DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health


AGENCY: Office for Protection from Research Risks, National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: On November 10, 1997, the Office for Protection from Research Risks (OPRR), in consultation with the Food and Drug Administration (FDA), requested written comments relating to the proposed republication of the list that identifies certain research activities involving human subjects which may be reviewed by the Institutional Review Board (IRB) through the expedited review procedure authorized in 45 CFR Part 46.110. The comment period closed on March 10, 1998. OPRR and FDA received a combined total of 108 comments. After a review of the comments, OPRR and FDA are now simultaneously publishing identical revised lists of categories of research activities that may be reviewed by the IRB through the expedited review procedure.

EFFECTIVE DATES: The revised list is effective as of November 9, 1998.

FOR FURTHER INFORMATION CONTACT: Michele Russell-Einhorn, Director of Regulatory Affairs, Office for Protection from Research Risks (OPRR), National Institutes of Health, 6100 Executive Blvd., Suite 3B01, Rockville, MD 20892-7507 or telephone (301) 435-6036.

SUPPLEMENTARY INFORMATION: The Federal Policy (Common Rule) for the Protection of Human Subjects was published in the Federal Register on June 18, 1991 (56 FR 28003) and is available at http://www.hhs.gov/ohrp/policy/index.html. The Common Rule is codified at 45 CFR 46.102. The Office of Protection from Research Risks (OPRR) of the National Institutes of Health (NIH) is responsible for implementing the Common Rule.

On November 10, 1997, the Office for Protection from Research Risks (OPRR), in consultation with the Food and Drug Administration (FDA), requested written comments relating to the proposed republication of the list that identifies certain research activities involving human subjects which may be reviewed by the Institutional Review Board (IRB) through the expedited review procedure authorized in 45 CFR 46.110. The comment period closed on March 10, 1998. OPRR and FDA received a combined total of 108 comments. After a review of the comments, OPRR and FDA are now simultaneously publishing identical revised lists of categories of research activities that may be reviewed by the IRB through the expedited review procedure. The revised list is effective as of November 9, 1998.

The comments received in response to the OPRR and FDA proposed revision of the 1981 expedited review list that was published on November 10, 1997 (62 FR 60607) overwhelmingly supported the proposed revision of the list. Three commenters suggested that there should be no expedited review available at all. OPRR and FDA disagree with these three comments and believe that expedited review is an appropriate part of the IRB review process. In addition, a deletion of the expedited review process would require a regulatory change to Section 110 which is beyond the scope of this revision. Several commenters suggested changing the scope of this revision. Several commenters suggested changing the scope of this revision.

Section 110 of the Federal Policy provides for expedited review procedures for certain categories of research involving no more than minimal risk, and for minor changes in approved research. This section gives the Secretary, HHS, the authority to amend and republish the expedited review list as needed after consultation with the departments and agencies that are subject to the Federal Policy. The expedited review list that is referenced in the Federal Policy was originally published by the Secretary, HHS in 1981 (46 FR 8392, 46 FR 8980). It listed categories of research that could be reviewed by the IRB through an expedited review procedure. The FDA also references an expedited review list (21 CFR Part 56) for matters under FDA's jurisdiction. The HHS and FDA lists have differed slightly, in that item nine (9) on the 1981 HHS expedited review list regarding certain types of behavioral research is not included in the list referenced in 21 CFR 56.110.

The comments received in response to the OPRR and FDA proposed revision of the 1981 expedited review list that was published on November 10, 1997 (62 FR 60607) overwhelmingly supported the proposed revision of the list. Three commenters suggested that there should be no expedited review available at all. OPRR and FDA disagree with these three comments and believe that expedited review is an appropriate part of the IRB review process. In addition, a deletion of the expedited review process would require a regulatory change to Section 110 which is beyond the scope of this revision. Several commenters suggested changing the scope of this revision. Several commenters suggested changing the scope of this revision.
The following discussion summarizes the 108 comments received and the resulting changes. In response to over forty comments, the introductory paragraph to the 1981 list has been reformatted into five general principles. The parenthetical in the introductory sentence in the 1981 list “(carried out through standard methods)” has been deleted in response to comments that this phrase served no particular purpose.

The reformatted general principles are set forth in paragraphs (A) through (F). Paragraph (C) makes it clear that the IRB must consider, for all categories, whether identification of the subjects or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. OPRR does not consider this to be a new or additional consideration. These concerns have always been an implicit part of the determination of whether an activity is a minimal risk activity. The words “insurability” and “be stigmatizing” have been added and are designed to serve as an aid to IRBs when genetic research is presented for review in an expedited review procedure. These changes were made in response to concerns raised in several comments that genetic testing may have consequences beyond those normally considered by the IRB.

Consistent with two comments, paragraph (D) prohibits expedited review for classified research involving human subjects. This is also in accordance with a March 27, 1997 Presidential Memorandum which proposed the elimination of an expedited review procedure for all classified research involving human subjects.

Paragraph (E) serves as a reminder to IRBs that informed consent and expedited review are two totally separate issues. This responds to concerns that allowing an increase in the scope of research eligible for expedited review would result in more waivers of informed consent. Research reviewed pursuant to an expedited review procedure is not necessarily eligible for waiver or alteration of informed consent. All research, whether reviewed by the full IRB or by way of expedited review, must conform to the applicable regulations for obtaining and documenting prospective informed consent, unless the research meets the conditions for waiving, excepting, or otherwise altering the informed consent requirements that are set forth in 45 CFR 46.116 and 117, 21 CFR 50.23 and 24, or 21 CFR 56.109(c).

Category one (1) preserves category ten (10) on the 1981 list. It also contains a new sentence that addresses the availability of the expedited review procedure for marketed drugs in research as well as specific citations in response to five comments that raised questions about these issues. The following changes have been made to category two (2) in response to over 45 comments which supported enhanced expedited review concerning collection of blood, but which suggested certain refinements. Collection of blood now includes finger stick, heel stick, or ear stick as well as venipuncture. The four proposed subcategories were recombined as two separate subcategories. The critical issues to be considered by the IRB include weight, physical condition, and amount of blood to be drawn. The first subcategory (a) concerns healthy nonpregnant adults. The second subcategory, (b), concerns all other adults and children. For this second subcategory, the IRB will need to make certain judgments including: consideration for the age, weight, and health of the subjects in light of the amount of blood to be collected, the frequency with which it will be collected, and the collection procedure. The final sentence of subcategory (b) reads: For these individuals, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more than 2 times per week. While an expedited review of research involving pregnant women is permissible under the revised section, this last sentence makes it clear that the amount of blood that can be drawn is subject to limitations greater than those on healthy nonpregnant adults. Also, in response to public comment, the phrase “medically vulnerable adults” that was proposed in November 1997 has been deleted.

In response to more than 24 comments, category three (3) (previously category one (1) in the 1981 list) has been changed in the following manner. The words “noninvasive means” have been added to clarify the manner of collection of research materials; and, the procedures outlined are set out as examples to the IRB of the types of procedures that could fall within this category. Category four (4) and five (5) on the proposed list have been combined into one new category five (5) on the 1998 list. This new section is added in response to comments that raised questions about the relationship of proposed categories four (4) and five (5) to exempt research and about separating out existing and prospectively collected materials. The term “nonresearch purposes” was maintained in new category five (5) to describe the origins of the research materials. An explanatory note has been added to categories five (5) and seven (7) to clarify that some research described in these categories may be exempt from IRB review under 45 CFR 46.101(b) of the HHS regulations for the protection of human subjects (there is no comparable exemption provision in the FDA regulations). Thus, the listing of those categories refers only to nonexempt research.

Category six (6), proposed in November 1997, is now category four (4) on the 1998 list and addresses the collection of data through noninvasive procedures. The words “noninvasive procedures” have been added and apply to all procedures that would fall within this category. Because of several comments that raised concerns about MRIs and the use of anesthesia and sedation, expedited review would not be allowed for any procedure employing either of these. In response to more than 24 comments, this category lists procedures as examples for the IRB of the types of procedures that would qualify for expedited review.

Category seven (7) on the list proposed in November 1997 is now category four (4) on the 1998 list and deals with the collection of data from voice, digital, or image recordings. The qualification that was proposed in November of 1998 requiring consideration of certain risks to subjects is now a general guiding principle. It has been incorporated into the general Applicability section in response to several comments that questioned limiting this consideration to this type of research.

Category eight (8) on the proposed list is now category seven (7) on the revised list. In response to over 30 comments, the following changes have been made. The word “stress” has been deleted; the subsections in the proposed list have been combined; research on oral history was separated out. In response to approximately six comments; and specific research and research techniques have been noted. As in new category six (6), the qualification that requires consideration of certain kinds of risks to subjects has been deleted as it is now a general guiding principle for these types of research.

Category nine (9) on the proposed list received more than 50 comments.
explicitly applauding this additional category. It has been divided into two
categories. Category eight (8) identifies three situations in which research that
is greater than minimal risk and has been initially reviewed by the convened
IRB, could undergo subsequent continuing review by the expedited
review procedure. New category nine (9) concerns continuing review of research
that is not greater than minimal risk but had to undergo initial review by a
convened IRB because it did not meet the criteria of categories two (2) through
seven (7) on the list.

Certain other minimal changes have been made for editorial purposes or to
clarify certain words that were used in the proposed list. Accordingly, the list
of categories of research which may be reviewed by the IRB through the
expedited review procedure is amended as set forth below.

Categories of Research That May Be Reviewed by the Institutional Review
Board (IRB) Through an Expedited
Review Procedure

Applicability

(A) Research activities that (1) present
no more than minimal risk to human
subjects, and (2) involve only
procedures listed in one or more of the
following categories, may be reviewed
by the IRB through the expedited review
procedure authorized by 45 CFR 46.110
and 21 CFR Part 110. The activities listed
should not be deemed to be of minimal
risk simply because they are included
on this list. Inclusion on this list merely
means that the activity is eligible for
review through the expedited review
procedure when the specific
circumstances of the proposed research
involve no more than minimal risk to
human subjects.

(B) The categories in this list apply
regardless of the age of subjects, except
as noted.

(C) The expedited review procedure
may not be used where identification of
the subjects and/or their responses
would reasonably place them at risk of
criminal or civil liability or be damaging
to the subjects’ financial standing,
employability, insurability, reputation,
or be stigmatizing, unless reasonable
and appropriate protections will be
implemented so that risks related to
invasion of privacy and breach of
confidentiality are no greater than
minimal.

(D) The expedited review procedure
may not be used for classified research
involving human subjects.

(E) IRBs are reminded that the
standard requirements for informed
consent (or its waiver, alteration, or
exception) apply regardless of the type
of review—expedited or convened—
utilized by the IRB.

(F) Categories one (1) through seven
(7) pertain to both initial and continuing
IRB review.

Research Categories

(1) Clinical studies of drugs and
medical devices only when condition
(a) or (b) is met.

(a) Research on drugs for which an
investigational new drug application (21
CFR Part 312) is not required. (Note:
Research on marketed drugs that
significantly increases the risks or
decreases the acceptability of the risks
associated with the use of the product
is not eligible for expedited review.)

(b) Research on medical devices for
which (i) an investigational device
exemption application (21 CFR Part
812) is not required; or (ii) the medical
device is cleared/approved for
marketing and the medical device is
being used in accordance with its
cleared/approved labeling.

(2) Collection of blood samples by
finger stick, heel stick, ear stick, or
venipuncture as follows:

(a) from healthy, nonpregnant adults
who weigh at least 110 pounds. For
these subjects, the amounts drawn may
not exceed 550 ml in an 8 week period
and collection may not occur more
frequently than 2 times per week; or
(b) from other adults and children,2
considering the age, weight, and health
of the subjects, the collection procedure,
the amount of blood to be collected, and
the frequency with which it will be
collected. For these subjects, the
amount drawn may not exceed the lesser of
50 ml or 3 ml per kg in an 8 week period
and collection may not occur more
frequently than 2 times per week.

(3) Prospective collection of biological
specimens for research purposes by
noninvasive means.

Examples: (a) Hair and nail clippings
in a nondisfiguring manner; (b)
deciduous teeth at time of exfoliation or
if routine patient care indicates a need
for extraction; (c) permanent teeth if
routine patient care indicates a need
for extraction; (d) excreta and external
secretions (including sweat); (e)
uncannulated saliva collected either in
an unstimulated fashion or stimulated
by chewing gumbase or wax or by
applying a dilute citric solution to the
tongue; (f) placenta removed at delivery;
(g) amniotic fluid obtained at the time
of rupture of the membrane prior to or
during labor; (h) supra- and subgingival
dental plaque and calculus, provided
the collection procedure is not more
invasive than routine prophylactic
scaling of the teeth and the process is
accomplished in accordance with
accepted prophylactic techniques; (i)
mucosal and skin cells collected by
buccal scraping or swab, skin swab, or
mouth washings; (j) sputum collected
after saline mist nebulization.

(4) Collection of data through
noninvasive procedures (not involving
general anesthesia or sedation) routinely
employed in clinical practice, excluding
procedures involving x-rays or
microwaves. Where medical devices are
employed, they must be cleared/approved
for marketing. (Studies intended to
evaluate the safety and effectiveness of
the medical device are not generally
eligible for expedited review, including
studies of cleared medical devices for
new indications.)

Examples: (a) Physical sensors that
are applied either to the surface of the
body or at a distance and do not involve
input of significant amounts of energy
into the subject or an invasion of the
subject’s privacy; (b) weighing or testing
sensory acuity; (c) magnetic resonance
imaging; (d) electrocardiography,
electroencephalography, thermography,
detection of natural radioactivity,
electroretinography, ultrasound, diagnostic
infrared imaging, doppler blood flow,
echocardiography; (e) moderate
exercise, muscular strength testing,
body composition assessment, and
flexibility testing where appropriate
given the age, weight, and health of the
individual.

(5) Research involving materials (data,
documents, records, or specimens) that
have been collected or will be collected
solely for nonresearch purposes (such as
medical treatment or diagnosis). (Note:
Some research in this category may be
exempt from the HHS regulations for the
protection of human subjects. 45 CFR
46.101(b)(4). This listing refers only to
research that is not exempt.)

(6) Collection of data from voice,
video, digital, or image recordings made
for research purposes.

(7) Research on individual or group
characteristics or behavior (including,
but not limited to, research on
perception, cognition, motivation,
identity, language, communication,
cultural beliefs or practices, and social

---

1 An expedited review procedure consists of a
review of research involving human subjects by
the IRB chairperson or by one or more experienced
reviewers designated by the chairperson from
among members of the IRB in accordance with the
requirements set forth in 45 CFR 46.110.

2 Children are defined in the HHS regulations as
“persons who have not attained the legal age for
counsel to treatments or procedures involved in
the research, under the applicable law of the
jurisdiction in which the research will be
conducted.” 45 CFR 46.402(a).
behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects 45 CFR 46.101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.)

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) Where no subjects have been enrolled and no additional risks have been identified; or

(c) Where the remaining research activities are limited to data analysis.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Gary B. Ellis,
Director, Office for Protection from Research Risks.

FOR PRIVACY ACT INFORMATION AND FOR FURTHER INFORMATION FROM SOURCE AGENCY CONTACT:
M.R. Taylor, Internal Revenue Service, Office of FedState Relations, 1111 Constitution Avenue, NW, Washington, DC 20224, telephone number (202) 622–5145 or Fax (202) 622–3041. (These are not toll-free numbers.)

REPORTING

In accordance with Pub. L. 100–503, the Computer Matching and Privacy Protection Act of 1988, as amended, and Office of Management and Budget (OMB), Bulletin 89–22, “Instructions on Reporting Computer Matching Programs to the Office of Management and Budget (OMB), Congress and the Public;” copies of this notice and report are being provided to the Committee on Government Reform and Oversight of the House of Representatives, the Committee on Governmental Affairs of the Senate, and the Office of Management and Budget.

AUTHORITY

The matching program will be conducted under the authority of section 6103(m)(2) of the Internal Revenue Code and 31 United States Code 3711, 3717 and 3718.

OBJECTIVES TO BE MET BY THE MATCHING PROGRAM

HUD expects that this computer matching program will enable it to quickly and effectively identify and locate individual debtors, and to obtain current mailing addresses of defaulted debtors.

RECORDS TO BE MATCHED

HUD will utilize its system of records entitled, Accounting Records, HUD/Dept-2. HUD will submit approximately 40,000 records annually of individuals with outstanding Federal debts for matching purposes. These records are extracted from the Privacy Act system of records, HUD/Dept-2, Accounting Records, maintained in the following programs and automated systems: (1) Title I—Debt Management Collection Systems; (2) Section 312—Loan Mortgage System; and (3) Departmental Claims—Delinquent Debt Control System. The IRS will extract taxpayer address information from Privacy Act System of Records: Individual Master File, Treas/IRS 24.030, maintained at the Martinsburg Computing Center, Martinsburg, WV. This file contains approximately 20 million records of taxpayers who have filed U.S. Individual Income Tax returns.