

## **FIFRA SAP Convenes First Nano Review**

**By Lynn L. Bergeson**

*NanoBusiness Alliance Newsletter*, Issue 13, January 18, 2010

On November 3-5, 2009, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) met to consider for the first time scientific issues related to the assessment of potential hazard and exposure associated with nanosilver and other nanometal pesticide products. This column briefly summarizes the discussion, and speculates on the outcome.

The decision to convene a SAP was motivated by the U.S. Environmental Protection Agency's (EPA) need to consider four applications pending at the Office of Pesticide Programs (OPP) seeking registration of products containing nanosilver-based active ingredients. The nanosilver products, which would take the form of textile additives, polymers, coatings, and/or plastics, would be used to protect a treated product from microorganisms or to impart antimicrobial activity to a treated material. They would be used in the same manner as some of currently registered silver products, including those used as materials preservatives and antimicrobial pesticides. Notably, many of the 110 currently registered silver-based products actually contain nanosilver.

Unmentioned in either the September 16, 2009, *Federal Register* notice announcing the public meeting or the SAP Background Document EPA prepared in connection with the meeting is a May 2008 petition submitted by the International Center for Technology Assessment (ICTA) and others requesting, among other actions, that EPA classify nanosilver as a pesticide, require the registration under FIFRA of nanosilver products, and determine that nanosilver is a new pesticide that requires a new FIFRA pesticide registration.

### **Key Science Issue**

EPA states in its Background Paper, the current state of the science does not contain sufficient information to determine definitively whether (and, if so, to what extent) various forms of nanosilver particles may cause toxic effects beyond those attributable to the release of silver ions. In light of this, the threshold question before the SAP relates to whether EPA can make its safety finding under FIFRA that a pesticide product will not cause unreasonable adverse effects on the environment with respect to the four pending applications.

According to EPA, the registration applicants claim that the mode of action for nanosilver is the same as for silver in that the release of silver ions is the source of antimicrobial activity. Because the pesticidal mode of action of nanosilver is the same as for conventionally sized silver, the potential hazards to human health and the environment resulting from the use of nanosilver as a pesticide will therefore be the same as from the use of silver. EPA likened the registrants' argument to that of the so-called 0-hypothesis put forward by S. Wijnhoven *et al.* (2009). The 0-hypothesis is that the toxic effects of nanosilver are proportional to the activity of free silver ions released by the nanoparticles. The question, then, for FIFRA regulatory purposes becomes whether sufficient data and information exist to validate the hypothesis. This requires a two-step

process: (1) determine whether nanosilver particles enter the body; and (2) determine whether nanosilver releases silver ions and to what extent the ions will be absorbed.

EPA further states that registration applicants posit that there will be no or only trivial levels of human exposure to nanosilver particles since these particles will not leach from finished products. As a result, any toxic effect to humans would be the result of exposure to silver ions and, as the argument goes, since the effects of exposure to silver are already well understood, no new toxicity testing is necessary.

EPA expressed several concerns with this argument. First, the acute toxicity studies that are routinely submitted with pesticide registration applications do not evaluate the effects of repeated low levels of exposure, and the only endpoints measured are mortality and clinical signs. In addition, acute toxicity studies on nanosilver or nanosilver composites were conducted according to guideline standards intended for conventionally sized antimicrobial pesticides, and there is no characterization of the test material provided in the study reports. The results may thus be biased or confounded. Finally, EPA is concerned about exposure to nanosilver by people handling or applying the nanosilver pesticide product, as well as consumers' exposure to nanoparticles when using the final product as intended.

### **SAP Charge**

EPA asked the SAP to consider whether pesticide products containing nanosilver as the active ingredient pose potential hazards different from those associated with products containing conventional silver, what types of data would EPA need to consider to address any potential risks associated with the use of nanosilver particles, how information concerning the percentages of the particles in a product falling in the nanoscale range could affect the risks of a product, what types of new information on individual products would be most useful to EPA in assessing the potential risks posed by antimicrobial pesticides containing nanosilver or nanosilver composites, and related issues.

During the public consultation meeting, panel members acknowledged the significant amount of data on conventional silver, particularly on elemental silver and monovalent silver ion, and the toxicological relevance of the type of study conducted on various silver forms (*in vitro* studies versus other types of studies) in terms of influencing the hazard profile of the silver. The panel cautioned, however, that there are significant data deficits pertinent to the effects of exposure to nanosilver particles over the lifecycle of a product. The panel also noted its uncertainty of the ability to bridge toxicity data between and among various kinds of nanosilver or nanometal oxide products with different physicochemical properties, as well as its concern about other crucially important science issues that, according to the panel, remain largely ill-defined.

### **What Is at Stake**

How the SAP addresses these issues and the recommendations it makes to EPA could have a significant impact on EPA's approach under FIFRA to nanosilver-based active ingredients and nanopesticides in general. To the listening public, the SAP appeared to conclude that the significant data deficits that exist preclude EPA from making the safety finding it must under

FIFRA to register a product. Until the SAP report is issued, however, it is unclear exactly how the SAP will respond to the charge questions, and, of course, whether and how EPA decides to rely upon the recommendations for regulatory purposes. As an immediate and preliminary step, EPA should consider obtaining from existing silver registrants more information about particle size distribution, surface area, and related physicochemical characteristics that would enable EPA to characterize better the nano potential of existing registrations.

Assuming EPA ultimately concludes it lacks sufficient data to make the FIFRA safety finding with respect to nanosilver pesticide products, an important issue that remains unclear is how EPA will ensure that the commercial playing field remains competitive. EPA acknowledges that many of the 110 currently registered silver-based products actually contain nanosilver. It will therefore need to consider how best to address the thorny question of treating nanosilver pesticide registrants and pending nanosilver pesticide applicants fairly.

How exactly EPA will decide to undertake this process is anything but clear. One regulatory response would be to register all such pending products conditionally, assuming all other aspects of the registration application are in order, and subject each to any new data requirements the SAP review may ultimately inspire. EPA has other options under FIFRA, including use limitation, product suspension, and use and/or product cancellation. The appropriate remedy may well be product-specific and require a resource-intensive review of the 110 silver-based products already registered as antimicrobial pesticides.

As the new Administration settles in, nano stakeholders are understandably eager to know how nanotechnology and the many, many science policy issues it inspires will fare. EPA's response to the SAP recommendations will be carefully watched, parsed, and dissected by the nano community as a harbinger of things to come.

*Lynn L. Bergeson is Managing Director of Bergeson & Campbell, P.C., a Washington, D.C. law firm focusing on conventional and engineered nanoscale chemical, pesticide, and other specialty chemical product approval and regulation, environmental health and safety law, chemical product litigation, and associated business issues, and President of The Acta Group, L.L.C. and The Acta Group EU, Ltd with offices in Washington, D.C. and Manchester, UK.*

74 Fed. Reg. 47575 (Sept. 16, 2009).

As noted in the SAP Background Paper, EPA has information suggesting that there are other pesticide products currently in the marketplace that contain nanosilver. The Silver Nanotechnology Working Group (SNWG), an industry group formed to promote the beneficial uses of silver nanoparticles that testified before and submitted comment to the SAP, went so far as to claim that *all* EPA registered silver products through to 1994 were nanoscale (emphasis added) and the majority of existing registered silver products are nanosilver, including the algaecides and water filters that have been used for decades.

Available at [http://www.icta.org/nanoaction/doc/CTA\\_nano-silver%20petition\\_final\\_5\\_1\\_08.pdf](http://www.icta.org/nanoaction/doc/CTA_nano-silver%20petition_final_5_1_08.pdf).

Other countries are considering similar issues. *See, e.g.*, U.K. Advisory Committee on Hazardous Substances Report on Nanosilver, available at <http://www.defra.gov.uk/environment/quality/chemicals/achs/documents/achs-report-nanosilver.pdf>.