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The Application of Post-Market Monitoring to Novel Foods

An Expert Group Opinion,
ILSI Europe Novel Foods Task Force.

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International Life Sciences Institute

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- Scientific Platforms > Clusters > Task Forces
- Assessment of Benefits and Risks
- Novel Foods (and Nanotechnology) Task Force

Objective

- To review how novel foods, novel food ingredients and new processing techniques should be evaluated scientifically from the safety and nutritional viewpoints
  - Expert Groups
  - Workshops
  - Concise monographs
  - ILSI Reports
  - Publications

EU Novel Food regulation EC 258/97

- Approval required if not used for human consumption in the EU community before 15 may 1997 ***and*** 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

- Produced from GM sources (EC 1829/2003)

History of Safe Use = Established Safety Profile

- Foods prepared and used in traditional ways (cultural practises) considered to be safe for the consuming population on basis of long-term human experience
- A level of safety, subject to appropriate risk management procedures, which is regarded as ‘acceptable’ by consumers of traditional food

IDENTITY

PREPARATION

USE PATTERNS

AVOIDANCE

Characterisation + Details of Use + Human Exposure + Health Effects

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

Food and Chemical Toxicology 2007, 45: 2513-2525

Safety Assessment of (Novel) Foods : Case by Case

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- Analytical/compositional/ nutritional characteristics of the novel food
  - Source of material / Changes due to new processing
- Previous history of human exposure
  - Comparison to traditional counterpart (if available)
- Expected applications and the *predicted* exposure
  - Purpose
  - Food categories and Use levels (usually worst-case; over-estimates)
- Neccessity, appropriateness and outcome of safety studies
  - Fate in biological systems
  - Standard toxicology , feeding studies
  - Focused toxicity studies
  - Allergenicity
  - Human studies : focused effects, target populations, efficacy….

Intern J Food Sciences and Nutrition 2003, 54: 1-32

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Ultimate Aims

- Risk Assessment (- ADI?)
  - *f* (Hazard x Exposure)
- To inform Risk Management decisions and Risk Communication
  - Regulatory Approval (or not);
  - Conditions/ limitations,
  - labelling as conditions of approval?
- Ensure foods placed commercially on the market are safe for the consumer and do not present undue risk
- Safe for the intended uses and Compliant with legislation

Concept of Post-launch monitoring?

- No mandatory requirement
- '*PMM should, where appropriate, be performed for foods derived from genetically modified sources, specifically where there is no traditional comparator available*'. (EFSA, 2004, 2006)
- PMM data '*will provide additional reassurance regarding long term safety of products, as well as their impact on the food supply*' (FSANZ, 2005)
- Condition for approval of phytosterol esters in fat spreads in EU

  ' Establish a surveillance programme accompanying the marketing of the product …….. in order to estimate the extent to which the product is reaching its target group, … and to estimate exposures to phytosterols from this source in other population groups……'

  (Committee Decision 2000/500/EC)

Definitions

- Post Market Surveillance (PMS)
- Post Market Monitoring (PMM)
- Post Launch Monitoring (PLM)
- Pharmacovigilance for Drugs
- Cosmetovigilance for Cosmetics

- PMM : a hypothesis driven, scientific methodology for obtaining information through consumer investigations relevant to the safety of a novel food after market launch (ILSI 2008).

PMS for Medicines v PMM for Foods

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PMS Medicines

- Prescriptive
- Specific population
- Pharmacies
- Small patient base
- Medical condition
- Health professionals
- Clear dose , cause v effect

PMM Foods

- No controls
- General population
- Freely available
- Large consumer base
- Health status unknown
- Consumer carelines
- Causality?

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Case Study : Aspartame (additive, sweetener)

- Reason for PMM
  - Pre-market assessment : EDI (8.3 - 34 mg/kg bw/d) close to ADI (40 – 50 mg/kg bw/d)
  - Consumer reports of adverse health effects post-launch
- Methodologies
  - Intake assessment by household menu survey (market research)
  - Collection and evaluation of anecdotal reports by independant authority (CDC/FDA)
- Outcome
  - Intake confirmed to be within limits
  - Safety confirmed by additional targeted studies in humans and animals
  - No link between aspartame consumption and reported adverse events

Case Study : Olestra (fat replacer)

- Reasons for PMM
  - Confirmation of pre-market assumptions concerning intake and consumer nutritional status (fat soluble vitamins), GI effects
  - Precautionary labelling

- Methods
  - Intake assessment in random cross-sectional population study by FFQ
  - Passive monitoring for consumer reports of adverse effects
  - Serum micronutrient levels measured in cohort study

- Outcomes
  - Intake/usage patterns : compliant with pre-market assessment
  - Expected effects confirmed as within background
  - Reported allergic reactions : not confirmed in follow up
  - Targeted clinical study :absence of effect on anti-coagulant medication
  - ➢ Labelling removed

Case Study : Fat spreads with Phytosterol esters (cholesterol reduction)

- Reason for PMM
  - Condition of pre-market approval to confirm predictions concerning intake and target populations

- Methods
  - Intake and pattern of use assessed by market research (direct survey of households)
  - Passive monitoring for consumer reports of adverse effects

- Outcome
  - Pre-market assumptions concerning intake and target group confirmed
  - No unexpected effects of any significance observed

More products, continuing monitoring (EFSA 2008, PHYTOST..)

Case Study 4 : StarLink Maize (Bt Cry9C; feed)

- Reason
  - Consumer complaints of adverse health effects
- Methods
  - Collection/evaluation of consumer reports by independant authority
  - Retrospective intake assessment in ‘positive’ cases by chemical analysis of food; measurements of biomarkers (IgE) in subjects
- Outcome
  - No association between putative allergic reactions and exposure to StarLink maize
  - no confirmation of allergic potential of Cry9C protein
  - No PMM strategy applied

Possible criteria to trigger a PMM?

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Intake

- If EDI is close to ADI - monitor real consumption patterns
- Original application for one product; further applications leading to different exposure patterns
- Product intended for use in foods in certain populations
- Monitor potential non-intended use

Health

- Possible (side-)effects identifed in pre-market
- Reassurance of no adverse effects – but need a reasoned hypothesis, system to collect signals.
- If significant number of complaints received?
- If new issues highlighted – further research?

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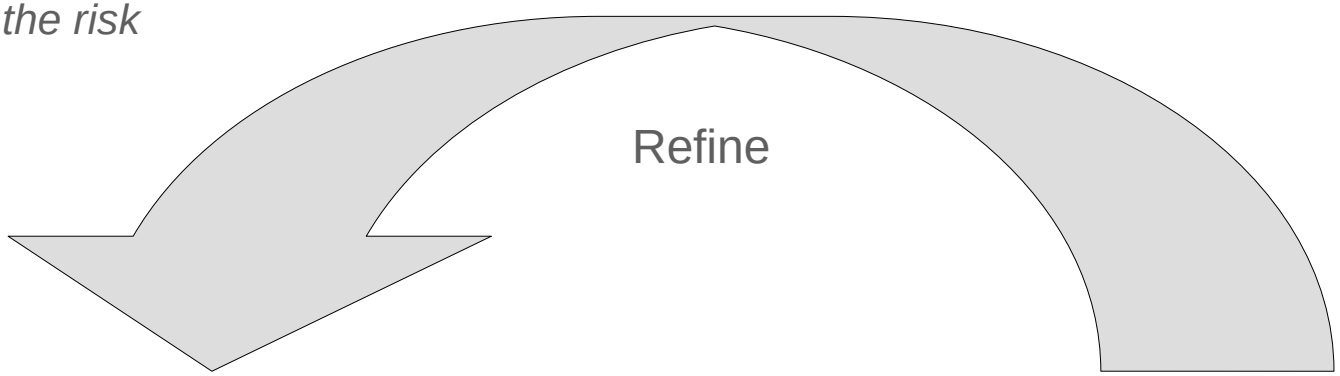
PMM : a Complement to Risk Assessment ?

A tool for getting market data which can be used for refinement of the risk assessment



Pre-market safety studies	Risk Assessment	Risk Management	Launch Product	Post-Launch
− Modelling − In-vitro − In-vivo − Human	Intake Estimate + Hazard characterisation	Regulatory approval − Limitations − Labelling	− Compliance − Advertising − Communication	PMM - Intakes - Health Effects

Methodology : Food Intake (1)

- Food *supply* data
  - Track production of agricultural commodoities
  - Measure volumes *available* for consumption
- *Household* food purchase data
  - National Food Surveys (eg UK - 6000 households since 1940)
  - Commercial market surveys
  - Retailer loyalty card info
    - Out of home ?
- Survey of *individual* intake
  - Dietary recalls

Methodology : Food Intake (2)

- Limitations/developments
  - Traceability (occurrence, food products)
  - Sources of info : Food composition databases (e.g. EuroFIR)
  - Brands v food products v ingredients
  - Statistical modelling : improve predicted intakes
  - Harmonisation of methodologies (different countries)

Methodology : Health Effects (1)

- Company Contact Centres (channels for consumer relations)
  - Collating information from consumers
  - Surveillance, detection of signals for follow-up
    - Reactive, Proactive
    - Specific (branded) food products
    - Contact (culture, country, motivation)
    - Long term effects not identified
    - Quality of information (asked and received)
    - Expert follow-up

- Disease Registers
  - Patient Care, Public Health
    - Planning of public health care
    - Do not cover all diseases
    - Difficult to link with dietary exposures
    - Ethical/data protection

Methodology : Heath effects (2)

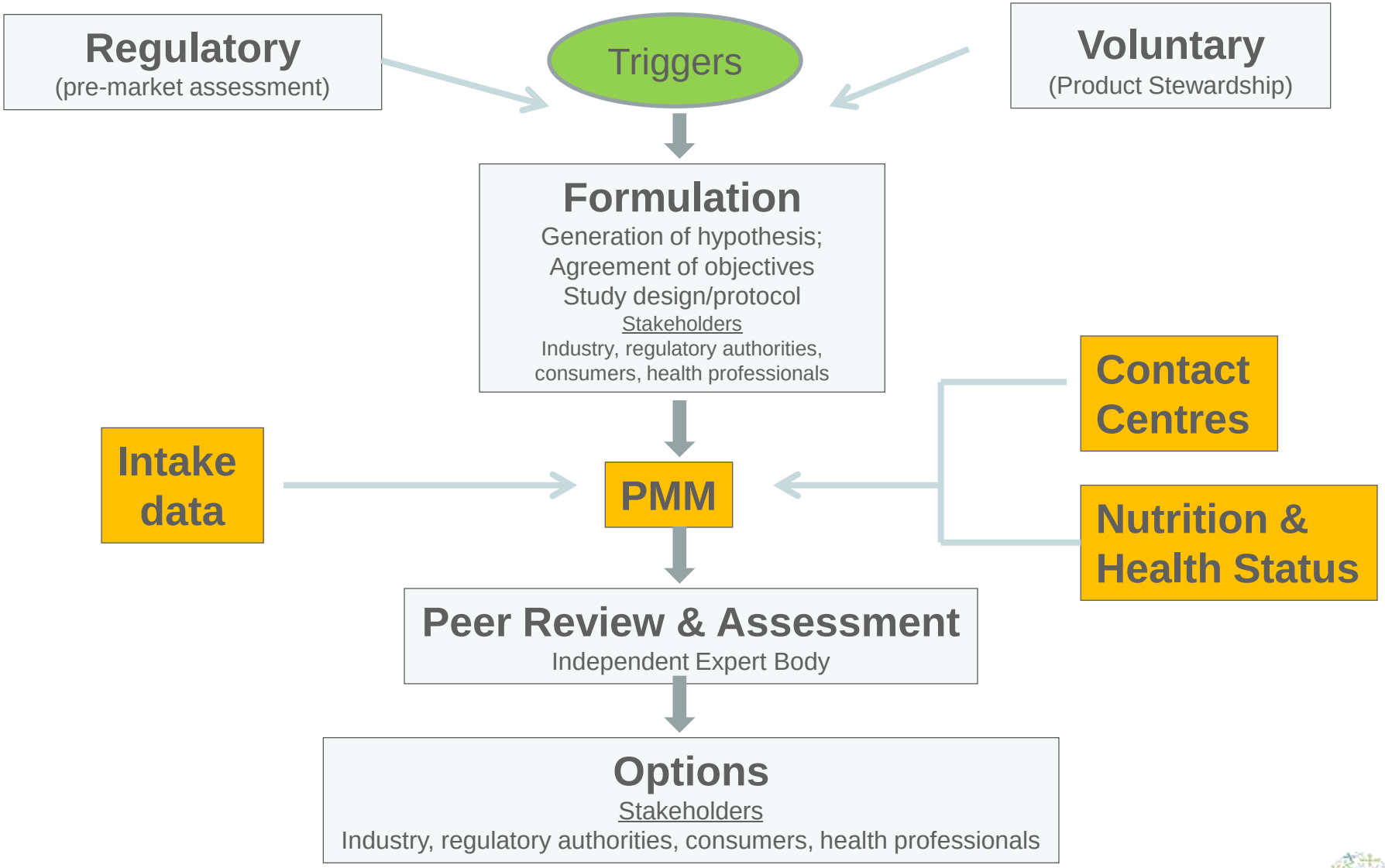
- Epidemiological Studies
  - Prospective studies (forward looking)
    - Monitor dietary practice and monitor health consequences
  - Case control studies
    - Investigate subjects with a particular disease in relation to previous dietary intake

- Needs/Developments/Improvements?
  - Detailed (accurate and continuous) dietary intakes
  - Link health effect to specific food/ingredient?
  - Early predictive (bio)markers of health effects - validation?
  - (Clinical trials in specific populations; v PMM)

Requirements for a PMM?

- Must be hypothesis driven
- Power of methodology employed must be sufficient to meet the needs of the PMM
- Study parameters must be clearly defined
- Timelines
- Adequate traceability and identification of the NF in question
- Reliable assessment of food intake
- Population must be large enough to ensure a statistically valid interpretation
- Collection, validation, recording checked for relevance and veracity by appropriate experts
- Characterised by codification in accordance with internationally recognised systems
- Transparent process fully involving all stakeholders.
- Decision making

Requirements for a hypothesis driven PMM



Conclusions (1)

PMM may be appropriate to:

- Confirm that product use is as predicted in the pre-market assessment
- Provide reassurance that effects observed in the pre-market assessment occur with no greater frequency or intensity in the post-market phase than anticipated
- Investigate the significance of any adverse effects reported by consumers after market launch

Conclusions (2)

- PMM should not replace any steps in the pre-market safety assessment
- PMM should only be used when triggered by specific evidence based questions
- Cannot be used to test hypothesis that effects are absent ; it is not possible to prove a negative.
  - Outcome is limited by power and nature of a study possible (duration).
  - (*Can provide a measure of confidence that effects will not occur*).
- Methodologies place limitations on what PMM can achieve

ILSI Europe Novel Foods Expert Group on PMM

- To discuss possibilities and limitations on PMM for Novel Foods
- Discussed in workshop Barcelona 2006.
- *Hepburn et al (2008). The application of Post-Market Monitoring to Novel Foods, Food Chemical Toxicology, 46(1) 9 – 33.*

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