Registration of New Cosmetic Ingredient with SFDA in China

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- Legal Framework and Guidelines

- Required Documents
  - Application Form for Licensing A New Cosmetic Ingredient
  - Research and Development Report
  - Brief Introduction and Illustration of Production Process
  - Quality and Safety Control of Ingredient
  - Toxicology Safety Assessment Data
  - Other Documents

- SFDA Format Check and Technical Review

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Definitions

“A new cosmetic ingredient is any natural or artificial ingredient that is used in cosmetics in China for the first time!”

3 Criteria for A Used Cosmetic Ingredient

✓ Listed on the Inventory of Existing Cosmetic Ingredients in China (IECIC 2003 or IECIC 2011) and is not a banned substance; or
✓ Has been used in a licensed special use cosmetic product (proof required); or
✓ Part of a plant that has been approved as cosmetic ingredient.

INCI 2007: 12,000 ingredients??
Legal Framework and Guidelines

- **Hygiene supervision over cosmetics (1990)**
  - The use of new ingredient for cosmetics production must be approved first;

- **Rules for the application of administrative licenses for cosmetics (2009)**
  - The use of new ingredient in cosmetics in China must be licensed;
  - Applicant can be the manufacturer of the new ingredient or the manufacturer of cosmetics;
  - Detailed requirements for registration of new cosmetic ingredient;
Legal Framework and Guidelines

Guidelines for the registration and evaluation of new cosmetic ingredient (2011)

- Toxicology data requirements and exemptions;
- Detailed guidelines for preparing other documents.

关于印发化妆品新原料申报与审评指南的通知

国家药品监督管理局
State Food and Drug Administration

2011年05月12日 发布

各省、自治区、直辖市食品药品监督管理局（药品监督管理局），有关单位：

为加强对化妆品新原料行政许可工作，确保化妆品产品质量安全，依据《化妆品卫生监督条例》及其实施细则等有关规定，国家食品药品监督管理局制定了《化妆品新原料申报与审评指南》，现予印发，请遵照执行。

附件：化妆品新原料申报与审评指南
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Application Form

Instructions

填表说明

1. 本表请从国家食品监督管理局网站下载使用。
2. 一式两份，一联申请者留存，一联由受理机关签章。
3. 本表每联均应填写，缺项不得受理。
4. 填写时要求实事求是，不得涂改。
5. 申请时应同时提交与该表相一致的电子文档。

New Ingredient Name

产品中文名称__________

公司及产品监督管理考核表

Declaration & Signature

声明书

公司和配方信息

Declaration & Signature

Declaration & Signature

Checklist

检查列表
Research & Development Report – Part 1

- **Background**

- **Process**
  - How?

- **Other Technical Materials**
  - Very Important;
  - Comparison studies
  - Literature data, test report
Research & Development Report – Part 2

- **Ingredient Identification**
  - Trade Name, Chinese Name, IUPAC, INCI Name, Molecular Formula, etc.
  - Source & Specification
  - Detailed Analytical Methods

- **Physio-chemical Properties**
  - Appearance, color, odor, solubility, Melting point, boiling point, vapor pressure, pH, Density, n-Octanol/Water, pKa, Refractive index, etc.
Intended Function
- Consistent with background info;
- Supporting data required;

Scope & Extent of Use
- Applicable types of cosmetics;
- Maximum concentration;
- Recommended concentration;

Wordings of Conditions of Use and Warnings

Has Been Approved or Used in Other Countries or Regions?
- Approval certificate required;
- Product label required;
Brief Introduction and Illustration of Production Process

Main steps, raw materials, solvents, additives, chemical reactions, temperature, pressure, purification steps, by products, possible impurities
Quality and Safety Control of Ingredient

- **Specification**
  - Requirement on the content of ingredient and unavoidable impurities;
  - Shelf-life, storage conditions, etc

- **Analytical Methods**
  - Required for both ingredient and Impurities (must be verified);

- **Quality and Safety Control**
  - How to minimize the content of hazardous and unavoidable impurities known as risk substances.
Toxicology Safety Assessment Data

Toxicology Safety Assessment for Ingredient
- Ingredient Characterization, Physio-chemical Properties and Toxicological Profile
- Hazard Identification;
- Dose-response assessment (Determination of NOAEL or LOAEL or VSD);
- Exposure assessment (Estimation of Systematic Exposure Dose (SED));
- Risk characterization (Calculation of MoS or MoE).

Chinese Summaries and Toxicology Studies for Ingredient
- Not all toxicology tests are required;
- Original test reports or certified copies required for toxicology tests conducted in overseas labs;
- Qualifications of overseas labs also required;
- Statement on the consistence between an ingredient and a tested material;

Safety Assessment of Risk Substances
- In most cases, such assessment is only qualitative;
- Not required if there is no risk substance. However, hazard identification must be done for every possible impurity.
Toxicology Safety Assessment Data

Required Toxicology Studies

1. acute oral and acute dermal toxicity;
2. skin and eye irritation/corrosion;
3. skin sensitisation;
4. skin phototoxicity and photosensitivity (required if the ingredient is used as UV-filters);
5. mutagenicity (should at least include a gene mutation test and a chromosome aberration test);
6. sub-chronic oral and dermal toxicity;
7. teratogenicity;
8. chronic toxicity/carcinogenicity;
9. toxicokinetics and dynamics;
### Toxicology Study Exemptions

<table>
<thead>
<tr>
<th>Exemption Criteria</th>
<th>Exempt endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) The ingredient is not used as a preservative, sun block agent, colorant or hair dye; and (2) The ingredient does not need to be added to restricted substances list in hygienic standard of cosmetics from the safety point of view.</td>
<td>7, 8, 9, sub-chronic oral or dermal toxicity depending on exposure route</td>
</tr>
<tr>
<td>(3) The ingredient has met criteria (1)+(2) and the ingredient has been included the inventory of existing ingredients in overseas authoritative organization for more than 4 years; and (4) The ingredient is not found to be hazardous in public literature when used.</td>
<td>6, 7, 8, 9</td>
</tr>
<tr>
<td>(5) The ingredient is proven to have a history of safe use as food ingredient by government or authoritative organizations.</td>
<td>1, 5, 6, 7, 8, 9</td>
</tr>
<tr>
<td>(6) Polymer with average molecular weight above 1000 Daltons;</td>
<td>1, 3, 5, 6, 7, 8, 9 and photosensitivity</td>
</tr>
<tr>
<td>(7) Risk assessment of the cosmetic ingredient has been carried out by overseas authoritative organizations and the conclusion is that the ingredient is safe to be used in cosmetics.</td>
<td>1, 2, 3, 4, 5, 6, 7, 8, 9</td>
</tr>
</tbody>
</table>
Toxicology Safety Assessment Data

Alternative to Animal Testing

- The word “动物替代方法” or “Alternative to Animal Test” is not mentioned in the guideline at all;
- Read-cross, clinical research, QSAR is mentioned in the guideline;
- In vitro method for phototoxicity published recently – a big step;
- It is worth a try to use alternative to animal testing for registration if the alternative method has been validated and accepted by authoritative organizations.
Toxicology Safety Assessment Data

Safety Assessment of Risk Substances

- Risk substances are the components (impurities or additives) that may cause potential harm to human health resulted from raw materials or brought in during the production process.
- Vital for successful registration;
- No required if there is no risk substance (hazard identification process and proof is required); Simple declaration is not enough;
- Not required if restriction limit has been established in cosmetic regulations in China or by other authoritative organizations;
- Risk assessment process similar to ingredient itself;
- Only abstracts of toxicology studies are required;
Other Documents

- Power of Attorney in case of appointing Chinese responsible agent;
- Contracted manufacturing agreement in case of contracted manufacturing;
- 1 Sample and other documents.
- All documents: 1 original, 4 copies.
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SFDA Format Check & Technical Review

- Format Check: 4 - 5 Days
- Technical Review: 4 – 5 months

Possible Conclusions:

- Safe without restrictions, approved;
- Safe with restrictions, proper warning and labeling, approved;
- Unsafe under proposed conditions of use, rejected;
- Request more data.
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Challenges & Trends

- Only a few new ingredients approved since 2004 (Only 8?)
- 2 new ingredients approved recently (PM-Lysine and Nivitol)

Possible Reasons?

- Lack of guidelines (Now it is available);
- Lack of alternative to animal tests (SFDA is improving this);
- Lack of exposure data (Less urgent);

Lessons Learned?

- 3 batch analysis is necessary before toxicology test starts in China;
- Monomer residue must be tested for polymers (GPC is not enough);
- Analytical methods must be verified in at least 3 labs recognized by SFDA if there is no standard method for a substance or impurity;
- If tests are carried out in overseas labs, only original reports or certified copies are accepted. Qualifications of labs are also required.
Thank you!