APPROACHES TO SAFETY
ASSESSMENT OF LOW AND NON-CALORIFIC SWEETENERS – GLOBAL PERSPECTIVES AND REGULATORY DEVELOPMENT STATUS

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Outline of the presentation
1. Current and Future Challenges – Globalisation
2. The Standards Setting Process
3. Risk Assessment & Risk Management
4. Food Additives
   - Regulation
   - Risk Assessments
4. Additive Case Studies
   - advantame
   - cyclamates
   - Benzoates
5. Summary

Future Challenges

Food Supply Local
Global Food Supply
An Era of Globalization

- Changes in Global Food Industry -

- The structure of the global food industry is continually changing and evolving
  - Mergers, acquisitions, consolidations
  - Expansion into foreign markets
  - Strategic partnerships – Countries/regions (e.g. Asia/Pacific) are negotiating multilateral Free Trade Agreements (APEC, TPP); bilateral agreements between countries are becoming more commonplace (e.g. Australia New Zealand Trans Tasman Mutual Recognition Agreement (TTMRA) for supply of specific food commodities.
Changes in Global Economy

- **Global Economy**
  - The **VOLUME** of foods and ingredients in international trade is ever increasing
  - The **TYPES** of foods and ingredients
    - 1980’s – primary grains and oilseeds
    - Today – processed foods, ingredients, food additives, processing aids, divergent food sources, food travelling for longer distances, food monopolies, changing diets and eating patterns (e.g. eating out)

Globalisation

- **Changing Food Supply**
- **Increasing reliance on imports**
- **Climate change**
  - Changes in manufacturing, production
- **Ethnic diversity**
  - Changes
  - Demographics
  - More “at-risk” consumers
- **Changes in eating patterns**
  - Increased choice

Food Health Risks Changing….

- **Classic Risk Factors**
  - Microbiological
  - Chemical – heavy metals, agricultural chemicals
  - Physical
  - Unknown (e.g. natural toxins)

- **Other Risk Factors**
  - New technologies
  - Changing nutrient profiles
  - Novel foods / functional foods
  - Increased reliance on food additives
  - Allergenic foods
  - Food intolerances
  - Demographics
  - Changing scientific methodologies in hazard assessment and risk assessment – need to update knowledge

More Opportunity for things to go wrong
Traditional Food Safety Concerns

- Microbiological
  - Salmonella spp.
  - Clostridium botulinum
  - Staphylococcus aureus
  - Clostridium perfringens
- Chemical
  - Heavy metals
  - Pesticides and agricultural chemicals
  - Food additives
- Physical
  - “Filth”
  - Foreign objects

Today’s Food Safety Issues

1975-1995
- Campylobacter jejuni
- Clostridium botulinum (infant)
- E. coli O157:H7
- E. coli O104:H4
- Listeria monocytogenes
- Salmonella Enteritidis
- Vibrio cholerae (Latin America)
- Vibrio vulnificus Yersinia enterocolitica
- Norwalk and Norwalk-like viruses
- Rotavirus
- Hepatitis A

Cryptosporidium parvum
Giardia lambia
Toxoplasma gondii
Bovine spongiform encephalopathy
Prion
Melamine
Acrylamide
Bisphenol A
Pthalates
Economically motivated adulterants — e.g. Sibutramine, Viagra in coffee, Phenolphthalein, Nanochemical safety
Etc.

Changes in Scientific Knowledge

- Greater understanding of foodborne pathogens
- More and better analysis and detection methods – ppb, ppt, ppqd!!
- Creating new issues re safe but non compliant for many low level chemicals e.g. BPA, ag/vet chemicals
- Processing technology
  - Aseptic
  - High pressure
  - Nanotechnology
  - Irradiation

Challenges for Responding to Food Safety Issues

- Short timeframes to respond
- Inadequate/incomplete data
- Uncertainties in data
- Perceptions and Communication
- Differing food standards across regions – lack of harmonization and trade disruption
- Differing approaches to risk assessment and risk management – lack of convergence and trade disruption
- Legal liabilities
- Political sensitivity
BUT more opportunities and more need to harmonise risk assessments and food standards across world!!

Opportunities to Harmonise Food Standards

- International
  - Codex – CCFA, CCFC, CCFH, CCPR etc
  - FAO/WHO JECFA, JMPR
  - WTO/SPS/TBT

- Regional
  - ASEAN, APEC FSCF
  - Multilateral and bilateral agreements – ANZ TTMRA, FTAs, TPP

Australian System

- Federal system
- Comprises Commonwealth Government,
- 6 States, and
- 2 Territories
- > local Government Authorities
FSANZ is a bi-national, independent, expertise-based statutory authority that develops food standards.

Food Standards Australia New Zealand (FSANZ)

Australia New Zealand Food Standards Code

- Chapter 1: General Food Standards
- Chapter 2: Food Product Standards
- Chapter 3: Food Safety Standards (Australia only)
- Chapter 4: Primary Production Standards (Australia only)

Who Does What?

- Standards setting: FSANZ
- Enforcement: States/Territories, Local government, Australian government (at border)
- Policy: Ministerial Council (States/Territories) (health/agriculture portfolios), FSANZ Act

Standards Setting Process

- Science and evidence based
- Consultative
- Regulatory Impact Statement
- Codex standards
- Based on Codex risk analysis model
- Other FSANZ responsibilities
**Codex Risk Analysis Paradigm**

- **Risk Assessment**
  - Science based
  - Identification of the hazard associated with the chemical
  - Hazard identification
  - Hazard characterisation
  - Dietary exposure

- **Risk Management**
  - Policy based
  - Risk characterisation

- **Risk Communication**
  - Interactive exchange of information & opinions concerning risks
  - Dialogue with all stakeholders

**Risk assessment at FSANZ**
- Chemical
- Microbiological
- Nutritional
- Novel foods, including GM
- Physical agents

**Risk Assessment: Elements**

1. **Hazard identification**
   - Identification of the hazard associated with the chemical

2. **Hazard characterisation**
   - Dose-response relationship

3. **Dietary exposure**
   - Estimate of intake of chemical

4. **Risk characterisation**
   - Probability of an adverse health effect

**Risk Management approach**

**Definition**
A consultative and decision-making process that identifies the problem; considers the risk assessment, social, economic and other factors; and develops, weighs and selects the option of greatest net benefit to the community. The process may also evaluate the implemented decision.
Principles of risk management

To ensure that FSANZ’s risk management measures are commensurate/proportionate to the risk to public health and safety, appropriate and ‘fit for purpose’:
- decisions are objective and transparent, including the associated uncertainties.
- effectively address the risk identified by the assessment process.
- decisions are independent and functionally separated from those providing advice.

Risk management – factors to consider

Consideration of policy options taking into account a number of factors, including:
- Scientific risk assessment & uncertainties
- Political, Economic, Social and Technological
- Cost-benefit/RIS
- WTO obligations (particularly the SPS agreement)
- Practicality – can the measure be implemented & enforced?

Food Additives – General Requirements

- A substance not normally consumed as a food or used as an ingredient of food, but intentionally added to a food to achieve a technological function (sweetener, emulsifier etc).
- Food additive or its by-products may remain in the food
- Pre-market approval required for new food additives

Approval of Food Additives

For food additives to be approved, it must be established that:
1. it must not pose an unacceptable risk to health when used in amounts up to the approved limits even after a lifetime of consumption
2. there is a technological need and it will provide a benefit to consumers
3. it will only be used up to a level commensurate with the function that the additive performs in food.
Typical Risk Assessment Questions

- What is the short- and long-term toxicity of the additive?
- What is the level of exposure to the additive?
- Is there a potential public health problem?

Regulation of Food Additives

- Pre-market safety assessment for new food additives
- Extensive animal toxicology data required
- Human toleration studies in some cases
- Dietary exposure assessment for all population groups
- Permissions of use based on potential to exceed the acceptable daily intake (ADI).

Risk Characterisation Outcomes

- Estimation of risk
- Identification of at-risk (sensitive) populations
  - e.g. children, elderly, pregnant women
- Uncertainties in the assessment

Risk management options

- Status quo
  - No change
- Non-legal or voluntary options for industry
  - Codes of Practice/QA programs/guidelines
- Non-legal or voluntary options targeted at consumers
  - Education/information/guidance
- Legal requirements
  - Requirements of existing Standards or Codes
Maximum Permitted Level

• The maximum amount of additive which may be present in the food as set out in relation to that food in Schedule 1 – risk management/trigger level

• Processed food means food which has undergone any treatment resulting in a substantial change in the original state of the food

Standard 1.3.1 – Similar to Codex GFSA

• Schedule 1 – Permitted uses of food additives by food type
• Schedule 2 – Miscellaneous additives permitted to GMP in processed foods specified in Schedule 1
• Schedule 3 – Colours permitted to GMP in processed food specified in Schedule 1
• Schedule 4 – Colours permitted to specified levels in processed foods specified in Schedule 1
• Schedule 5 – Technological functions which may be performed by food additives

Technological Function

• Means a function set out in Schedule 5 but harmonized with Codex GFSA as much as possible:
  • E.g. Acidity regulator - Alters or controls the acidity or alkalinity of a food - acid, alkali, base, buffer, buffering agent, pH adjusting agent
  • Flavouring
  • Sweetener
  • Colour
  • Preservative
  • Other

LOW AND NON-CALORIFIC SWEETENERS
Requirements for use of sweeteners ANZ FSC

Editorial note:

In general, the use of intense sweeteners is limited to:

1. foods meeting the definition of ‘reduced joule’ or ‘low joule’;
2. ‘no added sugars’ food e.g. artificially sweetened canned fruit without added sugar; or
3. specific foods in which the use of the sweetener is in addition to sugar rather than as an alternative e.g. chewing gum, brewed soft drink (these foods are listed in Schedule 1 on a case-by-case basis).

Save where otherwise expressly stated in Schedule 1 and not withstanding any specific level specified in a Schedule to this Standard, intense sweeteners may only be added to food in an amount necessary to replace the sweetness normally provided by sugars or as a flavour enhancer.

- Conditions relating to the use of reduced/low joule and no added sugar claims can be found in Standard 1.2.8 or in ANZFA’s Code of Practice on Nutrient Claims in Food Labels and in Advertisements (Commonwealth of Australia, AGPS 1995).
- Polyols, isomalt and polydextrose may be considered to be food additives when used as humectants and texturisers. Where these substances constitute a significant part of the final food they would be regarded as a food in their own right rather than food additives. Polyols, isomalt and polydextrose are not considered to be bulking agents if used in large amounts to replace sugars as they may contribute significantly to the available energy of the food.

Sweeteners – permissions in FSC

Sweeteners – permissions in FSC

Additives in Schedule 1

11.4. Tabletop sweeteners*

916 Maltol GMP
917 Ethyl maltol GMP
920 Glycyrrhizin GMP
921 Stevioside GMP
922 Cyclamate GMP
923 Azorvatin GMP
924 Aspartame GMP
925 Aspartame-acesulphame salt GMP
926 Steviol glycosides GMP
927 Polyvinylpyrrolidone GMP

11.4.1 Tabletop sweeteners – liquid preparation*

210 211 212 213 Sorbic acid and sodium, potassium and calcium sorbates GMP
230 231 232 233 Benzoic acid and sodium, potassium and calcium benzoates GMP
954 Saccharin GMP

11.4.2 Tabletop sweeteners – tablets or powder or granules packed in portion sized packages*

930 Saccharin GMP

14.1.3.1 Brewed soft drink*p

[Values for specific sweeteners like Aspartame, Saccharin, etc. with their respective limits are provided here.]
**Codex Committee on Food Additives (CCFA)**

**General Standard for Food Additives (GFSA) Food Additive Tables**
- ~ 300 additives assigned JECFA ADIs
- 125 Additives with Numeric or “Acceptable” ADIs – includes saccharin, sucralose, cynamates, aspartame, neotame, alitame and advantame
- 185 Additives ADI “Not Specified”
- 3770 Adopted Provisions
- For sweeteners, there are currently 459 adopted provisions, and 235 provisions in the step procedure.
- there are 25 sweeteners in the current GSFA.

The Codex process relies on a science – based approach but also takes into account “other legitimate factors”

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**Case study – advantame**

<table>
<thead>
<tr>
<th>Problem</th>
<th>New sweetener for use in energy reduced foods and drinks (20,000X) sweeter than sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Issue</td>
<td>First assessment in world – undertaken by FSANZ</td>
</tr>
<tr>
<td>Uses</td>
<td>Table top sugar substitutes (powdered only) and a range of powdered beverages including fruit flavoured drinks, milks and flavoured milk drinks, instant tea and coffee, and protein drinks.</td>
</tr>
<tr>
<td>Studies</td>
<td>Range of toxicological studies</td>
</tr>
<tr>
<td>Exposure</td>
<td>Applicant provided data to estimate the maximum levels of Advantame likely to be used as a sugar replacement in a range of common food products.</td>
</tr>
</tbody>
</table>

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**Advantame**

- Is Advantame: 
  - proposed to be added in a quantity and form which is consistent with achieving the stated purpose and technological functions (policy guideline)?
- Is there a need to establish a reference health standard for Advantame in order to protect public health and safety?
- If Advantame enters the food supply, would the resulting exposure pose an unacceptable risk for public health and safety for any consumer group?

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**What studies did we use**

- Independently evaluated the submitted toxicity studies on Advantame: 
  - including studies on kinetics, metabolism, acute toxicity, repeat-dose toxicity, genotoxicity, immunotoxicity, reproductive toxicity and developmental toxicity. Four human studies were also evaluated.
- Set an acceptable daily intake (ADI) of 5 mg/kg bw/day
- Well tolerated in human studies (including diabetics)
**Management**

- There was no specific risk that needed to be managed by setting a maximum permitted level in foods

- Schedule 2 (Good Manufacturing Practice permissions)

- General labelling: declared in the ingredient list by its class name ‘sweetener’ followed by its specific name ‘Advantame’

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**Case study – cyclamates**

<table>
<thead>
<tr>
<th>Problem</th>
<th>Soft drinks commonly consumed by children have high levels of cyclamates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Issue</td>
<td>Estimated dietary exposure for children aged 2-11 years exceeded ADI for cyclamate from a survey</td>
</tr>
<tr>
<td>Risk</td>
<td>Testicular atrophy in male rats – not known if applies to humans?</td>
</tr>
<tr>
<td>Solution</td>
<td>Discussions with industry to reduce use levels for soft drinks from 600 mg/kg to 350 mg/kg</td>
</tr>
<tr>
<td>Outcome</td>
<td>Safer food supply, costs to food business to change practices, possible increase in product price</td>
</tr>
</tbody>
</table>
Approach

- Cyclamate approved for use in a range of foods with maximum limits in the Code
- JECFA ADI of 11 mg/kg bw/day (1982)
  - Conversion to cyclohexylamine (testicular atrophy in rats)
- A post-market survey of intense sweeteners (2004):
  - Exceedance of ADI for high consumers (children aged 2-11 years)

Dietary exposure assessment

- Focus on major contributing food: soft drinks (water based beverages)
- Dietary exposure assessments: a range of scenarios were modelled:
  - Maximum permitted limit (600 mg/kg)
  - Manufacturers use levels: 300, 350 and 400 mg/kg

Risk Management

- Discussions with industry:
  - 300 mg/kg cyclamate may affect product characteristics such as taste and product stability
  - 400 mg/kg: ADI still exceeded
  - Compromised to 350 mg/kg: reduced exposure<ADI and was achievable and agreed by industry

How Sweet it is …… Sweeteners and the Consumer

Risk Communication is complicated

1. Consumer perception issues regarding safety
   - Perception regarding hazard – all chemicals have an intrinsic hazard e.g. water
   - Perception regarding risk – Risk = Hazard x Exposure
   - Misinformation/wrong information

Paracelsus: THE DOSE MAKES THE POISON! NO EXPOSURE… NO RISK! LCNS only used at safe levels and exposure.
2. Consumer Values

- Some communities don’t like food additives – colours/sweeteners e.g. EU member states
- Mostly values driven reasons
- Dislike of artificial sweeteners – “unnatural”
- Different ethnic populations with different traditional approaches to food

**BUT NOT ALL NEGATIVE!**

- Increased realisation that sweeteners have a role in public health
  - Diabetes
  - Rising Obesity with enormous public health sequelae

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**How Sweet it is ….. Sweeteners and the Consumer**

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**Sweeteners – Artificial versus “Natural”**

‘Naturally sweetened Dr. Pepper’—along with its companions 7UP and Canada Dry—now boast ‘natural sugar and Stevia’.

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**EFSA completes full risk assessment on aspartame and concludes it is safe at current levels of exposure**

- Aspartame and its breakdown products are safe for human consumption at current levels of exposure, EFSA concludes in its first full risk assessment of this sweetener. To carry out its risk assessment, EFSA has undertaken a rigorous review of all available scientific research on aspartame and its breakdown products, including both animal and human studies.
- “This opinion represents one of the most comprehensive risk assessments of aspartame ever undertaken. It’s a step forward in strengthening consumer confidence in the scientific underpinning of the EU food safety system and the regulation of food additives”, said the Chair of EFSA’s Panel on Food Additives and Nutrient Sources Added to Foods (ANS Panel), Dr Alicja Mortensen.

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**Summary**

- The Codex Risk Analysis Framework underpins FSANZ’s Risk assessment and management
- Risk-based approach to assessment of food additives
  - Range of toxicology studies assessed
  - Dietary exposure assessment (level and expected consumption)
  - Characterise the risk
- Risk management tailored to the risk characterisation
  - e.g. Maximum limits for specific foods versus GMP permissions (Advantame, aspartame)
- Post-market surveillance can lead to a review of an additives permission
  - Example of cyclamate
Food laws…

Ensure Everything They Eat is Safe… for 90 years

Thank you