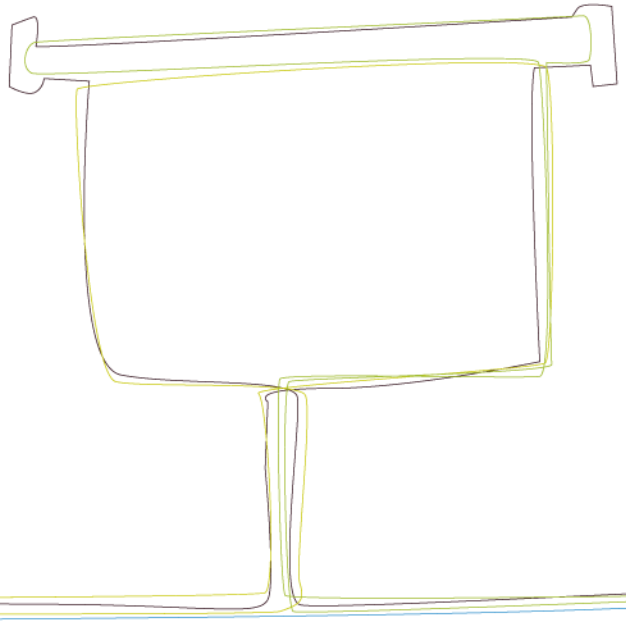
IDEA
International Dialogue for the Evaluation of Allergens

QRA: The hazard assessment challenge?



Prof. Jim Bridges
Emeritus Professor of Toxicology and Environmental Health and Chair of the IDEA Supervisory Group

IDEA Working Group meeting on the inclusion of alternatives to animal testing into QRA
April 26th, 2016 - Brussels

Outline of current QRA

Identify induction potential using LLNA test in mice (EC 3 used as threshold)

↓

Check threshold OK using human volunteers (Human Repeat Insult Protection Test)

↓

Confirm threshold for induction (NESIL) and use safety factors (SAF's) to set an acceptable exposure limit (AEL)

↓

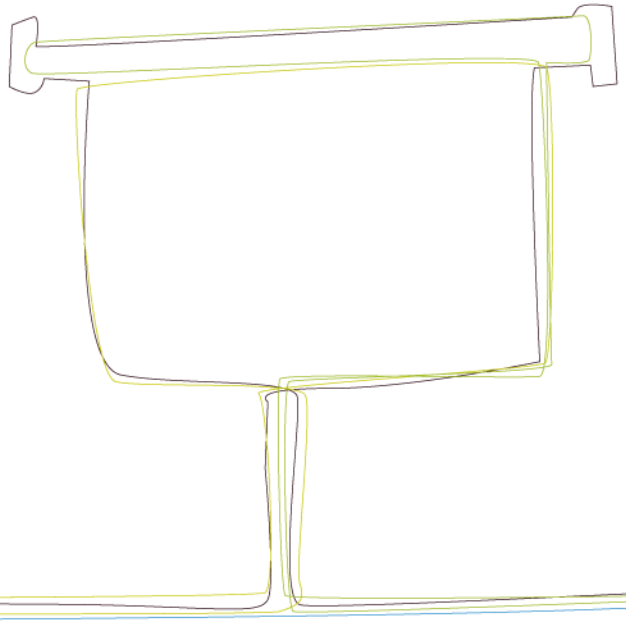
Based on levels of aggregate exposure involving high end usage calculate a consumer exposure limit (CEL)

IDEA

International Dialogue for the Evaluation of Allergens

‘Arriving at our goal is the starting point to another’

John Dewey



Framework for QRA 3 ?

Internal exposure

(total aggregate and toxicokinetics)

Hazard assessment

Non animal evaluation

(AOP based)

↓ ↓

↓ …..WoE evaluation …..**NESIL**

↓ ↓ ↓

→ **CEL** → ↓ **AEL** ← ←

↓ uncertainty analysis

Risk assessment

↑ assessment of the effectiveness of the QRA

Feedback from clinics and consumers

Developing in vitro test(s)for dermal sensitisation: Strategy

IDEA
International Dialogue for the Evaluation of Allergens

A four or more stages approach?

i) Identification of **phys-chem properties** (eg chemical reactivity and stability) and results of **SAR** application.

ii) Estimate of **upper exposure conditions**.

iii) Assessment of hazard. Some false positives acceptable but false negatives must be minimal.

iv) Assessment of potency. At a minimum this must enable reliable categorisation.

In vitro test(s)for dermal sensitisation: methodology?

IDEA
International Dialogue for the Evaluation of Allergens

- Gold standards for reference purposes/ positive and negative controls
- Suitable means for addition and retention of the test fragrances
- A well characterised, relevant, stable and easily available cellular/tissue based test system.
- Appropriate ‘drug’ metabolism capability.
- Endpoints that reflect the critical elements of the adverse outcome pathway(s)
- Strong evidence that the methodology adopted enable a high level of consumer protection

Non-animal tests: aim is hazard or risk assessment?

IDEA
International Dialogue for the Evaluation of Allergens

Is there an intermediary stage between the utilisation of tests for hazard identification and the availability of fully validated tests for potency? If so what should it comprise and should it be time limited?