



MEMORANDUM

Via E-Mail

DATE: September 8, 2005

TO: Firm Clients and Friends

FROM: Bergeson & Campbell, P.C.

RE: EPA Holds Stakeholder Briefing on Human Studies Proposed Rule

Yesterday, the U.S. Environmental Protection Agency (EPA) held a stakeholder briefing on its human studies proposed rule, which it expects to publish on **September 9, 2005**. The proposed rule focuses on third-party intentional dosing studies involving pesticides, although EPA “invites public comment on alternative approaches with broader scope.” The proposed rule would prohibit new third-party intentional dosing studies for pesticides involving pregnant women or children as subjects, as well as all first- and second-party intentional dosing studies of any substance involving pregnant women or children as subjects. More information on the proposed rule and stakeholder briefing is below. EPA’s proposed rule is available on the Internet at <http://www.epa.gov/oppfead1/guidance/fedreg-hs.pdf>, and additional EPA information is available at <http://www.epa.gov/oppfead1/guidance/human-test.htm>. Comments will be due 90 days after EPA publishes the proposed rule in the *Federal Register*. EPA expects the proposal to be published on **Friday, September 9, 2005**; if it is, comments would be due **December 8, 2005**.

Proposed Rule

First- and Second-Party Research

EPA’s proposed rule lists two actions with respect to human research conducted by EPA (first-party research) or by others with EPA’s support (second-party research):

- (1) Categorically prohibit any intentional dosing studies involving pregnant women or children as subjects; and



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- (2) Adopt the Department of Health and Human Services (HHS) regulations that provide additional protections to pregnant women and children as subjects of other than intentional dosing studies.

Third-Party Research

EPA lists four actions applicable to human research conducted by third parties (*i.e.*, by others without any support from EPA or other federal government agencies):

- (1) Categorically prohibit any third-party intentional dosing studies for pesticides involving pregnant women or children as subjects;
- (2) Extend the provisions of the Federal Policy for the Protection of Human Subjects of Research (the Common Rule) to all other third-party intentional dosing human studies intended for submission to EPA under the pesticide laws;
- (3) Require, before testing is initiated, submission to EPA of protocols and related information for proposed research covered by this extension of the Common Rule; and
- (4) Require information about the ethical conduct of covered human studies when the results of the research are submitted to EPA.

Other Actions

In addition, the proposed rule would establish an independent Human Studies Review Board to review proposals for covered intentional dosing human research and reports of completed research; specify measures EPA would consider to address non-compliance with the provisions of a final rule; define the ethical standards EPA would apply in deciding whether to rely on relevant, scientifically sound data derived from intentional dosing human studies for pesticides; and forbid EPA to rely in its decision-making under the pesticide laws on human research involving intentional exposure of pregnant women or children, with one potential exception noted below.

In the proposed rule, EPA discusses the ethical standards that it believes should apply to determine whether to rely on scientifically sound human studies with ethical deficiencies completed before promulgation of the final rule. For covered types of research conducted after the effective date of the rule, EPA would refuse to rely on data from



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scientifically sound and relevant human research “unless EPA has adequate information demonstrating that the research complied with the Common Rule.” For covered types of research conducted before the effective date of the rule, EPA would rely on data “from scientifically sound and relevant human research unless there is clear evidence to show the conduct of the research was fundamentally unethical or was significantly deficient relative to the ethical standards prevailing at the time the research was conducted.” Throughout the text of the rule and repeatedly in its description of the rule during the stakeholder briefing, EPA cited the results of the 2004 National Academy of Sciences (NAS) report on intentional human dosing studies as a basis for its proposal.

The proposed rule includes a formal process that EPA could use to make an exception to these standards when “scientifically sound but ethically deficient research” would provide “crucial support to a regulatory action more protective of public health than could be justified without relying on the ethically deficient research.” The “extraordinary procedure” would also apply if a scientifically sound study involving the intentional dosing of pregnant women or children as subjects “were found to be crucial to the protection of public health.” EPA will make decisions on a case-by-case basis, “taking into account the particular circumstances of the study and the way it could affect the regulatory action, and seeking the best possible advice.” EPA states that it “agrees such decisions should consider the importance of the research to a potential regulatory decision, and particularly whether it would support a regulatory position more protective of public health than would be justified without reliance on the data.” Under EPA’s proposed rule, EPA would consult the Human Studies Review Board and public comment before deciding whether to rely on such data.

Stakeholder Briefing

During the stakeholder briefing, EPA stated that it believes its proposed rule is consistent with the 2004 NAS report and that in some respects, its proposal is more protective than NAS recommends. EPA said that until it promulgates a final rule, in accordance with its understanding of Congress’s intent as expressed in the fiscal year **2006** appropriations bill for EPA (Pub. L. No. 109-54), it is discontinuing its reliance on human data. EPA expects to issue a final rule in late **January 2006**, as directed by Congress.

Stakeholders asked questions such as how many people will serve on the Human Studies Review Board and whether members will be chosen in a manner similar to that for EPA’s Science Advisory Board or Scientific Advisory Panel. EPA responded that the Review Board will be an independent entity and members will be subject to conflict of interest rules. Because EPA has only begun to look at the composition and procedures for the Review Board, it



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welcomes public comments on these issues. EPA intends to have the first Review Board in place when it issues its final rule.

When asked when EPA will issue guidance documents addressing issues such as the definition of a scientifically unsound document, EPA said that it does not have a schedule for when guidance documents will be available. According to EPA, in the absence of guidelines, the purpose of the protocol review is to ensure studies are conducted in an ethical and scientifically sound manner.

In response to a question regarding EPA's proposed catch-all exception and whether EPA would consider relevant "scientifically sound but ethically deficient" data supporting a less protective standard, EPA said that if the data tend to show that the compound is safer than would otherwise be expected by looking only at animal data or other ethical human studies, EPA stated that it believed the intent of the proposed provision is that EPA would not be able to avail itself of this exception. A stakeholder asked how EPA will define public health and described a situation wherein a registrant argues that an exception is necessary to increase crop yields to prevent starvation even though the higher standard is harmful to individuals exposed to the pesticide. EPA said that this scenario has not been discussed but that it would be appropriate to address in public comments.

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We hope this information is helpful. As always, please call if you have any questions.