# 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

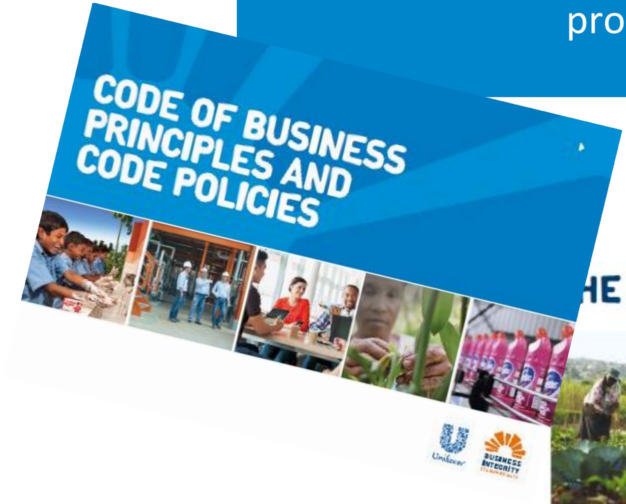
### SHARING SCIENCE

**COLLABORATION**

We partner with leading scientists from around the globe

# UNILEVER'S SAFETY GOVERNANCE

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
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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

# FOOD INDUSTRY IN INDIA

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

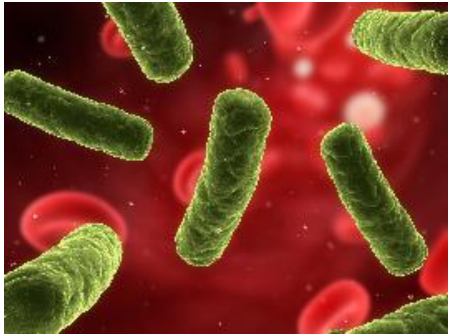
Add chemicals to kill/ prevent microbial growth

**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.


**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

## Hazard based

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

Precautionary approach
Zero tolerance policies

## Risk based

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

Hazard – What can go wrong?
Probability – How likely is 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

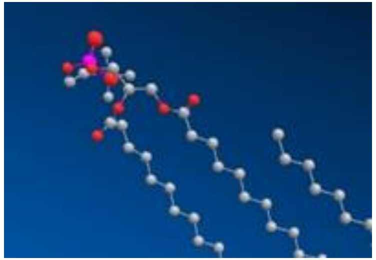
## Food Additives

- 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

[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**

1. Hazard Identification

2. Hazard Characterisation

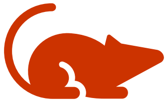
3. Exposure Assessment

4. Risk Characterisation

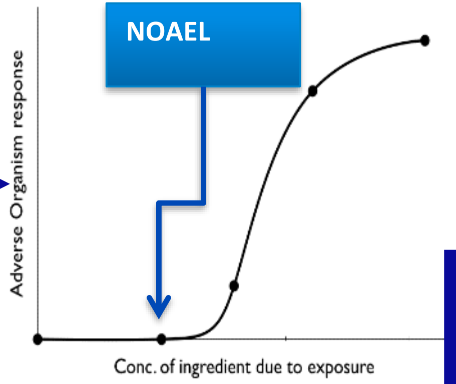
Exposure

**Ingestion**:
-Food & drink

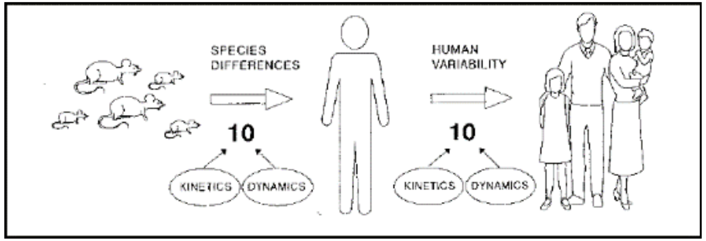
# CONVENTIONAL RISK ASSESSMENT APPROACH



Hazard characterisation

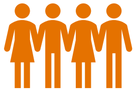



species extrapolation




Safety/uncertainty factors

Safe dose in humans



ADI* = NOAEL ÷ 100

Exposure < ADI ☺

Exposure > ADI ☹

* Acceptable Daily Intake

# WHOLE FOOD/ COMPLEX MIXTURE

## 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.

## 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

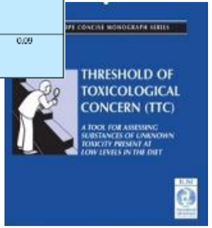
"Significant human consumption of food (over several generations and in a large diverse population) for which there exists adequate toxicological and allergenicity data to provide reasonable certainty that no harm will result from the consumption of the food"
Health Canada

<u>Safety assessment</u> (Constable et al, 2007)

- Characterisation
- Details of use
- Previous human exposure
- Health effects
- Potential hazards

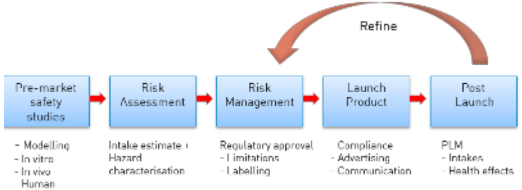
## Threshold of Toxicological Concern (TTC)

| CATEGORY | | DESCRIPTION | TTC (mg/person/day) |
|---|---|---|---|
| Cramer Class I | Low toxicity | Substances with simple structures for which efficient modes of detoxification exist in our body | 1.8 |
| Cramer Class II | Moderate toxicity | Substances that are less innocuous than in Class I, but do not contain structural features suggestive of toxicity like those in Class III. | 0.54 |
| Cramer Class III | High toxicity | Substances suggesting significant toxicity or containing reactive functional groups | 0.09 |




- 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

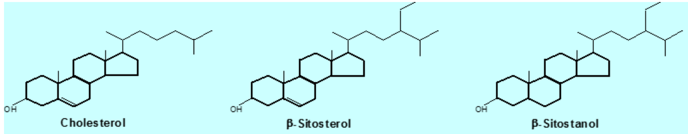
- Natural components of diet;
- Lowers blood cholesterol by blocking absorption

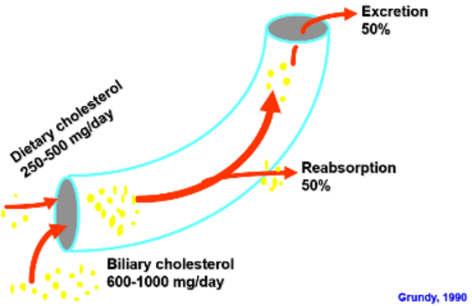
**Risk assessment**

- 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




FLORA pro-activ

# 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, specificatio 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**

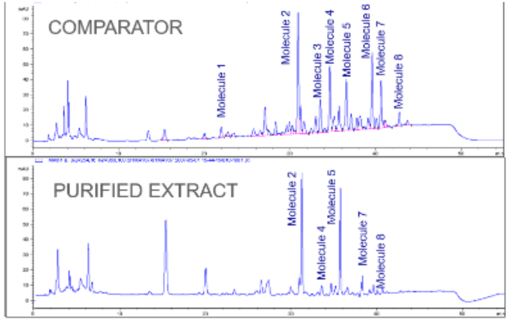
### Evidence of Concern - Hazard

- **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

Neely *et al* (2011). A multi-criteria decision analysis model to assess the safety of botanicals utilizing data on history of use. Tox. Int. 18 S20-9

**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
  - Threshold of toxicological concern
  - Post Launch Monitoring

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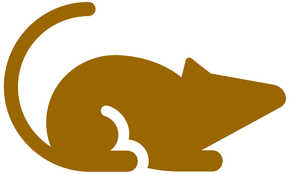
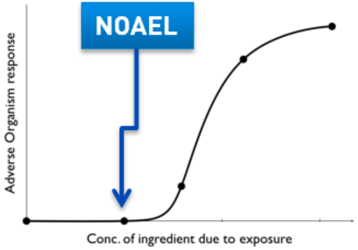
# 20$^{TH}$ CENTURY TOXICOLOGY

## Animal testing



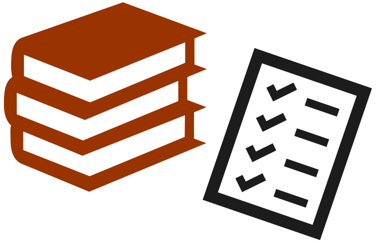
- Increase in animal numbers - 1950s onwards
- Testing guidelines e.g. OECD, US FDA Redbook
- Inbred animal strains
- Animal diets
- Good laboratory Practice (GLP)

## Risk Assessment




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

## Regulations

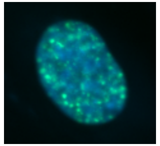


- US Pure Food & Drug Act (1906)
- US Food, Drug & Cosmetic Act (1938)
- Food Additive Amendment (1958) – GRAS, Delaney Clause
- Colour Additive Amendment (1960)
- Since 1970 -FDA review of GRAS substances
- Novel foods regulations (e.g. EU 1997)

# 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

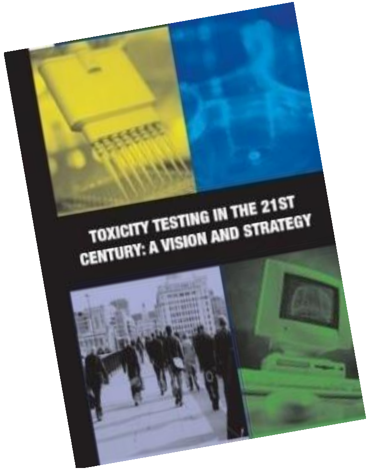
Scientific value of animal studies being challenged

Consumer demands to stop animal testing

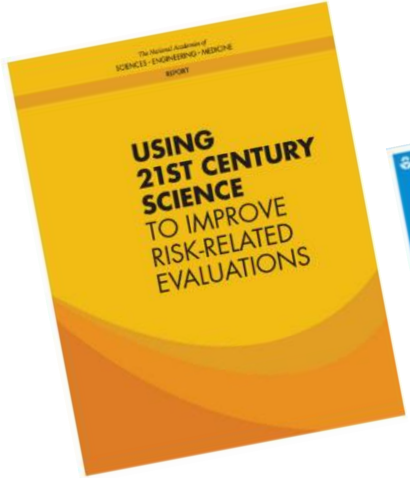
Too many chemicals – not enough animals/money/time !

# TOXICITY TESTING IN THE 21ST CENTURY (TT21C)

**2007**




**2017**





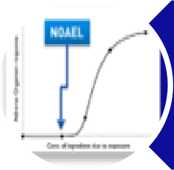
"Advances in toxicogenomics, bioinformatics, systems biology, epigenetics, and computational toxicology could transform toxicity testing from a system based on whole-animal testing to one founded primarily on *in vitro* methods that evaluate changes in biologic processes using cells, cell lines, or cellular 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

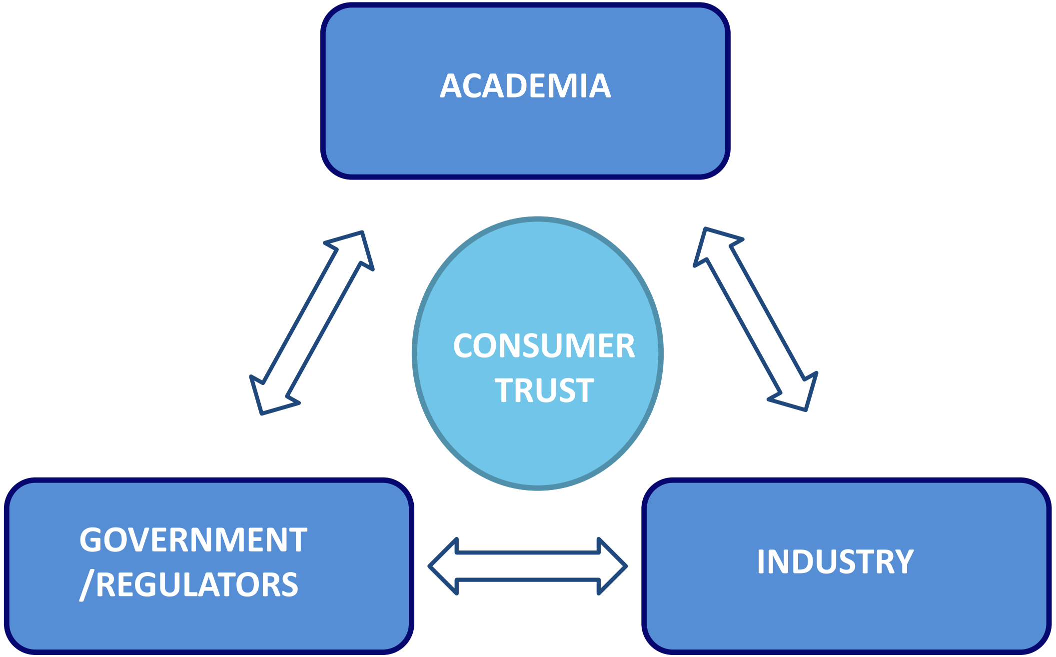
- Skill sets may be different to traditional approaches

Need regulatory frameworks to accommodate next generation approaches

- “regulatory acceptance”

# IMPORTANT TO COLLABORATE & FORM STAKEHOLDER PARTNERSHIPS

Unilever




CHIFSS
CII-HUL Initiative on Food Safety Sciences

ILSI
International Life Sciences Institute

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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

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