Registration of New Cosmetic Ingredient with SFDA in China

Enabling Chemical Compliance for A Safer World

18 April 2012, Yunbo Shi, CIRS China

Email: yunbo.shi@cirs-reach.com

CHEMICAL INSPECTION & REGULATION SERVICE

Table of Contents

CIRS
CHEMICAL INSPECTION & REGULATION SERVICE

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??

CHEMICAL INSPECTION & REGULATION SERVICE

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;*

CRS
CHEMICAL INSPECTION & REGULATION SERVICE

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

国食药监许[2011]207号

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

CIRS
CHEMICAL INSPECTION & REGULATION SERVICE

Table of Contents

- 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
- Challenges and Trends

CIRS
CHEMICAL INSPECTION & REGULATION SERVICE

Application Form

化妆品新原料行政许可

申 请 表

New Ingredient Name

产品中文名称_____

国家食品药品监督管理局制

Instructions

填 表 说 明

1. 本申请表可从国家食品药品监督管理局网站上下载使用。

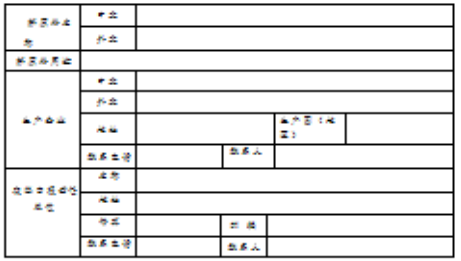
网址：HTTP：//WWW. SFDA. GOV. CN

2. 本表申报内容及所有申报资料均须打印。

3. 本表申报内容应完整，清楚，不得涂改。

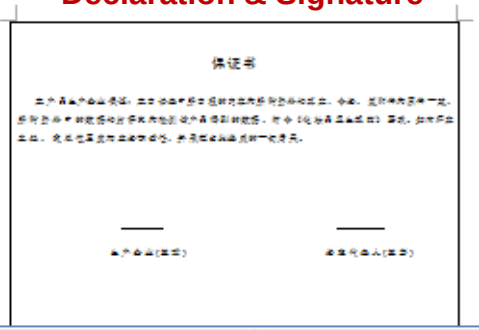
4. 填写此表前，请认真阅读有关法规及申报受理规定。

5. 申报时应同时提交与纸质申请表数据一致的电子表格。



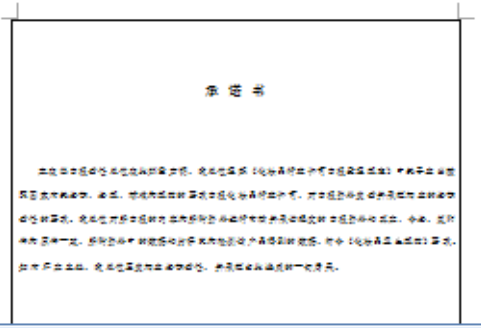
Company and Ingredient Info

Declaration & Signature



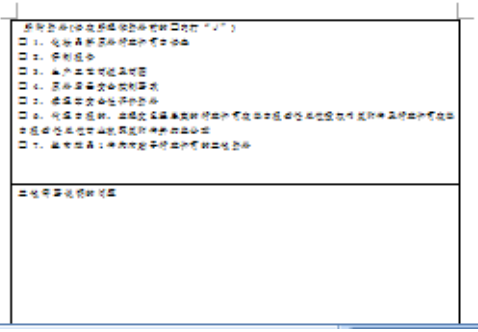
保证书

Declaration & Signature



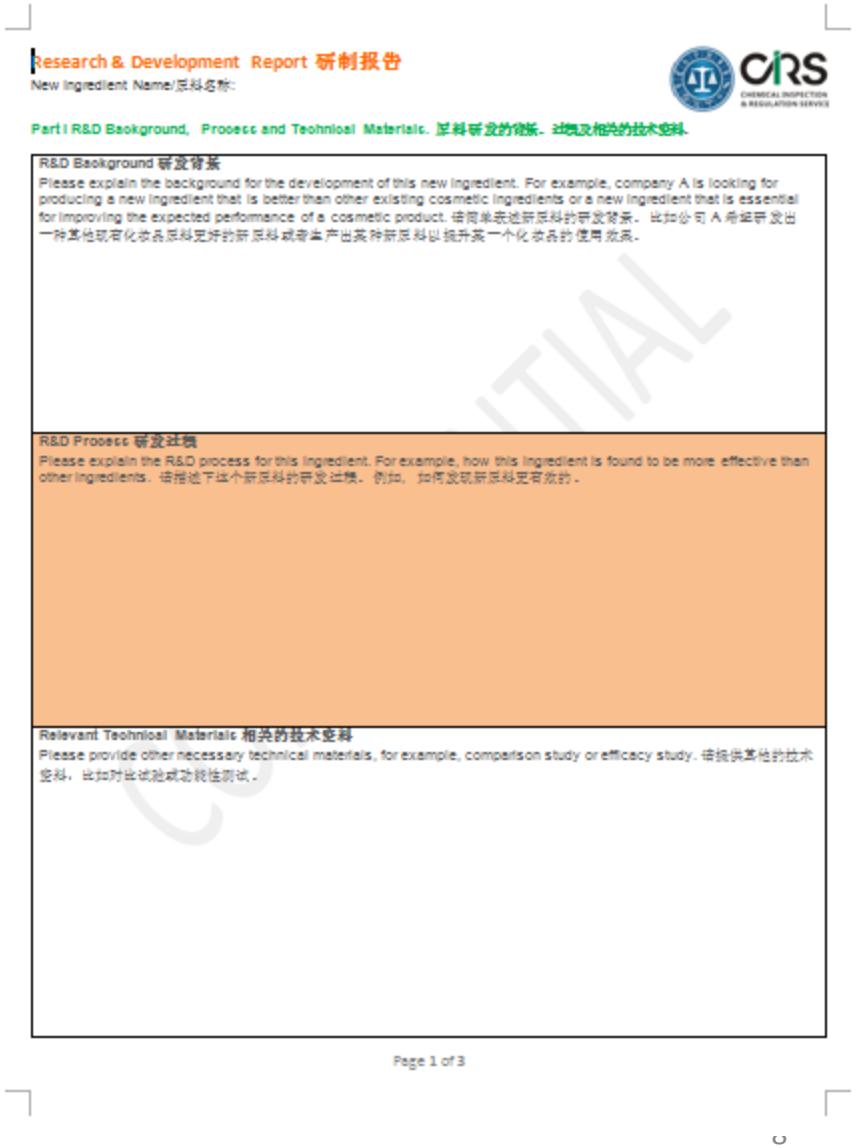
保 证 书

Checklist



Research & Development Report – Part 1

- Background
  - Why Better? Function & Safety.
- Process
  - How?
- Other Technical Materials
  - Very Important;
  - Comparison studies
  - Literature data, test report



Research & Development Report 研制报告

New Ingredient Name/原料名称:

Part I R&D Background, Process and Technical Materials. 原料研发的背景、过程及相关的技术资料.

R&D Background 研发背景

Please explain the background for the development of this new ingredient. For example, company A is looking for producing a new ingredient that is better than other existing cosmetic ingredients or a new ingredient that is essential for improving the expected performance of a cosmetic product. 请简单表述新原料的研发背景。比如公司 A 希望研发出一种其他现有化妆品原料更好的新原料或者生产出某种新原料以提升某一个化妆品的使用效果。

R&D Process 研发过程

Please explain the R&D process for this ingredient. For example, how this ingredient is found to be more effective than other ingredients. 请描述下这个新原料的研发过程。例如，如何发现新原料更有效的。

Relevant Technical Materials 相关的技术资料

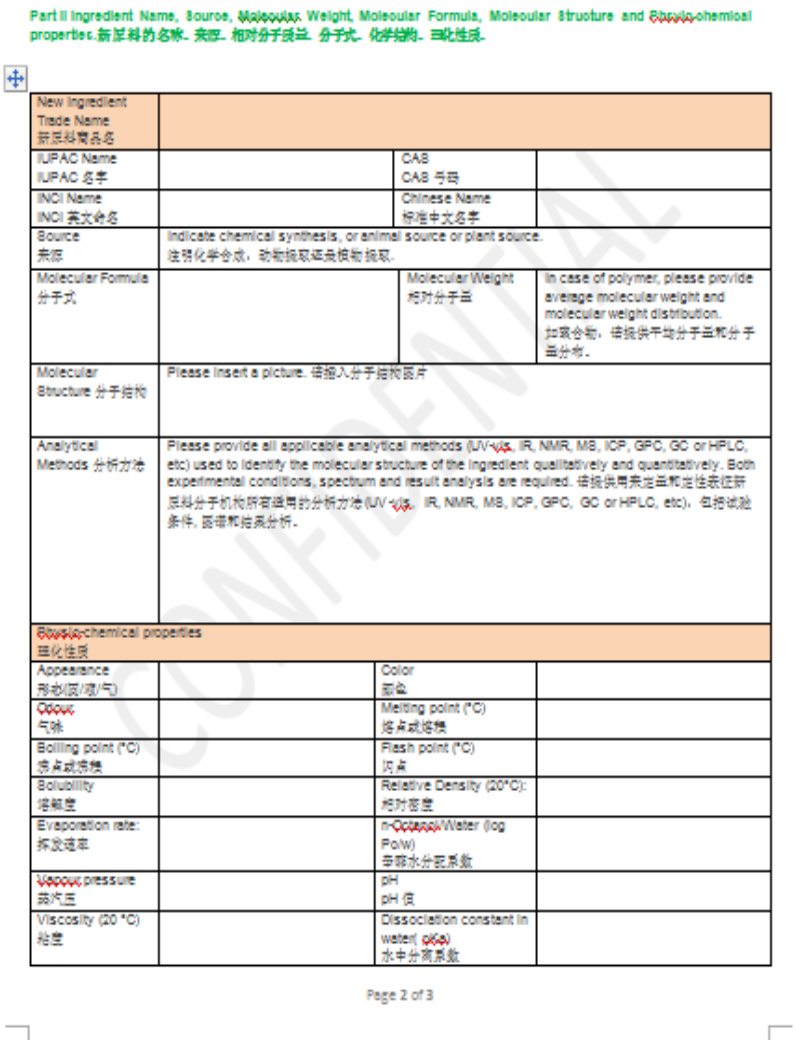
Please provide other necessary technical materials, for example, comparison study or efficacy study. 请提供其他的技术资料，比如对比试验或功效性测试。

Page 1 of 3

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, ordor, solubility, Melting point, boiling point, vapor pressure, pH, Density, n-Octanol/Water, pKa, Refractive index, etc.



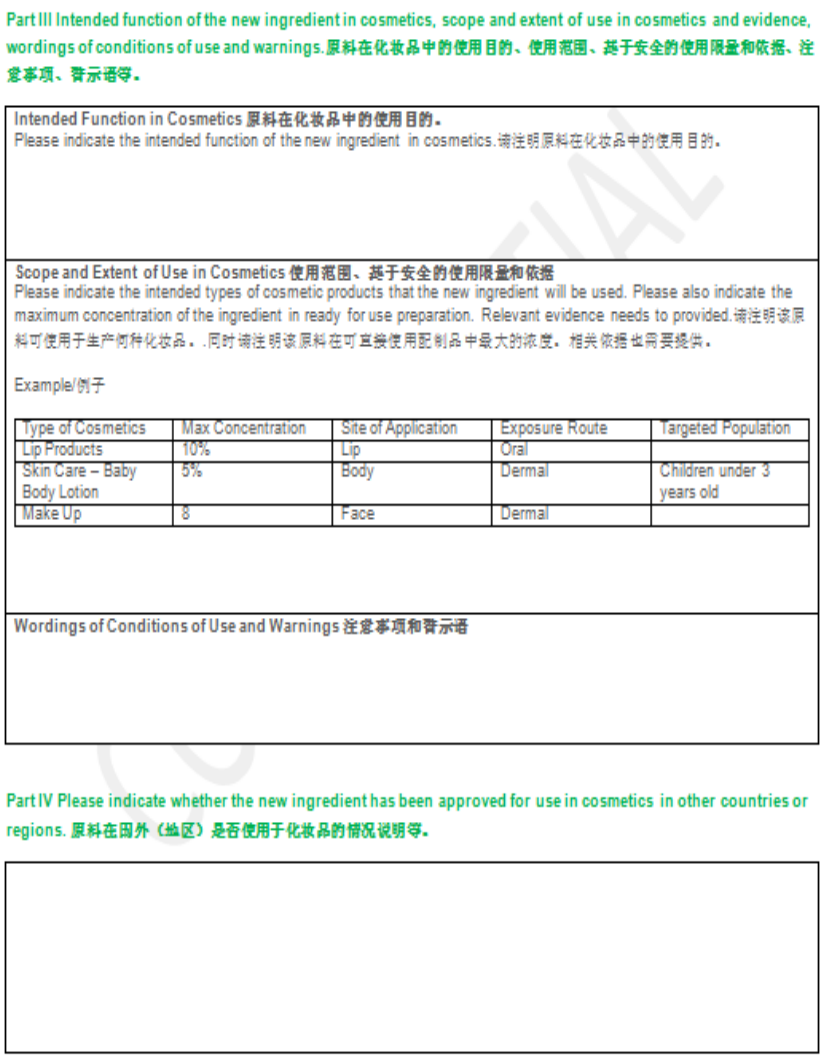
Part II Ingredient Name, Source, Molecular Weight, Molecular Formula, Molecular Structure and Physio-chemical properties.新原料的名称、来源、相对分子质量、分子式、化学结构、理化性质.

New Ingredient Trade Name 新原料商品名			
IUPAC Name IUPAC 名字		CAS CAS 号码	
INCI Name INCI 英文命名		Chinese Name 标准中文名字	
Source 来源	Indicate chemical synthesis, or animal source or plant source. 注明化学合成，动物提取还是植物提取.		
Molecular Formula 分子式		Molecular Weight 相对分子量	In case of polymer, please provide average molecular weight and molecular weight distribution. 如聚合物，请提供平均分子量和分子量分布.
Molecular Structure 分子结构	Please insert a picture. 请插入分子结构图片		
Analytical Methods 分析方法	Please provide all applicable analytical methods (UV-vis, IR, NMR, MS, ICP, GPC, GC or HPLC, etc) used to identify the molecular structure of the ingredient qualitatively and quantitatively. Both experimental conditions, spectrum and result analysis are required. 请提供用来定量和定性表征新原料分子机构所有适用的分析方法(UV-vis, IR, NMR, MS, ICP, GPC, GC or HPLC, etc)，包括试验条件，图谱和结果分析.		
Physio-chemical properties 理化性质			
Appearance 形状(固/液/气)		Color 颜色	
Odour 气味		Melting point (°C) 熔点或熔程	
Boiling point (°C) 沸点或沸程		Flash point (°C) 闪点	
Solubility 溶解度		Relative Density (20°C): 相对密度	
Evaporation rate: 挥发速率		n-Octanol/Water (log Pow) 辛醇水分配系数	
Vapour pressure 蒸汽压		pH pH 值	
Viscosity (20 °C) 粘度		Dissociation constant in water(pKa) 水中分离系数	

Page 2 of 3

Research & Development Report – Part 3

- 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;



Part III Intended function of the new ingredient in cosmetics, scope and extent of use in cosmetics and evidence, wordings of conditions of use and warnings.原料在化妆品中的使用目的、使用范围、关于安全的使用限量和依据、注意事项、警示语等。

Intended Function in Cosmetics 原料在化妆品中的使用目的。
Please indicate the intended function of the new ingredient in cosmetics.请注明原料在化妆品中的使用目的。

Scope and Extent of Use in Cosmetics 使用范围、关于安全的使用限量和依据
Please indicate the intended types of cosmetic products that the new ingredient will be used. Please also indicate the maximum concentration of the ingredient in ready for use preparation. Relevant evidence needs to provided.请注明该原料可使用于生产何种化妆品。.同时请注明该原料在可直接使用配制品中最大的浓度。相关依据也需要提供。

Example/例子

Type of Cosmetics	Max Concentration	Site of Application	Exposure Route	Targeted Population
Lip Products	10%	Lip	Oral	
Skin Care – Baby Body Lotion	5%	Body	Dermal	Children under 3 years old
Make Up	8	Face	Dermal	

Wordings of Conditions of Use and Warnings 注意事项和警示语

Part IV Please indicate whether the new ingredient has been approved for use in cosmetics in other countries or regions. 原料在国外（地区）是否使用于化妆品的情况说明等。

Brief Introduction and Illustration of Production Process

生产工艺简述及简图

Please indicate the main steps, processes and parameters during the production of the new cosmetic ingredient. To be more specific, please describe the raw materials used, reaction conditions (temperature, pressure, etc,), additives (catalyst, stabilizer, etc), intermediate product, by-products and key production steps (for example, mixing, reaction, purification, etc). In case of natural extracts, please indicate the processing methods, extraction method, solvent and possible residue of impurities or solvent in final product. 应说明化妆品新原料生产过程中涉及的主要步骤、流程及参数，如应列出原料、反应条件（温度、压力等）、助剂（催化剂、稳定剂等）、中间产物及副产物和制备步骤等；若为天然提取物，应说明加工、提取方法、提取条件、使用溶剂、可能残留的杂质或溶剂等。

Main steps, raw materials, solvents, additives, chemical reactions, temperature, pressure, purification steps, by products, possible impurities

Please insert a production diagram
请插入简图

CHEMICAL INSPECTION & REGULATION SERVICE

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.

Quality and Safety Control of Ingredient 原料质里安全控制要求

New Ingredient Name/原料名称:

Product Specification 产品规格

Product specification should include the requirements on the purity or concentration of main ingredient and inevitable impurities (for example, solvents, stabilizers, residue monomers in case of polymers, etc) due to technical reasons. Product specification also includes requirements on some physio-chemical properties, shelf life and storage conditions.

产品规格应包括纯度或含量、杂质种类及其各自含量（聚合物应说明残留单体及其含量）等质量安全控制指标，由于技术原因在原料中不可避免存在的溶剂、稳定剂、残体等的种类及其各自含量，其他理化参数，保质期及贮存条件等；若为天然植物提取物，应明确其质量安全控制指标。

Quantitative and qualitative analytical method for the ingredient and testing methods for impurities.

检测方法：原料的定性和定量检测方法、杂质的检测方法等。

Possible Risk Substances and Control Measures 可能存在的安全性风险物质及其控制措施。

Please indicate which substances/impurities might pose risk to human health and what measures could be taken to eliminate or reduce the presence of risk substances in the new ingredient. 请注明何种杂质可能对人体健康或安全性风险以及如何消除或减少风险物质的控制管理措施。

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.

CHEMICAL INSPECTION & REGULATION SERVICE

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;

CIRS
CHEMICAL INSPECTION & REGULATION SERVICE

Toxicology Safety Assessment Data

- Toxicology Study Exemptions

Exemption Criteria	Exempt endpoints
(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.	7, 8, 9, sub-chronic oral or dermal toxicity depending on exposure route
(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.	6,7,8,9
(5) The ingredient is proven to have a history of safe use as food ingredient by government or authoritative organizations.	1,5,6,7,8,9
(6)Polymer with average molecular weight above 1000 Daltons;	1,3,5,6,7,8,9 and photosensitivity
(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.	1,2,3,4,5,6,7,8,9

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.

CHEMICAL INSPECTION & REGULATION SERVICE

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;

CIRS
CHEMICAL INSPECTION & REGULATION SERVICE

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.

CHEMICAL INSPECTION & REGULATION SERVICE

Table of Contents

- 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
- Challenges and Trends

CIRS
CHEMICAL INSPECTION & REGULATION SERVICE

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.

CIRS
CHEMICAL INSPECTION & REGULATION SERVICE

Table of Contents

- 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
- Challenges and Trends

CRS
CHEMICAL INSPECTION & REGULATION SERVICE

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!