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August 22, 2000

Ms. Carol M. Browner
Administrator
Environmental Protection Agency
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Dear Administrator Browner:

We have conducted a comprehensive survey within EPA regarding the Agency's use of clinical human test data. We are furnishing you the results of our research and seek your views on its results.

EPA's Office of Pesticides Programs recently banned the use of any clinical human test data during its regulation of pesticides and herbicides under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA") and the Food Quality Protection Act ("FQPA"). In light of this new ban, and given the results of CRE's survey, we request that EPA respond to the following questions:

(1) Does EPA agree with CRE that the Pesticides Office's new ban on clinical human test data differs from and is inconsistent with the Pesticides Office's own prior practice and procedure?

(2) Does EPA agree with CRE that the Pesticides Office's new ban on clinical human test data differs from and is inconsistent with the current practice and procedure of other EPA Offices and Programs?

-- For example, CRE understands that other EPA Offices and Programs are bathing human test subjects in water contaminated with toxic substances.

-- As another example, CRE understands that other EPA Offices and Programs currently operate "Human Exposure Chambers" where human test subjects are exposed to toxic substances.

CRE also requests that EPA immediately reverse the Pesticides Office's refusal to consider any clinical human test data, and immediately allow consideration of such data, so long as it is generated in accordance with either the Common Rule or the Declaration of Helsinki. If the Pesticides Office wants to reconsider the use of clinical human test data, then EPA must address this issue in a public-notice-and-comment rulemaking conducted in accordance with the rulemaking requirements of the Administrative Procedure Act ("APA"). In the interim, clinical human test data must be accepted and utilized by the agency. Given EPA's own generation and use of clinical human test data in many other contexts, CRE doubts that there would be any rational basis for a rule banning such data during the regulation of pesticides and herbicides.

This letter is based on CRE's extensive review of EPA documents and discussions with EPA personnel. CRE's findings and conclusions are set forth below.

CRE'S SURVEY OF HUMAN TESTING PRACTICES AND PROCEDURES AT EPA

EPA's Pesticides Office Recently Banned Use of Clinical Human Test Data.

On July 27, 1998, EPA announced that the Pesticides Office would no longer consider any human test data when regulating pesticides or herbicides under FIFRA and the FQPA. EPA Statement dated July 27, 1998. In a Staff Background Paper prepared for the November 30, 1999 meeting of SAB/SAP Joint Subcommittee on Data from Human Subjects, EPA stated that "[t]he Agency's policy continues as it was first articulated in July 1998: we will not rely on [human] studies to support final decisions under the Food Quality Protection Act" until a final policy is in place regarding use of these studies. EPA spokespersons were recently quoted as stating, "We see no reason to change our policy, and our policy will remain no human testing of pesticides or toxics." BNA Daily Environment Report, June 8, 2000, p. A-11; *Washington Post*, June 7, 2000, p. A-02. Since its July 27, 1998 statement on this issue, the Pesticides Office has in several cases refused to consider clinical human tests when making FIFRA and FQPA regulatory decisions. Since that time, the Pesticides Office has not considered clinical human test data when making FIFRA and FQPA regulatory decisions.

Before 1998, the Pesticides Office Considered Clinical Human Test Data.

Until 1998, the Pesticides Office actively accepted and evaluated data from privately funded studies of human volunteers when regulating pesticides and herbicides. See EPA "Staff Background Paper" submitted to SAB/SAP Subcommittee on Data from Human Subjects for its November 30, 1999 Meeting. In fact, EPA has often stated that human test data are ethically acceptable and often scientifically preferable. For example, EPA's "Guidelines for Neurotoxicity Risk Assessment" dated May 14, 1998, at 35, explains that it is:

> ... ethically possible to perform human laboratory studies and obtain data relevant to the risk assessment process. Information from experimental human exposure studies have been used to set occupational exposure limits...[and] contributed to risk assessment and the setting of exposure limits for several solvents and other chemicals with acute reversible effects. Human exposure studies sometimes offer advantages over epidemiological field studies.

EPA's Neurotoxicity Guidelines are frequently used when performing risk assessments and making tolerance decisions for herbicides and pesticides. These Guidelines were published in final form in the *Federal Register* after public notice of and an opportunity to comment on proposed Guidelines. 63 FR 26926 (May 14, 1998); 60 FR 52032 (Oct. 14, 1995).

EPA Still Considers and Generates Human Test Data in Other Contexts.

At the December, 1998 meeting of the SAP/SAB Subcommittee on Data from Human Subjects, EPA representatives presented information on the Agency's acceptance and use of clinical human test data for the period from January 1, 1990 through August 31, 1998. During that period 26 human effects studies based on intentional clinical exposure were submitted that addressed metabolism, pharmokinetics, and absorption, and 8 that addressed a No Adverse Effects Level ("NOAEL").

EPA further noted in its "Staff Background Paper" prepared for the November, 1999 meeting of the SAB/SAP Subcommittee on Data from Human Subjects that the Agency itself still conducts and supports clinical tests involving human exposure to toxic substances, including the following:

- MTBE (methy tertiary butyl ether)
- Ozone
- SO2 (sulphur dioxide)
- NO2 (nitrogen dioxide)
- CO (carbon monoxide)

- Air particulate matter and acidic particles
- Methy mercury
- Hydrofluorocarbons

EPA's Office of Prevention, Pesticides, and Toxic Substances is in charge of the FIFRA and FQPA regulatory program. This EPA Office includes both the Office of Pollution Prevention and Toxics ("OPPT") and the Pesticides Office. OPPT, as well as EPA's Air Office and Water Office, continue to use human test data for several purposes, including risk assessments. *See, e.g.*, 65 FR 14186 (Mar. 15, 2000). Current practice by OPPT, the Air Office, and the Water Office is irreconcilable with Pesticides Office's new ban on clinical human test data.

EPA has its own "Human Studies Division" which still conducts clinical human studies involving toxic substances. Many of these EPA human tests are conducted at EPA's "Human Studies Facility" in Chapel Hill, North Carolina. EPA's "Human Studies Facility" contains eleven "Human Exposure Chambers" where human test subjects are exposed to hazardous air pollutants and other toxic substances.

EPA's Air Office is engaged in a major regulatory review of MTBE, a gasoline additive. In support of this effort, EPA's National Exposure Research Laboratory ("NERL") is conducting several human tests. These include, as described by NERL:

> "Human Exposure to Methyl Tertiary-Butyl Ether (MTBE) While Bathing with Contaminated Water";
>
> "Inhalation and Dermal Exposure to MTBE using Continuous Breath Analysis"; and
>
> "Controlled methyl tertiary-butyl ether (MTBE) exposure to humans through dermal, ingestion, and inhalation routes and the resultant biomarker tertiary butyl alcohol (TBA) as measured in exhaled breath and venous blood."

If CRE's research and survey are correct, then EPA itself is bathing human test subjects with contaminated water and making them breathe contaminated air. How can EPA reconcile its own human tests with the Pesticides Office's new ban on any industry-submitted clinical human test data?

THE PESTICIDES OFFICE'S NEW BAN ON CLINICAL HUMAN TEST DATA VIOLATES THE APA

The Pesticides Office's new ban on clinical human test data is a legislative rule under the Federal Administrative Procedure Act ("APA"), 5 U.S.C. §§ 551 et seq. Therefore, it is subject to the APA's rulemaking requirements.

The APA's definition of "rule" includes a statement of general or particular applicability and future effect designed to implement law or policy. 5 U.S.C. § 551(4). This definition is broadly construed to include not only formal regulations but other types of documents and even unwritten policies and procedures. *See, e.g., Ciba-Geigy v. EPA*, 801 F.2d 430 (D.C. Cir. 1986) (EPA's letter to the regulated community constitutes "legislative rule"); *United States v. Articles of Drug*, 634 F. Supp. 435 (N.D. Ill. 1985), *vacated as moot*, 818 F. 2d 569 (7th Cir. 1987) (unwritten procedures regarding the importation of animal drugs are rules under the APA).

EPA's new refusal to consider industry-submitted pesticide and herbicide human test data is not an "interpretive rule" under the APA. The "interpretive rule" exception to the APA's rulemaking requirements does not apply to rules and policies that have a "binding effect" on either EPA or private parties. *See McLouth Steel Products Corp*. v. *Thomas,* 838 F. 2d 1317, 1320 (D.C. Cir. 1988) ("If it appears that a so-called [interpretive rule] is in purpose or likely effect one that narrowly limits administrative discretion, it will be taken for what it is–a binding rule of subsequent law").

EPA cannot avoid the APA's rulemaking requirements by labeling the Pesticide Office's new refusal to consider human test data an "interim policy." "EPA's label of an agency action, although one factor to be considered, does not control whether the action is in fact a rulemaking. Instead, "it is the substance of what the [agency] has purported to do and has done which is decisive." *Limerick Ecology Action, Inc. v. United States Nuclear Regulatory Commission*, 869 F. 2d 719, 733 (3rd Cir. 1989) (quoting *Columbia Broadcasting System v. United States*, 316 U.S. 406, 407, 416 (1942)). *See also American Trucking Ass'n v. United States*, 688 F. 2d 1337, 1348 (11th Cir. 1982) ("the decision to reverse a longstanding and uniform practice by revoking all outstanding authorities of a particular type and implicitly indicating that no such authorities will be issued in the future is clearly a rule").

The Pesticide Office's new ban on clinical human test data establishes a binding norm that must be followed in all cases involving the regulation of pesticides and herbicides. Therefore, this new ban violates the APA because it was never proposed for public notice and comment in accordance with the APA's rulemaking provisions.

CONCLUSION

Based on CRE's research and survey, the Pesticides Office's new ban on human test data differs from and is inconsistent with the Office's past practice and procedure. It also differs from and is inconsistent with EPA's current practice and procedure in many other Offices and Programs. We request that you state whether you agree or disagree with CRE's conclusions. CRE further requests

that EPA initiate an APA rulemaking before the Pesticides Office continues its ban on the use of clinical human test data. Finally, CRE can see no rational basis for such a ban given EPA's current practice of generating and using clinical human test data in many other regulatory contexts.

We thank you for your prompt response to these requests.

Sincerely,

Jim J. Tozzi
Member, CRE Board of Advisors