage will "influence the long-run stability of the decision."[45] Thus a new piece of information during Stage 5 is only likely to result in a changed decision if it has not been anticipated and if contingency plans (both utilitarian and psychological) have not been prepared during Stage 3. For example, women who have sought information about abortion techniques, say by asking their physician, friends or by reading, are less likely to decide not to abort when the abortion procedures are described at the clinic. Improvement in the early decision-making process, according to this formulation, will reduce the risk of later indecision.

This brief description of the psychosocial concept of decision making under conflict does violence to a rather complicated theory based on a considerable amount of psychological evidence. It is sufficient, however, to make the point that the process of decision making is likely to be a more powerful predictor of later changes in the decision than is any one particular group of variables. Thus the search for situational factors which might contribute to a late decision not to abort is likely to be an elusive one.

The above discussion notwithstanding, four issues will be considered as having some likelihood of influencing the probability that a woman might change her decision to abort. These are (1) the gestational age of the pregnancy, (2) social and psychological considerations, (3) abortion counseling at the clinic, and (4) participation in a research project at the clinic.

Gestational Age of Pregnancy

There is some indication that increased gestational age is correlated with increased conflict during the decision process prior to arriving at the clinic (Table 1)[11] and a more difficult decision to abort.[11,13,14,29,32] Here, however, we are more concerned with the influence of gestation on a change in the decision to abort after visiting the clinic. Three considerations might contribute to late changes in the abortion decision. First, with later gestation, the abortion client may have experienced fetal movement which results in an increased emotional investment in the fetus. While the experience of fetal movement would be more likely to influence preclinic decisional change than it would be to produce a change in decision during the clinic visit itself, experience of fetal movement might be an important factor in influencing other considerations that do occur during the clinic visit.

Second, it would seem reasonable to propose that the principal influence of later gestation is on the change in the abortion procedure demanded by a second trimester pregnancy. It is likely that most women are unaware of the different abortion procedures for first and second trimester abortion until they arrive at the clinic. The second trimester procedure (usually saline instillation) has an approximately four-fold increased risk of major complications[31] and a seven- to nine-fold increased risk of death[46] and, on being confronted with a more serious procedure than expected, women who have not made a firm decision to abort may decide to deliver. Furthermore, the second trimester abortion procedure is more expensive[47,78] and requires an overnight hospital stay--considerations which might also be sufficient to change the decision in favor of not aborting.

Very few of the studies reported in Table 3 indicate the proportion of first trimester abortion patients who change their decision versus those in the second trimester. However, samples with the larger proportion of second trimester women are also those with a larger rate of decisional change. At Grady Memorial Hospital[18] 26.7 percent and at Yale-New Haven Hospital[21] 24.2 percent were in the second trimester. The data from the British Pregnancy Advisory Service[19] and King's College Hospital[16] indicate that 20 percent and 14.5 percent respectively were referred for abortion in the second trimester. Both of the women in the Yale-New Haven study sample[11] who decided to deliver were in the second trimester. The three large free-standing abortion clinics represented in Table 3 only include first trimester procedures.[15,20,27]

The third consideration results from the fact that women who present for abortion between the twelfth and fifteenth week of gestation are often asked to return beyond the fifteenth week because that is the optimal period for instillation procedures. There is neither empirical nor clinical documentation of the number of women who may, during this potentially vulnerable period, decide not to abort. Women who are refused abortion (many during the first telephone contact) because of advanced gestation at first trimester abortion clinics must often reregister for a second trimester abortion at another hospital. Records of the outcome of denied applications have not been maintained.

Of acute interest is the final pregnancy decision of women who visit a clinic or hospital abortion facility and who are only told following a medical examination that they are too advanced in pregnancy for a first trimester

procedure. These women are at risk of being asked to participate in research projects. While many first trimester abortion clinics maintain very close relationships with hospitals performing second trimester procedures, no data have been found which indicate what proportion of women denied first abortion do go on to abort in the second trimester. Some estimate of the prevalence of denied abortion because of advanced gestation is indicated by the data in Table 5.

Table 5. The Number and Proportion of Women Refused First Trimester Abortions Because of Advanced Gestational Age

| Source | Year | Number Refused | $\frac{\text{Total Refused}}{\text{Total Keeping Appointment}} \times 100$ |
|---|---|---|---|
| Erie Medical Center Buffalo, New York[28] | 1973 | 658 | 9.7 |
| | 1974 | 658 | 6.8 |
| Eastern Women's Center New York[20] | Feb 1 to Aug 1, 1972 | 454 | 18.6 |
| | 1973 | 553 | 15.1 |
| | Jan 1 to Oct 31, 1974 | 294 | 15.0 |

Social and Situational Factors

In this section a number of issues which emerge from the literature and which have not been previously considered are briefly discussed in terms of their implication for a change in the decision to abort.

A number of factors have been considered to contribute to conflict during pregnancy. Much of this research has dealt with "wanted" pregnancy and the factors include: hyperemesis,[48] common antenatal problems,[49] attitudes toward feminine role,[50,51] sexual attitudes toward mother, father, and husband,[52] "sick role" expectations in pregnancy,[53] and rejection of the pregnancy by the father and experience of having a previously defective or deformed child.[54] All of the above factors might be considered, if they occur during a pregnancy which is not unequivocally wanted, to contribute to an unchanged decision to abort. Evidence from studies of the reasons for seeking induced abortion also suggest situations in which the abortion decision is likely to remain firm. Among the more important are: social sanctions faced by single women who do not renounce motherhood,[51,55] inability to manage another child,[55-57] and anxiety over deformity of the child.[55]

The same body of literature suggests a number of situations which, in the absence of hard data can only lead us to speculate, may be associated with a changed decision to deliver and not abort either before or during the clinic visit. These include: deviant scores on psychological tests,[58] emotional immaturity,[59] attempts to involve the partner in marriage,[56,57,60] inadequate emotional supports,[55] mental abnormality,[56,61] previous psychiatric difficulty,[56,57] and anxiety of the abortion procedure itself[62] or surgery in general.[63]

## Abortion Counseling

Much of the early literature was written at a time when abortion "counseling" consisted of an interview during which the abortion applicant had to convince a psychiatrist that abortion was necessary for her mental, if not physical health. Reviewers of this literature[64-66] have pointed out the biases inherent in findings from that research. In this section we are concerned with the influence of abortion counseling as it currently is practiced in many abortion clinics in the United States.[23-26,67-69]

The essential feature of abortion counseling, as expressed by almost all writers and most pertinent for this inquiry, is that aspect of counseling in which the counselor determines the nature of the abortion client's decision-making process. The review of the pros and cons of the decision to abort, including an examination of any conflicts in the decision and how they were resolved, enables the counselor to assess the "quality" of the decision process. Particularly important, is whether the abortion client denied, negated or used other ego defense mechanisms leading her to ignore areas of conflict during the decision making which might result in an increased risk of post-decisional regret after the abortion. This type of counseling rarely leads to a unilateral decision on the part of the counselor to deny the client an abortion but, most frequently, the abortion client herself realizes during counseling that she is not yet prepared to commit herself to having an abortion. It was reported that the 31 women who decided not to abort while at Preterm in Boston (Table 3),[27] did so during extensive individual counseling with trained abortion counselors.

Abortion counseling, then, is a crucial process for screening out applicants for abortion who might be at higher risk for changing their decision to abort prior to the procedure itself.

## Participation in Research Projects

In order to gain some insight into the possible effect of participation in research prior to abortion on the decision to abort it is again useful to consider the "balance-sheet" model of decision making. At least two issues must be considered: (a) the extent to which a decision to abort is balanced in favor of abortion, and (b) the nature of the research activity itself.

Participation in research which has some risk to the fetus might be considered to reduce the choice which still remains for abortion or delivery. Evidence from psychological laboratories[73,75,76] suggests that the reduction of choice in a decision also reduces cognitive dissonance. These data imply, then, that participation in a higher risk fetal research project would incline the more ambivalent abortion patient toward a firmer decision to abort. Additionally, it might be argued, that only a relatively severe threat, such as fetal research involving drugs, would enhance an existing decision to abort. Less innocuous procedures, say the completion of questionnaires, might simply increase cognitive dissonance in the ambivalent patient[77] and act as an additional factor against the abortion decision.

## SUMMARY

1. Little available research has directly confronted the question of change in the decision to abort which is reviewed in this paper. All the evidence is drawn, second hand, from a variety of sources in which other issues were the object of interest. There is a clear demand for hard empirical data in this area.

2. Among women who abort as many as one third report having changed their decision to abort at least once prior to reaching the clinic. Difficult decisions and conflict during decision making are also quite prevalent.

3. Approximately 10 percent of appointments for abortion are not kept, a figure which probably overestimates the proportion of women who have decided to deliver.

4. In large volume free-standing clinics aborting women in the first trimester in the present socio-legal climate, less than 1 percent of abortion applicants are likely to decide not to abort after visiting the clinic. In facilities offering second trimester procedures it is unlikely that more than 2 percent of applicants will change their mind.

5. Women more at risk of changing their decision to abort are more likely to be characterized by psychological than by demographic factors. The style of coping with conflicts during decision making, rather than simply the presence of conflict, is more likely to predict late changes of decision.

6. Women aborting in the second, versus first, trimester may be at relatively greater risk of changing their decision to abort.

7. Between 5 percent and 20 percent of women examined at clinics performing first trimester procedures are refused abortion because of advanced gestational size. At other hospitals an unrecorded number of women have their abortion postponed because they are between 13 and 15 weeks pregnant. For either group of women there is no indication what proportion eventually go on to abort. In the absence of information to the contrary these women must be considered at elevated risk of changing their decision to abort.

8. Abortion counseling is a crucial procedure for selecting out of the clinic population women who are at increased risk of changing their decision to abort. An invitation to participate in a research project should only follow, and should be independent of, routine abortion counseling.

9. Women who have reached a firm decision to abort are unlikely to change their decision because of participation in a research project. Women more ambivalent about aborting are only likely to change their decision if the research maneuvers emphasize the viability of, and present no risk to, the fetus.

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# Part II

# SUPPLEMENTAL RESOURCE INFORMATION

# 17

# THE NUREMBERG CODE OF ETHICS IN MEDICAL RESEARCH

# The Nuremberg Code of Ethics in Medical Research

(1) The voluntary consent of the 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 other ulterior form of constraint or coercion and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

(2) The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

(3) The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

(4) The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

(5) No experiment should be conducted where there is an *a priori* reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subject.

(6) The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

(7) Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

(8) The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

(9) During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

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

# 18

# DECLARATION OF HELSINKI

**(Recommendations Guiding Doctors in Clinical Research
Adopted by the World Medical Association in 1964)**

# Declaration of Helsinki

## INTRODUCTION

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

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

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

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

## I. BASIC PRINCIPLES

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

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

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

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

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

## II. CLINICAL RESEARCH COMBINED WITH PROFESSIONAL CARE

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

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

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

## III. NON-THERAPEUTIC CLINICAL RESEARCH

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

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

3a. Clinical research on a human being cannot be undertaken without his free consent after he has been informed; if he is legally incompetent, the consent of the legal guardian should be procured.

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

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

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

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

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

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

**American Federation for Clinical Research**

**American Society for Clinical Investigation**

**Central Society for Clinical Research**

**American College of Physicians**

**American College of Surgeons**

**Society for Pediatric Research**

**American Academy of Pediatrics**

**American Medical Association**

19

# THE USE OF FETUSES AND FETAL MATERIAL FOR RESEARCH

Report of the Advisory Group,
Chaired by Sir John Peel, London, 1972

MEMBERS OF THE ADVISORY GROUP INCLUDE:

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Dr. Pauline M. Jackson, MB BS DCH
His Honour Judge E. B. McLellan

# The Use of Fetuses and Fetal Material for Research

## INTRODUCTION

1. We were appointed by the Secretary of State for Social Services and the Secretaries of State for Scotland and Wales on 19 May 1970, with the following terms of reference:

> "To consider the ethical, medical, social and legal implications of using fetuses and fetal material for research."

### Number of Meetings

2. We held our first meeting on 30 July 1970 and we have met six times altogether.

### Evidence

3. Factual information on the use of human fetuses and fetal material for research was obtained from the Medical Research Council and the Public Health Laboratory Service. This is summarized in later sections of the report. In addition to this evidence a number of organizations were invited to comment on the matters within the terms of reference and we received some spontaneous representations.

4. While there were differences of opinion in the evidence we were impressed by the substantial measure of agreement in the views expressed. Our work has been greatly assisted by the evidence received, which we have studied and taken into account when reaching our conclusions, and we wish to record our thanks to all those who contributed. Their names are listed in Appendix 1.

5. The Chairman and members of the Advisory Group would like to put on record their appreciation of the help they have received from the Joint Secretaries, Dr. Laycock and Mrs. S. E. Reeve. Throughout they have facilitated communication with the large number of people involved in the whole investigation, and made an invaluable contribution to the repeated draftings that became necessary. Without their help the enquiry would have been a much more difficult task.

## MEDICAL BACKGROUND

### Definitions

6. The ethical problems which have arisen in recent years in relation to organ transplantation have emphasized the difficulties of defining terms as "life" and "death." These difficulties have been encountered in the context of decisions relating to adults and children but in the case of the fetus in mid-pregnancy an additional difficulty arises in defining viability. In 1950 an Expert Committee of the World Health Organization attempted to meet the problem of definition but since that time advances in medical knowledge have made their definitions unsatisfactory. We have decided to introduce our own definitions of some of the more important terms used in this report, as we consider these to reflect more accurately the current state of medical knowledge. Our definitions are set out below:

> The Fetus: the human embryo from conception to delivery (and therefore including what is normally termed the embryonic state).
>
> A Viable Fetus: one which has reached the stage of maintaining the coordinated operation of its component parts so that it is capable of functioning as a self-sustaining whole independently of any connection with the mother.
>
> A Pre-Viable Fetus: one which, although it may show some but not all signs of life, has not yet reached the stage at which it is able, and is incapable of being made able, to function as a self-sustaining whole independently of any connection with the mother.
>
> Fetal Death: the state in which the fetus shows none of the signs of life and is incapable of being made to function as a self-sustaining whole.
>
> Fetal Tissue: a part or organ of the fetus, e.g., the lungs or liver.
>
> Fetal Material: any or all of the contents of the uterus resulting from pregnancy excluding the fetus, i.e., placenta, fluids and membranes.

### Research Involving the Use of the Dead Fetus and Fetal Material

7. Evidence was sought from a number of organizations known to use dead fetuses, fetal tissues and fetal material in the course of their work. Our enquiries showed that in most instances fetal tissues are used since tissues and cells may continue to live for a period after the fetus itself has died, even if they are separated from it. The use of the fetus as a whole is necessary only in a small number of investigations at present.

8. Fetal tissues may be used in various valuable ways, particularly in preventive medicine where there is generally no practical substitute for the fetal tissues used. This is especially the case in the field of virology. The enquiries we made showed that it is often difficult to distinguish between research uses and the diagnostic or therapeutic uses of the work which is being done. Some examples are described below and fuller details are given in Appendix 2.

9. Virology: Fetal tissues are used in the routine diagnosis of and research on viruses pathogenic to man, notably those affecting the respiratory tract; the largest present user for this purpose is the Public Health Laboratory Service. Identification of different strains of the rhino viruses (the most common causes of colds) has been made possible on a large scale only by using cultures obtained from fetal tissues since most of these organisms do not grow on cultures of non-human cells.

10. The properties of both established and new vaccines against viral infections are investigated in fetal tissue cultures, as these tissues provide excellent purity tests for the vaccines. For example, work is in progress on an influenza vaccine, and the vaccines for poliomyelitis and rubella (German measles) are manufactured from fetal tissue. Thus the use of fetal tissues has gone beyond basic research into the field of established practice in preventive medicine. For the future, it seems probable that the use of fetal tissues will offer the only chance for growing the viruses thought to cause hepatitis and infantile gastroenteritis.

11. Cancer Research: Fetal tissues provide the best source of human cells that can be kept growing in tissue culture for the study of induction of disordered growth (analogous to cancerous growth) and of the effect of various agents on that disordered growth. Research in this field opens up future possibilities of diagnosis and treatment of cancer in children and adults.

12. Arterial Degenerative Disease: Fetal tissue cultures provide material for research on the development of connective tissues in the arterial wall and so may contribute to the knowledge of the origins of arterial degenerative disease.

13. Immunology: Fetal thymus cells and bone marrow grafts are used in research into the treatment of certain diseases of infants where the normal mechanism for resistance against infection is deficient (immuno-deficient conditions). Fetal cells are used to investigate renal and liver transplant rejection phenomena in adults and for tissue typing in transplant surgery.

14. Congenital Deformities: Research on the whole dead fetus is essential for the advancement of knowledge of fetal development and to investigate factors that might interfere with this so as to produce congenital deformities. It has already been found that the infection of the fetus with rubella virus can cause congenital heart disease, blindness and deafness, and that certain drugs can cause deformities of the limbs or internal organs; but many other structural deformities remain to be investigated.

## Research on the Fetus in Utero

15. Observations have been made on the fetus in utero to estimate its growth especially that of the head, to study its responses to sensory stimuli and to investigate the changes in heart rate. Special attention has been given to the variations in blood composition during labour and to the circulatory and respiratory changes which occur during and after birth.

## Research on the Whole Pre-Viable Fetus

16. Research involving the whole pre-viable fetus has been carried out after delivery in certain countries to increase knowledge of perinatal physiology and pathology especially in regard to steroid metabolism. Stringent precautions have been taken to ensure that the fetuses used for such investigations are not viable.

## Supply of Fetuses, Fetal Tissue and Fetal Material

17. Since 1958 the Medical Research Council has provided a grant to support the collection, preservation and distribution of fetuses, fetal tissues and fetal material by the Royal Marsden Hospital, London. About 40 different establishments and individuals are supplied by this source. Inevitably costs for storage and transport are incurred and where appropriate these are met by the recipient. Outside the London area those requiring fetal tissues or material make similar arrangements with local hospitals.

# THE PRESENT LEGAL BACKGROUND

18. The law governing the issues under discussion falls naturally into four parts: the criminal, the civil, the administrative (the statutes governing registration of births and deaths etc.) and the disciplinary. In relation to both the criminal and civil law it is pertinent to note that the research under consideration is carried out in three separate legal jurisdictions (England and Wales, Scotland and Northern Ireland) in which the machinery of law enforcement is wholly, and the substantive law in part, different. An attempt to summarize the law in more than broad outline could therefore lead to confusion and no attempt is made to do so.

19. It is an important aspect of the law in all three jurisdictions that established practices over the whole range of medical and nursing treatment in the obstetric and paediatric field from the moment of conception until the fetus is firmly established as a live or dead child (in the normal colloquial sense) are subject to the strongest presumptions of legality.

## Criminal Law

20. The purpose behind the criminal law has always been the protection of the fetus at all stages. However, the law was developed and expounded before the great changes brought about by scientific advances and by the passing of the Abortion Act, with the result that the available authoritative statements of the law do not provide clear guidance in the present situation. Development of the law has also been limited by the rarity of cases in which the activities of the medical profession have given rise to prosecution.

21. The problem is essentially new and if, as we think, a measure of control is called for by both medical and lay opinion, the limited operation of the criminal law makes it an inadequate guide or instrument for this purpose. Having thus stated the limitations of criminal law, we have summarized what we understand to be its general effect. In all three jurisdictions the following acts may be taken to be criminal:

(a) deliberate or reckless injury to the fetus at any time between conception and delivery save under the provisions of the Abortion Act. (In this connection it is worth observing that the protection afforded to the fetus is continuous and is not abrogated by the fact that it may be the intention at the time of the infliction of the injury that the fetus should be prevented by a subsequent abortion from attaining life.)

(b) deliberate or reckless injury to the fetus which has become a child born alive or capable of being born alive. (In England and Wales and Northern Ireland there is a statutory presumption that a fetus of 28 weeks development is capable of being born alive.)

## Civil Law

22. Civil law requires of a medical practitioner who undertakes the treatment of a patient the exercise of reasonable skill and care and treats failure in such care as negligence. Any negligence in diagnosis or treatment (whether experimental or not) which causes injury to a fetus will found a claim for damages notwithstanding that the conduct of the practitioner has been neither criminal nor unethical. Such a claim could also arise from harm caused to a fetus following negligent certification that it was not viable.

## Administrative Law

23. The administrative law may be briefly summarised. In all three jurisdictions there are broadly similar statutory requirements for the registration of births, deaths and still-births, and for notification of births to the public health authority. These statutes have several purposes, statistical, administrative and protective of life. For present purposes only the last is relevant.

The requirement to register a birth applies only to live-births (irrespective of the duration of pregnancy) and to still-births, i.e., births not being live-births which take place after the 28th week of pregnancy. The delivery of a dead fetus before that stage is not registrable, nor is it notifiable to the public health authority.

## Disciplinary Law

24. Much more material to the present problem is the disciplinary jurisdiction of the Disciplinary Committee of the General Medical Council and, on appeal, the Judicial Committee of the Privy Council. The Disciplinary Committee are empowered by statute to erase a doctor's name from the register of medical practitioners or to suspend his registration if they are satisfied that his behavior constitutes "serious professional misconduct." They may also admonish a doctor on the same grounds. The limits of serious professional misconduct may extend far beyond those of criminal law. They reflect the high standard of ethical behavior demanded of and accepted by the medical profession. The Disciplinary Committee see their primary duty as protection of the public. Their proceedings are public and their decisions are publicly reported.

# THE IMPLICATIONS OF RESEARCH ON FETUSES AND FETAL MATERIAL

25. During our discussions we have been constantly aware of the public concern and of the ethical problems surrounding the use of fetuses, fetal tissues and fetal material for research. In reaching our conclusions, we have tried to maintain a balance between them and the contribution to medical science made by this form of research. In general, we feel that the contribution to the health and welfare of the entire population is of such importance that the development of research of this kind should continue subject to adequate and clearly defined safeguards. In the following paragraphs we consider the implications of undertaking research using the fetus, fetal tissue or fetal material and indicate the safeguards which we consider essential in the interests of both the public and the medical profession.

## Research on the Fetus in Utero

26. We have given careful consideration to the question of carrying out research involving the fetus during pregnancy. Investigations and tests may be carried out with the intention of benefiting the mother, her expected child or both, and in each instance ethical or legal objections do not arise. We understand that suggestions have been made if it is the intention to terminate the pregnancy with the idea of preventing a live-birth, then it would be permissible to administer substances to the mother in order to see if these are harmful to the fetus. We cannot accept this. In our view it is unethical for a

medical practitioner to administer drugs or carry out any procedures on the mother with the deliberate intent of ascertaining the harm that these might do to the fetus, notwithstanding that arrangements may have been made to terminate the pregnancy and even if the mother is willing to give her consent to such an experiment.

27. Apart from these ethical considerations such experiments are undertaken at the risk of the investigator since, if the fetus is alive on termination of pregnancy but is handicapped or subsequently dies as a result of experiments conducted during pregnancy, the persons concerned would be liable to prosecution. Also, if the fetus is born alive but is handicapped as a result of such experiments it would be open to the parent to seek compensation through the courts. The existence of arrangements to terminate the pregnancy made before the experiments are conducted would not necessarily constitute a valid defence.

Research on the Viable Fetus

28. We consider it is important that there should be no ambiguity about the circumstances in which research can be carried out on a viable fetus. In our view when the fetus is viable after delivery the ethical obligation is to sustain its life so far as possible and it is both unethical and illegal to carry out any experiments on it which are inconsistent with treatment necessary to promote its life, although in many instances the techniques used to aid a distressed fetus are so new that they are in some degree experimental.

29. In England and Wales evidence of pregnancy for a period of 28 weeks or more is accepted as prima facie proof that the mother is at that time pregnant of a child capable of being born alive (Infant Life [Preservation] Act 1929). However in our view advances in medical knowledge have made it no longer acceptable to take the 28th week of pregnancy as indicating the time at which a fetus becomes capable of survival as fetuses delivered before that date, may, by modern techniques, be enabled to live.

30. We noted that in April 1970 the International Federation of Obstetrics and Gynaecology said that advances in neonatology had made parameters for definition of the period of viability based on 28 weeks gestation age unrealistic. It recommended that the term "abortion" which implied that life could not be maintained in the fetus after expulsion from the mother should be restricted to terminations under 20 weeks (140 days). Similar views were expressed by a number of the organizations who submitted written evidence to us including the Royal College of Obstetricians and Gynaecologists and the Royal College of Midwives, although recommendations on the period of gestation which should be taken as prima facie evidence of viability varied from 18 to 24 weeks.

31. For ethical, medical and social reasons we recommend that for human fetuses evidence of a period of gestation of 20 weeks (140 days: this corresponds to a weight of approximately 400-500 grammes) should be regarded as prima facie proof of viability at the present time. This date should be reviewed regularly to

take account of the rapid changes taking place in medical knowledge. Accordingly consideration should be given to amendment of the Acts providing for registration and notification of births and deaths, the Infant Life (Preservation) Act 1929 and analogous legislation in Scotland and Northern Ireland.

## Research on the Pre-Viable Fetus

32. We have given long and careful consideration to the position of a fetus which, although it shows signs of life in some of its organs, is pre-viable in that it is incapable of attaining a state in which it could exist as a self-sustaining whole independently of the mother. In our view, if it has been shown that a missing vital function in a fetus cannot be established, for example that the lungs are solid and therefore cannot be inflated, then the fetus has not developed to the stage of being recoverable.

33. We have had to weigh the benefits of research involving pre-viable fetuses against the objections which may be generated and the reasoned ethical and social arguments which are involved. In considering whether it is ethically justifiable to undertake such research we noted that society through Parliament, in permitting abortion in certain circumstances has accepted that where an abortion under the Act is carried out the pre-viable fetus is prevented from attaining life. Given this situation we have considered whether through research on such fetuses new knowledge may be gained which would ultimately benefit viable infants.

34. The medical evidence we received showed that the whole pre-viable fetus has offered an important opportunity that cannot be obtained in any other way for making observations of great value on the transfer of substances across the human placenta, the reaction of the immature fetus to drugs, and on the endocrinological development of the placenta. There is a particular need to determine the ability or otherwise of the fetus to deal with substances including drugs given therapeutically to benefit the mother, which may cross the placenta. Observations on the pre-viable fetus are necessarily limited to a period of two or three hours. They have, however, already contributed significantly to our understanding of vital physiological and biochemical processes before birth on which the development of a fetus into a normal child essentially depends. As yet our knowledge is not sufficient to enable us either to control or compensate for any deviation from the normal in such processes. Research on the previable fetus promises, however, to be the most hopeful approach to understanding certain failures of the human brain to develop properly and the influence such factors as variants in sexual differentiation in utero may have on inherent behavioural patterns after birth.

35. We accept that in the case of single births any fetus of less than 20 weeks gestational age (400-500 grammes) is pre-viable and as such has not yet reached the stage at which it can exist as a living entity. We noted the evidence that in the pre-viable fetus of 300 grammes or less as distinct from the fetus approaching full term those parts of the brain on which consciousness depends

are, as yet, very poorly developed structurally and show no signs of electrical activity. After exhaustive consideration we have reached a unanimous view that it would be wrong to exclude the use of the pre-viable fetus for research, provided the following conditions are observed:

(1) Only fetuses weighing less than 300 grammes should be used.

(2) The responsibility for deciding that the fetus is in a category which may be used for this type of research must rest with the medical attendants at its birth and never with the intending research worker.

(3) Such research should only be carried out in departments directly related to a hospital and with the direct sanction of the ethical committee to which reference is made later in this report (paragraph 47).

(4) Before permitting such research the ethical committee should satisfy itself: (a) on the validity of the research; (b) that the required information cannot be obtained in any other way; and (c) that the investigators have the necessary facilities and skill.

Research on the Dead Fetus

36. When considering the implications of research on the whole dead fetus the difference in the Acts governing the use of human tissue for research makes it necessary to distinguish between the fetus which dies after birth and the fetus which is dead because separation from the mother involves the termination of its life.

37. Where a fetus dies after birth the provisions of the Anatomy Acts 1832 and 1871 and the Human Tissue Act 1961 apply as they would to any other deceased person. Subject to the proper implementation of these provisions there are no legal restrictions on the use of the whole fetus or parts thereof for research. Where a fetus is born dead the Anatomy Act and the Human Tissue Act do not apply and consequently there are no statutory restrictions on the use of the whole fetus or parts thereof for research.

38. After a thorough examination of the evidence, we are satisfied that the benefits to be derived from the use of the whole dead fetus in the prevention and treatment of disease and deformity are such that it would be a retrogressive step to prevent it. In our view it should be allowed to continue, provided it is carried out within the context of the general recommendations which we made later in this report on the control to be exercised whenever fetuses, fetal tissues or fetal material are used for research.

## Research on Fetal Tissues and Fetal Material Other Than the Fetus

39. Having regard to the essential contribution that is made by this research to preventive medicine there is, in our view, no reason to object to the use of fetal tissues and fetal material for these purposes subject to our general recommendations for control over research referred to later in the report.

40. Since 1968 commercial use of the placenta and retroplacental blood, not otherwise used by the National Health Service, has been accepted practice provided that the products to be derived from them are intended for therapeutic use. We see no ethical or legal objections to this practice.

## Consent to Research

41. Where a fetus is viable the overriding responsibility of the doctor is to promote and preserve its life and the parent's consent can normally be inferred for procedures consistent with this aim. There are also areas of research which whilst not jeopardising the health and welfare of the fetus are not of direct benefit to that particular fetus. In such cases we consider that express consent should be obtained from the parent. As stated in paragraph 37, where the fetus is born alive and later dies the provisions of the Human Tissue Act and the Acts concerned with certification of causes of death and investigation by coroners (in Scotland, Procurators Fiscal and Sheriffs) apply and enquiry must be made as to whether there is no objection on the part of the parent before the body can be used for research.

42. Where the separation of the fetus from the mother leads to the termination of its life there is no statutory requirement to obtain the parent's consent for research, but equally there is no statutory power to ignore the parent's wishes. A number of organizations who discussed this question in their evidence expressed the view that to seek consent could be an unnecessary source of distress to parents. We share this view but believe the parent must be offered the opportunity to declare any special directions about the disposal of the fetus. In our view this opportunity could be provided by adding an appropriate clause to the form giving the patient's consent to the operation thus minimising any possible distress.

## Conscientious Objections

43. The evidence we received strongly suggested that some members of staff may have conscientious objections to the use of fetuses or fetal tissues for research. We recommend that no member of staff should be under any duty to participate in research on the fetus, fetal tissue or fetal material if he or she has a conscientious objection. We also received representations that experiments on the fetus or dissections for fetal tissues should not be carried out within the operating theatre or place of delivery. We have no reason to believe that this has ever occurred, but we agree that it should not happen.

Finance

44. The public disquiet voiced about the use of fetuses, fetal tissue and fetal material for research has been influenced in part by the suggestion that financial transactions are involved. In our view any charges made are acceptable only if they do no more than meet the necessary costs incurred in administering these services, such as those provided by the Royal Marsden Hospital. In no other circumstances should there be monetary exchange for fetuses, fetal tissue or fetal material.

Record of Fetuses, Fetal Tissue and Fetal Material

45. We recommend that wherever fetuses, fetal tissue or fetal material are used for research the relevant institutions should ensure that a record is kept of all such material supplied or received and of its source and destination. In our view this record would be a valuable safeguard and should be available to central advisory body to which we refer later in the report.

## FUTURE CONTROL OF RESEARCH

46. Because of the concern expressed generally over this form of research we have given particular attention to its future control. He note that a report published in 1967 by the Committee on the Supervision of the Ethics of Clinical Investigations in Institutions set up by the Royal College of Physicians of London recommended that:

> "The competent authority (e. g., Board of Governors, Medical Schools Council, Hospital Management Committee, or equivalent body in non-medical institutions) has a responsibility to ensure that all clinical investigations carried out within its hospital or institution are ethical and conducted with the optimum technical skill and precautions for safety. This responsibility would be discharged if, in medical institutions where clinical investigation: is carried out, it were ensured that all projects were approved by a group of doctors including these experienced in clinical investigation. This group should satisfy itself of the ethics of all proposed investigations. In non-medical institutions or wherever clinical investigation (i. e., any form of experiment on man) is conducted by investigators with qualifications other than medical the supervisory group should always include at least one medically qualified person with experience in clinical investigation. "

This was accepted by the Ministry of Health and Hospital Memorandum (68) 33 asked hospital authorities in England and Wales to arrange with the medical staff of their hospitals for it to be put into effect.

47. We recommend that all research using the fetus, fetal tissue or fetal material should be approved by such a committee whatever the institution in which the research is undertaken; research involving the previable fetus should only be carried out in departments directly related to hospitals. The committee should accept responsibility for ensuring that such investigations are ethical. In approving research projects using the fetus, fetal tissue or fetal material the committee should use as a guideline the principles which we set out in the suggested Code of Practice at the end of this report.

48. We considered whether this type of research justified any safeguards additional to those mentioned already, in particular whether a lay member should be appointed to the ethical committee. Our conclusion was that clinical decisions are the responsibility of the clinician, and the ethical questions are for the profession to consider. Given a change in the minimum limit of viability (see paragraph 31), and guidance to the profession in a code of practice, together with the overall safeguards of the law, particularly the disciplinary control referred to in paragraph 24, we consider that the interests of all concerned would be sufficiently protected.

49. Some of the evidence received suggested that there should be legislation to provide for the licensing of those who wished to undertake research using fetuses, fetal tissue or fetal material similar to the licenses issued to those undertaking research on animals. In our view a system of licensing would be unnecessarily cumbersome and a code of ethical practice would be an adequate safeguard as it is in the case of research involving all patients. A code would have the advantage of flexibility in that it could be modified in the light of future experience without recourse to amending legislation, and it would not entail the establishment of permanent machinery for the issue of licenses and an inspectorate.

50. We also considered whether any central body should be set up to advise in cases where the local committee is uncertain of the ethics of particular investigations. We concluded that it would not be necessary to have a permanent body to handle the limited number of enquiries which are likely to rise. Instead we recommend that arrangements should be made for a small informal advisory body with legal representation and including members drawn from the Medical Research Council, the Royal College of Obstetricians and Gynaecologists, the General Medical Council and the British Paediatric Association to be convened when the need for central advice arises. It might be considered appropriate for this advisory body to cover the United Kingdom.

## RECOMMENDED CODE OF PRACTICE

This code has no binding legal force but is the result of a careful consideration of all relevant factors in the light of the available evidence. It is hoped that it will prove acceptable to the bodies statutorily responsible for disciplinary matters in the medical and nursing professions.

1. Where a fetus is viable after separation from the mother it is unethical to carry out any experiments on it which are inconsistent with treatment necessary to promote its life.

2. The minimal limit of viability for human fetuses should be regarded as 20 weeks' gestational age. This corresponds to a weight of approximately 400-500 grammes.

3. The use of the whole dead fetus or tissues from dead fetuses for medical research is permissible subject to the following conditions:

(i) The provisions of the Human Tissue Act are observed where applicable;
(ii) Where the provisions of the Human Tissue Act do not apply there is no known objection on the part of the parent who has had an opportunity to declare any wishes about the disposal of the fetus;
(iii) Dissection of the dead fetus or experiments on the fetus or fetal material do not occur in the operating theatre or place of delivery;
(iv) There is no monetary exchange for fetuses or fetal material;
(v) Full records are kept by the relevant institution.

4. The use of the whole previable fetus is permissible provided that:

(i) The conditions in paragraph 3 above are observed;
(ii) Only fetuses weighing less than 300 grammes are used;
(iii) The responsibility for deciding that the fetus is in a category which may be used for this type of research rests with the medical attendants at its birth and never with the intending research worker;
(iv) Such research is only carried out in departments directly related to a hospital and with the direct sanction of its ethical committee;
(v) Before permitting such research the ethical committee satisfies itself: (a) on the validity of the research; (b) that the required information cannot be obtained in any other way; and (c) that the investigators have the necessary facilities and skill.

5. It is unethical to administer drugs or carry out any procedures during pregnancy with the deliberate intent of ascertaining the harm that they might do to the fetus.

APPENDIX 1

Organizations and Individuals Who Submitted Evidence to **the** Advisory Group

(i) The following organizations submitted evidence to the Group:

Blair Bell Research Society
Board for Social Responsibility of the National Assembly of the Church of England
British Council of Churches
British Medical Association
British Paediatric Association
Karolinska Institute-Department of Obstetrics and Gynaecology (Stockholm)
Medical Research Council (evidence was also submitted by the Reproduction and Growth Research Unit of the MRC)
Medical Women's Federation
National Association of Theatre Nurses
National Institute of Health, Bethesda, United States
Office of the Chief Rabbi
Patients Association
Public Health Laboratory Service
Roman Catholic Church
Royal College of Midwives
Royal College of Nursing and National Council of Nurses in the United Kingdom
Royal College of Obstetricians and Gynaecologists
Society for the Protection of Unborn Children
Swedish Committee on International Health Relations
Swedish Medical Research Council-Reproductive Endocrinology Unit
Union of Liberal and Progressive Synagogues
Universities of Aberdeen, Dundee and Edinburgh

(ii) The following individuals submitted evidence to the Group:

Mr. Michael Wilkinson, FRCS
Mr. R. Wilson, MSc

## APPENDIX 2

### Projects Utilizing Human Fetuses, Fetal Tissue and Fetal Material

The work reported has been loosely grouped into physiological and anatomical categories. Items mentioned here include some of those already referred to in the text.

#### General Fetal Metabolism

1. Fetal head measurements to confirm the accuracy of ultrasonic cephalometry.
2. Fetal size in relation to amniotic fluid production.
3. Fetal size in relation to maternal smoking habits in and before pregnancy.
4. Water exchange between maternal, fetal and amniotic fluid environments.
5. The changes in oxygen partial pressures and acid base balance in hypoxia at various stages of pregnancy.
6. Carbohydrate metabolism in hypoxic fetuses and the effects of maternal dextrose infusions.
7. Glycoprotein synthesis in fetal liver.
8. Study of glucoronide metabolism for future treatment of neonatal jaundice or steroid imbalance.

#### Endocrinology

1. Detection of hormones that are solely fetal in origin and could possibly be measured in maternal tissues to enable the degree of fetal well-being to be determined.
2. Adrenal steroid metabolism in the fetal gland and the excretion of such steroids into the amniotic fluid at various stages.
3. Investigation of prolactin using fetal pituitary glands.
4. Cholesterol metabolism in relation to plasma protein levels.
5. Insulin secretion in the fetal pancreas and the effects on carbohydrate metabolism.
6. Gonadotrophin assay in fetal pituitary glands and stimulation of fetal pituitary activity *in vitro*.
7. Fetal intracellular binding site of progesterone with reference to possible blocking of histocompatible antigens.
8. Parathyroid metabolism in early pregnancy.

#### Haematology

1. Blood volume studies at different maturities.
2. Changes in fetal blood composition and development of plasma proteins.
3. Bone marrow maturation in relation to peripheral fetal blood.
4. Folate metabolism in the fetus and its accumulation in various tissues—notably liver and pancreas.

5. Studies of rhesus incompatibility using fresh suspensions of fetal liver cells.
6. Structure and properties of fetal haemoglobin and its variants.

Cardiology

Fetal electrocardiography performed directly on hysterotomy specimens and correlation with records made whilst the fetus **was** *in utero.*

Alimentary Tract

1. Fetal swallowing mechanisms in mid-trimester and the effects of anencephaly.
2. The pharmacology and innervation of small gut of the fetus.
3. The activity of some liver enzymes and their alteration with maturity.
4. Vitamin A content and activity of liver (and brain).

Renal and Urinary Tracts

1. Urine excretion and the production of amniotic fluid.
2. Changes in constitution of fetal urine in relation to renal maturity.
3. Culture of renal tissues to elucidate the development of fetal renal malignancies.

Skin

1. The origin and shedding of skin cells into the liquor.
2. Permeability of fetal skin and its variations with maturity.
3. The growth of fetal oral squamous epithelium in tissue culture.
4. Steroid metabolism in various skin sites of the body.
5. Biochemical assay of glycogen in fetal skin as a means of glycogen storage.

Amniotic Fluid Physiology

1. The circulation of fluid in relation to fetal and placental weight.
2. Composition of fluid in relation to fetal blood.
3. The origin and development of cells in the amniotic fluid.
4. Electrical conductivity of fluid and its effects in fetal electrocardiographic studies.
5. Secretion of steroid hormones from the vessels of the umbilical cord into the liquor.
6. Alterations in trace metal metabolism in relation to proteins and electrolytes levels in amniotic fluid.

## Placental Metabolism

Much work is proceeding in the transfer of various drugs and macromolecules, while other research is investigating glucose, amino-acid and steroid transfers.

## Immunology

1. Fetal antibody production in hosts of other species with subcellular fractions from hemogenates of the fetal tissues.
2. Carcinoma embryonic antigens present in adult tumours and fetal tissue only. Developments in their use in diagnosis of cancer in the adult and possibly their use for cancer therapy.
3. Fetal thymus cells are used in the investigation of human antilymphocyte globulin and other immunosuppressive agents.
4. Research on auto-immune conditions and immunopathological states using fetal tissue.

## Chromosome Studies

1. Abnormalities in therapeutic abortions (providing background figures to those produced after spontaneous abortions).
2. Y chromosome detection by fluorescent techniques.
3. Effect of X irradiation on chromosomes in ovarian tissue culture and total numbers of ova.

## Anatomy

1. Fetuses are used at all stages of development for teaching of medical and nursing students.
2. Studies of neuro-anatomy using fetal brain tissue.

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# 20

# PROTECTION OF HUMAN SUBJECTS: POLICIES AND PROCEDURES

**Federal Register, November 16, 1973, DHEW**

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FRIDAY, NOVEMBER 16, 1973
WASHINGTON, D.C.

Volume 38 • Number 221

PART II

# DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

■

## NATIONAL INSTITUTES OF HEALTH

### Protection of Human Subjects

### Policies and Procedures

NO. 221—Pt. II----1

## DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

National Institutes of Health

### PROTECTION OF HUMAN SUBJECTS

Policies\ and Procedures

In the FEDERAL REGISTER of October 0, 1973 (38 FR 27882 et seq.), the Secretary of Health, Education, and Welfare issued a notice of proposed rulemaking concerning the protection of human subjects and mentioned that DHEW through *the* National Institutes of Health, had appointed a special study group to review and recommend policies and special procedures for the protection of children, prisoners, and the institutionalized mentally infirm in research, development, and demonstration activities. The report of this study group has been completed in *draft* form and reviewed by the Director, NIH.

There may well be elements in the recommendations which will provoke debate and controversy. We recognize that public consideration and comment are vital to the development of our final recommendations to the Secretary and are inviting such comment now even though the materials are still pending final review and completion. The product of our effort after considering public comment will be transmitted to the Assistant Secretary for Health, HEW to recommend to the Secretary, HEW that it appear again in the FEDERAL REGISTER as proposed rulemaking for further public comment. Such a procedure is consistent with long established DHEW policy for permitting extensive public opportunity to affect the promulgation of DHEW regulations.

It must be clearly understood by the reader that the material that follows is *not* proposed rulemaking in the technical sense, and is not presented as Departmental, Public Health Service, or NIH policy. Rather it is a draft working document on which early public comment and participation is invited.

Please address any comments on these draft policies and procedures to the Director, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20014. All comments should be received by January 4,1974.

Additional copies of this notice are available from the Chief, Institutional Relations Branch, Division of Research Grants, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20014.

Dated: November 6, 1973.

ROBERT S. STONE,
*Director,*
*National Institutes of Health.*

### RESEARCH, DEVELOPMENT, AND DEMONSTRATION ACTIVITIES: LIMITATIONS or INFORMED CONSENT

SPECIAL POLICY CONSIDERATIONS

*Summary*

NOVEMBER 5,1973.

The mission of the Department of Health, Education, and Welfare Includes the improvement of the health of the Nation's people through research, development, and demonstration activities which at times involve human subjects. Thus, policies and procedures are required for the protection of subjects on whose participation these activities depend.

Informed consent is the keystone of the protection of human subjects involved in research, development, and demonstration activities. Certain categories of persons have limited capacity to concent to their involvement in such activities. Therefore, as a supplement to DHEW policies, special protections are proposed for *children, prisoners,* and the *mentally infirm* who are to be involved in research, development, and demonstration activities.

Agency "Ethical Review Boards" are to be established to provide rigorous review of the ethical issues in research, development, and demonstration activities involving human subjects, in order to make judgments regarding societal acceptability in relation to scientific value. "Protection Committees" are to be established by the applicant to provide "supplementary judgment" concerning the reasonableness and validity of the consent given by, or on behalf of, subjects. The intent of this policy is that institutions which apply for DHEW funds or submit research in fulfillment of DHEW regulations, must be in compliance with these special protections, whether or not particular research, development, or demonstration activities are Federally act!* Ities.

1. *Children.* If the health of children is to be improved, research activities involving their participation is often essential. Limitation of their capacity to give informed consent, however, requires that certain protections be provided to assure that scientific importance is weighed against other social values in determining acceptable risk to children. Therefore, research, development, and demonstration activities which involve risk to children who participate must:

a. Include a mechanism for obtaining the consent of children who are 7 years of age or older;

b. Include the applicant's proposal for use of a Protection Committee which is appropriate to the nature of the activity;

c. Be reviewed and approved, in conformity with present DHEW policy, by an Organizational Review Committee; and

d. Be reviewed by the appropriate agency Primary Review Committee, the Ethical Review Board, and the appropriate secondary review group.

2. *Special categories.*—a. *The Abortus.* No research, development, or demonstration activity involving the non-viable abortus shall be conducted which:

1. Will prolong heart beat and respiration artificially solely for the purpose of research:

2. Will of itself terminate heart beat and respiration;

3. Has not been reviewed by the agency Ethical Review Board; and

4. Has not been consented to by the pregnant woman with participation of a Protection Committee.

(An abortus having the capacity to sustain heart beat and respiration is in fact a premature infant, and all regulations governing research on children apply.)

b. *The fetus in utero.* No research involving pregnant women shall be conducted unless:

1. Primary Review Groups assure that the activity is not likely to harm the fetus;

2. the agency Ethical Review Board has reviewed the activity;

3. a Protection Committee is operating in a manner approved by the agency; and

4. the consent of both prospective legal parents has been obtained, when reasonably possible.

c. *Products of in vitro fertilization.* No research involving implantation of human ova which have been fertilized in *vitro* shall be approved until the safety of the technique has been demonstrated as far as possible in sub-human primates, and the responsibilities of the donor and recipient "parents" and of research institutions and personnel have been established. Therefore, no such research may be conducted without review of the Ethical Review Board and of a Protection Committee.

3. *Prisoners.* Research, development, and demonstration activities involving human subjects often require the participation of normal volunteers. Prisoners may be especially suitable subjects for such studies, although there are problems concerning the voluntariness of the consent of normal volunteers who are confined in institutions. Certain protections are required to compensate for the diminished autonomy of prisoners in giving voluntary consent. Research, development, and demonstration activities involving prisoners must:

a. Include the applicant's proposal for use of a Protection Committee which is appropriate to the nature of the activity;

b. Be reviewed and approved by an Organizational Review Committee which may already exist in compliance with present DHEW policy or which must be appointed in a manner approved by the appropriate DHEW agency;

c. Be reviewed by the agency Primary Review Committee; and

d. Be conducted in an institution which is accredited by the Secretary of Health, Education, and Welfare.

4. *The mentally infirm.* Insofar as the institutionalized mentally infirm might lack either the competency or the autonomy <or both) to give informed consent, their participation in research requires additional protection:

a. Research, development and demonstration activities involving the mentally infirm will be limited to investigations concerning (1) diagnosis, etiology, prevention, or treatment of the disability from which they suffer, or (2) aspects of institutional life, *per se,* or (3) information which can be obtained only from such subjects.

All research, development and demonstration activities involving such persons must:

1. Include the applicant's assurance that the study can be accomplished *only*

with the participation of the mentally infirm;

2. Include the applicant's proposal for use of a Protection Committee which la appropriate to the activity; and

S. Be reviewed and approved by an Organisational Review Committee, in conformity with present DREW policy.

TABLE *or* CONTENTS



## INTRODUCTION

The mission of the Department of Health, Education, and Welfare includes the improvement of the health of the Nation's people through biomedical research. This mission requires the establishment of policy and procedures for the protection of subjects on whose participation that research depends. In DHEW policy, as well as in ethical codes pertaining to research in human subjects, the keystone of protection is informed consent.

An uncoerced person of adult yean and sound mind may consent to the application of standard medical procedures in the case of illness, and when fully and properly informed, may legally and ethically consent to accept the risks of participating in research activities. Parents and legal guardians have authority to consent on behalf of their child or ward to established therapeutic procedures when the child is suffering from an illness, even though the treatment might involve some risk.

There is no firm legal basis, however, for parental or guardian consent to participation in research on behalf of subjects who are Incompetent, by virtue of age or mental state, to understand the Information provided and to formulate the judgments on which valid consent must depend. In addition, current policies for clinical research afford such subjects inadequate protection. Nevertheless, to proscribe research on all such subjects, simply because existing protections are inadequate, would be to deny them potential benefits, and is, therefore, Inequitable. Knowledge of some diseases and therapies can be obtained only from those subjects (such as children) who suffer from the disease or who will be receiving the therapy. Their participation in research is necessary to progress in those fields of medicine. When such subjects participate in research, they need more protection than is provided by present policy.

There are other individuals who might be able to comprehend the nature of the research, but who are involuntarily confined in institutions. Insofar as incarceration might diminish their freedom of choice, and thus limit the degree to which informed consent can be freely given, they too need additional protection. Current policies do not recognize the limitations on voluntariness of consent which may emanate front incarceration.

This addition to existing policy is offered as a means of providing adequate protection to subjects who, for one reason or another, have a limited ability to give truly informed and fully autonomous consent to participate in research. The aim is to set standards which are both comprehensive and equitable, in order to provide protection and, to the extent consistent with such protection, maintain an environment in which clinical research may continue to thrive.

1. *Definitions.* For purposes of this policy:

A. *Subject at risk* means any individual who might be exposed to the possibility of harm (physical, psychological, sociological, or other) as a consequence of participation as a subject in any research, development or demonstration activity (hereinafter called "activity") which goes beyond the application of established and accepted methods necessary to meet his needs.

B. *Clinical* research means an investigation involving the biological, behavioral, or psychological study of a person, his body or his surroundings. This includes but is not limited to any medical or surgical procedure, any withdrawal or removal of body tissue or fluid, any administration of a chemical substance, any deviation from normal diet or daily regimen, and any manipulation or obseravtion of bodily processes, behavior or environment. Clinical research com' prises four categories of activity:

*1.* Studies which conform to established and accepted medical practice with respect to diagnosis or treatment of an illness.

2. Studies which represent a deviation from accepted practice, but which are specifically aimed at improved diagnosis, prevention, or treatment of a specific illness in a patient.

3. Studies which are related to a patient's disease but from which he or she will not necessarily receive any direct benefit.

4. Investigative, non-therapeutic research in which there is no intent or expectation of treating an illness from which the patient is suffering, or in which the subject is a "normal control" who is not suffering from an illness but who volunteers to participate for the potential benefit of others.

It is important to emphasize that "non-therapeutic" is not to be understood as meaning "harmful." Understanding of normal processes is essential; it is the prerequisite, in many instances, to recognition of those deviations from normal which define disease. Important knowledge can be gained through such studies of normal processes. Although such research might not in any way benefit the subjects from whom the data are obtained, neither does it necessarily harm them.

Patients participating in studies identified in paragraph B-I, above, are not considered to be at special risk by virtue of participating in research activities, and this policy statement offers no special protection to them. When patients or subjects are involved in procedures identified in paragraphs B2, B3, and B4, they are considered to be "at risk," and the special policy and procedures set forth in this document pertain. Excluded from this definition are studies in which the risk is negligible, such as research requiring only, for example, the recording of height and weight, collecting excreta, or analysing hair, deciduous teeth, or nail clippings. Some studies which appear to involve negligible physical risk might, however, have psychological, sociological or legal implications which are significant. In that event, the subjects are in fact "at risk," and appropriate procedures described in this document shall be applied.

C. *Children* are individuals who have not attained the legal age of consent to participate in research as determined under the applicable law of the jurisdiction in which the proposed research is to be conducted.

D. *Pregnancy* encompasses the period of time from implantation until delivery. All women during the child bearing years should be considered at risk of pregnancy; hence, prudence requires definitive exclusion of pregnancy when women in this period of life are subjects for experimentation which might affect the fetus.

E. *Fetus* means the product of conception from the time of implantation to the time of delivery from the uterus.

F. Abortus means a fetus when it is expelled whole, whether spontaneously or as a result of medical or surgical intervention undertaken with the intention of terminating a pregnancy, prior to viability. This definition, for the purpose of this policy, excludes the placenta, fetal material which is macerated at the time of explusion, a dead fetus, and isolated

fetal tissue or organs excised from a dead fetus.

G. *Viability of the fetus,* means the ability of the fetus, after either a spontaneous delivery or an abortion, to survive to the point of independently maintaining vital functions; such a "viable" fetus is a premature infant. Determination of viability entails a subjective and objective Judgment by the physician attending labor or examining the product of conception, and must be made by a physician other than the investigator wishing to use fetal tissue in research. In general, and all other circumstances notwithstanding, a beating heart is not sufficient evidence of viability. At least one additional necessary condition is the possibility that the lungs can be inflated. Without this precondition, no currently available mechanisms to initiate or maintain respiration can sustain life; and in this case, though the heart is beating, the fetus or abortus is in fact non-viable.

H. I*n vitro fertilization is* any fertilization of human ova which occurs outside the body of the female, either through admixture of donor sperm and ova or by any other means.

I. *Prisoner is* any individual involuntarily confined in a penal institution. The term in intended to encompass individuals sentenced to such an institution under a criminal or civil statute, or individuals detained by virtue of statutes which provide alternatives to criminal prosecution.

J. *Mentally infirm* includes the mentally ill, the mentally retarded, the emotionally disturbed, the psychotic, the senile, and others with impairments of a similar nature, residing as patients in an institution, regardless of whether or not the individual has been determined to be legally incompetent.-

K. *Informed content* has two elements: comprehension of adequate information and autonomy of consent. Consent is a continuing process. The person giving consent must be informed fully of the nature and purpose of the research and of the procedures to be used, including Identification of those procedures which are experimental, the possible attendant short or long term risks and discomforts, the anticipated benefits to himself and/or others, any alternative methods of treatment, expected duration of the study, and of his or her freedom to ask any questions and to withdraw at any time, should the person wish to do so. There must also be written evidence of the process used for obtaining informed consent, including grounds for belief that the subject has understood the information given and has sufficient maturity and mental capacity to make such choices and formulate the requisite judgment to consent. In addition, the person must have sufficient autonomy to choose, without duress, whether or not to participate. Both the comprehension of information and the autonomy of consent are necessary elements; to the extent that either of these is in doubt, the adequacy of informed consent may be in doubt.

L. *Supplementary judgment* is the Judgment made by others to assent, or to refuse to assent, to procedures for which the subject cannot give adequate consent on his or her own behalf. For the purposes of this document, supplementary Judgment will refer to Judgments made by local committees in addition to the subject's consent (when possible) and that of the parents or legal guardian (where applicable), as to whether or not a subject may participate in clinical research. This supplementary judgment is to be confirmed by the signature of the Chairman of the Protection Committee on the consent form. In accordance with the procedures approved by the agency for the Protection Committee, the Chairman's signature may be affixed on a standard consent form, or may need to be withheld until the Committee approves the participation of the individual subject.

II. General *policy considerations. In* general, clinical research, like medical practice, entails some risk to the subjects. When the potential subject is unable fully to comprehend the risks which might be involved, or to make the Judgment essential to consent regarding the assumption of those risks, current guidelines suggest obtaining the consent of the parents or legal representative.

Whereas it is clear by law that consent of a parent or legal representative is valid for established and generally accepted therapeutic procedures performed on a child or an incompetent adult, it is far from clear that it is adequate for research procedures. In practice, parental or guardian consent generally has been accepted as adequate for therapeutic research, although the issue has not been definitively resolved in the courts. When research might expose a subject to risk without defined therapeutic benefit or other positive effect on that subject's well-being, parental or guardian consent appears to be insufficient.

In the case of prisoners, confinement imposes limitations on freedom of choice which brings into question their ability to give voluntary consent. A prisoner's ability to give consent may be restricted by overt or potential coercion, or by the loss of personal autonomy generally considered to result from incarceration itself. Therefore, additional protection must be afforded this group even though an individual's competency to understand what is involved might not be in doubt.

The institutionalized mentally infirm are doubly limited: as with children, they might not be competent to make informed judgments, and, as with prisoners, they are confined under conditions which limit their civil freedom and autonomy. Therefore, their participation in research requires special protections.

The law is not clear on these issues. Even if the law were clear, however, ethical questions would remain; specifically, whether, and under what conditions research involving these subject groups may proceed. Resolution of these ethical questions requires Judgments concerning both the ethics of conducting a particular research project, and the adequacy of procedures for protecting the individual subjects who will be asked to participate. The intention of this policy is to broaden the scope of review, preclude or resolve conflicts of interest, and invoke social as well as scientific judgments to protect potential subjects who might have diminished capacity to consent.

The proposed mechanism for protecting subjects with limited ability to give informed consent culminates in a form of supplementary Judgment, which Is to be supportive and protective of the subject's best interests and wishes, to the extent that he or she is capable of formulating and expressing a judgment. In the case of children and the mentally infirm, it will supplement their judgment and that of their parents or guardians. In the case of competent individuals who have restricted autonomy, it will support and protect their wishes. Through this mechanism, these subjects will be protected as fully as possible by community review; however, the nature of some research procedures might be such that, in addition, court review ultimately will be required.

III. *Participation of children* to research—A. *Policy considerations.* Children have generally been considered inappropriate subjects for many research activities because of their inability to give informed consent. There are circumstances, however, which not only Justify, but even require their participation. Children do differ from adults in their physiologic responses, both to drugs and to disease; if the health of children is to be improved, it is necessary to know the nature and extent of these differences, and to have a full understanding of normal patterns of growth and development, metabolism, and biochemistry in the perinatal, infant, early childhood, pubertal and adolescent stages of development. Studies of normal physiology and behavior can also provide significant benefit to children suffering from disease; children are the only subjects from whom these data can be obtained. Furthermore, there are diseases which cannot be induced in laboratory animals and occur only rarely, if at all, in human adults. In such cases, children are the only subjects in whom the disease process and possible modes of therapy can be studied.

The Kefauver-Harris Act[1] requires that drugs be tested for safety, efficacy and dosage in children and pregnant women before being approved for use to treat illness in such patients. Food and Drug Administration (FDA) approval for the use of a new drug depends upon submission of proposed labeling for a new drug, which must include "adequate directions for use" and "adequate warnings" as to unapproved uses,3 Acceptance of a new drug

1 Federal Food, Drug, and Cosmetic Act, 1962 (FDC Act), 31 U.S.C. SCO. 301 et. seq.
2 FDC Act Sec. 802(f), 21 U.S.C. Sec. 362(f).

rests on the adequacy of the research it-ports submitted with the application to support the proposed labeling.8 Thus, in order (or a drug to be distributed in Interstate commerce for use in children or pregnant women, sufficient testing must have taken place in children or pregnant women to substantiate claims on the label regarding safety, efficacy, and dosage for those groups. If the safe and efficacious dosage for children and pregnant women has not been determined, the label must so state. Thus, participation of children in drug research might be the only means of meeting licensing requirements for new drugs for use in children, Just as studies in pregnant women might be the only means of meeting licensing requirements for new drugs for use in that class of patients.

When the risk of a proposed study is generally considered not significant, and the potential benefit is explicit, the ethical issues need not preclude the participation of children in biomedical research. However, the progression from innocuous to noxious, in terms of risk, is often subtle. Therefore, additional review procedures are necessary for research activities which expose children to risk, in order to provide sharp scrutiny, vigorous review, and stringent procedural safeguards for all subjects of such research.

Judgment* concerning the ethical propriety of research depend partly upon the scientific assessment of the potential risks and benefit*. Risk has several important elements: severity, probability, frequency, and the timing of possible advene effects. While it might not always be easy to distinguish these elements, they must be evaluated in the assessment of risk, and in the determination of the acceptable limits of specific risk for an anticipated benefit. The first Judgment to be made is whether it is possible to assess the risk. If studies in animals or adults do not provide sufficient information to assess these elements of risk, then the research should not be conducted on children. If the risks can be determined from studies in animal and adult human populations, application to children may be considered.

In addition to results from investigations on animals and adult subjects, there are unknowns which must be considered in the weighing of risk to children. These include: (1) differences in physiologic or psychologic response from adult patterns; (2) delayed expression of injury (for example, until puberty); (3) effects on developing organs (especially the central nervous system) ; (4) degree of interference with normal routine required by the study; and (8) possibility of misuse of data by institution or school personnel.

Once the severity and probability of risks in a particular study have been identified, a second Judgment must be made: given potential benefits of described dimensions, what are the acceptable limits of risk to which children ethically may be subjected? Value Judgments which must be weighed here transcend scientific issues and suggest that the decision requires interaction among individuals in society with diverse training and perspectives. Further, given the complexity of the issues and the opportunity for conflict among the interests of several parties (the child, the parents or guardian, the attending physician, and the research personnel), decisions regarding participation of individual subjects in research activities involving children should not rest solely with persons directly involved in the research.

In order to provide both impartial ethical review of projects and maximum protection of individual subjects, two procedures are proposed in addition to those currently required: review by an Ethical Review Board at the sponsoring DHEW agency, and participation by a Protection Committee at the institution in which the research is to be conducted. Both groups will provide community involvement in decisions and attempt to balance scientific value and societal acceptability of proposed research involving children.

B. E*thical Review Board: Ethical revita of projects.* Each DHEW agency shall appoint an Ethical Review Board to provide rigorous review of ethical issues in research involving human subjects by people whose interests are not solely those of the scientific community. Its functions will include:

1. Advising the agency on ethical issues including review of questions of policy, and development of guidelines and procedures;

*2. F*ostering inter-agency coherence through cognisance of the policies and procedures of other agencies;

3. Reviewing specific proposals or classes of proposals submitted to the Board by the agency. These will include proposals stipulated herein as requiring review by the Board, as well as proposals submitted on an *ad hoc* basis by agency staff. In addition, the Board may recommend that certain additional classes of research be reviewed.

The acceptability of a research project rests on questions of scientific merit as well as on questions of ethics. The agency Primary Review Committees are responsible for evaluating scientific merit and experimental design. The Ethical Review Board will be concerned with ethical issues and questions of societal acceptability in relation to scientific value. In reaching its determination of acceptability, the Board will rely upon the Primary Review Committees for Judgments on scientific merit and design, existence of prerequisite animal and adult human studies, estimated risks and benefits (taking into account the competence and experience of Investigators and the adequacy of their resources), and scientific importance. It will review proposals received from these Primary Review Committees.

An investigator proposing research activities which expose children to risk must document, as part of the application for support, that the Information to be gained can be obtained in no other way. The investigator must also stipulate either that the risk to the subjects will be insignificant, or that although some risk exists, the potential benefit is significant and far outweighs that risk. In no case will research activities be approved which entail substantial risk, except in the case of clearly therapeutic procedures in which the benefit to the patient significantly outweighs the possible harm. The Ethical Review Board shall review all proposals approved by Primary Review Committees involving children in research activities, except when the Primary Review Committees determine that the subjects are not at risk.

In addition to reviewing ethical issues, the Board will review procedures proposed in the research application to be employed by the institution's Protection Committee (see below), and may suggest modifications of these procedures. The Board's recommendation may vary from a general concurrence with the proposal, as submitted by the investigator, to a recommendation that each parental and subject consent must be obtained with the concurrence of the full Protection Committee. Any specific recommendations for procedures to be followed by the Protection Committee' will be included in the report, of the Ethical Review Board which will be forwarded to the National Advisory Councils or other secondary review groups of the agency. Appropriate information will be provided by the agency to assist the Protection Committee.

Inasmuch as the articulation of decisions might clarify both the objectives and the assumptions on which they are based, records of testimony and deliberations, as well as final decisions, should be maintained pursuant to existing regulations. Such records will serve additionally as the basis for public accountability and will facilitate the review of any decision, should such action be requested.

Members of the Board, which shall number 15, shall be drawn from the general public, and shall include, for example, research scientists (including social scientists), physicians, lawyers, clergy, or ethicists, and other representatives of the public, none of whom shall be employees of the agency establishing the Board. Appointments shall be made by the agency, which will establish the terms of office and other administrative procedures of the Board. No more than 1/3 of the members of the Board may be actively engaged i3n research, development, or demonstration activities involving human subjects.

C. *Protection Committee: Protection of individual subjects.* The determination that it is Justifiable to conduct a particular investigation in children, however, does not mean that all children are equally appropriate subjects for inclusion in that research. Numerous considerations might affect the proper choice of subjects. Therefore, the sponsoring institution shall designate a Protection Committee to oversee: (1) the process of

4 FDC Act Sec. 505 (b), (d), 21 USC. Sec. 355 (b), (d).

selection of subjects who may be included in the project; (2) the monitoring of their continued willingness to participate in the research; and (3) the design of procedures to permit intervention on behalf of the subject, should that become necessary. This Committee should consider the reasonableness and validity of the consent of the child participants (see below) as well as that of the parents, and should assure that the issue of risk and discomfort has been fully and fairly disclosed to parents and subjects. The procedure employed by the institution to achieve these goals will vary; the latitude for such procedures will be great since it will be related in part to the issue of risk. Investigators proposing research involving children shall include a description of their planned use of the Protection Committee In their research proposal; the proposed use of this Committee will be considered an integral part of the research proposal under review by the agency. Relevant Information arising in the review process, including information about safety, risk, efficacy, and protection procedures, will be provided to the Protection Committee by the agency supporting the research.

One member of the Committee shall be designated a representative for the project to whom any participant (or parent of a participant) may go to discuss questions or reservations concerning the child's continued participation in the project.

The signature on the consent form of the Chairman of the Protection Committee, when all the stipulations and conditions identified above have been met, will constitute, for DHEW, *supplementary judgment* on behalf of the child subject.

The institution's Protection Committee shall be comprised of at least 5 members so selected that the Committee will be competent to deal with the medical, legal, social, and ethical issues involved in the research and to represent the community from which the subject population is to be drawn. The Committee should include members of both sexes. No more than two of the members may be employees of the institution sponsoring or conducting the research. The Protection Committee may operate as a subcommittee of the Organizational Review Committee. The composition of the Committee must be approved by the awarding agency.

D. *Special provisions*—1. *Consent of both parents.* Even where State law may permit one parent alone to consent to medical care, both parents have an interest in the child, and therefore, consent of both parents should be obtained before any child may participate in research activities. Since the risks of research entail the possibility of additional burdens of care and support, the consent of both parents to the assumption of those risks should be obtained,[6] except when the identity or whereabouts of either cannot be ascertained or either has been judged mentally incompetent. If the consent of either parent is not obtained, written explanation or justification should be provided to the Protection Committee. Consent of school or institutional authorities is no substitute for parental concern and consent.

2. *The child's consent.* An important addition to the requirement for parental consent is the consent of the child subject. Clearly infants have neither the comprehension nor the independence of judgment essential to consent: older children might or might not have these capabilities. Although children might not have the capacity to consent on their own to participate in research activities, they must be given the opportunity (so far as they are able) to refuse to participate. The traditional requirement of parental consent for medical procedures is intended to be protective rather than coercive. Thus, while it was held to be unlawful to proceed merely with the consent of the child, but without consent of the parent or legal guardian,[6] the reverse should also hold. Therefore, in addition to consent of both parents, consent of the child subject must also be obtained when the child has attained the common law "age of discretion" of 7 years, unless the agency Ethical Review Board specifically exempts a project from this requirement.

3. *Exclusions.* Despite all the protections afforded by these procedures, certain children are categorically excluded from participation in research involving risk. These include children with no natural or adoptive parents available to participate in consent deliberations, and children detained by court order in a residential facility, whether or not natural or adoptive parents are available.

E. *The fetus.* Respect for the dignity of human life must not be compromised whatever the age, circumstance, or expectation of life of the individual. Therefore, all appropriate procedures providing protection for children as subjects in biomedical research must be applied with equal rigor and with additional safeguards to the fetus.

The recent decision of the Supreme Court on abortion * does not nullify the ethical obligation to protect the developing fetus from avoidable harm. This obligation, along with the right of every woman to change her decision regarding abortion, requires that no experimental procedures entailing risk to the fetus be undertaken in anticipation of abortion. Further, since the fetus might be at risk in research involving pregnant women, all research involving pregnant women must be reviewed by the Ethical Review Board, unless the Primary Review Committee determines that the research involves no risk to the fetus. Recruitment of pregnant subjects for research reviewed by the Board must involve the institution's Protection Committee in a manner approved by the Board, to provide supplementary judgment.

The consent of both parents must be obtained for any research involving the fetus, any statutes to the contrary on consent for abortion notwithstanding. Both the mother and the father have an interest in the fetus, and legal responsibility for it, if it is born. Therefore, the father's consent must be obtained for experimental procedures involving the fetus; consent of the father may be waived if his identity or whereabouts cannot be ascertained, or if he has been judged mentally incompetent.

IV. Special *categories*—A. *The abortus.* Prematurity is the major cause of infant death in this country; thus, research aimed at developing techniques to further viability is of utmost importance. Such research has already contributed significantly to improvement in the care of the pregnant woman and of her fetus. In addition, knowledge of fetal drug metabolism, enzyme activity, and the development of organs is essential to progress in preventing or offsetting certain congenital defects. After thorough research in animal models, it often eventually becomes essential to undertake studies in the non-viable human fetus.

The decision of the Supreme Court on abortion does not eliminate the ethical issues involved in research on the non-viable human fetus. No procedures should be undertaken on the non-viable fetus which clearly affront societal values. Nevertheless, certain research is essential to improve both the chance of survival and the health status of premature infants. Such research must meet ethical standards as well as show a clear relation either to the expectation of saving the life of premature infants through the development of rescue techniques, or to the furthering of our knowledge of human development and thereby our capacity to offset the disabilities associated with prematurity. It is imperative, however, that the investigator first demonstrate that appropriate studies on animals have in fact been exhausted and that therefore the research in question requires that the work be done on the non-viable human fetus. Specific reasons for this necessity must be identified. A thorough review of the ethical issues in proposed research involving the non-viable fetus is of utmost importance.

It must be recognized that consent for abortion does not necessarily entail disinterest on the part of the pregnant woman in what happens to the product of conception. Some women feel strongly about what may, or may not, be done to the aborted fetus; others do not. In order to give every woman the opportunity to declare her wishes, consent of the pregnant woman for application of any research procedures to the aborted fetus must be secured at the time of admission to the hospital for the abortion.

Because research on the abortus involves ethical as well as scientific issues, all projects involving the abortus must be reviewed by the Ethical Review Board, and recruitment of individual pregnant women for such research must involve

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6 59 *Am. JUR.* 2d, Sect. 129, p. 229.

6 *Banner v. Moran,* 76 U.S. App. D.C. 156, 126 P. 3d 121, 139 A.L.R. 1366 (1911).

• *Roe* V. *Wade.* 410 U.S. 113 (1973).

the institution's Protection Committee in • manner approved by the Board to provide supplementary judgment. In addition to the requirement for maternal consent, both the Ethical Review Board and the Protection Committee shall, in their deliberations, consider the ethical and social issues surrounding research on the non-viable fetus. The Protection Committee must be satisfied that maternal consent is freely given and based on full disclosure, each time approved research is conducted on an abortus.

In order to insure that research considerations do not influence decisions as to timing, method, or extent of a procedure to terminate a pregnancy, no investigator encaged in the research on the abortus may take part in these decisions. These are decisions to be made by the woman and her physician.

The attending physician, not the investigator, must determine the viability of the abortus at the termination of pregnancy. If there is a reasonable possibility that the life of the fetus might be saved, experimental and established methods may be used to achieve that goal. Artificial life-support techniques may be employed only if the physician of record determines that the fetus might be viable. If the physician determines that the fetus is not viable, it is not acceptable to maintain heart beat or respiration artificially in the abortus for the purpose of research. Experimental procedures which of themselves will terminate respiration and heart beat may not be undertaken.

This policy and these protections apply with equal force to the products of spontaneous abortions.

B. *The products of in vitro fertilization.* In the interest of improving human health and development, the biology of human fertilization and the early events surrounding this phenomenon, including implantation, should be studied. To the extent that in vitro studies of human fertilization might further this aim, they are permissible at the present time within the limits outlined below.

Current technology limits the in vitro development of the human fertilized ovum to a period of several days. This is a rapidly advancing field of biomedical research, however, and the time might come when it is possible to extend in vitro development beyond the stage of early cell division and possibly even to viability.

It is contrary to the interests of society to set permanent restrictions on research which are based on the successes and limitations of current technology. Still, it is necessary to impose restraints prospectively in order to provide reasonable protections, while at the same time permitting scientific advancements which might well benefit society. A mechanism is required to weigh, at any given time, the state of the art, a specific proposal, legal issues, community standards, and the availability of guidelines to govern the research situation. This mechanism is provided by the Ethical Review Board. Ultimately, the Board will determine the acceptability of a project involving in vitro fertilization, and by recognizing the state of the art, as well as societal concerns, propose appropriate research policy.

Care must be taken not to bring human ova fertilized *in vitro* to viability—whether in the laboratory or implanted in the uterus—until the safety of the technique has been demonstrated as far as possible in sub-human primates. To this end:

1. All proposals for research involving human in vitro fertilization must be reviewed by the Ethical Review Board.

2. No research involving the implantation of human ova fertilized in the laboratory into recipient women should be supported until the appropriate scientific review boards are satisfied that there has been sufficient work in animals (including sub-human primates) to demonstrate the safety of the technique. It is recommended that this determination of safety include studies of natural born offspring of the products of in vitro fertilization.

3. No implantation of human ova fertilized in the laboratory should be attempted until guidelines are developed governing the responsibilities of the donor and recipient "parents" and of research institutions and personnel.

V. *Prisoners—A. Policy considerations.* Clinical research often requires the participation of normal volunteers; for example, in the early stages of drug or vaccine evaluation. Sometimes, the need for standardization certain variables, or for monitoring responses over an extended period of time, requires that the subjects of research remain in a controlled environment for the duration of the project Prisoners may be especially suitable subjects for such studies, since, unlike most adults, they can donate their time to research at virtually no cost to themselves. However, the special status of prisoners requires that they have special protection when they participate in research.

While there is no legal or moral objection to the participation of normal volunteers in research, there are problems surrounding the participation of volunteers who are confined in an institution. Many aspects of institutional life may influence a decision to participate; the extent of that influence might amount to coercion, whether it is intended or not. Where there are no opportunities for productive activity, research projects might offer relief from boredom. Where there are no opportunities for earning money, research projects offer a source of income. Where living conditions are unsatisfactory, research projects might offer a respite in the form of good food, comfortable bedding, and medical attention. While this is not necessarily wrong, the inducement (compared to the deprivation) might cause prisoners to offer to participate in research which would expose them to risks of pain or incapacity which, under normal circumstances, they would refuse. In addition, there is always the possibility that the prisoner will expect participation in research to be viewed favorably, and to his advantage, by prison authorities (on whom his other few privileges depend) and by the parole board (on whom his eventual release depends). This is especially true when the research involves behavior modification and may be termed "therapeutic" with respect to the prisoner. In such instances, participation inevitably carries with it the hope that a successful result will increase the subject's chances for parole. Thus, the inducement involved in therapeutic research might be extremely difficult to resist; and for this reason, special protection is necessary for prisoners participating in research, whether or not the research is therapeutic.

The first principle of the Nuremburg Code requires that subjects of biomedical research must be "so situated as to be able to exercise free power of choice" concerning their participation. Whether prisoners can be considered to be "so situated" is ultimately a matter for the courts and the legislatures to resolve. In the meantime, it must be recognized that where liberty is limited, and where freedom of choice is restricted, there is a corresponding limitation of the capacity to give truly voluntary consent. Although the prisoner might be adequately informed, and competent to make judgments, the voluntariness of the person's consent remains open to question. This policy statement is designed to provide additional protections to prisoners participating in research.

The mission of the Department of Health, Education, and Welfare does not include rendering judgments on the administration of justice or the management of the correctional system. At the same time, the Department should not support activities which take unethical advantage of those who are under the jurisdiction of the courts and who, for that reason, lack some of the usual defenses to their personal integrity. Participation of prisoners in the research activities of the DHEW in the pursuit of medical knowledge might be beneficial to all concerned, but the relationship which involves a class of persons with diminished autonomy requires careful supervision.

Many prisoners are strongly motivated to participate in research, and view as unfair suggestions that they be denied this opportunity. Unless society, through its judicial and legislative bodies, decides that such participation should be halted, it is essential to develop mechanisms to protect those who may participate, or who are now participating, from the coercive aspects of incarceration which diminish their capacity for voluntary consent. Pursuant to the obligation to protect the rights of all subjects participating in research conducted under its auspices, the DHEW is proposing special guidelines for the protection of prisoners as subjects in any biomedical or behavioral research.

Two aspects of research involving prison populations require special review and procedural safeguards in addition to those provided by current DHEW policies.

First, when research is conducted under the auspices of • commercial manufacturer or an individual investigator, it is not always subject to review by an Organisational Review Committee, as is required (or similar research conducted at a hospital or a university. Thus, local review has not heretofore been required for ethical considerations or for specific problems related to the population or institution which is to be directly involved. Second, because of the loss of individual dignity, the limitations of personal freedom, and the possibility of real or potential coercion which may accompany confinement in an institution, special safeguards must be provided to mitigate the inequalities of bargaining power between the prisoners and those who are in positions of authority. While it is important that prisoners have the opportunity to participate in research, it is equally important that they not feel compelled to do so.

a. *Organisational Review Committee.* All research Involving prisoners must be conducted at an accredited correctional faculty (see Section F, below) and be reviewed Initially, and on a continuing basis, either by the Organisational Review Committee of that correctional facility or by the Organisational Review Committee of the institution sponsoring the research. The Organisational Review Committee shall have the duties and responsibilities identified in current DHEW regulations. In addition, for each project, it shall determine the adequacy of clinic or hospital facilities for the particular activity to be conducted, assess the appropriateness of the subject population for that activity, and weigh the questions of scientific importance, social need, and ethical acceptability. In addition to the foregoing, the Organisational Review Committee shall have the following duties, with respect to research involving prisoners as subjects:

1. To review and approve or modify the process proposed by the principal investigator for involvement of the Protection Committee (see below) in overseeing the selection of subjects who may be included in the research, and the process of obtaining their voluntary and informed consent.

a. To set rates of remuneration, if any, consistent with the expected duration and discomfort or risk of the proposed study, and consistent with other opportunities for employment, if any, at the facility in question.

b. To monitor the progress of the research as required by the sponsoring DHEW agency.

The recommendations of this Committee, along with a report describing any site visits, shall be included with the investigator's application to the agency. For facilities which have filed no general assurance, composition as well as recommendations of the Organisational Review Committee will be considered an integral part of the proposal in the agency review.

C. *Protection Committee.* The primary function of the Protection Committee is to provide supplementary judgment by overseeing the selection of subjects who may be included in a research project to assure that their consent Is as voluntary as possible under the conditions of confinement.

Consent is a continuing process. To assure the voluntariness of consent, subjects must be able to withdraw from the research project without prejudice. Each Protection Committee shall establish such a withdrawal mechanism.

The duties of the Protection Committee, therefore, shall include:

1. Reviewing the information given the potential subjects, with special attention to: adverse effects, the importance of reporting all deviations from normal function, the continuing option of withdrawing from participation at any time, and the identification of a member of the committee who will be available, at reasonable intervals upon request, for consultation regarding the research project. All of this information shall appear on the consent form, a copy of which will be given to each participant. When oral representations are made procedures described under DHEW regulations shall be followed.

a. Overseeing the process of selection of subjects who may be included In the research, to the extant stipulated in the recommendation of the Organizational Review Committee. Tills may vary from overall approval of the recruitment process, to reviewing a sample of subject selections, to interviewing as. a full Committee each individual subject to be included in the project.

3. Visiting the institution on a regular basis to invite questions, to monitor the progress of the research, and to assess the continued willingness of subject participation. The frequency of these visits will be determined by the nature of the research, and any recommendations of the Organisational Review Committee. Depending upon the circumstances and the number of subjects involved, these visits may be made either on a rotating basis by various members of the Committee, or by the full Committee.

4. Maintaining records of its activities including contacts initiated by subjects in the project between regular site visits. These records shall be made available to the agency upon request.

The Protection Committee shall be comprised of at least S members so selected that the Committee will be competent to deal with the medical, legal, social, and ethical issues involved. No more than 1/3 of the members shall be scientists engaged in biomedical research or physicians; at least 1 shall be a prisoner or a representative of an organisation conearned with the prisoners' interests; no more than 1 (except prisoners or their representatives) shall have any affiliation with the prison faculty or with the unit of government having Jurisdiction over the facility, with the exception of persons employed by the department of education of a relevant jurisdiction in a teaching capacity. The composition and the investigator's proposed use of the Committee must be reviewed and approved by the DHEW agency.

D. Payment to prisoners. The amount paid for participation in research will vary according to the risks and discomforts involved, and the other employment opportunities in the facility in which the research is to be conducted. The specific amount for each project will be determined by the Organisational Review Committee, which will forward its recommendation as part of the application to the sponsoring agency. The amount paid shall provide a compensation for services, but shall not be so great as to constitute undue inducement to participate.

Any reduction of sentence as a consequence of participation in research shall be comparable to other opportunities at the facility for earning such a reduction.

Any subject who is required by the investigator or prison physician to withdraw, for medical reasons, before completion of the investigation, shall continue to be paid for a period to be determined by the Protection Committee in consultation with the investigator. This does not apply to subjects who withdraw for other reasons. Any disputes regarding certification of withdrawal for medical reasons shall be heard and resolved by the Protection Committee.

Prisoners who serve on the Protection Committee shall be paid an amount consistent with that received by the research subjects.

E. *Accreditation.* The Secretary, DHEW, shall establish standards for accreditation of correctional facilities offering to act as sites for the performance of clinical research, or offering to act as a source of volunteer subjects for clinical research when the research is supported in whole or in part by Departmental funds or the research Is to be performed in compliance with requirements of Federal statutes.

The review for certification shall include, but not be limited to:

*1.* Standard of living in the prison facility.

2. Other opportunities for employment and/or constructive activity, either within the prison, or in a work-release program.

3. Adequacy of (a) medical care for the general prison population (so that participation in research is not the only means of obtaining medical attention), and (b) the proposed methods for maintaining medical records and for protecting the confidentiality of those records.

4. The nature, structure, function, and composition of the Organisational Review Committee (whether located at the prison or at the institution sponsoring the research) which is to review clinical research in that correctional facility.

The Secretary shall also set general guidelines to assist the Organisational Review Committees in determining rates of remuneration, and shall indicate groups who may be considered to represent the prisoners' interests for the purpose of appointment to membership on the Protection Committee. No institution shall be accredited if research, whether or not supported by funds from the DHEW, is conducted under its auspices,

or by members of its staff, which is not in conformity with these guidelines. No DHEW funds will be granted for research in institutions lacking such accreditation.

F. *Special provisions.* 1. Persons detained in a correctional facility while awaiting sentence, or in a hospital facility for pre-sentence diagnostic observation, are excluded from participation in research.

2. A child may not be included as a subject in research involving risk if he is detained in an institutional setting pursuant to a court order, whether or not the parents and the child have consented to the child's participation.

VI. *The mentally infirm.*—A. *Policy considerations.* The institutionalized mentally infirm are dou
respect to participation in research activities. First, as with children, they might lack the clear capacity to comprehend relevant information, and to make informed judgments concerning their participation. Second, as with prisoners, they experience a diminished sense of personal integrity as a result of confinement in an institution. Such confinement restricts their freedom of choice and imposes elements of coercion, which limit their capacity to give truly voluntary consent. In addition, the mentally infirm who are confined in institutions have more pressures to cooperate with custodial authorities than do prisoners, for their release might depend entirely upon their behavior and on the impression they make upon those having the power to make decisions concerning termination of their confinement.

Legal guardians, who have authority to consent for medical treatment, might have interests in the matter which do not necessarily coincide with those of the patient. Long-term management of patients with mental disabilities is expensive and time-consuming. Any proposal which might reduce either the expense or the supervision required in caring for such persons might be appealing, whether or not there is correlative benefit to the patient. This is certainly the case in projects offering new therapy; it might also occur, albeit in a more subtle form, where free medical or custodial services are perceived to be contingent upon the patient's participation as a subject in research.

The courts have begun to recognize that persons confined in institutions might not be able to give truly voluntary consent in such matters. It is important to recognize, as well, that persons encumbered with the economic or custodial responsibility for the mentally infirm might not be sufficiently objective to make judgments which are fully in the best interest of the institutionalized person.

The circumstances are limited under which it is justifiable to include the mentally infirm as subjects in biomedical research. These circumstances include projects in which: the proposed research concerns diagnosis, treatment, prevention, or etiology of the disability from which they suffer; the necessary information can be obtained only from those subjects; or the studies concern institutional life *per se*. With these exceptions, the general rule is that the participation of the mentally infirm as subjects in research is not acceptable.

B. *Ethical review of projects and protection of subjects.* In instances in which a research protocol requires the participation of mentally infirm subjects, the research must be overseen by a Protection Committee in the manner described in Section III–C, pertaining to children. This Protection Committee must be supervised on a continuing basis, as described in Section V–B, by the Organizational Review Committee of the institution in which the research is to be conducted or of the institution sponsoring the research.

VII. *General provisions.* These provisions apply to all research activities covered by this policy.

A. *Referrals to the Ethical Review Board.* Whenever a Primary Review Committee, secondary review group, or the agency staff perceives an apparent and significant question of ethics or an unusual element of risk—whatever the subject group involved—the research proposal in question may be forwarded to the Ethical Review Board for an opinion. In addition to offering an opinion of acceptability from an ethical viewpoint, the Board may choose to recommend the establishment of a Protection Committee, and suggest guidelines for its operation.

B. *Procedures requiring special consideration.* All other recommendations notwithstanding, DHEW may identify certain procedures which: (1) Require Protection Committee review of the selection of each individual subject; (2) are acceptable for stipulated subjects only if approved by affirmative declaratory judgment of a court of competent jurisdiction; or (3) are unacceptable.

C. *Research conducted in Foreign Countries.* All regulations governing research conducted in the United States apply to research conducted in foreign countries under DHEW auspices, and the ethical review must be of equal rigor.

There are sometimes special constraints encountered in foreign settings. Therefore, in addition to the requirement that consent procedures for research to be conducted abroad conform with the policy and regulations set forth in this document, there must be written assurance that the proposed research enjoys local acceptance, and offends no local ethical standards.

D. *Research submitted pursuant to DHEW regulatory requirements.* Research or testing which is performed pursuant to or in fulfillment of any regulation issued by any agency of the DHEW will be acceptable to the government only if conducted in compliance with these procedures and regulations.

E. *Clinical research not funded by DHEW.*

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

If, in the judgment of the Secretary, an organization fails to discharge its responsibilities for the protection of the rights and welfare of the subjects in its care, whether or not DHEW funds are involved, he may, upon reasonable notice to the organization of the basis for such action, determine that its eligibility to receive further DHEW grants or contracts involving human subjects shall be terminated. Such disqualification shall continue until it is shown to the satisfaction of the Secretary that the reasons therefor no longer exist.

If, in the judgment of the Secretary, an individual serving as principal investigator, program director, or other person having responsibility for the scientific and technical direction of a project or activity, has failed to discharge his responsibilities for the protection of the rights and welfare of human subjects in his care, the Secretary may, upon reasonable notice to the individual of the basis for such action, determine that such individual's eligibility to serve as a principal investigator or program director or in another similar capacity shall be terminated. Such disqualification shall continue until it is shown to the satisfaction of the Secretary that the reasons therefor no longer exist.[1]

In reaching a determination on compliance, with respect to subjects with limited capacity for consent, the Secretary will consider the extent and the nature of the procedures by which the institution offers protection in all studies conducted in or by that institution regardless of the source of funds, with the expectation that there shall be an ethical review similar to that required of the agency Ethical Review Board (III–B). The existence of a Protection Committee, overseen by an Organizational Review Committee and acting to afford supplementary judgment, will be accepted as evidence of responsibility in this regard.

F. *Confidentiality of information and records.* Nothing in this policy shall be construed as permitting the release of confidential research protocols nor the violation of State law applicable to the confidentiality of individual medical records.

VIII. *Draft additions to proposed regulations* (See FEDERAL REGISTER, Vol. 38, No. 194, Part 2, Tues., Oct. 9, 1973, pp. 27882–27885).

To amend the proposed Part 46 of Subtitle A of Title 45 of the Code of Federal Regulations by deleting §§ 46.20 through 46.23, redesignating §§ 46.1 through 46.19 thereof as Subpart A, and adding the following new Subparts B through F:

SUBPART B—ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED AS SUBJECTS IN DHEW ACTIVITIES

Sec.
46.21 Applicability.
46.22 Purpose.
46.23 Need for legally effective consent.
46.24 Definitions.
46.25 Ethical Review Board; Composition; Duties.

[1] FEDERAL REGISTER, Vol. 38, No. 194, Part 2, Tuesday, October 9, 1973, § 46.22, p. 27885.

AUTHORITY: 5 U.S.C. 301.

SUBPART B—ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED AS SUBJECT IN DHEW ACTIVITIES

Section 46.21 *Applicability.* (a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare research, development, or demonstration activities in which children may be at risk.

(b) The requirements of this subpart are in addition to those imposed under subpart A of this part.

Section 46.22 *Purpose.* It is the purpose of this subpart to provide additional safeguards in reviewing activities to which this subpart is applicable inasmuch as the potential subjects in activities conducted thereunder might be unable fully to comprehend the risks which might be involved and are legally incapable of consenting to their participation in such activities.

Section 46.23 *Need for legally effective consent.* Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will necessarily result in a legally effective consent under applicable State or local law to a subject's participation in any activity; nor in particular does it obviate the need for court approval of such participation where court approval is required under applicable State or local law in order to obtain a legally effective consent.

Section 46.24 *Definitions.* As used in this subpart:

(a) "DHEW activity" means:

(1) The conduct or support (through grants, contracts, or other awards) of biomedical or behavioral research involving human subjects; or

(2) Research, development, or demonstration activities regulated by any DHEW agency.

(b) "Subject at risk" means any individual who might be exposed to the possibility of harm (physical, psychological, sociological, or other—as a consequence of participation as a subject in any DHEW activity which goes beyond the application of those established and accepted methods necessary to meet his needs.

(c) "Child" means an individual who has not attained the legal age of consent to participate in research as determined under the applicable law of the jurisdiction in which such research is to be conducted.

(d) "DHEW" means the Department of Health, Education and Welfare.

Section 46.25 *Agency Ethical Review Board; composition; duties.* (a) The head of each agency shall establish an Ethical Review Board, hereinafter referred to as the "Board," to review proposals for research, development, and demonstration activities to which this subpart is applicable, as well as to advise him or her on matters of policy concerning protection of human subjects. The Board shall be composed of research scientists (biomedical, behavioral, and/or social), physicians, lawyers, clergy, ethicists, and representatives of the public. It shall consist of 15 members appointed by the agency head from outside the Federal Government. No more than one-third of the members may be individuals engaged in research, development, or demonstration activities involving human subjects.

(b) It shall be the function of the Board to review each proposed activity to which this subpart applies, and advise the agency concerning the acceptability of such activities from the standpoint of societal need and ethical considerations, taking into account the assessment of the appropriate Primary Review Committees as to: (1) The potential benefit of the proposed activity, (2) scientific merit and experimental design, (3) whether the proposed activity entails risk of significant harm to the subject, (4) the sufficiency of animal and adult human studies demonstrating safety and clear potential benefit of the proposed procedures and providing sufficient information on which to base an assessment of the risks, and (5) whether the information to be gained may be obtained from further animal and adult human studies.

(c) The Board shall review the procedures proposed by the applicant to be followed by the Protection Committee, provided for in § 46.26 of this subpart, in carrying out its functions as set forth in § 46.26. In addition, the Board may recommend additional functions to be performed by the Protection Committee in connection with any particular activity.

(d) In decisions regarding activities covered by this subpart, the agency shall take into account the recommendations of the Board.

Section 46.26 *Protection Committees; composition; duties.* (a) No activity covered by this subpart will be approved unless it provides for the establishment by the applicant of a Protection Committee, composed of at least five members so selected that the Committee will be competent to deal with the medical, legal, social and ethical issues involved in the activity. None of the members shall have any association with the proposed activity, and at least one-half shall have no association with any organization or individual conducting or supporting the activity. No more than one-third of the members shall be individuals engaged in research, development, or demonstration activities involving human subjects. The composition of the Protection Committee shall be subject to DHEW approval.

(b) The duties of the Protection Committee, proposed by the applicant, and reviewed by the agency including the Ethical Review Board shall be to oversee: (1) The selection of subjects who may be included in the activity; (2) the monitoring of the subject's continued willingness to participate in the activity; (3) the design of procedures to permit intervention on behalf of one or more of the subjects if conditions warrant; (4) the evaluation of the reasonableness of the parents' consent and (where applicable) the subject's consent; and (5) the procedures for advising the subject and/or the parents concerning the subject's continued participation in the activity. Each subject and his or her parent or guardian will be informed of the name of a member of the Protection Committee who will be available for consultation concerning the activity.

(c) The Protection Committee shall establish rules of procedure for conducting its activities, which must be reviewed by DHEW, and shall conduct its activities at convened meetings, minutes of which shall be prepared and retained.

Section 46.27 *Certain children excluded from participation in DHEW activities.* A child may not be included as a subject in DHEW activities to which this subpart is applicable if:

(a) The child has no known living parent who is available and capable of participating in the consent process: *Provided*, That this exclusion shall be inapplicable if the child is seriously ill, and the proposed research is designed to substantially alleviate his condition; or

(b) The child has only one known living parent who is available and capable of participating in the consent process, or only one such parent, and that parent has not given consent to the child's participation in the activity; or

(c) Both the child's parents are available and capable of participating in the consent process, but both have not given such consent;

(d) The child is involuntarily confined in an institutional setting pursuant to a court order, whether or not the parents and child have consented to the child's participation in the activity; or

(e) The child has not given consent to his or her participation in the research: *Provided*, That this exclusion shall be inapplicable if the child is 6 years of age or less or if explicitly waived by the DHEW; or

(f) The Protection Committee established under § 46.26 of this subpart has not reviewed and approved the child's participation in the activity.

Section 46.28 *Activities to be performed outside the United States.* In addition to satisfying all other applicable requirements in

this subpart, an activity to which this subpart is applicable, which is to be conducted outside the United States, must include written documentation satisfactory to DHEW that the proposed activity is acceptable under the legal, social, and ethical standards of the locale in which it is to be performed.

SUBPART C—ADDITIONAL PROTECTION FOR CERTAIN CLASSES OF DHEW ACTIVITIES

Section 46.31 *Applicability.* (a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare research, development, or demonstration activities: (1) Involving pregnant women, unless there is a finding by DHEW that the activity will have no adverse effect on the fetus, or is clearly therapeutic with respect to the fetus involved, (2) involving the abortus or the non-viable fetus, or (3) involving in vitro fertilization of human ova.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will in any way render inapplicable pertinent State or local laws bearing upon activities covered by this subpart.

(c) To the extent the requirements of subpart A of this part are applicable to activities also covered by this subpart, the requirements of this subpart are in addition to those imposed under subpart A.

Section 46.32 *Purpose.* It is the purpose of this subpart to provide additional safeguards in reviewing activities to which this subpart is applicable to assure that they conform to appropriate ethical standards and relate to important societal needs.

Section 46.33 *Definitions.* As used in this subpart:

(a) "DHEW" means the Department of Health, Education, and Welfare.

(b) "DHEW activity" means:

(1) The conduct or support (through grants, contracts, or other awards) of biomedical or behavioral research involving human subjects; or

(2) Research, development, or demonstration activities regulated by any DHEW agency.

(c) "Board" means the Board established under § 46.25.

(d) "Protection Committee" means a committee referred to in § 46.26.

(e) "Pregnancy" means the period of time from implantation of a fertilized ovum until delivery.

(f) "Fetus" means the product of conception from implantation until delivery.

(g) "Abortus" means the fetus when it has been expelled whole, whether spontaneously or as a result of medical or surgical intervention to terminate a pregnancy, prior to viability. This definition, for the purpose of this policy, excludes the placenta, fetal material which is macerated at the time of expulsion, a dead fetus, and isolated fetal tissue or organs excised from a dead fetus.

(h) "Viability of a fetus" means capability given the benefit of available therapy, of independently maintaining heart beat and respiration.

(i) "In vitro fertilization" means any fertilization of human ova which occurs outside the body of a female, through admixture of human sperm and such ova.

Section 46.34 *Duties of the Ethical Review Board.* (a) It shall be the function of the Board to review each activity to which this subpart applies and advise the agency concerning the acceptability of such activities from the standpoint of societal need and ethical considerations, taking into account the assessment of the appropriate Primary Review Committees as to: (1) The potential benefit of the proposed activity, (2) scientific merit and experimental design, (3) the sufficiency of studies involving animals demonstrating the clear potential benefit of the proposed procedures and (4) whether the information to be gained may be obtained from further animal or adult human studies.

(b) The Board may recommend the establishment by the sponsoring institution of a Protection Committee to carry out such functions as the Board deems necessary.

Section 46.35 *Maternal consent to activities involving the abortus.* (a) No activity to which this subpart is applicable may involve an abortus or a non-viable fetus unless maternal consent has been obtained.

(b) No activity to which this subpart is applicable may involve an abortus or a non-viable fetus unless: (1) Individuals involved in the activity will have no part in the decision as to timing, method, or extent of the procedure used to terminate the pregnancy, or in determining viability of the fetus at the termination of the pregnancy; (2) vital functions of the abortus will not be maintained artificially for purposes of research; and (3) experimental procedures which would terminate heart beat or respiration in the abortus will not be employed.

Section 46.37 *Prohibition on certain activities involving pregnant women where the fetus may be adversely affected.* The Board shall review all research, development, and demonstration activities involving pregnant women. No activity to which this subpart is applicable may involve a pregnant woman if the Primary Review Committee finds that the fetus might be adversely affected, unless the primary purpose of the activity is to benefit that fetus. In addition, no activity to which this subpart is applicable may involve pregnant women unless all the requirements of this subpart are satisfied.

Section 46.38 *Parental consent to activities which might affect the fetus.* No activity involving a pregnant woman which might affect the fetus but which nevertheless is permissible under § 46.37 shall be conducted unless maternal consent has been obtained, as well as the consent of the father if he is available and capable of participating in the consent process.

Section 46.39 *Activities to be performed outside the United States.* In addition to satisfying all other applicable requirements in this subpart, activities to which this subpart is applicable, which are to be conducted outside the United States, must include written documentation satisfactory to DHEW that the proposed activity is acceptable under the legal, social, and ethical standards of the locale in which it is to be performed.

SUBPART D—ADDITIONAL PROTECTIONS FOR PRISONERS INVOLVED AS SUBJECTS IN DHEW ACTIVITIES

Section 46.41 *Applicability.* (a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare research, development, and demonstration activities involving prisoners as subjects.

(b) The requirements of this subpart are in addition to those imposed under subparts A and B of this part.

Section 46.42 *Purpose.* It is the purpose of this subpart to provide additional safeguards for activities to which this subpart is applicable inasmuch as the potential subjects in activities conducted thereunder, because of their incarceration, might be under constraints which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate in such activities.

Section 46.43 *Definitions.* As used in this subpart:

(a) "DHEW activity" means:

(1) the conduct or support (through grants, contracts, or other awards) of biomedical or behavioral research involving human subjects; or

(2) research, development, or demonstration activities regulated by any DHEW agency.

(b) "Prisoner" means any individual involuntarily confined in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute and also individuals detained by virtue of statutes which provide alternatives to criminal prosecution.

(c) "DHEW" means the Department of Health, Education, and Welfare.

Section 46.44 *Additional duties of Organizational Review Committee where prisoners are involved.* (a) In carrying out its responsibilities under subpart A of this part for activities also covered by this subpart, the Organizational Review Committee provided for under subpart A shall also certify: (1) That there will be no undue inducements to participation by prisoners as subjects in the activity, taking into account among other factors, the sources of earnings generally available to the prisoners as compared with those offered to participants in the activity, (2) that the clinic and hospital facilities are adequate for the proposed activity, (3) that all aspects of the activity would be appropriate for performance on nonprisoners, and (4) that no prisoner will be offered any reduction in sentence or parole for participation in such activity which is not comparable to that offered for other activities at the facility not of a research, development, demonstration or similar nature.

(b) In addition, the Organizational Review Committee shall have the following duties: (1) To review, approve, or modify the procedures proposed for the Protection Committee in carrying out its functions as set forth in § 46.45; (2) To recommend any additional functions to be performed by the Protection Committee in connection with a particular activity; (3) To set rates of remuneration, if any, consistent with the anticipated duration, discomfort, and/or risk of the activity but not in excess of that paid for other employment generally available to inmates of the facility in question; and (4) To carry out such other responsibilities as may be stipulated by DHEW in the contract or grant award.

(c) Activities to which this subpart is applicable must provide for the designation of an Organizational Review Committee, where no such Committee has been established under subpart A.

Section 46.45 *Protection Committees; duties; composition.* (a) No activity covered by this subpart will be approved unless it provides for the establishment of a Protection Committee to carry out the following functions, as well as any others recommended by the Organizational Review Committee or by DHEW: (1) Reviewing the procedure for soliciting participation by prisoners in the research activity to determine that all elements of informed consent, as outlined in § 46.3, are satisfied; (2) overseeing the selection of prisoners who may participate in the activity; (3) monitoring the progress of the research and the continued willingness of subject participation; and (4) intervening on behalf of one or more subjects if conditions warrant. In addition, each subject will be informed of the name of a member of the Protection Committee who will be available to the subject for consultation concerning the activity.

(b) Each Protection Committee shall be composed of at least five members appointed by the applicant and so selected that the Committee will be competent to deal with the medical, legal, social, and ethical issues involved. At least one member of the Committee shall be either a prisoner or a representative of an organization having as a primary concern protection of the interests of prisoners.

No more than one-third of the members may be physicians or scientists engaged in biomedical or behavioral research, and no more than one member, other than a prisoners' representative, may have any affiliation with the prison facility or the legal entity having jurisdiction over the facility, except for persons employed by a Department of Education in a teaching capacity. Any prisoners serving on the Committee shall be compensated at a rate consistent with that set for prisoners participating as subjects in activities at the facility to which this subpart is applicable.

(c) The Protection Committee shall establish rules of procedure for conducting its activities which must be reviewed by DHEW, and shall conduct its activities at convened meetings, minutes of which shall be prepared and retained. The composition of the Committee shall be subject to DHEW approval.

Section 46.46 *Prohibition on participation in activities prior to conviction.* No individual confined pending arraignment, trial, or sentencing for an offense punishable as a crime may be used as a subject in any activity supported in whole or in part by a grant or contract to which this subpart is applicable.

Section 46.47 *Remuneration to subjects.* Where rates of remuneration are set pursuant to § 46.44 of this subpart, any subject who, for medical reasons, is required by a representative of the prison facility, grantee, contractor, or sponsor of the activity, to withdraw before completion of his or her participation in the activity shall continue to be compensated for a period to be set by the Protection Committee after consultation with the grantee or contractor.

Section 46.48 *Accreditation.* It is the intention of DHEW to accredit prison facilities as sites for the performance of activities to which this subpart applies. Accreditation will be based on certification of the acceptability of the facilities and compliance with the procedures required by this subpart, as determined by the Secretary. No activity covered by this subpart may involve prisoners incarcerated in a facility not accredited by Secretary of DHEW.

Section 46.49 *Activities to be performed outside the United States.* In addition to satisfying all other applicable requirements in this subpart, an activity to which this subpart is applicable, which is to be conducted outside the United States, must include written documentation satisfactory to DHEW that the proposed activity is acceptable under the legal, social, and ethical standards of the locale in which it is to be performed.

### Subpart E—Additional Protections for Institutionalized Mentally Infirm Individuals Involved as Subjects in DHEW Activities

Section 46.51 *Applicability.* (a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare activities involving the institutionalized mentally infirm as subjects.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein in connection with activities permitted under § 46.54 of this subpart will necessarily result in a legally effective consent under applicable State or local law to a subject's participation in such an activity; nor in particular does it obviate the need for court approval of such participation where court approval is required under applicable State or local law in order to obtain a legally effective consent.

(c) The requirements of this subpart are in addition to those imposed under Subparts A, B, and D of this part.

Section 46.52 *Purpose.* It is the purpose of this subpart to provide additional safeguards for the mentally infirm involved in research, development, and demonstration activities, inasmuch as the potential subjects in such activities are: (1) Confined in an institutional setting; (2) might be unable fully to comprehend the type risks which may be involved; and (3) might be legally incompetent to consent to their participation in such activities.

Section 46.53 *Definitions.* As used in this subpart:

(a) "DHEW activity" means:

(1) The conduct or support (through grants, contracts, or other awards) of biomedical or behavioral research involving human subjects; or

(2) Research, development, or demonstration activities regulated by any DHEW agency.

(b) "Mentally infirm" includes the mentally ill, the mentally retarded, the emotionally disturbed, the psychotic, the senile, and others with impairments of a similar nature, regardless of whether or not the individual has been determined to be legally incompetent.

(c) "Institutionalized" means confined, whether by court order or voluntary commitment, in an institution for the care and/or treatment of the mentally infirm.

Section 46.54 *Limitations on activities involving the institutionalized mentally infirm.* No institutionalized mentally infirm individual may be included as a subject in a DHEW activity unless:

(a) The proposed activity is concerned with: (1) The diagnosis, treatment, prevention, or etiology of the impairment with which he or she is afflicted; or (2) the proposed activity is concerned with the effect of institutional life on the subject and involves no risk of harm to the subject; or (3) the information can be obtained only from such subjects.

(b) The individual's legal guardian has given consent to the individual's participation in such activity;

(c) Where the individual has sufficient mental competency to understand what is proposed and to express an opinion as to his or her participation, the individual's consent to such participation has also been secured; and

(d) The Protection Committee, provided for in § 46.56 of this subpart, has reviewed and approved subject participation in the activity (by class or by individual).

Section 46.55 *Additional duties of Organizational Review Committee where the mentally infirm are involved.* (a) In addition to its responsibilities under Subpart A of this part, the Organizational Review Committee shall, with respect to activities to which subpart applies:

(1) Certify that all aspects of the activity would be ethically appropriate for performance on healthy individuals;

(2) Conduct at least one on-site visit to the institution and prepare a report of the visit, including discussion of such matters as living conditions, availability of medical care, and quality of food, to be submitted to DHEW along with the application;

(3) Review and approve or modify the procedures proposed by the applicant to be followed by the Protection Committee, provided for in § 46.56, in overseeing the recruitment of the mentally infirm subjects who may be included in such activity;

(4) Recommend any additional functions to be performed by the Protection Committee in connection with any particular activity; and

(5) Carry out such other responsibilities as may be recommended by DHEW.

(b) Activities to which this subpart is applicable must provide for the designation of an Organizational Review Committee where no such Committee has been established under subpart A.

Section 46.56 *Protection Committees; duties; composition.* (a) No activity covered by this subpart will be approved unless it provides for the establishment of a Protection Committee to carry out the following functions, as well as any others prescribed by the Organizational Review Committee or by DHEW: (1) Overseeing the process of selection of subjects who may be included in the activity, (2) monitoring the progress of the activity with special attention to adverse effects on subjects, (3) intervening on behalf of one or more of the subjects if conditions warrant, (4) evaluating the process and reasonableness of consent of the legal guardian and (where applicable) of the subject, and (5) advising the legal guardian and/or the subject concerning the latter's continued participation in the activity if conditions warrant.

(b) The composition of each Protection Committee shall conform to the requirements set forth in § 46.26(a).

(c) The Protection Committee shall establish rules of procedure for conducting its activities, which must be reviewed by DHEW, and shall conduct its activities at convened meetings, minutes of which shall be prepared and retained.

Section 46.57 *Activities to be performed outside the United States.* In addition to satisfying all other applicable requirements in this subpart, an activity to which this subpart is applicable, which is to be conducted outside the United States, must include written documentation satisfactory to DHEW that the proposed activity is acceptable under the legal, social, and ethical standards of the locale in which it is to be performed.

### Subpart F—General Provisions

Section 46.61 *Applicability.* The following regulations are applicable to all activities covered by this part.

Section 46.62 *Records.* (a) Copies of all documents presented or required for initial and continuing review by any Organizational Review Committee or Protection Committee and minutes, transmittals on actions, instructions, and conditions resulting from committee deliberations are to be made part of the official files of the grantee or contractor for the supported activity.

(b) Records of subject's and representative's consent shall be retained by the grantee or contractor in accordance with its established practice, or, if no practice has been established, in project files.

(c) Acceptance of any DHEW grant or contract award shall constitute consent of the grantee or contracting organization to inspection and audit of records pertaining to the assisted activity by authorized representatives of the Secretary.

(d) All documents and other records required under this part must be retained by the grantee or contracting organization for a minimum of three years following termination of DHEW support of the activity.

Section 46.63 *Reports.* Each organization with an approved assurance shall provide the Secretary with such reports and other information as the Secretary may from time to time prescribe.

Section 46.64 *Early termination of awards: sanctions for noncompliance.* (a) If, in the judgment of the Secretary, an organization has failed to comply with the terms of this part with respect to a particular Federal activity, he may require that said grant or contract be terminated or suspended in the manner prescribed in applicable grant or procurement regulations.

(b) If, in the judgment of the Secretary, an organization fails to discharge its responsibilities for the protection of the rights and welfare of the subjects in its care, whether or not DHEW funds are involved, he may, upon reasonable notice to the organization of the basis for such action, determine that its eligibility to receive further DHEW grants or contracts or participate in DHEW assisted activities, involving human subjects, shall be terminated. Such disqualification shall continue until it is shown to the satisfaction of the Secretary that the reasons therefor no longer exist.

(c) If, in the judgment of the Secretary, an individual serving as principal investigator, program director, or other person having responsibility for the scientific and technical direction of a project or activity, has failed to discharge her or his responsibilities for the protection of the rights and welfare of human subjects in his or her care, the Secretary may, upon reasonable notice to the individual of the basis for such action, determine that such individual's eligibility to serve as a principal investigator or program director or in another similar capacity shall be terminated. Such disqualification shall continue until it is shown to the satisfaction of the Secretary that the reasons therefor no longer exist.

Section 46.65 *Conditions.* The Secretary may with respect to any activity or any class of activities impose conditions, including conditions pertaining to informed consent, prior to or at the time of the approval of any activity when in the Secretary's judgment such conditions are necessary for the protection of human subjects.

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# PROTECTION OF HUMAN SUBJECTS:
# PROPOSED POLICY

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# DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

## Office of the Secretary

■

# PROTECTION OF HUMAN SUBJECTS

## Proposed Policy

## DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

### Office of the Secretary

### [45 CFR Part 46]

### PROTECTION OF HUMAN SUBJECTS

### Proposed Policy

In the FEDERAL REGISTER of May 30, 1974 (39 FR 18914), regulations were published as Part 46 of Title 45 of the Code of Federal Regulations providing generally for the protection of human subjects involved in research, development, or related activities supported by Department grants or contracts. At that time it was indicated that notices of proposed rulemaking would be developed concerning minors, fetuses, abortuses, prisoners, and the institutionalized mentally disabled.

Coincidentally with the development of the notice of proposed rulemaking set forth below, both Houses of Congress reached agreement on the "National Research Act," and the President signed P.L. 93-348 into law. Among other things, the Act establishes an eleven-member National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research to "* * * (i) conduct a comprehensive investigation and study to identify the basic ethical principles which should underlie the conduct of biomedical and behavioral research involving human subjects, (ii) develop guidelines which should be followed in such research to assure that it is conducted in accordance with such principles, and (iii) make recommendations to the Secretary (I) for such administrative action as may be appropriate to apply such guidelines to biomedical and behavioral research conducted or supported under programs administered by the Secretary, and (II) concerning any other matter pertaining to the protection of human subjects of biomedical and behavioral research."

This notice of proposed rulemaking is published today to continue the public dialogue begun in November 1973 when the Director of the National Institutes of Health published draft proposals on these issues in the FEDERAL REGISTER. The comments addressed in this preamble are the result of that issuance.

The comments received as a result of this notice of proposed rulemaking will not only assist the Department to develop final regulations but will also be available to the Commission for their use during the course of their deliberations over the next two years.

In the light of the 450 responses received as a result of the November issuance, largely from grantee and contractor organizations, the Department now proposes that, in addition to the protection afforded generally to all subjects of research, development, and related activities supported by the Department by virtue of Part 46, further protective measures should be provided for those subjects of research whose capability of providing informed consent is or may be absent or limited.

This would be accomplished by amending Part 46 to delete § 46.19 through 46.22, redesignating § 46.1 through 46.18 as Subpart A, and adding new Subparts B through F. If this proposal is accepted, the regulations would be structured as follows:

Subpart A would be the basic regulation, substantially as promulgated on May 30, 1974. This provides that no activity involving any human subject at risk shall be supported by a DHEW grant or contract unless the applicant or offering organization has established an organizational review committee which has reviewed and approved such activity and submitted to DHEW a certification of such review and approval. This subpart also provides that all grant and contract proposals involving human subjects at risk are to be additionally evaluated by the Secretary for compliance with the requirements of said subpart.

Subpart B is reserved for a separate, future proposed rulemaking providing additional protection for children.

Subpart C as described in the present proposed rulemaking would call for the utilization of two special mechanisms for the protection of the pregnant woman and unborn child or fetus, where the pregnant woman participates in a research, development, or related activity. While these mechanisms are designed to allow sufficient flexibility for the pursuit of new information about the perinatal process, they are also designed to provide additional safeguards to assure that the research is acceptable from an ethical standpoint.

Subpart D as described in the present proposed rulemaking would give added responsibilities to an organizational review committee where the contemplated research would involve prisoners as subjects and also would require in such instances that a consent committee be established to supervise the selection and participation of prisoners in the research. Prisoner groups are particularly valuable in properly conducted clinical trials since they provide a stable subject population which can be followed over a period of weeks or months rather than days or hours. From the point of view of the prisoner subject, participation in research offers an opportunity to make a contribution to society and to provide an income, much as other jobs in prison do. Nevertheless, the dangers of abuse of prisoners' rights are obvious. For this reason, the proposed rulemaking calls for additional safeguards for the rights of prisoners whose capability to provide informed consent may be affected by the very fact of their incarceration.

Subpart E as described in the present proposed rulemaking offers additional protections for the rights of the mentally ill, the mentally retarded, the emotionally disturbed, and the senile who are confined to institutions, whether by voluntary or involuntary commitment. Such persons, by the very nature of their disabilities, may be severely limited in their capacity to provide informed consent to their participation in research. At the same time, the nature of their disabilities requires extensive research efforts to the study of the etiology, pathogenesis, and therapy of their conditions. The proposed rulemaking limits the research in which such subjects may be allowed to participate to that which is most likely to be of assistance to them or to persons similarly disabled.

In developing the present proposed rulemaking, the Department has taken into consideration the public's comments relevant to certain parts of the Introduction, Definition, and General Policy Sections of the draft regulations published at 39 FR 18914, November 16, 1973, as well as to the draft regulations themselves. The major comments, and the Department's present proposals, are as follows:

#### INTRODUCTION, GENERAL POLICY CONSIDERATIONS

A. Commentators suggested, in several different contexts, that the regulations should (i) apply to all research, regardless of the degree of risk or academic discipline concerned, and (ii) provide for the exclusion of certain types of research, particularly behavioral and social science research as distinguished from biomedical research.

The Department, having considered these comments, notes that the applicability provisions of the basic regulations (45 CFR 46.1) permit the Secretary to determine whether specific programs place subjects at risk. Such determination is to be made only after careful study and publication in the FEDERAL REGISTER, providing an opportunity for comment on the merits of each determination. With respect to research in the social sciences, the Department has already indicated its intention of issuing public rulemaking on this matter (see 39 FR 18914, paragraph A).

B. Comments also included suggestions that regulations should be proposed specifically dealing with activities involving students, laboratory employees, seriously ill or terminal patients, the non-institutionalized mentally disabled, and other special groups.

The Department considers that any abuses relating to these groups are less evident and that they are afforded the protection of the existing regulations published in 39 FR 18914.

C. Several comments suggested the provision of additional guidelines with respect to the distinction between established and accepted methods on the one hand and experimental procedures on the other.

While the Department recognizes the theoretical desirability of such guidelines, and that the practical necessity of making such a distinction is arising with increasing frequency, the feasibility of making this distinction on a generalized basis has yet to be demonstrated. At the moment a regulatory approach to this issue does not appear justified.

D. It was suggested that all meetings of organizational review committees and similar groups established pursuant to

these regulations should be open to the public.

The Department notes that since the purpose of these committees is, for the most part, to advise with respect to the conduct of individual projects and proposals by individual investigators, a blanket provision to this effect would appear to be inconsistent with the need to protect the confidentiality of the proceedings and records of institutional review and evaluation committees.

DEFINITIONS

A. Comments on the definition of "Subject at Risk" suggested changes in language that would (i) limit the concept of risk to that encountered only in addition to that normally experienced, (ii) eliminate demonstration projects as a possible source of risk, since these are nominally limited to application of established and accepted methods, (iii) specifically identify failure to maintain confidentiality as a source of risk, and (iv) provide a mechanism for identifying activities essentially free of risk.

These comments are similar to those made with respect to the same definition as incorporated in an earlier proposed rulemaking (38 FR 27882). In responding to the criticism, the Department has already (i) redefined "Subject at Risk" in 45 CFR 46.3(b) so as to exclude any activity which does not increase the ordinary risks of daily life or the recognized risks inherent in a chosen occupation or field of service, (ii) substituted in 45 CFR 46.1(a) the term "development" for "demonstration," (iii) provided in 45 CFR 46.19(b) specific prohibitions against disclosures of information which refers to or can be identified with a particular subject, and (iv) provided in 45 CFR 46.1(b) authority for determination in advance as to whether a particular Federal program or an investigational method or procedure may place subjects at risk.

B. Comments on the definition of "Clinical Research" suggested inclusion in said definition of the behavioral aspects of research and facets of medical research necessarily concerned with diagnosis and other nonetherapeutic aspects of research.

Since the term "clinical research" does not occur in the present rulemaking, the Department reserves its opinion with respect to these suggestions. However, the proposed regulations are applicable to all departmental research, development, and related activities except with respect to Subpart C, where applicability is limited to "biomedical research" (§ 46.303(b)).

C. Comments on "Informed Consent" suggested the addition of language concerning (i) full and complete disclosure, (ii) the likelihood of success or failure of the experiment, (iii) the use of placebos or other control procedures, (iv) provision of information as to the progress of the research, (v) publication of names of all persons, institutions, and review committees involved in approval of consent procedures, (vi) provision of legal counsel and technical advice, and (vii) assurance that the subject comprehends the disclosure.

The Department, having considered these comments, notes that "Informed Consent" is presently defined in 45 CFR 46.3(c) and not in the present proposed rulemaking. With respect to the specific suggestions the Department notes that: as far as (i) is concerned, the regulations already call for a "fair explanation" of the procedures and a description of risks and benefits reasonably to be expected; (ii) reflects a basic misunderstanding of the experimental process which begins, essentially, with the comparison of two or more methods, procedures, or modalities on the *a priori* hypothesis that there will be no difference; (iii) is implicit in the existing regulations and is better emphasized in interpretive materials; (iv) would not be an element of informed consent unless interim findings affected the risk of benefit involved; and (v) touches on the subject of a possible future proposed rulemaking and the Department reserves its options for the present. The suggestion in (vi) is met in part by the proposals in the present proposed rulemaking to employ consent committees to advise potential subjects. The last suggestion (vii) goes beyond requirements for informed consent as they have generally been articulated by the courts.

D. Comments also included suggestions for the inclusion of additional definitions of (i) Institutions, (ii) Legal Guardian, (iii) Organizational Review Committee, (iv) Institutionalized Mentally Infirm, and (v) Children (with regard to age of consent), Parents, and Father.

The Department, having reviewed these comments, notes that (i) "Organization" is defined for the purpose of these regulations to include "institutions" at 45 CFR 46.3(a); (ii) "Legally authorized representative" is defined for the purpose of these regualtions to include legal guardian at 45 CFR 46.3(h); (iii) the definition of "organizational review committee" is implicit in 45 CFR 46.6; (iv) "Institutionalized mentally disabled" has been defined in the present proposed rulemaking at 46.503(d) to meet the suggestion; and (v) definition of "Children," "Parents," and "Father" will be reconsidered prior to the issuance of a future rulemaking covering research on children.

E. Several commentators criticized provisions of the draft policy that would have required that activities to be conducted outside the United States satisfy all requirements of the Departments regulations including those based on ethical concepts peculiar to the Judeo-Christian moral heritage or to English common law. It was noted that this would create substantial problems for United States investigators working overseas since these concepts are often inconsistent if not in conflict with normal, ethical, and legal concepts in certain foreign countries. For the same reasons, it was argued that these provisions would create problems for United States citizens assigned, detailed, seconded, or acting as consultants to international organizations or to foreign governmental or private institutions.

Having considered these objections, the Department proposes to retain the basic concept that activities supported by Departmental funds should, in general, be subject to a uniform ethical policy wherever they are conducted, but to permit the Secretary to modify consent procedures if it can be demonstrated to his satisfaction that such procedures, as modified, are acceptable under the legal, social, and ethical standards of the locale in which the activities are to be performed.

FETUSES, ABORTUSES, AND PREGNANT WOMEN

Since comments on the draft provisions in 38 CFR 31738 providing additional protections for fetuses, abortuses, *in vitro* fertilization, and pregnant women were integrated with those on children, it is difficult to identify the communications specifically concerned with these subjects. However, it is estimated that the majority of the more than 400 letters received on research with children, born and unborn, touched on one or more aspects of research with fetuses, abortuses, and pregnant women.

A. A large number of respondents disagreed entirely with the idea of permitting research with the fetus, with the abortus (whether living or dead), or with the pregnant woman if the research might conceivably endanger the fetus.

The Department, having carefully considered these comments and similar proposals reflected in general correspondence and in articles in the public media, notes that their adoption would seriously hamper the development of needed improvements in the health care of the pregnant woman, the fetus, and the newborn. The opposition to research involvement of the fetus and abortus appears to be based in part on the assumption that the needed information can be obtained through research with animal species or with adults. Unfortunately, these assumptions are not valid. While much useful research can be conducted in animals, differences in species are nevertheless so great that any research finding in nonhuman species must ultimately be repeated in man before its general application in human medicine. In addition, the fetus and the newborn are not small adults. They suffer from some diseases not encountered in the adult. They may react differently to the diseases commonly affecting both adult and young, and they may have a different response to the same treatment, both with regard to its effectiveness and to its safety. The Department therefore proposes that (i) the ethical probity of any application or proposal for the support of any activity covered by subpart C be reviewed by an Ethical Advisory Board as described in § 46.304, and (ii) the conduct of any such activity supported by the Department be subject to oversight and monitoring by a consent committee as described in § 46.305.

B. Opinion was divided as to the need for an Ethical Advisory Board. Many respondents called it a welcome addition in the review process. Others felt that it would duplicate the function of the local organizational review committee and that its existence would encourage the organizational review committee to be less critical and would impose an additional roadblock that would delay or prohibit important research while needlessly consuming time, energy, and money, and posing potential danger to a patient waiting for treatment. Complaints were voiced that such decisions should be made locally, not in Washington, and that the investigator should be able to present his case in person. Numerous comments suggested that the Board's function should be limited to advising on policy, guidelines, or procedures, and not be concerned with the review of individual projects. This would avoid duplicating the function of the organizational review committee. Others suggested that the Ethical Advisory Board should serve as an appeal body from the organizational review committee.

There were also numerous comments to the effect that it is unwise and impossible to totally separate ethical and scientific review. Approval based only on ethics would be unethical if the science were bad. Both should be reviewed jointly.

The Department, having reviewed these comments, concludes that Ethical Advisory Board remains, in concept, a useful addition to the review process. It does not duplicate the functions of the local organizational review committee, since the latter is primarily concerned with matters of organizational regulations, local standards of professional practice, applicable law within its jurisdiction, and local community attitudes. The Ethical Advisory Board will be primarily concerned with similar issues at the national level. Applications and proposals should be capable of passing scrutiny at both levels. It is therefore proposed that the Ethical Advisory Board be retained as part of the additional protection mechanism.

Specific comments regarding the establishment of an Ethical Advisory Board touched principally on (i) the possibility that appointment of members at an agency level might lead to "loaded" Boards, while appointment at a higher level, i.e., by a joint Congressional committee or by independent outside bodies, might produce a more objective group, and (ii) disagreement as to the proper balance between scientist and nonscientist members, with a majority of the commentators suggesting that more than one-third of the members should have the scientific expertise necessary to identify risks and their possible consequences. It was specifically suggested that different sizes, compositions, and administrative locations of the Board be tried before selecting a final mechanism. In addition, it was suggested (iii) that a fifteen member Board was too large, (iv) that all members be human geneticists, (v) that at least one member be a psychologist, if behavioral issues were to be considered, (vi) that there be an absolute ban on departmental agency employees, (vii) that all proceedings be confidential, (viii) that all meetings be open to the public, and (ix) that an appeal mechanism be established.

The Department, having considered these views, proposes that while an Ethical Advisory Board to deal with biomedical research involving fetuses, abortuses, pregnant women, and *in vitro* fertilization might logically be established at the National Institutes of Health, (i) the power of appointment should be reserved to the Secretary, (ii) while the membership should include research scientists, physicians, lawyers, clergy or ethicists, and representatives of the general public, the balance between callings should rest with the Secretary as should also (iii) the number of members, so that the membership (iv, v) can be adjusted to the needs of the Board as the workload and the issues before it dictate. The specific suggestion (see vi) that departmental agency employees be excluded is adopted and expanded to include all full-time employees of the Federal Government. The decisions with regard to suggestions (vii) and (viii) will be governed by the provisions of the Federal Advisory Committee Act which generally require that meetings of similar advisory groups be open to the public for the purposes of policy discussion, but closed and confidential for the purpose of review of specific applications and proposals. Since the Board will be advisory to funding agencies, the final action will be that of existing awarding authorities, and appeal mechanisms (ix) will be provided only to the extent available under other existing departmental regulations and policies. These proposals are incorporated into § 46.304.

C. A number of respondents recommended that the policy governing *in vitro* fertilization be strengthened, on the one hand, or liberalized, on the other. The Department has considered these recommendations, and has provisionally chosen not to stipulate at this time protections for the product of *in vitro* fertilization which is not implanted, but rather to leave that series of issues to the Ethical Advisory Board established under § 46.304(a). The Board will be required to weigh, with respect to specific research proposals, the state of the art, legal issues, community standards, and the availability of guidelines to govern each research situation.

Because biomedical research is not yet near the point of being able to maintain for a substantial period the nonimplanted product of *in vitro* fertilization, no clear and present danger arises from not stipulating in these regulations the protections for it. Given the state of the research, we believe that such stipulation would be premature.

It is the Department's intent that the definition of the term "fetus" (§ 46.303 (d)) be construed to encompass both the product of *in vivo* conception and the product of *in vitro* fertilization which is subsequently implanted in the donor of the ovum. Whatever the nature of the conception process, it is intended that upon implantation the protections of subpart C apply to all fetuses. It is only with respect to the protections available to the non-implanted product of *in vitro* fertilization that the regulations are silent.

With respect to the fertilization of human ova *in vitro*, it is expected that the Board will consider the extent to which current technology permits the continued development of such ova, as well as the legal and ethical issues surrounding the initiation and disposition of the products of such research.

With respect to implantation of fertilized human ova, it is expected that the Board will consider such factors as the safety of the technique (with respect to offspring) as demonstrated in animal studies, and clarification of the legal responsibilities of the donor and recipient parent(s) as well as the research personnel.

Since the Department does reserve the option of later specifying such protections by regulation, we invite comment on the question of appropriate regulations in the future.

D. The draft proposals included a suggestion for the establishment of a protection committee which elicited numerous comments that the use of the term "protection committee" implies that the Department recognizes a clear, present need for protection against the investigator, the uncertain relation of this committee to the organizational review committee, and the uniform need for and desirability for such protection.

Having reviewed these comments, the Department proposes an extensive revision in this innovative concept. Initially, it acknowledges that the term "protection committee" is pejorative and proposes the term "consent committee" as more appropriate and consistent with the primary purpose of such bodies. Further, it proposes to eliminate specific requirements for the size and composition of such committees. Instead, applicants and offerors are to propose the establishment of such a committee, specifying its size, composition, and rules of procedure. In addition, where the applicant or offeror believes that the activity involves only negligible risks, it may ask the Secretary to waive or modify the requirement for a consent committee. All proposals for the establishment, modification, or waiver of a consent committee shall be subject to review and approval at the local level by the organizational review committee and at the departmental level by the Ethical Advisory Board. The Ethical Advisory Board may prescribe additional duties for the consent committee. These changes are incorporated in § 46.305. In view of this drastic change in concept of the committee, detailed discussion of the many excellent and often thought-provoking comments concerned with details of the original draft seems inappropriate.

E. Many critical comments were addressed to the definitions used in this subpart, specifically:

1. "Pregnancy." It was suggested that pregnancy should be defined (i) conceptually to begin at the time of fertilization of the ovum, and (ii) operationally by actual test unless the woman has been surgically rendered incapable of pregnancy.

While the Department has no argument with the conceptual definition as proposed above, it sees no way of basing regulations on the concept. Rather, in order to provide an administerable policy, the definition must be based on existing medical technology which permits confirmation of pregnancy. This approach is reflected by § 46.303(c).

2. "Viability of the Fetus". Many recommendations were received concerning the definition of viability of the fetus after premature delivery or abortion. Some respondents urged that presence of fetal heartbeat be definitive (whether or not there is respiration) while others urged that identifiable cortical activity be specified as an alternative sign of viability. The Department has concluded that the issue of viability is a function of technological advance, and therefore must be decided with reference to the medical realities of the present time. We reserve the option of redefining the parameters as conditions warrant.

Only upon the basis of a definition which is both precise and consistent with current medical capability can a regulation realistically be interpreted and enforced. Current technology is such that a fetus, given the benefit of available medical therapy, cannot survive unless the lungs can be inflated so that respiration can take place. Without this capability, even if the heart is beating, the fetus is nonviable. In the future, if technology has advanced to the point of sustaining a fetus with non-inflatable lungs, the definition can and should be modified.

The Department has therefore chosen to specify, in the definition of viability of the fetus (§ 46.303(e)), that heart beat and respiration are, jointly, to be the indicator of viability.

3. "Abortus." Various comments noted that this definition is more restrictive than the usual medical definition of the abortus as a "nonviable fetus," and suggested substitution of the broader definition.

The Department proposes to retain the original definition for the purposes of these regulations. There is general agreement that there are distinct ethical problems involved in decisions concerning research use of the intact fetus, or use of organs or tissues obtained from a fetus that has died *in utero* or from an abortus at autopsy. The definition recurs with minor editorial changes in § 46.303(f).

F. Several comments were critical of the draft regulation's provisions limiting activities involving pregnant women to those not adversely affecting the fetus, except where the primary purpose of the activity was to benefit the fetus. It was suggested that the regulations (i) should contain language permitting exceptions for research necessary to meet the health needs of the mother, and (ii) should grant the right to participate in research aimed at improvement of methods of abortion, birth control, and genetic intervention.

The Department concurs with the first suggestion, (i), and proposes that the regulations permit research whose primary interest is to benefit the particular fetus or to respond to the health needs of the pregnant woman. It does not fully accept the second suggestion, (ii), and proposes that the regulations permit fetal research concerned with diagnosis and prevention of perinatal disease, and to offset the effects of genetic abnormality or congenital injury, but only when such research is done as part of a procedure properly performed to terminate a pregnancy. These changes are incorporated into § 46.306(a). The Department has tentatively concluded that consideration of risk vs. benefit with respect to fetal research does not seem to be appropriate.

G. Draft regulation provisions required maternal consent and the consent of the father if he were available and capable of participating in the consent process. This provision was strongly criticized on the grounds that it could permit the father of the fetus to deny needed health care to the woman or to the fetus even though he had no marital obligations, and that it might result in undue delay in the delivery of health care. It was also pointed out that the regulation did not touch on the question of the validity of consent by a pregnant minor.

The Department agrees. It is now proposed that paternal consent be sought only if the activity is not responding to the health needs of the pregnant woman and the father is reasonably available. These changes are reflected by § 46.306(b).

H. The Department has provisionally chosen, in § 46.306(a), to permit research to be undertaken from which there will be risk of harm to the fetus if such research is conducted as part of the abortion procedure. This decision, upon which we invite comment, has been made in the expectation that such research may produce new technology which will enable countless premature infants to live who now cannot.

It is not intended that this provision be construed to permit fetal research in anticipation of abortion prior to the commencement of the termination procedure itself.

While it is true that the class of fetuses for whom abortion is contemplated will be placed at greater research risk than all fetuses in general, such risk can arise only after implementation of the double safeguard of parental consent to the contemplated abortion, and second parental consent to the research procedure itself.

I. Comments regarding activities involving the abortus were concerned with the issue of maintaining vital functions and signs. It was argued that maintaining vital functions at the level of the organ, tissue, or cell is essential to studies and involves no prolongation of the dying of the abortus. At the same time, it was argued that termination of the heart beat should not be prohibited since temporary cardiac arrest has proved essential in the development of surgical techniques necessary to correct congenital heart defects.

Neither of these objections appear valid and no significant changes in § 46.307 are proposed. However, in order to emphasize again the distinction between research with the whole fetus or abortus, functioning as an organism with detectable vital signs, and with the dead fetus or abortus, the Department has added § 46.308, concerning activities involving a dead fetus or abortus, and § 46.309, concerning the abortus as an organ or tissue donor. Also § 46.307(d) has been expanded to permit the artificial maintenance of vital functions of an abortus where the purpose is to develop new methods for enabling the abortus to survive to the point of viability.

The Department feels that there is evident distinction between "termination" and "arrest" of the clinical signs as applied to the fetus or premature infant, but that no such distinction is valid or applicable where the abortus is concerned.

### PRISONERS

Forty-seven responses spoke to the provisions regarding additional protection for prisoners involved as subjects. Of these, two were from individuals identifying themselves as prisoners, seven were from State correctional institutions or State agencies, and four were from representatives of the pharmaceutical industry.

A. In comments directed at the overall nature of the draft regulations providing additional protection for prisoners, approximately equal numbers of respondents (i) denied that any significant additions were necessary, and (ii) proposed either the exclusion of prisoners from any research or experimentation not intended for the personal benefit of a prisoner, or highly restrictive regulations to accomplish the same purpose.

The Department, having reviewed these comments, has not been persuaded that any change should be made in the initial proposal.

B. A number of comments were concerned with the relationship between the existing organizational review committees and the proposed Protection Committee. It was pointed out by several that, as proposed, the two committees would not only have overlapping functions and authority but could operate independently of each other with conflicting directives and objectives that would not practicably provide additional protection of prisoners used as subjects.

The Department, recognizing the importance of preserving the authority of the organizational review committee as the primary institutional focus for the implementation of the Department of Health, Education, and Welfare regulations, proposes to assign to the organizational review committee the additional duties specified under § 46.404(a).

A committee auxiliary to the organizational review committee, now designated the consent committee, will have the character and responsibilities specified in § 46.406. In keeping with this modified position it should be noted that when the organizational review committee determines that an activity would involve no risk or negligible risk to any prisoner while serving as a subject, the organization may request the Secretary to consider a modification or waiver of the requirement for a consent committee.

C. Comments on the proposed prohibition of research involvement of persons awaiting arraignment, trial, or sentencing expressed doubts that these individuals should be denied the benefits of innovative procedures, particularly those concerned with sociological research.

The Department agrees that the uniform exclusion of any such person from research should not be mandatory and proposes to permit his participation in an activity as a subject when the risk is negligible and the intent of the activity is therapeutic for him or relates to the nature of his confinement. This modification is incorporated into § 46.406.

D. The draft requirement for DHEW accreditation of prison facilities as sites for the performance of research, development, and related activities involving prisoner subjects was severely criticized, principally because of the jurisdictional problems inherent in any attempt to impose a Federal regulatory requirement on an autonomous State facility.

The Department concludes that this draft proposal was ill-advised. However, in order to attain the objective on an activity basis, certain specific prerequisites for the protection of prisoner subjects within facilities have been added to § 46.404(a) to properly relate conditions in a facility to the issue of undue inducements to participation by prisoners as subjects in an activity.

MENTALLY DISABLED

Over 40 of the responses spoke directly to the section of the draft concerned with the "mentally infirm." Many of these objected initially to the use of the word "infirm" as reflecting an antiquated notion of mental illness.

The Department agrees, and proposes to substitute "disabled" for "infirm," though noting that there is no clearly preferable collective term for the groups described.

A. Comments on the purpose of this section expressed satisfaction with the intent to provide additional protection for this group but dissatisfaction with the actual language employed. Specifically, they noted that not institutionalization but rather the limitation of personal rights and freedom imposed by institutionalization is the determining issue. Similarly, it is not only the potential subject's difficulty in comprehending risks that is at issue, but his ability to comprehend generally.

The Department concurs. Proposed changes in language are incorporated in § 46.52.

B. Many of the respondents objected to one or more of the definitions peculiar to this subpart. The criticisms and the Department's proposed changes are as follows:

1. "Mentally infirm." In addition to requesting substitution of another term for "infirm," respondents raised conflicting objections to the definition's coverage. Some felt that it was overly inclusive; others felt it was too narrow. Some felt that epileptics should be specifically included, as well as those who are temporarily or permanently mentally incapacitated as a result of a physical condition such as stroke, brain damage, trauma, etc.

The Department, having carefully reviewed these comments, proposes no basic change in the definition. It concurs with many reviewers in the opinion that the definition is broad enough to include any category of subjects proposed for specific addition. Minor editorial changes have been made in § 46.503(b).

2. "Institutionalized." Commentators noted that (i) the regulations should cover all mentally disabled persons regardless of institutionalization, (ii) not all involuntary commitments are by order of a court, (iii) the draft refers to "residence" and "confinement" in similar contexts, though the terms do not carry the same connotation, and (iv) the definition does not specify halfway houses, lodges, day/night hospitals, nursing homes, and psychiatric wards of hospitals as places where subjects might be institutionalized.

The Department notes that (i) the non-institutionalized mentally disabled are covered by the existing regulations published as 39 FR 18914 and need not be included under these additional protections. Such individuals are not necessarily subject to all limitations on their freedom and rights as described in § 46.502 of this proposed rulemaking. Consideration will be given, however, to dealing with the noninstitutionalized legally incompetent who are mentally disabled in a subsequent notice of proposed rulemaking. With regard to (ii), the implication that court orders are the sole basis for involuntary confinement is incorrect and should be removed. Editorial changes have been made in § 46.503 to emphasize that concern therein is with those "* * * confined * * * in a residential institution * * *" (see iii) and, in order to designate the type of institutions concerned (see iv), it is proposed to separately define "Institutionalized mentally disabled individuals" in § 46.503 to include examples of such institutions. These changes are incorporated in § 46.503(c) and § 46.503(d).

C. While most respondents endorsed the intent of the draft limitations on activities involving the institutionalized mentally disabled, there were several specific criticisms of the terms used. Several persons suggested that any limitation of research to that related to a particular subject's "impairment" be worded so as to include any illness from which the person suffers so that, for example, an institutionalized mentally disabled person with cancer could not be denied the benefits of research in cancer therapy.

Further, this limitation could exclude the use of such subjects as controls in research which might benefit those suffering from a mental disability other than the specific one from which a particular subject suffers. Still further, mentally disabled people should be involved as subjects in research on infirmities other than their own because of lack of knowledge of the causes of mental and emotional disorders.

Many respondents felt that there was inadequate recognition of the need for research with the mentally disabled on basic psychological processes (e.g., learning, perception, and cognitive functions) which are fundamental to the study of the treatment, etiology, pathogenesis, prevention, and treatment of such disabilities.

The Department agrees that the language of the draft limiting research to the disease entities affecting individual subjects is probably not in the interests of the institutionalized mentally disabled as a class. The Department does not agree that it would be appropriate to permit this class of subjects to be involved in research unrelated to the causes, nature, or circumstances of their institutionalization. While there are possible disadvantages to the institutionalized mentally disabled inherent in this restriction, the possible risks of using the mentally disabled in such research outweigh its advantages. The proposed changes are incorporated in § 46.504(a). Editorial changes are reflected in § 46.504 (b) and § 46.504(c).

D. Criticisms of the draft's suggestion of the establishment or a protection committee in connection with each activity conducted in an institution for the mentally retarded were similar to those aimed at the protection committee to be established in connection with research on the pregnant woman and on the fetus. The Department proposes to change the title of the committee to "consent committee" and to change the regulations governing size, composition, and operating rules to conform to those previously described for § 46.305. Such changes are incorporated in § 46.506.

E. With respect to § 46.603(b), the Department reserves the right to amend this section if legislation now being developed by the Executive Branch on the safe guarding of individually linked data used for statistical and research purposes is enacted.

Written comments concerning the proposed regulation are invited from interested persons. Inquiries may be addressed and data, views, and arguments relating to the proposed regulations may be presented in writing, in triplicate, to the Chief, Institutional Relations Branch, Division of Research Grants, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20014. All comments received will be available for inspection at the National Institutes of

Health, Room 303, Westwood Building, 5333 Westbard Avenue, Bethesda, Maryland, weekdays (Federal holidays excepted) between the hours of 9:00 a.m. and 4:30 p.m. All relevant material received on or before November 21, 1974 will be considered.

Notice is also given that it is proposed to make any amendments that are adopted effective upon publication in the FEDERAL REGISTER.

Dated: August 15, 1974.

CASPAR W. WEINBERGER,
*Secretary.*

It is therefore proposed to amend Part 46 of Subtitle A of Title 45 of the Code of Federal Regulations by:

1. Revising §§ 46.19 through 46.22 and renumbering them as §§ 46.603 through 46.606, reading as set forth in Subpart F below.

2. Designating §§ 46.1 through 46.18 as Subpart A, renumbering these §§ 46.101 through 46.118, and modifying all references thereto accordingly.

3. Reserving Subpart B.

4. Adding the following new Subparts C through F.

**Subpart C—Additional Protections Pertaining to Biomedical Research, Development, and Related Activities Involving Fetuses, Abortuses, Pregnant Women, and In Vitro Fertilization**

Sec.
46.301 Applicability.
46.302 Purpose.
46.303 Definitions.
46.304 Ethical Advisory Board.
46.305 Establishment of a consent committee.
46.306 Activities involving fetuses *in utero* or pregnant women.
46.307 Activities involving abortuses.
46.308 Activities involving a dead fetus or abortus.
46.309 Activities involving the abortus as an organ or tissue donor.
46.310 Activities to be performed outside the United States.

**Subpart D—Additional Protections Pertaining to Activities Involving Prisoners as Subjects**

46.401 Applicability.
46.402 Purpose.
46.403 Definitions.
46.404 Additional duties of the organizational review committee where prisoners are involved.
46.405 Establishment of a consent committee.
46.406 Special restrictions.
46.407 Activities to be performed outside the United States.

**Subpart E—Additional Protections Pertaining to Activities Involving the Institutionalized Mentally Disabled as Subjects**

46.501 Applicability.
46.502 Purpose.
46.503 Definitions.
46.504 Activities involving the institutionalized mentally disabled.
46.505 Additional duties of the organizational review committee where the institutionalized mentally disabled are involved.
46.506 Establishment of a consent committee.
46.507 Activities to be performed outside the United States.

**Subpart F—General Provisions**

46.601 Applicability.
46.602 Multiple consent committee requirements.
46.603 Organization's record; confidentiality.
46.604 Reports.
46.605 Early termination of awards; evaluation of subsequent applications.
46.606 Conditions.
46.607 Activities conducted by Department employees.

AUTHORITY: 5 U.S.C. 301.

**Subpart C—Additional Protections Pertaining to Biomedical Research, Development, and Related Activities Involving Fetuses, Abortuses, Pregnant Women, and In Vitro Fertilization**

**§ 46.301 Applicability.**

(a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare grants and contracts supporting biomedical research, development, and related activities involving: (1) the fetus *in utero*, (2) the abortus, as that term is defined in § 46.303, (3) pregnant women, and (4) *in vitro* fertilization. In addition, these regulations are applicable to all such activities involving women who could become pregnant, except where the applicant or offeror shows to the satisfaction of the Secretary that adequate steps will be taken in the conduct of the activity to avoid involvement of women who are pregnant.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will in any way render inapplicable pertinent State or local laws bearing upon activities covered by this subpart.

(c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

**§ 46.302 Purpose.**

It is the purpose of this subpart to provide additional safeguards in reviewing activities to which this subpart is applicable to assure that they conform to appropriate ethical standards and relate to important societal needs.

**§ 46.303 Definitions.**

As used in this subpart.

(a) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(b) "Biomedical research, development, and related activities" means research, development, or related activities involving biological study (including but not limited to medical or surgical procedures, withdrawal or removal of body tissue or fluid, administration of chemical substances or input of energy, deviation from normal diet or hygiene, and manipulation or observation of bodily processes).

(c) "Pregnancy" encompasses the period of time from confirmation of implantation until delivery.

(d) "Fetus" means the product of conception from the time of implantation to the time of delivery.

(e) "Viability of the fetus" means the ability of the fetus, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. If the fetus has this ability, it is viable and therefore a premature infant.

(f) "Abortus" means a fetus when it is expelled whole, prior to viability, whether spontaneously or as a result of medical or surgical intervention. The term does not apply to the placenta: fetal material which is macerated at the time of expulsion; or cells, tissue, or organs excised from a dead fetus.

(g) "*In vitro* fertilization" means any fertilization of human ova which occurs outside the body of a female, either through admixture of donor sperm and ova or by any other means.

**§ 46.304 Ethical Advisory Board.**

(a) All applications or proposals for the support of activities covered by this subpart shall be reviewed by an Ethical Advisory Board, established by the Secretary within the National Institutes of Health, which shall advise the funding agency concerning the acceptability of such activities from an ethical standpoint.

(b) Members of the Board shall be so selected that the Board will be competent to deal with medical, legal, social, and ethical issues and shall include, for example, research scientists, physicians, lawyers, and clergy and/or ethicists, as well as representatives of the general public. No Board member may be a regular, full-time employee of the Federal Government.

**§ 46.305 Establishment of a consent committee.**

(a) Except as provided in paragraph (c) of this section, no activity covered by this subpart may be supported unless the applicant or offeror has provided an assurance acceptable to the Secretary that it will establish a consent committee (as provided for in the application or offer and approved by the Secretary) for each such activity, to oversee the actual process by which individual consents required by this subpart are secured, to monitor the progress of the activity and intervene as necessary, and to carry out such other duties as the Secretary (with the advice of the Ethical Advisory Board) may prescribe. The duties of the consent committee may include:

(1) Participation in the actual selection process and securing of consents to assure that all elements of a legally effective informed consent, as outlined in § 46.3, are satisfied. Depending on what may be prescribed in the application or offer approved by the Secretary, this might require approval by the committee of individual participation in the activity or it might simply call for verification (e.g., through sampling) that procedures prescribed in the approved application or offer are being followed.

(2) Monitoring the progress of the activity. Depending on what may be prescribed in the application or offer approved by the Secretary, this might

include: visits to the activity site, identification of one or more committee members who would be available for consultation with those involved in the consent procedure (i.e., participants) at the participant's request, continuing evaluation to determine if any unanticipated risks have arisen and that any such risks are communicated to the participants, periodic contact with the participants to ascertain whether they remain willing to continue in the activity, providing for the withdrawal of any participants who wish to do so, and authority to terminate participation of one or more participants with or without their consent where conditions warrant.

(b) The size and composition of the consent committee must be approved by the Secretary, taking into account such factors as: (1) the scope and nature of the activity; (2) the particular subject groups involved; (3) whether the membership has been so selected as to be competent to deal with the medical, legal, social, and ethical issues involved in the activity; (4) whether the committee includes sufficient members who are unaffiliated with the applicant or offeror apart from membership on the committee; and (5) whether the committee includes sufficient members who are not engaged in research, development, or related activities involving human subjects. The committee shall establish rules of procedure for carrying out its functions and shall conduct its business at convened meetings, with one of the members designated as chairperson.

(c) Where a particular activity, involving fetuses *in utero* or pregnant women, presents negligible risk to the fetus, an applicant or offeror may request the Secretary to modify or waive the requirement in paragraph (a) of this section. If the Secretary finds that the risk is indeed negligible and other adequate controls are provided, he may (with the advice of the Ethical Advisory Board) grant the request in while or in part.

(d) The requirements of this section and § 46.304 do not obviate the need for review and approval of the application or offer by the organizational review committee, to the extent required under Subpart A of this part.

**§ 46.306 Activities involving fetuses in utero or pregnant women.**

(a) No activity to which this subpart is applicable, involving fetuses *in utero* or pregnant women, may be undertaken unless: (1) the purpose of the activity is to benefit the particular fetus or to respond to the health needs of the mother, or (2) the activity conducted as part of (but not prior to the commencment of) a procedure to terminate the pregnancy and is for the purpose of evaluating or improving methods of prenatal diagnosis, methods of prevention of premature birth, or methods of intervention to offset the effects of genetic abnormality or congenital injury.

(b) Activities covered by this subpart which are permissible under paragraph (a) of this section may be conducted only if the mother and father are legally competent and have given their consent, except that the father's consent need not be secured if: (1) the purpose of the activity is to respond to the health needs of the mother or (2) his identity or whereabouts cannot reasonably be ascertained.

(c) Activities covered by this subpart which are permissible under paragraph (a) (2) of this section may not be undertaken unless individuals engaged in the research will have no part in: (1) any decisions as to the timing, method, or procedures used to terminate the pregnancy, and (2) determining the viability of the fetus at the termination of the pregnancy.

**§ 46.307 Activities involving abortuses.**

No activity to which this subpart is applicable, involving an abortus, may be undertaken unless:

(a) Appropriate studies on animals have been completed;

(b) The mother and father are legally competent and have given their consent, except that the father's consent need not be secured if his identity or whereabouts cannot reasonably be ascertained;

(c) Individuals engaged in the research will have no part in: (1) any decisions as to the timing, method, or procedures used to terminate the pregnancy, and (2) determining the viability of the fetus at the termination of the pregnancy;

(d) Vital functions of an abortus will not be artificially maintained except where the purpose of the activity is to develop new methods for enabling the abortus to survive to the point of viability; and

(e) Experimental procedures which would terminate the heart beat or respiration of the abortus will not be employed.

**§ 46.308 Activities involving a dead fetus or abortus.**

Activities involving a dead fetus or abortus shall be conducted in accordance with any applicable State or local laws governing autopsy.

**§ 46.309 Activities involving the abortus as an organ or tissue donor.**

Activities involving the abortus as an organ or tissue donor shall be conducted in accordance with any applicable State or local laws governing transplantation or anatomical gifts.

**§ 46.310 Activities to be performed outside the United States.**

Activities to which this subpart is applicable, to be conducted outside the United States, are subject to the requirements of this subpart, except that the consent procedures specified herein may be modified if it is shown to the satisfaction of the Secretary that such procedures, as modified, are acceptable under the laws and regulations of the country in which the activities are to be performed and that they comply with the requirements of Subpart A of this part.

## Subpart D—Additional Protections Pertaining to Activities Involving Prisoners as Subjects

**§ 46.401 Applicability.**

(a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare grants and contracts supporting research, development, and related activities involving prisoners as subjects.

(b) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

**§ 46.402 Purpose.**

It is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable, inasmuch as, because of their incarceration, they may be under constraints which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate in such activities.

**§ 46.403 Definitions.**

As used in this subpart:

(a) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(b) "Prisoner" means any individual involuntarily confined in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute and also individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution.

**§ 46.404 Additional duties of the organizational review committee where prisoners are involved.**

(a) In addition to the responsibilities prescribed for such committees under Subpart A of this part, the applicant's or offeror's organizational review committee shall, with respect to activities covered by this subpart, carry out the following additional duties:

(1) Determine that there will be no undue inducements to participation by prisoners as subjects in the activity, taking into account such factors as whether the earnings, living conditions, medical care, quality of food, and amenities offered to participants in the activity would be better than those generally available to the prisoners;

(2) Determine that (i) all aspects of the activity would be appropriate for performance on nonprisoners, or (ii) the activity involves negligible risk to the subjects and is for the purpose of studying the effects of incarceration on such subjects;

(3) Determine that the application or proposal contains adequate procedures for selection of subjects, securing consents, monitoring continued subject participation, and assuring withdrawal with-

out prejudice, in accordance with § 46.405 of this subpart;

(4) Determine that rates of remuneration are consistent with the anticipated duration of the activity, but not in excess of that paid for other employment generally available to inmates of the facility in question, and that withdrawal from the project for medical reasons will not result in loss of anticipated remuneration; and

(5) Carry out such other responsibilities as may be assigned by the Secretary.

(b) Applicants or offerors seeking support for activities covered by this subpart must provide for the designation of an organizational review committee, subject to approval by the Secretary, where no such committee has been established under Subpart A of this part.

(c) No award may be issued until the applicant or offeror has certified to the Secretary that the organizational review committee has made the determinations required under paragraph (a) of this section.

### § 46.405 Establishment of a consent committee.

(a) Except as provided in paragraph (c) of this section, no activity covered by this subpart may be supported unless the applicant or offeror has provided an assurance acceptable to the Secretary that it will establish a consent committee (as provided for in the application or offer and approved by the organizational review committee and the Secretary) for each such activity, to oversee the actual process by which individual subjects are selected and their consents secured, to monitor the progress of the activity (including visits to the activity site on a regular basis) and the continued willingness of the subjects to participate, to intervene on behalf of one or more subjects if conditions warrant, and to carry out such other duties as the Secretary may prescribe. The duties of the consent committee may include:

(1) Participation in the actual process by which individual subjects are selected and their consents secured to assure that all elements of a legally effective informed consent, as outlined in section 46.3 of this part, are satisfied. Depending on what may be prescribed in the application or offer approved by the Secretary, this might require approval by the committee of each individual's participation as a subject in the activity or it might simply call for verification (e.g., through sampling) that procedures prescribed in the approved application or offer are being followed.

(2) Monitoring the progress of the activity and the continued willingness of subjects to participate. Depending on what may be prescribed in the application or offer approved by the Secretary, this might include: visits to the activity site, identification of one or more committee members who would be available for consultation with subjects at the subjects' request, continuing evaluation to determine if any unanticipated risks have arisen and that any such risks are communicated to the subjects, periodic contact with the subjects to ascertain whether they remain willing to continue in the study, providing for the withdrawal of any subjects who wish to do so, and authority to terminate participation of one or more subjects with or without their consent where conditions warrant.

(b) The size and composition of the consent committee must be approved by the Secretary, taking into account such factors as: (1) the scope and nature of the activity; (2) the particular subject groups involved; (3) whether the membership has been so selected as to be competent to deal with the medical, legal, social, and ethical issues involved in the activity; (4) whether the committee includes a prisoner or a representative of an organization having as a primary concern protection of prisoners' interests; (5) whether the committee includes sufficient members who are unaffiliated with the applicant or offeror apart from membership on the committee; and (6) whether the committee includes sufficient members who are not engaged in research, development, or related activities involving human subjects. The committee shall establish rules of procedure for carrying out its functions and shall conduct its business at convened meetings, with one of its members designated as chairperson.

(c) Where a particular activity involves negligible risk to the subjects, an applicant or offeror may request the Secretary to modify or waive the requirement in paragraph (a) of this section. If the Secretary finds that the risk is indeed negligible and other adequate controls are provided, he may grant the request in whole or in part.

### § 46.406 Special restrictions.

Persons detained in a correctional facility pending arraignment, trial, or sentencing or in a hospital facility for pre-arraignment, pre-trial, or pre-sentence diagnostic observation are excluded from participation in activities covered by this subpart, unless (a) the organizational review committee finds that the particular activity involves only negligible risk to the subjects and (b) the activity is therapeutic in intent or relates to the nature of their confinement.

### § 46.407 Activities to be performed outside the United States.

Activities to which this subpart is applicable, to be conducted outside the United States, are subject to the requirements of this subpart, except that the consent procedures specified herein may be modified if it is shown to the satisfaction of the Secretary that such procedures, as modified, are acceptable under the laws and regulations of the country in which the activities are to be performed and that they comply with the requirements of Subpart A of this part.

## Subpart E—Additional Protections Pertaining to Activities Involving the Institutionalized Mentally Disabled as Subjects

### § 46.501 Applicability.

(a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare grants and contracts supporting research, development, and related activities involving the institutionalized mentally disabled as subjects.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will necessarily result in a legally effective consent under applicable State or local law to a subject's participation in such an activity; nor in particular does it obviate the need for court approval of such participation where court approval is required under applicable State or local law in order to obtain a legally effective consent.

(c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

### § 46.502 Purpose.

It is the purpose of this subpart to provide additional safeguards for the protection of the institutionalized mentally disabled involved in activities to which this subpart is applicable, inasmuch as: (a) they are confined in an institutional setting where their freedom and rights are potentially subject to limitation; (b) they may be unable to comprehend sufficient information to give an informed consent, as that term is defined in § 46.103; and (c) they may be legally incompetent to consent to their participation in such activities.

### § 46.503 Definitions.

As used in this subpart:

(a) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(b) "Mentally disabled" includes those institutionalized individuals who are mentally ill, mentally retarded, emotionally disturbed, or senile, regardless of their legal status or basis of institutionalization.

(c) "Institutionalized" means confined, whether by voluntary admission or involuntary commitment, in a residential institution for the care or treatment of the mentally disabled.

(d) "Institutionalized mentally disabled individuals" includes but is not limited to patients in public or private mental hospitals, psychiatric patients in general hospitals, inpatients of community mental health centers, and mentally disabled individuals who reside in halfway houses or nursing homes.

### § 46.504 Activities involving the institutionalized mentally disabled.

Institutionalized mentally disabled individuals may not be included in an activity covered by this subpart unless:

(a) The proposed activity is related to the etiology, pathogenesis, prevention, diagnosis, or treatment of mental disability or the management, training, or rehabilitation of the mentally disabled and seeks information which cannot be obtained from subjects who are not institutionalized mentally disabled;

(b) The individual's legally effective informed consent to participation in the

activity or, where the individual is legally incompetent, the informed consent of a representative with legal authority so to consent on behalf of the individual has been obtained; and

(c) The individual's assent to such participation has also been secured, when in the judgment of the consent committee he or she has sufficient mental capacity to understand what is proposed and to express an opinion as to his or her participation.

**§ 46.505 Additional duties of the organizational review committee where the institutionalized mentally disabled are involved.**

(a) In addition to the responsibilities prescribed for such committees under Subpart A of this part, the applicant's or offeror's organizational review committee shall, with respect to activities covered by this subpart, carry out the following additional duties:

(1) Determine that all aspects of the activity meet the requirements of § 46.50 (a) of this subpart;

(2) Determine that there will be no undue inducements to participation by individuals as subjects in the activity, taking into account such factors as whether the earnings, living conditions, medical care, quality of food, and amenities offered to participants in the activity would be better than those generally available to the mentally disabled at the institutions;

(3) Determine that the application or proposal contains adequate procedures for selection of subjects, securing consents, protecting confidentiality, and monitoring continued subject participation, in accordance with § 46.506 of this subpart; and

(4) Carry out such other responsibilities as may be assigned by the Secretary.

(b) Applicants or offerors seeking support for activities covered by this subpart must provide for the designation of an organizational review committee, subject to approval by the Secretary, where no such committee has been established under Subpart A of this part.

(c) No award may be issued until the applicant or offeror has certified to the Secretary that the organizational review committee has made the determinations required under paragraph (a) of this section.

**§ 46.506 Establishment of a consent committee.**

(a) Except as provided in paragraph (c) of this section, no activity covered by this subpart may be supported unless the applicant or offeror has provided a separate assurance acceptable to the Secretary that it will establish a consent committee (as provided for in the application or offer and approved by the organizational review committee and the secretary) for each such activity, to oversee the actual process by which individual subjects are selected and consents required by this subpart are secured, to monitor the progress of the activity (including visits to the activity site on a regular basis) and the continued willingness of the subjects to participate, to intervene on behalf of one or more subjects if conditions warrant, and to carry out such other duties as the Secretary may prescribe. The duties of the consent committee may include:

(1) Participation in the actual process by which individual subjects are selected and their consents secured to assure that all elements of a legally effective informed consent, as outlined in § 46.3, are satisfied. Depending on what may be prescribed in the application or offer approved by the Secretary, this might require approval by the committee of each individual's participation as a subject in the activity or it might simply call for verification (e.g., through sampling) that procedures prescribed in the approved application or offer are being followed.

(2) Monitoring the progress of the activity and the continued willingness of subjects to participate. Depending on what may be prescribed in the application or offer approved by the Secretary, this might include: visits to the activity site, identification of one or more committee members who would be available for consultation with subjects at the subjects' request, continuing evaluation to determine if any unanticipated risks have arisen and that any such risks are communicated to the subjects, periodic contact with the subjects to ascertain whether they remain willing to continue in the study, providing for the withdrawal of any subjects who wish to do so, and authority to terminate participation of one or more subjects with or without their consent where conditions warrant.

(b) The size and composition of the consent committee must be approved by the Secretary, taking into account such factors as: (1) the scope and nature of the activity; (2) the particular subject groups involved; (3) whether the membership has been so selected as to be competent to deal with the medical, legal, social, and ethical issues involved in the activity; (4) whether the committee includes sufficient members who are unaffiliated with the applicant or offeror apart from membership on the committee; and (5) whether the committee includes sufficient members who are not engaged in research, development, or related activities involving human subjects. The committee shall establish rules of procedure for carrying out its functions and shall conduct its business at convened meetings, with one of its members designated as chairperson.

(c) Where a particular activity involves negligible risk to the subjects, an applicant or offeror may request the Secretary to modify or waive the requirement in paragraph (a) of this section. If the Secretary finds that the risk is indeed negligible and other adequate controls are provided, he may grant the request in whole or in part.

**§ 46.507 Activities to be performed outside the United States.**

Activities to which this subpart is applicable, to be conducted outside the United States, are subject to the requirements of this subpart, except that the consent procedures specified herein may be modified if it is shown to the satisfaction of the Secretary that such procedures, as modified, are acceptable under the laws and regulations of the country in which the activities are to be performed and that they comply with the requirements of Subpart A of this part.

## Subpart F—General Provisions

**§ 46.601 Applicability.**

Sections 46.602 through 46.606 are applicable to all grant or contract supported activities covered by this part.

**§ 46.602 Multiple consent committee requirements.**

Where an application or proposal would involve human subjects covered by more than one consent committee requirement imposed under this part, upon approval by the Secretary, these multiple requirements may be satisfied through use of a single consent committee appropriately constituted to take account of the nature of the subject group.

**§ 46.603 Organization's records; confidentiality.**

(a) Copies of all documents presented or required for initial and continuing review by the organization's review committee or consent committee, such as committee minutes, records or subjects' consent, transmittals on actions, instructions, and conditions resulting from committee deliberations addressed to the activity director, are to be retained by the organization, subject to the terms and conditions of grant and contract awards.

(b) Except as otherwise provided by law, information in the records or possession of an organization acquired in connection with an activity covered by this part, which information refers to or can be identified with a particular subject, may not be disclosed except:

(1) With the consent of the subject or his legally authorized representative; or

(2) As may be necessary for the Secretary to carry out his responsibilities under this part in the exercise of oversight for the protection of such subject or class of subjects.

**§ 46.604 Reports.**

Each organization with an approved assurance shall provide the Secretary with such reports and other information as the Secretary may from time to time prescribe.

**§ 46.605 Early termination of awards; evaluation of subsequent applications.**

(a) If, in the judgment of the Secretary, an organization has failed materially to comply with the terms of this policy with respect to a particular Department of Health, Education, and Welfare grant or contract, he may requre that said grant or contract be terminated or suspended in the manner prescribed in applicable grant or procurement regulations.

(b) In evaluating proposals or applications for support of activities covered by this part, the Secretary may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) whether the offeror or applicant has been subject to a termination or suspension under paragraph (a) of this section, (2) whether the offeror or applicant or the person who would direct the scientific and technical aspects of an activity has in the judgment of the Secretary failed materially to discharge his, her, or its responsibility for the protection of the rights and welfare of subjects and (3) whether, where past deficiencies have existed in discharging such responsibility, adequate steps have in the judgment of the Secretary been taken to eliminate these deficiencies.

§ 46.606 Conditions.

The Secretary may with respect to any grant or contract or any class of grants or contracts impose additional conditions prior to or at the time of any award when in his judgment such conditions are necessary for the protection of human subjects.

§ 46.607 Activities conducted by Department employees.

The regulations of this part (except for this subpart) are applicable as well to all research, development, and related activities conducted by employees of the Department of Health, Education and Welfare, except that: (a) subpart C is applicable only to biomedical research, development, and related activities and (b) each agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint.

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## DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

### Office of the Secretary

[ 45 CFR Part 46 ]

### PROTECTION OF HUMAN SUBJECTS

### Correction of Preamble to Proposed Policy

In the August 23, 1974 issue of the FEDERAL REGISTER (39 FR 30648), the Department of Health, Education, and Welfare published a notice of proposed rulemaking governing research, development, and related activities, supported by the Department, involving the fetus, abortus, pregnant women, in vitro fertilization, prisoners, and the institutionalized mentally disabled.

After publication the following errors were noted in the preamble to the proposed rulemaking:

(1) The initial three paragraphs of Section C on page 30650 fail to indicate that, because of the Department's concern about the ethical issues surrounding in vitro fertilization (whether or not implantation is contemplated), the proposed rulemaking would require that all activities involving in vitro fertilization be reviewed by the Ethical Advisory Board prior to funding. In order to make clear this concern these paragraphs have been revised to read as follows:

* * * * *

C. A number of respondents recommended that the policy governing in vitro fertilization be strengthened, on the one hand, or liberalized, on the other. The Department has considered these recommendations, and concluded that while it is necessary to impose certain restraints, it is contrary to the interests of society to set permanent restrictions on research which are based on the successes and limitations of current technology. Therefore, the Department would expect the Ethical Advisory Board, which must review all applications involving in vitro fertilization (whether or not implantation is contemplated) to weigh, with respect to specific proposals, the state of the art, legal issues, community standards, and the availability of guidelines to govern each research situation. In sum, if there is a possibility that the conceptus might be sustained in vitro beyond the earliest stages of development, the Ethical Advisory Board is to consider this possibility, and determine what guidelines should govern decisions affecting that fetus, if the research is to be permitted. If, on the other hand, implantation is attempted and achieved, then regulations governing the fetus in utero shall apply.

* * * * *

(2) Several sentences were inadvertently omitted from the first and second paragraphs of the discussion of "Viability of the Fetus" in the first column on page 30651. These sentences are now inserted and as revised, the paragraphs read as follows:

2. "Viability of the Fetus." Some respondents suggested specific criteria such as birth weight, crown-rump length, or gestational age, similar to those used in England, such criteria to be reviewed and reissued periodically by the Department. It was emphasized that the use of such objective criteria might simplify problems involved in determining what types of research might be permissible. Some respondents urged that presence of fetal heartbeat be definitive (whether or not there is respiration) while others urged that identifiable cortical activity be specified as an alternative sign of viability. Others objected strenuously to any distinction as to the nature of fetal life, holding that the physician's obligation should be the same to any fetus regardless of weight, size, or age of gestation.

The Department, having reviewed these comments, concludes that the distinction between a viable and a nonviable fetus is both valid and meaningful. At the same time, the Department does not believe that the use of weight, size, gestational age and/or cortical activity is a valid substitute for the judgment of a physician, particularly in view of the wide variation in the facilities and arts available to him both in this country and abroad. The Department further concludes that the issue of viability is a function of technological advance [see § 46.303(e) of the regulations], and therefore must be decided with reference to the medical realities of the present time, while reserving the right to redefine the parameters as conditions warrant."

* * * * *

(3) Section H on page 30651 incorrectly implies that, under the proposed rulemaking, fetuses for which abortion is contemplated may be placed at greater risk than fetuses in general. In fact, however, as is stated already in section F on page 30651, the proposed rulemaking bans the undertaking of research, development, or related activities involving the fetus prior to the commencement of the abortion procedure, at which point the question of risk to the fetus is no longer an issue. Such activities which are permitted under the regulations would be reviewed by the Ethical Advisory Board prior to funding. Section H should therefore be deleted and section I on the same page relettered section H.

Dated: October 21, 1974.

CASPAR W. WEINBERGER,
*Secretary.*

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