

BioReliance

Toxicology Services



Reconstructed Skin Micronucleus Assay

The Reconstructed Skin Micronucleus Assay (RSMN) is a new and novel in vitro alternative test that uses a 3D skin system consisting of normal, human-derived epidermal keratinocytes (NHEK) which have been cultured to form a multilayered, highly differentiated model of the human epidermis.

Why An In Vitro Micronucleus Assay?

Assessing induction of chromosome damage is an important step in prioritizing compounds early in the drug/product development process, as well as for meeting regulatory requirements. One of the most common assays for measuring chromosome damage is the micronucleus assay, which detects small, extra nuclei in the cell cytoplasm that represent chromosome fragments or whole chromosomes excluded from nuclei at the cell division.

The micronucleus assay is an accepted part of genetic toxicology testing worldwide. An OECD guideline (487) for the In Vitro Micronucleus Assay was finalized in July of 2010. In November of 2011, the updated guideline for pharmaceuticals, ICH S2(R1) was accepted. This guideline includes the micronucleus assay.

Why A Reconstructed Skin (3D) Model?

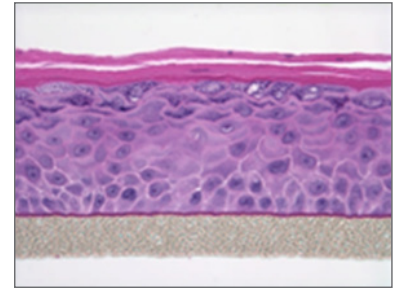
The current testing approach for genotoxicity typically involves the conduct of a battery of in vitro assays, with follow up testing for positive results with in vivo assays. Based on the high rate of misleading positive results in the standard in vitro battery (positive results for non-carcinogens and/or chemicals not genotoxic in vivo), there has been an increasing emphasis to reduce or eliminate animal testing:

- 3 R's: Reduce, Refine, Replace (the use of animals in testing)
- 7th Amendment to EU Cosmetics Directive
 - Animal tests for cosmetic ingredients are banned starting in March 2009
- Animal assays are not compatible with large testing programs like REACH

Why RSMN Assay?

- 3D Skin MN Assay
 - More predictive than traditional in vitro cell cultures
 - Utilizes a regulatory accepted endpoint (micronuclei)
- 3D tissues for genotoxicity
 - More closely resemble human organs (than other in vitro models)
 - Could be expanded to liver, kidney or other target organ models
- Experts support this assay
 - SCCS (Sci. Committee on Consumer Safety), 14, Dec 2010 acknowledges 3D skin MN assay is an alternative method undergoing development and "it is not excluded that these could add to a weight of evidence approach"
 - A useful tool in assessing safety of cosmetics (Pfuhrer, et al 2011)

BioReliance offers the first commercially available service GLP for the Reconstructed Skin Micronucleus Assay



Some advantages of a Reconstructed Skin Micronucleus Assay:

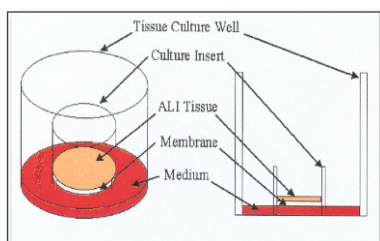
- No Animals Used
- Accepted in Guidelines
- More Physiologically Relevant
- More predictive
- Similar sensitivity as other in vitro tests
- Greater specificity than in vivo tests

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EpiDerm™ Skin Model

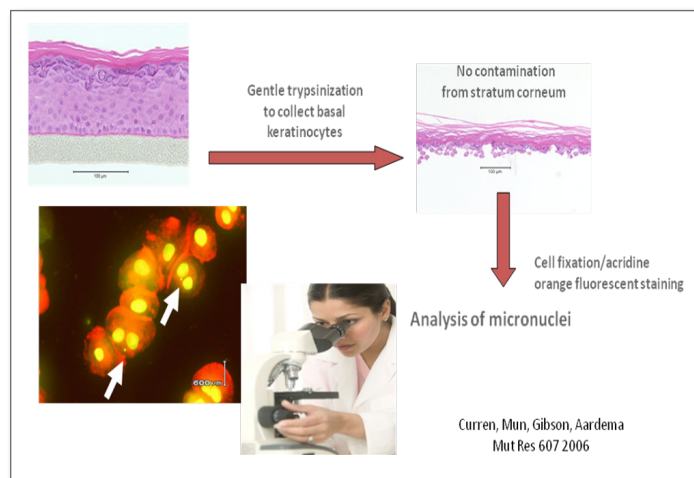
BioReliance uses the EpiDerm™ Skin Model available from MatTek. This model is a human 3-D skin-like tissue structure produced from normal (non-transformed) human epithelial keratinocytes.



RSMN Assay

BioReliance has qualified the RSMN Assay for GLP use (Roy, et al, "Development of a GLP 3D EpiDerm™ Reconstructed Human Skin Micronucleus Assay- a Promising Animals Alternative Model" – presented at EMS 2012)

Method Summary



References

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