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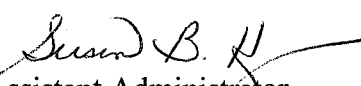
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

April 29, 2004
(Supercedes March 2, 2004 memorandum)

MEMORANDUM

SUBJECT: Consideration of Prions as a Pest under FIFRA

FROM: Susan B. Hazen 
Principal Deputy Assistant Administrator
Office of Prevention, Pesticides, and Toxic Substances

TO: The Record

The attached document embodies my decision on September 10, 2003, that prions should be considered to be a pest under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended (FIFRA).

Attachment

**Record of Decision by Principal Deputy AA/OPPTS Regarding
Status of Prions under FIFRA**

April 29, 2004

Supercedes March 2, 2004

Summary of Decision

On September 10, 2003, Susan Hazen, Principal Deputy Assistant Administrator for the Office of Prevention, Pesticides, and Toxic Substances (OPPTS), decided that prions should be considered to be a "pest" under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended. She said a multi-part approach should be followed:

1. The Agency should proceed on the basis that prions are pests under FIFRA.
2. Applications for registration and for emergency exemptions for products for use against prions should be examined and appropriate decisions made.
3. EPA should follow an appropriate regulatory process to make explicit the Agency's interpretation that prions are pests because they share many of the characteristics of deleterious microorganisms. At the same time, EPA should exercise its authority to declare prions to be a form of plant or animal life which is injurious to health or the environment and which is a pest under Section 25(c)(1) of FIFRA.
4. Coordinate with other EPA offices and other federal agencies as necessary (e.g., USDA/APHIS).

As background for this decision, OPPTS evaluated a large body of available scientific information about prions, and consulted with other EPA offices, including the Office of General Counsel, the Office of Research and Development, and the Office of Enforcement Compliance and Assurance. This document summarizes the factual basis and the rationale for the decision that prions should be considered to be pests.

Background on Prions

- Certain proteins found in cells of the central nervous system of humans and animals appear to exist in both a normal (correctly folded), noninfectious form and in an abnormal (misfolded), infectious form. The normal proteins, which are believed to be involved in cell-to-cell communication, are designated as PrP. The abnormal, infectious proteins are called "prions," and are designated either as PrP^{Sc} (for the prion isoform found in sheep-scrapie) or PrP^{res} (for "resistant" prion isoforms) (1, 2). Dr. Stanley Prusiner, who won a Nobel Prize for identifying prions, initially described prions as "proteinaceous infectious particles that resist inactivation by procedures which modify nucleic acids" (3). He later described prions as proteinaceous particles that lack nucleic acids (4).

- There is a growing consensus that prions can invade and attack the central nervous systems of both animals and man, causing fatal diseases called "transmissible spongiform encephalopathies" (TSE) (5). In order to demonstrate that prions are the infectious agents responsible for TSEs, researchers had to establish several principles of infectivity. First, the prions had to be isolated from infected hosts with known cases of prion disease. Then the prions had to be re-inoculated into susceptible hosts. Finally, the prions had to be re-isolated from the susceptible hosts following the onset of disease. Following these principles, researchers have developed persuasive evidence that prions are the infectious, causative agents for TSEs such as Scrapie in sheep, Bovine Spongiform Encephalopathy (BSE) in cattle, and Creutzfeldt-Jakob Disease (CJD) in humans. BSE is of considerable public health interest and concern because it has been associated with the variant form of CJD; both have no known cure and can take many years to manifest symptoms. Symptoms in humans are severe and can include personality change, dementia and ataxia (loss of motor skills). Once symptoms are exhibited, death usually occurs within six months to one year.
- Prions appear to be most infectious when they come into direct contact with susceptible tissue. They may be transmitted from host to host by contaminated surgical instruments, direct transfer of infected tissue, or the ingestion of contaminated food or feed. Cases of TSE diseases appear to have resulted in humans and animals via all three of these routes of infectivity. For example, BSE appears to have been transmitted in herds throughout England because offal, bones and wastes from infected carcasses were processed and incorporated into animal feeds. Variant CJD (vCJD) then appears to have been transmitted from cattle to humans through ingestion of BSE prion-contaminated beef products.
- Prions (while not viruses) share characteristics with viruses, which are listed in FIFRA Section 2(t)(2) among the things that the Administrator may declare to be pests pursuant to FIFRA section 25(c)(1). Prions, like viruses, lack certain characteristics commonly associated with life (and are not currently considered to be "living"): they neither eat nor excrete and have no apparent metabolic activity on their own. Neither prions nor viruses reproduce sexually or asexually, however, both replicate through infection of living tissue. Prions and viruses differ in several ways. First, prions appear to contain only protein and lack genetic material, whereas viruses contain proteins and either DNA or RNA. Also, prions appear to propagate by inducing certain normal proteins present in host cells to fold into the same abnormal, infectious form. In contrast, viruses attach themselves to host cells, utilize the host's genetic material, and replicate using the host's mechanisms for reproducing cells. Despite the difference in the mechanisms of replication, both prions and viruses utilize a host or host tissue, both disrupt normal cell function, both increase in number in the host, and, in the process, both produce disease.
- Prions are extremely resistant to inactivation by ultraviolet light, irradiation, boiling, dry heat, formalin, freezing, drying and changes in pH. Methods for inactivating prions in

infected tissues or wastes include incineration at very high temperatures and alkaline hydrolysis. There is no known method of inactivating prions within living host tissue.

- There are currently no EPA registered products approved for inactivation of CWD agents from contaminated surfaces. Several states in Region 8 have applied for an emergency exemption under FIFRA for the use of a commercial aqueous acid phenolic product for inactivation of the CWD agent on contaminated surfaces. If an emergency exemption is granted, the product must be used according to the conditions of the exemption. The Centers for Disease Control and Prevention (CDC) and the World Health Organization recommend sodium hydroxide and sodium hypochlorite (bleach) for inactivating TSE agents on surfaces (6). However, these chemicals would need to be granted an exemption (or a registration) prior to sale and distribution in the U.S. with claims for this use.

Rationale

The Principal Deputy AA/OPPTS decided that prions should be considered to be a "pest" under FIFRA for the following reasons, based on the information presented to her:

- As discussed above, prions are unquestionably injurious to the health of humans and other animals. They cause TSE diseases that attack the nervous system, inflict irreversible damage, and are always fatal to infected animals and humans. These infectious particles, once introduced into an animal or human, induce neuronal cells to replicate other prions that in turn attack other neuronal cells, primarily in the central nervous system. Finally, prions are considered among the most difficult of all biological entities to inactivate and few methods are available for effectively destroying them.
- FIFRA section 2(t) provides that "[t]he term 'pest' means (1) any insect, rodent, nematode, fungus, weed, or (2) any other form of terrestrial or aquatic plant or animal life or virus, bacteria, or other micro-organism (except viruses bacteria, or other micro-organisms on or in living man or other living animals) which the Administrator declares to be a pest under section 25(c)(1)." Thus, Congress has determined that all members of the classes listed in section 2(t)(1) are pests, and has in addition authorized EPA to declare as pests members of the classes listed in section 2(t)(2). Section 25(c)(1) authorizes the Administrator, after notice and opportunity for hearing, "to declare a pest any form of plant or animal life (other than man and other than bacteria, virus, and other micro-organisms on or in living man or other living animals) which is injurious to health or the environment." Pursuant to section 25(c), EPA promulgated the rule now codified at 40 C.F.R. §152.5, where it declared any microorganism to be a pest under circumstances that make it deleterious to man or the environment (other than those on or in living man or other living animals). As explained below, since prions share many of the characteristics of deleterious microorganisms, they can be considered to be pests inasmuch as they are clearly deleterious to man and the environment.
- Microorganisms are defined differently in different dictionaries. The American Heritage

Dictionary (7) defines "microorganism" as "[a]n animal or plant of microscopic size, especially a bacterium or a protozoan." Dorland's Medical Dictionary (8) defines "microorganism" as "a minute living organism, usually microscopic. Those of medical interest are bacteria, rickettsiae, viruses, molds, yeasts, and protozoa." This definition explicitly considers viruses to be living organisms, so prions might fall within its scope as well. Webster's Collegiate Dictionary (9) defines "microorganism" as "an organism of microscopic or ultramicroscopic size;" and "organism" as "1: a complex structure of interdependent and subordinate elements whose relations and properties are largely determined by their function in the whole." Whether prions may be considered to be a "microorganism" is subject to interpretation. Prions might reasonably be considered to share many of the characteristics of microorganisms because they may have "a complex structure of interdependent and subordinate elements whose relations and properties are largely determined by their function in the whole," and because they are "of microscopic or ultramicroscopic size."

- Another view is that prions are a "form of ... plant or animal life" because they originate in living organisms, they replicate within those host organisms by converting parts of the host into prions, and they can be transmitted to other host organisms. Like viruses, prions lack certain characteristics commonly associated with life, however, prions share with other pests the characteristics of being able to increase in number and spread by attacking host organisms, with catastrophic harm to the host organism. In addition, prions consist of protein, one of the critical components of life. Thus, one can reasonably argue that prions can be considered to be a "form of plant or animal life" along with viruses, bacteria and other microorganisms. If so, the Administrator might declare these forms of life to be pests pursuant to section 25(c)(1).
- Under FIFRA, EPA regulates a wide range of pesticide products that are intended to prevent or destroy microorganisms. Such products include biocides, sanitizers, disinfectants, and sterilants. EPA's charge under FIFRA is to assure that "no unreasonable adverse effects" will result from the use of these products. In particular, for products intended to kill microorganisms of public health significance, the EPA reviews product performance (efficacy) data to determine that the product will kill the target microorganisms. If products claimed to prevent or destroy prions were not regulated under FIFRA, it is not clear that an adequate mechanism for regulatory oversight of the safety and efficacy of such products could be put into place in a timely manner to address a public health crisis. Absent regulatory oversight such as that provided under FIFRA, persons who need to control prions would have no assurance that products claiming to control prions were either effective or safe.
- In 2002, pursuant to FIFRA section 28(d), EPA issued a list of pests of "significant public health importance" in Pesticide Registration Notice 2002-1. This list, which included prions, was compiled in coordination with the Departments of Health and Human Services and Agriculture, and issued after public notice and opportunity to comment. There were no comments objecting to EPA's inclusion of prions on this list of pests of

significant public health importance.

- For the foregoing reasons, the Agency believes that prions share enough characteristics of either "micro-organism" or of "form of ... plant or animal life" to fall within the scope of FIFRA section 2(t)(2). The Administrator has declared deleterious microorganisms to be pests in 40 C.F.R. §152.5, and the Administrator might also declare prions to be forms of life which are injurious to health or the environment and which are pests, pursuant to FIFRA section 25(c)(1).
- The reasonableness of EPA's decision to consider prions pests is supported by the fact that Congress has also considered prions to be pests – albeit in the context of animal health legislation. The Animal Health Protection Act (AHPA) of 2002 includes prions within the definition of a "pest." That statute states that a pest is: "any of the following that can directly or indirectly injure, cause damage to, or cause disease in livestock...(E) A virus or viroid...(F) An infectious agent or other pathogen...(I) A prion... (K) Any organism similar to or allied with any of the organisms described in this paragraph."¹ This definition is more expansive than the definition of "pest" in FIFRA, which includes "(1) any insect, rodent, nematode, fungus, weed, or (2) any other form of terrestrial or aquatic plant or animal life or virus, bacteria, or other micro-organism... which the Administrator declares to be a pest under section 25(c)(1)."²
- Finally, the definition of "pest" as it appears in FIFRA Section 2(t)(2) has not been changed by Congress since 1972. The existence of prions was widely not postulated or demonstrated until well after that date. Given Congress' inclusion of viruses in that definition, even though viruses are not living microorganisms, it is reasonable to suggest that the intent of Congress was that EPA, under FIFRA, should regulate deleterious forms of animal or plant life that share the characteristics of viruses and other microorganisms.

Conclusion

¹ 7 U.S.C. §8302(13). This statute was passed in order to effectuate the finding of Congress that "[T]he prevention, detection, control and eradication of diseases and pests of animals are essential to protect... the health and welfare of the people of the United States." See 7 U.S.C. §8301(2).

² 7 U.S.C. §136(t).

The Principal Deputy AA/OPPTS has decided, based on the best available scientific information and a reasonable interpretation of FIFRA, that EPA should regulate on the basis that prions are a pest under FIFRA. The Agency will follow the four-step approach outlined above.

References

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- (5) Collinge J. 2001. "Prion Diseases of Humans and Animals: Their Causes and Molecular Basis." *Annual Reviews, Neuroscience*. 24: 519-550.
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- (8) Dorland's Illustrated Medical Dictionary. 1974. W.B. Saunders Company, USA
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