Place: Neuroscience Center, National Institutes of Health, 6001 Executive Blvd., Bethesda, MD 20892.

Open: January 19, 2001, 8:30 a.m. to adjournment.

Agenda: Presentation of NIMH Director's Report and discussion of NIMH program and policy issues.

Place: National Institute of Health, 9000 Rockville Pike, Building 31, Conference Room 6, Bethesda, MD 20892.

Contact Person: Jane A. Steinberg, PHD, Director, Division of Extramural Activities, National Institute of Mental Health, NIH, Neuroscience Center, 6001 Executive Blvd., Room 6154, MSC 9609, Bethesda, MD 20892–9609, 301–443–5047.

(Catalogue of Federal Domestic Assistance Program Nos. 93.242, Mental Health Research Grants; 93.281, Scientist Development Award, Scientist Development Award for Clinicians, and Research Scientist Award; 93.282, Mental Health National Research Service Awards for Research Training, National Institutes of Health, HHS)

Dated: December 4, 2000.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 00–31520 Filed 12–11–00; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institutes of Mental Health; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b((c)(6), Title 5 U.S.C., as amended. The contract proposals and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Mental Health Special Emphasis Panel.

Date: December 18, 2000.

Time: 1:30 p.m. to 3:30 p.m.

Agenda: To review and evaluate contract proposals.

Place: Neuroscience Center, National Institutes of Health, 6001 Executive Blvd., Bethesda, MD 20892 (Telephone Conference Call).

Contact Person: Michael J. Moody, Scientific Review Administrator, Division of Extramural Activities, National Institute of Mental Health, NIH, Neuroscience Center, 6001 Executive Blvd., Room 6154, MSC 9609, Bethesda, MD 20892–9609, 301–443–3367.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.242, Mental Health Research Grants; 93.281, Scientist Development Award, Scientist Development Award for Clinicians, and Research Scientist Award; 93.282, Mental Health National Research Service Awards for Research Training, National Institutes of Health, HHS)

Dated: December 4, 2000.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 00–31521 Filed 12–11–00; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Office of Biotechnology Activities; Recombinant DNA Research: Proposed Actions Under the NIH Guidelines

AGENCY: National Institutes of Health (NIH), PHS, DHHS.

ACTION: Notice of proposed actions under the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines).

SUMMARY: The NIH is proposing changes to the NIH Guidelines to enhance its oversight of human gene transfer research by making modifications to the reporting and analysis of serious adverse events in human gene transfer research studies. The purpose of this Notice is to inform the public about the proposed changes and to seek public comment on them. The proposed changes involve four main issues: (1) The scope and timing of serious adverse event reporting; (2) public access to information about serious adverse events; (3) protection of individually identifiable patient information as it relates to serious adverse event reporting; and (4) a new mechanism for the review and assessment of data on serious adverse events and other relevant safety information.

The NIH currently requires all serious adverse events to be reported immediately whether or not they are expected or considered to be associated with the gene transfer product. The first proposed change would require expedited reporting for those serious adverse events that are unexpected and considered possibly associated with the use of the gene transfer product. The proposed change also provides timeframes for expedited reporting and definitions of serious, associated, and unexpected adverse events. Under this proposal, other reportable serious adverse events would be included in annual reports.

The second proposed change would clarify that serious adverse event reports submitted to the NIH may not be classified as confidential information and that trade secret or other commercial confidential information should not be included in serious adverse event reports.

The third proposed change adds specific language to the NIH Guidelines to prohibit the submission of individually-identifiable patient information in serious adverse event reports.

The fourth and final change is the establishment of a working group of the NIH Recombinant DNA Advisory Committee (RAC), to be known as the NIH Gene Transfer Safety Assessment Board, that will be responsible for the review and analysis of serious adverse event reports and other relevant safety information in gene transfer research studies. The working group will report safety information to the RAC and information will, thereby, be disseminated to the scientific and patient communities and the public.

DATES: The public is encouraged to submit written comments on these proposed changes. Comments may be submitted to NIH Office of Biotechnology Activities (OBA) in paper or electronic form. Comments received on or before February 10, 2002 will be reproduced and distributed to the RAC for consideration at a future meeting to be announced.

All comments received in response to this notice will be considered by the NIH and will be available for public inspection in the NIH OBA office weekdays between the hours of 8:30 a.m. and 5 p.m.

FOR FURTHER INFORMATION: If you have questions, or require additional information about these proposed changes, please contact OBA by e-mail at oba@od.nih.gov, or telephone at 301–496–9838. Comments can be submitted to the same email address or by fax to 301–496–9839 or mail to the Office of Biotechnology Activities, National Institutes of Health, Building 1, Room 103, Bethesda, Maryland 20892.

For additional information about the RAC meeting at which these proposed changes will be deliberated, please visit the NIH/OBA Web site at: *http://www.nih.gov/od/oba/.*

SUPPLEMENTARY INFORMATION:

Introduction

NIH's oversight of human gene transfer research, especially its requirements for serious adverse event reporting in human gene transfer research, has been the subject of an in-depth, year-long, public debate and discussion. In September 1999, the RAC initiated a discussion relating to public access to serious adverse event reports. The RAC's interest in this issue was prompted by claims from several human gene transfer investigators and sponsors that serious adverse event reports were confidential, commercial information and, therefore, should not be made publicly available. In November, following the death of a participant in a human gene transfer research protocol—a death directly attributable to the study—a number of new concerns arose about the collection, analysis, and dissemination of gene transfer safety information. The RAC subsequently expanded its discussions to include the scope and timing of NIH reporting requirements for serious adverse events and investigator compliance with those requirements.

In December 1999, the NIH Director established the Advisory Committee to the Director (ACD) Working Group on NIH Oversight of Clinical Gene Transfer Research. The charge to this Working Group was to review the role of NIH in oversight of this area of research, including an assessment of protocol review, analysis of serious adverse event reports, and the interaction between the various Federal agencies and local oversight bodies involved in regulation and oversight of this research. The ACD Working Group met four times and issued a final report to the ACD, which concurred with the Working Group's recommendations. The ACD Working Group report is posted at the following URL:

The changes proposed in this Notice respond to recommendations made by the ACD and by the RAC. They also reflect the views expressed by patients, patient advocates, investigators, industry representatives, and professional associations regarding the purpose, public good, and appropriate scope of toxicity and safety data collection and dissemination in human gene transfer research subject to the NIH Guidelines.

Background

The NIH Guidelines (Appendix M–I–C–4) currently require immediate reporting of all serious adverse events to NIH OBA, the IBC, the IRB, and, if applicable, the Office for Human Research Protections. This NIH requirement for immediate reporting of all serious adverse events, whether or not they are associated with the gene transfer product, was added to the NIH Guidelines in 1990, shortly after human gene transfer studies began. Because gene transfer was a novel and untested area of clinical investigation and because of the potential risks, NIH determined, with advice from the RAC, that it would be prudent to collect information on all serious adverse events in these studies.

These and other provisions of the NIH Guidelines apply to NIH-funded as well as non-NIH-funded gene transfer projects that are conducted at or sponsored by an institution that receives NIH support for recombinant DNA research. All human gene transfer research studies are also subject to FDA regulations found in volume 21 of the Code of Federal Regulations (CFR), including specific requirements at 21 CFR 312.32 related to adverse events.

Roles and Responsibilities of NIH and FDA. The scope and timeframe of the serious adverse event reporting to the NIH and the FDA currently differ. As noted above, NIH requires immediate reporting of all serious adverse events. FDA requires expedited reporting of only those serious adverse events that are unexpected and considered possibly associated with the gene transfer product.

The two agencies also have different roles and responsibilities with respect to adverse event reports and initiate different, but complementary, processes in response to these reports. The FDA conducts an analysis of an adverse event(s) and related data and, if necessary, places the study, and others like it, on clinical hold until the safety issues have been adequately addressed. The FDA is required by law to maintain the confidentiality of all information connected with an investigational new drug (IND). In contrast, the reporting of serious adverse events to NIH enables the identification of trends in serious adverse events, the assessment of their significance for the safety of patients enrolled in similar human gene transfer studies, and public discussion by the RAC of important developments in the safety of human gene transfer research.

Confidentiality of Adverse Event Reports. In September 1999, the RAC initiated discussions regarding public access to serious adverse event information. This discussion was in response to several serious adverse event reports submitted to OBA which were labeled as confidential. The NIH has always acknowledged and affirmed the need to protect trade secret and other proprietary information, such as the details of a sponsor's manufacturing process, and this principle is accommodated in the NIH Guidelines. The concept that reports of serious adverse events should be considered from a commercial standpoint as confidential, however, is contrary to NIH's commitment to public access to information about the safety of human gene transfer research. Since the NIH Guidelines were not explicit about the confidentiality of serious adverse event reports, NIH OBA asked the RAC to consider whether the NIH Guidelines should be modified to clarify the requirement for public access to these reports. In response, the RAC issued the following consensus statement:

> Adverse event reports shall not be designated as confidential, either in whole or in part. Adverse event reports are essential to decision-making by IBCs, IRBs, and potential subjects of gene transfer research in humans. The public disclosure of adverse events is also essential to public understanding and evaluation of gene transfer in humans. Adverse event reports must be made available for public discussion without the inclusion of proprietary or trade secret information.

Compliance with NIH Adverse Event Reporting Requirements. Subsequent to the death of a participant in a human gene transfer research protocol, which was directly attributable to the study, NIH OBA called on investigators conducting related studies to submit comprehensive pre-clinical and clinical data from their trials. In the course of gathering and assessing this data, it became evident that serious adverse events were not being reported to OBA, as required by the NIH Guidelines. Concerted efforts were immediately initiated to ensure enhanced awareness of, and compliance with, the reporting requirements. NIH also proposed that the NIH Guidelines be amended to make the requirements for reporting serious adverse events more explicit. The proposed amendments were published for public comment in the November 22, 1999, **Federal Register** (64 FR 63827). The proposed amendments added explicit definitions and spelled out timeframes for immediate reporting of serious adverse events.

In response to the notice, NIH OBA received a wide range of public comments from investigators, sponsors, industry, and patient advocacy organizations. Some commenters expressed vigorous support for the requirement that all serious adverse events be reported to OBA immediately, arguing that the requirement was warranted for the same reasons it was established in the first place'the field

was still young and the manipulation of genetic material posed risks that were still not fully known or understood. Other commenters suggested that NIH harmonize its requirements with those of the FDA so that it would receive, on an expedited basis, only those serious adverse events that are unexpected and considered to be possibly associated with the gene transfer product, and, on an annual basis, a summary of adverse events that are expected or considered to have other causes such as disease progression or concurrent medications. According to these commenters, requiring the immediate submission of all serious adverse events was counter-productive given the priority that should be placed on events that are unexpected and considered to be possibly associated with the gene transfer product. Other commenters stated that reporting any serious adverse event to OBA was unnecessary because FDA receives such reports by law and has authority to stop trials when necessary for safety concerns. Given that most serious adverse events are associated with disease progression, not the experimental gene transfer product, some commenters expressed concern that reporting of all serious adverse events had the potential to mislead or confuse the public about the cause of adverse events. They argued that the reporting of all such events would give the public the wrong impression about the risks involved in human gene transfer research.

Members of the RAC also expressed differing views about the appropriate scope of reporting. At its December 10, 1999, meeting, the Committee did not reach a consensus on whether the proposed amendments making more explicit the requirement for immediate reporting of all serious adverse events should be adopted. Consideration of the proposed amendments was deferred pending further RAC deliberations. Moreover, as noted previously, the ACD Working Group, formed in early December 1999, was also charged with considering the issue of serious adverse event reporting in the context of its broader review of NIH's role in the oversight of human gene transfer studies.

After extensive deliberations, the ACD Working Group submitted a report to the NIH ACD which concluded that: (1) public discussion of serious adverse events is an important component of the NIH oversight process; (2) serious adverse events should not be considered trade secrets or proprietary; (3) serious adverse event data should be disseminated to the public in an analyzed and interpreted form; and (4) because FDA is unable to disclose information, NIH OBA should continue to receive reports of serious adverse events directly from investigators or sponsors. With regard to the scope of what should be reported, the ACD Working Group recommended that NIH and FDA work together to simplify, streamline, and harmonize reporting of serious adverse events. The ACD Working Group also agreed that all reasonable measures be taken to protect the privacy of the individual who experienced the adverse event, without compromising the health of others in similar trials.

In addition, the ACD Working Group affirmed the need to gather cumulative data on gene transfer trials to improve the conduct and overall safety of such research, noting that systematic analyses of adverse event data could reveal trends related to, for example, specific diseases, routes of administration, or vectors. In this regard, the ACD Working Group recommended that a new mechanism was needed for ongoing analyses of the nature and frequency of adverse events reported over time, analyses that would be made available to the RAC, FDA, scientific community, and public. They recommended that a standing expert body be established to conduct ongoing analyses of adverse event data. The standing expert body should include basic scientists, clinicians, patient advocates, and ethicists. Ad hoc members could be appointed to provide additional expertise on an as-needed basis. The standing body should review all reports of adverse events, analyze the data for trends, develop a cumulative report that should be presented annually at a public RAC meeting and made available to the public, and identify trends or even single events that may warrant further public discussion or Federal action.

In June 2000, the RAC reviewed the conclusions and recommendations of the ACD Working Group and, after engaging in further discussion about the appropriate timing and scope of serious adverse event reporting, endorsed the ACD Working Group recommendations by a unanimous vote. In September 2000, the full ACD reviewed and endorsed the recommendations of the Working Group at a publicly accessible teleconference.

The public deliberations of the ACD and the RAC affirmed the importance of NIH's role in ensuring the safety of human gene transfer research studies. This role differs from, and in important ways complements, the role of the FDA, which is to respond on a timely basis to serious, life-threatening, unexpected events that are associated with the investigational product. NIH's role is to gather information about the safety of the field in general and to disseminate that information to investigators and the public with the purpose and goal of developing a body of knowledge about the risks and benefits of this form of clinical investigation.

The NIH concurs with the need to harmonize Federal requirements for reporting serious adverse events and other safety information. With this action, NIH is proposing to amend the NIH Guidelines to require expedited reporting of serious adverse events that are unexpected and considered to be possibly associated with the use of the gene transfer product. The scope and timeframe for reporting these events and other safety information, as well as definitions used, would parallel those of the FDA as set forth in volume 21 of the CFR. Submission of a comprehensive summary of serious adverse event data will be required on an annual basis, again in harmony with the FDA requirements.

The comprehensive public review of serious adverse event data by the RAC is a critical component of Federal oversight of human gene transfer research. A systematic and publicly accountable review and assessment of toxicity and safety data from these trials over time is essential for identifying trends and recognizing patterns that may have important implications for the future development of human gene transfer research. In order to enhance NIH's ability to perform this critical function, and in accordance with the recommendations of the ACD, the NIH is proposing to establish a new mechanism for the review and assessment of serious adverse events. The specific proposed mechanism is a working group of the RAC, to be known as the NIH Gene Transfer Safety Assessment Board. The working group's specific functions would involve: (1) Reviewing serious adverse event reports, annual reports, and other relevant safety information and assessing toxicity and safety data across all gene transfer trials and analyzing the data for trends; (2) identifying significant trends or single events; (3) developing information that will enhance the development, design, and conduct of human gene transfer clinical trials; and (4) reporting aggregated data to the RAC to enhance review of new protocols and to enhance public understanding and awareness of the safety of human gene transfer research studies as well as the informed decision-making of potential trial participants. The working group would

be composed of government and non-governmental experts in relevant clinical specialties; pediatric, adult, and geriatric medicine; relevant basic science disciplines such as genetics, virology, and immunology; biostatistics; bioethics; and patient advocacy. The working group would include liaison representation from the FDA. The working group would consist of approximately 15 members, at least two of whom would be RAC members, appointed by the NIH Director. The working group would meet quarterly or more frequently if needed.

Patient safety is the utmost concern. NIH believes that the proposed changes will expand knowledge, advance the science and ethics of the field of human gene transfer research, and optimize NIH oversight of the field.

Proposed Amendments to the NIH Guidelines

Although the NIH has received a considerable amount of valuable advice and a range of perspectives from the public and advisory groups, NIH wishes to provide another opportunity for public comment before finalizing these proposed amendments regarding serious adverse event reporting. The specific proposed amendments to the NIH Guidelines are as follows: (1) Change the requirements for expedited reporting of serious adverse events; (2) clarify that trade secret or other commercial confidential information should not be included in serious adverse event reports and that serious adverse event reports may not be classified as confidential information; (3) add a new section prohibiting individually identifiable patient information from being included in serious adverse event reports; and (4) establish a working group of the RAC, to be known as the NIH Gene Transfer Safety Assessment Board, to be responsible for the review and analysis of serious adverse events and other relevant safety information in gene transfer research studies and dissemination of safety information to the RAC, and, thereby, to the scientific and patient communities, and the public.

A new Section I–E–8 is proposed to be added to read:

''Section I–E–8. A 'serious adverse event' is any event occurring at any dose that results in any of the following outcomes: Death, a life-threatening event, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization also may be considered a serious adverse event when, upon the basis of appropriate medical judgment, they may jeopardize the human gene transfer research subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.''

A new Section I–E–9 is proposed to be added to read:

''Section I–E–9. An adverse event is 'associated with the use of a gene transfer product,' when there is a reasonable possibility that the event may have been caused by the use of that product.''

A new Section I–E–10 is proposed to be added to read:

''Section I–E–10. An unexpected serious adverse event is any serious adverse event for which the specificity or severity is not consistent with the risk information currently available in the protocol.''

Section IV–B–7. Principal Investigator (PI) is modified to read:

Section IV–B–7. Principal Investigator (PI)

On behalf of the institution, the Principal Investigator is responsible for full compliance with the NIH Guidelines in the conduct of recombinant DNA research. A Principal Investigator engaged in human gene transfer research may delegate to another party, such as a corporate sponsor, the reporting functions set forth in Appendix M, with written notification to NIH OBA of the delegation and of how the delegate may be contacted. The Principal Investigator is responsible for ensuring that the reporting requirements are fulfilled and will be held accountable for any reporting lapses.''

Current M–I–C–3, Annual Reporting, is proposed to be modified proposed to read in its entirety:

Appendix M–I–C–3, Annual Reports

Within 60 days of the one-year anniversary of the date on which the clinical trial was initiated and of each subsequent anniversary until the trial is completed, the Principal Investigator (or delegate) shall submit a summary report of the progress of the investigation that includes:

(a) Clinical Trial Information. A brief summary of the status of each trial in progress and each trial completed during the previous year. The summary is required to include the following information for each trial: (1) The title and purpose of the trial; (2) clinical protocol identifiers, including the NIH OBA protocol number, NIH grant number(s) (if applicable), and the FDA IND application number; (3) participant population; (4) the status of the trial; (5) the total number of participants planned for inclusion in the trial; the number entered into the trial to date; the number whose participation in the trial was completed; and the number who dropped out of the trial for any reason; and (6) if the trial has been completed, a brief description of any study results.

(b) Progress Report and Data Analysis. Information obtained during the previous year's clinical and non-clinical investigations, including: (1) A narrative or tabular summary showing the most frequent and most serious adverse experiences by body system; (2) a summary of all serious adverse events submitted during the past year; (3) a summary of serious adverse events that are expected or considered to have causes not associated with the use of the gene transfer product such as disease progression or concurrent medications; (4) the number of participants who died during participation in the investigation and causes of death; (5) a brief description of any information obtained pertinent to an understanding of the gene transfer product's actions, including, for example, information about dose-response, information from controlled trials, and information about bioavailability.

(c) A copy of the updated clinical protocol including a technical and non-technical abstract.

Current Appendix M–I–C–4, Serious Adverse Event Reporting is proposed to be modified in its entirety to read:

Appendix M–I–C–4, Safety Reporting

Principal Investigators must submit, in accordance with this section, Appendix M–I–C–4–a and Appendix M–I–C–4–b, a written report on: (1) Any serious adverse event that is both unexpected and possibly associated with the use of the gene transfer product; and (2) any finding from tests in laboratory animals that suggests a significant risk for human research participants including reports of mutagenicity, teratogenicity, or carcinogenicity. The report must be clearly labeled as a ''Safety Report'' and must be submitted to the Office of Biotechnology Activities (OBA) and to the local Institutional Biosafety Committee within the timeframes set forth in Appendix M–I–C–4–b.

Principal Investigators should adhere to any other serious adverse event reporting requirements in accordance with Federal regulations, state laws, and local institutional policies and procedures, as applicable.

Principal Investigators may delegate to another party, such as a corporate sponsor, the reporting functions set forth in Appendix M, with written notification to NIH OBA of the delegation and of how the delegate may be contacted. The Principal Investigator is responsible for ensuring that the reporting requirements are fulfilled and will be held accountable for any reporting lapses.

The three alternative mechanisms for reporting serious adverse events to OBA are: by e-mail to oba@od.nih.gov; by fax to 301–496–9839; or by mail to the Office of Biotechnology Activities, National Institutes of Health, MSC 7010, 6000 Executive Boulevard, Suite 302, Bethesda, Maryland 20892–7010.

Appendix M–I–C–4–a, Safety Reporting: Content and Format

Reports of serious adverse events should follow the format provided in the Adverse Event Reporting Format available on NIH OBA's web site at: http://www.nih.gov/od/oba/. The serious adverse event report must include, but need not be limited to: (1) The date of the event; (2) designation of the report as an initial report or a follow-up report; (3) a complete description of the event; (4) relevant clinical observations; (5) relevant clinical history; (6) relevant tests that were or are planned to be conducted; (7) the suspected cause of the event; (8) gene delivery method; (9) vector type, *e.g.*, adenovirus; (10) vector subtype, *e.g.*, type 5, relevant deletions; (11) dosing schedule; (12) route of administration; (13) identification of all safety reports previously filed with the clinical protocol concerning a similar adverse event and an analysis of the significance of the adverse event in light of previous similar reports; (14) clinical site; (15) the principal investigator; (16) NIH Protocol number; and (17) FDA's Investigational New Drug (IND) Application number.

Serious adverse event reports must not contain individually identifiable patient information.

Reports from laboratory animal studies must be submitted in a narrative format.

Unless NIH OBA determines that there are exceptional circumstances, all information submitted in accordance with Appendix M–I–C will be considered public. Safety reports submitted in accordance with Appendix M–I–C will not be considered to contain any trade secret or commercial or financial information that is privileged or confidential as defined under the Freedom of Information Act, 5 U.S.C. 552.

Appendix M–I–C–4–b, Safety Reporting: Time-Frames for Expedited Reports

Any serious adverse event that is fatal or life-threatening, that is unexpected, and possibly associated with the use of the gene transfer product must be reported to NIH OBA as soon as possible, but not later than 7 calendar days after the sponsor's initial receipt of the information (*i.e.*, at the same time the event must be reported to the FDA).

Serious adverse events that are unexpected and possibly associated with the use of the gene transfer product, but are not fatal or life-threatening, must be reported to NIH OBA as soon as possible, but not later than 15 calendar days after the sponsor's initial receipt of the information (*i.e.*, at the same time the event must be reported to the FDA).

If, after further evaluation, an adverse event initially considered not to be possibly associated with the use of the gene transfer product is subsequently determined to be possibly associated, then the event must be reported to NIH OBA within 15 days of the determination.

Relevant additional clinical and laboratory data may become available following the initial serious adverse event report. Any follow-up information relevant to a serious adverse event must be reported within 15 calendar days of the sponsor's receipt of the information. If a serious adverse event occurs after the end of a clinical trial and is determined to be possibly associated with the use of the gene transfer product, that event shall be reported to NIH OBA within 15 calendar days of the determination.

Any finding from tests in laboratory animals that suggests a significant risk for human research participants including reports of mutagenicity, teratogenicity, or carcinogenicity must be reported as soon as possible, but not later than 15 calendar days after the sponsor's initial receipt of the information (*i.e.*, at the same time the event must be reported to the FDA).''

A new Appendix M–I–D is proposed to be added:

Appendix M-I-D, Safety Assessment in Human Gene Transfer Research

A standing working group of the RAC, the NIH Gene Transfer Safety Assessment Board, will: (1) Review serious adverse event reports, annual reports, and other relevant safety information made to OBA for the purpose of assessing toxicity and safety data across all gene transfer trials and analyzing the data for trends; (2) identify significant trends or single events; (3) develop information that will enhance the development, design, and conduct of human gene transfer clinical trials; and (4) report aggregated trend data to the RAC to enhance review of new protocols and to enhance public understanding and awareness of the safety of human gene transfer research studies as well as the informed decision-making of potential trial participants. The working group members are appointed by the NIH Director.''

Current Appendix M–IV. Privacy and Confidentiality is proposed to be amended by the addition of the following sentence at the end of the section:

Current Appendix M–IV. Privacy and Confidentiality

''* * * These measures should protect the confidentiality of information that could indirectly enable identification of study participants, as well as information that would directly identify study participants.''

OMB's ''Mandatory Information Requirements for Federal Assistance Program Announcements'' (45 FR 39592) requires a statement concerning the official government programs contained in the Catalog of Federal Domestic Assistance. Normally, NIH lists in its announcements the number and title of affected individual programs for the guidance of the public. Because the guidance in this notice covers virtually every NIH and Federal research program in which recombinant DNA techniques could be used, it has been determined not to be cost effective or in the public interest to attempt to list these programs. In addition, NIH could not be certain that every Federal program would be included as many Federal agencies, as well as private organizations, both national and international, have elected to follow the NIH Guidelines. In lieu of the individual program listing, NIH invites readers to direct questions to the information address above about whether individual programs listed in the Catalog of Federal Domestic Assistance are affected.

Dated: December 4, 2000.

Ruth L. Kirschstein,

Principal Deputy Director, National Institutes of Health.

[FR Doc. 00–31524 Filed 12–11–00; 8:45 am]

BILLING CODE 4140–01–P