Risk Assessment of Chemicals in Food – International Approaches

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Risk assessment is an estimate of the likelihood or probability of adverse effects resulting from exposure to certain health hazards. In this presentation, we will discuss the risk assessment process for use of food additives. Risk assessment is defined as a scientifically based process consisting of the following steps:

1) **Hazard identification**
   Hazard identification determines whether food additives can cause adverse effects, and what is the nature of the adverse effects.

2) **Hazard characterization**
   Hazard characterization, also called dose-response assessment, determines the relationship between dose and incidence of effects. This requires extensive toxicology testing in different species at multiple doses. These data are used to establish the Acceptable Daily Intake (ADI). The ADI is an estimate of the amount of a food additive in food or beverages expressed on a body weight basis that can be ingested daily over a lifetime without appreciable health risk to the consumer.

3) **Exposure assessment**
   The exposure assessment is based on the food categories that will contain the food additive and the proposed use levels of the food additive.

4) **Risk characterization**
   In the risk characterization step, the probable exposure to the food additive is compared with the ADI.

The steps of hazard identification and characterization of food additives, as well as the factors that affect the ADI and its applicability to the general population will be discussed in this presentation.

Risk Assessment of Chemicals in Food – International Approaches"

Berna Magnuson, PhD
Fellow Academy of Toxicological Sciences

contaminants → unintentional

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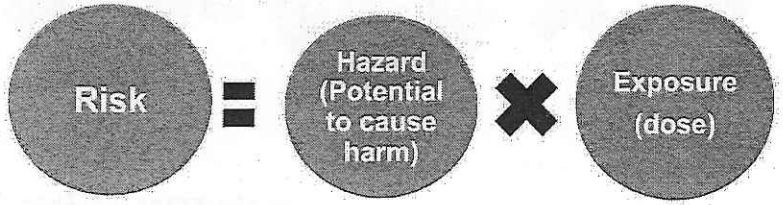
Safety = absence of risk



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Purpose

- **To foster further understanding of the nature of the safety assessment of food additives**
  - Describe risk assessment paradigm
  - Explain the factors that are considered in the establishment of the ADI.

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If low exposure, can accept high hazard –

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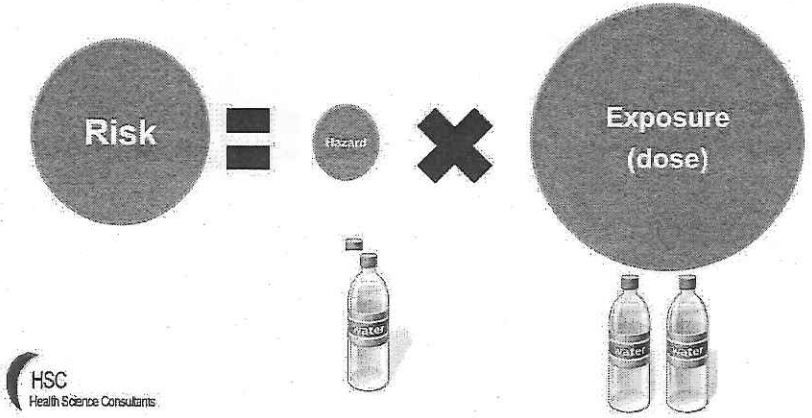
But, there is always a dose that can cause harm

Drinking Too Much Water Can Kill: People can and do drink themselves to death.

If low hazard, can accept higher exposure –



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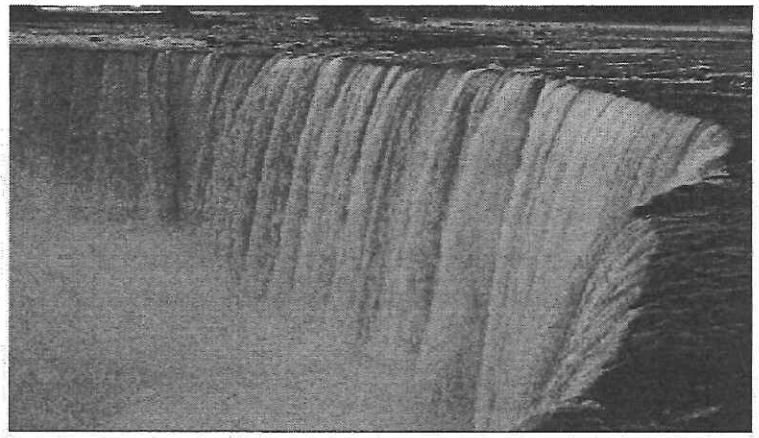
Type of Exposure to Hazard?



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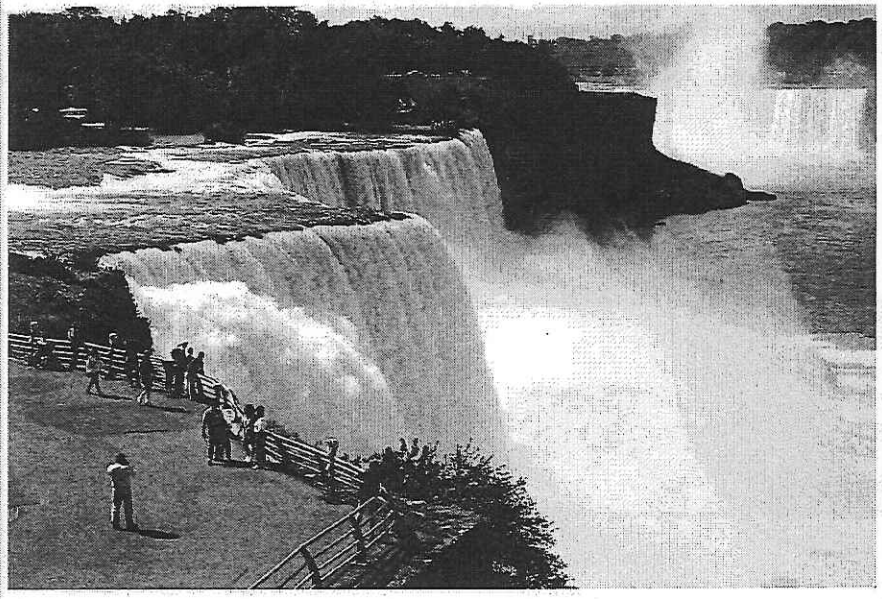
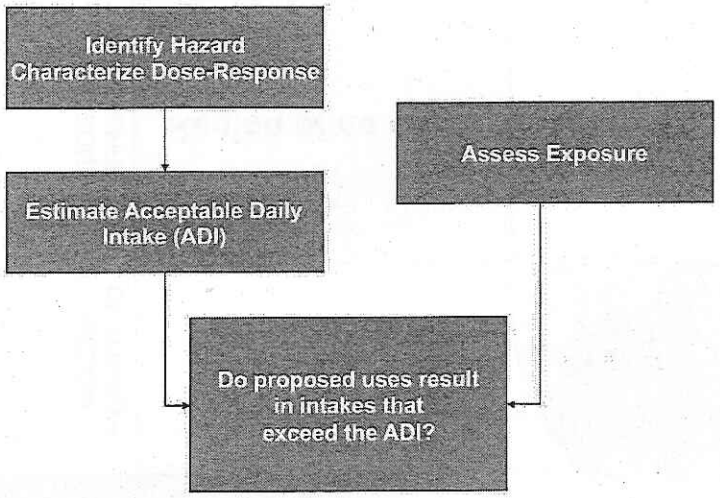
Exposure



Risk assessment paradigm



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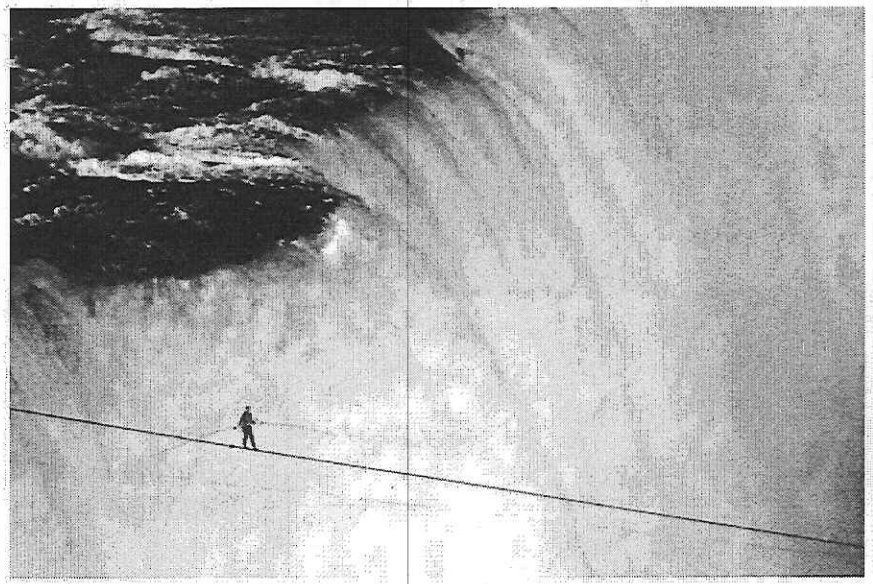
Exposure



Identify Hazard

- Extensive toxicology testing required.
- What happens to the compound when we consume it?
- Toxicity following long-term consumption?
- Any effect on mutations or cancer development?
- Reproductive toxicity?
  - before and during pregnancy
- Teratogenicity – effect on development?
- Also human clinical studies may be conducted

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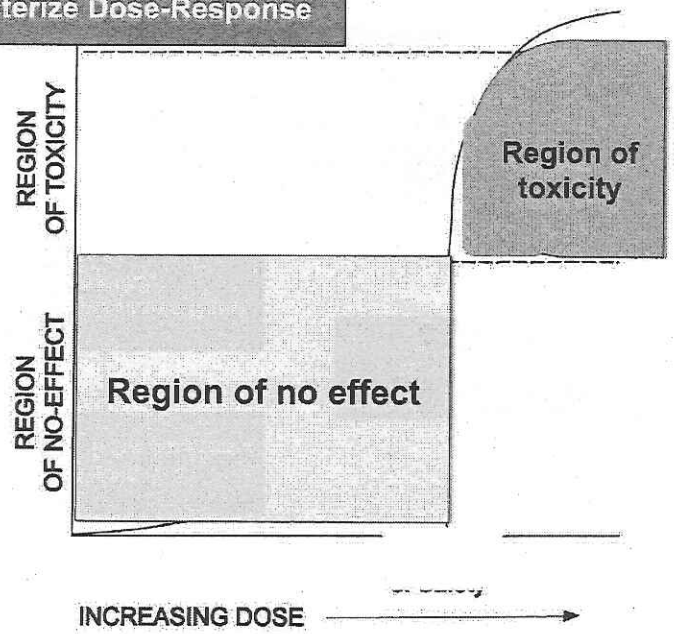
life time level depends on the species rat: 2 years (rodent)
study
in 2 species

Characterize Dose-Response



No Observed Adverse Effect Level (NOAEL) dog.

-From most comprehensive long term study with several doses tested in appropriate species

- Is not an inherent property of the compound
- Is an experimental **observation dependent upon the conditions** of the experiment:
  - Doses tested – where in the no effect region?
  - Species and strain of animal,
  - Method of exposure to test compound, oral food
  - May also depend on diet and other conditions of the experiment.

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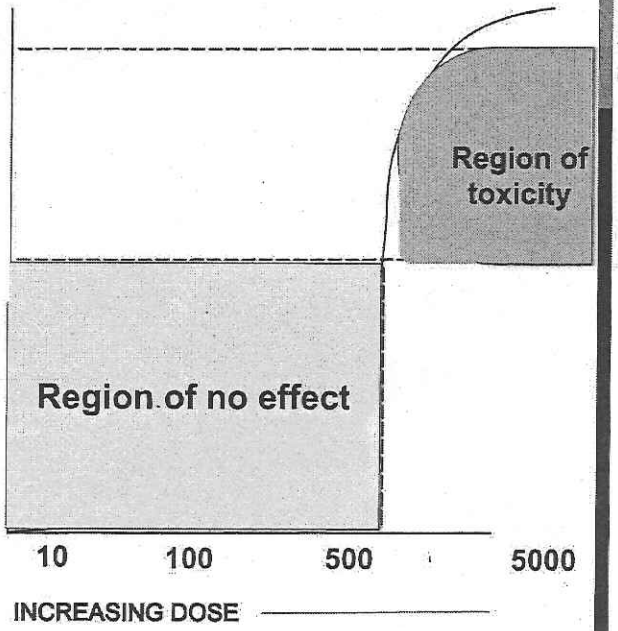
Dose selection, affects NOAEL.

What is NOAEL if doses tested: 0, 100 and 500?

NOAEL = 500 mg/kg



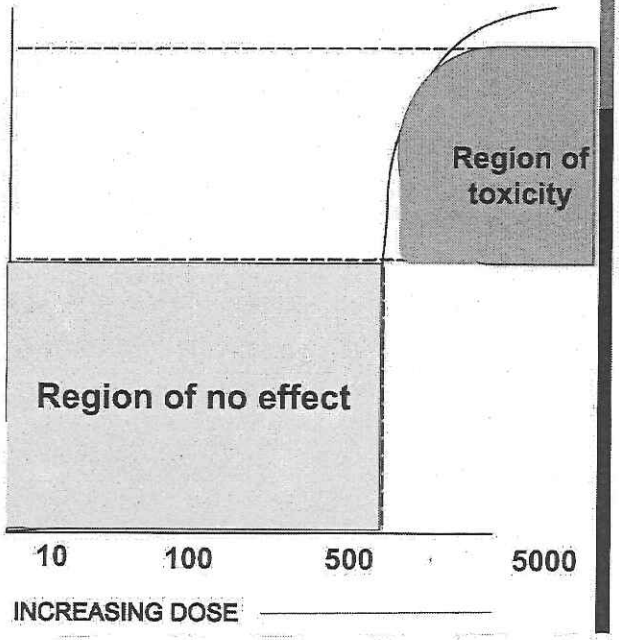
Dose selection, affects NOAEL.

What if doses tested are: 0, 10 and 100?

NOAEL = 100 mg/kg

If doses tested: 0, 10 and 1000?

NOAEL = 10 mg/kg



Adverse effect?

Need to distinguish **statistically significant** changes from **biologically relevant effects**.

- Need to know normal range variability for animal species and strain;
- Decreased body weight gain accompanied by decreased food consumption? may be caused by palatability, *i.e.* not an adverse health effect.
- Observed with high intensity sweeteners due to feed refusal of very high levels.

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Acceptable Daily Intake

"is an estimate of the amount of a food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk."

(Environmental Health Criteria No. 70, JECFA 1987)

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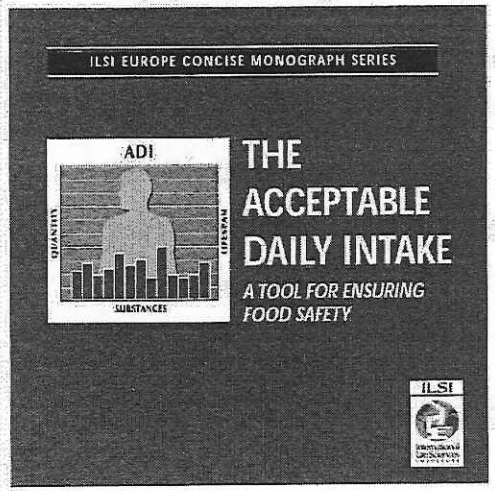
Acceptable Daily Intake



- **Based on general principles for evaluation of food additives set out in 1950s**
- **by Joint FAO/WHO Expert Committee on Food Additives (JECFA).**
- **Considered a valuable regulatory tool internationally.**

ADI Values

Established by

- determining the amount animals can consume every day without adverse effect, or
- No Observed Adverse Effect Level (NOAEL)

- Application of "safety factors" to account for
  - differences between individuals
  - differences between humans and animals

NOAEL/safety factors = ADI

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Safety Factors used may depend on

young / old
male / female
↑
within the species

- **Intraspecies sensitivity,**
- **Interspecies differentiation,** between the species
  rat/mice/dog/rabbit
- **Study duration,**
- **Adequacy of toxicology database,**
- **Sub-population susceptibility,**
- **Endpoints identified (*e.g.*, severity).**

ex. contaminant
intentionally added substance } different end point

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Extrapolation of animal data to humans

- **Assess relevance of animal species used in toxicity studies for extrapolation to humans:**
  - Comparison of pathways of metabolism in animals and humans,
  - Investigation of toxicity in animals of major metabolites found in humans,
  - Testing at high levels may result in severe chronic repair and effects that are not relevant to lower levels of exposure.

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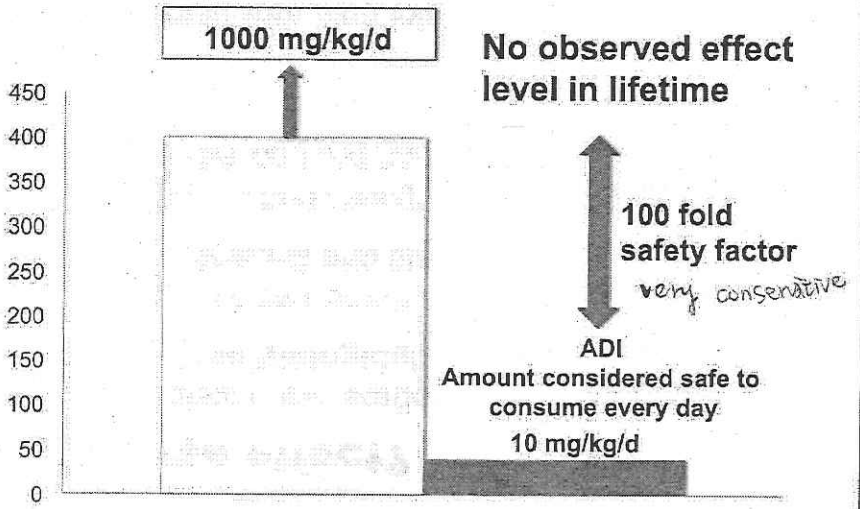
Acceptable Daily Intake



ADI categories

Permanent ADI	• most food additives
ADI not specified	• potential intake from all current uses does not represent a hazard to health. Use at GMP levels
Temporary ADI	• Database not adequate. Additional safety factors applied.
Group ADI	• If similar chemical structure and/or common metabolite. Example: Steviol glycosides

no necessity to establish a numerical ADI

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APPLICABILITY OF THE ADI TO SPECIAL SUBGROUPS?

all populations.

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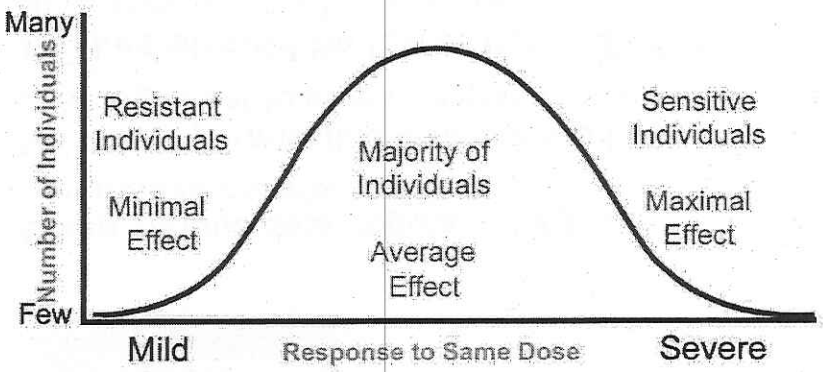
Variability in Response to Same Dose



Infants and children

Are infants (from birth to 12 months of age) and children (1 to 12 years of age) adequately protected by the ADI? Infants are not protected by ADI.

- infants and children may differ in their capacity to detoxify and eliminate chemicals from the body);
- infants and children may be more sensitive to toxicity.

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Infants and Children

- Variation between infants and adults is addressed within safety factor.
- If effects are seen during growth and development in animal studies, be reflected in establishing the NOAEL and ADI
- In general, **ADI does not apply to infants, but does apply to children**

>1 year old

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Pregnant Women

- reproductive studies designed to cover stages of conception, gestation and development
- detects effects on the fetus, the newborn and the immature animal as well as on the adult.
- If effects are seen on reproductive ability or developing offspring, these studies will be used in establishing the NOAEL.
- Safety factors address increased susceptibility.
- Thus **ADI does protect pregnant women.**

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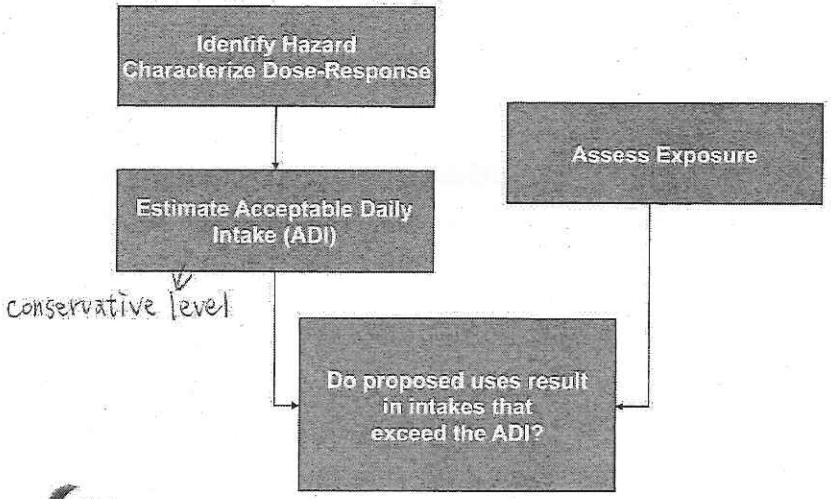
Risk assessment paradigm



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People with Food Allergies?

Potential for causing allergies is part of testing.

- People with unique food allergies or genetic disorders cannot be protected by the ADI, and must learn to "manage the risk" by avoiding foods containing the substance.
- Are very few convincing reports of true allergy to food additives.

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Assess Exposure

Using various data, regulatory agency determines possible intakes.

Maximum permissible levels in foods & beverages set to ensure exposures < ADI

Intakes should be lower than ADI for all users, including highest consumers.

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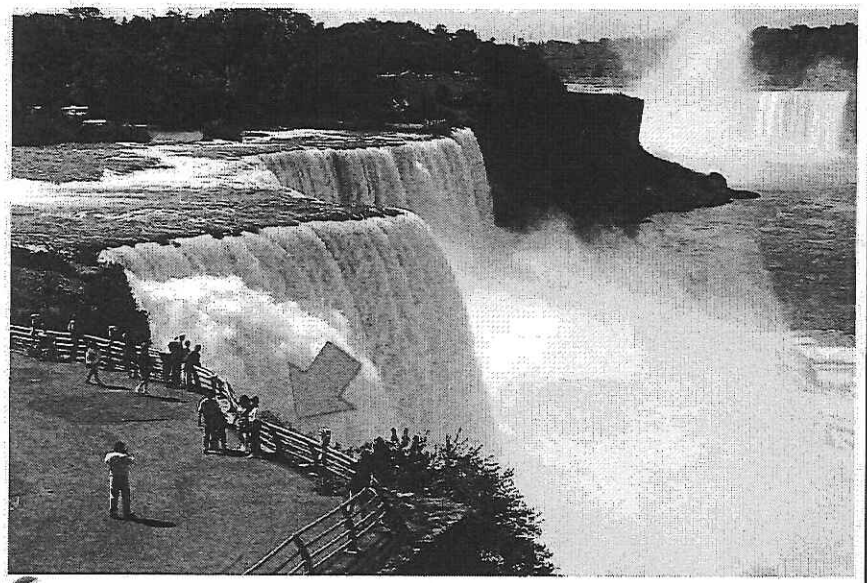

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set maximum use level

1. the amount to acheive the technical purpose

2. the amount of consumption of food

Summary

Risk is determined by assessment of both hazard and exposure.

ADIs for food additives are based on the No Observed Effect Level and safety factors;

Consumption of levels below the ADI is safe for all members of the population.

Occasional consumption >ADI not predicted to cause adverse effects due to safety margins in ADI.

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Intakes above the ADI?

- methods of intake estimation are over-estimations;
- changing dietary patterns - even an individual with extreme dietary habits is unlikely to have high intakes daily over an entire lifetime.

Considering hidden and overt safety margins, JECFA concluded that occasional excursions > ADI will not result in harm, provided that intakes averaged over a longer period are <ADI.

Consumption > ADI, particularly for prolonged periods, however, are generally undesirable as represent increased risk of potential adverse effect.

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Total Diet Studies in Malaysia

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Malaysia is one of the ASEAN countries that conducted Total Diet Study (TDS) on a national basis. Malaysia acknowledged the importance of TDS as an assessment program that provides indicators of chemical exposure in whole diet and generates a baseline for food safety measures. The Food Safety and Quality Division under the Ministry of Health Malaysia was responsible for conducting TDS in Malaysia. The planning to conduct TDS in Malaysia was initiated in year 2000 where the most important initial requirements were identified including the development of adequate TDS capability and capacity, collection of food consumption data for Malaysian population, and implementation of a pilot project for TDS. Malaysia started the pilot project for TDS in 2005. Over the years, Malaysia has improved the implementation of TDS by strengthening the capacity and capability as well as standard operating procedure (SOP). Establishing an SOP that suit each country's requirement is a very important element to ensure the consistency in conducting and implementing national TDS. Malaysia will share the experience and lesson learnt in the implementation of TDS in this presentation.

Total Diet Studies (TDS) in Malaysia

Nur Hidayah Jamaludin

Food Safety and Quality Division
Ministry Of Health Malaysia

CONTENT

INTRODUCTION

What is Total Diet Studies (TDS)?

TDS is

- Assess exposure of chemicals in whole diet
- Involved foods as normally consumed (table ready)
- Consistent approach, allowing comparison of results (use of science-based risk assessment, international approach)
- Require lowest detection limit possible

TDS is not

- Focus on chemicals in individual food
- Focus on commodity or uncooked food
- Surveillance which may differ in approaches
- Nutrition survey – finding out how much and what people eat (though this info is needed for TDS) consumption data
- Compliance with regulatory requirements (where detection limit meets regulatory limit)

TDS in Different Countries

- Since 1960s, various countries have been conducting TDS i.e. UK, USA, Canada, Australia, NZ and China.
- TDS may vary from country to country
  - types of contaminants
  - approaches and methodologies
    - "food group composite approach" – samples from same food group prepared and then combined to form a single food group sample for laboratory analysis; small number of samples; less flexibility in dietary exposure estimation
    - "individual food approach" – samples are analysed separately, larger number of samples, greater flexibility in calculating dietary exposures

TOTAL DIET STUDIES (TDS) IN MALAYSIA

How TDS Get Started in Malaysia

- The planning to conduct TDS in Malaysia was initiated in year 2000
- The initial requirements for conducting TDS were identified as follows:
  - Develop adequate TDS capability and capacity
  - Obtain appropriate food consumption data for Malaysian population
  - Implementing a pilot project on TDS

TDS Milestone in Malaysia...(i)

Since 2001	• Planning & Capacity building
2003	• Food Consumption Statistics of Malaysia
2005	• Pilot project
2006	• 1st MTDS
2007/ 2008	• 2nd MTDS

Planning & Capacity Building (Since 2001)

- **Planning**
- Establish technical committee on TDS
- Develop plan of action for TDS
- Develop general procedure for TDS
- Build up analytical capacity

- **Capacity Building**
- JICA Consultation (2001-2003)
- Study Visit on TDS in Japan (2004)
- WHO TDS Training and Workshop, Beijing (2006)
- WHO TDS Training Course, Hong Kong (2008)
- WHO Consultation Programme (2009)

Food Consumption Statistics (2003)

WHO recommend each country have their own consumption dat

- 1st Malaysian Food Consumption Survey
  - Adult Population (18 to 59 years)
  - Method: Food Frequency Questionnaire (FFQ)
  - 126 food items grouped into 13 food categories
  - Food consumption statistics presented according to geographical zones, stratum (rural/urban), ethnic groups and sex

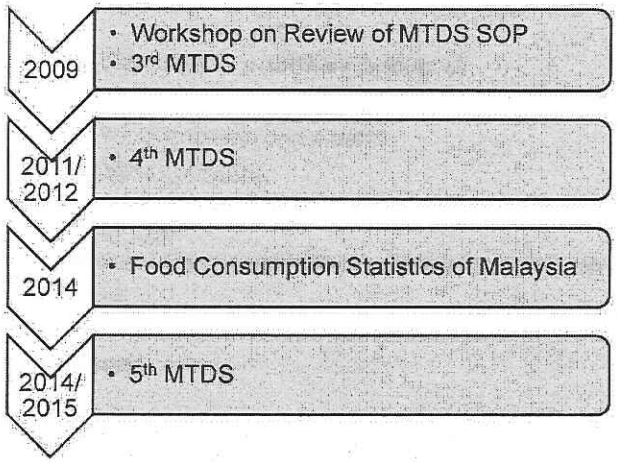
Pilot Project (2005)

- Objectives:
  - to pre-test all systems for foods sampling, preparation, and analysis
  - to determine and evaluate the readiness of MOH to carry out national TDS
- Pilot project involves:
  - 1 zone (consists of 3 states)
  - 39 food items based on individual food sample
  - 1 parameter – 1 analysis laboratory
- The experience gained also used to improve the SOP for national TDS implementation

Malaysian TDS Food Group Composite Approach (2006-2008)

2006	• 1st MTDS • 1 parameter • 86 food items • 25 composite samples
2007/2008	• 2nd MTDS • 2 parameters • 105 food items • 57 composite samples

TDS Milestone in Malaysia...(ii)



Review of MTDS SOP (2009)

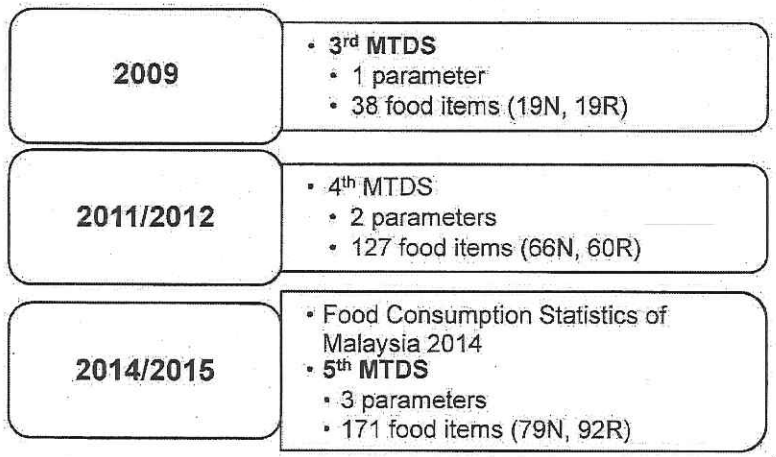
- Objectives:
  - To review the implementation of TDS
  - To improve current protocols for TDS

Topic	Previous TDS	Improvement
Sampling and analytical plan	No specific plan	Develop sampling and analytical plan in order to reduce workload, cover seasonal food, smooth sampling and analysis
Food item	No category	Categorise food items into National & Regional food item in order to significantly reduce sampling, sample preparation and transport efforts and costs associated with these foods
Sampling point	2 sampling points in all states	1 sampling points in in each state (3 sampling point for each region)

Review of MTDS SOP (2009)

Topic	Previous TDS	Improvement
Sample preparation	All laboratory in each state	Assign regional preparation laboratory in order to be more cost effective and reduce uncertainty and probability
LOD	Never checked, as provided by laboratory	Get the low enough LOD by using theoretical spreadsheet calculation and the LOD will be verified every time before TDS implementation
Sample analysis	All laboratory in each state	Assign centralise laboratory for analysis in order to reduce uncertainty and probability as well as increase precision

Malaysian TDS Individual Food Approach (2009-2015)



How TDS Conducted in Malaysia

SOP is very important in order to conduct TDS.
Four (4) important elements in Malaysian TDS SOP are:

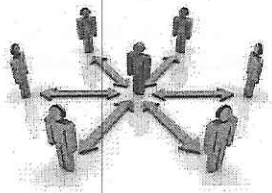
Management

Sample Purchasing

Sample Preparation

Sample Analysis

MANAGEMENT

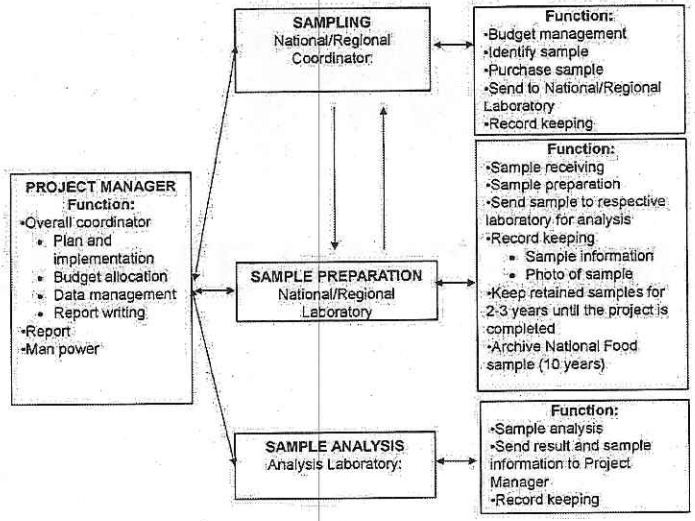


SOP for Management

❑Objective:

- To provide scope, objective, roles and responsibilities of TDS Committee as well as planning in order to ensure clear direction and communication in implementing TDS

Function and Line of Communication for TDS Committee



Sampling and Analytical Plan

- Specific time for sampling, preparation and analysis documented in SOP
- Frequency of MTDS: Every 2 years

No	Activities	Year 1												Year 2											
		Ja	Fb	Mc	Ap	My	Ju	Jl	Ag	Sp	Oct	Nv	Dc	Ja	Fb	Mc	Ap	My	Ju	Jl	Ag	Sp	Oct	Nv	Dc
1	Analysis laboratory preparation for lowest LOD																								
2	Briefing on TDS Implementation																								
3	Sampling for: Cereal Products																								
4	Sampling for Egg & Egg Products																								
5	Sampling for Nut & Nut Products																								
6	Sampling for Seasoning Products																								
7	Sampling for Drinks																								
8	Sampling for Meat Products																								
9	Preparation and Analysis for Sample Composite																								
10	Data compilation/ data checking																								
11	Re-analyse samples																								
12	Sampling for: Fruit Products																								
13	Sampling for Fish																								
14	Sampling for Dairy Products																								
15	Sampling for Vegetable Products																								
16	Sampling for Sweet and Spreads																								
17	Sampling for Alcoholic Beverages																								
18	Preparation and Analysis for Sample Composite																								
19	Data compilation/ data checking																								
20	Re-analyse samples																								
21	Data analysis																								
22	Report writing																								
23	Finalise report																								
24	Publish report																								

SAMPLE PURCHASING

SOP for Sample Purchasing

- Objective:
  - To provides proper harmonised food purchasing process in order to ensure consistency, quality, integrity and traceability of the sample for further preparation and analysis
- Consist of shopping list, purchasing instruction, location of sampling and food purchasing checklist

Food Categories

The food items are split into two (2) categories which are National Food and Regional Food

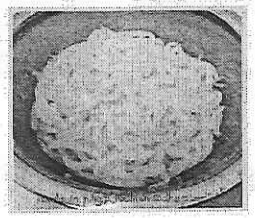
National Food (N)

- Foods that are processed / imported foods and likely to contain homogenous levels of contamination with respect to their production and / or processing methods.
- N will only be collected at one (1) sampling point in the Central Region

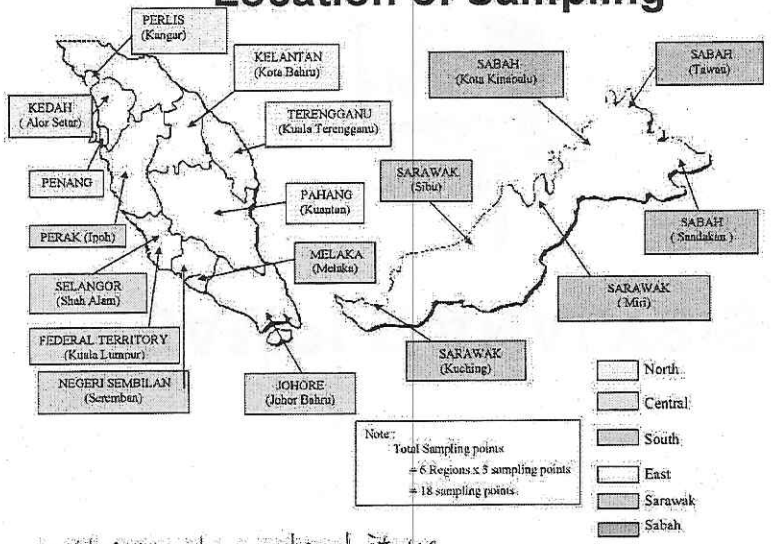
Food Categories

Regional Food (R)

- Foods that might contain heterogeneous levels of contamination resulting from production and / or preparation method specific to the region
- R will be collected at all identified 18 sampling points in all six (6) regions

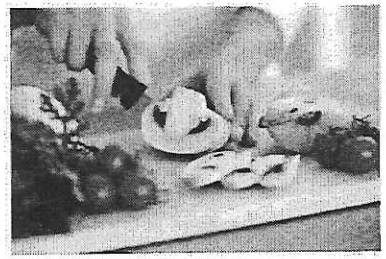


Location of Sampling



most commonly purchased items

SAMPLE PREPARATION



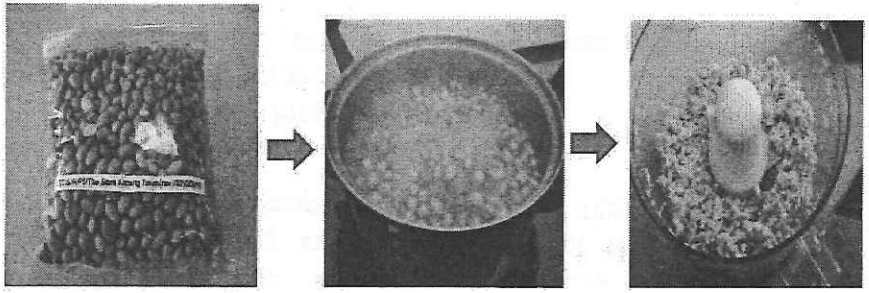
SOP for Sample Preparation

- Objective:
  - To provide a standard procedure to ensure consistency in the preparation of National and Regional composite samples for the TDS
- Principles:
  - Regional Preparation Laboratory - to ensure consistency and reduce uncertainty
  - Sample prepared as consumed based on individual food composite approach
  - Avoid cross contamination from utensils and environment

Steps in Sample Preparation

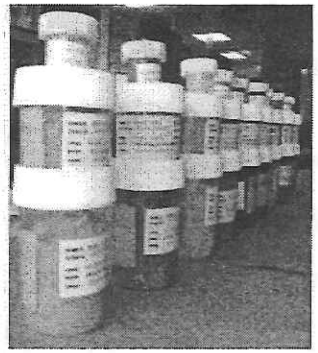
Subsampling	• Take equal portion and mix/homogenize before preparation
Preparation	• Use as it is after washing without cooking • Prepare as on the label • Cooking (Boiling, Blanching, Dry fry) Standardized & harmonized
Compositing as individual food	• Mixing, blending, chopping of indicated amount of sample
Retained and Archive sample	• Retained – for reanalysis/traceability of problematic food or until completion of TDS project (2 years) • Archive – for referral or comparison including reanalysis of new parameter (10 years)

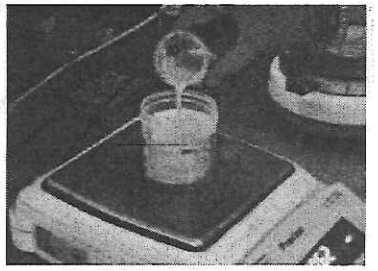
Example of Flow of Sample Preparation



Peanut Boil Grind

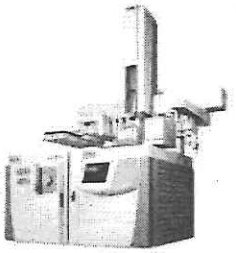
Individual Composite





keep the sample

SAMPLE ANALYSIS



SOP for Sample Analysis

- Objective:
  - To provide the requirement to ensure quality and integrity of the data generated from the analysis
- Sample analysis will be conducted in centralised laboratory (specific for each substance)
  - to reduce uncertainty and probability
  - to increase precision
- All laboratories have to verify the LOD and the instrument before the implementation of TDS

CONCLUSION

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- Knowledge and experience from previous TDS should be used to strengthen the capacity and capability on TDS implementation
- To ensure the consistency in conducting TDS, it is recommended to develop SOP to suit each countries requirement
  - SOP should provide detailed description for each component of TDS i.e. communication, sampling, sample preparation and sample analysis

Terima Kasih

Khawp khun

Ar kun

Thank You

Chezu ba

Salamat

cảm ơn bạn

Khawp jai