

III. EPA's Rulemaking Process and Request for Public Comment

EPA intends to undertake notice-and-comment rulemaking on the subject of its consideration of or reliance on research involving human subjects. The Agency will particularly focus on third-party intentional dosing human studies, but recognizes that the principles applicable to third-party studies may also be relevant to studies conducted or supported by the federal government. The first step in this process is this ANPR which calls for comments and suggestions from all interested parties. The next step the Agency would expect to undertake would be to issue a proposed rule for public comment. In developing any proposed rule, EPA will consider the advice in the National Academy of Sciences committee report, along with comments received in response to this ANPR. Comments received on any proposed rule would then be taken into consideration in developing a final rule or policy.

In general, the Agency expects that any rule or policy coming out of this process may do one or more of the following:

- Specify, if and to the extent determined by EPA to be appropriate, whether EPA would accept, consider, or rely on results from particular types of studies involving intentional dosing of human subjects or from human studies with particular characteristics.
- Establish minimum standards relating to the protection of human subjects which would be required to be met in the design and conduct of a study with human subjects, in order for EPA to accept, consider, or rely on the results of the study.
- Establish procedures for ensuring that any minimum standards for the conduct of third-party research with human subjects had been adhered to in the conduct of any such study that EPA intended to accept, consider, or rely on.

A. Legal Authority

Section 25(a) of FIFRA gives the Administrator authority to “prescribe regulations to carry out the purposes of [FIFRA].” Such a rule would implement EPA’s authority to require data in support of registration of pesticides (see, for example, FIFRA sections 3(c)(1)(F) and 3(c)(2)(B)) and to interpret the provision making it unlawful for any person “to use any pesticide in tests on human beings unless such human beings (i) are fully informed of the nature and purposes of the test and of any physical and mental health consequences which are reasonably foreseeable therefrom, and (ii) freely

volunteer to participate in the test.” (FIFRA section 12(a)(2)(P)). In addition, section 408(e)(1)(C) of the FFDCA authorizes the Administrator to issue a regulation establishing “general procedures and requirements to implement this section.”

The Clean Air Act gives EPA general rulemaking authority in 42 U.S.C. 7601(a). The Clean Water Act, 33 U.S.C. 1361, authorizes the Administrator to promulgate regulations necessary to carry out the Agency’s functions under that Act. Section 42 U.S.C. 9615 in the Comprehensive Environmental Response, Compensation, and Liability Act authorizes the President to establish regulations to implement the statute; this authority has been delegated to EPA by Executive Order 12580. The Emergency Planning and Community Right-to-Know Act also contains a general rulemaking provision, 42 U.S.C. 11048, authorizing the Administrator to promulgate rules necessary to carry out the Act. The Resource Conservation and Recovery Act specifically authorizes the Administrator to prescribe regulations necessary to carry out EPA’s functions under the Act, 42 U.S.C. 6912. The Safe Drinking Water Act contains similar language, authorizing the Administrator to prescribe such regulations “as are necessary and appropriate” to carry out EPA’s functions under the Act, 42 U.S.C. 300j-9. In addition, EPA has authority under 5 U.S.C. 301 and 42 U.S.C. 300v-1(b).

B. Request for Comments

Neither this ANPR nor the specific questions presented below for public comment are intended to indicate that EPA now favors any particular policy approaches regarding the Agency’s consideration of or reliance on third-party intentional dosing human studies. Similarly, neither this ANPR nor the specific questions presented below for public comment are intended to indicate that EPA has decided on a particular scope for any potential future rulemaking. Nor is this ANPR intended to impede or otherwise delay any Agency assessments or actions. Rather, this ANPR is designed to encourage public input from all interested parties on a broad range of issues that could help inform any rule or policy that EPA eventually promulgates or issues, respectively.

The Agency fully appreciates the number, the range, and the interconnectedness of the scientific and ethical concerns raised especially by intentional dosing human studies of the wide range of environmental agents addressed by EPA’s programs. Reflecting the breadth of issues that

have been raised, the Agency has identified specific questions on which it particularly invites comment. These questions are intended to help organize and focus the discussion, but not to constrain it. Commenters should feel free to address any other relevant topics as well.

1. *Applicability of existing standards*—a. Is it appropriate to use a standard intended to guide the conduct of research (e.g., the Common Rule, Declaration of Helsinki, or the Nuremberg Code) to assess the acceptability for review of completed research?

b. Is it appropriate to use a standard intended to guide the conduct of therapeutic or diagnostic medical research or to clarify causes of disease, such as the Declaration of Helsinki, to assess the acceptability for review of other kinds of research without diagnostic or therapeutic intent, conducted with healthy subjects?

c. Should the Agency apply the same standard of acceptability independent of the type of substance tested (e.g., pharmaceutical, pesticide, pathogen, or environmental contaminant)? If not, how might differing standards be applied when a single substance has multiple uses, e.g., as both a pesticide and a drug?

d. Does it matter who maintains a standard, or by what process it is maintained? For example, would it be appropriate for EPA to accept and apply a standard maintained by a private, non-governmental organization, as is the Declaration of Helsinki?

e. Should the Agency extend the requirements of the Common Rule to the conduct of third-party research with human subjects intended for submission to EPA? What are the advantages and disadvantages of conducting a rulemaking or undertaking other Agency action for this purpose alone?

2. *Should the standard of acceptability vary depending on the research design?*—a. Should the Agency apply the same standard of acceptability independent of whether the research design involves intentional exposure? For example, should the same standard apply to research involving intentional exposures to human subjects, to research designed to follow-up accidental exposure, and to studies of individuals occupationally or incidentally exposed?

b. Should the Agency apply the same standard of acceptability independent of the level of exposure of the human subjects? For example, does it matter if the level of exposure to a chemical is below the Reference Dose or other established health standard designed to