FOOD TOXICOLOGY AND NEXT GENERATION RISK ASSESSMENT APPROACHES

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OUTLINE

• Introduction to SEAC
• Risk based approaches
• Food toxicology safety assessment
  - conventional approach
  - new tools in risk assessment
  - risk assessment of ‘Naturals’
• New approaches in toxicology/ Next Generation Risk Assessment (NGRA)
• Conclusions
SAFETY & ENVIRONMENTAL ASSURANCE CENTRE (SEAC)

PROTECTING CONSUMERS, WORKERS & OUR ENVIRONMENT BY ENSURING UNILEVER’S PRODUCTS & PROCESSES ARE SAFE & SUSTAINABLE BY DESIGN

CENTRE OF EXCELLENCE – SAFETY & ENVIRONMENTAL SUSTAINABILITY SCIENCES

APPLYING SCIENCE

GOVERNANCE
We provide scientific evidence to manage safety risks & environmental impacts for new technologies.

ADVANCING SCIENCE

NEW CAPABILITY
We harness the latest science to create new tools to assess innovations of the future.

SHARING SCIENCE

COLLABORATION
We partner with leading scientists from around the globe.
We use scientific evidence-based risk and impact assessment methodologies to ensure that the risks / impacts of adverse human health and/or environmental effects from exposure to chemicals used in our products, processes & packaging are acceptably low.
RISK BASED THINKING

Risk based thinking is science and evidence-based - ensures that the risk of adverse health effects from exposure to pathogens / chemicals in foods is acceptably low.

Hazard based

- Check-list compliance
- Unnecessary testing
- Doesn’t consider how product is used
- Yes / No decisions
- Overly conservative

Risk based

- Expertise- & evidence-driven
- Essential testing only
- Product use / exposure determines outcome
- Options to manage risks
- Uncertainties explicit

Precautionary approach
Zero tolerance policies

Hazard – What can go wrong?
Probability – How likely is it to happen?
Severity – If it happens what are the consequences on health?

Science based policies
Priorities are clear
Acceptable levels
### CHEMICALS IN FOOD

#### Naturally occurring

- **Nutrients** e.g. carbs, fats, protein, vits, minerals
- **Biologically active** e.g. lectins, tetrodotoxin, cyanogenic glycosides, caffeine, cocaine, resveratrol, flavones.
- **Other chemicals** e.g. colours, aromas

#### Intentionally added

- **Food additives** e.g. colours, preservatives, flavours, sweeteners
- **New ingredients** e.g. GM, novel foods
- **Processing aids** e.g. enzymes, antifoaming agents
- **Adulterants** e.g. diethylene glycol, melamine, Sudan 1

#### Unintentionally added (contaminants)

- **Environmental** e.g. dioxins/PCBs, heavy metals (Pb, Hg), pesticide/vet drug residues
- **Process** e.g. PAHs, maillard reactions (acrylamide)
- **Food contact materials** e.g. bisphenol A
- **Food spoilage** e.g. aflatoxin, ochratoxin
CAN WE USE A NEW INGREDIENT (OR PROCESS) SAFELY IN FOOD?

Can we safely use \( x \)% of ingredient \( y \) in product \( z \)?
SAFETY ASSESSMENT OF INGREDIENTS IN CONSUMER PRODUCTS

1. Consider product type and consumer habits
2. Determine route and amount of exposure
3. Identify toxicological endpoints of potential concern
4. Identify critical endpoint(s) for risk assessment
5. Identify available toxicology data
6. Identify supporting safety data (e.g. QSAR, HoSU)
7. Evaluate required vs. available support
8. Conduct toxicology testing as required
9. Conduct risk assessment for each critical endpoint
10. Overall safety evaluation for product – define acceptability and risk management measures
RISK ASSESSMENT PRINCIPLES

Risk = f (Hazard x Exposure)

Toxicological Hazard
- Acute toxicity
- Allergy (type I)
- Systemic toxicity
  - sub-chronic
  - chronic
- Reproductive toxicology
- Teratogenicity
- Genotoxicity
- Carcinogenicity

Exposure

Ingestion:
- Food & drink

1. Exposure Assessment
2. Hazard Identification
3. Hazard Characterisation
4. Risk Assessment
CONVENTIONAL RISK ASSESSMENT APPROACH

ADI* = NOAEL ÷ SF**

Exposure < ADI 🌸
Exposure > ADI 😞

* Acceptable Daily Intake
** Safety factor

Hazard characterisation

Safe dose in humans

species extrapolation

Safety/uncertainty factors
Whole Foods

- Macro components of the diet
- Complex mixture of different chemicals
- Toxicological testing is more difficult - 100-fold safety factors often can not be achieved without unbalancing the nutritional content of the animal diet

Substantial Equivalence

- Does the new food share health and nutritional characteristics with an existing, familiar food?
- Safety evaluation - focus on differences
- Recognises that existing foods often contain anti-nutrients that can be consumed safely e.g. potatoes (solanine) and tomatoes (α-tomatine alkaloids)

1 Antinutrients are natural or synthetic compounds found in a variety of foods that interfere with the absorption of vitamins, minerals and other nutrients.
NEW TOOLS IN FOOD SAFETY

History of Safe Use

“Significant human consumption of food (over several generations and in a large diverse population) for which there exists adequate toxicological and allergenicity data to provide reasonable certainty that no harm will result from the consumption of the food”

Health Canada

Safety assessment (Constable et al, 2007)
- Characterisation
- Details of use
- Previous human exposure
- Health effects
- Potential hazards

Threshold of Toxicological Concern (TTC)

- Threshold of exposure for chemicals of known structure below which there is no appreciable risk to human health
- Based on structure chemicals are classed as low, mod, high toxicity
- Useful for chemicals present in food at low concn. e.g. contaminants
- Little or no toxicity data required
- Reliable estimate of intake possible

Post Launch Monitoring (PLM)

- A hypothesis driven scientific approach for obtaining information through investigations relevant to the safety of a (novel) food after market launch
- Uses market data [e.g. food intakes, consumer complaints] to refine safety assessment
- A complement to safety assessment (not replacement)
CASE STUDY: ALGAL OILS

Genetically Modified algae
• Produce chemically tailored edible oils e.g. rich in oleic
• Benefits for product structuring and nutrition

Risk assessment
• Exposure assessment
  • What will the consumer be exposed to?

• Hazard assessment
  • Chemical analysis (impurities from algae and fermentation media, specification, algal toxins?)
  • Genotoxicity
  • ‘read-across’ from published algal tox studies

• Risk
  • If there are no hazards then there is no risk

Risk = f (Hazard x Exposure)
Increased interest in the use of “Naturals” in consumer products, including Foods & Beverages

Key principle - “not all naturals are safe & not all synthetic chemicals are unsafe”

History of Safe Use is an important tool for establishing safety of “Naturals”.
HISTORY OF SAFE USE (HoSU) – risk assessment of naturals

Establishing Similarity

- Appropriate comparator – HoSU at levels equal to or greater than the substance e.g. theanine, a component of black/green tea

Key Criteria

- Evidence – History of Use
  - Substance - Origin & id
  - No. people consuming
  - Consumption frequency
  - Similarity
    - i) population;
    - ii) ingredient spec;
    - iii) processing

- Evidence - concern
  - Safety data
  - Adverse effects in man
  - Components of concern
  - Biological effects/MoA

- Published (Constable et al, 2007; Neeley et al, 2011)

Fingerprinting

- Comparative analysis
- Safety analysis focusses on differences
HISTORY OF SAFE USE (HoSU) – understanding chemical composition

Qualitative & Quantitative Protein Analysis

Comparative Analyses - Fingerprinting

Multidimensional analyses

Individual chemical identification and quantification
HISTORY OF SAFE USE – KEY PUBLICATIONS

History of safe use as applied to the safety assessment of novel foods and foods derived from genetically modified organisms

A. Constable a, D. Jonas b, A. Cockburn c, A. Davi d, G. Edwards e, P. Hepburn f, C. Herouet-Guicheney g, M. Knowles h, B. Moseley i, R. Oberdörfer j, F. Samuels k, l,

Review

Similarity analyses of chromatographic herbal fingerprints: A review

Mohammad Goodarzi a, Paul J. Russell b, Yvan Vander Heyden c, d,

A Multi-Criteria Decision Analysis Model to Assess the Safety of Botanicals Utilizing Data on History of Use


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ABSTRACT

Botanicals (herbal materials and extracts) are widely used in traditional medicines throughout the world. Many have an extensive history of safe use over several hundreds of years. There is now a growing consumer interest in food and cosmetic products, which contain botanicals. There are many publications describing the safety assessment approaches for botanicals, based on the history of safe use. However, they do not define what constitutes a history of safe use, a decision that is ultimately a subjective one. The multi-criteria decision analysis (MCDA) is a model that enables the decision to be formalized. This is a methodology that enables the subjective information to be formalized and turned into an objective decision. The primary objective of this paper is to use the MCDA approach to formalize the criteria for what constitutes a history of safe use and to assess the impact of these criteria on the safety assessment of botanicals.
CASE STUDY: BRAHMI IN TEA

Brahmi (Bacopa monnieri)
• Traditionally used in Ayurveda as a tea
• Key components are saponin glycosides linked to enhanced cognitive performance

Risk assessment – defining History of safe Use

History of Use - Exposure
• Origin of ingredient
• Specification
  • Finger print analysis
• Preparation/ processing
• Population exposed
• No of people exposed
• Duration of exposure
• Pattern of use
• Bioavailability

Evidence of Concern - Hazard
• Toxicology data
  • High Concern: Reproductive or developmental toxicity, mutagenicity, organ toxicity, carcinogenicity
• Biological effects/mechanism of action
• Evidence of adverse effects in man (literature review or existing clinical data)

Fingerprint analysis
FOOD SAFETY RISK BASED APPROACHES: SUMMARY

• Basic principle is to understand the toxicological hazard and how the consumer is exposed (Risk = f(Hazard x Exposure)

• Characterise the risk e.g.
  Acceptable Daily Intake (ADI) = NOAEL ÷ SF

• Substantial equivalence is a useful concept for whole foods

• Additional safety assessment tools include
  • History of Safe Use – particular importance for ‘Naturals’
  • Threshold of toxicological concern
  • Post Launch Monitoring
The world is changing

- Rapid advances in scientific knowledge e.g. genomics, exposure science
- Speed of innovation creating novel materials e.g. nano, biotechnology
- Consumer demands to stop animal testing. Increasing demand for vegan.
- Huge technological advances e.g. HTS, informatics, computational toxicology
- Scientific validity and human relevance of animal studies is being challenged
- Too many chemicals – not enough animals/money/time!
“Advances in toxicogenomics, bioinformatics, systems biology, epigenetics, and computational toxicology could transform toxicity testing from a system based on whole-animal testing to one founded primarily on in vitro methods that evaluate changes in biologic processes using cells, cell lines, or cellular components, preferably of human origin.”

“A primary objective for improving exposure science is to build confidence in the exposure estimates used to support risk-based decision-making, by enhancing quality, expanding coverage and reducing uncertainty.... An important focus has been on the development of PBPK models for translating exposures between test systems and human exposure scenarios”
21st Century Toxicology: Challenges

Accept and embrace the new science (next generation toxicology) - there is no going back

Evolution of risk assessment in response to the new science

Need for trained scientists - Skill sets may be different to traditional approaches

Need regulatory frameworks to accommodate next generation approaches - “regulatory acceptance”
NEXT GENERATION RISK ASSESSMENT (NGRA)

- Using new tools and approaches to build a risk assessment to enable decisions to be made (without animal tests)
- An exposure-led risk assessment solution to biological pathway-indicated hazard concerns

Exposure led  Mechanistic  Hypothesis driven
IMPORTANT TO COLLABORATE & FORM STAKEHOLDER PARTNERSHIPS

ACADEMIA

CONSUMER TRUST

GOVERNMENT /REGULATORS

INDUSTRY
CONCLUDING REMARKS

• Toxicological risk based approaches are critical for establishing acceptable levels of food additives and ingredients in foods and beverages
  - Established in international regulations and CODEX

• Toxicology and risk assessment science is evolving rapidly.
  - Toxicology in the 21st Century (TT21C)
  - Next Generation Risk Assessment Approaches (NGRA)
  - Opportunity for India to engage in this evolution

• Stakeholder partnerships involving academia, industry and regulatory authorities are needed
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