



## Center for Regulatory Effectiveness

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May 10, 2002

Hon. Stephen L. Johnson  
Assistant Administrator for Prevention,  
Pesticides and Toxic Substances  
U.S. Environmental Protection Agency  
Mail Code 7101M  
1200 Pennsylvania Ave., N.W.  
Washington, D.C. 20460

**Re: The Data Quality legislation and OMB's final implementing guidelines have superceded and prohibited EPA's categorical ban on its consideration and use of "third-party" human volunteer clinical studies**

Dear Mr. Johnson:

On December 14, 2001, EPA issued a press release announcing that it would not consider or rely on any "third-party" clinical human test data studies in its regulatory decision making pending the outcome of an EPA-requested National Academy of Sciences' review of unspecified issues involved in such studies. (A copy of the press release is attached as Exhibit A). The announcement also stated that the ban will continue following receipt of the NAS report while EPA formulates a formal policy on future acceptance, consideration or regulatory reliance on such human studies.

The NAS study has still not begun, and a subsequent agency rulemaking is likely to be lengthy and its outcome uncertain. It could well be several years, if ever, before the agency formulates a "formal policy". The December 14, 2001, EPA announcement imposing a ban on the use of such studies therefore amounts to an interim final rule under the APA definition. It is as final as can be for the foreseeable future, and may or may not be revised.

However, this December 14, 2001, interim final rule contains an important qualification. It states that the ban will not apply if EPA is "legally required" to consider or rely on any such human study during this interim period.

When the December 14 rule was issued, the Office of Management and Budget had not yet issued its final "guidelines" implementing the new Data Quality legislation. The final OMB

guidelines were issued on January 3, 2002, and reissued with corrections on February 22, 2002.<sup>1</sup> The legislation<sup>2</sup> and OMB rules are legally binding on all federal agencies, including EPA. Although denominated “guidelines”, they clearly constitute legal requirements issued to implement Congressional mandates. Agencies are now in the process of developing agency-specific guidelines; but those guidelines must, as a matter of law, be in conformance with the legislation and the OMB rules.

There is no indication that EPA has yet considered the impact of the Data Quality legislation and OMB rules on its December 14, 2001 interim final rule banning use or reliance on human clinical studies.

As explained below, EPA is now “legally required” by the legislation and OMB rules to consider and appropriately incorporate “third-party” clinical human volunteer studies in risk assessments and related regulatory decisions.

Consequently, the Center for Regulatory Effectiveness now requests EPA to review its interim final ban on use of human volunteer clinical studies in light of the new OMB legal requirements.<sup>3</sup> We believe that those requirements clearly require that the agency now take the following actions to modify its December 14 policy statement:

- Announce that, in view of the new OMB rules, EPA has now determined it is legally required to consider and rely on such studies in its risk assessments and regulatory decisions if the studies are determined to have been conducted in accordance with generally accepted ethical standards and are scientifically relevant.<sup>4</sup>
- Announce that any such studies that have previously been reviewed and relied on by the Agency will be considered acceptable now for consideration and use by EPA in regulatory decision making.
- Refrain from taking any affected regulatory actions until EPA’s current ban on consideration of third-party clinical human test data is modified or rescinded, and the new policy identified in this letter is implemented.

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<sup>1</sup> 67 Fed.Reg. 369-78; 67 Fed.Reg. 8452-60.

<sup>2</sup> 44 U.C.C. § 3501 *et seq.* and § 515, P.L. 106-554; 44 U.S.C. § 3516 note.

<sup>3</sup> This request should be considered a petition for modification or rescission of a rule under the APA, 5 U.S.C. § 553(e).

<sup>4</sup> Consensus ethical standards are already embodied in the Declaration of Helsinki and the federal Common Rule, which EPA subscribes to. The Common Rule even provides for acceptance of human studies conducted in accordance with the Declaration of Helsinki. It is not clear what EPA had in mind in requesting the NAS to consider ethical issues.

## **THE DATA QUALITY LEGISLATION AND OMB'S GUIDELINES REQUIRE EPA TO CONSIDER AND USE THE BEST AVAILABLE DATA AND STUDIES**

The Data Quality legislation and OMB's implementing guidelines require that EPA disseminate information, including risk assessments, based on the best available data and studies, particularly if such data or studies have been peer-reviewed. This requirement stems in part from the "objectivity" standard imposed by the Act and OMB's guidelines. In order to meet this standard, risk assessments and other information disseminated by EPA have to be "accurate, clear, complete, and unbiased." 67 FR 8453, 8459. Disseminated information that excludes the available and relevant data and studies cannot be accurate, clear, complete and unbiased.

The OMB guidelines specifically address quality aspects of human health risk assessments. The guidelines require agencies to apply the quality standards specified by Congress in the Safe Drinking Water Act Amendments of 1996 ("SDWAA"). Agencies must either "adopt or adapt" these Congressional requirements in their agency-specific data quality guidelines. 67 Fed.Reg. 8457-58, 8460. The OMB guidelines make clear that use of the term "adapt" does not relieve agencies of the responsibility for applying these basic quality standards; rather, the term "adapt" "is intended to provide agencies with flexibility in applying these principles to various types of risk assessment." 67 Fed.Reg. 8458 1<sup>st</sup> col.

The SDWAA quality principles specifically quoted in the OMB guidelines as applicable, and which are particularly relevant to the consideration and use of data from human volunteer clinical studies, include the following:

- "[T]o the degree that an agency action is based on science", the agency is directed "to use...the best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices..." 67 Fed.Reg. 8457 3d col.
- The presentation of information in the risk assessment must be "comprehensive". *Id.*
- The risk assessment must specify, to the extent practicable, "each significant uncertainty identified in the process of the assessment of [risk] effects and the studies that would assist in resolving the uncertainty'." 67 Fed.Reg. 8458 1<sup>st</sup> col.
- The risk assessment must also specify "peer-reviewed studies known to the [agency] that support, are directly relevant to, or fail to support any estimate of [risk] effects . . . ." *Id.*

Data and studies that have previously been peer-reviewed, including peer-review by the SAB or SAP, and relied upon in developing risk assessments and determining reference doses have already been "peer-reviewed" and require no further peer-review in order to comply with these principles.

**HUMAN VOLUNTEER CLINICAL STUDIES PROVIDE  
SOME OF THE BEST AVAILABLE AND MOST RELIABLE DATA  
FOR EVALUATING HUMAN HEALTH RISKS**

Attached as Exhibits B and C are two published articles by distinguished scientists which explain that clinical human test data are often the best available data on a substance or product's risk to human beings. This point is further demonstrated by the fact that EPA itself frequently conducts clinical human tests to assess risk, and has also frequently used third-party clinical human tests to assess risk. Ongoing EPA clinical human tests include those conducted at EPA's "inhalation chambers" in North Carolina where human volunteers, including asthmatics, are exposed to various air pollutants. (Exhibits D, E and F). The United States Court of Appeals for the District of Columbia recently relied on this type of EPA clinical human test to uphold the Agency's ozone standards under the Clean Air Act. *American Trucking Association, Inc. v. EPA*, 2002 WL 452092, \*22 (D.C. Cir., March 26, 2002).

There is no rational basis for distinguishing categorically between clinical human tests conducted by EPA and by third parties. Therefore, under the Data Quality legislation and OMB's guidelines, EPA cannot disseminate risk information that categorically excludes consideration and use of third-party human volunteer clinical data and studies. For the same reasons, under the Data Quality legislation and OMB's guidelines, EPA cannot propose and promulgate guidelines that allow the categorical exclusion of third-party clinical human test data and studies.

**CONCLUSIONS AND RECOMMENDATIONS**

The agency's December 14, 2001, interim final rule banning consideration and use of human volunteer clinical studies has been superseded by the legal requirements contained in the final OMB guidelines on data quality. There is no conceivable way in which such studies can be excluded from the applicable OMB directives noted above. Accordingly, EPA should --

- Issue, as soon as possible, an announcement or notice acknowledging these new legal requirements and modifying or rescinding the ban contained in the December 14 announcement.
- Announce that any such studies that have previously been reviewed and relied on by the Agency will be considered acceptable now for consideration and use by EPA in regulatory decision making.
- Refrain from taking any affected regulatory actions until EPA's current ban on consideration of third-party clinical human test data is rescinded, and the new policy identified in this letter is implemented.

Thank you for your prompt consideration of this matter. Please feel free to contact me if you feel you need clarification of any of the points in this petition or wish to discuss it.

Sincerely,

A handwritten signature in black ink, appearing to read "Jim J. Tozzi". The signature is stylized with a large initial "J" and "T".

Jim J. Tozzi  
Member, CRE Board of Advisors

Attachments

cc (w. attach.):

Hon. Christine Todd Whitman  
Hon. Kimberly T. Nelson, OEI/CIO  
Marcia Mulkey, OPP  
Philip J. Ross, OGC  
Michele Knorr, OGC