

BSC Nomination Review

Meeting of the National Toxicology Program Board of Scientific Counselors

National Institute of Environmental Health Sciences
Rall Building, Rodbell Conference Center
Research Triangle Park, NC

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NTP Study Nomination: o-Phthalaldehyde

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BSC Reviewer: Drs. Nancy Kerkvliet and Jean Regal

1. Does the NTP research concept address the needs of the nomination?

NIOSH nominated o-phthalaldehyde (OPA) for study due to its widespread and increasing use as a disinfectant in health care settings. Its increasing use is attributed to its marketing as a safer alternative to glutaraldehyde, which is a strong skin, eye and respiratory irritant and has been linked to skin and respiratory sensitization in exposed workers or patients. Although toxicity and sensitization data for OPA exist, they are not publically available. The research concept proposed by NTP will characterize the potential for o-phthalaldehyde (OPA) to cause dermal and respiratory sensitization using mouse models, and will assess ADME and systemic toxicity following a yet-to-be-determined route of exposure. NTP will also determine the vapor pressure of OPA. These studies will address the needs of NIOSH.

2. Is the proposed study approach as outlined in the research concept document appropriate in scope given the merit of the nomination? Are there other studies that should be considered for this substance?

Given the uses and marketing of OPA, it is important to have data on the systemic toxicity and sensitization potential of OPA, especially in comparison to glutaraldehyde. However, several Board members expressed frustration that the NTP needs to propose such studies given that relevant data already exist but are not available due to confidentiality. All effort should be extended to obtain this data before any new studies are undertaken. The studies to assess systemic toxicity and ADME were not considered compelling.

Given that OPA is already widely used, the rationale for any additional animal studies were also questioned by some Board members. Rather, since the greatest concern is hypersensitivity (which is difficult to extrapolate from animal tests to human risk), some Board members suggested that research in workers (epidemiology, skin testing, etc,) would be more direct and relevant to the needs of the nomination. With such information,

efforts could be directed more quickly at minimizing exposures in the workplace and educating workers to minimize the chance of allergic sensitization.

3. Does the proposed research program address an important area of biomedical research (e.g. children's health, genetic susceptibility, specific environmental disease) and/or advance the field of environmental health sciences?

The proposed research program would allow comparison of new data with OPA to historical data obtained with glutaraldehyde by NTP and provide some evidence to indicate whether OPA may be less hazardous than glutaraldehyde as a sensitizer at concentrations used for disinfection.

4. Do the nomination and proposed research program merit NTP evaluation and if so, what priority (low, moderate, or high) should it be given?

Low to moderate priority for NTP evaluation based on the specific research proposed. The studies to determine the sensitization potential of OPA should have been done prior to approval of the compound. The sensitization potential of OPA seems high based on its structural similarity to other sensitizers and the available evidence. It is important for the investigators to review the existing privileged and unpublished data in the guinea pig and LLNA to prevent unnecessary duplication of experiments.

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