# BLUE RIDGE ENVIRONMENTAL DEFENSE LEAGUE

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December 12, 2005

Stephen Johnson, EPA Administrator
c/o Public Information and Records Integrity Branch (PIRIB) (7502C)
Office of Pesticide Programs (OPP)
Environmental Protection Agency
1200 Pennsylvania Ave., NW., Washington, DC 20460- 0001
E-mail: opp-docket@epa.gov

**Attention: Docket ID Number OPP-2003-0132.**

Dear Mr. Johnson:

On behalf of the Blue Ridge Environmental Defense League, I write to comment on the proposed human testing rule change being considered by EPA. The rule promulgated under the Office of Pesticide Programs would have severe negative effects within the context of pesticide regulation. Further, the Agency acknowledges that the impact of this rule change would have implications for new rulemakings at other federal agencies. **But the rule cannot and must not be approved because it does not meet minimum standards of ethical medical practice**.

General Comments

First, the human testing rule is contrary to well-established jurisprudence:

*Qui in utero est pro jam nato habetur, quoties de ejus commodo quaeritur.*

That is, "He who is in the womb is held as already born, whenever his benefit is in question." Therefore, a fetus has the right to be born without being deliberately subjected to toxic pesticides or other harmful chemicals in the womb. This principle also applies to children and others who are mute, incompetent or otherwise unable to give their explicit, individual consent. The United States Environmental Protection Agency must not allow medical testing on anyone without express consent, nor by its actions or lack thereof give approval to others to perform unethical experiments which would form the basis for EPA regulations.

Second, the foundation for the rulemaking is economics, not public health. I draw your attention to some of the most troubling language in the proposed rule. According to the rules definitions, *"Research involving intentional exposure of a human subject means a study of an environmental substance in which the exposure to the substance experienced by a human subject participating in the study would not have occurred but for the human subject's participation in the study."* [Sec. 26.102(k) Definitions] If the proposed rule is approved, the substances to which human subjects would be exposed include about a dozen pesticide products which do not meet health

protective requirements of the Food Quality Protection Act. Therefore, the principal reason for the rule is the financial benefit for a few pesticide manufacturers who seek to justify the use of dangerous chemicals while safer alternatives exist. The industry juggernaut pushing this rule is led by CropLife America, a national trade association which challenged and halted EPA's announced intent to prohibit consideration of third-party studies based on unethical human testing [*CropLife America v. EPA*, 329 F.3d. 876 (D.C.Cir. 2003)]. Regional partners of CropLife include the Southern Crop Production Association whose membership includes 95 percent of the companies which "manufacture, formulate and distribute pesticide products in fifteen southern states." [website at http://www.southcrop.org] Croplife would have us believe that its products are tools for protecting public health, but pesticides represent a major threat to public health and to the environment, else they would not be regulated at all.

Specific Comments

**40 CFR § 26.221 Prohibition of EPA reliance on research involving intentional dosing of pregnant women, fetuses, or newborns**

Despite the title, the proposed rule would allow the EPA to rely on testing done on pregnant women; it would allow the Agency to accept studies funded and carried out by third parties for the purpose of future pesticide decision-making. The proposed rule states:

> In its regulatory decision-making under the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq.) or section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a), EPA shall not rely on any research involving intentional dosing of any pregnant women, fetuses, or newborns, except when such research is deemed scientifically sound and crucial to the protection of public health, under the procedure defined in Sec. 26.603. (emphasis added) [40 CFR § 26.221 Prohibition of EPA reliance on research involving intentional dosing of pregnant women, fetuses, or newborns]

As cited above in *qui in utero*, the intentional administration of toxic chemicals to the unborn cannot be "deemed sound" because no consent can be given and none may be inferred. If the EPA intended to prohibit such practice altogether, this clause would be unnecessary. To approve this rule would wrongly establish unethical practice in the Code of Federal Regulations.

**40 CFR § 26.401 To what do these regulations apply?**

This proposal under Part D, "Protections for Children Involved as Subjects in Research," would allow unethical research to be conducted or supported by EPA involving children in Asia, Africa, Europe, South America, Canada and Mexico. Section 40 CFR 26.401(a) outlines the rule's applicability and states:

> It also includes research conducted or supported by EPA outside the United States, but in appropriate circumstances, the Administrator may, under Sec. 26.101(e), waive the applicability of some or all of the requirements of these regulations for research of this type. [40 CFR 26.401 (a)(2)] (emphasis added)

What on earth are the "appropriate circumstances" which would prompt EPA to waive the

protections afforded to American children? There can be none; this clause is an affront to billions of children outside the United States.

**40 CFR § 26.408 Requirements for permission by parents or guardians and for assent by children**

Subpart D also details the obtaining of consent of children for research conducted or supported by EPA in the United States. But paragraph (a) authorizes an Institutional Review Board (IRB) to determine that consent is unnecessary if the children have limited capacity to understand what is to be done to them; it states:

> If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. [40 CFR § 26.408(a)]

Even if children are capable of giving their consent, the proposed rule allows the IRB to waive the requirement under certain circumstances. Here, the EPA carves a loophole through which children who are fully able to understand and agree may be subjected to research testing without their approval.

In paragraph (c) of this section, EPA specifically targets neglected or abused children for research testing, thereby subjecting those who have no parental protection to further abuse at the hands of the federal agency. The language of the proposed rule states:

> In addition to the provisions for waiver contained in Sec. 26.116, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, State or local law. [40 CFR § 26.408(c)]

What would be an "appropriate mechanism" for protecting neglected or abused children? I think it would be a good home and a caring guardian or a loving family member. The EPA should rule out neglected or abused children as subjects of research—period. Why would American society subject them to the possibility of further injury?

**40 CFR § 26.421 Prohibition of EPA reliance on research involving intentional dosing of children.**

The EPA relies heavily on research done by third parties for the setting of exposure limits to pesticides and for determining the safety of drugs and cosmetics. If such research is not in compliance with minimum ethical standards, the proposed rule provides EPA with a method for washing its hands of the matter. The rule states:

> In its regulatory decision-making under the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq.) or section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a), EPA shall not rely on any research involving intentional dosing of any child, except when such research is deemed scientifically sound and crucial to the protection of public health, under the procedure defined in Sec. 26.603. [40 CFR § 26.421] (emphasis added)

The proposed rule prohibits nothing with regard to intentional dosing of children so long as the research is "deemed sound." Within this context, what drug company would submit flawed research? What chemical company?

**40 CFR § 26.603 Exceptions for human research**

Subpart E centers on non-compliance and details certain administrative penalties for errant research institutions. However, the EPA's proposed rule would allow sub-standard research which intentionally exposes a pregnant woman, fetus, newborn, or child to be incorporated.

> Before reaching a decision not to rely on scientifically useful and relevant data derived from research that does not meet the applicable standards of Sec. Sec. 26.601 through 26.602, or that involves intentional exposure of a pregnant woman, fetus, newborn, or child, EPA will consider whether the data are crucial to a regulatory decision that would be more protective of public health than could be justified without relying on the data. [40 CFR § 26.603(a)] (emphasis added)

If and when sub-standard research were to be utilized, EPA could merely include a *discussion* of why the data was used despite public comments to the contrary.

> If EPA decides to rely on data derived from a study that does not meet the applicable standards of Sec. Sec. 26.601 through 26.602, EPA will include in the explanation of its decision a thorough discussion of the significant ethical deficiencies of the study, as well as the full rationale for concluding that relying on the study is crucial to protection of public health. [40 CFR § 26.603(c)] (emphasis added)

**Ethical Principles for Research**

The World Medical Association's Declaration of Helsinki* contains comprehensive guidance which should inform EPA as to the grievous error in its approach to this matter. The American Medical Association is listed as a member group of the WMA. I have included below seven of the principles which I believe should deter EPA from approving the proposed rules.

- 5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
- 6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease.
- 16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

- 20. The subjects must be volunteers and informed participants in the research project.

- 22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

- 24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

- 25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

In summary, the Declaration of Helsinki states that the welfare of the individual takes precedence over the needs of science, that medical research serves the needs of medicine—not industry, that all such research must be made freely available to the public, that consent must be informed and voluntary and able to be withdrawn, that risks and benefits are to be fully explained to the subject, that research on incompetent persons shall be for the direct benefit of those persons, and that consent must be obtained even from minor children.

The EPA must not proceed with the proposed rule as drafted.

Respectfully,

Louis Zeller

Attachment: proposed amendment to 40 CFR § 26

CC: Office of Information and Regulatory Affairs
Office of Management and Budget (OMB)
Attn: Desk Officer for EPA
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*End Note*
* World Medical Association, *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects* (2000), available at http://www.wma.net/e/policy/pdf/17c.pdf. The Declaration of Helsinki (Document 17.C) is an official policy document of the World Medical Association, the global representative body for physicians. It was first adopted in 1964 (Helsinki, Finland) and revised in 1975 (Tokyo, Japan), 1983 (Venice, Italy), 1989 (Hong Kong), 1996 (Somerset-West, South Africa) and 2000 (Edinburgh, Scotland).

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**Therefore, it is proposed that 40 CFR chapter I be amended as follows: [[Page 53863]] PART 26--[AMENDED]**

**1. By revising the authority citation for part 26 to read as follows**: Authority: 5 U.S.C. 301; 7 U.S.C. 136w(a)(1); 21 U.S.C. 346a(e)(1)(C); and 42 U.S.C. 300v-1(b).

**2. By redesignating Sec. Sec. 26.101 through 26.124 as subpart A and adding a new subpart heading to read as follows:** Subpart A--Basic Federal Policy for Protection of Human Research Subjects

**3. By amending Sec. 26.101 by adding paragraphs (j) and (k) to read as follows:** Sec. 26.101 To what does this policy apply? * * * * * (j) Except as provided in paragraphs (a) and (b) of this section, this policy applies to all research involving intentional exposure of a human subject if, at any time prior to initiating such research, any person who conducted or supported such research intended: (1) To submit results of the research to EPA for consideration in connection with any regulatory action that may be performed by EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq.) or section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a); or (2) To hold the results of the research for later inspection by EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq.) or section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a). (k) For purposes of determining a person's intent under paragraph (j) of this section, EPA may consider any available information relevant to determining the intent of a person who conducts or supports research with human subjects after the effective date of the rule. EPA shall rebuttably presume such intent existed if: (1) The person or the person's agent has submitted or made available for inspection the results of such research to EPA; or (2) The person is a member of a class of people who, or whose products or activities, are regulated by EPA under FIFRA or the FFDCA and, at the time the research was initiated, the results of the research would be relevant to EPA's exercise of its authority under FIFRA or the FFDCA with respect to that class of people, products, or activities.

**4. By amending Sec. 26.102 by adding paragraph (k) to read as follows:**
Sec. 26.102 Definitions. * * * * * (k) Research involving intentional exposure of a human subject means a study of an environmental substance in which the exposure to the substance experienced by a human subject participating in the study would not have occurred but for the human subject's participation in the study.

**5. By revising Sec. 26.124 to read as follows:** Sec. 26.124 Conditions. (a) With respect to any research project or any class of research projects the department or agency head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects. (b) Prior submission and review of proposed human research. Any person who intends to conduct human

research covered by Sec. 26.101(j) shall, after receiving approval from all appropriate IRBs, submit to EPA at least 90 days prior to initiating such research all information relevant to the proposed research specified by Sec. 26.115(a) to be prepared and maintained by an IRB, and the following additional information, to the extent not otherwise covered: (1) A discussion of: (i) The potential risks to human subjects; (ii) The measures proposed to minimize risks to the human subjects; (iii) The expected benefits of such research, and to whom they would accrue; (iv) Alternative means of obtaining information comparable to what would be collected through the proposed research; and (v) The distribution and balance of risks and benefits of the proposed research. (2) The information for subjects and written informed consent agreements as provided to the IRB, and as approved by the IRB. (3) Information about how subjects will be recruited, including any advertisements proposed to be used. (4) All correspondence between the IRB and the investigators or sponsors. (5) Following initial evaluation of the protocol by Agency staff, EPA shall submit the protocol and all supporting materials, together with the staff evaluation, to the Human Studies Review Board. This Board shall consist of members who are not employed by the Agency, who meet the ethics requirements for special government employees, and who have expertise in fields appropriate for review of human research. The Board shall review and comment on the scientific and ethical aspects of research proposals and reports of completed intentional dosing research with human subjects which EPA intends to rely on in its decision-making under FIFRA or FFDCA, and, on request, advise EPA on ways to strengthen its programs for protection of human subjects of research. (c) Submission of information pertaining to ethical conduct of completed human research. Any person who submits to EPA data derived from human research covered by this subpart shall also provide to EPA information documenting compliance with the requirements of this subpart. Such information should include: (1) Copies of all of the records relevant to the research specified by Sec. 26.115(a) to be prepared and maintained by an IRB. (2) Copies of sample records used to document informed consent as specified by Sec. 26.117, but not identifying any subjects of the research. (3) Copies of all correspondence, if any, between EPA and the researcher or sponsor pursuant to paragraph (b) of this section.

**6. By adding new subparts B through F to read as follows:**

Subpart B--Additional Protections for Pregnant Women, Fetuses, and Newborns Involved in Research Sec.
Sec. 26.201 To what do these regulations apply?
Sec. 26.202 Definitions.
Sec. 26.203 Duties of IRBs in connection with research involving pregnant women, fetuses, and neonates.
Sec. 26.204 Research involving pregnant women or fetuses.
Sec. 26.205 Research involving neonates.
Sec. 26.206 Research involving, after delivery, the placenta, the dead fetus, or fetal material.
Sec. 26.207-26.219 [Reserved]
Sec. 26.220 Prohibition of research involving intentional dosing of pregnant women, fetuses, or newborns.
Sec. 26.221 Prohibition of EPA reliance on research involving intentional dosing of pregnant women, fetuses, or newborns.

Subpart C--Additional Protections Pertaining to Research Involving Prisoners as Subjects [Reserved]

Subpart D--Additional Protections for Children Involved as Subjects in Research
Sec. 26.401 To what do these regulations apply?
Sec. 26.402 Definitions.
Sec. 26.403 IRB duties.
Sec. 26.404 Research not involving greater than minimal risk.
Sec. 26.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.
Sec. 26.406 [Reserved]
Sec. 26.407 [Reserved] [[Page 53864]]

## Subpart B--Additional Protections for Pregnant Women, Fetuses, and Newborns Involved in Research

Sec. 26.201 To what do these regulations apply? (a) Except as provided in paragraph (b) of this section, this subpart applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates conducted or supported by the Environmental Protection Agency (EPA). This includes all research conducted in EPA facilities by any person and all research conducted in any facility by EPA employees. This subpart also applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates covered by Sec. 26.101(j). (b) The exemptions at Sec. 26.101(b)(1) through (b)(6) are applicable to this subpart. (c) The provisions of Sec. 26.101(c) through (i) are applicable to this subpart. Reference to State or local laws in this subpart and in Sec. 26.101(f) is intended to include the laws of federally recognized American Indian and Alaska Native Tribal Governments. (d) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

Sec. 26.202 Definitions. The definitions in Sec. 26.102 shall be applicable to this subpart as well. In addition, the definitions at 45 CFR 46.202(a) through (f) and at 45 CFR 46.202(h) are applicable to this subpart. For purposes of this part, Administrator means the Administrator of the Environmental Protection Agency and any other officer or employee of the Environmental Protection Agency to whom authority has been delegated.

Sec. 26.203 Duties of IRBs in connection with research involving pregnant women, fetuses, and neonates. The provisions of 45 CFR 46.203 are applicable to this section.

Sec. 26.204 Research involving pregnant women or fetuses. The provisions of 45 CFR 46.204 are applicable to this section.

Sec. 26.205 Research involving neonates. The provisions of 45 CFR 46.205 are applicable to this section.

Sec. 26.206 Research involving, after delivery, the placenta, the dead fetus, or fetal material. The provisions of 45 CFR 46.206 are applicable to this section.

Sec. 26.207-26.219 [Reserved]

Sec. 26.220 Prohibition of research involving intentional dosing of pregnant women, fetuses, or newborns. Notwithstanding any other provision of this part, under no circumstances shall EPA or a person when covered by Sec. 26.101(j) conduct or support research involving intentional dosing of any pregnant woman, fetus, or newborn.

Sec. 26.221 Prohibition of EPA reliance on research involving intentional dosing of pregnant women, fetuses, or newborns. In its regulatory decision-making under the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq.) or section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a), EPA shall not rely on any research involving intentional dosing of any pregnant women, fetuses, or newborns, except when such research is deemed scientifically sound and crucial to the protection of public health, under the procedure defined in Sec. 26.603.

**Subpart C--Additional Protections Pertaining to Research Involving Prisoners as Subjects [Reserved]**

**Subpart D--Additional Protections for Children Involved as Subjects in Research**

Sec. 26.401 To what do these regulations apply? (a) This subpart applies to all research involving children as subjects, conducted or supported by EPA. This subpart also applies to all research involving children covered by Sec. 26.101(j). (1) This includes research conducted by EPA employees, except that each head of an Office of the Agency may adopt such nonsubstantive, procedural modifications as may be appropriate from an administrative standpoint. (2) It also includes research conducted or supported by EPA outside the United States, but in appropriate circumstances, the Administrator may, under Sec. 26.101(e), waive the applicability of some or all of the requirements of these regulations for research of this type. (b) Exemptions at Sec. 26.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at Sec. 26.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at Sec. 26.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed. (c) The exceptions, additions, and provisions for waiver as they appear in Sec. 26.101(c) through (i) are applicable to this subpart.

Sec. 26.402 Definitions. The definitions in Sec. 26.102 shall be applicable to this subpart as well. In addition, as used in this subpart: (a) Children are persons who have not attained the age of 18. (b) Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. (c) Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research. (d) Parent means a child's biological or adoptive parent. (e) Guardian means an individual who is authorized under applicable State, Tribal, or local law to consent on behalf of a child to general medical care.

Sec. 26.403 IRB duties. The provisions of 45 CFR 46.403 are applicable to this section.

Sec. 26.404 Research not involving greater than minimal risk. EPA will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the [[Page 53865]] permission of their parents or guardians, as set forth in Sec. 26.408.

Sec. 26.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. EPA will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds and documents that: (a) The risk is justified by the anticipated benefit to the subjects. (b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches. (c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in Sec. 26.408.

Sec. 26.406 [Reserved]

Sec. 26.407 [Reserved]

Sec. 26.408 Requirements for permission by parents or guardians and for assent by children. (a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with Sec. 26.116(d). (b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by Sec. 26.116, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under Sec. 26.404 or Sec. 26.405. (c) In addition to the provisions for waiver contained in Sec. 26.116, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in

the research is substituted, and provided further that the waiver is not inconsistent with Federal, State or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition. (d) Permission by parents or guardians shall be documented in accordance with and to the extent required by Sec. 26.117. (e) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented. Sec.

Sec. 26.409-26.419 [Reserved]

Sec. 26.420 Prohibition of research involving intentional dosing of children. Notwithstanding any other provision of this part, under no circumstances shall EPA or a person when covered by Sec. 26.101(j) conduct or support research involving intentional dosing of any child.

Sec. 26.421 Prohibition of EPA reliance on research involving intentional dosing of children. In its regulatory decision-making under the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq.) or section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a), EPA shall not rely on any research involving intentional dosing of any child, except when such research is deemed scientifically sound and crucial to the protection of public health, under the procedure defined in Sec. 26.603.

**Subpart E--Administrative Actions for Noncompliance**

Sec. 26.501 Lesser administrative actions. (a) If apparent noncompliance with the applicable regulations in subparts A through D of this part concerning the operation of an IRB is observed by a duly authorized investigator during an inspection, the inspector will present an oral or written summary of observations to an appropriate representative of the IRB. EPA may subsequently send a letter describing the noncompliance to the IRB and to the parent institution. The agency will require that the IRB or the parent institution respond to this letter within a time period specified by EPA and describe the corrective actions that will be taken by the IRB, the institution, or both to achieve compliance with these regulations. (b) On the basis of the IRB's or the institution's response, EPA may schedule a reinspection to confirm the adequacy of corrective actions. In addition, until the IRB or the parent institution takes appropriate corrective action, the Agency may: (1) Withhold approval of new studies subject to the requirements of this part that are conducted at the institution or reviewed by the IRB; (2) Direct that no new subjects be added to ongoing studies subject to this part; (3) Terminate ongoing studies subject to this part when doing so would not endanger the subjects; or (4) When the apparent noncompliance creates a significant threat to the rights and welfare of human subjects, notify relevant State and Federal regulatory agencies and other parties with a direct interest in the agency's action of the deficiencies in the operation of the IRB. (c) The parent institution is presumed to be responsible for the operation of an IRB, and EPA will ordinarily direct any administrative action under this subpart against the institution. However, depending on the evidence of responsibility for deficiencies, determined during the investigation, EPA may restrict its administrative actions to the IRB or to a component of the parent institution determined to be responsible for formal designation of the IRB.

Sec. 26.502 Disqualification of an IRB or an institution. (a) Whenever the IRB or the institution has failed to take adequate steps to correct the noncompliance stated in the letter sent by the Agency under Sec. 26.501(a) and the EPA Administrator determines that this noncompliance may justify the [[Page 53866]] disqualification of the IRB or of the parent institution, the Administrator may institute appropriate proceedings. (b) The Administrator may disqualify an IRB or the parent institution if the Administrator determines that: (1) The IRB has refused or repeatedly failed to comply with any of the regulations set forth in this part, and (2) The noncompliance adversely affects the rights or welfare of the human subjects of research. (c) If the Administrator determines that disqualification is appropriate, the Administrator will issue an order that explains the basis for the determination and that prescribes any actions to be taken with regard to ongoing human research, covered by subparts A through D of this part, conducted under the review of the IRB. EPA will send notice of the disqualification to the IRB and the parent institution. Other parties with a direct interest, such as sponsors and investigators, may also be sent a notice of the disqualification. In addition, the agency may elect to publish a notice of its action in the Federal Register. (d) EPA may refuse to consider in support of a regulatory decision the data from human research, covered by subparts A through D of this part, that was reviewed by a disqualified IRB or conducted at a disqualified institution, unless the IRB or the parent institution is reinstated as provided in Sec. 26.504, or unless such research is deemed scientifically sound and crucial to the protection of public health, under the procedure defined in Sec. 26.603.

Sec. 26.503 Public disclosure of information regarding revocation. A determination that EPA has disqualified an institution and the administrative record regarding that determination are disclosable to the public under 40 CFR part 2.

Sec. 26.504 Reinstatement of an IRB or an institution. An IRB or an institution may be reinstated if the Administrator determines, upon an evaluation of a written submission from the IRB or institution that explains the corrective action that the institution or IRB plans to take, that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in this part. Notification of reinstatement shall be provided to all persons notified under Sec. 26.501(c).

Sec. 26.505 Debarment. If EPA determines that an institution or investigator repeatedly has not complied with or has committed an egregious violation of the applicable regulations in subparts A through D of this part, EPA may recommend that institution or investigator be declared ineligible to participate in EPA-supported research (debarment). Debarment will be initiated in accordance with procedures specified at 40 CFR part 32.

Sec. 26.506 Actions alternative or additional to disqualification. Disqualification of an IRB or of an institution is independent of, and neither in lieu of nor a precondition to, other statutorily authorized proceedings or actions. EPA may, at any time, on its own initiative or through the Department of Justice, institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of, or after, disqualification. The Agency may also refer pertinent matters to another Federal, State, or local

government agency for any action that that agency determines to be appropriate. Subpart F--Ethical Standards for Assessing Whether to Rely on the Results of Human Research in EPA Regulatory Decisions

Sec. 26.601 Human research conducted prior to [effective date of the final rule]. Unless there is clear evidence that the conduct of that research was fundamentally unethical (e.g., the research was intended to seriously harm participants or failed to obtain informed consent), or was significantly deficient relative to the ethical standards prevailing at the time the research was conducted, EPA will generally accept and rely on relevant, scientifically valid data from research that: (a) Was initiated prior to [effective date of the final rule], (b) Involved intentional exposure of a human subject, (c) Did not involve intentional exposure of a pregnant woman, fetus, newborn, or child, and (d) Is being considered under the Federal Insecticide, Fungicide, and Rodenticide Act or the Federal Food, Drug, and Cosmetic Act.

Sec. 26.602 Human research conducted after [effective date of the final rule]. EPA will generally accept and rely on relevant, scientifically valid data from research that: (a) Was initiated after [effective date of the final rule], (b) Involved intentional exposure of a human subject, (c) Did not involve intentional exposure of a pregnant woman, fetus, newborn, or child, and (d) Is being considered under the Federal Insecticide, Fungicide, and Rodenticide Act or the Federal Food, Drug, and Cosmetic Act only if EPA has adequate information to determine that the research was conducted in a manner that substantially complies with subparts A through D of this part.

Sec. 26.603 Exceptions for human research. (a) Before reaching a decision not to rely on scientifically useful and relevant data derived from research that does not meet the applicable standards of Sec. Sec. 26.601 through 26.602, or that involves intentional exposure of a pregnant woman, fetus, newborn, or child, EPA will consider whether the data are crucial to a regulatory decision that would be more protective of public health than could be justified without relying on the data. (b) Before making a decision under this section, EPA will solicit the views of the Human Studies Review Board and provide an opportunity for public comment. (c) If EPA decides to rely on data derived from a study that does not meet the applicable standards of Sec. Sec. 26.601 through 26.602, EPA will include in the explanation of its decision a thorough discussion of the significant ethical deficiencies of the study, as well as the full rationale for concluding that relying on the study is crucial to protection of public health.
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