HISTORY OF SAFE USE: APPLICATION IN NOVEL FOOD SAFETY ASSESSMENT

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WHAT IS A NOVEL FOOD?

- EU Regulation on Novel Foods, (EC) No. 258/97
- Approval required if the food was not used for human consumption in the European Community before 15 may 1997
- Novel foods fall into the following categories:
  - new or intentionally modified primary molecular structure;
  - consisting of, or isolated from, micro-organisms, fungi or algae;
  - consisting of, or isolated from plants, or food ingredients isolated from animals except for those obtained by traditional propagating or breeding practices, and having a history of safe food use; or
  - has been applied a production process not currently used, resulting in significant changes in the composition/structure which affect their nutritional value, metabolism or level of undesirable substances
- If substantially equivalent to existing foods with a history of safe use, then a simplified notification procedure can be used

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EU REGULATORY UPDATE

- Proposal for a new Novel Foods Regulation is under consideration
- The Common Position of the Council makes new provisions for ‘traditional foods from third countries’:
  - "traditional food from a third country" means novel food,…, derived from primary production, with a history of food use in any third country, such that the food in question has been and continues to be part of the customary diet for at least 25 years in a large part of the population of the country
  - "history of safe food use in a third country" means that the safety of the food in question is confirmed with compositional data and from experience of use and continued use for at least 25 years in the customary diet of a large part of the population of a country.
- The information requirements in support of such traditional foods include:
  - documented data demonstrating the history of safe food use in any third country
- The European Parliament Second Reading Vote scheduled for the w.c. 5th July, 2010

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HOSU IN NOVEL FOOD SAFETY ASSESSMENT

- ‘ a long history of use is a reassuring and practical starting point’ for the evaluating the safety of a Novel Food’ (OECD 1999)
- Can also apply to a ‘Conventional Counterpart’

- ‘a similar food or feed produced without the help of genetic modification and for which there is a well established history of safe use’

(GMOs: EU Regulation 1829/2003)

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HISTORY OF SAFE USE

?

- What does it mean ?
- Can it be better defined ?
- How can it be used in new product safety assessment?

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TRADITIONAL FOODS

- Few traditional foods have been subjected to standard toxicological tests to establish Acceptable Daily Intakes (ADI)
- Foods are complex and potential hazards do exist:
  - Inherent toxins
  - Nutrients
  - Anti-nutritional components
  - Bioactive compounds
  - Environmental contaminants

- Taking into account that:
  - 'Complete freedom from risks is an unattainable goal' FAO (1997)
- Must be managed so that :
  - 'Reasonable certainty of no harm results from consumption' CODEX (2001)

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EXPERIENCE

IDENTIFICATION

PROCESSING and PREPARATION

MODERATION

AVOIDANCE

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TRADITIONAL FOOD SAFETY

- Foods prepared and used in traditional ways (cultural practises) considered to be safe for the consuming population on basis of long-term human experience
-  NOT absolutely safe!
- A level of safety, subject to appropriate risk management procedures, which is regarded as ‘acceptable’ by consumers of traditional food
- HISTORY OF SAFE USE = ESTABLISHED SAFETY PROFILE

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EXAMPLES OF DEFINITIONS

- 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

- ‘the qualified presumption of safety making the food generally recognised as safe in the community’
  - TEMANORD 2005

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CHARACTERISATION

- Correct identification
- Biology (origin, genetic diversity)
- Geographic/demographic distribution
- Composition:
  - Proximate analysis
  - Nutritional profiles
  - Chemical hazards (toxicants, allergens, heavy metals)
  - Bioactive compounds
- Chemical identity, potential impurities arising from manufacture

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EVIDENCE OF PREVIOUS HUMAN CONSUMPTION

- Significant human consumption
- Several generations
- Diverse population
- Genetic backgrounds and age groups

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DETAILS OF USE

- How is the food prepared for human consumption?
- Preparation and processing:
  - Fermentation, soaking, peeling, cooking
- Purpose:
  - Food, ingredient, supplement, pharmaceutical
- Pattern of consumption:
  - Regular, occasional, co-administration
- Intake:
  - Levels, means, extremes
  - Populations exposed
- Known limitations of use:
  - Specific processing for specific uses/populations
  - Cultural practice

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HEALTH EFFECTS

- Evidence from human exposure
  - Known adverse effects
  - Case reports – toxicity, allergenicity, intolerance
  - Known precautions
  - Over-consumption
  - Mis-use
  - Specific sub-populations

- Potential Hazards
  - Toxicity data, details of known natural toxicants
  - Nutritional data, known anti-nutritional factors
  - Allergens
  - Known health compromising contaminants
  - Bioactive compounds e.g. phytoestrogens
  - Metabolic / gastrointestinal effects

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HISTORY OF SAFE USE

- A body of knowledge on which to establish the existing safety profile of a food, with known limitations.

- Sources of information – Robust and reliable
  - Peer reviewed scientific publications, government documents, scientific expert opinions
- Non-scientific, anecdotal data

- Collect information on:
  - the food on which we want to establish History of Safe Use
  - and the new food under evaluation where that is a different food, e.g. GMO

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NOVEL FOOD SAFETY ASSESSMENT

NEW FOOD

RAW MATERIAL
PROCESSING
MANUFACTURE
+
CHARACTERISATION
+
EXPECTED USE/
ESTIMATED INTAKE

COMPARITOR / REFERENCE

History of Safe Use

(established safety profile under conditions of use)

⇔

↓

≈

'As safe as'
Limitations identified +
can be managed ?

≠

Differences:
Assess health consequences

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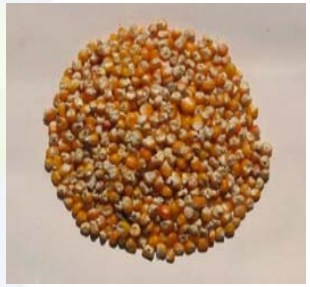
EXAMPLE: GM

- GA21 Maize : modified 5-enolpyruvyl-shikimate-3-phosphate gene (5-EPSP) resulting in tolerance to herbicide glyphosate
- Comparator : Conventional Maize - long history of safe use
- Assessment compared
  - Growth criteria ≈
  - Phenotypic characteristics ≈
  - Yield ≈
  - Chemical composition ≈
  - Nutritional profile ≈
  - Derived products ≈
- Focus on EPSPS protein
  - Toxicity studies
  - Allergenicity studies
- Glyphosate tolerant maize ‘As safe as’ maize and derived products from conventional varieties
- (SCF 2002)



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EXAMPLE: FOOD (1)

- Noni juice

- *Morinda citrifolia L*
- Polynesia, S.E. Asia
- Marketed in US and elsewhere
- No untoward reactions noted
- Additional info provided:
  - Absence of anthraquinones
  - Sub-acute, Sub-chronic
  - Genotoxicity
  - Allergenicity

- Acceptable at observed intake (30 ml) (SCF 2002)

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EXAMPLE: FOOD (2)

- Chia seeds : ingredient in bread (5%), source of omega-3 FAs

- Salvia hispanica L
- Pre-Columbian civilisations
- Roast, ground – porridge/drink
- Insufficient 'history of safe use' in modern society
- Incomplete information on:
  - Composition/bioavailability
  - Storage/processing
  - Possible allergen cross-reactivity?
  - Anti-nutritional/toxicity?
- Additional clarification required (EFSA 2005)
- This was provided subsequently (2009)

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EXAMPLE: FOOD (3)

Ngali nuts

- From the Nangai tree *Canarium indicum L*
- Native to Pacific
- Exported to Japan, Hawaii, Australia
- Consumption in Western Melanesia 70g/person/day
- 'History of safe' use in that region
- Unable to draw conclusions on consumer safety due to lack of information on:
  - Analytical procedures for nutritional composition
  - Extent of variation of data
  - No toxicity data
  - Possible allergenicity? (History of safe use of nuts?)

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EXAMPLE: FOOD (4)

Baobab fruit

- Fruit of the Baobab tree (*Adansonia digitalis*), also known as the 'upside down tree'
- Grown primarily in Southern African countries
- Submission via the UK in 2007based on:
  - Information on identity, harvesting, processing, composition, contaminants and projected exposure
  - Dried fruit pulp to be used as an ingredient in products such as smoothies and cereal bars
- Positive opinion to the Commission leading to authorisation in 2008.
- History of safe use with the above supporting information was sufficient to achieve authorisation

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EXAMPLE : CHANGE OF USE/EXTRACT

- Phytosterol esters – reduce serum cholesterol levels
- Extracted from edible oils, esterified with sunflower oil FAs
- Occur naturally in food - 0.5 – 4% in oils
- Pharmaceuticals, with good safety profile
- Incorporation into food products > significant increase in consumption (8-12 fold)
- Extensive toxicological testing
  - ADME
  - Toxicology studies
  - Human studies
- No safety concerns at use levels of 8% in fat spreads
  - Labelling – cholesterol medication
  - Children/pregnant women
- New products – notification as 'substantially equivalent'

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HISTORY OF SAFE USE: USA

- In the United States foods may be considered Generally Recognised as Safe (GRAS)
- GRAS status was first applied to foods in 'common use' prior to January 1, 1958
- 'Common use in food' is defined as 'substantial history of consumption of a substance for food use by a significant number of consumers
- Food not in common use before January 1958 may achieve GRAS status through scientific procedures

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HISTORY OF SAFE USE: CANADA

- Novel foods are regulated by Division 28 of Part B of the Canadian Food and Drugs Regulations
- 'novel food means
  - (a) a substance, including a micro-organism, that does not have a history of safe use as a food
- Within the information required in a notification:
  - (c) (v) information respecting its history of use as a food in a country other than Canada, if applicable, and
- History of Safe Use may be a determinant of novelty or supporting information, depending on the circumstances

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HISTORY OF SAFE USE: FSANZ

- Since 1999 Food Standards Australia New Zealand (FSANZ) regulates novel foods through Standard 1.5.1 of the Food Standards Code
- Foods are classified as either 'traditional' or 'non-traditional'
- 'Non-traditional food' means a food which does not have a history of significant human consumption by the broad community in Australia and New Zealand.
- 'Novel food' means a non-traditional food for which there is insufficient knowledge in the broad community to enable safe use in the form or context in which it is presented,
- The determination of novelty thus depends on whether or not there is a history of safe use.

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CONCLUSIONS

- History of Safe Use is:
  - A body of knowledge accumulated from the use and experience of a food within its cultural context and conditions of use
  - A description of its safety profile
- A good description of History of Safe Use can be used:
  - As a STARTING point in the safety assessment of a new product
  - To choose an appropriate reference material
  - Highlight knowledge gaps and focus further testing
  - Facilitate the regulatory status?
- Caution:
  - May require intensive research/generation of data
  - Must consider the NF as consumed: quality and quantity

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ILSI EUROPE NOVEL FOODS TASK FORCE (2007)

- INDUSTRY MEMBERS
  - Bayer Crop Science
  - Coca-Cola European Union Group
  - DSM
  - Groupe Danone
  - McNeil Nutritionals
  - Nestlé
  - Südzucker
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ILSI EUROPE: HOSU PUBLICATION

- **'History of safe use as applied to the safety assessment of novel foods and foods derived from genetically modified organisms'.**
- Constable A., Jonas D., Cockburn A., Davi A., Edwards G., Hepburn P., Herouet-Guicheney C., Knowles M., Moseley B., Oberdörfer R., Samuels F (2007).
- *Food and Chemical Toxicology,* 45(12): 2513-2525

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