Animal Testing
An update on Regulations and Science

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Lifetime achievement award in cosmetics Paris 2010
EU Regulation

• EU Cosmetic Directive 7th Amendment published in 2004 bans all animal testing on finished cosmetic products;

• EU Cosmetic Regulation published 30 November 2009 bans all animal testing on ingredients used in cosmetic products:
  • Performance of animal test (to assess human health) in the EU for the EU Cosmetic purpose is not allowed after 11 March 2009;
  • Ingredients tested outside the EU: deadline 11 March 2013;
EU Regulation: Are all animal tests banned?

• Tests performed outside the EU “not to meet the requirements of the EU Regulation” are not banned;

• These include:
  • Tests done to meet other regulations i.e. Quasi Drug regulation in Japan, REACH in EU;
  • Tests performed by Authorities e.g. in China;
  • Tests done on ingredients used in Drugs;
EU Regulation: Are all animal tests banned?

• Caveat to this: the results cannot be used to determine the safety of the finished product;
Other countries

- Many other countries have followed and are banning animal tests on cosmetic finished products and cosmetic ingredients:
  - Norway in the same time as EU;
  - India as of June 2013;
  - Israel as of January 1, 2013;
  - State of Sao Paulo in Brazil as of March 2014;
  - New Zealand as of March 2015;
  - Turkey as of July 2015;
Korea

• Korea has banned animal testing on cosmetic finished products as of March 2015;
• The Korean bill only bans animal testing where Korean accepted non-animal alternatives are available. If an alternative is not available, the animal test will be allowed;
What’s next?

• Bills to ban animal testing have been introduced in Australia, Brazil, Russia, Taiwan and the USA. They should be passed within the near future;
• Discussion in place to introduce bills in Argentina, Canada, Colombia and Peru;
Alternative Methods

- Alternative methods to animal testing have been developed since the 80’s and many have been validated;
- Alternative methods are now accepted by China regulators (July 2013) and Centers for the Validation of Alternative Methods (CVAM) have been established in Japan and Korea;
- Today many alternative methods can be used to replace animal testing;
- Under ethical review, human testing can be used on finished products;
Alternative Methods: some facts

• Alternative methods are:
  • More accurate than animal tests with a far better correlation to human tests;
  • Cheaper to perform than animal tests;
  • More reproducible;
  • Easy to be repeated;

• For most of the methods, no heavy investment in training or equipment is required;
Human Tests

• No human test should be conducted unless the safety assessment is done and shows the risks to be minimal;
• Usual human tests include:
  • Single patch: primary irritation – photo irritation;
  • Repeated patch: cumulative irritation;
  • hRIPT: allergy potential – photo allergy;
  • Human use test: normal or sensitive skin;
  • Comedogenicity test;
Finished products

• Alternative methods for the testing of eye or skin irritation and allergy give higher correlation to human data than animal methods: as such, for finished products, companies around the World have replaced animal testing since the 90’s for all or most finished products;
## Alternative methods

<table>
<thead>
<tr>
<th>Skin irritation</th>
<th>Human skin models</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye irritation</td>
<td>Several methods in place: ex vivo; HET CAM, cell cultures, etc.</td>
</tr>
<tr>
<td>Eye corrosion</td>
<td>Ex-vivo eye tests, Corositex</td>
</tr>
<tr>
<td>Skin corrosion</td>
<td>Human skin models</td>
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<td>Skin absorption</td>
<td>Franz cell, human skin models</td>
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<td>Phototoxicity</td>
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<td>Photo irritation – Photoallergy</td>
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<td>Mutagenicity</td>
<td>Test on bacteria</td>
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<tr>
<td>Allergy</td>
<td>hRIPT on human</td>
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<tr>
<td>Skin sensitization</td>
<td>Direct Peptide Reactivity Assay, KeratinoSens™, THP-1 Human Cell line activation Test (h-CLAT), Myeloid U-937 Skin sensitization test (MUSST)</td>
</tr>
</tbody>
</table>
What about ASEAN?

- While in ASEAN the testing of finished products is left to the consideration of the company placing the product in the market, companies that do test their finished products can move away from animal testing;
- Alternative methods are offered by many labs around the World;
Ingredients

• In order to evaluate the safety of finished products, one needs the safety data on ingredients:

• ACD Article 8.1.d states that “Companies responsible for placing the product on the market… have to assess the safety for human health of the finished product (based on) its ingredients, (their) chemical structure and level of exposure”;

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Ingredients

• With the ban on animal testing on ingredients it is difficult to get information on some of the end points like systemic toxicity (NOAEL) or reproductive toxicity;

• New methods are being developed using multiple end points to evaluate systemic toxicity with promising results;
Ingredients

- The burden is with raw material suppliers as they have to prove the safety of their ingredients without the usual animal tests;
- Cosmetic product companies have to be aware of the difficulties and ensure the ingredients they use are safe;
EU Regulation Signification

• All cosmetic products manufactured or imported in the EU must not have been tested on animals after 2004;

• All cosmetic products manufactured or imported in the EU must not contain ingredients that have been tested on animals after 11 March 2013 (11 March 2009 if the test is done in EU);
Consequence for cosmetic companies

- Cosmetic companies making finished products have to ensure the safety of the ingredients they use and establish the safety of the finished product (safety assessment);
- Ingredient manufacturers have to turn to alternative methods;
EU Regulation impact

• Companies that export finished products or ingredients to the EU have to abide by the EU Regulation: no animal test on finished products after 2004 and no ingredient that has been tested (for long term toxicity) on animals after 11 March 2013;

• Same applies to companies exporting to India (June 2013) and a growing number of countries;
A view to the Future

• Correlation between animal tests and human tests on irritation or allergies have been shown to be low: 50-60% at best;

• Alternative to animals are the future:
  • Better science;
  • Easier to do, reproduce, replicate, and interpret;
  • Better correlation to human: >80%;
A view to the Future

• Alternative methods do not yet exist for some of the end points while active research is going on;
• Structure – activity relationship is a first step to evaluate the risks;
• ASEAN has published a Guideline for the safety assessment of botanical ingredients (available on ASEAN Secretariat and ACA web sites);
• Centers for validation of methods have been set up in the EU (ECVAM), in the US (CAAT), and now in Japan and Korea;
A view to the Future

- All MNCs have eliminated animal testing;
- Within 5 years the number of countries banning animal testing will increase to cover the major markets;
- Within 5 years most if not all countries will accept data based on alternative methods;
- Within 10 years it will be impossible to run an international cosmetic business with animal tests done;
Thank You