SAFETY EVALUATION OF FOODS: NOVEL INGREDIENTS & ADDITIVES

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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.
OUTLINE

• Challenges for India
• Risk based approaches
• Food toxicology safety assessment
  - chemicals in food
  - conventional approach
• Challenges/ new approaches in toxicology
• Conclusions
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ISSUES IMPACTING FOOD SAFETY

Global

- Changing food habits - convenience
- Increased food processing
- Globalisation of food trade
- Depletion of resources
- Climate change

India

- Good agricultural practice not fully adopted
- High population density
Countries Producing Most Food:
#1 China
#2 India
#3 USA
#4 Brazil
#5 Russia

Largest Food Exporters:
#1 US $149Bn
#2 Netherlands $93Bn
#6 China $63 Bn
#12 India $37 Bn

• India accounts for <1.5% of international food trade
• India has the highest number of Food industry plants approved by USFDA outside USA
• Vast opportunity for India
NATIONAL FOOD SAFETY AGENDA

Challenges

• Balancing food availability/ access and food safety

• Legislation and enforcement – enabling innovations to ensure
  • Consumers access safe wholesome food
  • Food waste is stopped

• Data gaps on food safety information

• Lack of expertise

Acknowledgement: Sanjiv Mehta, HUL CEO
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Priorities

- Risk based thinking
  - Pragmatic science based regs without compromising health
- Hygiene promotion
  - Reduce the burden of food-borne illness
- Consumer engagement
  - Informed consumers critical to food safety
- Stakeholder partnerships
  - Jointly build trust; capacity building; shaping national food safety agenda

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EATING FOOD CAN BE DANGEROUS!
(but not as dangerous as not eating)

Nutrients & Energy

• Food provides nutrients & energy for growth & activity
• Eating is enjoyable
• But, is a source of microbes & chemicals (Hazards)

Preservation/cooking → kill bugs

Add chemicals to kill/ prevent microbial growth

Preservation
- Chemicals (e.g. benzoate, sorbate, nitrite)
- Processes (curing, smoking)
- Environment (low water activity, low pH)

Cooking
- Can improve taste/flavour, but introduces chemicals (toxic, mut., or carc.)

• Important to tackle the microbial burden
HAZARD VERSUS RISK

**Hazard:** Biological, chemical or physical agent in, or condition of, food with potential to cause an adverse health effect

**Risk:** A function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard(s) in food.

\[
\text{Risk} = f (\text{Hazard} \times \text{Exposure})
\]

Low Risk \rightarrow High Risk

Risk = f (Hazard x Exposure)
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**

<table>
<thead>
<tr>
<th>Hazard based</th>
<th>Risk based</th>
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<tbody>
<tr>
<td>• Check-list compliance</td>
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<tr>
<td>• Unnecessary testing</td>
<td></td>
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<td>• Doesn’t consider how product is used</td>
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<td>• Yes / No decisions</td>
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<td>• Overly conservative</td>
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<td>• Expertise- &amp; evidence-driven</td>
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<tr>
<td>• Essential testing only</td>
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<tr>
<td>• Product use / exposure determines outcome</td>
<td></td>
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<tr>
<td>• Options to manage risks</td>
<td></td>
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<tr>
<td>• Uncertainties explicit</td>
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</tbody>
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**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**
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CHEMICALS IN FOOD

**Naturally occurring**
- Food constituents e.g. carbs, fats, protein, vits, minerals
- Natural toxins e.g. lectins, tetrodotoxin, cyanogenic glycosides, caffeine, cocaine, aflatoxin
- Other chemicals e.g. isoflavones, fragrances

**Intentionally added to food**
- 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

**Unintentionally added to food (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
**REGULATED FOOD CHEMICALS**

### Food Additives
- Added intentionally to foodstuffs to perform certain technological functions e.g. colour, sweeten, preserve.
- Identified in EU by E-number
- Regulators set safe levels for potential life-time use – ADI\(^1\)

### Novel Foods
- A type of food that does not have a significant history of human consumption* or is produced by a method that has not previously been used for food.
- Regulators establish that it is safe or at least as safe as the food it replaces

### Contaminants
- Not intentionally added to food, but may be present as a result of the production process, packaging, transport, or environment.
- Regulations to minimise contaminants in foodstuffs and reduce impact to human health.
- Establish TDI\(^2\)

### Supplements (vitamins/ minerals)
- Products taken by mouth that contain a dietary ingredient (e.g. vitamins, minerals, amino acids, botanicals) that can be used to supplement the diet.
- Safety and health claims

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\(^1\) ADI = acceptable daily intake; \(^2\) TDI = tolerable daily intake

* In EU relates to significant consumption before 15 May 1997
CHEMICALS IN FOOD

• The diet contains a diverse range of thousands of chemicals (naturally occurring; intentionally added; unintentionally added/ contaminants)

• Human consumes 30 tons of food during a lifetime
  - a lot of chemicals for the body to process!

• Substances found in food might be harmful to those who consume sufficient quantities of the food containing such substances.

• Understanding the chemical composition is fundamental to safety assessment

• Use scientific evidence-based risk assessment approaches in the development of safe food products, where both the hazard and the exposure are considered
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. Hazard Identification
2. Hazard Characterisation
3. Exposure Assessment
4. Risk Characterisation
CONVENTIONAL RISK ASSESSMENT APPROACH

\[ \text{ADI}^* = \frac{\text{NOAEL}}{100} \]

Exposure < ADI  😊
Exposure > ADI  😞

* Acceptable Daily Intake

Hazard characterisation

Safe dose in humans

Exposure < ADI
Exposure > ADI

Safety/uncertainty factors

Species extrapolation

Species differences

Human variability

Genetics

Demographics
Whole Foods

- Macro components of the diet
- Complex mixture of different chemicals
- Toxicological testing is more difficult - 100-fold safety factors often cannot be achieved.

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\(^1\) 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 STUDIES: PLANT STEROLS
- NOVEL FOOD IN EU

Plant Sterols – blood cholesterol lowering
  • Natural components of diet;
  • Lowers blood cholesterol by blocking absorption

Risk assessment
  • Extensive safety package – all studies published
    • ADME, genotoxicity, sub-chronic rat feeding study, reproduction studies
    • Extensive clinical studies

• Standard risk assessment
  • NOAEL = 3900mg/kg BW/day; ADI = 130mg/kg BW/day

• Risk assessment supported by
  • History of safe Use
  • Post Launch Monitoring
CASE STUDIES: 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, 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)
CASE STUDIES: 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)

➡️ Unilever has developed a HoSU scoring tool

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
  • Threshold of toxicological concern
  • Post Launch Monitoring
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20TH CENTURY TOXICOLOGY

Animal testing

• Increase in animal numbers - 1950s onwards
• Testing guidelines e.g. OECD, US FDA Redbook
• Inbred animal strains
• Animal diets
• Good laboratory Practice (GLP)

Risk Assessment

• Benchmark dose
• Physiologically based kinetic modelling
• Threshold of toxicological concern
• Margins of exposure
• History of safe use
• Post market monitoring

Regulations

• US Pure Food & Drug Act (1906)
• US Food, Drug & Cosmetic Act (1938)
• Food Additive Amendment (1958) – GRAS, Delaney Clause
• Colour Additive Amendment (1960)
• Since 1970 -FDA review of GRAS substances
• Novel foods regulations (e.g. EU 1997)
THE WORLD IS CHANGING

Rapid advances in scientific knowledge e.g. genomics, exposure science

Huge Technological advances e.g. HTS, informatics, computational toxicology

Speed of innovation creating novel materials e.g. nano, biotechnology

Scientific value of animal studies being challenged

Consumer demands to stop animal testing

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”
IMPORTANT TO COLLABORATE & FORM STAKEHOLDER PARTNERSHIPS
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CONCLUDING REMARKS

• Risk based approaches are critical for establishing acceptable levels of food additives and ingredients in decision making
  - Established in international regulations and CODEX

• Toxicology and risk assessment science is evolving rapidly.
  - Opportunity for India to engage in this evolution

• Priorities for the India national food safety agenda
  - Risk based thinking
  - Stakeholder partnerships