Pesticide Scientific Advisory Panel Rejects EPA Effort to Use the Mouse Local Lymph Node Assay for Quantitative Assessment of Dermal Sensitization

EPA convened its FIFRA Scientific Advisory Panel (SAP) on May 4-6, to review a new approach to dermal sensitization risk assessment for pesticides. The Agency's Office of Pesticide Programs (OPP) developed and planned to use this approach to evaluate pending applications to register Acid Copper Chromate (ACC) wood preservative. Hexavalent chromium is a known dermal sensitizer in humans, and EPA staff thought it best to apply this new technique, based upon the Mouse Local Lymph Node Assay (LLNA), to establish acceptable levels of chromium residues on the surface of treated wood. The SAP did not accept EPA's view that the LLNA provides an appropriate basis for quantitation of sensitization responses. With respect to hexavalent chromium, the SAP suggested that EPA base its sensitization risk assessment on the unique body of human data on this material.

Staff at EPA's Antimicrobials Division (which has responsibility for wood preservatives) developed the LLNA-based technique for determining a minimum elicitation threshold (MET) for dermal sensitizers with the intention of using it to evaluate pesticides and pesticide-treated articles (such as preserved wood or plastics). The LLNA was developed by industry as a screening tool for dermal sensitization. It has been validated by a number of laboratories, but never has been used to quantify the level at which a sensitization reaction is likely to occur. EPA's approach was the first effort to use the LLNA in this manner.

At the SAP, EPA presented its proposed assessment methodology along with a 3000 fold safety factor it planned to apply to METs calculated from LLNA data. Several industry representatives made the point that the LLNA had not been developed for use in quantitative assessment, and that there was inadequate experience with it to allow its use in that manner. They also emphasized the importance of using a weight-of-the-evidence approach in evaluating this endpoint.

The SAP reached its conclusion immediately following the close of the public presentations. It concluded that the LLNA is a useful screening tool, and could be useful as part of a weight-of-the-evidence analysis. However, the Panel concluded that the assay is not at this time an appropriate basis for quantitative assessment of dermal sensitization risk. Therefore, the Panel rejected EPA's effort to calculate an MET using the LLNA.

The EPA, industry and members of the public also presented the SAP with information about the dermal sensitization properties of hexavalent chromium and with views on acid copper chromate wood preservative. The Panel concluded that EPA should seek additional information on the reduction of hexavalent chromium to the trivalent form. It also advised EPA to perform a quantitative assessment of the dermal sensitization potential of chromium based upon human patch test data. The SAP performed this analysis and presented its results at the meeting. These indicated that the MET for chromium should be two orders of magnitude greater than the threshold EPA had sought, principally due to the rejection of the 3000 fold safety factor EPA had imposed on the LLNA-derived threshold. The SAP concluded that a much smaller safety factor was appropriate because the threshold was derived from human patch test data, which is known to be reliable and to be approximately ten times more potent than environmental or workplace exposures to tested compounds.

This result is a significant rebuff of EPA's effort to base dermal sensitization thresholds on LLNA data. It means that traditional methods of evaluating sensitization likely will continue to be used. Information on the meeting, including SAP members, the Agenda, EPA's questions to the SAP and the complete docket can be found on the EPA FIFRA SAP website.