COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

STATEMENT ON PHTHALATES IN INFANT FORMULAE

1. The Committee was provided with details of the recently completed MAFF surveillance work on phthalates in food and infant formulae in the form of the published Food Surveillance Information Sheets Nos 82 and 83 dated March 1996.[1,2] The Committee understands that the survey of individual phthalates in infant formulae is the first of its kind to be carried out in Europe and welcomes the new information it provides.

2. Phthalates are common environmental contaminants and they have high solubility in fat. Their presence as contaminants in infant formulae and other fat-containing foods is not unexpected. The Committee noted that surveys have found phthalates not only in infant formulae but also in fresh cows milk, meat, poultry, fish and eggs. The Committee is not aware of any information on phthalate levels in human breast milk but would anticipate from the nature of phthalates and the high fat content of breast milk that they are likely to be present in breast milk, as are other fat-soluble environmental contaminants.

3. The Committee was informed that 59 samples from 15 brands of infant formulae were obtained and composite samples of each brand prepared for analysis. All brands tested are widely available in the UK. Although the analytical results only reflect the situation from purchases made at one point in time, they were likely to be generally representative of the UK market as a whole. The Committee noted that phthalates were found in all the infant formulae tested and that levels of total phthalates in the various formulae were similar, all being within one order of magnitude of each other. Levels of individual phthalates were also similar across the various formulae. Whilst the survey gives a good overall picture, there are insufficient data to assess whether any particular brand may have consistently higher phthalate levels than others.

4. The Committee noted that the estimated intakes of individual phthalates were all below the relevant Tolerable Daily Intakes (TDIs) set by the EC Scientific Committee for Food.[3,4] Looking at the overall picture, average intakes of total phthalates from infant formulae were estimated to range from 0.10 to 0.13 mg/kg bodyweight/day over the first 6 months of life. These exceed by 2-3 fold the temporary "group restriction" of 0.05 mg/kg bodyweight/day set by the SCF for those phthalates for which further toxicity testing is required. The Committee notes that TDIs are derived from doses which produce no effect in animal studies divided by a 100-fold safety factor. However the

Committee was aware that new evidence on the reproductive effects of phthalates has been published since these TDIs were set. The Committee therefore gave separate and particular consideration to this aspect.

5. Earlier reproduction and teratology studies on phthalates have shown effects on the testis and on embryonic development only at very high doses and these effects were taken into account by the SCF in setting the TDIs. However in new work, two of the phthalates identified in infant formulae, butylbenzyl phthalate (BBP) and dibutyl phthalate (DBP), have been shown to have weak oestrogenic activity in sensitive *in vitro* assays.[5]

6. BBP has also been shown recently in an *in vivo* study by Sharpe et al[6] to have an effect on the developing rat testis in male offspring whose mothers were given BBP in their drinking water. In this study, a single concentration of 1 mg/l was given throughout pregnancy and lactation, resulting in an estimated maternal oral intake of 0.1-0.4 mg/kg bodyweight/day, but a dose-response relationship was not studied. Testis size in male offspring at 90 days of age was reduced by around 10% and sperm count reduced by around 20%. The mechanism(s) of these effects is unclear, as are the contributions of *in utero* compared with postnatal exposure. The Committee also notes that the critical period for testis development in both humans and rats begins prenatally and in rats extends for two weeks postnatally, but in humans it may extend up until puberty. Thus it may not be satisfactory to use an experimental study on BBP in rats in which exposure has covered the entire prenatal and postnatal critical period to assess the risk of exposure of humans via infant formulae after birth.

7. For DBP there are also recent reassuring data from a US National Toxicology Program (NTP) study on rats using dietary administration over a range of doses.[7] In this study, male offspring were exposed to DBP via their mothers throughout pregnancy and lactation and subsequently directly exposed via the diet until they were adult. The study showed effects on adult testis weight and histopathological lesions at doses of 570 mg/kg bodyweight/day and above, with a no-effect level of 250 mg/kg bodyweight/day.

8. Utilising these new but limited data, the highest estimated intake of BBP in infants on infant formula is 11.5 times lower than the dose said to cause minimal effects in rodents.[6] The average estimated intake of BBP for all the formulae tested is 33 times lower than the dose said to cause minimal effects in rodents. The safety margins based on the data from Sharpe et al[6] are lower than the 100-fold safety margin we would usually wish to see. It should be noted however that the recent *in vitro* studies on BBP and DBP[5] and the *in vivo* study on BBP[6] were not designed for risk assessment purposes and caution should be exercised in extrapolating from these results to humans. In the case of DBP, a risk assessment can be made from the NTP study[7] and even the highest estimated intake of DBP from infant formulae is over 17,000 times lower than the no-effect level found in that study.

9. The Committee considers that further studies are required before a definitive overall risk assessment can be made. These studies would need to establish not only whether the putative oestrogenic or other activities of phthalates have a significant effect in the whole animal and, if so, at what dose they are without effect, but also should screen as yet untested phthalates. It would also be helpful to have data on phthalate levels in human breast milk.

10. In conclusion, the Committee considers that, on the basis of the evidence available to date, the levels of individual and total phthalates found in the recent survey of infant formulae are unlikely to pose any risk to the health of infants being fed on infant formulae, but it would be prudent to ensure there are adequate safety margins. The Committee therefore endorses the action which has already been taken to ask the manufacturers to trace the sources of phthalates present in infant formulae so that levels may be reduced. However, the Committee notes that given the widespead distribution of phthalates and their occurrence in ingredients of infant formulae, it is unlikely it will be possible to eliminate phthalates completely from infant formulae.

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References

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