July 15, 2022
Japan Tissue Engineering Co., Ltd.

Toward creation of a database for results of skin irritation tests using an alternative to animal testing

- With a grant from JSAAE, 6 corporations continue contributing jointly to the cosmetics industry –

Japan Tissue Engineering Co., Ltd. ("J-TEC", headquarters in Gamagori, Aichi, Japan; President & CEO, Ken-ichiro Hata) manufactures and markets the reconstructed three-dimensional human skin models for a skin irritation test. With a focus on the skin irritation that is one of the safety evaluation items, a total of 6 companies – J-TEC together with Mandom Corp., Kobayashi Pharmaceutical Co., Ltd., Nihon Kolmar Co., Ltd., ROHTO Pharmaceutical Co., Ltd., etc. – have been striving to expand data on alternatives to animal testing and enrich testing conditions. The results of this research were presented in a poster presentation at the 49th Annual Meeting of the Japanese Society of Toxicology held from June 30, 2022 (Thursday) to July 2, 2022 (Saturday) at Sapporo Convention Center.
Having been awarded the "8th Research Grant on the Evaluation of Testing Methods for Ensuring the Safety of Cosmetics, etc.", the 6-company group is proceeding with the further expansion of data and the creation of a database of the test results and findings obtained, to continue contributing to the cosmetics industry.

1. Background, results, and future development of the 6-company joint enterprise

Use of safety testing through alternatives to animal testing is now advancing in the cosmetics industry, but information published in scientific journals or by public institutions is limited. Moreover, there is little information on the ingredients of quasi-drugs and cosmetics, and individual companies tend to keep the results they have obtained independently confidential.

Similarly, in OECD TG439*, which is listed in "Guidance on the System for Evaluating Skin Irritation in the Evaluation of the Safety of Quasi-Drugs and Cosmetics (PSEHB/PED Notification No. 0422-3)" issued by the Ministry of Health, Labour and Welfare on April 22 of last year, there is still little usable information on the raw ingredients of cosmetics, and expansion of test data and enrichment of testing conditions, etc., will be needed in order to promote its utilization in safety testing.

This is why the 6 companies have jointly tested 16 ingredients commonly used in cosmetics, using reconstructed three-dimensional human skin model EPI-MODEL24 (Fig. 1, left), a J-TEC product. Through testing and verification by multiple companies, it has been possible to obtain reliable data that will be instructive to companies in the cosmetics industry when they use this testing method in safety testing. (Fig. 1, blue circle)

Moreover, it was found that even with ingredients and concentrations that are judged to be non-irritant by EPI-MODEL24 (a reconstructed three-dimensional human skin model assuming normal skin), there are cases in which they would be found irritant in a reconstructed three-dimensional human skin model of skin with a thin stratum corneum (Fig., 1, right), such as in sensitive skin. (Fig. 2, red circle) This suggests that by using a reconstructed three-dimensional human skin model assuming sensitive skin, it would be possible to evaluate the risk associated with cosmetic ingredients (probability and degree of irritation).

Findings that could be used to improve the dilution concentration of ingredients, solvents, and other testing conditions, as well as the sensitivity of irritant detection, were also obtained.

These activities will be continued with the "8th Research Grant on the Evaluation of Testing Methods for Ensuring the Safety of Cosmetics, etc." sponsored by the Japanese Society for Alternatives to Animal Experiments. With this grant, the 6 companies plan to proceed with the further expansion of effective data and the creation of a database that can also be used by other companies that were not involved in the joint research for the development of the cosmetics industry.

The 6 companies aim to connect further expansion of findings to the continued provision of safe

products that consumers can use with peace of mind.

Fig. 1. Reconstructed three-dimensional human skin model

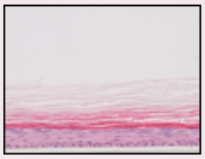
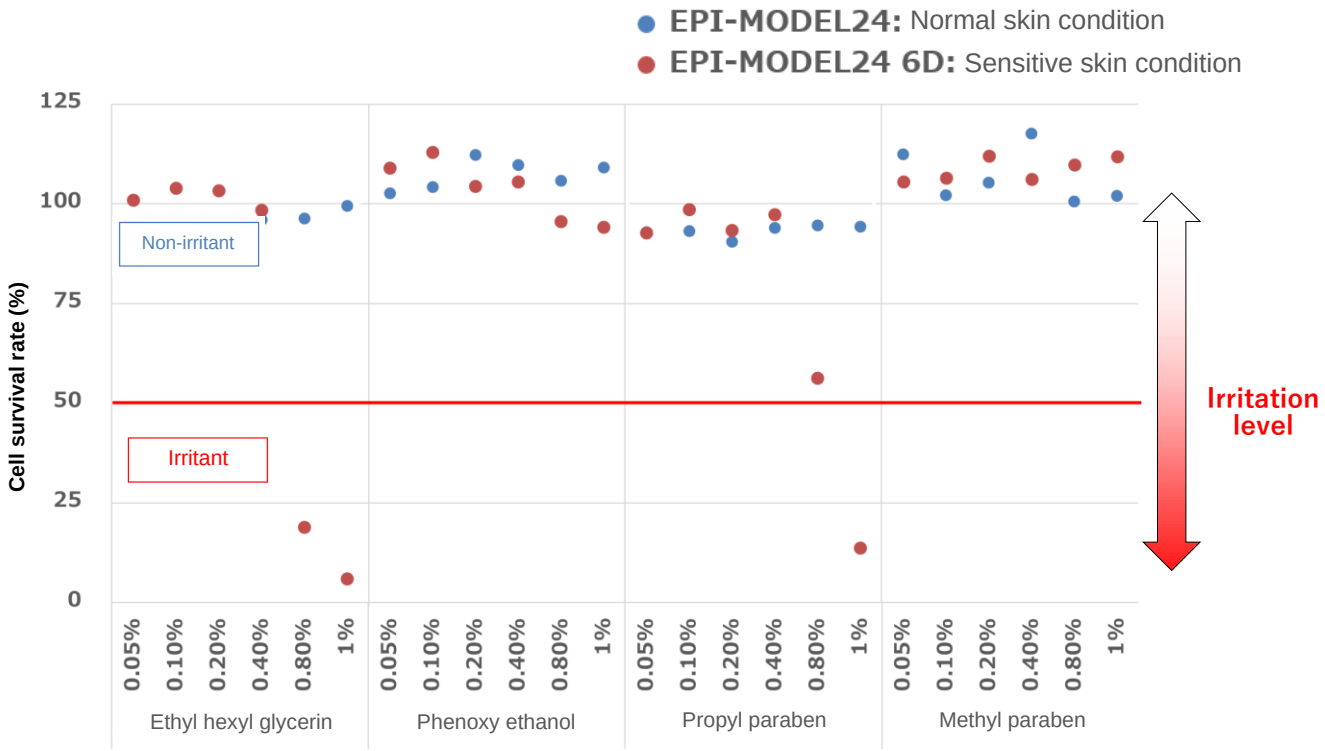
Product name	EPI-MODEL24	EPI-MODEL24 6D
Listed in OECD TG439	○	×
Figure of tissue section		
Transepidermal water loss	Low	High
Barrier function	High	Low
Skin condition	Assuming ordinary skin condition	Assuming sensitive skin condition

Fig. 2. Example results of skin irritation test of preservative ingredient



2. J-TEC's efforts to promote the spread of alternatives to animal testing

J-TEC has applied the advanced culturing technology accumulated through the regenerative medical products of cultured epidermis and cultured cartilage to develop, manufacture, and market cultured human tissue for research use. This is a reconstructed tissue model using human cells cultured outside the body. It can be applied to various experiments as an alternative to animals and simple cultured cells as it can replicate a structure that is extremely close to human tissue. Reconstructed three-dimensional human skin model EPI-MODEL24 is a product that is listed in OECD TG431 (Skin Corrosion Test) and OECD TG439 (Skin Irritation Test). J-TEC will go on contributing to the spread of alternatives to animal testing by making efforts to expand the market for this product.

* OECD TG439: The Organisation for Economic Co-operation and Development (OECD) adopted in vitro method for skin irritation "Test method using Reconstructed human Epidermis (RhE)" as OECD Test Guideline (TG) 439.

(Reference: About J-TEC)

J-TEC is a maker of regenerative medical products whose corporate vision is “creating a future for regenerative medicine,” and has been a member of the Teijin Group since March 2021. As Japan’s top runner in regenerative medicine, J-TEC obtained marketing approval for autologous cultured epidermis “JACE”, Japan’s first regenerative medical product, in October of 2007, and began marketing the product in January of 2009. J-TEC then went on to obtain marketing approval for Autologous Cultured Cartilage “JACC” in July of 2012, for Autologous Cultured Corneal Epithelium “Nepic” in March of 2020, and for Autologous Cultured Oral Mucosal Epithelium “Ocural” in June 2021. “JACC” was Japan’s first regenerative medical product for use in orthopedic surgery, and “Nepic” was the first for use in ophthalmology. Of the 16 regenerative medical products that have been approved in Japan, four are J-TEC products.

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