

Review Summary

NTP Executive Committee Working Group for the Report on Carcinogens (RG2)

Nomination: Diazoaminobenzene (DAAB)

Review Date: 7/22/2003

Major issues discussed

Application of criteria

Exposure

There was no data available on US production of DAAB or on environmental or occupational exposures. However, there are 7 US suppliers of DAAB and it is allowed as an impurity in dyes permitted for use in drugs and cosmetics.

Carcinogenicity

Animal Data:

The RG2 felt that the oral, dermal and injection studies in mice published in the late 1940s were inadequate to evaluate the carcinogenicity of DAAB in experimental animals.

Human Data:

No human study data are available for DAAB.

Other Scientific Concerns

DAAB is metabolized to benzene, a known human carcinogen, and to aniline, a chemical that induced tumors in animals. It was noted that there are other chemicals (e.g. benzidine dyes) that are listed in the RoC in part based on their metabolism to *known* or *reasonably anticipated* to be human carcinogens. In oral studies on the absorption, distribution, metabolism, and excretion of DAAB in mice and rats, benzene and aniline were detected in blood, benzene was measured in exhaled breath, and metabolites of aniline and benzene were excreted in urine. Reductive metabolism of DAAB to benzene, aniline and nitrogen likely occurs in the GI tract. Metabolism may also occur in liver as *in vitro* studies indicate cytochrome P450 reductase will catalyze the reductive cleavage. *In vitro* studies with human hepatocytes indicate that DAAB can be reduced to aniline and benzene in humans. *In vivo* ESR studies show that phenyl radicals are produced as intermediates in the metabolism of DAAB to benzene. In addition, DAAB and benzene induced micronuclei in mice; however, the effect of DAAB was greater than a mixture containing equivalent doses of benzene plus aniline. DAAB is also mutagenic in *Salmonella* with metabolic activation, whereas benzene and aniline are not. The RG2 noted that even though there is little exposure information available, they felt it important to identify this chemical as a cancer hazard because it is allowed as an impurity in dyes permitted for use in drugs and cosmetics.

Recommendation

Motion:

Recommend that Diazoaminobenzene be listed in the RoC as *reasonably anticipated to be a human carcinogen* based on its metabolism to benzene, a *known human carcinogen* and its demonstrated genotoxicity.

Vote on the motion: 8 yes votes to 1 no vote. Negative vote because member felt there was not sufficient evidence for DAAB to list in the RoC.