# Cosmetic Product Safety Report

李钟瑞 （Ray.Li）

毒理安全评估

Toxicological safety assessment

# 个人介绍


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**风险评估师，欧盟毒理学会继续教育课程（巴黎）：风险评估**

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曾就职于天祥专家服务组服务（前Ciba专家服务），负责化学品的毒理评估、报告审核、卷宗制作和注册等。目前负责化妆品、玩具和日化产品的风险和安全评估。

参与和完成的行业机密报告有：中国首份和多份REACH主注册卷宗和化学品风险安全报告；中国环保部第一份新化学物质申报（常规申报）;某些石油产品和染料的毒代动力学评估报告；某化学品推导无影响程度（DNEL）报告;某些化学品毒理评估和分类（GHS/CLP）提案;化妆品和玩具的毒理风险评估和欧盟化妆品安全报告等。

# Valued Quality. Delivered.

Intertek是全球领先的质量和安全服务公司，可以为众多行业和产品提供相关服务。

我们的服务涉及几乎所有行业，包括纺织、玩具、电子、建筑、加热设备、医药、石油、食品和货物扫描等，可以为产品、货物和体系提供包括测试、检验、认证在内的一系列服务。

Intertek实验室和办事处网络遍布全球100多个国家，员工人数超过30,000人。

天祥集团成员, 英国富时100强的公司

# Cosmetic Definition

欧盟化妆品的定义：

化妆品是用于人体外部任何部位（皮肤、毛发、指甲、口唇、和外阴部）或牙齿及口腔粘膜的物质（substance)或混合物（mixture)，主要起到清洁、香化或保护作用，以达到保护良好状况、美容或消除体臭的目的。

**停留类产品**（Leave-on）：

是化妆品将在皮肤、头发或粘膜上停留一段时间。

**冲洗类产品**（Rinse-off）：

是指化妆品接触到皮肤、头发或粘膜后将被迅速冲洗掉。





# BackGround

欧盟化妆品指令76/768 EEC于1976年正式实施以来，欧盟各个成员国根据该指令相继制定并颁布了本国的化妆品法规，如英国化妆品安全法规 （S.I. 2004/2152）等。由于欧盟指令只是框架协议，加上成员国为适应各自国情而对该指令进行一定的修改和追加特定条款，因此在欧盟内部造成了一定的贸易壁垒，如法国(France)要求所有的化妆品必须到法国毒物中心（Poison Centre）进行备案。英国(UK)化妆品法规规定毒理风险评估人必须是特许的生物学家或化学家（Chartered Biologist or Chemist）。

有鉴于此，欧盟于2009年通过了第一部化妆品法规（EC）1223/2009,从而达到规范整个市场，消除贸易壁垒和促进产品流通的目的。该法规第15(1)和(2)条款中关于致癌、致畸和致突变（Carcinogenic, Mutagenic or Toxic for Reproduction, 以下简称 CMR）禁令已经于2010年09月01日正式开始执行，第16(3)条款关于纳米材料的通告将于2013年01月11日开始执行，其它剩余条款将于2013年07月11日正式执行。

# 指令于法规对比

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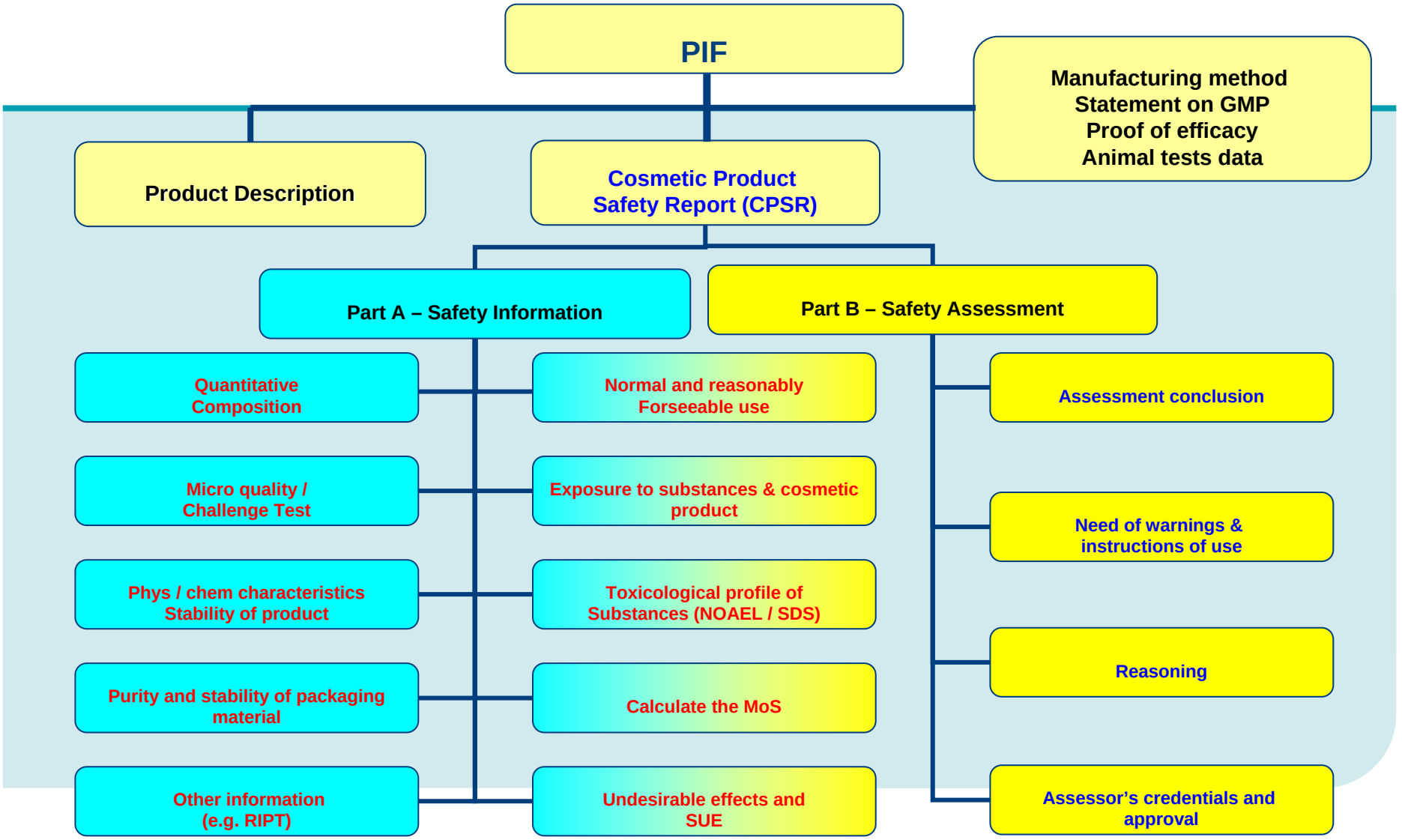
## Directive: 76/768/EEC

- 各成员国国家法规
- 责任人未明确定义
- GMP 要求含糊不清
- 每个成员国做单独的“通告”
- PIP 包含产品技术文档
- 毒理评估 (TRA)

## Regulation: 1223/2009

- 适用于整个欧洲经济区EEA
- 详细规定了责任人的义务
- 需要证明遵从GMP(ISO 22716)
- 统一的电子通告
- 增加新要求 PIP → PIF
- ★ 化妆品安全报告 (CPSR)

# Product Information File



# PART A — COSMETIC PRODUCT SAFETY INFORMATION

## 1.Quantitative and qualitative composition of the cosmetic product

The qualitative and quantitative composition of the cosmetic product, including chemical identity of the substances (incl. chemical name, INCI, CAS, EINECS/ELINCS, where possible) and their intended function. In the case of perfume and aromatic compositions, description of the name and code number of the composition and the identity of the supplier.

| INCI/Chemical Name * INCI/化学名* | Trade Name * 商品名* | EINECS/ELINCS No | CAS / CI No. * | Cosmetic Function 化妆品功能 | % active in raw material / trade name* 原材料/商品名中活性成分的浓度%* | %* 产品中的浓度 |
|---|---|---|---|---|---|---|
| MCI | Kathon CG | | | | | |
| MI | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

香料香精(fragrance):

Please supply Allergen Declarations and IFRA certificate for all perfumes/fragrances/flavours/essential oils/aromas/essences.

请提供完整的香精/香料/ 精油的的过敏原声明（26）以及IFRA证书

26过敏原声明/测试：和产品的标签相关，欧盟规定，26个致敏源在终产品中超过了0.001%（停留类产品），0.01%（冲洗类产品）则需要将该致敏源的INCI名称标注在产品标签上，去警告那些已经对这些原料过敏的消费者不要使用该产品。

IFRA certificate: 根据IFRA 方法评估该香精在不同产品中允许使用的的最高浓度。

## 2. Physical/chemical characteristics and stability of the cosmetic product

The physical and chemical characteristics of the substances or mixtures, as well as the cosmetic product.

The stability of the cosmetics product under reasonably foreseeable storage conditions.

**1.Physical/chemical characteristics of substances or mixtures**

Technical data sheet（TDS）/Certificate of Analysis(CoA) , Safety Data Sheet (SDS)

如 UV-absorbers, 吸收光谱（ absorption spectra）

***2.Physical/chemical characteristics of the finished cosmetic product***

Formulation is liquid, powder or gel? Colour, Odor and pH

## 产品的稳定性(stability)：

- Based on principle of reaction rate
  基于反应速率的原理
- Reaction rate double on every 10 °C increase in temp 温度每增加10摄氏度则反应速率加倍
- 6 months at 40-45 °C ≈ 2 years at RT
  处于40-45摄氏度中6个月约等于在常温中2年
- Controlled parameters 控制参数：
  - Basic physico-chemical 基本理化指标
  - Microbial 微生物，challenge test
  - Compositional 成分

## 3. Microbiological quality

"The microbiological specifications of the substance or mixture and the cosmetic product. Particular attention shall be paid to cosmetics used around the eyes, on mucous membranes in general, on damaged skin, on children under three years of age, on elderly people and persons showing compromised immune responses.

1.Microbiological Test

2.Challenge test

NB： Challenge test is not necessary for single use products and low microbiological risk products

## 4. Impurities, traces, information about the packaging material

"The purity of the substances and mixtures. In the case of traces of prohibited substances, evidence for their technical unavoidability. The relevant characteristics of packaging material, in particular purity and stability."

化妆品的包装材料不仅仅是展示产品个性的平台，也是保护产品免受外界环境影响的重要屏障。

化妆品包装材料质量的好坏往往也影响着产品的安全， 由包材引起的产品召回案例屡见不鲜。一些劣质的塑料的包材往往含有的塑化剂；玻璃或陶瓷的材质含有过量重金属；色彩鲜艳的材质含有偶氮染料。这些有毒和有害的物质在长期储存过程中与产品相互反应，或者是迁移到产品中导致了产品违规而被召回和曝光。

# Packaging Test-

- 参考欧盟食品接触材料标准 (EC) No 1935/2004
  - 总迁移率(塑料)
  - 重金属（玻璃和陶瓷）
  - 特定的有毒杂质(phthalates, bisphenol A)
  - REACH SVHC Test
  - Packaging Waste 94/62/EC Directive (4大重金属)

- 原材料供应商须提供： 包材的组分信息，杂质信息和SDS 等，甚至还需要提供GMP(ISO22716)去证明“technical unavoidability”。

## 5. Normal and reasonably foreseeable use

“The normal and reasonably foreseeable use of the product. The reasoning shall be justified in particular in the light of warnings and other explanations in the product labelling.”

reasonably foreseeable use: shampoo ? Shower gel?

产品设计标签时要包括： 使用说明（Instruction to use）和警示语（Warning）等信息。

警示语（Warning）信息来源于TRA或CPSR

## 6. Exposure to the cosmetic product

1) The site(s) of application;

2) The surface area(s) of application;

3) The amount of product applied;

4) The duration and frequency of use;

5) The normal and reasonably foreseeable exposure route(s);

6) The targeted (or exposed) population(s). Potential exposure of a specific population shall also be taken into account.

# 成品暴露评估

| | |
|---|---|
| Product Class: | Baby soap |
| Product Type: | **Cosmetic** |
| Physical Form: | Liquid |
| Specific Applications: | |

**Secrecy**

## Assessment Of Exposure

| | |
|---|---|
| Targeted Population: | Newborn babies 4.8kg |
| IFRA Product type: | Baby Hair Shampoo |
| IFRA product Type for report: | Baby Hair Shampoo |
| IFRA Category: | Category 9 |
| Amount per application/g: | 10.460 |
| Skin Surface Area of Application/cm$^2$: | 1430.000 |
| Total Amount applied per day/g: | 10.46 |
| Amount Per Unit Area of Skin per day mg/cm$^2$/day: | 0.073 |
| Estimated Daily Exposure mg/kg bw/ day: | - |
| Retention factor: | 0.01 |
| Number of applications per day: | Once per day |
| Exposure time Solvent Inhalation: | Not Applicable |
| Exposure time Aerosol Inhalation: | Not Applicable |
| Exposure Time Neat: | Diluted immediately |
| Exposure Time Dilute: | 4 Minutes |
| Amount of Product Used Per Application: | 200 mg per application |
| Part of Body Exposed to Undiluted Product: | Hands |
| Frequency of Exposure to Undiluted Product: | Twice a day |
| Time of Exposure to Undiluted Product: | Washed off immediately |
| Dilution Factor | Diluted 1 to 25 with water |
| Part of body exposed to diluted product | Body |
| Time of exposure to the diluted product | Washed off after 2 - 3 minute delay |
| Frequency of exposure to the diluted product | Four times a day |

**Summary of assessment of exposure and justifications to be discussed below**

## Exposure Evaluation

Ingredient Tox Reviews

Transport Regulation ADR 2011

CIR Compendium2010

Cosmetic Web Cos Ing

CIR Reference

Biocides Directive

Canadian Hotlist

UK Cosmetic Regulations

Saudi Cosmetic Reg

Wiley Website

CTFA Resources links

REACH Regs

EU INCI LIST

FDA Colour Status List

## 7. Exposure to the substances

"Data on the exposure to the substances contained in the cosmetic product for the relevant toxicological endpoints taking into account the information under Section 6."

第六项，第七项和第八项要求通常结合在一起衡量。

## 8. Toxicological profile of the substances

contained in the cosmetic product for all relevant toxicological endpoints. A particular focus on **local toxicity evaluation** (skin and eye irritation), skin sensitisation, and in the case of UV absorption photo-induced toxicity shall be made.

All significant toxicological routes of absorption shall be considered as well as the **systemic effects** and margin of safety (MoS) based on a no observed adverse effects level (NOAEL) shall be calculated. The absence of these considerations shall be duly justified.

局部毒性和系统性毒性，纳米材料

# Endpoints

- Acute toxicity via relevant routes of exposure
- Irritation and corrosivity:
- skin irritation and skin corrosivity
- mucous membrane irritation (eye irritation)
- Skin sensitisation
- Dermal/percutaneous absorption
- Repeated dose toxicity (normally 28- or 90-day studies)
- Mutagenicity/genotoxicity
- Carcinogenicity
- Reproduction toxicity
- Toxicokinetics (ADME studies)
- Photo-induced toxicity

# 单个组分的毒理文档 TPS

完成TPS所需材料：

产品中所使用原料的Certificate of Analysis (COA)、 Technical Data Sheet (TDS)、安全技术说明书（MSDS/SDS）。如果产品使用了香料或香精则要提供国际香精协会证书（IFRA Certificate）和26个致敏源声明。另外，如果产品中使用的动植物提取物，则要原材供应商提供农药残留和所使用防腐剂的信息。

**NOAEL shall be selected to calculate MoS.**

**Hazardous assessment AND Risk assessment**

## 9. Undesirable effects and serious undesirable effects

"All available data on the undesirable effects and serious undesirable effects to the cosmetic product or, where relevant, other cosmetic products. This includes statistical data."

1. **Undesirable effects (UEs):** "adverse reactions for human health attributable to the normal or reasonably foreseeable use of a cosmetic product."

2. **Serious Undesirable effects (SUEs):** "undesirable effects which result in temporary or permanent functional incapacity, disability, hospitalisation, congenital anomalies or an immediate vital risk or death."

一般指的是同款（或类似）产品已经在欧盟以外的国家和地区（如中国）上市销售，如果有任何的不良反应和严重不良反应则须将该资料放到CPSR中。如果产品在欧盟上市后有任何不良反应或严重不良反正，则须要向官方当局和签署CPSR的毒理学家报告。

## 10 Information on the cosmetic product

"Other relevant information, e.g. existing studies from human volunteers or the duly confirmed and substantiated findings of risk assessments carried out in other relevant areas."

如斑贴试验（Path-Test），重复斑贴试验（HRIPT），SPF test, Marketing Investigate Test等测试结果。

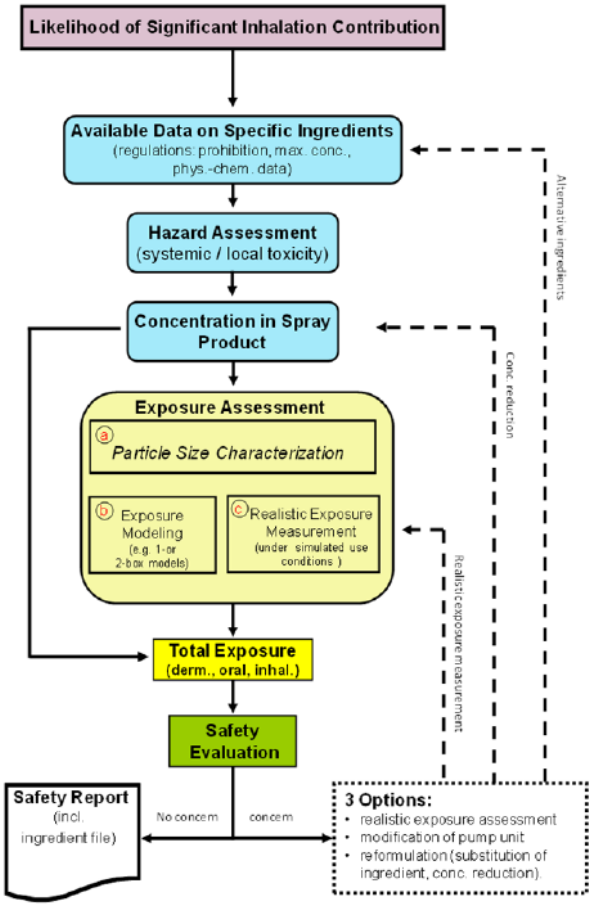
# PART B — COSMETIC PRODUCT SAFETY ASSESSMENT

## 1. Assessment conclusion

"Statement on the safety of the cosmetic product "

The conclusion should state if the product is safe, safe with restrictions or not safe for human health when used under normal or reasonably foreseeable conditions of use. (Colipa Guidline)

化妆品须保证在正常可可预见的使用条件下的产品安全性。




Color code in boxes: Blue related to ingredients / yellow related to product

**Fig. 4:** Basic principles for the safety assessment of inhalable cosmetic products and their substances.

## 2. **Labelled warnings and instructions of use**

“Statement on the need to label any particular warnings and instructions of use ”

毒理学家责任

警示语（**Warning Statement**）e.g. avoid eye contact

26 个致敏源名称

根据法规附录须要特殊标识的， e.g Not to be used by children under 3 years of age

厂商责任

**SPF** 值（COMMISSION RECOMMENDATION 2006/647/EC）: **low, medium, high and very high**

使用说明等

## 3. **Reasoning**

“This explanation shall be based on the descriptions set out under Part A.”

推论和解释须要基于Part A部分。

There shall be inter alia a specific assessment for cosmetic products intended for use on children under the age of three and for cosmetic products intended exclusively for use in external intimate hygiene.

婴幼儿产品和用在特殊部位的产品需要特殊考虑。

如：异丙基、异丁基、戊烷基、苯基和苯甲基尼泊金酯禁止在化妆品中使用；羟苯丁酯和羟苯丙酯的允许使用浓度从0.4%下降至0.19%（单个或混合）；产品中的尼泊金酯类成分总和不能超过0.8%。（SCCS Opinion）

"Possible interactions of the substances contained in the cosmetic product shall be assessed."

所使用成分是否发生了相互反应并评估反应后的的毒性（混合物毒性）

The consideration and non-consideration of the different toxicological profiles shall be duly justified.

毒理评估人需要考虑TPS中的毒性信息

Impacts of the stability on the safety of the cosmetic product shall be duly considered.

稳定性对于产品安全的影响

注：不仅仅要考虑每一个成分的毒性还需要衡量产品总体毒性

# 化妆品风险评估

欧盟化妆品安全报告中要求计算出产品中单一组分的安全边际系数（MoS）。MoS是将动物试验结果（如NOAEL）通过计算外推到人类本身，并包括那些特殊敏感人群的一种风险评估方法。通过统计学和毒理试验结果，世界卫生组织（WHO）建议的MoS的最小值为100，此时该物质被认为是风险可控且可以安全使用的。该最小值源于动物和人种种见区别的最大不确定因子10和人类物种种内区别的最大不确定因子10，将两项值相乘即为100

$$MoS = \frac{NO(A)EL}{SED}$$

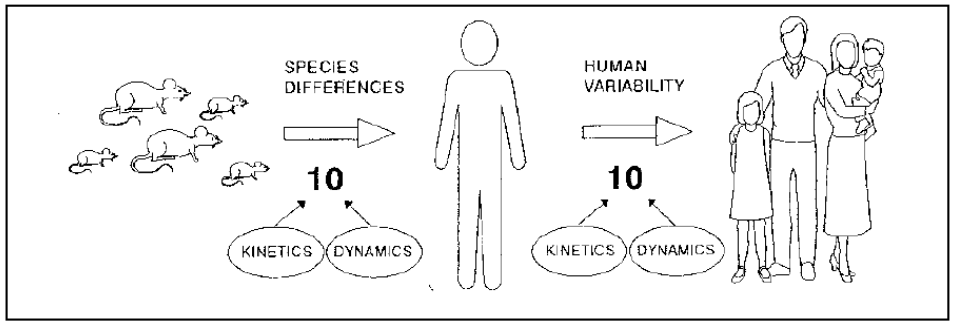



**Fig.2:** Schematic representation of the extrapolation from animal to man [Renwick, 1998].

## 4. Assessor's credentials

"Name and address of the safety assessor.

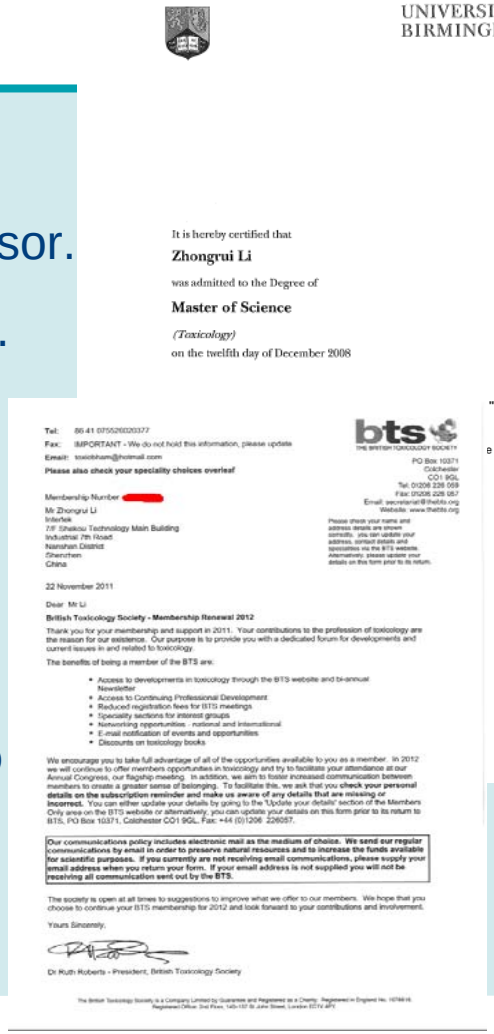
Proof of qualification of safety assessor.

Date and signature of safety assessor."

签名，日期，住址和资质信息。

Colipa Guideline:

个人简历（CV）和毕业证书（Diploma）



UNIVERSITY OF BIRMINGHAM

It is hereby certified that

**Zhongrui Li**

was admitted to the Degree of

**Master of Science**

*(Toxicology)*

on the twelfth day of December 2008

bts

22 November 2011

Dear Mr Li

**British Toxicology Society - Membership Renewal 2012**

Thank you for your membership and support in 2011. Your contributions to the profession of toxicology are the reason for our existence. Our purpose is to provide you with a dedicated forum for developments and current issues in and related to toxicology.

The benefits of being a member of the BTS are:

- Access to developments in toxicology through the BTS website and bi-annual Newsletter
- Access to Continuing Professional Development
- Reduced registration fees for BTS meetings
- Specialist sections for interest groups
- Networking opportunities - national and international
- E-mail notification of events and opportunities
- Discounts on toxicology books

We encourage you to take full advantage of all of the opportunities available to you as a member. In 2012 we will continue to offer members opportunities in toxicology and try to facilitate your attendance at our Annual Congress, our flagship meeting. In addition, we aim to foster increased communication between members to create a greater sense of belonging. To facilitate this, we ask that you **check your personal details on the subscription reminder and make us aware of any details that are missing or incorrect.** You can either update your details by going to the 'Update your details' section of the Members Only area on the BTS website or alternatively, you can update your details on this form prior to its return to BTS, PO Box 10371, Colchester CO1 9GL. Fax: +44 (0)1206 226057.

**Our communications policy includes electronic mail as the medium of choice. We send our regular communications by email in order to preserve natural resources and to increase the funds available for scientific purposes. If you currently are not receiving email communications, please supply your email address when you return your form. If your email address is not supplied you will not be receiving all communication sent out by the BTS.**

The society is open at all times to suggestions to improve what we offer to our members. We hope that you choose to continue your BTS membership for 2012 and look forward to your contributions and involvement.

Yours Sincerely,

Dr Ruth Roberts - President, British Toxicology Society

Eurotox 2011 PARIS

**CERTIFICATE OF ATTENDANCE CEC COURSES**

We hereby certify that

**Mr Zhongrui LI**

attended the Continuing Education Course
**"CEC 3 - Risk Assessment: a panaceafor nearly everything "**
on Sunday, August 28 2001 from 10:00 to 16:00.

e took place on the occasion of the 47th Congress of the European Societies of Toxicology (Paris - August 28-31, 2011).

**Paris, August 28 2011**

Nancy Claude

Congress President

# 总结

1. 现在的CPSR Part A = 70% Product Information File (PIF)
2. Part A 部分一般由生产厂商或责任人提供
3. 须要厂商和毒理学评估人紧密合作,相互支持
4. Part B 由毒理学家在 Part A 部分上完成
5. 技术难点：TPS （Toxicological Profile of Substance）

# Intertek CPSR 流程介绍

初步评估（草稿版）：用来确定配方的符合性. 问卷里的相关信息应填写完整，客户应提供问卷中的第一至第六部分所涉及到的相关文件。如果第三项至第六项无相关信息，请签署相关声明。当初始评估完成并通过后，客户可着手开始进行第七部分的实验。

完整报告：提供第七部分要求的所有的测试报告和信息后，将着手进行最终的CPSR报告.

| | |
|---|---|
| 1 | 请提供完整的香精/香料/ 精油的的过敏原声明以及IFRA证书（如果含有香精/香料/精油，必须提供） |
| 2 | 请提供原材料的SDS，技术数据表以及成分鉴定的相关资料 |
| 3 | 请提供纳米材料的相关信息（如果有） |
| 4 | 请提供毒理测试数据，特别是由制造商，代理商或者供应商对产品或单个成分进行的有关开发和安全评估的动物测试数据（如果有） |
| 5 | 请提供此产品或相关产品的不良反应以及严重不良反应的所有信息（如果有） |
| 6 | 请提供原材料和终产品已有的人体测试报告（如果有） |
| 7 | 请提供微生物/挑战性实验、稳定性、包材、重金属的测试报告及相关信息（可接受其它单位出具的符合EU/国际标准和格式的报告） |

# PIF细则

1. 产品的名称，数量，类别和详细描述
2. 责任人信息（地址，资质和联系方式）
3. 生产商信息
4. 产品的定性和定量信息
5. 产品和原材料物理和化学信息
6. 微生物检测
7. 原材料的SDS(不是MSDS，符合欧盟CLP规范)
8. 稳定性测试
9. 化妆品安全报告 （CPSR）
10. 化妆品安全报告评估师的信息
11. 生产方法
12. 良好生产规范（GMP）
13. 有效性说明
14. 不良反应
15. 成分（INCI）和浓度信息，产品标签
16. 申报书 （Notification）
17 其它相关资料，如动物测试或临床测试报告

**PIF中的内容70%与化妆品安全报告相同**

**企业应对突发安全事件，证明产品安全的有力证据**

# Thanks and Questions?