

US EPA ARCHIVE DOCUMENT

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460



OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 2/25/09

SUBJECT: Transmission of Background Materials and Charge to the Panel for the March 31-April 1, 2009 FIFRA Scientific Advisory Panel (SAP) Session Entitled "Scientific Issues Associated with Designating a Prion as a 'Pest' under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and Related Efficacy Test Methods"

TO: Myrta Christian, Designated Federal Official
Office of Science Coordination and Policy
Scientific Advisory Panel (7201M)

FROM: Joan Harrigan-Farrelly
Director, Antimicrobials Division (7510C)
Office of Pesticide Programs

Attached are 25 pairs of compact discs containing background documents and the Charge to the Panel for the March 31-April 1, 2009 FIFRA SAP session: Scientific Issues Associated with Designating a Prion as a "Pest" under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and Related Efficacy Test Methods. These materials contain neither any information protected under statute as Confidential Business Information (CBI) nor any information protected from disclosure to foreign and multi-national pesticide producers under FIFRA Section 10(g). Some of these materials, which are placed on separate CDs, include information protected by copyright. The Antimicrobials Division (AD) has obtained permission from the publishers to reproduce these copyrighted materials for purposes of the FIFRA SAP review. A list of these documents is attached. A second list of references that may be useful to the SAP but for which copyright permission was not granted to EPA is also attached.

Attachments

Charge to the Panel

1. White Paper Issue: Whether EPA's draft review paper, "Scientific Information Concerning the Issue of Whether Prions Are a 'Pest' under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)," adequately identifies and summarizes available, relevant scientific studies.

In 2005, EPA established a Work Group to develop a Notice of Proposed Rulemaking (NPRM) that defines a prion as a "pest" under FIFRA. To assure that it considers key available scientific studies that are relevant to the issue of whether a prion is a "pest" under FIFRA, the Work Group drafted a review paper. While the paper received intra-Agency review, it was not subjected to peer review outside of EPA. Accordingly, EPA seeks the SAP's peer review of the attached, draft review paper (USEPA 2008). Some of the key references cited in the review paper have been provided to the SAP.

EPA wishes to point out that the NPRM will also focus on legal and policy matters that are not addressed in depth in the "white paper." EPA is presenting this paper to the SAP solely for review as to its characterization of the scientific issues, and is not asking the SAP to interpret legal/policy issues such as Congress' intent in drafting FIFRA.

- **Please comment on the accuracy of the characterization of the nature of prions, and the adequacy of the review of the relevant scientific information to support that characterization, as presented in EPA's draft paper, "Scientific Information Concerning the Issue of Whether Prions Are a 'Pest' under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)."**

2. Efficacy Guidance Test Method Issue: Whether the specific test systems recommended in the draft guidance document are scientifically appropriate to support the registration of pesticide products with prion-related claims.

The draft efficacy guidance document (USEPA 2009) recommends a carrier-based, animal infectivity test method, if the intended use of a product is for treating environmental surfaces, and a suspension-based, animal infectivity test method if the intended use of a product is for treating liquids. The draft efficacy guidance document also states that the test methods may either be end-point titration or incubation time interval assays. EPA is interested in knowing the SAP's opinion on whether these recommended test systems are scientifically sound and

appropriate approaches to evaluating the efficacy of pesticide products with prion-related claims. EPA would also like to know whether the SAP recommends that other test methods be considered to evaluate the efficacy of pesticide products used either on environmental surfaces or in liquid media.

- **Please comment on the scientific appropriateness of:**
 - a. **Carrier-based, animal infectivity assays recommended by EPA's guidance for evaluating the efficacy of pesticide products used on environmental surfaces (e.g., hard, nonporous surfaces).**
 - b. **Suspension-based, animal infectivity assays recommended by EPA's guidance for evaluating the efficacy of pesticide products used in liquid media (e.g., wastewater).**
 - c. **Any other known test methods for evaluating the efficacy of pesticide products used on either environmental surfaces or in liquid media.**

3. Efficacy Guidance Performance Criterion Issue: Whether the product performance criterion specified in the draft guidance document to support the registration of pesticide products with prion-related claims is scientifically sound.

The draft efficacy guidance document recommends a target efficacy criterion of six (6) logs of reduction of infectivity in the treated versus untreated (control) groups. This criterion is widely used in the current scientific literature. EPA would like the SAP's comment on this proposed product performance criterion.

- **Please comment on the scientific soundness of the product performance criterion recommended in the draft guidance document to support the registration of pesticide products with a prion claim.**

4. Efficacy Guidance Labeling Claim Issue: Whether the labeling claim described in the draft guidance document is scientifically appropriate based on the recommended test systems and product performance standard.

The draft efficacy guidance document recommends a carefully worded labeling claim statement: "Has been demonstrated to reduce infectivity of prions (TSE agents) based on testing using (insert type of organism in

which the prions were raised) (insert prion type)." EPA believes that claims that may normally be applied to microorganisms (e.g., "destroy," "mitigate," "eliminate," "control") may be misleading when applied to prions. Because currently available test methods can only measure a reduction in infectivity, and the total elimination or destruction of prions cannot be measured, EPA believes that "reduce infectivity" is the only appropriate claim.

- **Please comment on the scientific appropriateness of the term "reduce infectivity" in a label claim to reflect the action of a pesticide on prions.**

5. Efficacy Guidance Hierarchy Issue: Whether different prion types exhibit variation in the degree of resistance to inactivation by pesticide chemicals and whether a hierarchy of resistance by prion type can be reliably determined at this time.

Comparisons of different types of prions in a common animal infectivity assay indicate there may be significant differences with regard to their ability to resist inactivation by pesticide chemicals. For example, Peretz et al. (2006) compared the resistance of hamster scrapie and human CJD prions in transgenic mice expressing either hamster PrP or a chimeric mouse-human PrP transgene and found that human sCJD prion tested was 100,000 fold more difficult to inactivate than hamster Sc237 prion. Preliminary additional studies indicate that the cow BSE prion may be even more resistant to inactivation than the human CJD prion (Giles et al. 2006; 2008 in press).

- **Please comment on whether a hierarchy of resistance among prion types can be reliably demonstrated for different pesticide chemicals based on the available data.**

References being provided to the SAP by EPA with copyright permission

Aguzzi A, Baumann F, and Bremer J. 2008. The prion's elusive reason for being. *Annu. Rev. Neurosci.* 31:439-477. *Reprinted with permission from the Annual Review of Neuroscience.*

Bolton DC, McKinley MP, and Prusiner, SB. 1982. Identification of a protein that purifies with the scrapie prion. *Science* 218:1309-1311. *Reprinted with permission from AAAS.*

Chen JHS. 1975. Comparison of virus recovery techniques for assessing the virucidal activity of disinfectant spray products. *JAOAC* 1975; 58(1):130-2. *Reprinted with permission from AOAC International.*

Chesebro B, Trifilo M, Race R, Meade-White K, Teng C, LaCasse R, Raymond L, Favara C, Baron G, Priola S, Caughey B, Masliah E, and Oldstone M. 2005. Anchorless prion protein results in infectious amyloid disease without clinical scrapie. *Science* 308: 1435-1439. *Reprinted with permission from AAAS.*

Colby DW, Zhang Q, Wang S, Groth D, Legname G, Riesner D, and Prusiner SB. 2007. Prion detection by an amyloid seeding assay. *PNAS* 104:20914-20919. *Reprinted with permission from National Academy of Science USA.*

Collinge J. 2001. Prion diseases of humans and animals: Their causes and molecular basis. *Annu.Rev. Neurosci.* 24:519-550. *Reprinted with permission from the Annual Review of Neuroscience.*

Legname G, Baskakov IV, Nguyen OAB, Riesner D, Cohen FE, DeArmond SJ, Prusiner SB. Synthetic mammalian prions. 2004. *Science* 305; 673-676. *Reprinted with permission from AAAS.*

Manuelidis L, Yu Z-X, Barquero N, and Mullins B. 2007. Cells infected with scrapie and Creutzfeldt_Jacob disease agents produce intracellular 25-nm virus-like particles. *PNAS* 104:1965-1970. *Reprinted with permission from National Academy of Science USA.*

Peretz D, Supattapone S, Giles K, Vergara J, Freyman Y, Lessared P, Safar JG, Glidden DV, McCullooch C, Nguyen O-H B, Scott M, DeArmond SJ, and Prusiner SB. 2006. Inactivation of prions by sodium dodecyl sulfate. *J. Virol.* 80:322-331. *Reprinted with permission from ASM.*

Prusiner SB. 1982. Novel proteinaceous infectious particles cause scrapie. *Science* 216:136-144. *Reprinted with permission from AAAS.*

USEPA. 2004. Considerations of Prions as a Pest under FIFRA. Memorandum to The Record from Susan B. Hazen, Principal Deputy Assistant Administrator, Office of Prevention, Pesticides, and Toxic Substances. April 29, 2004.

USEPA. 2008. Scientific Information Concerning the Issue of Whether Prions Are a 'Pest' under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Unpublished draft; 12/17/08.

USEPA. 2009. Product Performance Test Guidelines OPPTS 810.XXXX
Products with Prion-Related Claims. Unpublished draft; 2/19/09.

Zobeley E, Flechsig E, Cozzio A, Enari M, and Weissman C. 1999. Infectivity of scrapie prions bound to a stainless steel surface. *Molecular Medicine* 5:240-243. *Reprinted with permission from Molecular Medicine.*

Additional references that may be useful but cannot be provided to the SAP by EPA because copyright permission was not granted

Aguzzi A, Baumann F, and Bremer J. 2008. The prion's elusive reason for being. *Annu. Rev. Neurosci.* 31:439-477.

Castilla J, Saa P, Hetz C, and Soto C. 2005. In vitro generation of infectious scrapie prions. *Cell* 121: 195-206.

Castilla J, Morales R, Saa P, Barria M, Gambetti P, and Soto C. 2008. Cell-free propagation of prion strains. *The EMBO Journal* 27:2557-2566.

Collinge J. 2001. Prion diseases of humans and animals: Their causes and molecular basis. *Annu.Rev. Neurosci.* 24:519-550.

Giles K, Peretz D, Glidden DV, and Prusiner SB. 2006. Poster SA-05. Prion 2006: strategies advances and trends towards protection of society. Turin, Italy, 3-6 October.

Manuelidis L. 2007. A 25 nm virion is the likely cause of transmissible spongiform encephalopathies. *J. Cell Biochem.* 100:897-915.

Prusiner SB, Cochran SP, Downey DE, Groth DF. 1981. Determination of scrapie agent titer from incubation period measurements in hamsters. *Adv Exp Med Biol.* 134:385-99.

Prusiner SB, Cochran SP, Groth DF, Downey DE, Bowman KA, Martinez HM. 1982. Measurement of the scrapie agent using an incubation time interval assay. *Ann. Neurol.* April;11(4):353-8.

Prusiner SB, Groth DF, Bolton DC, Kent SB, and Hood LE. Prusiner, S.B. 1984. Purification and structural studies of a major scrapie prion protein. *Cell* 38:127-134.

Weissmann C, Enari M, Klohn PC, Rossi P, Flechsig E. 2002. Transmission of prions. *J Infect Dis* 186 Suppl 2:S157-65.