Scientific workshop on non-animal approaches for chemical safety in China: Current Progress and Outlook

Jin Li, Sandy Li, Paul Carmichael, Jie-Bing Zhu, Carl Westmoreland, Shuangqing Peng, Jiabin Guo, Chao Liu, Weidong Hao, Ping Xu, Feng Xu, Jingbo Pi, Shengnan Liu, Wei Sun, Yuan Pang, Aiqian Zhang, Rong Kuang, Lei Wen, Ying Yang, Erin Hill, Quanshun Zhang, Yongbo Lu, Jianhua Qin, Zhongyu Li, Xiaowei Zhang
Changing world - towards non-animal approaches

Political: Regulations
Increasing regulatory restrictions on marketing ingredients that have been tested on animals

Social: Consumers/NGOs
Millennials demand cruelty free cosmetics
Low trust in safety of chemicals, foods & new innovations may cause rise in animal testing

Technology: 21st Safety Science
New technologies & scientific knowledge are transforming how we assess chemical safety
Significant changes in Safety and Cosmetics

2021 in China

1st May: New regulation for the placing of cosmetic products on the market came into force in China. The Cosmetic Supervision and Administration Regulation (CSAR) now allows “general-use cosmetics” to be imported into China without the need for pre-market animal testing of those products.

1. A safety assessment must be submitted for the cosmetic product to confirm the safety of product.

2. The manufacturer provides an official production qualification management certificate (e.g. GMP or ISO) issued by competent authority in the country of origin.
Recognition of NGRA in cosmetic safety assessment

Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients


European Commission: Scientific Committee on Consumer Safety (2021)
2019: Workshop in Shanghai, China (10-11 April)

Brought together 70 scientists from across China and globally to:

- Address challenges and gaps in China to maximise the impact of New Approach Methodologies (NAMs) in chemical safety
- Raise awareness and acceptance of NAMs to accelerate their uptake into regulations
Breakout Groups

1. Group 1 – In vitro models
2. Group 2 – In silico models
3. Group 3 – Regulatory sciences
4. Group 4 – Education and training
5. Group 5 – Next Generation Risk Assessment
Talks from Chinese scientists

Prof ShuangQing Peng - Development and Application of Non-animal Toxicity Testing Alternatives in China

- Two scientific communities set up and organised annual China conferences from 2014 to 2021
- 3 books published in Chinese on NAMs
- Rising governmental funding on NAMs (in both chemical and food risk assessments)
- Challenges remain
  - Need for increased lab capability
  - Safety regulations need to evolve to adopt NAMs
- Perspectives
  - Willing to innovate
  - Science is advancing with the next generation of young scientists
Talks from Chinese scientists

• Dr Jiabin Guo (AMMS) - A tiered pathway approach in an exposure-led framework for NGRA
• Prof Xiaowei Zhang (Nanjing Univ) - Dose-dependent transcriptomic approach for screening and prediction of chemical toxicity
• Prof Ping Xu (BPRC) - Multi-omics studies for chemical risk assessment - Ping Xu (Beijing Proteomics Research Centre)

Li et al (2021) Toxicology in Vitro, 74, 105171
Talks from Chinese scientists

- Organs-on-chips platform to advance chemical safety assessment – Prof Jianhua Qin (Dalian Institute of Chemistry Physics / CAS)

3DP In Vitro Model for Drug Testing

- Limited human clinical trials
- Not feasible for testing
- Ethic issues

- Cell micro-environment different from human
- Different immune system
- Different from human clinical trials

Bio-Printing in vitro Physiological Model for Drug Testing

- Not a true physiological environment
- Difficult to simulate 3D tissue
- Not reliable to cancer drug testing

- Simulated physiological model
- More close to 3D human tissue
- Reduce using animals

Using cells and/or other biological compounds as basic building blocks to 3D Printing in vitro biological models.

Bio-3D Printing

Y. Li¹, SS Mao¹, Y. Song¹, Y. Zhao¹, Zhou¹, ZZ., Y. Pang¹, T. Zhang¹, W. Sun¹, ²

¹ Tsinghua University, China
² Drexel University, USA
Chinese 3D models by BioCell™
(e.g. 3D Eye irritation test models for cosmetic products)

3D角膜上皮模型: BioOcular™
reconstructed 3D cornea epithelium model: BioOcular™

人角膜组织学结构, Native Cornea

角膜模型组织学结构, Histology of BioOcular

3D Skin Model

角膜模型（BioOcular）高度接近于天然角膜
Talks from Chinese scientists

Predictive toxicology: from and beyond structural basis
Prof Aiqian Zhang (Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences)

Assays for safety mechanisms: how to interpret the data on cellular adaptive stress responses?
Prof Jingbo Pi (China Medical University)
Talks on China regulations by Dr Kuang Rong (ZJ-IFDC*) & Yang Ying (GD-CDC*)

• Regulations rely mainly on animal testing

• Steps taken already
  1. Cosmetics
     • no mandated animal testing for locally made general-use cosmetics and any imported cosmetics via online
     • No mandated animal testing for imported general use cosmetics (2021)
  2. Chemical: QSAR/Read-across can be used when appropriate
  3. Authority engagements with international organisations on future developments with New Approach Methodologies / Next Generation Risk Assessment (e.g. ICCR)

* Zhejiang Institute for Food and Drug Control
Guangdong Provincial Center for Disease Control
Overview of content of undergraduate and graduate toxicology education

**3Rs Rules**
- 3Rs rules and other methods in toxicology research

**Toxicology alternatives**
- Embryonic stem cell test (embryonic stem cell test, EST)
- Replacement (replacement) and optimization (refinement) methods
- Animal models

**OECD采用的主要替代方法**
- 急性毒性替代方法
  - 固定剂量法 (fixed dose procedure)
  - 急性毒性分级法 (acute toxic class method)
- 皮肤腐蚀性体外替代方法
  - (transcutaneous electrical st. test, TES)
  - (human skin model test)

**替代毒理学的发展**
# Student Poster Awards

<table>
<thead>
<tr>
<th>Name</th>
<th>Poster title</th>
<th>Organization</th>
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<tbody>
<tr>
<td>Chi Zhang</td>
<td>Integration of in vitro data from 2D/3D culture HepaRG cells and PBPK-based simulation for predicting acetaminophen hepatotoxicity</td>
<td>Academy of Military Medical Sciences</td>
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<tr>
<td>Yuan Pang</td>
<td>Personalized tumor model: from patient tumor to three-dimensional printing of in vitro model and drug testing</td>
<td>Tsinghua University</td>
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<tr>
<td>Bayindala Xlagedeer</td>
<td>Mode of action of androgen receptor antagonists on HepG2 cells based on ToxCast open source data</td>
<td>Peking University</td>
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<tr>
<td>Zhong Yu Li</td>
<td>Organ-on-a-chip to advance the assessments of chemical and product safety</td>
<td>Chinese Academy of Sciences</td>
</tr>
<tr>
<td>Yuan Yuan Yin</td>
<td>Nrf2 deficiency disrupts autophagy and sensitizes ZnO nanoparticles induced cytotoxicity in HaCat cells</td>
<td>Academy of Military Medical Sciences</td>
</tr>
<tr>
<td>Liu Shengnan</td>
<td>Hyperoxidation of peroxiredoxin renders bistable $H_2O_2$ signalling and nonlinearity for redox circadian oscillation</td>
<td>China Medical University</td>
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Conclusions and next steps

Significant advances in China on NAM science (*in silico* and *in vitro* methods as well as application in risk assessment)

Uptake and progress with NAMs is a multi-stakeholder process

Programmes of training and educations on non-animal approaches to chemical safety
Assessment and application of NAMs

Discussion of regulatory developments and approval of alternative methods in China (including recent adoption of OECD non-animal methods into Chinese technical guidance).

Workshop report in preparation for publication
Thank you!

谢谢！