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Dear Dr Stokes

This public comment is delivered in response to Federal Register Notice Volume 69, Number 212, Pages 64081-64082. It provides some overview comments from the Procter & Gamble Company on the Background Review Document (BRD) published on November 1, 2004 for the Isolated Chicken Eye Test.

The Procter & Gamble Company is very supportive of ICCVAM's activity to address *In Vitro* Test Methods For Detecting Ocular Corrosives and Severe Irritants and congratulates ICCVAM on the work accomplished to date in this activity. As a consumer products company that has many years of experience conducting eye safety assessments as an integral part of the overall consumer safety assessment of a product and as a data submitter for this particular ICCVAM activity, the Procter & Gamble Company would like to offer the following technical comments on the BRD for the Isolated Chicken Eye Test:

Isolated Chicken Eye (ICE):

- The Procter & Gamble data for ICE submitted in response to the Federal Notice noted above is included in the BRD in Section 9: Other Scientific Reports and Reviews. These data have not been included in the evaluation and analysis of ICE on the basis that the reference data were identified as not having been generated with the standard *in vivo* protocol (Draize Test). However historical *in vivo* data submitted (LVET) with the ICE Test data is a 3Rs alternatives test to the Draize test which corresponds to an optimized protocol within the system of the American Society for Testing of Materials (ASTM E1055-85). Reviews and publications in peer reviewed journals support LVET as being an appropriate *in vivo* methodology for the evaluation of eye irritation potential that more accurately predicts the human response to accidental eye exposure to chemicals than the Draize Test[1,2,3]. These historical *in vivo* data represent a relevant source of information in a weight of evidence evaluation of ICE. As such, we request that these data are incorporated into the overall evaluation of ICE. If requested, the Procter & Gamble Company will provide additional data, such as individual animal data, from *in vivo* tests conducted historically.
- The types of surfactants included in the database would appear to be too limited to draw the general conclusion that ICE under-predicts the irritancy of surfactants as a class of materials.
- We would encourage further review of the incorporation of histological evaluation as an additional evaluation parameter addressing depth of injury to optimise the usefulness of this method for classification and labelling and in a weight of evidence

assessment of ocular irritancy. Additional qualification of this method would be helpful in the development of a prediction model for mechanistic understanding of ocular injury and for correlation with other *ex vivo* methods where area and depth of injury have been shown to be important in determining time for reversibility of ocular injury.

The comments detailed above are in addition to the overview comments provided by the European Cosmetics Toiletries and Perfumery Trade Association COLIPA on December 20, 2004 with which we are in agreement.

Representatives of the Procter & Gamble Company will be present at the expert panel meeting to be held on 11/12 January 2004. We will be happy to expand on the above comments on the BRD for ICE and provide further in-depth technical comments at that time.

Yours sincerely,

Dr. R.A. Rapaport,
Associate Director,
Product Safety & Regulatory Affairs,
The Procter & Gamble Company

[1]Griffith, J.F., Nixon, G.A., Bruce, R.D., Reer, P.J. & Bannan, E.A. (1981). Dose response studies with chemical irritants in the albino rabbit eye vs. a basis for selecting optimum testing conditions for predicting hazard to the human eye. Toxicol. Appl. Pharmacol. **55**, 501-513.

[2]Freeberg, F.E., Griffith, J.F., Bruce, R.D. & Bay, P.H.S. (1984). Correlation of animal test methods with human experience for household products. J. Toxicol. Cut. & Ocular Toxicol. **1** (3), 53-64.

[3]Cormier E.M., Parker R.D., Henson C., Cruse L.W., Merritt A.K., Bruce R.D. & Osborne R. (1996). Determination of the intra- and interlaboratory reproducibility of the Low Volume Eye Test and its statistical relationship to the Draize eye test. Regulatory Toxicology and Pharmacology. **23**, 156-161.