Title of Research:

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The validation study of EpiSensA (Epidermal Sensitization Assay); the *in vitro* skin sensitization assay based on reconstructed human epidermis

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Summary of Research:

Lipophilic chemicals are difficult to correctly evaluate by existing in vitro tests because these tests employ aqueous-phase systems. To overcome the limitation, we focused on a reconstructed human epidermis (RhE) and developed the Epidermal Sensitization Assay (EpiSensA) based on the expression of four marker genes related to induction of skin sensitization. Based on the comparison with the results of animal test, we confirmed that EpiSensA has better predictive performance for a variety of chemicals including lipophilic chemicals than existing in vitro tests. Therefore, the validation study of EpiSensA was started from July 2018 at JaCVAM (Japanese Center for the Validation of Alternative Methods) to adopt it for OECD test guideline. We have reported that the validation management team (VMT) concluded the technical transfer from the lead laboratory to three participating laboratories (Food and Drug Safety Center, KOSÉ Corporation and LION Corporation) was successfully completed.

For evaluation of within laboratory reproducibility (WLR), three laboratories tested 15 coded chemicals in three independent experiments during Phase I study, and target criteria was established at 85% by the VMT. Several protocol modifications and additional experiments were performed as appropriate, and the mean WLR resulted in 91% and satisfied the target criteria. The VMT concluded that the Phase I study was successful. Regarding subsequent Phase II study for evaluation of between laboratory reproducibility (BLR), three laboratories tested 12 coded chemicals once, and target criteria was established at 80%. The BLR was calculated using 27 test chemicals including Phase I and Phase II chemicals, and the final prediction for the chemicals that were tested 3 times in each laboratory was based on the median classification. As a result, the BLR was 89% and satisfied the target criteria. In addition, protocol modification was proposed to avoid the potential cross-contamination effect of volatile strong sensitizers. Furthermore, hazard predictive performances at participating laboratories were evaluated using 27 test chemicals, the performances were similar to that of the lead laboratory. From these results, the VMT concluded that the Phase II study was successful, and the protocol modification was accepted.

Timeline: April 1, 2018-

Topics:

Presentations at 2018,2019, 2020, and 2021 JCIA-LRI Workshop

Publications:

The 34th Annual Meeting of the Japanese Society for Alternatives to Animal Experiments, Okinawa and On-line, Japan, Nov. 2021.