COMMENTS BY THE CENTER FOR REGULATORY EFFECTIVENESS ON DEVELOPMENT OF ECAS FOR PFOA/FLUORINATED TELOMERS (Docket No. OPPT-2003-0012)

I. INTRODUCTION

The Center for Regulatory Effectiveness ("CRE") submits the following initial comments on EPA's *Federal Register* notice regarding negotiation of Enforceable Consent Agreements ("ECAs) for perfluorooctanoic acid ("PFOA") and fluorinated telomers ("telomers). CRE understands that the primary purpose of these ECAs is to require testing necessary to fill significant data gaps regarding PFOA exposure and effects. [1] CRE's comments make the following main points.

• CRE agrees with EPA that the current data base is inadequate to assess the risks of PFOA and its salts. For example, the human and animal blood, serum and plasma ("blood") data for PFOA are derived from tests that have never been validated, and that have never been shown to be accurate, reliable and reproducible.

• The Data Quality Act and EPA's implementing Guidelines require that all EPA-disseminated data regarding PFOA risks be demonstrated to be accurate and reliable. [2]

• The PFOA human and animal blood data, and the PFOA risk assessment itself, are influential scientific information that must meet the highest reproducibility and other quality standards under the Data Quality Act and EPA's Data Quality Act Guidelines. Consequently, before EPA disseminates any original or supporting data regarding PFOA risks, the Agency must ensure the reproducibility of the data, including the blood data. [3]

• Any negotiated ECAs should contain provisions requiring the development of tests for PFOA in human and animal blood that are accurate, reliable and reproducible.

• EPA should correct its Preliminary Risk Assessment for PFOA to state that there are currently no tests for PFOA in human or animal blood that have been demonstrated to be reliable, accurate, and reproducible. All other EPA disseminations of information regarding PFOA that discuss human or animal PFOA blood levels should be corrected in the same manner.

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[1] 68 FR 18626, 18628-31 (April 16, 2003).

[2] 44 U.S.C. § 3516 historical and statutory notes (Data Quality Act); http://www.epa.gov/oei/qualityguidelines/EPA_OEI_IQG_FINAL_10-2002.pdf ("EPA Guidelines"), pp. 15-16.

[3] EPA Guidelines, pp. 19-21, 47.

CRE registered for "interested party" status because this proceeding raises significant Data Quality Act issues. CRE has been a proponent of the Data Quality Act from the Act's drafting to its implementation by OMB and other agencies, including EPA. CRE commented extensively on OMB and EPA's proposed Data Quality Act Guidelines. CRE's website, http://www.TheCRE.com, has several sections devoted to Data Quality Act issues. CRE filed with EPA one of the first Requests for Correction ("RFC") under the Data Quality Act. [4] This RFC addressed an issue that is also raised by EPA's proposal to negotiate ECAs for PFOA: test accuracy, reliability, reproducibility and validation.

II. EPA-DISSEMINATED INFORMATION REGARDING PFOA RISKS MUST MEET THE DATA QUALITY ACT STANDARDS FOR INFLUENTIAL SCIENTIFIC INFORMATION

EPA has already disseminated substantial information to the public about PFOA risks. That information includes the Agency's *Federal Register* notice about the ECA negotiations, the Preliminary Risk Assessment, and other information on a website exclusively devoted to PFOA. [5] This information must meet the Data Quality Act Standards and EPA Guidelines before it is disseminated.[6] If this information is disseminated in violation of the Data Quality Act Standards and EPA Guidelines, then it is subject to a Request for Correction under the Act and EPA Guidelines. [7]

The ECAs contemplated by EPA's *Federal Register* notice would require additional tests generating data that EPA would use in its PFOA risk assessment. These data would be publicly disseminated in subsequent revisions of the Risk Assessment and probably in other forums. These data must also meet the Data Quality Act Standards and Guidelines. [8]

The Preliminary Risk Assessment relies heavily on data generated and submitted by parties outside EPA. The contemplated ECAs would require additional testing and data submissions by parties outside EPA. Outside-party tests and data must also meet the Data Quality Act Standards and EPA Guidelines before EPA can use them in subsequent risk assessments or in other public

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[4] CRE's RFC, EPA's Response to it, and other related information are accessible at http://www.thecre.com/atrazine/fedactions.htm.

[5] EPA's Preliminary Risk Assessment for PFOA can be accessed by the public at http://www.epa.gov/opptintr/pfoa/pfoara.htm. Other EPA information regarding PFOA can be accessed by the public at http://www.epa.gov/opptintr/pfoa/index.htm.

[6] 44 U.S.C. § 3516 historical and statutory notes; EPA Guidelines, pp. 15-16, 29.

[7] 44 U.S.C. § 3516 historical and statutory notes; EPA Guidelines, pp. 30-34.

[8] 44 U.S.C. § 3516 historical and statutory notes; EPA Guidelines, pp. 15-16, 29.

disseminations. [9]

The PFOA risk assessment and the test data used in it are influential scientific information subject to the most stringent Data Quality Act Standards because:

• The PFOA Risk Assessment is scheduled for external peer review by the Science Advisory Board (68 FR 18630);

• The Preliminary Risk Assessment has already undergone external "letter" peer review (68 FR 18630);

• EPA's review of PFOA is controversial and precedent setting; and

• EPA's review of PFOA could have a wide-spread and major impact on the private sector. [10]

For Influential Scientific Information like this, the EPA Guidelines require that EPA "ensure reproducibility for disseminated original and supporting data according to commonly accepted scientific, financial, or statistical methods." [11]

III. CRE AGREES WITH EPA THAT THE CURRENT DATABASE DOES NOT MEET DATA QUALITY ACT STANDARDS

EPA has correctly identified flaws and gaps in the current PFOA database.[12] In particular, EPA has acknowledged that "[t]he technical difficulties of detecting and accurately measuring the chemical in all these various media, particularly in the low concentrations that EPA would anticipate, are

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[9] EPA Guidelines, p. 28; OMB/OIRA Memorandum to Agencies Subject to the Data Quality Act, pp. 6-7 (June 10, 2002)(accessible on CRE's website at http://www.thecre.com/pdf/omb-6-10memo.pdf).

[10] EPA Guidelines, p. 20 (criteria for determining influential scientific information). EPA's press release for the PFOA Preliminary Risk Assessment quotes EPA Assistant Administrator Stephen L. Johnson as stating that "'the Agency will be conducting its most extensive scientific assessment ever undertaken on this type of chemical.'" (accessible at http://www.epa.gov/opptintr/pfoa/pfoaprsl.pdf). This is a precedent-setting and extremely controversial proceeding.

[11] EPA Guidelines, pp. 21, 47.

[12] *E.g.*, 68 FR 18628-31.

considerable." [13] The affected industry has sent letters to EPA stating their intent to validate and, after validation and approval, perform the necessary tests. [14] EPA has correctly queried the participating industry regarding "the validation status and accuracy and precision of each test method" proposed by them. [15]

EPA is focusing on developing reliable tests for various environmental media and exposure pathways. EPA is apparently not considering "the validation status and accuracy and precision" of tests for PFOA in human and animal blood. EPA has not publicly identified any efforts to address the blood test issue. Accurate, reliable and reproducible blood tests are a prerequisite for the dissemination of any PFOA risk information that complies with the Data Quality Act Standards and Guidelines. CRE understands that, at this time, there are no such tests.

CRE is aware of efforts by several different laboratories to test human blood for PFOA. [16] These laboratories used different tests and got different results. None of them confirmed their test results by having another laboratory reproduce them.

The most influential guidance for bioanalytical test validation is FDA's *Guidance for Industry*. [17] Like the Data Quality Act and Guidelines, FDA's Guidance also requires reproducibility:

> Bioanalytical method validation includes all of the procedures that demonstrate that a particular method for quantitative measurement of analytes in a given biological matrix, such a blood, plasma, serum, or urine, is reliable and reproducible for its intended use. The fundamental parameters for this validation include (1) accuracy, (2) precision, (3) selectivity, (4) sensitivity, (5) reproducibility, and (6) stability. [18]

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[13] 68 FR 18630.

[14] 68 FR 18631.

[15] Emails from Ward Penberthy accessible in EPA's electronic docket OPPT-2003-0012.

[16] *E.g.*, Yu-lin *et al.*, "*Chinese Journal of Chromatography*, Vol 20, No. 1 (January 2002); Masunaga *et al.* , *Organohalogen Compounds*, Vol. 59, p. 319 (2002); Hansen, *et al.*, *Environ. Sci. Technol.* 35, pp. 766-70 *(*2001); Sottani *et al.*, *Rapid Commun Mass Spectrom 2002,* Vol. 16, No. 7 , pp. 650-4 (2002).

[17] *Guidance for Industry: Bioanalytical Method Validation* (FDA, May 2001)("FDA Guidance").

[18] *Id*. at p. 2.

None of the PFOA blood tests so far could be approved under the FDA Guidance. For example, the FDA Guidance requires "reproducibility." It defines this term in part as "precision between two laboratories." [19] The term "precision" is defined as "closeness of agreement (*degree of scatter*) between a series of measurements obtained from multiple sampling of the same homogenous sample under the prescribed conditions." [20] The FDA Guidance further requires that "[t]he precision determined at each concentration level should not exceed 15% of the coefficient of variation (CV) except for the LLOQ, where it should not exceed 20% of the CV." [21] To the best of CRE's knowledge, none of the PFOA blood tests have been demonstrated to meet this quality standard on an inter-laboratory basis.

Based on news reports, 3M and DuPont are working together to validate a test for PFOA in human blood. One purpose of this effort is to develop a standardized protocol that is reproducible among different laboratories. [22] Until and unless such a test is developed and validated, EPA cannot disseminate information regarding PFOA levels in human blood that complies with the Data Quality Act Standards and Guidelines.

EPA has also disseminated information regarding PFOA levels in animal blood. [23] To the best of CRE's knowledge, no standardized test protocol for determining PFOA levels in animal blood has been demonstrated to be reproducible. Until and unless such a test is developed and validated, EPA cannot disseminate information regarding PFOA levels in animal blood that complies with the Data Quality Act Standards and Guidelines.

The PFOA blood level determinations are an essential part of the animal toxicity tests discussed in EPA's Preliminary Risk Assessment. The Interagency Coordinating Committee for the Validation of Analytical Methods ("ICCVAM") has established a Government-wide data quality standard that requires proper validation of this type of animal toxicity test before the test can be considered reliable. Proper validation includes reproducibility among laboratories:

> Before a new or revised test method is used to generate information to support regulatory decisions, it must be (a) validated to determine its reliability and relevance for its proposed use, and (b) determined to be acceptable by one or more regulatory agencies to fill a specific need.

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[19] *Id.* at p. 21.

[20] *Id*. at p. 20.

[21] *Id*. at p. 5.

[22] "Daily Environment Report," BNA, Inc. , p. 8 (April 17, 2003).

[23] *E.g*., Preliminary Risk Assessment, pp. 1-3.

> Criteria for validation and regulatory acceptance have been prepared and are described in the report, *Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the Ad Hoc Interagency Coordinating Committee on the Validation of Alternative Methods*. Prior to the initiation of any test method development or validation efforts, sponsors are encouraged to consider the validation and acceptance criteria developed by the Federal government.[24]
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> For a new or revised test method to be considered validated for regulatory risk assessment purposes, it should generally meet the following criteria....
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> The extent of within-test variability, and the reproducibility of the test within and among laboratories must have been demonstrated. Data must be provided describing the level of intra- and interlaboratory reproducibility and how it varies over time. The degree to which biological variability affects this test reproducibility should also be addressed.[25]

EPA is a member of ICCVAM. EPA is one of the authors of the *Validation Guidelines* and *Validation Criteria* that established the government-wide validation requirement for toxicity test reliability and reproducibility.[26] Thus, according to EPA's own data quality standards, there is currently no reliable and reproducible information regarding PFOA levels in animal blood.

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[24] *Evaluation of the Validation Status of Toxicological Methods: General Guidelines for Submissions to ICCVAM,* Prepared by Interagency Coordinating Committee on the Validation of Alternative Methods , *et. al.*, p. v., October 1999. *("Validation Guidelines").*

[25] *Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the ad hoc Interagency Coordinating Committee on the Validation of Alternative Methods*, "Executive Summary", p. 2, Prepared by ICCVAM and NICEATM (March1997) *("Validation Criteria").*

[26] *Validation Guidelines*, p. iii; *Validation Criteria*, "Agency Representatives and Participants," p. 1.

IV. RECOMMENDATIONS

The Data Quality Act, the EPA Guidelines, and principles of sound science require that:

• Any negotiated ECAs should contain provisions requiring the development of tests for PFOA in human and animal blood that are accurate, reliable and reproducible; and

• EPA should correct its Preliminary Risk Assessment for PFOA, and all other EPA disseminations of information regarding PFOA that discuss human or animal PFOA blood levels, to state that there are currently no tests for PFOA in human or animal blood that have been demonstrated to be reliable, accurate, and reproducible. [27]

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[27] Some of the EPA statements that need correction appear in the PFOA Preliminary Risk Assessment at pages 1-5, 9-16, 23-27, 34-35, 40-45, 47-55.