Comments on the opinion expressed by the CSTEE regarding the report "Validation of methodologies for the release of diisononylphthalate (DINP) in saliva simulant from toys (2001 EUR 19826 EN)"

Prepared by Greenpeace International, July 2001

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Greenpeace Research Laboratories Technical Note 09/2001

1. At its 25th Plenary meeting, held in Brussels on 20th July 2001, the Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) of the European Commission expressed its opinion[1] on the report recently published by the Joint Research Centre regarding validation of methodologies for DINP release from PVC toys[2]. The comments below relate to the CSTEE's opinion and the quality of the underlying research on which that opinion is based.

2. In its response to the two questions posed by the European Commission, the CSTEE firstly concluded that the validation studies, involving the use of three methods by more than 15 laboratories (in both USA and Europe) were of "good scientific quality", although some important information was missing regarding the rationale for the absence of certain data from some laboratories. More significantly from the perspective of the validation of methods for use as the basis of regulations, the CSTEE concluded that the repeatability (within lab variation) and reproducibility (between lab variation) of one of the methods (namely the head over heals, or HoH, extraction method developed by TNO, Netherlands) were "good" and "acceptable" respectively. In turn, this implies that in the view of the CSTEE, the HoH method might be considered as a sound basis for the development of future regulations concerning the leaching of phthalates from PVC toys.

3. Detailed study of the validation studies themselves, however, reveal that the conclusions of "good repeatability" and especially "acceptable reproducibility" are highly questionable. Moreover, the results of these studies, despite the further efforts of the last two years to develop and validate the methodologies, continue to indicate that the *in vitro* measurement of leaching rate can never form a reliable, nor acceptable, basis for responsible and protective regulation of the use of plasticising additives in PVC.

4. The CSTEE note the calculated inter-laboratory reproducibility of the HoH method of 35-65%, but nevertheless conclude that this is acceptable. This judgement is remarkable, especially given the very high degree of variation between analyses by individual laboratories which underlies this summary calculation. Table 2A of the CSTEE opinion, and the corresponding data in the validation report itself, indicate that DINP release rates determined for individual toys by different laboratories using the HoH/GCMS method (judged to be the most reliable) varied by a factor of between 2.5 and 5. Moreover, the range of values for two of the toys tested (identified as Gloworm and Nikki) fell either side of the proposed maximum acceptable release rate of 6.7 ug/10 cm^2/min. In other words, on the basis of the test results presented, some laboratories would accept these toys whereas others would reject them. This poor reproducibility is immediately clear from the "detailed graphs" presented in Annex 5 of the JRC report.

5. This degree of variation persists despite the use by all laboratories involved of identical apparatus and reagents, indicating that this represents inherent methodological variation which would be extremely difficult, if not impossible, to reduce further. Indeed, despite the substantial additional effort which has clearly been expended in conducting this study, compared to the previous validation attempts co-ordinated by TNO[3], the reproducibility of the HoH technique has barely improved (previously 33-73%, now 35-65%). This is also despite the switch from HPLC to GCMS analysis, a factor which TNO previously judged would further improve reproducibility.

6. The CSTEE stress that mean (average) release rates determined by this technique for all five toys did not exceed the proposed maximum of 6.7 ug/10 cm^2/min. While this is true (see, e.g. Table 1 of the CSTEE opinion), it is significant that mean release rates determined by individual laboratories for some of the toys did exceed this value. For the Gloworm toy, analysed using the HoH/GC method, 6 laboratories reported means above 6.7 and 8 laboratories, below this value. This is important in a regulatory context, as future inter-laboratory calibration exercises are likely only to be periodic and in most cases, judgements as to the acceptability or otherwise of individual products will depend on the analytical data from individual laboratories. Such extensive inter-laboratory calibration as conducted during the validation exercise is unlikely ever to be repeated.

7. It must also be remembered that the current validation tests rely on the use of toy samples specifically manufactured for the purpose of these studies, with all the attendant efforts to ensure homogeneity of plasticizer content and distribution which this implies. The validation attempts have also focussed exclusively on only phthalate ester (DINP) from the numerous which are known to be used in PVC toys on sale in the EU[4]. This is entirely misrepresentative of the manufacturing processes, and range of origins, which underlie the diversity of individual products available through retailers in the EU. In practice, a much greater degree of batch-to-batch, and even individual toy-to-toy, variability in content, homogeneity and structure must be expected. Faced with this additional source of error, compounded with the substantial errors which remain in the analytical method itself, the regulators will have an impossible task to ensure that only those products yielding "acceptable" release rates are available on the shelves. Such an approach would be entirely inconsistent with the Commission's commitment to ensure a high level of protection for human health.

8. At the base of all the attempts at method validation are the results of the rather limited study of *in vivo* release rates from PVC toys conducted by RIVM in 1998[5]. The fundamental limitations of this study have been highlighted previously[6], but include the small number of volunteers involved, the numerous unverifiable assumptions underlying the calculation of leaching rates and the high degree of variability between individuals (greater than one order of magnitude even for a standardised PVC disk). At the same time, other similar studies have reported even higher *in vivo* leaching rates[7]. Moreover, the judgements made in that study regarding the timing of exposure and the "acceptability" of certain levels of intake are largely subjective.

9. In short, the results of the JRC study confirm that DINP can be extracted from standardised PVC toys (manufactured specifically for the purpose of the test) into artificial saliva at rates which depend on the precise methodology and conditions employed. The data also indicate that leaching rates for some toys may be higher than for others under the particular conditions employed. Beyond that, however, the study yields very little and certainly

cannot be described as providing a sound basis for the development of regulatory controls. The degree of inter-laboratory variation even for the best of the three methods investigated remains very high. The lack of improvement in this variability despite the intensive resourcing which these studies have received over the last two years indicates strongly that this is inherent variability which will not be resolved through further refinement. Rather, the European Commission should conclude from this exercise that attempts to develop regulations based on the measurement of leaching rates using a "validated" *in vitro* method will never ensure the high degree of protection for children's health to which the Commission aspires.

10. Greenpeace International retains its position, therefore, that the only effective and acceptable protective regime remains the making permanent of the current temporary prohibition on the use of six phthalates in toys for children under 36 months designed to be chewed. Furthermore, this prohibition must be extended to include all other soft PVC products in the light of evidence that significant exposure can arise through mouthing of items not intended for such use.

11. The only responsible option is to take progressive steps to avoid exposure of young children to phthalates and other chemicals contained in, and leaching from, soft PVC toys rather than to attempt to regulate such exposure within levels deemed to be tolerable. The high variability which remains even within the CSTEE's preferred *in vitro* method reaffirms our position. Avoidance of exposure can be achieved simply and most effectively by ensuring that only suitable alternative materials to soft PVC, which do not require leachable chemical additives of any type, are used in the manufacture of teethers and other toys designed for use by young children. Such alternatives are already widely available within the EU. To follow such an approach would additionally obviate the need for further resources to "refine" an inherently unreliable and (in a regulatory context) practically inapplicable methodology in which public confidence is likely to remain extremely low.

References

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