

Skin Sensitization Test “human Cell Line Activation Test (h-CLAT)” Adopted as a OECD Test Guideline

The skin sensitization test called the human Cell Line Activation Test (h-CLAT), jointly developed by Shiseido Company Limited and Kao Corporation, was adopted as the globally recognized official test method, the OECD Test Guideline*1, on July 29th. As the skin sensitization (cutaneous allergic reaction) is a complex mechanism of biological reactions, evaluation with alternative to animal testing had been regarded as difficult. Amid this situation, “h-CLAT” was adopted as the world-first alternative method for skin sensitization test focusing on the in vitro replication of functions in immune cells, the first stage in the course of allergic response. As a result, it is now expected that a combination of “h-CLAT” with other alternative methods, testing other stages of allergic response and already adopted in the Guidelines, will give equal to or more accurate skin sensitization evaluation on chemicals compared to animal testing.

Looking ahead, we can expect a shift to alternative methods when testing the skin sensitization to tens of thousands of chemicals around the world yearly. In particular, Europe has already prohibited animal testing on all cosmetics products, hence alternative methods are regarded as an essential requirement. Alternative methods are also expected to be applied to REACH, the Registration, Evaluation, Authorization and Restriction of Chemicals. “h-CLAT” is also being considered to employ for quasi-drug application in Japan under the Ministry of Health, Labour and Welfare research grant.

In addition, h-CLAT is now well established by practical application at various cosmetics companies. Since it is highly superior to the existing animal testing in terms of cost and testing period, a significant contribution to efficient development of new chemicals in the industry is also expected.

Shiseido and Kao started joint research on alternative methods for skin sensitization in January 2003 and successfully established the elaborate test method. Since then, both companies pursued further research for its practical application with a concerted effort of industry, government and academia and in a partnership with other cosmetics companies*2 around the globe, as well as support from the Cosmetics Europe, Ministry of Health, Labour and Welfare of Japan, and The Japanese Society for Alternatives to Animal Experiments. Later, validation was conducted under the directions of the European Commission, and with successful results, “h-CLAT” was adopted as the OECD Test Guideline 442E.

These two major Japanese cosmetics companies were the first companies in Japan to commit themselves to the development of “h-CLAT” over the years, resulting in this adoption of h-CLAT in the global guidelines for test methods. This achievement will be an outstanding example to present Japanese technology to the world.

*1: Test methods that is designated by OECD (Organization for Economic Co-operation and Development) and internationally agreed for use in evaluating the safety of chemicals.

*2: Henkel AG & Co. KGaA, Kanebo Cosmetics Inc., KOSÉ Corporation, Lion Corporation, L'Oréal S.A.,
Menard Cosmetic Co., POLA INC., The Procter & Gamble Company (in alphabetical order)

Alternative Method for Skin Sensitization Testing, "h-CLAT"

Skin sensitization is an allergic response of the skin exposed to the same chemical that was recognized as a foreign substance at its first contact with the skin. Skin sensitizers vary from natural ingredients to chemical compounds, and characteristic substances include nickel and platinum for metals, or lacquer and primrose for plants.

"h-CLAT" is an alternative method for evaluating the skin sensitization to chemicals in an accurate and prompt manner with lower cost based on the system in which two types of proteins (CD86*³ and CD54*⁴) increase on the cell surface of the human acute monocytic leukemia cell line, THP-1.

The skin sensitization is very important as one of the safety assessment items for chemicals to be applied on human skin. However, since it involves the complex immune system, development of alternative methods has been regarded as extremely difficult. In recent years, OECD has played a leading role in evaluating the skin sensitization by combining alternative methods which test various stages of an allergic reaction. Of which, "h-CLAT" was adopted as the first alternative method in the world to replicate "dendritic cell activation", a complex and important phenomenon.

*3, *4: Important cell surface proteins to activate other immune cells.

Shiseido's Initiatives and Future Outlook

Shiseido has been engaged in research and development of alternative methods for more than 20 years and abolished animal testing on the cosmetics products and quasi-drugs developed after April, 2013. Also the company solely acquired its patent right regarding the basic technology of "h-CLAT" in 2009, however, with the aim of promoting this technology, the company allows its free use from December 1, 2014 for skin sensitization testing purposes only. Shiseido will continue to pursue this research going forward and will also actively publish the research results to help utilize alternative methods globally.