P S G
PERCHLORATE STUDY GROUP

A coalition of aerospace, defense, chemical and allied industries

December 3, 2003

Information Quality Guidelines Staff
Mail Code 28220T
U.S. Environmental Protection Agency
1200 Pennsylvania Ave., N.W.
Washington, D.C., 20460
quality.guidelines@epa.gov

This letter is submitted with regard to these documents as a petition for correction pursuant to agency-specific information quality guidelines published by EPA (EPA/260R-02-008, December 2002). EPA's guidelines implement but do not supercede government-wide guidelines published by the Office of Management and Budget (OMB) (67 Fed. Reg. 8452-8460, February 22, 2003) implementing section 515 of the Treasury and General Government Appropriations Act for Fiscal Year 2001 (Public Law 106–554; H.R. 5658).

1. Contact name, organization, and contact information (phone number and at least one of the following: e-mail, physical address or fax number).

This petition is filed by the Perchlorate Study Group (PSG), an alliance of manufacturers and users of perchlorate established in 1993 to fund and perform scientific research to identify and estimate the human health effects of perchlorate exposure. PSG is an affected person under the language of OMB guidelines, and this petition is submitted pursuant to EPA's "administrative mechanisms allowing affected persons to seek and obtain correction of information maintained and disseminated by the agency that does not comply with these OMB guidelines" (§II.2, 67 FR 8458).

Please address all communications to:

Mr. Michael Girard, Chairman
The Perchlorate Study Group
c/o Aerojet
Bldg. 20001 Dept. 0330
PO Box 13222
Sacramento, CA 95813-6000

2. Description of the information you believe does not comply with the Office of Management and Budget or EPA Information Quality Guidelines, including specific citations to the information and to the guidelines, if applicable.

On or about November 7, 2003, EPA posted on its website a set of documents that it had submitted to the National Research Council Committee to Assess the Health Implications of Perchlorate Ingestion.[1] These documents include:

- Disposition of Comments and Recommendations for Revision to "Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization" (External Review Draft, January 16, 2002)
- Compilation of Public Comments Received by the U.S. EPA on "Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization" (2002 External Review Draft)
- References Associated with Disposition of Comments on the U.S. EPA's "Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization" (2002 External Review Draft)

In addition, EPA disseminated slides from the presentation delivered by Agency personnel at the first meeting of the Committee on October 27, 2003:

- Perchlorate Risk Characterization: US EPA Technical Perspective

For the specific reasons discussed below, certain information contained within the above bulleted documents does not comply with applicable OMB and EPA Information Quality Guidelines. With limited exceptions, the information addressed in this petition concerns information that is not capable of being reproduced (OMB guidelines, §V.10). This procedural requirement is an essential prerequisite for an independent, external reviewer to evaluate whether the information satisfies the information quality standard of objectivity (OMB guidelines, §V.3).

a. Some of this information is covered by information quality guidelines.

Three of the four bulleted items above meet the definition of "information" set forth by EPA. EPA defines "information" as follows:

> "Information," for purposes of these Guidelines, generally includes any communication or representation of knowledge such as facts or data, in any medium or form. Preliminary information EPA disseminates to the public is also

[1] http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=72117

> considered "information" for the purposes of the Guidelines. Information generally includes material that EPA disseminates from a web page. However not all web content is considered "information" under these Guidelines (e.g., certain information from outside sources that is not adopted, endorsed, or used by EPA to support an Agency decision or position).

Only the Compilation of Public Comments Received by EPA is not "information" covered by information quality guidelines except insofar as these comments are "adopted, endorsed, or used by EPA to support an Agency decision or petition."

b. Covered information is "influential" scientific or technical information.

Covered information is "influential" scientific information as that term has been defined by both OMB and EPA. OMB guidelines define "influential" information as covered information that "the agency can reasonably determine that dissemination ... will have or does have a clear and substantial impact on important public policies or important private sector decisions" (§V.9). EPA guidelines define as "influential" covered information "that the Agency can reasonably determine that dissemination of [which] will have or does have a clear and substantial impact (i.e., potential change or effect) on important public policies or private sector decisions" (p. 19).

Covered information disseminated by EPA clearly meets this test. It will be used by EPA as the scientific foundation for enforceable drinking water and/or remediation standards. The dissemination of any draft or final risk assessment constitutes a regulatory action under Executive order 12866:

> "Regulatory action" means any substantive action by an agency (normally published in the Federal Register) that promulgates or is expected to lead to the promulgation of a final rule or regulation..."[2]

Any draft or final risk assessment disseminated by EPA constitutes an "economically significant regulatory action" if it is:

> likely to result in a rule that may ... have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities.[3]

[2] See 58 FR 51737-51738.
[3] Id.

A primary national drinking water standard for perchlorate is universally expected to be an economically significant regulatory action. In addition, EPA draft risk assessments have been cited as authorities for site-specific remediation standards

This petition concerns EPA's Disposition of Public Comments document (hereinafter *Disposition* document) and References Associated with Disposition of Comments document (hereinafter *References* document). The *Disposition* document is, in its entirety, influential scientific information. To the extent that EPA relies on documents identified in the *References* document as the scientific basis for the *Disposition* document, these references are also influential scientific information and must satisfy the same information quality standards.

As a general matter, the information sought herein is essential for reproducing EPA's results. In selected cases, this information is essential for understanding and testing the reliability and validity of EPA's scientific claims. If EPA is unable or unwilling to disclose the information sought, then the information in question is incapable of being reproduced—a necessary procedural element of the objectivity test. The information in question would have to be identified as falling below applicable standards and rejected for dissemination as influential scientific information, including subsequent dissemination by reference in risk assessment or risk management contexts. Further, both the National Academy committee charged with reviewing perchlorate science and the public would need to be informed that this information does not satisfy applicable information quality standards. Influential scientific information that cannot be reproduced could, under highly restrictive circumstances such as national security, still satisfy the information quality standard of objectivity. These circumstances do not apply in this case, however. The burden of proof that the information challenged herein is in fact objective would be shifted to EPA.

3. Explanation of how the information does not comply with the Information Quality Guidelines.

a. Missing high resolution images in Consultants in Veterinary Pathology (2003)[4] and criteria for assignment to data

[4] Morphometry Review Report. Protocol 1416-003. Hormone, Thyroid, and Neurohistological Effects of Oral (Drinking Water) Exposure to Ammonium Perchlorate in Pregnant and Lactating Rats and in Fetuses and Nursing Pups Exposed to Ammonium Perchlorate During Gestation or Via Maternal Milk. Task 1—Review of Selective Morphometric Data F1 Generation Day 22 Postpartum Rats, Including New Morphometric Data Obtained From Additional Step Sections. February 3, 2003.

This reference is a summary report on new data obtained by EPA and on which the Agency relies in the *Disposition* document. The reference summarizes these new data but does not include the high resolution images of the brain sections from which the summaries were derived. The analysis of these summary data presented in the reference can be reproduced, but the underlying data cannot be reproduced without the high resolution images. Whether these measurements are accurate and complete is a fundamental scientific issue because, as EPA knows, the morphometric data in the so-called "Effects Study" have been a matter of significant controversy. These data are essential to EPA's scientific claim that the "Effects Study" showed evidence of neurodevelopmental effects from perchlorate exposure. EPA apparently obtained these new data precisely because the original data were controversial, and did so in hopes that these new data would resolve the controversy. However, the pathologist's measurements cannot be reproduced without access to the same high resolution images. Thus, neither an independent, external reviewer nor a member of the National Academy panel can reproduce the results reported in the reference.

A second critical issue is that EPA's pathologist did not disclose the criteria he used to assign plate numbers to data. These plate numbers come from the atlas of the rat brain by Paxinos and Watson cited in the reference. An independent, external reviewer cannot evaluate the appropriateness of the pathologist's assignment without examining the high-resolution scanned images, *and* knowing what criteria he used to make the assignments. Hence, disclosure of the high resolution images is necessary *but not sufficient* for this reference to be adequately transparent.

Recommended corrective actions. First, to satisfy the minimum procedural requirements for transparency and reproducibility that apply to influential scientific information, EPA must disclose the high resolution images obtained by its pathologist. As noted in the *Disposition* document, these high resolution images clearly exist:

> All measured sections were digitally scanned using a PathScan Enabler™ and a Polaroid SprintScan 35® film scanner. These sections were scanned at a resolution of 2700 dpi using a calibrated frame measuring 2004 x 1104 pixels in order to standardize the image size and allow for subsequent analysis of the digital images *via* more sophisticated stereologic methodologies (not included in Task One). Each scan includes the hand-written number for the corresponding atlas plate. The digital images were saved in "TIFF" format, and these images transferred to CD-R compact discs. Each file is 6.33 MB in size (p. 5).

Without disclosure of these images, the data summarized in this reference is incapable of being reproduced and therefore could not satisfy the applicable information

standard for objectivity. If EPA does not possess these high resolution images it must obtain them from its hired pathologist, Consultants in Veterinary Pathology (CVP), which obtained the data under contract to EPA, and make them available immediately to the public and the National Academy panel. The Agency also must explain how it conducted an effective pre-dissemination review to ensure that CVP's data satisfied applicable information quality standards. EPA is required to have effective pre-dissemination review procedures in place, and it is unclear how these procedures could have been effective without access to the underlying data summarized in the CVP report. EPA may believe that the CVP report fully and accurately characterizes the raw data, but its legal obligation goes well beyond a mere statement of belief in its contractor.

Second, EPA must disclose the criteria used by the pathologist to assign plate numbers from the atlas to each observation in the data set. It is true that this assignment requires significant scientific judgment. However, scientific judgment also must be transparent and reproducible to satisfy the information quality standard applicable to influential scientific information.

b. Critical details missing from the discussion of materials and methods in Consultants in Veterinary Pathology (2003)

The histology for the "Effects Study" was performed by Experimental Pathology Labs (EPL). This histology was utilized by CVP for this reference and by EPA in the *Disposition* document, but only for the perchlorate treated groups II, III, IV and V. The reference describes new brain sections taken by CVP, but from the control rats only.

Reproducing this work requires additional information not reported in the reference, including:

- What were the tissue storage conditions since the first Effects Study was performed?
- How was the tissue prepared for sectioning?
- What steps were taken to ensure that the degree of tissue compression during sectioning and shrinkage during processing was equivalent in the two series; or alternatively, what steps were taken to measure the extent of tissue compression and shrinkage *in each series of sections* to allow for arithmetic correction necessary to place the measures of the two series on the same scale?
- Who actually sliced the paraffin-embedded brains, what microtome was used, and with what kind of knife?

- What was the temperature of the water bath and how was this determined?

As EPA knows, it is widely believed that the neurodevelopmental effects observed by EPA were artifacts of laboratory errors. This information is essential because there is a serious danger that differences in tissue compression during the histology could have created an apparent perchlorate effect by artifact alone.

Recommended corrective actions. EPA must disclose all pertinent information necessary to enable an independent, external reviewer to discern whether the latest results reported by EPA are also artifacts of laboratory errors. Without this information, the data contained in the reference is incapable of being reproduced. A failure to fully disclosure pertinent information, especially given past controversy concerning laboratory errors, would be persuasive evidence that this information does not satisfy the applicable information quality standard for objectivity.

c. Discrepancies in EPA's statistical analysis of the data in Consultants in Veterinary Pathology (2003)

In its 2002 external review draft health assessment, EPA reported the results of a multivariate profile analysis that, as shown in its Figure 5-15, suggested a strong perchlorate dose effect as a possible inverted U-shaped function. In the *Disposition* document, EPA also reports such a statistical analysis. However, EPA does not provide graphical descriptions of the results of this analysis or sufficient details for the analysis to be capable of being reproduced. The absence of these details appears irregular given the high degree of prominence that EPA attached to this analysis (and its graphical summary) in its 2002 external review draft. This raises obvious questions about the presentational objectivity of EPA's report.

Recommended corrective actions. EPA should report the details of the multivariate profile analysis performed on the new brain sections—in particular, results for posterior corpus callosa at the level of plates 30, 31, 32, and 33. If EPA is unable or unwilling to disclose this information, serious doubts arise as to whether the Agency has satisfied the applicable requirement for presentational objectivity. A reasonable inference would be that EPA no longer has confidence in the statistical analysis reported in its 2002 external review draft.

d. Missing data in Consultants in Veterinary Pathology (2003)

An examination of Tables 1-4 in the above reference indicates that a great deal of data appear to be missing. For example, there are only data for six out of 16 rats in Group I, CC Plate 15 (third column, Table 1). In Group II, there are only data for four out of 16 animals (last column, Table 2). In Table 4, none of the columns contain values for more than two out of 16 animals. Although statistical analyses were not performed with brain section levels with less than five data points, EPA should explained the lack of data and justify the criteria it used for statistical analysis especially given the large number of missing data. The reference does not adequately explain why these data are missing, nor does it explain the basis for performing statistical tests on only those data which are reported. The reference does not explain the disposition of the 19 sections between the step sections that were mounted on slides and stained. It appears that critical sections may have been missed or their results not disclosed. Finally, the reference does not indicate whether any of the sections for which data are reported were measured, analyzed and reported in the original report. The reference is not transparent and the results presented are not reproducible without this information.

This information is essential to interpret reported measures of thickness of structures in the serial coronal sections and to establish the correspondence between sections measured in the Argus 2001 report and EPA's new reference. Conventional practice requires that section numbers be assigned to each section sliced from a block of brain tissue. These sections numbers were not provided in the report of the original 2001 data, nor were they memorialized on the scanned images of sections that were measured, and they are not included in this reference. Section numbers must be disclosed so that independent, external reviewers can reproduce the results reported in the reference based on the high resolution scanned images (see [a] above). Transparency also requires that this reference state explicitly which of the sections measured and reported in Tables 1 through 4 correspond to scanned images of sections that were included in the Argus 2001 report. If section numbers cannot be disclosed because they were not recorded at the time they were collected, then this should be clearly stated and acknowledged as a material defect that makes the data incapable of being reproduced.

Recommended corrective actions. EPA must ascertain and publicly disclose all data obtained by its contractor, including section numbers for each section obtained. Where no data were obtained, the Agency needs to explain the reasons why data are missing and provide a credible explanation why their absence should not materially detract from their inferential value as influential scientific information.

e. Affirmative Showing of GLP compliance for Consultants in Veterinary Pathology (2003)

The data obtained by CVM and reported in this reference are new, but come from tissues collected as part of an earlier study funded by PSG and performed by Argus Research Laboratories.[5] Argus (now Charles River Laboratories) is GLP-certified pursuant to EPA regulations set forth in 40 C.F.R. Parts 160 and 792. The reference does not discuss GLP compliance, and the matter also is not discussed by EPA in its *Disposition* document relying on this reference for critical, influential scientific information.

GLP compliance was a requirement for PSG funding of the original study and is generally required by EPA for laboratory data submitted by third parties for use in regulatory decision making. GLP compliance is highly persuasive evidence that data meet the highest standards of information quality. EPA relies on GLP data for risk assessments and does not require that such data be independently peer reviewed.[6]

An independent and external review of this reference requires documentation of GLP compliance related to a number of study elements including recordkeeping, documentation, and chain of custody. EPA did not disclose this information within its references to the *Disposition* document. This information is essential for evaluating whether the reference satisfies the applicable information quality standards of objectivity and integrity.

Recommended corrective actions. Because the original study was performed in compliance with EPA's GLP regulations, the public has reason to presume that the data summarized in this reference also comply. To enable independent verification, EPA must disclose documentation sufficient to show that the new data summarized by this reference were in fact obtained via GLP-compliant procedures.

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[5] Argus Research Laboratories, Inc. 2001. Hormone, Thyroid and Neurohistological Effects of Oral (Drinking Water) Exposure to Ammonium Perchlorate in Pregnant and Lactating Rats and in Fetuses and Nursing Pups Exposed to Ammonium Perchlorate During Gestation or via Maternal Milk: with Abbreviated Morphometry Report with Appended Thumbnails of Scanned Sections. March, 2001. Horsham, PA. Protocol No. 1416-003.

[6] Environmental Protection Agency, 2002. Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency, http://www.epa.gov/oei/qualityguidelines/EPA_OEI_IQG_FINAL_10-2002.pdf. p 24.

f. Material information from Garman (2003)[7] is not disclosed

EPA relies on the above reference for influential scientific information. In particular, it is EPA's scientific basis for concluding that "morphometric measurements from anterior corpus callosum and striatum taken at a brain depth identified as plate 17 (block level I) and from posterior corpus callosum taken at plate 31 (block level II) ... were reasonably representative of the brain areas examined" (pp. 4-33, -34). However, EPA did not disclose any material information about this reference. Independent, external reviewers do not have enough information from what EPA has disclosed to reproduce it.

Recommended corrective actions. If EPA intends to rely on this reference for influential scientific information, the Agency must publicly disclose all notes, transcripts, derivative notes, and internal memoranda, produced for or by Annie M. Jarabek and other "attending team members" related to this teleconference. For an independent, external reviewer to be able to reproduce the data on which EPA's conclusion rests, the same information available to EPA and its employees (including employees of other federal agencies assigned to this project) must be made available to the public. This includes all materials that make up the pre-dissemination review undertaken by the Agency to ensure that applicable information quality standards were met. Except in areas where disclosure is contrary to the public interest (e.g., national security, privacy), federal information quality guidelines do not permit an agency to withhold critical information.

g. Attachment in Marcus (2003c)[8] is not disclosed

The above reference is one of three internal EPA memoranda that make up the Agency's new analysis of existing human data. According to the memorandum, "The modeling approach and results are described more fully in the attachment" (p. 3). EPA did not disclose the attachment to this memorandum, however. The reference thus does not satisfy procedural requirements for transparency sufficient to enable independent, external reviewers to reproduce the information contained in the memo and relied upon by EPA in its *Disposition* document.

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[7] Garman, R.H., 2003. Personal communication [with Annie M. Jarabek and attending team members on February 28, 2003 teleconference regarding 2003 brain morphometry analyses and neurodevelopmental endpoints]. Research Triangle Park, NC: U.S. Environmental Protection Agency, National Center for Environmental Assessment, February 28.

[8] Marcus, A. H., 2003. Analyses of dose-response functions for effects of perchlorate on serum hormone from data of Greer et al. (2000, 2002) and Merrill (2001a) [memorandum with attachment to Annie M. Jarabek]. Washington DC: U.S. Environmental Protection Agency, National Center for Environmental Assessment, October 1.

Recommended corrective actions. EPA must publicly disclose the attachment to this reference. In addition, EPA must disclose any other information that is needed for independent, external reviewers to reproduce the information contained in the memo.

4. Explanation of how the alleged error affects or how a correction would benefit you.

The Perchlorate Study Group is an alliance of firms engaged in the production or use of perchlorate. PSG has funded much of the scientific research related to the potential human health effects of perchlorate, including much of the data EPA has relied upon for its draft risk assessment. PSG's sole interest is in an accurate, fair and unbiased characterization of potential human health risks. Both presentational and substantive objectivity are essential to achieve this goal. Conversely, PSG may be irreparably harmed if EPA disseminates influential scientific information that does not satisfy applicable information quality standards.

Thank you for your prompt and complete attention to this request for correction. As EPA knows, the National Research Council Committee to Assess the Health Implications of Perchlorate Ingestion has scheduled meetings in December 2003 and March 2004. A prompt response by EPA is essential for PSG to participate effectively and constructively in this scientific review. More importantly, the Committee cannot fulfill its obligations without a prompt and complete EPA response. Like PSG, the Committee is almost certain to be incapable of reproducing this information.

Sincerely,

Mr. Michael Girard, Chairman
The Perchlorate Study Group