Preface

Toxicity tests should be reconsidered in light of new developments in toxicology. Recent concerns about animal rights have made it necessary to consider a number of ethical issues as well as social concerns.

The Draize eye irritation test (Draize test) is the most commonly used method for evaluating the irritancy potential of drugs and cosmetics. However, public outcry over the use of the test has aroused concern for animal welfare and has prompted scientists to develop alternative tests. In the face of these concerns, many new methods have been reported.

The "Research group on test methods for safety evaluation tests of new cosmetic ingredients" was established in 1990 by scientists from universities, from the regulatory research institute, and from the cosmetics industries (Headed by: Dr. Tanaka, National Institute of Health Sciences, until March 1994). The mandate of the group was to obtain basic information on the characteristics (usefulness and limitation) of Draize test and alternative test systems that could be used to evaluate the eye irritancy potential of cosmetic ingredients.

We first reviewed the literature on alternatives to the Draize test. It appear that these alternatives might offer valuable information on the irritancy potential of various chemicals, and that it might be possible to replace the current *in vivo* method with an *in vitro* method suitable for evaluating most, but not all substances of interest. However, in order to obtain regulatory acceptance of the new methods as alternatives to the already established toxicity test, it is necessary to demonstrate the validity of the new methods on a wide variety of chemicals by using the tests in many laboratories. Thus, we decided to undertake inter-laboratory validation in an attempt to obtain more detailed information on intra- and inter-laboratory test variation, reproducibility, specificity, and relevance. The approach was divided into three stages. The first was a primary validation using a relatively large number of methods and a small number of chemicals (surfactants). The second stage was designed to obtain more information on the selected methods when used with a wider variety of chemicals. The third stage was intended to supplement the required data and to confirm the characteristics of the methods. In total, 39 cosmetic ingredients were to be used. All of these substances were also evaluated using the Draize test in order to allow reliable comparison of *in vitro* data with *in vivo* data and to obtain further insight into the Draize test.

The present volume presents the results of primary validation of 12 alternative methods using 9 surfactants and physiological saline solution as a negative control. The results of the cell culture method, trypan blue staining method using hen eggs, and the hemolysis method were in good agreement with the obtained Draize scores.

The second phase of validation has completed and we are now conducting the third stage. For the final evaluation of the alternative method, it is necessary to combine the validation results of all three stages. Consideration of the characteristics of the Draize test itself is also indispensable for a rational evaluation of the alternative methods. Because of the limited number of chemicals used in the present validation, other validation data obtained in Europe, in the United States, and in Japan should be also considered.

It is necessary to recognize the extensive contribution of the many scientists in the cosmetic industry who belong to the Japan Cosmetic Industry Association, National Institute of Health Science, Yokohama City University, and Showa University. We wish to extend our sincere appreciation to Toyobo Corp. Ltd., Kurabo Industry Ltd., Oriental Yeast Co. Ltd., and In Vitro International, Ltd. for their kind technical cooperation and for supplying the test kits. Thanks

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