

exposed to iPB daily for 9 weeks (Kamijima, 1997a, 1997b; Yu, 2001). Daily exposure of male rats to iPB at 300, 1000, and 3000 ppm was associated with effects ranging from reduced body and organ (e.g., kidneys, liver, testis) weight, reduced sperm counts and sperm motility, abnormal sperm, reduced red blood cell and platelet counts, and hemoglobin volume (Ichihara, 1997). A recent study has been published (Sekiguchi, 2002) in which the effects of iPB exposure on the reproductive physiology of female F344 rats were investigated. The rats were exposed to air (in the control group, the number of animals, n, is 7) or 50 (n=6), 200 (n=7), or 1000 (n=9) ppm of iPB via whole-body inhalation for 8 hours/day for 21–24 days (exact number of days not specified in the article). A larger number of females at the high concentration exhibited an estrous cycle of >6 days (7 of 9 animals) than those at the control, low- and mid-concentration (4, 2, and 3, respectively) which corresponded to the greater number of estrous cycles lasting >6 days (9 of 34 animals) in the high-concentration group as compared to the other groups (4 of 31, 4 of 30, 3 of 30). A dose-dependent increase in the number of days/cycle was observed in rats at 200 and 1000 ppm. These increases did not reach statistical significance, however. A smaller number of females per group was analyzed for uterine and ovary weights because only rats showing the estrous stage upon vaginal smear test were chosen for autopsy (5, 5, 5, and 7, respectively in the low-, mid-, and high-concentration groups). No changes were noted in the weights of ovaries or uterus, or in the number of ovulated ova among any of the female groups (exposed or controls). Although this study indicates that iPB was not a strong reproductive toxin in the female rat, the small number of animals exposed is a significant limitation to the study. The dose dependent increase in estrous cycles observed at 200 and 1000 ppm suggest the potential for reproductive failure from exposure to this compound. These results also indicate the need for additional studies using greater numbers of exposed animals.

Both male and female workers occupationally exposed to iPB have been found to exhibit some of the same effects reported in animal toxicological studies. Ichihara (1999) reported low sperm motility, low semen volume, abnormal sperm cells, and decreased blood cell count, hemoglobin and hematocrit in otherwise healthy Chinese male workers exposed to a wide range

of iPB concentrations (2.5–111 ppm). Abnormal or an absence of menstruation was associated with iPB exposure in several female workers, as well as reduced blood cell count, hemoglobin, and hematocrit. Employees of an electronics factory in South Korea showed similar effects following exposure to iPB (Kim, 1996). In female workers, disrupted or absent menstruation, abnormal hormone levels, hot flashes, and abnormal bone marrow were found, while male workers exhibited significantly reduced sperm counts and sperm motility.

CERHR convened an Expert Panel to consider existing toxicological studies on effects of both nPB and iPB. (See section IV.A.1.c. for a discussion of CERHR review process and the Expert Panel Report.) The CERHR Expert Panel came to the following conclusions on the existing studies on iPB (CERHR, 2002b, p. 44):

- Available human and animal data are insufficient to draw conclusions on the potential for developmental toxicity due to iPB.
- There is sufficient evidence that iPB is a reproductive hazard in men and women, particularly based upon the epidemiological data from Korea.
- At low levels (less than 0.004 ppm), there is minimal concern for human reproduction. At higher levels up to 1.35 ppm, there is some concern.
- For reproductive data from male rats, the panel identified a NOAEL of 100 ppm.

The toxicological studies on male reproductive endpoints for iPB have limitations which (e.g., small number of dose groups) make them inappropriate for use in quantitative risk assessment. Although the occupational exposure studies also are limited, given the mutagenicity of the compound and that human exposures have resulted in significant health effects consistent with those reported in the available animal studies, the Agency considers it appropriate to limit the amount of iPB exposure resulting from nPB use to the maximum extent feasible.

Today's action proposes to limit SNAP acceptability of nPB to those formulations of nPB that contain concentrations less than 0.05% iPB by weight before adding stabilizers or other chemicals. The current American Society for Testing and Materials (ASTM) standard for vapor degreasing grade and general grade nPB specifies that unstabilized nPB must have less than 0.1% of iPB as a contaminant. EPA believes that this level should be reduced to 0.05% given the toxicity of iPB, and the fact that achieving a level of 0.05% is technologically feasible and

would not cause significant economic impacts (US EPA, 2003). The Agency also requests comment on the appropriateness of alternative concentration limits for iPB in nPB, including 0.1%. If this provision is finalized, the iPB concentration limit would be a condition that all users in the U.S. must observe in all sectors and end uses where nPB is listed as acceptable.

In order to show compliance with the use condition, end users would need to keep records to demonstrate that the nPB used in the product contains no more than 0.05% iPB by weight before adding stabilizers or other chemicals. Documentation could involve, for example, keeping a certificate of analysis or purity provided by the manufacturer or formulator for two years from the date of creation of that record. Such records are customary business information that chemical companies provide to their customers, so we do not expect that this requirement will impose an additional paperwork burden.

B. Ozone Depletion Potential

The ozone depletion potential (ODP) of a chemical compound provides a measure of its impact on stratospheric ozone levels relative to the impact of an equal mass emission of CFC-11. The Parties to the Montreal Protocol have used the ODP benchmark index as a means of characterizing the relative risks associated with the various ozone-depleting compounds subject to the requirements of the Protocol and to calculate the total allowable production and consumption of different classes of ozone depleting substances. Every four years the World Meteorological Organization publishes the *Scientific Assessment of Ozone Depletion*. These assessments are authored by leading experts in the fields of atmospheric science and atmospheric chemistry, and include the most current research findings relevant to the science of ozone depletion. These assessments, along with other studies in the field of atmospheric chemistry, have traditionally focused on compounds with relatively long atmospheric lifetimes (in excess of 3 months).

Two-dimensional (2-D) models that base calculations on latitude and altitude are sufficient for calculating the ODP of long-lived chemicals. However, 2-D models cannot simulate the complex atmospheric transport pathways that are necessary to determine the ODP of short-lived compounds like nPB (Wuebbles, 2000). nPB is estimated to remain in the atmosphere for only 11 to 20 days after