

# **Prioritization of Chemicals for Developmental and Reproductive Toxicant (DART) Identification Committee Review:**

## **Proposed Chemicals for Committee Consideration September 2007**

### **Reproductive and Cancer Hazard Assessment Branch Office of Environmental Health Hazard Assessment California Environmental Protection Agency**

#### **Summary**

In October 2004, the Office of Environmental Health Hazard Assessment (OEHHA) adopted a prioritization process by which the Developmental and Reproductive Toxicant Identification Committee (DART IC) will review and select chemicals for preparation of a hazard identification documents and consideration of listing under Proposition 65. Based on this process, endorsed by the DART IC and adopted in 2004, OEHHA is requesting the DART IC to review preliminary data on eight chemicals that have been subjected to an epidemiology data screen and a preliminary toxicological evaluation. These chemicals are: bisphenol-A, bromodichloromethane, caffeine, chlorpyrifos, chromium (hexavalent), dichlorodiphenyldichloroethylene (DDE), methylisocyanate and sulfur dioxide. The eight chemicals and relevant documentation are being released to the public for comment for a 60-day comment period in preparation for consultation with the DART IC during its fall/winter 2007 meeting. At that meeting, the DART IC will recommend to OEHHA whether hazard identification materials should be prepared for these chemicals as the next step toward future consideration of their listing.

#### **Background**

In 2002, the Carcinogen Identification Committee (CIC), the state's qualified experts for carcinogenicity under Proposition 65, asked OEHHA to improve its process for prioritizing chemicals for review and potential listing. Leads from the CIC were identified to provide consultation to OEHHA in developing the improved process. Subsequently, the Chair of the DART IC identified leads from that committee to also provide consultation to OEHHA. It was suggested that an improved process should more fully reflect exposure in California to chemicals under consideration, populations exposed, and the degree and extent of potential harm. In consultation with members of the DART IC and CIC, OEHHA undertook development of the improved process. There were two 30-day public comment periods on the draft prioritization process document. During the first of these, a public workshop was also held, at which additional comments were accepted. The prioritization process document was revised based upon the public comments and input from members of the DART IC and CIC. The proposed revised prioritization process was presented to the DART IC at a public meeting on November 4,

2004, and to the CIC at a public meeting on November 1, 2004. After opportunity for additional public comment at each of these meetings, the proposal was discussed and endorsed by both committees. Accordingly, on December 17, 2004, OEHHA adopted this prioritization process that it now uses to select chemicals for DART IC and CIC and review.

In accordance with the 2004 prioritization process, OEHHA used a focused literature review to conduct a preliminary appraisal of exposure potential and evidence of hazard on candidate chemicals in its database. The evidence of hazard used in this round of prioritization was an epidemiologic data screen, as described below. The chemicals that passed the screen were then subjected to preliminary toxicological evaluation. In the next step, OEHHA will release the results of the evaluation for public comment. At its December 2007 meeting, the DART IC will provide advice and consultation to OEHHA regarding possible development of hazard identification materials on the chemicals presented here. The following is a description of the process OEHHA conducted to screen potential chemicals and select chemicals for possible future consideration by the DART IC.

## **Chemicals screened**

Following the process outlined in Figure 1, OEHHA screened all candidate chemicals in the tracking database for data suggesting that they cause reproductive and developmental effects and have potential for exposure in California. The evaluation of exposure potential was qualitative, based primarily on data concerning production and use of the chemical, or monitoring data. Candidate chemicals were not screened if they had already been assigned a final priority under OEHHA's former prioritization process or if they were candidates for listing via an administrative listing mechanism.

## **Applying the epidemiology data screen**

The epidemiology data screen was applied to 286 chemicals (or chemical groups). The screen entailed the identification of chemicals with epidemiologic studies suggesting evidence of adverse developmental or reproductive effects. OEHHA conducted a literature search to identify epidemiologic studies of the chemical that report an association between exposure to the chemical and increased risk of adverse developmental or reproductive effects. More weight was given to analytical studies, and less weight to descriptive studies and case reports. Single case reports were not sufficient to satisfy the screen. For those chemicals with studies available, the abstracts were examined in detail to determine whether there was a positive finding of developmental or reproductive effects associated with exposure to the chemical. The abstracts were further reviewed to determine whether the effect might be attributed with some confidence to exposure to the chemical of concern. Two or more analytical studies of adequate quality were required for the chemical to pass the screen.

## **Preliminary toxicological evaluation**

After applying the epidemiologic data screen, OEHHA then conducted a preliminary evaluation of the animal toxicology data for the chemicals identified. This involved a further search of the literature to identify animal reproductive or developmental toxicity studies, studies on the mechanism of action, metabolism, and pharmacokinetics. This additional information was used in conducting a preliminary evaluation of the overall evidence of reproductive or developmental toxicity for each of the chemicals identified by the epidemiology data screen. Chemicals for which the preliminary evaluation indicated that developmental and reproductive toxicity might be a concern are being proposed here for DART IC consideration.

## **Chemicals proposed for DART IC consideration**

The above process yielded eight chemicals: bisphenol-A, bromodichloromethane, caffeine, chlorpyrifos, hexavalent chromium, dichlorodiphenyldichloroethylene (DDE), methylisocyanate and sulfur dioxide. A ninth chemical, nitrous oxide, also passed the screen for potential DART IC review. However, this chemical was subsequently identified as a candidate for listing under the Labor Code listing mechanism (Health and Safety Code section 25249.8(a)). Therefore, this chemical is not being proposed for committee review at this time.

The Appendix provides an explanation of why each of the eight chemicals was chosen. Briefly, for each chemical chosen there were available at least two analytical epidemiologic studies of adequate quality reporting an association between exposure to the chemical and increased risk of adverse developmental or reproductive outcomes (the basic criterion for selection), plus additional relevant studies in humans and animals. The number of analytical epidemiologic studies of adequate quality reporting such an association for each chemical was:

- Bisphenol-A, 2
- Bromodichloromethane, 4
- Caffeine, 30
- Chlorpyrifos, 6
- Chromium (hexavalent), 5
- Dichlorodiphenyldichloroethylene (DDE), 17
- Methylisocyanate, 2
- Sulfur dioxide, 7

Epidemiological studies and other data relevant to the reproductive or developmental toxicity of these eight chemicals are provided in papers and other materials listed in the Appendix. Abstracts of studies obtained, when available, from sources such as on-line journals or PubMed have been included verbatim in the Appendix.

## Next Steps

With the publication of this document on September 7, 2007, OEHHA opened the public comment period on the chemicals proposed for DART IC consideration. The comment period closes on November 6, 2007.

The DART IC will deliberate on the eight chemicals proposed for its consideration at its December 10 meeting, and provide advice and consultation regarding possible development of hazard identification materials. Written public comments received by OEHHA before November 6, 2006, will be provided to the DART IC for review.

At the DART IC meeting, the public will be given the opportunity to comment on the chemicals being proposed for possible hazard identification materials preparation. The DART IC could vote on recommendations or provide less formal advice to OEHHA concerning which chemicals should be brought back for future consideration for listing. In addition, the DART IC may also suggest other chemicals for which hazard identification materials should be prepared.

OEHHA will prepare hazard identification materials for any chemicals that the DART IC recommends for further consideration. These materials will summarize the available scientific evidence on the developmental and reproductive toxicity potential of the selected chemicals, based on an exhaustive search and evaluation of the scientific literature. OEHHA will provide these materials to the DART IC and release them for public comment. The DART IC will then hold another public meeting to deliberate the listing of the chemicals.

Further details on prioritization, the development of hazard identification materials, and committee consideration of the listing of chemicals under Proposition 65 are given in the OEHHA document cited below.

## Reference

Office of Environmental Health Hazard Assessment (OEHHA, 2004). *Process for Prioritizing Chemicals for Consideration under Proposition 65 by the "State's Qualified Experts."* California Environmental Protection Agency, OEHHA, Sacramento, CA, December. Available online at:  
[www.oehha.ca.gov/prop65/CRNR\\_notices/state\\_listing/pdf/finalPriordoc.pdf](http://www.oehha.ca.gov/prop65/CRNR_notices/state_listing/pdf/finalPriordoc.pdf)