2019化妆品风险评估及非动物测试新技术方法应用研讨会

2019 Workshop on Cosmetic Risk Assessment and Regulatory Application of Non-animal Testing Technology

会议手册

Workshop Handbook

2019年4月14 – 17日 • 上海
Apr 14 –17, 2019 • Shanghai

组织机构（ORGANIZATION）

主办单位（HOSTS)

中国毒理学会毒理学替代法与转化毒理学专业委员会

The Society of Toxicological Alternatives & Translational Toxicology, CSOT

中国环境诱变剂学会毒性测试与替代方法专业委员会

The Society of Toxicity Testing and Alternative Methods, CEMS

协办单位（SPONSORS）

国际人道对待动物协会（Humane Society International）

欧莱雅中国研发和创新中心（L'Oréal R&I China）

玫琳凯（中国）有限公司（Mary Kay (China) Co., Ltd.）

上海美迪西生物医药股份有限公司（Shanghai Medicilon Inc.)

组织委员会（ORGANIZATION COMMITTEE）

主席（Presidents）：彭双清

秘书长（Secretaries in General）：瞿小婷 帅怡

委员（Members）（按姓氏拼音字母排序）：卞倩，蔡磊明，蔡臻子，曹征宇，高珉之，郭家彬，郝卫东，贺争鸣，李津，江以竑，Kate Willett, 匡荣，彭双清，邱璐，瞿小婷，帅怡，王慧，汪明英，王艳，杨杏芬，杨颖，苑晓燕，赵晓红，周显青

参会须知（NOTICES)

热烈欢迎各位代表来到上海参加 **2019 化妆品风险评估及非动物测试新技术方法应用研讨会**，衷心感谢您的参与和支持！请各位会议代表仔细阅读会议须知，并随时留意会务组发布的通知。

Welcome to participate in **2019 Workshop on Cosmetic Risk Assessment and Regulatory Application of Non-animal Testing Technology**, your participation and support are very much appreciated. Please read these notices carefully and pay attention to the notifications issued by the conference secretary during this meeting.

(一) 报到、住宿与用餐事项（Check-in, Accommodation, and Dining）

1. 会议报到登记、会务费、会议资料和用餐凭证、发票和培训证书等事宜由会务注册组负责。参会报到时，请仔细核对确定个人信息、发票单位名称等信息。

   Please check your information, and collect all conference materials such as badge, proceedings, meal tickets, and invoice, at registration desk.

2. 具体住宿安排请在宾馆服务台办理，早餐包含在房费之中。

   Please register your accommodation at the hotel front desk. The cost of the breakfast is included in your room fees.

3. 凭会务组发放的相应餐券在宾馆用餐。

   Please show your meal tickets when dining in the hotel.

4. 会议能提供国家认可的继续教育学分，如有需要者，请与会议注册组联系。

   This conference can provide with national continuing education credits, please contact with conference secretary at Registration if you need.

(二) 会场要求（Conference Requirements）

1. 为了维护您的安全和大会秩序，请参会代表佩戴胸牌进入会场；会场内请关闭您的手机或将手机调成静音模式；会议中有需要提问，请向主持人举手示意。

   For your security and the conference order, please attend each session with your badge; please turn off your cell phone or switch it to silent mode during the meeting; please raise your hand if you have any questions.

2. 每个大会报告或专题报告均含 3 分钟讨论时间。由于会议报告较多、时间有限，请各报告人按时到会，控制好报告时间，同时也请主持人做好提醒。

Each presentation includes 3 min discussion. All speakers are requested to present on time and keep their talk within the time allowed. The chairs will remind the timing.

3. **未经许可，不得对报告人和幻灯片进行拍照、录音或录相。**

   Without permission, photographing, sound recording, and video recording of the speaker or slides are **NOT** allowed in this conference.

4. 会议谢绝从会务组拷贝代表上传的 PPT 等材料，如有需要请直接与报告人联系。

   It is **NOT** allowed to copy the uploading materials such as slides from the conference. Please contact the speaker if you need.

(三) 其它事项 (Others)

与会期间请代表务必注意自身安全，妥善保管好个人财物。

Please pay attention to your personal security and keep your belongings carefully.

日程安排总览 (PROGRAM OVERVIEW)

日期 (Date)	时间 (Time)	内容 (Events)	地点 (Location)
4 月 14 日，星期日 (Apr 14th, Sunday)	08:30 – 21:00	报到、注册 (Check in, Registration)	一楼大堂 Lobby of 1st floor
4 月 15 日，星期一 (Apr 15th, Monday)	09:00 - 09:15	开幕式 (Opening Ceremony)	三楼宴会厅A厅 3F Grand Ballroom A
	09:15 - 12:30	大会报告 (Plenary Speeches)	
	12:30 - 13:30	午餐 (Lunch)	铂雅西餐厅(Poya)
	13:30 - 17:20	主题 I. 基于化妆品原料的产品安全风险评估 Theme I: Cosmetic risk assessment: principles and frameworks	三楼宴会厅A厅 3F Grand Ballroom A
	17:20-18:00	海报展示 (Poster exhibition)	
	18:00 - 20:00	欢迎晚宴 (Banquet)	三楼韦尔斯顿+马萨诸塞厅 3F Wellston + Massachusetts
4 月 16 日，星期一 (Apr 16th, Tuesday)	09:00 - 12:15	主题 II. 现有化妆品替代测试方法、新方法开发及法规采纳进程 Theme II. Current available cosmetic alternatives, newly developed methods & regulatory acceptance	三楼宴会厅A厅 3F Grand Ballroom A
	12:15 - 13:30	午餐 (Lunch)	铂雅西餐厅(Poya)
	13:30 - 16:45	主题III. 化妆品安全评估的整合测试与评估策略（IATA）及案例 Theme III. Integrated Approaches to Testing and Assessment (IATA) for cosmetic safety assessment and case studies	三楼宴会厅A厅 3F Grand Ballroom A
	16:45 - 16:55	闭幕式 (Closing Ceremony)	三楼宴会厅A厅 3F Grand Ballroom A
	18:00 - 20:00	晚餐 (Dinner)	铂雅西餐厅(Poya)
4 月 17 日，星期三 (Apr 17th, Wednesday)	全天 Whole day	代表离会 Departure	

学术报告安排 (SCIENTIFIC PROGRAM)

► 2019 年 4 月 15 日，星期一 (Apr 15th, 2019; Monday)

时间 (Time)	内容 (Events)		主持人 (Chair)
09:00 - 09:15	**开幕式 (Opening Ceremony)** 1. 介绍主席台就坐领导和嘉宾 Introduction of the guests 2. 大会主席宣布大会开幕并致辞 Address by the Workshop Chair, Prof. Shuangqing Peng 3. 嘉宾代表致辞 Address by a representative of guests 4. 欧洲体外毒理学学会合作签约仪式暨新闻发布 European Society of Toxicology *In Vitro* (ESTIV) cooperation signing ceremony and press release		帅怡 Yi Shuai
大会报告 (Plenary Lectures)			
时间 (Time)	**报告人 (Speaker)**	**报告题目 (Topic)**	**主持人 (Chairs)**
9:15-9:45	**李波 (Bo Li)** 中国食品药品检定研究院 National Institutes for Food and Drug Control	替代方法在我国化妆品评估中应用的法规认证与发展状况 The development and regulatory acceptance of alternative methods for cosmetic evaluation in China	郝卫东 Weidong Hao 贺争鸣 Zhengming He
9:45-10:15	**戚柳彬 (Liubin Qi)** 国家药品监督管理局化妆品监督管理司 Department of Cosmetics Supervision and Administration, National Medical Products Administration	我国化妆品法规监管政策及展望 Cosmetics regulatory policies and prospects	

10:15-10:45	**Gerald Renner** 欧洲化妆品协会 Cosmetics Europe	确保化妆品的安全:欧盟化妆品法规和市场合规控制 Ensuring safety of cosmetic products: EU cosmetic regulations and in-market control of compliance	
10:45-11:00	**茶歇（Coffee Break）**		
11:00 - 11:30	**Catherine Willett** 国际人道对待动物协会 Humane Society International	全球化妆品监管改革15年 15 years of transformational change in global cosmetics regulation	杨杏芬 Xingfen Yang Gerald Renner
11:30 - 12:00	**金鑫 (Xin Jin)** 上海市药品监督管理局 Shanghai Medical Products Administration	上海市化妆品事中事后法规监管体系发展现状 Development of cosmetic interim and post-market surveillance system in Shanghai	
12:00-12:30	**Vera Rogiers** 布鲁塞尔自由大学/欧盟消费者安全委员会 Vrije Universiteit Brussel/ Scientific Committee on Consumer Safety	化妆品安全评价原则 Principles of safety assessment of cosmetics	

► **2019 年 4 月 15 日，星期一 (Apr 15th, 2019; Monday)**

主题 I．基于化妆品原料的产品安全风险评估 **Theme I: Cosmetic risk assessment: principles and frameworks**			
时间 (Time)	**报告人 (Speaker)**	**报告题目 (Topic)**	**主持人 (Chairs)**
13:30-14:00	**James Wakefield** Delphic HSE	如何应对化妆品非动物测试策略合规 Compliance with non-animal testing strategy for cosmetic	王艳 Yan Wang Catherine Willett
14:00-14:30	**Vera Rogiers** 布鲁塞尔自由大学/欧盟消费者安全委员会 Vrije Universiteit Brussel/ Scientific Committee on Consumer Safety	如何将安全信息转化为安全评价报告 Transformation of safety information into a safety evaluation report	
14:30-15:00	**卢立新 (Lit-Hsin Loo)** 新加坡科技研究局生物资讯研究院 Bioinformatics Institute, A*STAR, Singapore	基于表型分析和机理研究的化学危害评价 Chemical hazard assessment based on phenotypic profiling and mechanistic reasoning	
15:00-15:15	**茶歇（Coffee Break）**		
15:15-15:40	**高原（Yuan Gao）** 北京宝洁技术有限公司 P&G Technology (Beijing) Co., Ltd.	化妆品安全评估中的暴露评价 Exposure assessment in cosmetics safety evaluation	周显青 Xianqing Zhou 江以竑 Yihong Jiang
15:40-16:05	**李津 (Jin Li)** 联合利华安全与环境保障中心(英国) Unilever Safety and Environmental Assurance Centre (UK)	安全使用史：化妆品中植物原料的非动物安全评估 History of safety use: a non-animal approach to risk assess botanicals in cosmetics products	
16:05 -16:30	**邢泰然(Ted Xing)** 欧莱雅亚太区法规部 L'OREAL APAC Regulatory	化妆品产品安全生命周期安全评价和风险管理 Safety evaluation and risk management during the whole life cycle of cosmetic product	

16:30-16:55	**胡丽萍(Liping Hu)** 强生公司全球临床前安全毒理学部门 Global Preclinical Safety Toxicology Resource, Johnson and Johnson Company	婴幼儿产品的安全性评价:替代方法的实施 Baby product safety assessment, implement of alternative methodology	
16:55-17:20	**刘宇红(Yuhong Liu)** 北京东方淼森生物科技有限公司/北京工商大学中国化妆品协同创新中心 Nutri-woods Bio-tech (Beijing) Co.,Ltd; Beijing Technology and Business University, China Cosmetic Collaborative Innovation Center	化妆品植物原料安全风险评估体系建设 Establishment of safety evaluation system of botanical ingredients for cosmetics and instance sharing	

► 2019 年 4 月 16 日，星期二 (Apr 16, 2019; Tuesday)

主题 II. 现有化妆品替代测试方法、新方法开发及法规采纳进程
Theme II. Current available cosmetic alternatives, newly developed methods & regulatory acceptance

时间 (Time)	报告人 (Speaker)	报告题目 (Topic)	主持人 (Chairs)
9:00-9:30	**邱璐(Lu Qiu)** 上海海关技术中心 Shanghai Customs District Technical Center	非动物测试在检验检疫领域的建立和应用 Establishment and application of non - animal test in CIQ	蔡磊明 Leiming Cai 卞倩 Qian Bian
9:30-10:00	**帅怡(Yi Shuai)** 上海市疾病预防控制中心 Shanghai Municipal Center for Disease Control & Prevention	重组人皮肤模型在日用化学品皮肤刺激性评价中的应用研究 Application of the reconstructed human epidermis model to evaluate the skin irritation of topical products used in daily life	
10:00-10:30	**杨颖(Ying Yang)** 广东省疾病预防控制中心 Guangdong Provincial Center for Disease Control and Prevention	3D 模型在化妆品整合检测策略中的应用研究 Application of 3D models in integrated testing strategy of cosmetics.	

10:30-10:45	**茶歇（Coffee Break）**		
10:45-11:15	**Donna Macmilan** Lhasa Limited	Derek Nexus 在化学品安全评估中的应用:案例研究 The use of Derek Nexus for chemical safety assessment: a case study	蔡臻子 Zhenzi Cai 苑晓燕 Xiaoyan Yuan
11:15-11:45	**桑 晶 (Jing Sang)** 浙江省食品药品检验研究院 Zhejiang Institute for Food and Drug Control	一种过敏试验细胞模型-嗜碱性粒细胞激活试验模型的建立 Establishment of basophil activation test, an allergic model *in vitro*	
11:45-12:15	**黄黎珍 (Lizhen Huang)** 华南理工大学 South China university of technology	新型化妆品皮肤致敏预测细胞模型 EndoSens 的建立以及评估 Development and evaluation of a novel cell model for skin sensitization prediction	

主题 III. 化妆品安全评估的整合测试与评估策略（IATA）及案例
Theme III. Integrated Approaches to Testing and Assessment (IATA) for cosmetic safety assessment and case studies

时间 (Time)	报告人 (Speaker)	报告题目 (Topic)	主持人 (Chairs)
13:30-14:00	**Hajime Kojima** National Institute of Health Sciences (NIHS), Japan 日本国立卫生研究院	ICCR 关于化妆品成分的安全性评估最新进展 ICCR update for the safety assessment of cosmetic ingredients	高珉之 Minzhi Gao Vera Rogeirs
14:00-14:30	**Carl Westmoreland** Unilever Safety and Environmental Assurance Centre (UK) 联合利华安全与环境保障中心（英国）	用于化妆品安全评估和案例研究的下一代风险评估(NGRA)策略 Next Generation Risk Assessment' (NGRA) for cosmetic safety assessment and case studies	
14:30-15:00	**张全顺 (Quanshun Zhang)**	基于 AOP 的皮肤致敏危害及强度评估整合测试方法	

	Institute for *In Vitro* Sciences 美国体外科学研究院	AOP based integrated approaches to testing and assessment for skin sensitization hazard and potency	
15:00-15:15	**茶歇（Coffee Break）**		
15:15-15:45	**Nathalie Alepee** L'OREAL R&I 欧莱雅全球研发与创新中心	通过化妆品行业应用案例探究新兴的皮肤致敏性体外评估策略 Dealing today's emerging *in vitro* evaluation of skin sensitization: a cosmetic industrial case study	郭家彬 Jiabin Guo 瞿小婷 Xiaoting Qu
15:45-16:15	**郭隽 (Jun Guo)** 安利（中国）研发中心有限公司 Amway (China) R&D Center	直接多肽结合试验与人源细胞系激活试验联合策略在多产地菊花提取物皮肤致敏性应用的研究 Combination of DPRA and h-CLAT to evaluate skin sensitization of chrysanthemum extracts from different habitats	
16:15 -16:45	**卢永波 (Yongbo Lu)** 广东博溪生物科技有限公司 Guangdong BioCell Biotechnology Co. Ltd	化妆品刺激性的体外整合测试策略 Integrated *in vitro* test strategy for cosmetics irritation	
16:45 – 16:55	**闭幕式 (Closing ceremony)** 大会总结 (Summary of the Conference) 宣布大会闭幕 (Close of the Conference)		彭双清 Shuangqing Peng

联系（CONTACT)

组别（Group)	姓名（Name)	电话（Mobile)
注册组 (Registration)	帅怡(Yi Shuai)	13671890609
学术组 (Scientific Services)	瞿小婷(Xiaoting Qu)	15821305679
会场保障组 (Workshop Venue Coordination)	汪明英(Mingying Wang)	15026845392
会议赞助与展商 (Sponsorship and Exhibition)	瞿小婷(Xiaoting Qu)	15821305679
新闻媒体 (News Media)	瞿小婷(Xiaoting Qu)	15821305679
继续教育学分 (Continue education credits)	苑晓燕(Xiaoyan Yuan)	13051109960
住宿餐饮组 (Accommodation and Dining)	苑晓燕(Xiaoyan Yuan)	13051109960

会议宾馆(CONFERENCEHOTEL)

名称/ Name：上海浦东绿地铂骊酒店（The QUBE Pudong)

地址/ Address：上海浦东新区川沙 5500 号（5500 Chuansha Rd, Pudong Xinqu, Shanghai Shi, China)

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邮箱/ Email: red.spd@thequbehotels.com

电话/ Tel:86-21-61871888

演讲嘉宾介绍

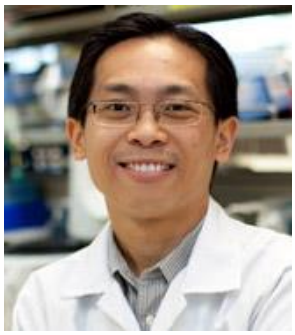
Biography of Speakers

Gerald Renner
Director of Technical Regulatory Affairs，Cosmetic Europe
Management of Cosmetics Europe's activities in the implementation of the new EU Cosmetics Regulation; Application of the EU Cosmetics Regulation and its technical adaptations with an emphasis on ingredient defence and borderline of cosmetics to other EU legislations; Responsibility for Cosmetics Europe's international alignment activities (China, Russia ICCR, ISO).

Kate Willett
Senior Director, Science and Federal Affairs for the Research and Toxicology, Humane Society International
Work on the science, policy and regulatory aspects of replacing animals in human health research and as the basis of chemical safety assessment. Coordinates with regulatory agencies, scientists and policy makers in the US and internationally. Focus on the OECD Test Guideline and Adverse Outcome Pathway Programs.

Vera Rogiers
***In Vitro* Toxicology and Dermato-Cosmetology (IVTD)**
Vrije Universiteit Brussel (VUB)
Besides teaching at the VUB and University of Ghent, she organizes international courses on Cosmetics and Risk Assessment. Work as director of the Innovation Centre-3Rs (IC-3Rs) and director of the Chair Mireille Aerens at the VUB. She has coordinated 2 EU research projects and was partner in several FP6 andFP7 EU projects concerned with *in vitro* methodology development.

James Wakefield
Asia-Pacific Director, Delphic HSE
Overseeing day-to-day activities within the region as well as acting as the regional representative in Asia-Pacific and expert for Delphic HSE. Responsible for leading the team in undertaking toxicological safety and regulatory assessments of many types of consumer product globally, particularly specialising in cosmetic safety and compliance.



Lit-Hsin Loo

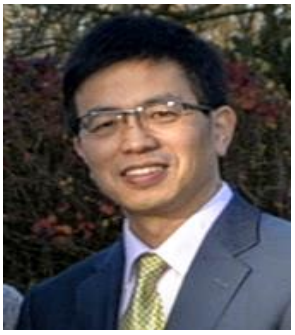
Senior Principal Investigator at the Agency for Science, Technology, and Research (A*STAR), Singapore.

Leading the Toxicity Mode of Action Discovery (ToxMAD) Platform under the Innovations in Food and Chemical Safety Program. Responsible for integrating various unique molecular and phenotypic profiling technologies developed in multiple A*STAR research institutes into a single platform for elucidating the MOA of chemicals.

Yuan Gao

Senior R&D Manager, Global Product Management of P&G

She is responsible for cosmetics products safety assessment, supporting cosmetics marketed in different regions in the world. She also works on the application of none animal testing methods in safety assessment, skin sensitization alternative methods and integrated testing strategies etc.

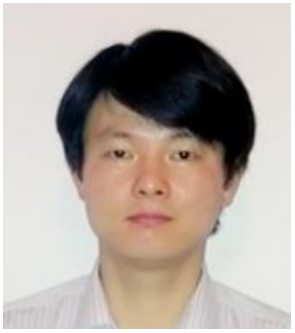


Jin Li

Senior safety scientist

Safety & Environmental Assurance Centre, Unilever

His principle responsibilities in Unilever are to develop and apply non-animal approaches to risk assessment on chemical safety with a focus on 1) the integration of in silico, in vitro and in vivo multiscale data for chemical safety assessments; and 2) the development of novel pathway-based risk assessment approaches.



邢泰然

欧莱雅亚太区法规部产品安全与评估资深经理

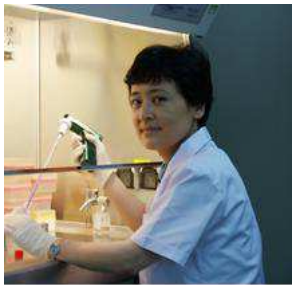
2009 年毕业于中国科学技术大学，获生物学博士学位。博士期间主要从事重金属及阻燃剂的毒理研究。毕业后从事一般化学品及农化产品毒理学安全评价工作。2012 年加入欧莱雅亚太地区产品安全评价部，先后负责皮肤护理产品以及发用产品的原料及成品的安全评价，2018 年开始负责整个亚太区产品安全评价部工作。

Liping HU

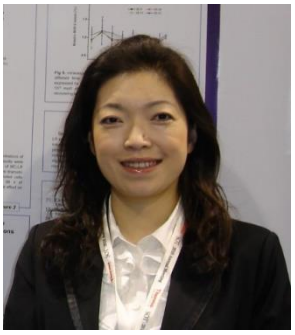
Toxicology senior manager, Global Preclinical Safe Toxicology Resource,

M.D., European Registered Toxicologist (ERT). Postdoctoral in Boston University and University of Maryland. Experienced in toxicology research on pharmaceutical compounds as well as safety evaluation on cosmetic product and ingredients. Now responsible for Johnson and Johnson consumer product safety in China.

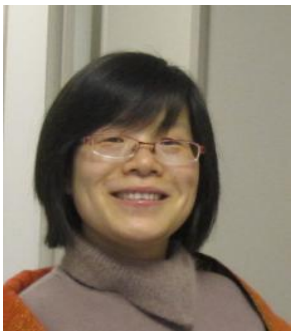
刘宇红
北京东方淼森生物科技有限公司首席科学家
北京工商大学中国化妆品协同创新中心特聘专家
主要从事以中医理论为指导的化妆品植物功效原料的研究、开发；创建化妆品植物原料安全评价体系、功效评价体系以及进行体系研究，并结合皮肤表观生理学和皮肤科学，对作用机理和通路进行研究。



Qiu Lu
Director of the laboratory of technology center, Shanghai Customs
She joined the toxicology laboratory of technical center of Shanghai Entry-Exit Inspection and Quarantine Bureau (CIQ) in May,2003. Mainly engaged in toxicology safety test and evaluation, especially the research, application and promotion of alternatives. Pioneer in participating international standard validation activity.



Yi Shuai,
PhD/DABT/ERT, Associate Director of the Division of Chemical Toxicity and Safety Assessment, Shanghai CDC.
More than 11 years of toxicology related professional experience and safety evaluation experience. Established more than 10 toxicological *in vitro* assays in her institution. She is the board member of CEMS, committee member of TATT, ST, BMT and etc. Secretary of the Society of Toxicology, Shanghai Preventive Medicine.



Yang Ying
Chief Physician, Deputy Director of the Institute of Hygiene Toxicology, Guangdong CDC
Participated in the formulation of national food safety standards and safety technical standards for cosmetics. A member of Working Group in Validation of Cosmetic Alternative Test of the SFDA, Deputy Secretary of the TATT. Chinese observer of the International Coordinating meeting of OECD, ICATM, ESAC and SACATM.

Donna Macmillan
Principal Scientist at Lhasa Limited and the lead scientist in the skin sensitisation research team
Initially worked in the development of mutagenicity and skin sensitisation alerts in the Derek knowledge base then moving into the role of lead scientist in skin sensitisation. Currently involves the promotion of research, seeking collaborations, and encouraging data-sharing to improve the performance of Lhasa's toxicity models.

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Associate chief pharmacist in Zhejiang Institute for Food and Drug Control

Mainly working on genetic toxicology and *in vitro* toxicology research. Graduated from Shanghai Jiaotong University School of Medicine in 2011. Worked as postdoctoral fellow in Toronto University Sunnybrook Research Institute in 2012-2013. Trained for *in vitro* technology and GLP in IIVS in 2016.

黄黎珍

华南理工大学副教授，硕士生导师

长期从事基因编辑体外细胞模型的开发及应用研究，应用CRISPR/Cas9 等系统建立了一系列灵敏特异的药物代谢肝毒性、药药相互作用及皮肤过敏评估等体外细胞模型。主持国家自然基金项目 2 项，作为技术骨干参与 2019 年国家重点研发项目精准医学项目。

Hajime Kojima

Secretary general of Japanese Center for the Validation of Alternative methods (JaCVAM) and the section chief of Division of risk assessment, Biological Safety Research Center (BSRC) in National Institute of Health Sciences (NIHS)

The councilor of the Japanese Society of Toxicology, the Japanese Environmental Mutagen Society and the Japanese Society for Alternatives to Animal Experiments. He is also a vice-chair of the Working Group of the National Coordinators for the Test Guidelines Programme and is also an expert of skin & eye irritation, skin sensitisation, validation management group of non-animal for endcrine disrupter in OECD.

Carl Westmoreland

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Carl is responsible for scientific leadership in SEAC with respect to current and future requirements in the area of consumer safety. He focuses on Unilever's ongoing effort to develop novel ways of delivering consumer safety without the need for animal testing. Carl is currently a member of ESAC (the scientific advisory committee for the European Centre for Validation of Alternative Methods).

Quanshun Zhang
Senior scientist and director of education and outreach programs at the Institute for In Vitro Sciences (IIVS)
Graduated from Nanjing Agricultural University School of Veterinary Medicine, worked at Tufts University School of Veterinary Medicine and also worked at Shanghai Animal and Plant Quarantine Bureau as a Senior Veterinarian. Currently work for IIVS which is a non-profit research and testing laboratory dedicated to *in vitro* methods.

Nathalie Alépée
L'Oréal Research & Innovation, France
Twenty-year experience in leadership of investigative toxicology with proof of accountability for relationship of European bodies on Alternative to Animal Testing having being an ESAC member (ECVAM Scientific Advisory Board) and research partner in EU projects. Involved in international regulatory acceptance bodies, i.e. OECD Test Guidelines and Guidance.

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会议论文集

目录

大会报告(Plenary lectures)

Ensuring safety of cosmetic products: EU cosmetic regulations and in-market control of compliance

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Abstract: Today there are more than 700.000 cosmetics products on the EU market (considering the different shades and variants within product lines). With a turnover of 20 % every year, cosmetics are truly fast moving consumer goods. When considering something as intimate and personal as cosmetic products, business success is closely linked to consumer confidence : Confidence in the brand, confidence in the efficacy of the product but most importantly confidence that the product will not cause harm. One key avenue to create and keep consumer confidence - product-by-product as well as for a whole sector - is through credible and efficient safety regulation. There are a three key success criteria for a successful safety legislation of fast moving consumer goods: 1. Clear requirements on safety, based on modern scientific approaches; 2. Safe products that comply with the regulation can quickly enter the market without unnecessary administrative lead times. 3. Unsafe products don't reach the market, or in the rare cases that they do, are quickly detected and removed. Over the past 45 years, the EU has developed and refined a regulatory approach for cosmetics that ensures a high level of consumer protection whilst allowing rapid market access innovation of compliant products. The EU Cosmetics Regulation is based on a system of industry responsibility and authorities' in-market control. The technical product dossier (Product Information File, PIF) and the Product Safety Assessment are corner stones of this approach. The presentation will introduce the regulatory approach of the EU and the interplay between safety assessment, in-market control and cosmetovigilance.
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15 years of transformational change in global cosmetics regulation

Catherine Willett

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Abstract: The first law restricting the testing of cosmetics on animals was passed in the European Union in 2004, fifteen years ago this year, although the work that laid the foundation for that law began many years before. Consumers have long rejected the idea that animals should be used to test cosmetics, and initially, the major driver for legislative change was public pressure. In the intervening years, similar prohibitions on the testing and sale of cosmetics and cosmetic ingredients have been passed now in some 37 countries, the US state of California, and 6 states in Brazil; a majority of the major cosmetics markets. The prohibitions created a large incentive for the development of non-animal methods or "new

approach methodologies" (NAMs). What is evident following the development of several NAMs is that they actually provide information that more accurately reflects the human response to chemicals. So the motivation for development and implementation of NAMs has evolved to include better human health protection; this was the driver for the inclusion of a section limiting animal testing in the recently updated US law regulating chemicals. There has been a tremendous evolution in not only the science of the test methods, but in the thinking about chemical safety assessment, which enables more efficient, effective safety assessment of cosmetic ingredients. As part of this evolution, we have initiated a new partnership, Non-Animal Cosmetic Safety Assessment (NACSA) that aims to provide the science and training to allow complete safety assessment of cosmetics without animals globally by 2023.

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Principles of safety assessment of cosmetics

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Abstract: Cosmetics need to be safe for the general population when applied under normal conditions of use. Therefore, safety assessment is carried out on the active ingredients, based on hazard identification, dose-response assessment and exposure assessment, forming together risk characterization. By calculating the probability that harm will happen under a defined exposure scenario, a safe dose is determined for each of the actives present. When for an ingredient the thus obtained Margin of Safety is higher or equal to 100, the compound is considered to be safe. Safety assessment needs to be carried out prior to marketing. It is an objective, predictive and living scientific exercise, which needs updating whenever new relevant information becomes available. As in most parts of the world, animal studies are increasingly being forbidden for cosmetics, alternative ways using animal-free new approach methodologies are being developed to guarantee human health.
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Compliance with Non-Animal Testing Strategies for Cosmetics

Dr James Wakefield

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Abstract: Objective Since the introduction of the ban on the use of animal testing for the substantiation of safety of cosmetics came into force in the European Union, there has been an increased need for alternative strategies for determining the safety of cosmetic products and ingredients. Globally, the regulations of cosmetics are moving towards the banning of animal testing of cosmetics, with more and more countries either already banning or in the process of banning cosmetic testing using laboratory animals. The safety assessment for cosmetics and ingredients has become more and more important, in the absence of new data from animal

studies. It now requires the comprehensive knowledge on the use and interpretation of in vitro, in silico, in chemico and historical in vivo data, which can be challenging to the safety assessors and the cosmetic industry to collect large amounts of varied data and analyse the validity. **Methods** The historical use of typical Points of Departure (PoD) such as acute toxicity, skin and eye irritation potential, skin sensitisation potential, chronic toxicity, phototoxicity, genotoxicity, carcinogenicity and reproductive and developmental toxicity has become well accepted for determining the safe use of ingredients to humans. Since the animal testing bans, new data for these points of departure can not be determined for cosmetic ingredients, and as such alternative strategies are required. Interpretation of alternative data, including in vitro studies, whether formally validated or non-validated, computational modelling such as Quantitative Structure Activity Relationships (QSAR), read-across to compounds with structural or functional similarities and History of Safe Use may all be considered, but should be carefully applied with expert judgment on the applicability in each scenario. **Conclusion** Based on professional experience in toxicology and computational chemistry it is possible to utilise these alternative strategies in order to substantiate the safety of ingredients for cosmetic use, without relying on new data from animal testing.

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Transformation of safety information into a safety evaluation report

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Abstract: A comprehensive safety evaluation of a cosmetic product is based on reliable safety information on the product and all its ingredients, with emphasis on those substances for which some concern exists for human health. It starts with an unambiguous identification of its composition. Elements to be addressed for the product and its ingredients - by a qualified safety assessor - consist of the physico-chemical characteristics, microbiological quality, stability, the presence of impurities and traces, the toxicological profile and the exposure under the foreseen conditions of use. In addition, information on the composition of the packaging material and possible impurities along with manufacturing, GMP procedures and complaints received should be present. The final statement on the safety of the cosmetic product is based on all-inclusive reasoning, covering also the calculations of the margin of safety of the actives and any regulatory and health issues.
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Chemical hazard assessment based on phenotypic profiling and mechanistic reasoning

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Abstract: Current chemical safety assessments are mostly based on phenotypic endpoints derived from animal models. New approach methods based on predictive *in vitro* molecular and phenotypic endpoints have the potential to enable assessments based on mechanistic reasoning that are more efficient and relevant to human health. I will provide an update on the development of the Toxicity Mode-of-Action Discovery (ToxMAD) Platform in A*STAR. The platform is aimed to provide fit-for-purpose assays tailored to specific regulatory or industrial needs. I will focus on a key ToxMAD module called "High-throughput In-vitro Phenotypic Profiling for Toxicity prediction" (HIPPTox), which uses high-throughput cellular imaging and machine learning to automatically identify cell models and phenotypic endpoints predictive of chemical-induced toxicity. I will also discuss how HIPPTox can be used to rapidly and efficiently estimate the Points of Departure (POD) in cellular responses, and accelerate the prioritization of chemicals with little or no human safety data.

Exposure Assessment in Cosmetics Safety Evaluation

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Abstract: Exposure refers to a quantitative measure of the magnitude, duration and frequency of exposure to a potential hazard. Exposure to a potential hazard must be of sufficient magnitude, duration and frequency (i.e. dose) in order for harm to occur. In the words of the fifteenth century 'father of toxicology' Paracelsus, "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy." In cosmetics safety evaluation, exposure assessment plays an essential role. Consumer exposure to the ingredients is determined through assessment of the cosmetic product's target consumer groups, use scenario, amount, frequency, duration, contact with the skin surface area, and concentration of the ingredient in the finished product. Consumer "Habits and Practices" data from different sources will be leveraged, such as the Personal Care Product Council studies for cosmetic use in US, the SCCS guidelines for cosmetics in Europe, or EPA or EU DPD Technical guidance document exposure handbooks. We also conduct studies to understand consumer use "Habits and Practices" in relevant regions/populations to get more profound understanding of consumer exposure scenarios. In the absence of skin absorption data, consumer exposure is based on habits and practices and 100% skin uptake is typically assumed of the applied dose. Exposure assessment can be further refined by measuring how much of the ingredient is absorbed. This can be achieved by toxicokinetics study, including dermal absorption study. There are in vitro methods established for dermal absorption e.g. described in OECD TG 428. Other tools like PBPK modeling can also help to describe toxicokinetics and calculate the absorbed dose. Skin absorption data is helpful in the refinement of both systemic exposure and site-of-contact exposure, which is relevant for skin sensitization

endpoint. In a recent in vitro dermal absorption study we conducted, a novel design of measurements was used with the preservative, methylisothiazolinone (MI), in beauty care (BC) and household care (HHC) products using realistic consumer exposure conditions. A difference between measured exposure levels (MELs) for MI in leave-on versus rinse-off BC products, and lower MELs for MI in HHC rinse-off compared to BC products was demonstrated. For repeated product applications, the measured exposure was lower than estimations based on summation of applied amounts. Compared to rinse-off products, leave-on applications resulted in higher MELs, correlating with the higher incidences of allergic contact dermatitis associated with those product types. Lower MELs for MI in rinse-off products indicate a lower likelihood to induce skin sensitization, also after multiple daily applications. These in vitro skin exposure measurements indicate conservatism of default exposure estimates applied in risk assessment and might be helpful in future risk assessment refinements.

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History of Safety Use: A non-animal approach to risk assess botanicals in Cosmetics products

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Abstract: There is now a growing consumer interest in cosmetic products which contain botanicals (herbal material or extracts). Many botanicals have an extensive history of safe use for several hundreds of years. However, robust and transparent safety assessment on such types of ingredients in cosmetics without generation of new animal data still poses a challenge. This talk will present a novel non-animal approach, History of Safety Use (HoSU), which has been developed and used by Unilever for many years for risk assessing safety of botanical ingredients [1]. Following risk-based risk assessment principles, the approach integrates both exposure and hazard information of botanicals using a multi-criteria decision analysis (MCDA) tool. The MCDA evaluates the similarity of the botanical ingredient of interest to its historic counterpart - the comparator, the evidence supporting the history of use, and any evidence of concern. The assessment made is whether a botanical ingredient is as safe as its comparator botanical, which has a history of use. We will illustrate the approach with a case study on green tea. The study generates some objective, transparent, and transferable safety assessment outcomes, which help us with decision making.

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The whole life cycle safety evaluation and risk management of cosmetics

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Abstract Cosmetics safety is the key responsibility of cosmetics manufactures and also the focus of authorities. The safety evaluation of cosmetic products is a systemic process constituted by several key segments. According to the life cycle of cosmetic products usually we divide the safety evaluation into two parts, pre-marketing evaluation and post marketing surveillance, and the pre-marketing evaluation includes the raw material risk assessment and product safety evaluation two segments. Raw material risk assessment is key during the process. The objective of raw material risk assessment is to control the safety risk of the raw material when it is used in cosmetic products. hazard characterization is one of the two key elements, another one is exposure evaluation. Therefore, acquire appropriate toxicological data based on the exposure properties is the basic requirement in the evaluation, i.e. which level of toxicological data is needed is decided by the exposure properties of the cosmetic product. the assessment cannot be carried on if no sufficient toxicological data available, but focus to much time on the creation of the full toxicological data set is also a waste of resource. Understanding the composition of the raw material is the prerequisite of the risk assessment. The composition not only includes the key ingredients and other Intentionally added ingredients like solvents, preservatives, and antioxidants, but also the impurities including byproducts, residues etc. Due to the consideration of the animal welfare, the cosmetic industry made a lot effort on the investigation of animal test alternative methods, while many non-test methods are also the alternatives to minimal or reduce the animal tests. Based on the composition of raw material, historical use experiences and publications can be collected to sustain the safety of the ingredients in raw material, also other methods such as read across, computer modelling, and Threshold of Toxicological Concern etc. Test is not the only solution for raw material risk assessment. Generally speaking, the safety evaluation of finished products is based on safety of individual ingredients. However, the efficiency of preservative system and product stability need to be checked at product level as safety requirements. In some conditions, the local tolerance of product can be confirmed by non-animal test models and human tests. The dominant data is human study in supporting the good local tolerance of the product. In the product safety evaluation, we need to be noted that the hazard of cosmetics is not zero, while the safety risk can be well controlled with good risk management. The risk management methods are made according to the hazard information of the product and also the foreseeable use of consumer. The product safety evaluation is not finished after product launched on the market. Close monitor the safe of consumers to insure the safety evaluation conclusion is correct and the risk management is appropriate is essential in the product life cycle. If there are any signals on the market show that this product has higher ratio of adverse reactions comparing with other products in the same category, further actions should be made and the product need to be reevaluated. Though the post market surveillance, we can eventually guarantee the product is safe to our consumer.
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Botanic Extract Safety Evaluation on Baby Product: Implement of Alternative Methodology

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Abstract: Objective Evidence based safety is the foundation of our product development. Our common focus and commitment is to ensure products founded on safety to protect and advance the health of our baby consumers. In this effort, each formulation must go through our rigorous Five-Level Safety Assurance Process: 1) approach to sourcing ingredients, 2) ingredient toxicological safety assessment, 3) an exaggerated confirmatory clinical evaluation and 4) in-use testing in the intended population. (5) ongoing global post market evaluation. Throughout this process, we engage leading science, alternative methodology, and medical experts from around the world to ensure that we're holding ourselves to the very highest standards. In this case we are addressing the safety of Empetrum Nigrum Fruit Juice ingredient in a Baby Cream used at concentration of 0.002%.

Method

Botanical information: Empetrum Nigrum Fruit also known as black crowberry, moss berry, curlew berry and belongs to Ericaceae (Empetraceae) family. The raw material which contains this ingredient is Black Crowberry Hydroglycerined Extract. The composition is: Glycerin, water and Empetrum Nigrum Fruit Juice (1%). The Raw Material is used at 0.2% in the product. Hence the effective concentration in the product is 0.002%. The safety profile of Glycerin and Water is well characterized and hence not elucidate here.

Systemic safety: Crowberry provides the third largest harvest of all berries (after blueberries and lingonberries). Crowberry is used in jams and jellies; beer or sparkling wines can be made from the juice. It is also used in a number of traditional medicines. Given its extensive food- and traditional herbal medicinal use, the systemic exposure of this berry extract has no systemic toxicological concern and is considered safe in this application.

Local safety profile

a. Eye irritation potential: Acute eye irritation potential of the raw material (RM) was studied undiluted by measuring its cytotoxic effects in a GLP compliant *in-vitro* EpiOcular™ reconstructed human cornea-like epithelium model (OECD TG492). The true MTT mean viability of the tissues treated with the RM should be > 60% after the MTT reduction, to be concluded as not an eye irritant in in-vitro Epi-ocular model.

b. Skin irritation potential: The Skin irritation potential of RM was studied undiluted in a GLP compliant *in-vitro* Epi-skin reconstructed human epidermis (OECD TG439). Following a 15 minutes exposure and 42 hours of recovery period, the relative mean viability of the tissues treated with the test item (RM) and reference item was measured and should be > 50% after the MTT reduction to qualify as not a skin irritant. In addition, secretion of the inflammatory cytokine IL-1α was measured at the end of recovery period. The conclusion was made based on the IL-1α concentration values as well as the cytotoxicity of the test item-treated tissues.

c. Skin sensitization potential: By following the Adverse Outcome Pathway for Skin sensitization described by OECD, the skin sensitization potential of the Empetrum Nigrum Fruit juice (1%) was evaluated by using 3 *in vitro* test methods:

a) Direct Peptide Reactivity Assay (DPRA, OECD 442C) to evaluate the reactivity of the berry extract to synthetic cysteine and lysine peptides. b) Human Cell Line Activation Test (h-CLAT, OECD 442E). and c) In-Vitro Keratinosens Test (protocol similar to OECD test guideline No. 442D). The ability of berry extract to activate Nrf2 transcription factor

was studied on immortalized and genetically modified Human adherent HaCaT keratinocyte cell line. The interpretation is if any two tests out three indicate negative results, the chemical is considered to be non-sensitizer. These are all validated *in vitro* methods, which are globally accepted and published by OECD for acceptance.

d. Phototoxic potential: The raw material was studied in a GLP compliant in-vitro 3T3 NRU photo-toxicity test by following the protocol of OECD TG432.

Clinical safety data: Clinical safety testing of the formula (Human Repeat Insult Patch Test (HRIPT), Photoallergy (PA) and Phototoxicity (PT) studies were performed on adult volunteers. HRIPT studies and Photoallergy studies are performed in adults rather than babies since the immune system of adult is more developed and sensitive as compared to babies. Phototoxicity studies involve irradiation with UV rays and hence babies cannot be used for testing this potential.

Results and conclusion

The *in-vitro* EpiOcular™ study indicated that the raw material Black Crowberry Hydroglycerined Extract 80 was non-irritant to the reconstructed human cornea like epithelium. The *in-vitro*, skin irritation in Episkin™ study indicated that the raw material was non-irritant to skin. Skin sensitization potential evaluated by 3 *in vitro* studies - DPRA, h-CLAT and Keratinosens™ Test indicated negative results and hence the raw material can be considered as non-sensitizer to the skin. Phototoxic potential of the raw material evaluated in an *in-vitro*, 3T3 NRU phototoxicity test indicated no phototoxic potential. Clinical safety studies – HRIPT, PA and PT performed on the formula containing 0.002% of Empetrum Nigrum Fruit juice did not indicate adverse effects in the tested volunteers. Hence, Crowberry is an edible fruit used in jams, beers and wines. Based on the available set of local safety data on the raw material Black Crowberry Hydroglycerined Extract 80 containing 1% Empetrum Nigrum Fruit juice, it is not expected to be eye irritant, not a skin irritant, not a skin sensitizer and not a photo-toxic and hence safety concerns are anticipated from the use of the INCI - Empetrum nigrum fruit juice in the formula baby cream at 0.002%.

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Establishment of Safety Evaluation System of Botanical Ingredients for Cosmetics and Instance Sharing

化妆品植物原料安全评价体系建设及实例分享

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北京工商大学中国化妆品协同创新中心

摘要:化妆品安全性是第一要素。植物原料安全风险评估是化妆品安全评价的组成部分，但植物原料安全评价难度大，主要表现在：国际上可借鉴的化妆品安评做法以及数据主要针对结构明确的物质，现行欧盟化妆品安全评估指导原则主要着眼于化学成分清晰的化妆品原料，而植物原料属于化学结构不完全明确物质范畴，无法照搬欧盟化妆品做法，这类风险评估参考文献有限，在我国基本空缺。与其形成强烈反差的是国内外民众对天然、绿色化妆品的追求有增无减，势不可挡。因此，化妆品植物原料如何进行

安全风险评估是一个亟待研究和解决的课题。本研究先从国际、中国法规或规定中寻找直接或间接依据，即做事的合规性；再从科学的角度，摸索出了化妆品植物原料安全风险评估体系组成要素，主要包括：风险评估基本原则（危害识别，剂量反应评定，暴露评定和风险特征描述），化妆品植物提取物安全评价决策树，减少动物毒理学试验策略，系统毒性评估，以及局部耐受性动物替代评价组合测试策略。报告的第二个部分是实例分享，首先，对无慢性毒理学数据的植物原料，用实例说明如何进行系统毒性评价；第二，实际工作中我们发现，在对植物原料进行局部耐受性测试中，不能完全照搬化妆品做法，否则会造成假阴性或假阳性，而误导评价结果，本部分就我们所进行的方法学研究用实例进行分享。总之建立植物原料安全风险评估体系，遵循 3R 原则，以保障化妆品植物原料其品质的安全性。

Establishment and application of non - animal test in CIQ

Lu Qiu

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Abstract: The Entry-Exit Inspection and Quarantine Bureau has been integrated into the Customs in April 2018. Its functions remain basically, and it will continue to provide technical support for the supervision of import and export trade, including cosmetics. Therefore, our organization pays more attention to the internationalization tendency in the field of laboratory testing, the transfer and application of related methods. Around 2003, CIQ with a positive attitude, keep track international laws and regulations on cosmetics, was committed to the application of international alternatives and research. Up to now, CIQ has basically established a testing platform for alternative methods for safety testing of cosmetics. In addition, CIQ has always paid attention to the international communication of alternatives ，and communication with enterprises. Take an active part in the international validation activities of alternatives. The four laboratories of CIQ also participated in the formal validation of human epidermal model for skin irritation testing organized in China, and actively conduct the test items in the CNAS recognition, which improved the acceptance of test results. With the concept of social responsibility, CIQ has set up some website and public Weixin to promote the concept of non-animal testing and provide useful information. At the same time, we are also expanding the research of non-animal tests in the efficacy evaluation of cosmetics, striving for standardized evaluation model, to provide the best help for the industry.

Application of the reconstructed human epidermis model to evaluate the skin irritation of topical products used in daily life

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Abstract: Detergent, personal care, and cosmetics products are widely used in daily life for cleaning, moisture, and refresh purposes. The increasing demands for safety evaluation of these products in China urge the development of *in vitro* methods for toxicological safety assessment. This study was conducted to evaluate the skin irritation of topical usage products

in daily life by using the reconstructed human epidermis model EpiSkin^{TM} (produced in China). First, 10 Proficiency Substances (PS) recommended by OECD TG439 with known irritation scores, such as isopropanol and cyclamen aldehyde, were tested according to OECD TG439. PS were applied directly to EpiSkin for 15 minutes and removed by rinsing with PBS. After42h post-treatment incubation, tissue viability was measured by MTT test. A threshold to identify the irritant is that 50% OD value of untreated control in MTT test. The results showed that the classification of the 10 PS was in good accordance with the data provided by validated reference methods in OECD TG439. Next, 32 finished products (including 6 fundamental cosmetics, 10 make-up and beauty cosmetics, 12 cleansing cosmetics and 4 detergent products) were evaluated by the improved method (18 hours exposure and without post-treatment incubation) and the results were compared to the traditional Draize test. The results showed that the predictability of 32 products reached 59.4%. Among the 32 products, 16 fundamental and beauty cosmetics were 100% correctly predicted. While the predictability of the cleansing cosmetics and detergent products was only 18.8%. Considering the complex compositions and surfactant types in these cleansing agents and laundry products, the excessive amount of surfactants in these products might cause irreversible damage to the lipid layer of the cell membrane, therefore the exposure time (i.e. 2 hours or 4 hours) used in Draize test was applied to the current *in vitro* method and the above cleansing cosmetics and laundry products were evaluated again. Then the predictability was improved from 18.8% to 93.8%. Thus, based on our study results, EpiSkin^{TM} skin irritation test has very good predictability for the safety evaluation of fundamental cosmetics, beauty cosmetics and cleansing cosmetics as well as detergent products. In the future, more samples would be included to validate the feasibility of the protocol adopted in our study and provide more information of the feasibility of this alternative method.

Acknowledgments:

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Application of 3D models in integrated testing strategy of cosmetics

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Abstract: In the ethics management of experimental animal, 3R principle, which refers to reduction, replacement and refinement, has attracted an increasing globalization attention of animal welfare. With the development of science and technology, law orientation and globalization of animal welfare, traditional risk assessment method no longer meets the need for human hazard evaluation of cosmeitc raw materials and products. In this context, cosmetics safety evaluation shifts from traditional animal-based toxicity testing to non-animal testing strategy and IATA based on human cells, commercial cell lines or cellular components. The three-dimensional (3D) human sexual organ is an in vitro model that is reconstructed by tissue engineering technology using human cells, and nowadays it has been widely used in animal alternative research owing to a high similarity to human physiological structure and metabolic function. In recent years, our center works on applying 3D reconstructed artificial skin model

and three-dimensional corneal model in cosmetics non-animal testing, IATA and risk assessment. Here, we reviewed the progression in application of 3D skin models in IATA on skin irritation/corrosion, eye irritation, phototoxicity, genotoxicity assessments and progress in application of 3D cornea models in eye irritation evaluation.

The use of Derek Nexus for chemical safety assessment: a case study

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Abstract: Purpose Due to increased regulatory and public pressure, interest in non-animal approaches for skin sensitisation has grown significantly in recent years. **Objectives** To describe a 'defined approach' combining *in silico/in chemico/in vitro* data to predict skin sensitisation. **Methods** Using five exclusion criteria, a '2 out of 3' approach is used to provide a prediction of hazard. A potency category (and GHS classification) is then assigned using a k-Nearest Neighbours model containing human and mouse data. **Results** The defined approach correctly identifies hazard for 86% and the GHS classification for 76% of the dataset when compared to human data. Comparable results are observed for animal data, 85% and 73%, respectively. **Conclusions** *In silico* predictions from Derek Nexus can be used in combination with results from OECD-validated *in chemico* and *in vitro* assays in a defined approach to provide hazard and potency information about a potential skin sensitiser without the use of animal models.
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Establishment of basophil activation test, an allergic model *in vitro*

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Abstract: Objective This study aims to establish human basophil activation test in vitro by flow cytometry, and to explore the feasibility of assessment of type I allergy reaction. **Methods** The expression of CD63 and CD203 in human basophil KU812 activated by positive agents was used to establish in vitro model of type I allergy, which was verified by the result of human histamine enzyme-linked immunosorbent assay. **Results** Human basophil activation test were set up with 2μg /ml of positive agent fMLP for 2 hours of incubation. Human histamine ELISA assay confirmed the result at the same time. **Conclusion** Human basophil activation test in vitro is relatively simple and objective. It is a good animal alternative test for sensitization test with guinea pigs.

Development and evaluation of a novel cell model for skin sensitization prediction

新型化妆品皮肤致敏预测细胞模型 EndoSens 的建立以及评估

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摘要 目的 建立皮肤致敏预测细胞模型并根据 OECD 的指导原则对该模型进行准确度、灵敏度和特异性评估，同时应用该细胞模型进行化妆品中药成分的致敏性检测。**方法：** 利用 CRISPR/Cas9 以及同源重组介导的精准基因编辑技术建立实时精准的 HMOX1 报告追踪细胞模型—EndoSens。选择 OECD 指导原则推荐的 20 种标准参考化合物进行皮肤致敏预测能力评估和比较，同时对化妆品中药成分进行致敏性检测。**结果** EndoSens 可以准确地区分化学物的皮肤致敏性，其准确度达 90%，灵敏度达 91.7%，特异性达 87.5%，预测能力达到了 OECD 指导原则的要求，超过了已验证认可的 KeratinoSen™ 模型。同时，EndoSens 也准确预测了含致敏成分的肉桂提取物的致敏性。**结论** EndoSens 皮肤致敏预测细胞模型不仅可以实现对单一化合物的准确预测，还可以对复杂成分的化妆品中药植物提取物进行皮肤致敏性评价，具有较好的皮肤致敏预测能力，可用于化妆品原料皮肤致敏性筛查，提高化妆品使用的安全性。

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ICCR update for the safety assessment of cosmetic ingredients

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Abstract The International Cooperation on Cosmetics Regulation (ICCR) is an international group of regulatory authorities from Brazil, Canada, the European Union, Japan, and the United States. ICCR members work together to promote regulatory alignment, in order to maximize consumer protection while minimizing barriers to trade. ICCR was held its ninth annual meeting (ICCR-9) on November 5, 2015 in Brussels, Belgium. At this meeting, discussions related to the evolution of the working group on *in silico* methods/quantitative structure activity relationships (QSARs) and updates on alternatives to animal testing approaches took place. These led to the formation of a new joint working group, covering a holistic approach to identify modern methods and Integrated Approaches to Testing and Assessment (IATA), relevant to the safety assessments of ingredients used in cosmetics. In 2017 ICCR published a white paper entitled “Integrated Strategies for Safety Assessments of Cosmetic Ingredients – Part I”. This white paper was written by an ICCR ad hoc Joint Regulators-Industry Working Group (JWG) and outlined the principles that underpin the integration of novel methods and data in the safety assessment of cosmetic ingredients. The white paper was followed in 2018 by a peer-reviewed paper entitled “Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients”. The 9

principles outlined in these documents describe the goals of a next generation risk assessment (NGRA) for cosmetics (to be human-relevant, exposure-led, hypothesis-driven and designed to prevent harm), how an NGRA should be conducted (using a tiered and iterative approach, following an appropriate literature search and evaluation of the available data, and using robust and relevant methods and strategies); and how the assessment should be documented (transparent and explicit about the logic of the approach and sources of uncertainty). In addition, In addition, this joint WG will be holding a workshop on July 11th -12nd, 2019 in Montreal, Canada. The goal of this workshop is to investigate how these 9 principles are currently being applied to NGRA case studies being performed in different organizations and explore how application of these principles can aid safety decision in risk assessments which use novel assessment methodologies (NAMs). Four case studies will be presented at the workshop. The case studies will describe how non-animal approaches have been used to complete an exposure-led risk assessment, and will cover a variety of health effects relevant to cosmetics. Workshop participants will discuss how application of the 9 ICCR principles can underpin the use of new approaches in safety decision making. Gaps that may prevent decision making will also be identified and discussed.

Next Generation Risk Assessment (NGRA) for cosmetic safety assessment and case studies

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Abstract: The principles for the use of non-animal approaches in consumer safety risk assessments were recently outlined by the International Cooperation on Cosmetics Regulation (ICCR1). A key principle is that modern risk assessments should be exposure-led. This means that novel methods that are used to make decisions about human safety must be quantitative, so that any predictions relating to dose must be interpretable in the context of actual levels of consumer exposure. Interpreting dose-response data from in vitro toxicity assays requires an understanding of both cellular exposure in in vitro assays and how these relate to in vivo internal concentrations. Understanding both dosimetry and physiologically-based kinetic (PBK) modelling have been identified as essential components for robust decision-making in Next Generation Risk Assessments (NGRA). An NGRA approach for skin allergy risk assessment (SARA2) evaluated using six case study ingredients in two different product exposure scenarios will be described. This is a tiered model-based approach that integrates predictive chemistry expertise, historical in vivo data, in silico predictions and in vitro data to predict the probability of human skin sensitisation occurring following a given product exposure with explicit uncertainty. For evaluation of systemic toxicity using NGRA approaches, a series of case study chemicals (including caffeine, curcumin and coumarin) are being evaluated in a joint research programme between Unilever and the US Environmental Protection agency (EPA). This uses selected ToxCast assays and high throughput transcriptomics together with in silico chemistry tools and PBK modelling. A key challenge with respect to the application of these tools for safety decision-making is a reliance on

quantification of in vitro-to-in vivo extrapolation. These case study examples are providing increasing confidence in the application of the ICCR principles for 'Integrated Strategies for Safety Assessments of Cosmetic Ingredients' for robust decision-making in consumer safety.

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AOP based integrated approaches to testing and assessment for skin sensitization hazard and potency

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Abstract Skin sensitization is a common toxicity endpoint of concern in various industries and accounts for 10-15% of known occupational illness in the U.S. and Europe. Mechanisms of skin sensitization have been investigated intensively for many years and are documented by the Organization for Economic Co-operation and Development (OECD) in its publication, "The Adverse Outcome Pathway for Skin Sensitization Initiated by Covalent Binding to Proteins". The adverse outcome pathway (AOP) includes four key mechanistic events: (1) binding of haptons to endogenous proteins in the skin, (2) keratinocyte activation, (3) dendritic cell activation, and (4) proliferation of antigen-specific T cells. The most commonly used animal test, the murine local lymph node assay (LLNA) is based on the understanding of this complex series of events underlying the immune response after expose to a chemical sensitizer, and covers all key events. However, the construction of the AOP for skin sensitization has enabled the development of a multitude of non-animal test methods that are associated with one or more of the AOP key events. However, the complexity of the underlying biology indicates that no single measurement is yet sufficient to predict sensitizer potency. Therefore, it is generally assumed that only a combination of several methods in an integrated testing strategy will obviate the need for animal testing. Many testing strategies combining non-animal methods are developed with defined approaches. The defined approaches are able to either predict skin sensitization hazard (sensitizer versus non-sensitizer) or assign the test substance to one of three skin sensitization potency categories. Here we will introduce an evaluation of defined approaches (Das) representing non-animal skin sensitization testing strategies performed by the Cosmetics Europe skin tolerance task force and the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods.

Dealing Today's Emerging In Vitro Evaluation of Skin Sensitization: A Cosmetic Industrial Case Study

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L'OREAL R&I

Abstract The field of non-animal testing for skin sensitization has increased over the past

decade, leading to the publication by the OECD of the adverse outcome pathway for skin sensitization, which has divided the sensitization process into mechanistic key events (OECD, 2012). Hence there is broad agreement that the non-animal's methods cannot be used as stand-alone tools and that information from several methods needs to be integrated to perform sensitization hazard identification and potency prediction in a weight of evidence approach, the ways of integrating such data to allow risk assessment of new ingredients is still in its investigational stage. In the present talk, application of a defined approach with a DIP previously published (del Bufalo, et al., 2018) along with additional lines of evidence in an IATA which serves as point of departure (PoD) is presented. The approach is exemplified with specific case studies on six chemicals across 2 exposure scenarii (face cream and shampoo). Among the 6 tested chemicals, propyl paraben and lactic acid are predicted non sensitizer in our first tier strategy Sensitizer/Non-Sensitizer. Concerning the positive calls, a second-tier step on potency predicted DNCB and PTD as strong/extreme sensitizers while eugenol and resorcinol were predicted moderate/weak, allowing their usage at 0.2% in both product types. These case studies reflect an approach on how to move from animal testing into an evaluation of new ingredients based on alternative information only in a weight of evidence approach.

Combination of DPRA and h-CLAT to Evaluate Skin Sensitization of Chrysanthemum Extracts from Different Habitats

直接多肽结合试验与人源细胞系激活试验联合策略在多产地菊花提取物皮肤致敏性应用的研究

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摘要 目的:皮肤致敏性是化妆品原料安全性评估中的一项重要内容，植物提取物被广泛应用在化妆品产品中，然而植物提取物的致敏性缺乏相关研究数据。有报道菊花具有潜在的皮肤致敏风险，本研究拟建立改良的直接多肽结合试验（Direct Peptide Reaction Assay，DPRA）法与人源细胞系激活试验（Human Cell Line Activation Test，h-CLAT）法联合策略，确认菊花提取物体外皮肤致敏性，比较不同产地菊花提取物致敏性差异，为菊花提取物应用于化妆品产品提供安全性依据。**方法:**选择 9 种不同产地的菊花提取物，将受试物分别与半胱氨酸多肽和赖氨酸多肽避光共孵育 24h，样品过滤后加入 1ml 进样瓶，运用高效液相色谱法（HPLC），分析各菊花提取物对两种多肽的消耗。当受试物不与两种多肽发生共洗脱时，则按两种多肽消除率均值判断；当受试物与赖氨酸多肽发生共洗脱时，则按半胱氨酸多肽消除率计；当受试物与半胱氨酸多肽及赖氨酸多肽都发生共洗脱时，则该受试物无法判断。同时，设置 8 个不同浓度的菊花提取物与体外培养的人急性单核细胞白血病细胞（THP-1）共孵育 24h 后，通过流式细胞仪检测受试物孵育后的细胞表面标记物 CD54 和 CD86 的表达。通过比较两种方法的预测结果综合判断其产生过敏反应的可能性。**结果:**DPRA 法对菊花提取物致敏性的预测中，发现编号为 HBAG 的祁白菊和 TX 的杭白菊为皮肤致敏疑似物质，ABRC 杭白菊为非致敏物。h-CLAT 法预测中，ABRC 杭白菊同样为非致敏物。**结论:** DPRA 和 h-CLAT 的组合策略可以应用于菊花提取物致敏性评估，不同品种、不同产地菊花提取物的致敏性

存在差异性。DPRA 和 h-CLAT 的组合策略可把控植物提取物安全性，降低其应用于化妆品产品后引发皮肤致敏的风险。

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Integrated in vitro test strategy for cosmetics irritation

化妆品刺激性的体外整合测试策略

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摘要 随着化妆品产业与认知的发展，伴随着高比例的因消费者自身皮肤屏障功能不足而导致的轻微刺激性现象。消费者对化妆品安全性提出更严格的要求，促使化妆品不仅要满足传统刺激性检测的标准，更要满足轻微刺激性检测的要求。因此，如何建立一个化妆品刺激性检测整合策略，以高效地判定化妆品刺激性水平，优化产品开发，就体现出显著的应用价值。我们在本研究中探讨，皮肤刺激性尤其是轻微刺激性发生的机理，并以 3D 皮肤模型（EpiKutis）为基础，建立化妆品配方的整合测试策略，包括单时间点与多时间点检测体系。同时，通过对分子、细胞以及组织活力等多维度的指标检测，对皮肤刺激性与轻微刺激性进行判定，以提高体外化妆品刺激性测试结果与临床测试的吻合度。

其他摘要 (Other Abstract)

3D 人源性重组皮肤模型微核试验方法初探

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摘要 3D 人源性重组皮肤模型（Reconstructed human skin models）是模拟人体天然皮肤结构，由体外分离出的正常人角质形成细胞在特定的培养环境下生成的活性组织。3D 皮肤模型在体外研究方面具有众多优势，如其人源性及 3D 立体培养特性，能更好地模拟体内正常细胞的生长环境，反映受试物在靶器官的作用情况等。目前 3D 人源性重组皮肤模型在遗传毒性评价方面得到了国际组织的广泛认可。欧洲化妆品、盥洗用品和香料协会协会和欧洲替代试验有效性验证中心已将 3D 皮肤模型微核试验和彗星试验用于化学品、化妆品的体外遗传毒性试验。我国在此领域尚未完全建立相应的试验方法，本课题旨在探索并建立我国 3D 皮肤模型体外微核试验方法，助力我国体外遗传毒性研究。

本课题使用两种 3D 人源性重组皮肤模型，Epikutis®RhE（广东博溪生物科技有限公司）和 Episkin®（上海斯安肤诺生物科技有限公司）开展体外微核试验。目前阳性物选用环磷酰胺（Cyclophosphamide，CP）、甲磺酸甲酯（methyl methane sulfonate，MMS)和硫酸长春碱（vinblastine sulfate，VB）。对微核试验中关键步骤如 3D 皮肤组织的消化方法反复多次确定，最终标准化 3D 皮肤微核试验方法（复苏，染毒，消化，固定，制

片），并且对微核的计数方法进行了统一。同时增加阳性物种类和数量，验证其敏感性和可重复性。并与体内遗传毒性试验对比，验证其准确性。

尽管应用 3D 皮肤模型进行遗传毒性评价有很多优势，仍需要在如下问题上进行深入研究：如 3D 模型的代谢酶与人体组织代谢酶之间存在差异；3D 皮肤模型还处于验证阶段，尚需增加受试物的种类进一步验证其敏感性；受试物处理方法以及减少受试物沉淀对试验结果的影响；减少运输过程对模型的影响等。

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Human brain organoid-on-a-chip to probe impaired neurogenesis induced by cadmium

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Abstract Objective: As an industrial metal, cadmium has received considerable concern in environmental and occupational health. Once absorbed, cadmium rapidly accumulates in human body over time due to a low excretion rate. In particular, women are more susceptible to cadmium toxicity compared to men, and cadmium might affect the female reproductive system and fetal development. Cadmium was examined to cross human placenta, which is not a complete barrier, and finally accumulate in fetal tissues. Such prenatal exposure to cadmium poses a health threat particularly to the fetal brain, however there are few studies to explain the relationships between prenatal cadmium exposure and adverse effects in the early developing brain. Given the inherent differences between species in brain development, architecture, and function, it is highly desirable to develop in vitro models of the human brain to explore the complicated mechanisms of neuronal dysfunctions caused by cadmium. **Method:** Herein, we establish a human induced pluripotent stem cell-derived brain organoid model on a pillar array, which is amenable to explore the pathogenesis of fetal brain development with cadmium exposure in vitro. An array of octagon-shaped micropillars allows for the reaggregation of dissociated hiPSCs, termed embryoid bodies. These aggregates were subsequently induced into neural identities in suspension and finally differentiated into millimeter-sized 3D brain organoids with rapid expansion of polarized neuroepithelium in the extracellular matrix. The growth of these organoids recapitulates key aspects of human brain development, including authentic cell types, well-defined organization, and orderly neural differentiation, reminiscent of the early developing brain. With Cd exposure, it has a lasting effect on neural differentiation, maturation, and cellular death. Immunostaining and real-time PCR was carried out to investigate the impaired neurogenesis in Cd-treated brain organoids. **Result:** In this study, we engineered an in vitro model of hiPSC-derived brain organoids on a

micropillar chip and explored neural dysfunctions under Cd exposure. With cadmium treatment, these brain organoids exhibited the increased cell death, impaired neurogenesis, skewed neural maturation, and disturbed brain regionalization. Such changes might be potential causes for various learning and behavioral deficits observed in various neurological diseases due to Cd exposure. **Conclusion:** Engineeered brain organoid-on-an-array chip incorporates microfabrication technology with stem cell biology, which allows examination of abnormal neurogenesis induced by many different toxic factors in vitro and might contribute to our better understanding of the mechanisms underlying clinical features observed in postnatal neural disorders.

皮肤致敏替代方法的整合策略研究

The integration study of alternative tests in skin sensitization

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摘要 目的: 基于皮肤致敏的 AOP 分子起始事件，建立直接多肽反应（DPRA）、人细胞系激活试验（h-CLAT）和基于 ARE-Nrf2 致敏细胞株（JSens）的检测平台，对化妆品原料是否有致敏潜能进行预测。**方法:**DPRA：将受试物与半胱氨酸和赖氨酸共孵育，通过 HPLC 检测反应体系中多肽的消耗率，从而评估受试物的肽反应性；h-CLAT：通过受试物与 THP-1 细胞共孵育 24h，检测细胞表面抗原 CD54 和 CD86 的表达上调情况，预判受试物是否有皮肤致敏的潜能；JSens：基于 ARE-Nrf2 的细胞毒性通路，设计携带目的基因的 pGL4.17 质粒，构建稳转 HaCaT 细胞株。将不同浓度受试物与细胞共孵育 48 h，通过检测细胞荧光素酶的表达量，作为判断受试物致敏潜力的量化指标。**结果:**在 3 个方法中，分别对包括 2,4-二硝基苯酚、肉桂醇、苯乙醛等阳性物质和乳酸、甘油等阴性物质在内的 20 多种标准物质进行验证，发现该 3 个方法的整合使用不仅能很好地区分致敏物与非致敏物，并对 SDS 等有皮肤刺激但非致敏的物质也能进行较好地区分。**结论:**3 个方法的联合使用能够较好地对受试物的致敏潜能进行预测。本研究后续将扩大检测范围，提升平台的应用型。

New Approach for Assessing Photo-genotoxicity/mutagenicity of Cosmetic Ingredients

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Abstract Animal Testing Ban & Lack of Formally Validated Methods for Photo-genotoxicity/mutagenicity Since March 2013, there is a complete ban on animal testing and marketing of cosmetic products, which themselves or their constituent ingredients are tested on animals solely for the purpose of cosmetic use, in European Union. A number of in vitro assays have been developed and validated since then, including the 3T3 Neutral Red Uptake Photo-toxicity Test (OECD Testing Guideline 432) for testing of phototoxic potential.

However, the 3T3 test is not designed to predict other adverse effects that may arise from combined actions of a chemical and light, e.g. photo-clastogenicity, photo-mutagenicity, or photo-carcinogenicity. **Guidance for Assessing Photo-genotoxicity/mutagenicity (new in SCCS Notes of Guidance 10th version)** First of all, photo-genotoxicity testing are not required routinely as part of a photo-safety assessment. Only for specific cases when there is a structural alert for that molecule, and the molecule has a high light absorbing potential or it has a high possibility to be photo-activated, especially when the substance could reach the eyes or light-exposed areas of skin, either by direct contact or through systemic distribution, then evidence of lack of photo-genotoxicity/photo-mutagenicity should be provided, in addition to data for gene mutations and clastogenicity/aneugenicity endpoints. For these molecules, UV-VIS spectra should be provided together with the Molar Extinction Coefficient (MEC) determined. Photo-toxicity 3T3 test should then be performed if the test material absorbs at wavelengths higher than 313 nm with a MEC higher than 1000 L mol−1 cm−1. As a second tier, the photo-toxicity effect can be further evaluated with reconstructed human skin model with barrier properties. A positive control should always be included. A negative result is usually accepted and no photo-mutagenicity tests are needed. **Current status of available Photo-genotoxicity/mutagenicity alternative methods and challenges** Several OECD assays have been adapted to a combined treatment of chemicals with UV-VIS light for the detection of photo-clastogenicity/mutagenicity, which were summarized in the report of the Gesellschaft für Umweltmutationsforschung (GUM) Task Force on photochemical genotoxicity. The methods include photo-Ames test, photo-mouse lymphoma assay, photo-micronucleus test, photo-chromosome aberration test and photo-Comet assay. However, the validity and usability of photo-genotoxicity tests are still being questioned. Experience with photo-clastogenicity tests by US Food and Drug Administration (FDA) indicated that these tests are oversensitive and incidences of pseudo-photo-clastogenicity have been reported. UK Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM) on the other hand stated that photo-genotoxicity testing had a negligible impact in the overall assessment for potential of photo-carcinogenicity. The International Conference on Harmonisation (ICH) guideline on photo-safety evaluation of pharmaceuticals also stated that the mechanism by which compounds induce photo-genotoxic effects is identical to those that produce photo-toxicity, and thus separate testing of both endpoints is not warranted. With all the comments above, COM, ICH, FDA, European Medicines Agency (EMA), and European Food Safety Authority (EFSA) agreed that no photo-mutagenicity testing is not required for the time being. It is clear that the validity of photo-genotoxicity testing is still being challenged and further guidance would be necessary when there are positive results in the photo-toxicity tests.

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替代毒理学方法在化妆品检测中的应用研究进展

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摘要 进入 21 世纪前，以不使用实验动物为核心的 1R 原则经历了一个漫长的缓慢发展

时期。近些年来，受益于现代生物科学技术的飞速发展，1R 原则进入了快速发展期。时至今日，体外方法（（*in vitro* methods））已成为生物学检测与研究手段的重要组成部分，在化妆品法规性测试、生物学机制研究以及功效性原料的筛查等方面扮演着重要角色。不同于替代方法（alternative methods），体外方法泛指一切利用无知觉材料替代活体哺乳动物的安全性与功效学的测试。只有经过严格验证并被法规接受，可用于取代毒理学动物实验的体外方法方可被称为绝对“替代方法”。广义的体外方法既包括符合法规要求的替代方法，还包括大量应用于化妆品原料和产品安全性或功效性测试的非动物以及非临床测试方法。根据实验系统和适用范围的不同，可将体外方法分为用于风险评估和毒性预测的非生物测试方法、法规认可和列入标准测试指南的替代方法，以及大量多元化和个性化的方法。体外方法覆盖化妆品质量和安全评价的整个过程，可以被应用于原料筛查、配方优化、组合测试、定制化评估以及产品监管等方面。自 OECD2004 年发布首个法规认可的替代方法-3T3 中性红摄取光毒性实验（3T3 NRUPT，指南 432）以来，截止目前，列入指南的替代方法已经超过 20 项。自 2006 年起，我国开始接受替代方法成为国家标准和检验检疫行业标准，累计发布标准 30 余项。在全球化妆品毒性测试标准一体化的背景下，建立在检测标准基础上的方法创新和优化将不断涌现，这些技术的应用将助力行业的健康发展，同时对保护消费者权益也有积极促进作用。

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化妆品质量安全检测技术研究进展

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摘要 随着经济的快速发展和人民生活水平的不断提高，化妆品日益成为人们日常生活的必需品。在化妆品行业高速发展的大背景下，纷繁多样的化妆品新原料被用于化妆品生产。一方面，新原料的引入对化妆品品质和功效有一定的改善作用。另一方面，新原料的使用也带来了潜在风险。许多国际知名品牌化妆品相继检出含有禁用物质或限用物质，化妆品质量安全问题日益成为公众关注的焦点。为加强对化妆品质量安全的监管，规避不断涌现的化妆品质量安全事件，保护消费者的健康，保障化妆品贸易良好运行，世界各国先后制定了严格的化学品质量安全法律法规，明确规定了在化妆品生产过程中禁止和限制添加的物质。与此同时，研究人员采用现有的分析测试技术，研发了一系列检测化妆品中安全性风险物质的方法。新的检测方法的不断涌现有效提升了化妆品质量安全检测技术水平。该文对近年来国内外在化妆品质量安全检测技术方面的重要研究进展作了综述，并对代表性的化妆品质量安全检测新方法作了较为详尽的介绍，以期为化妆品检测领域研究人员提供理论支持和技术参考。

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应用体外替代方法预测化妆品中常用化学防晒剂的皮肤致敏性及光敏性

Application of in vitro alternative methods to predict skin sensitization and photosensitivity of chemical sunscreens commonly used in cosmetics

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摘要 目的：应用体外替代方法DPRA及photo-DPRA预测化妆品中常用的13种化学防晒剂的皮肤致敏性及光敏性。**方法：**本研究使用的13种化妆品常用化学防晒剂包括：苯基苯并咪唑磺酸、乙基己基三嗪酮、亚甲基双-苯并三唑基四甲基丁基酚、双-乙基己基苯酚甲氧苯基三嗪、丁基甲氧基二苯甲酰甲烷、奥克立林、4-甲氧苄亚基樟脑、二乙氨基羟基甲酰基甲酸己酯、二苯酮-3、p-甲氧基肉桂酸异戊酯、水杨酸乙基己酯、胡莫柳酯和甲氧基肉桂酸辛酯。DPRA方法：使用100mM的样品溶液作为受试物，把不同受试物分别按照1:10和1:50的比例加入含半胱氨酸和赖氨酸的多肽溶液，在室温下避光孵育24h后，用配有220nm紫外检测器的高效液相色谱分析仪器检测两种多肽的消耗情况。photo-DPRA方法：使用20mM的样品溶液作为受试物，把不同受试物按照1:10的比例加入含半胱氨酸的多肽溶液，在5 J/cm^2 UVA下光照50min后，在室温下避光孵育24h，用配有220nm紫外检测器的高效液相色谱分析仪器检测多肽的消耗情况。**结果：**所有受试物与半胱氨酸多肽和赖氨酸多肽均无共洗脱现象，通过计算两种多肽的清除百分率均值发现，二苯酮-3对两种多肽的清除百分率均值大于临界值6.38%，可判断为致敏性阳性。苯基苯并咪唑磺酸经UVA照射后，对半胱氨酸多肽的清除百分率大于临界值13.89%，可判断为光致敏性阳性。**结论：**二苯酮-3可预测为致敏物，而苯基苯并咪唑磺酸可预测为光致敏物。化学防晒剂由于具有紫外线吸收特性，因此对其进行安全性评价时需要将光照因素引入研究模型。

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Nrf2 deficiency disrupts autophagy and sensitizes ZnO nanoparticles induced cytotoxicity in HaCaT cells

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Abstract Zinc oxide (ZnO) nanoparticles are widely used in cosmetics and sunscreens. ZnO nanoparticles can enter into human epidermal keratinocytes either directly through topically applied cosmetics or indirectly through any breaches in the skin integrity. Increasing evidences indicate ZnO nanoparticles induces unignorable harmful effects to human skin. Nrf2 (Nuclear factor erythroid derived 2 like 2) is a key nuclear transcriptional factor for intracellular antioxidant reaction and electrophilic pressure. Nrf2 pathway is emerged as an important

toxicity pathway mediating chemical induced skin injury. Herein, the present study was aimed to investigate the role of Nrf2-mediated autophagy in dermal toxicity induced by ZnO nanoparticles. Size and zeta potential were determined by dynamic light scattering and phase analysis light scattering. Cellular uptake of nanoparticles was investigated by scanning electron microscopy and transmission electron microscopy. A specific knockdown of Nrf2 (*Nrf2*-KD) HaCaT cells by lentiviral shRNA and the scramble cells were exposed to ZnO nanoparticles at the concentrations ranging from 50 to 500 μM. Our results demonstrated that the mean hydrodynamic diameter and zeta potential of the ZnO nanoparticles was 219 nm and −14.8 mV, respectively. ZnO nanoparticles concentration-dependently reduced cell viability and increased intracellular reactive oxygen species (ROS) levels in the cells. In contrast, Nrf2-KD cells were more vulnerable to ZnO nanoparticles induced cytotoxicity as well as ROS accumulation. ZnO nanoparticles increased Nrf2 and its downstream antioxidant genes, such as Gclc, Gclm, and HO-1. Moreover, the proteins expression of autophagy related proteins p62, LC3, Beclin, and PINK1 were also increased by ZnO nanoparticles. Nrf2 deficiency was found to reduce the gene expression of Gclc, Gclm and HO-1, and to enhance the proteins expression of LC3, PINK1, and Parkin. Taken together, these findings demonstrated that Nrf2 deficiency disrupts autophagy and sensitizes HaCaT cells to ZnO nanoparticles-induced oxidative stress and cytotoxicity.

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对乙酰氨基酚对 2D/3D HepaRG 细胞的毒作用比较与体外-体内数据外推研究

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目的：选择合适的体外模型成为药物性肝损伤评价与毒性发现的关键问题之一。理想的肝毒性体外评价模型应该具有类似体内肝脏表型、代谢能力，并适合于长期体外培养和高通量筛选。本文采用体外单层培养（2D）和三维（3D）培养的人肝癌 HepaRG 细胞模型，对临床常用的解热镇痛药对乙酰氨基酚（APAP）进行体外肝毒性评价，应用基于生理的药代动力学（PBPK）模型进行体外-体内数据外推研究。旨在比较 APAP 对 2D/3D HepaRG 细胞的毒性作用，并建立肝毒性评价的整合测试方法。**方法：**采用液滴重叠法构建 3D 类器官培养模型。APAP（0.16、0.8、4 和 20 mM）分别处理 HepaRG 2D 和 3D 细胞 24 h，Alamar blue 法测定细胞存活率。应用高内涵图像分析（HCA）检测线粒体活性氧（ROS）、线粒体膜电位（MMP）和线粒体数丰度以评价 APAP 引起的肝损伤。此外，利用 GastroPlus™ 的参数估计功能和文献资料获取的模型参数建立 APAP 的人体 PBPK 模型，并应用人体实测药物动力学数据对模型进行验证和修正。基于 PBPK 模型计算 APAP 产生肝毒性时肝细胞暴露的药物浓度，并与体外试验中 APAP 致肝细胞损伤的浓度进行比较。**结果：**APAP 可剂量依赖性地降低 2D 和 3D 细胞的存活率。3D 细胞对 APAP 诱导的线粒体损伤更为敏感，表现为活性氧积累增加，线粒体膜电位下降和线粒体丰度下降。通过 PBPK 模拟计算发现，APAP 在 3D 模型中诱导线粒体损伤的浓度与 PBPK 模型预测的 APAP 致体内肝损伤的药物浓度更为接近。**结论：**

3D HepaRG 模型可以更准确地评估药物诱导的肝毒性，整合体外数据与 PBPK 模型为肝毒性评价提供了有力的工具。

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Establishment and application of high throughput qualitative screening method for chemical oxidative stressor

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Abstract Objective: The public has been concerned about the safety of chemicals used in production and life for a long time. Human expose to chemicals in complicated ways. The evaluation of chemicals health hazard is a big challenge. Multiple mechanisms have been proposed of chemicals toxicity, among which oxidative stress is the most important one. Oxidative stress is a pathophysiological condition, in which the imbalanced of reactive oxygen species (ROS) production and clearance can be induced by a variety of *in vivo* and *in vitro* factors. Oxidative stress is closely associated with the development of various diseases such as cancers, diabetes, atherosclerosis, hypertension and heart diseases. Hence, precise identification and determination of chemical oxidative stressors are crucial for the evaluation of chemicals health hazard. This study aims to establish a high-throughput chemical oxidative stressors screening system based on ARE (antioxidant response element) activity and intracellular ROS levels. **Methods:** The ARE-luciferase reporter stable transfected cell lines were used to establish the high-throughput screening system. Intracellular ROS levels were detecting by using DCFH probes through microplate reader. **Results:** The chemical oxidative stressors identification system based on ARE activity and intracellular ROS levels is successfully established. Around 7500 chemicals tested by this screening system, 146 ARE-activators and 50 ARE-inhibitors (including isoniazid and camptothecin) were recognized by this oxidative stressors screening system. And we have successfully established high-throughput methods of intracellular ROS levels at two-points (1h and 6h). **Conclusion:** The high-throughput screening system based on ARE activity and intracellular ROS levels can identify chemical oxidative stressors rapidly and efficiently. Furthermore, ARE-activators and inhibitors can be distinguished by this ARE activity screening platform. Combined with the ROS detection, we might be able to further classify the chemicals into ROS producer or sulfhydryl-based oxidants. These classifications will provide a basis for the identification and toxicity evaluation of chemical oxidative stressors.

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基于线虫 33 个表型指标的化学物毒性高通量筛检方法

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摘要 研究非啮齿类动物的大规模高通量的快速毒性筛检和评价体系，可以预测新的化学品的传统动物急性毒性效应，从而达到减少或替代啮齿类动物的目的，符合“3R”原则，是当前化学品毒性风险评估和风险管理研究中的前沿领域。传统的毒性测试主要依赖于大量的动物实验，测试周期长、通量低、费用高，难以满足大量化学物的测试需求。本项目拟采用 384 孔板的线虫急性毒性实验，通过图像采集软件和图像处理软件，量化染毒后线虫的各项指标（平均长度、平均宽度，分散情况和分布情况等），初步研究化学品毒性的线虫快速筛检及毒性评价体系（包括线虫染毒剂量、检测指标、方法和评价模式等）。得到的五大类 33 个线虫表型变化相关的指数包括线虫死活相关的指数、线虫大小相关的指数、灰度值相关的指数、卷曲度相关的指数、活动度相关的指数等。参照 BIC-SK 算法，通过对指数的聚类分析和 PCA 分析，并结合 T 检验方法等，得出数据间的差异性，从而快速高通量筛检比较化合物的急性毒性效应。如应用于啮齿类动物实验之前，可预先快速筛查出可疑或毒性较高的化学物，有助于形成传统毒性测试的优先排序名单，能够减少、优化甚至替代部分啮齿类实验动物的使用。该技术方法的发明与应用，符合国际 21 世纪毒理学发展计划所提出的毒性测试新战略与风险评估新框架，即倡导改变以啮齿类等整体动物实验为主的传统毒性测试体系，向基于高通量体外测试和计算毒理学等方法的低等模式生物及人源性细胞等体外毒性测试体系转型。

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灭活菌条件优化及硫化汞的线虫毒性研究

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摘要 目的：探索线虫化学品毒性测试模型中喂饲用大肠杆菌（OP50）灭活的优化条件，确定钴 60 灭活 OP50 的最佳照射剂量。以秀丽隐杆线虫的体长、体宽和咽泵震动频率为检测终点，研究硫化汞（HgS）对秀丽隐杆线虫幼虫生长发育的影响。**方法：**采用钴 60 不同照射剂量（8kGy、10kGy、20kGy、30kGy）灭活的 OP50（未浓缩和 10:1 浓缩）及未处理的 OP50 分别喂饲 L1 期线虫，在 0h、24h、48h、72h 分别测量线虫的体长和体宽，以喂饲 48h 对线虫体长和体宽无影响的钴 60 照射剂量为优选实验条件。在此实验条件下，秀丽线虫幼虫暴露不同浓度的 HgS（10mg/ml、60mg/ml、120mg/ml）48h，

测定线虫体长、体宽和咽泵震动频率的变化。**结果：**不同喂饲时间、不同照射剂量对线虫的生长发育影响不同。大于等于 10kGy 的钴 60 照射剂量可将 OP50 完全灭活，未浓缩 OP50 经 10kGy 的钴 60 灭活后喂饲线虫 48h，对其体长和体宽均无显著影响，故确定 10kGy 为钴 60 的最佳照射剂量，且 OP50 不浓缩。在此优化条件下， 60mg/ml 和 120mg/ml 的 HgS 暴露 L1 期线虫 48h，线虫体长、体宽均减小；10mg/ml 的 HgS 对线虫生长发育没有影响。不同浓度的 HgS 对线虫的咽泵震动频率未见显著影响。**结论：**在本文灭活菌喂饲的优化实验条件下，60mg/ml 及以上浓度的 HgS 对秀丽线虫的生长发育具有一定的抑制作用。

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应用 SOS/umu 试验研究 PM2.5 的致 DNA 损伤性效应

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摘要 目的 采用 SOS/umu 试验评价国内北方某市区的大气细颗粒物（$PM_{2.5}$）的 DNA 损伤效应。**方法** 采集大气中的细颗粒物（$PM_{2.5}$）并制成水溶性样品悬液，以采集时间分为“供暖期 $PM_{2.5}$”和“非供暖期 $PM_{2.5}$”两组，每组分别以 62.5、125、250、500 μg/ml 四个剂量，用 SOS/umu 试验评价并比较两组 $PM_{2.5}$样品的致 DNA 损伤效应。**结果** 62.5、125、250、500 μg/ml 供暖期 $PM_{2.5}$组 I_R值均大于 1.5，且有明显的剂量-反应关系，提示具有 DNA 损伤；非供暖期 $PM_{2.5}$组样品仅 500 μg/ml 高剂量组的 I_R值高于 1.5。**结论** 该地区采集的 $PM_{2.5}$样品具有致 DNA 损伤性，且供暖期组显著高于非供暖期组。

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基于体外生物检测技术的大气微细颗粒物（PM2.5）不同组分遗传毒性的比较研究

Comparative study on genotoxic activity of different components of fine particulate matter ($PM_{2.5}$) using *in vitro* bioassays

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摘要 目的：研究上海市区及郊区两个位点（浦东及惠南）冬、夏两季$PM_{2.5}$样本不同组分的遗传毒性特征。**方法：**冬、夏两季采集$PM_{2.5}$样本至石英滤膜上，每张滤膜采集时间为24h。同天采集的滤膜三等分，分别用于总颗粒物（TP）、有机组分（OE）及水溶性组分（WS）的抽提。上述抽提组分冻干后溶于二甲基亚砜（DMSO）中，以灭菌生理盐水（0.85%，w/v）稀释至实验浓度。采用5种鼠伤寒沙门氏菌菌株（*Salmonella typhimurium* strains TA98、TA100、TA97a、TA1535及WP2）研究抽提后样本的基因点突变诱变性、基于大肠杆菌菌株（*E. coli* PQ37 ）的SOS Chromotest® 试剂盒进行基因损伤活性分析并以中国仓鼠肺成纤维细胞株（CHL）进行染色体畸变研究。同时，进行添加代谢活化物S9的间接遗传毒性研究。**结果：**各组分在添加S9后，遗传毒性效应均明显减弱，各组分效应以直接毒性效应为主。TP、WS及OE的遗传毒性各异，相对TP及WS而言，OE的遗传毒性几乎可忽略，尤其在较低剂量暴露时（如实际大气体积≤$10m^3$时）。尽管OE的遗传毒性随暴露时间的延长而增加，但始终低于TP及WS。SOS Chromotest® 分析中，冬季浦东TP及WS的遗传毒性诱导因子（IF）分别为4.04~4.76及3.58~4.10，惠南分别为3.71~4.05及3.00~3.49 ；夏季两点TP及WS的IF分别为3.13~3.31及2.06~2.74、2.79~3.07 及2.01~2.58。鼠伤寒沙门氏菌暴露于冬季浦东的TP及WS ，最高致突变率分别为31.43±3.69% 及27.09±5.85%，冬季惠南点的最高致突变率为27.09±5.85%及24.83±2.02%；夏季两点TP及WS的最高致突变率分别为20.84±5.19%及18.06±5.15%、14.07±7.15%及12.16±5.30%。TP及WS对5种菌株的致突变活性类似，诱变活性从大到小均依次为：TA97a> TA100> TA98>TA1535>WP2。CHL细胞株暴露于TP及WS，冬季浦东及惠南点的致畸变率分别为9.83±1.89%及7.67±1.44%、7.17±2.08%及6.83±0.29% ；夏季两点TP及WS致畸变率分别为 5.67±1.04%及5.50±1.32%、2.50±0.08%及 2.67±0.29%。OE暴露下，仅在冬季两点观察到轻微致畸变效应，致畸变率分别为2.67±0.29%及2.33±0.29% 。**结论：**两位点$PM_{2.5}$总颗粒物及其提取组分的遗传毒性效应各异并具明显季节性差异，冬季的遗传毒性明显高于夏季。市区浦东及郊区惠南两点相同季节的遗传毒性效应无显著性差异，表明郊区污染日益严重。体外研究结果表明，TP及WS具相似的遗传毒性效应，表明水溶性组分是导致两点$PM_{2.5}$遗传毒性效应的主因，TP及WS均表现出代谢减毒现象。后续研究将关注上海大气$PM_{2.5}$中的水溶性组分组成。

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槲皮素和槲皮苷的抗炎功效及对活性氧的影响

The anti-inflammatory effects of quercetin and quercetin and their effects on reactive oxygen species

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摘要 目的：探讨槲皮素（quercetin）和槲皮苷（quercitrin）对脂多糖（lipopolysaccharide，LPS）诱导的巨噬细胞 RAW264.7 炎症因子分泌及活性氧的影响。**方法：**采用不同剂量的槲皮素和槲皮苷作用于 LPS 诱导的 RAW264.7 细胞炎症体外模型，CCK-8（Cell Counting Kit-8）法测定细胞存活率，Griess 法测定一氧化氮（NO）含量，ELISA 法测

定炎症因子 TNF-α、IL-1β 和 IL-6 水平，DCFH-DA 法测定活性氧（ROS）含量，采用 Materials Studio 计算软件包从理论角度考察槲皮素和槲皮苷不同位置羟基的抗氧化性能力。**结果：**槲皮素与槲皮苷能明显减少 LPS 诱导的 NO 释放、炎症因子 TNF-α、IL-1β、IL-6 的生成；减少 ROS 的产量；理论计算结果表明，B 环是黄酮类物质抗氧化、清除自由基的主要活性部位。**结论：**一定浓度的槲皮素和槲皮苷具有抗炎和抗氧化效果，推断槲皮素和槲皮苷抗炎作用的产生可能与抗氧化协同作用有关。

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应用转基因鱼胚胎测试技术把关化妆品雌激素安全

Apply Fish Embryo Toxicity Tests to Ensure Cosmetics Safety

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摘要 目的：化妆品的安全性一直备受关注。当前毒理学研究专注于纯化学品而忽略了现实产品中的混合物毒性效应，使得建立高通量完整生物体毒性测试技术用于把关化妆品的整体安全性就变得非常重要。**方法：**通过对化妆品进行前处理，将化妆品样本中会对测试造成干扰的成分剔除，将有毒物质提取出来。应用斑马鱼（*Danio rerio*）胚胎，参照 OECD 236 标准，对提取物进行急性毒测试找出半致死浓度（LC50）；通过建立同类型产品急性毒数据库来反应测试样本的急性毒风险。同时，应用 *Choriogenin H* - Green *Fluorescence Protein* 转基因鲭鳉鱼（*Oryzias melastigma*）胚胎对提取物进行雌激素活性测试并将测试结果表达为雌激素当量值(Estrogen Equivalent, EEQ--—即相当于多少雌二醇)。测试结果比对参照粮农组织/世卫组织食品添加剂联合专家委员会(JECFA)关于雌二醇日摄取量指引所计算出的各类型产品的雌激素当量风险值来评估样本的雌激素毒性风险。**结果：**目前已建立绝大部分常见化妆品的鱼胚胎毒性测试方法并建立了数千款在售化妆品的生物毒性数据库。数据库显示，即使是同类型的化妆品，其急性毒和/或雌激素当量值可相差几十倍甚至几百倍。以 BB 霜为例，雌激素当量值可从未检出到 20,000 ng/g（一粒普通口服避孕药的雌激素当量值约为 10,000 ng），对化妆品的原料进行毒性溯源发现化妆品原料的雌激素当量值从未检出到 5,000,000 ng/g 不等。通过鱼胚胎测试对化妆品原料进行毒性溯源和配方验证，可以高效地发现问题，改善配方，最终提升产品品质。**结论：**斑马鱼因基因、器官组织和生理反应与人类高度相似，已成为第 3 重要的模式生物，广泛用于药物的毒性测试和功效评估，对斑马鱼胚胎有毒的物质对人类也很可能有害。同时，*Choriogenin H* 是雌激素依赖的雌激素受体(Estrogen Receptor)下游基因；在内源性雌激素含量非常低的鱼胚胎时期，该基因不表达或者说表达水平达不到可检出水平。因此，*choriogenin H: GFP* 转基因的表达反应了雌激素信号通道的启动，从技术原理避免了假阳性检测结果的出现。而脊椎动物之间高度保守的雌激素调控机理机制则使得测试结果可以推及致人。根据欧盟实验动物相关法律，鱼胚胎不属于动物。因此，鱼胚胎测试技术可作为一种简单有效地动物测试替代方法来获取可靠的科学数据用于化妆品及其原料的安全性评价和风险评估。

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稀有鮈鲫胚胎和成鱼对几种化学品的敏感性比较研究

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摘要 目的：通过比较稀有鮈鲫胚胎和成鱼对化学品的急性毒性效应，评价稀有鮈鲫胚胎的敏感性，确定其在鱼类替代试验中的应用潜力。**方法：**选取 3,4-二氯苯胺、重铬酸钾、七水硫酸锌和五水硫酸铜四种常用参比化学品，按照《OECD 化学品测试准则 No.236 鱼类胚胎急性毒性试验》和《OECD 化学品测试准则 No.203 鱼类急性毒性试验》，分别开展稀有鮈鲫胚胎和成鱼急性毒性试验。**结果：**3,4-二氯苯胺、重铬酸钾、七水硫酸锌和五水硫酸铜对稀有鮈鲫胚胎的 96 小时半数致死浓度（96h LC_{50}）分别为 12.8mg/L、534mg/L、10.4mg/L 和 1.76mg/L；对成鱼的 96h LC_{50} 分别为 6.52mg/L、116mg/L、37.5mg/L 和 1.29mg/L。比较 96h LC_{50} 值发现，除 3,4-二氯苯胺外，稀有鮈鲫胚胎和成鱼对其余三种化学品的敏感性类似，即获得的毒性分级一致。**结论：**稀有鮈鲫作为一种中国本土的标准试验鱼种，其胚胎与成鱼敏感性类似，具有应用于鱼类急性毒性替代试验的潜力。

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椰子油脂肪酸单乙醇酰胺引起眼刺激的分子机制及结构基础

Molecular mechanism and structural base for cocamide monoethanolamide-induced eye irritation

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目的：椰子油脂肪酸单乙醇酰胺（Cocamide monoethanolamide，CMEA）作为表面活性剂广泛、大量用于日化用品中，能够引起皮炎与眼刺痛，然而其作用机制尚不明确。辣椒素受体（Transient receptor potential vanilloid 1，TRPV1）主要在感觉神经元包括三叉神经节（Trigeminal ganglion，TG）表达，介导疼痛感觉的传导。本研究将阐明 CMEA 激活 TRPV1 通道从而导致眼刺痛的作用机制及结构基础。**方法：**在动物模型上考察 CMEA 对大鼠眼刺痛的影响，运用电生理技术考察 CMEA 对 TRPV1 的激动作用阐明 CMEA 直接激动 TRPV1 从而导致眼刺激性；通过化学分离，构效关系研究，发现 CMEA 中激动 TRPV1 的活性成分；最后通过热动力学计算，定点突变，阐明 CMEA 激活 TRPV1 通道的氨基酸位点。**结果：**CMEA 显著引起鼠眼刺激，并能够被 TRPV1 抑制剂 SB-366791 抑制；CMEA 可引起 TG 神经元动作电位发放频率及内钙增加，此作用可被 SB-366791 抑制；在稳定转染表达 TRPV1 的 HEK-293 细胞上，CMEA 增加 TRPV1 的全细胞电流（EC_{50}=2.55 μg/mL）及开放几率；通过 HPLC 分离并进行活性鉴定，发现月桂酸单乙醇酰胺为主要活性化合物；通过热动力学计算及点突变研究发现 hTRPV1 的辣椒素活性氨基酸 Y512、S513、T551、E571 为月桂酸单乙醇酰胺产生活性的关键氨

基酸。**结论：**CMEA 通过结合 TRPV1 的辣椒素活性氨基酸激动 TRPV1 从而引起眼刺痛。

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高透膜性、皮下靶向释放型 hEGF 的构建和表达

Construction and expression of hEGF with high permeability and subcutaneous targeted release

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摘要 目的：表皮生长因子（epidermal growth factor，EGF）是一种含有 53 个氨基酸多肽单链小分子，对各种细胞增殖和表皮组织生长有很强的促进作用。在医学上已用于烧伤烫伤、溃疡和角膜损伤等方面治疗，在护肤品中也起到美白、抗皱、延缓衰老的作用，具有巨大的潜在应用价值和广阔的市场前景。然而研究表明， EGF 的透皮吸收效果十分微弱。因而构建高透膜型、靶向释放的 EGF，增强 EGF 的透皮吸收效率，提高其生物利用度。**方法：**首先采用重叠 PCR 技术将 MMP-2 的酶切位点编码基因插入于 EGF 和穿膜肽基因中间，构建筛选出最适工业化生产的表达体系为携带 pET22b-P-hEGF 质粒的 *E.coli* BL21-TrixB（DE3），并确定其最佳发酵条件，采用高密度发酵法，提升 P-hEGF 表达产量。同时，以毕赤酵母 GS115 为宿主菌构建 Ppic9k-P-hEGF，并确定其发酵工艺。利用细胞 MTT 法检测 P-hEGF 对细胞的增值能力，利用免疫荧光和离体模拟皮肤模型分析 P-hEGF 的跨膜能力，并检测 P-hEGF 的靶向释放能力。**结果：**经 Western blot 检测，表达获得的重组目的蛋白 P-hEGF 均正确无误；免疫荧光及 MTT 分析显示重组 P-hEGF 具有很好的跨越角质细胞 Hacat 的能力，并能有效的促进 Balb/c 3T3 成纤维细胞的增殖，同时利用 Transwell 小室构建 3D 水平的离体模拟皮肤模型，重组 P-hEGF 能高效的跨越角质细胞层，并扩散作用于成纤维细胞中。最后，利用 MMP-2 金属基质蛋白酶在体外对 PME 进行了酶切实验分析。结果表明 MMP-2 可以对 PME 进行有效的切割，并且随着酶切时间的延长，酶切效率表现出一定的增强。**结论：**构建了一种具有高效跨膜转运与透皮吸收能力、并能实现皮下靶向释放的重组 hEGF，建立了其大肠杆菌和酵母菌的表达制备工艺，将有助于大大提高 hEGF 在药品及化妆品中的生物利用度及功效，从而为其相关产品的品质提升奠定了较好的基础。

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以牛奶为原料制备脂质体眼霜的研究

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摘要 目的:牛奶中丰富的营养成分如牛乳蛋白、氨基酸、维生素、烟酸、抗坏血酸、乳铁蛋白、超氧化物歧化酶、共轭亚油酸等使其具有良好的滋养美白、抗氧化、抗炎、修复和抑菌等功效。但直接使用牛奶仅能营养表面皮肤，因对于皮肤的渗透能力有限，无法营养深层皮肤。脂质体是由磷脂双分子层闭合形成的囊泡，是目前研究最为成熟的纳米药物递送系统，具有很强的皮肤渗透作用，适合作为眼霜制剂，水溶性活性物质可

包载于内水相，脂溶性活性物质可包载于磷脂双分子层间。然而，常规制备脂质体的人工合成磷脂材料十分昂贵，成本过高且制备工艺复杂。本研究以牛奶为原料制备脂质体，即可提高皮肤渗透营养和保湿的作用，同时作为纳米载体，可包载递送其他活性成分到基底组织细胞，还可降低成本，简化制备工艺。**方法：**将普通牛奶稀释一系列倍数后，以不同超声功率在冰浴条件下超声，混合一定比例的纳米氧化银、生育酚，再由0.22μm 无菌滤膜过滤，形成牛奶脂质体溶液保存。利用马尔文粒度仪表征不同条件下溶液的粒径和电位。**结果：**制备所得牛奶脂质体呈电负性，电位-26.56±1.38mv，粒径为163.53±2.41nm，多分散系数 0.134±0.003。室温敞口放置一个月后，状态良好不变性，无细菌生长，实验结果重现性好。**结论：**利用牛奶中的天然脂质成分和蛋白取代人工合成磷脂制备牛奶脂质体，无有机防腐剂添加，具有很强的新颖性和实用性，简化工艺，降低成本，极具应用开发潜力。

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Target audiences

Regulatory and industry risk assessors, including SMEs, safety and regulatory compliance consultants, academic scientists, students, NGOs and informed consumers.

Scope

Exposure-led assessment and decision-making approaches for consumer safety and regulatory compliance without using animals. Development of frameworks and case studies showing how new types of information are used, and how decisions are made. Collaboration between industry, consultants, CROs, regulators and other experts is needed.

Languages & regions

Our efforts will initially focus on the development and dissemination of a comprehensive set of educational resources in English, Additional languages and national outreach efforts will be added as the project develops.

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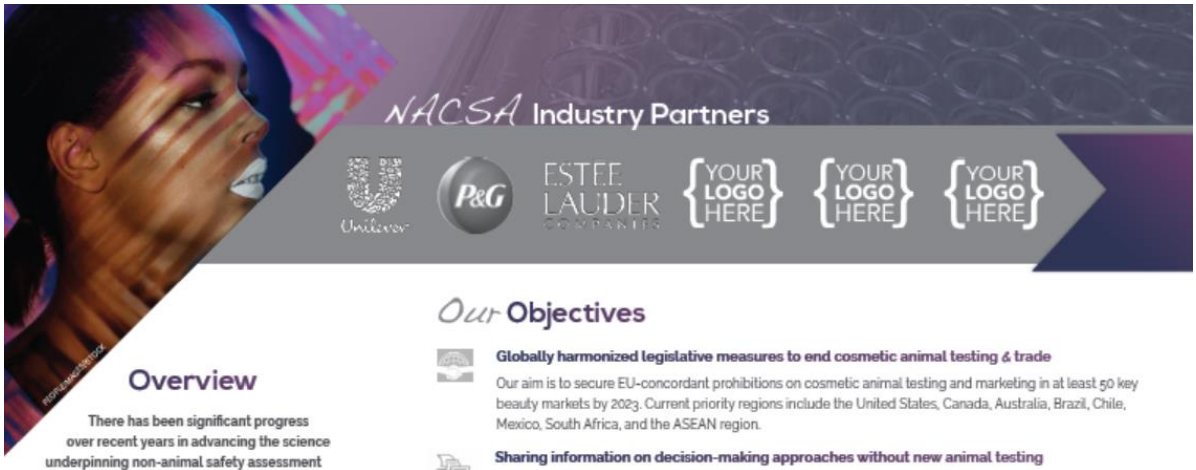
Collaboration for *Non-Animal* Cosmetic Safety Assessment (NACSA)



NACSA Industry Partners

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Overview

There has been significant progress over recent years in advancing the science underpinning non-animal safety assessment for cosmetics. This has evolved in parallel with legislative change in a number of beauty markets; however, if we are to achieve a true global end to the use of animals in cosmetic safety assessment by 2023, there is still more to do. This collaboration between Humane Society International and industry partners intends to help shape future cosmetics legislation and share the decision-making approaches which are being applied to assess safety without animals. The associated investment in education and training will ensure that there is the ongoing ability to satisfy regulations which require non-animal safety approaches.

Our Objectives

Globally harmonized legislative measures to end cosmetic animal testing & trade

Our aim is to secure EU-concordant prohibitions on cosmetic animal testing and marketing in at least 50 key beauty markets by 2023. Current priority regions include the United States, Canada, Australia, Brazil, Chile, Mexico, South Africa, and the ASEAN region.

Sharing information on decision-making approaches without new animal testing

As non-animal testing methods and approaches develop, they can be used for many different purposes, including decision-making on the consumer safety of cosmetics. We will share information on these evolving risk assessment processes which are necessarily exposure-led, product and use-specific and iterative. The expertise of multiple stakeholders and relevant case studies will be used to provide clarity on how to make risk-based cosmetic safety decisions through the integration of scientific evidence from multiple sources.

Investment in education & training

Capacity building is necessary within both the regulated and regulatory cosmetic communities for the long-term acceptance and implementation of these new approaches. Many tools and information are currently available; this project involves developing curricula that are engaging and accessible with specific focus on the application of the data generated for safety decision making. Since this is a global effort, this will require translation and modification of the curricula to meet the needs of different countries.

Join us » **Interested companies are invited to join the *NACSA* collaboration to achieve a global end to cosmetic animal testing by 2023 through harmonized national legislation, education & capacity building in next-generation safety assessment**

SHANGHAI EPISKIN

Reconstructed Human Epidermis
三维重建表皮模型

- **SkinEthic™ RHE** 三维重建表皮模型是由正常人类角质形成细胞在聚碳酸酯膜上经过体外培养而成。该组织模型具有良好的分层和完整结构，其结构和功能与人类的表皮非常接近。该模型是OECD测试指南 431（体外皮肤腐蚀性测方法）和 439（体外皮肤刺激性测方法）采纳认可的表皮模型。
- **SkinEthic™ RHE** 模型参与了国际ISO医疗器械皮肤刺激性测试验证，使用该模型的预测结果与样品结果的一致率为100%。由此，SkinEthic™ RHE 模型现已被纳入最新的ISO 10993-23医疗器械皮肤刺激性试验标准的草案中。

为客户提供实时的技术支持

- 皮肤和角膜模型操作
- 协助客户设计专属或创新的测试研究方案
- 解决日常测试的相关问题
- 三十余年的组织模型开发和体外测试技术背景

检测医疗器械的皮肤刺激性

皮肤刺激性
2008年经过ECVAM 验证 OECD测试指南 439

皮肤腐蚀性
2006年ECVAM验证 OECD测试指南 431

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海恩斯莫里斯（瑞典）公司 (H&M GBC AB)

玫琳凯（中国）化妆品有限公司 (Mary Kay (China) Co., Ltd)

广东博溪生物科技有限公司 (Guangdong BioCell Biotechnology Co., Ltd.)

禄亘生物科技（大连）有限公司 (Logan Biotechnology (Dalian) Corp)

北京慧荣和科技有限公司

上海美迪西生物医药股份有限公司 (Shanghai Medicilon Inc.)

解放军疾病预防控制中心 (Institute of Disease Control and Prevention, PLA)