Overview of pesticide residues in food – application of pesticides in agriculture, their safety and regulation. *JMPR perspectives.*

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Consumers: no pesticide residue

Producer: pesticides needed for economic production

Compromise

Pesticide use is acceptable if:

- residues are not harmful to human health

AND

- no more pesticide is used than necessary to be effective (ALARA)

- What is the nature of the residue?
- How toxic is the pesticide and what are the toxic effects?
- What happens to the residue during food processing?
- What levels of residue occur in food?
- What are the methods of analysis?

This paper will deal with:

1) national controls
2) Codex and JMPR
3) toxicological assessment
4) pesticide residues in food
5) diets or food consumption data
6) dietary risk assessment
7) trade issues

1) National controls

National controls on pesticide use

- Assessment of the four risks
  1) occupational health
  2) public health, residues in food
  3) environment
  4) trade
- Pesticide registration
- Label directions for use
- Control-of-use regulations
- Monitoring

Proposed use and efficacy

- Compatible with integrated pest management systems.
- Allow for resistance management.
- Efficacy trials: range of treatment rates, various agricultural conditions → lowest effective rate for that pest-crop combination. - ALARA
- Results of efficacy trials → details in label directions for use, i.e. pests controlled, rates of application and timing. [**Note: these label instructions ultimately determine the MRL**].

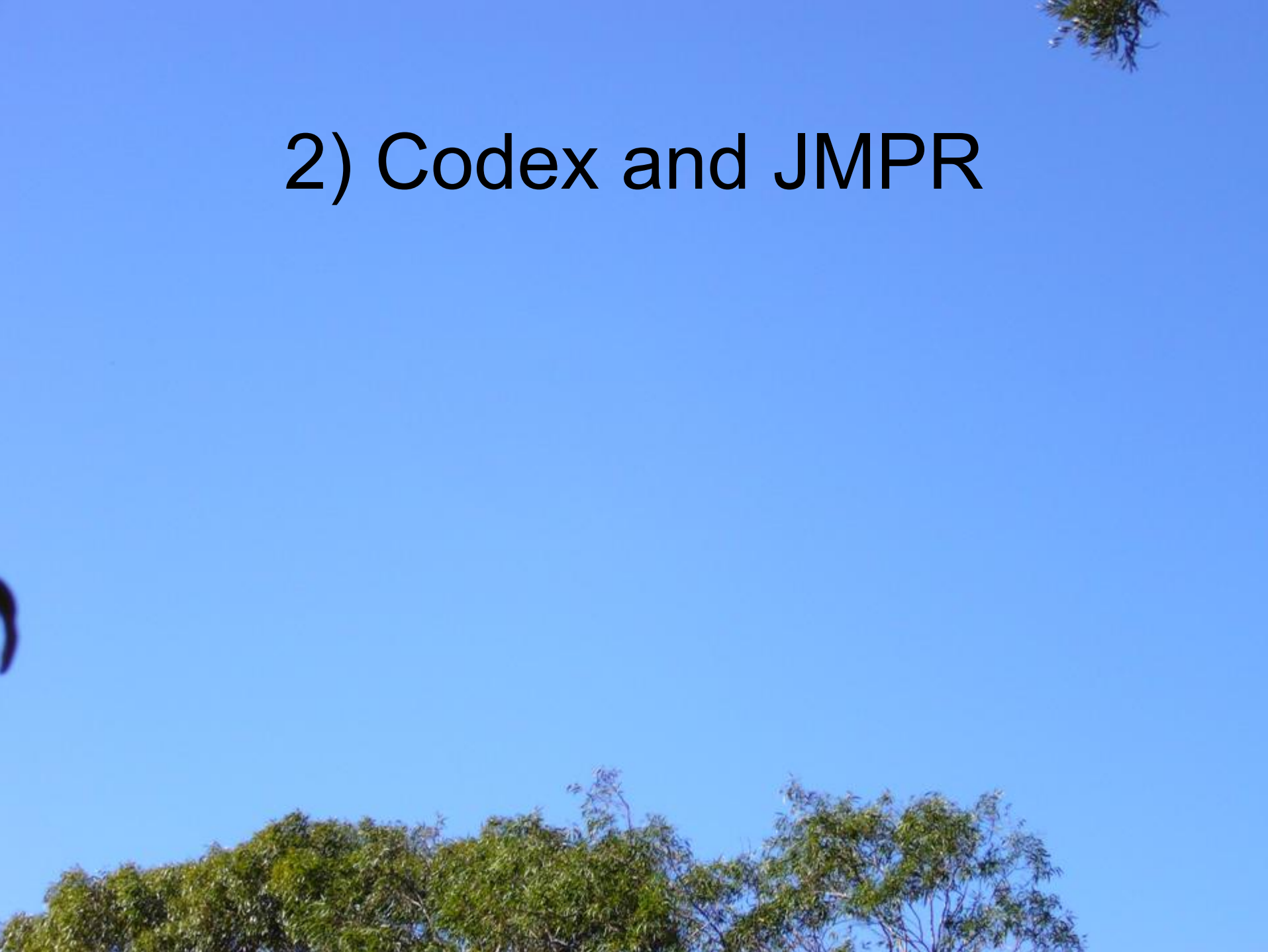
Good Agricultural Practice - FAO

- Good agricultural practice in the use of pesticides (GAP) includes the nationally authorized safe uses of pesticides under actual conditions necessary for effective pest control. It encompasses a range of levels of pesticide applications up to the highest authorized use, applied in a manner which leaves a residue which is the smallest amount practicable.
  - ALARA – as low as reasonably achievable

National monitoring

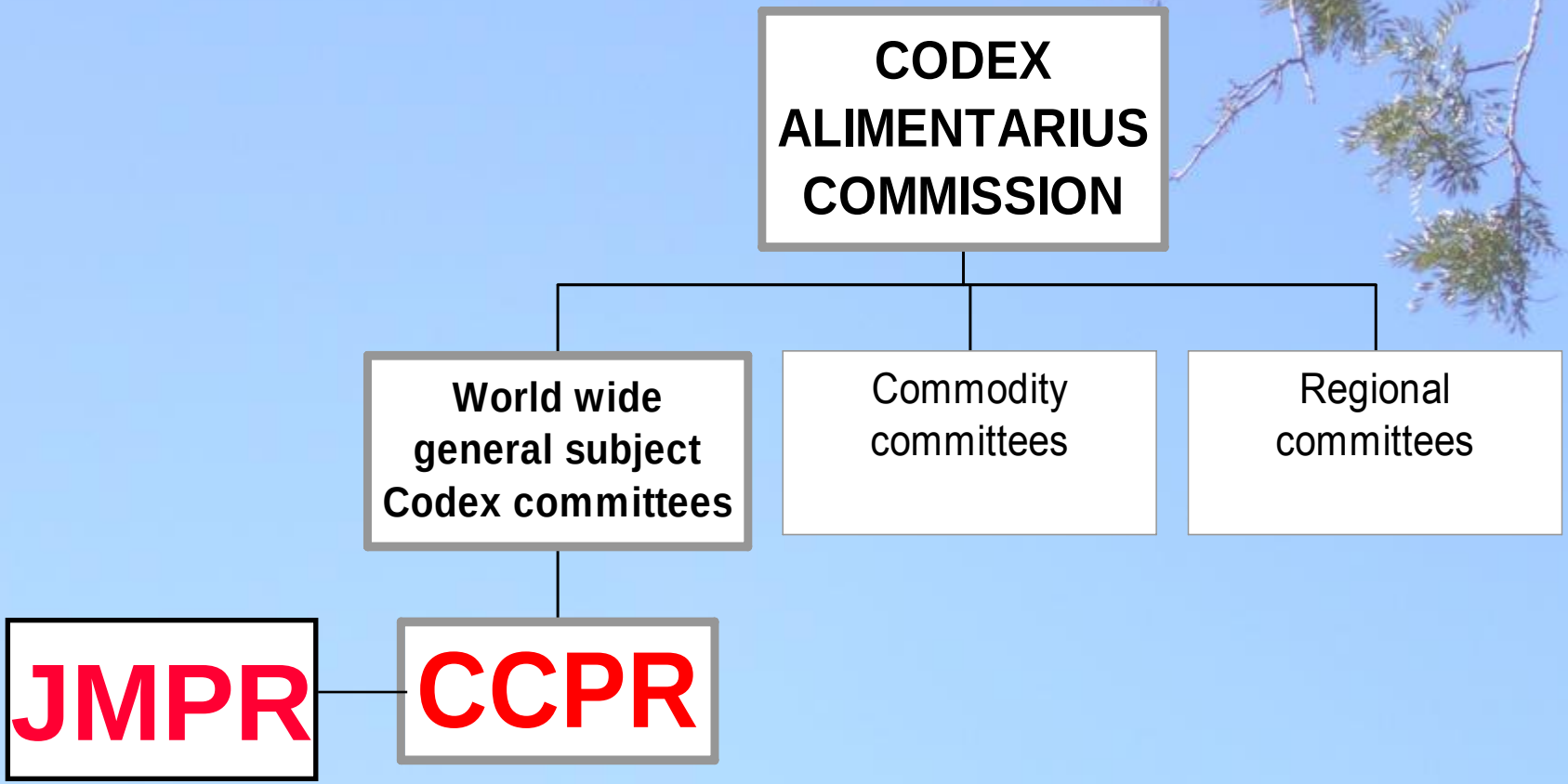
1) **Control-of use.** Monitoring of residue levels in domestically produced food commodities to observe if pesticides are being used according to label directions.
2) **Consumer exposure**. Monitoring, in total diet studies, of residue levels in food ready for consumption to provide data on actual exposure for comparison with pesticide acceptable daily intakes.
3) **Trade**. Monitoring of residue levels in import and export food commodities to check if the pesticide residue levels comply with the relevant standards – Codex MRLs or national MRLs.

2) Codex and JMPR



Codex Alimentarius

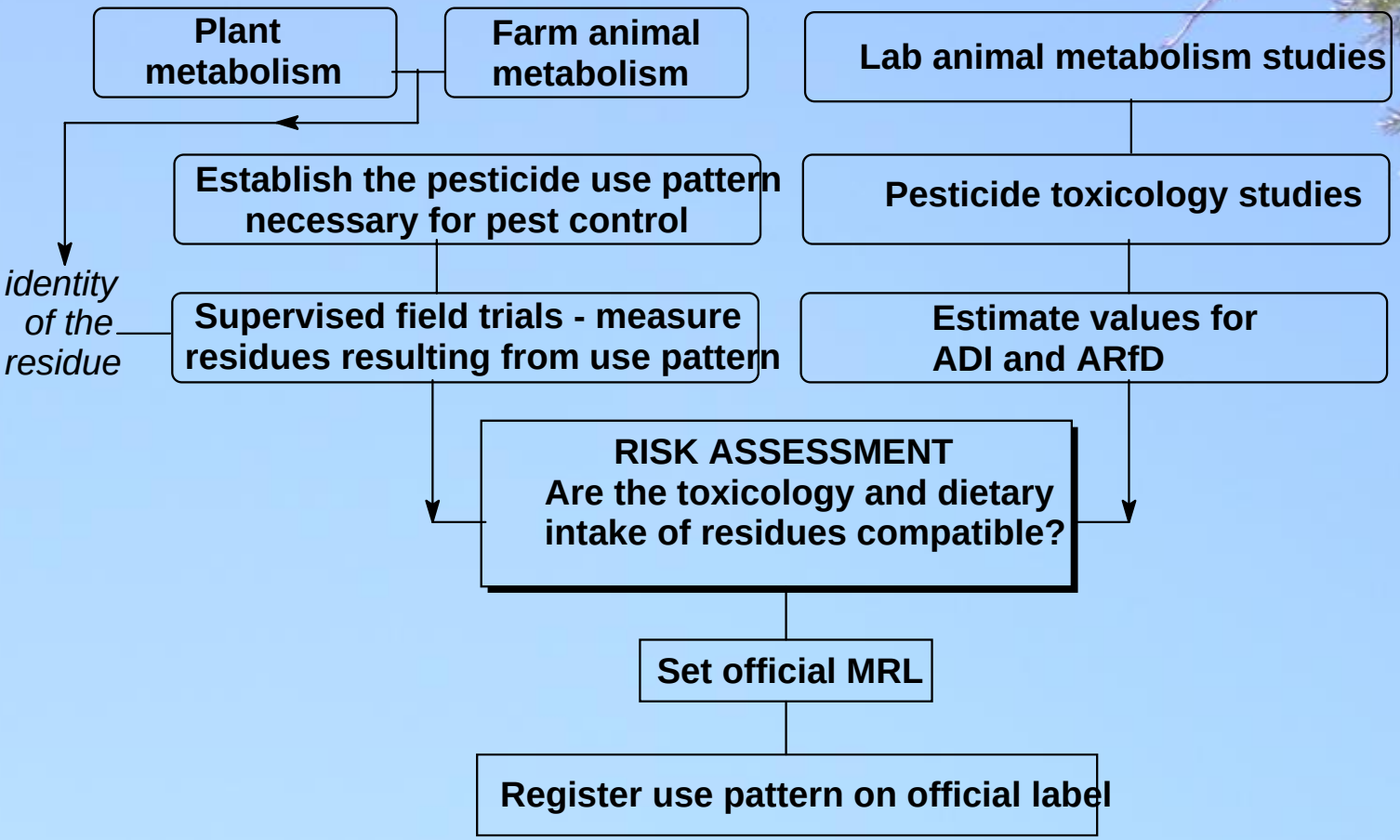
- aims to protect the health of consumers and ensure fair practices in the food trade
- CCPR
  - Codex Committee on Pesticide Residues
  - a committee of national representatives
  - establishes maximum limits for pesticide residues in food commodities in trade
  - receives scientific advice and recommendations from JMPR
  - CCPR is the risk manager


CODEX ALIMENTARIUS COMMISSION
World wide general subject Codex committees
Commodity committees
Regional committees
JMPR
CCPR

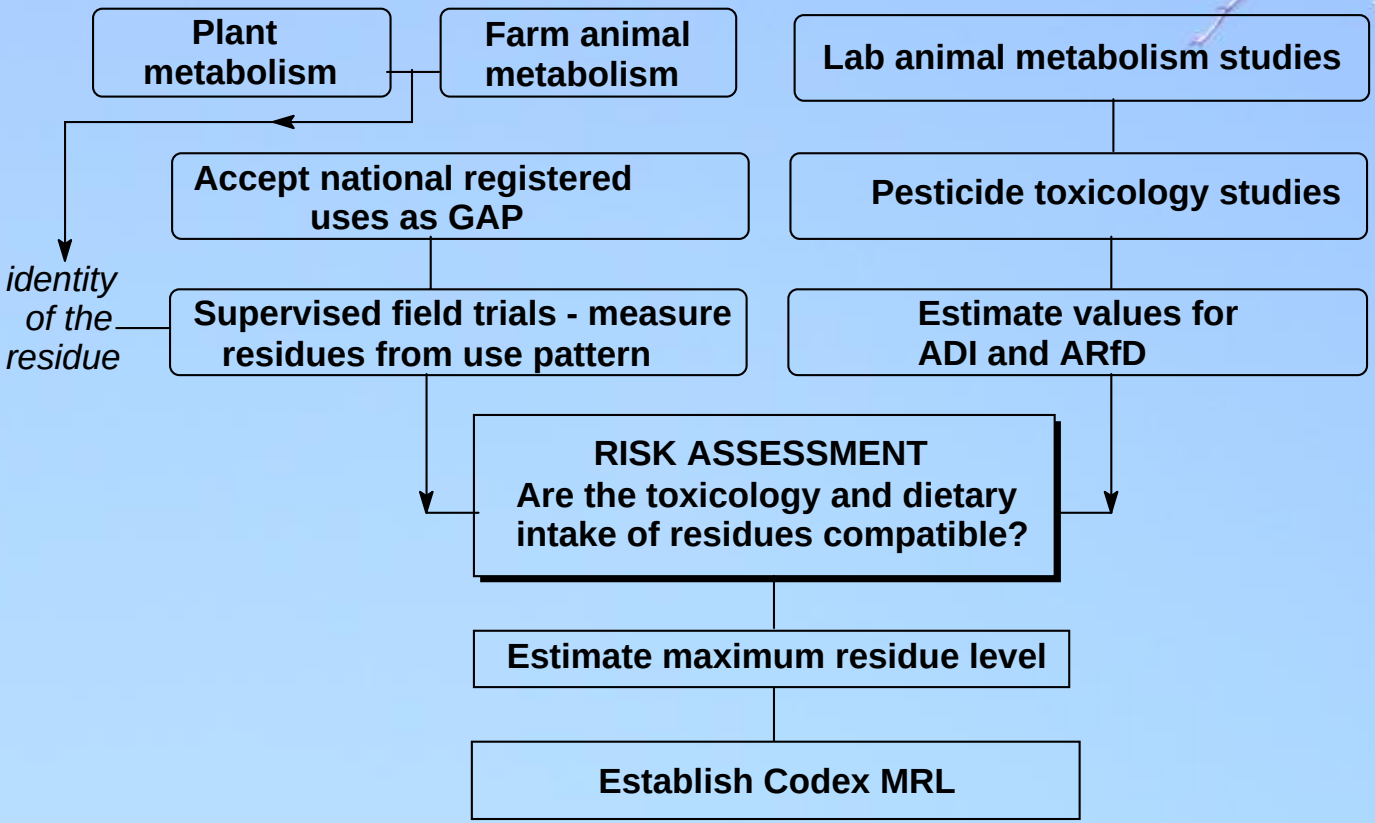
Joint Meeting on Pesticide Residues (JMPR)

- **Members serve in personal capacities, not as government representatives.**
- **WHO Group**
  - **review metabolism, toxicological data**
  - **estimate ADIs and ARfDs**
- **FAO Panel**
  - **review chemistry, environmental fate, metabolism , analytical methods, use patterns, residue trials**
  - **estimate MRLs and STMRs**
- **Both WHO Group and FAO Panel**
  - **risk assessment**

Evaluation process for national registration

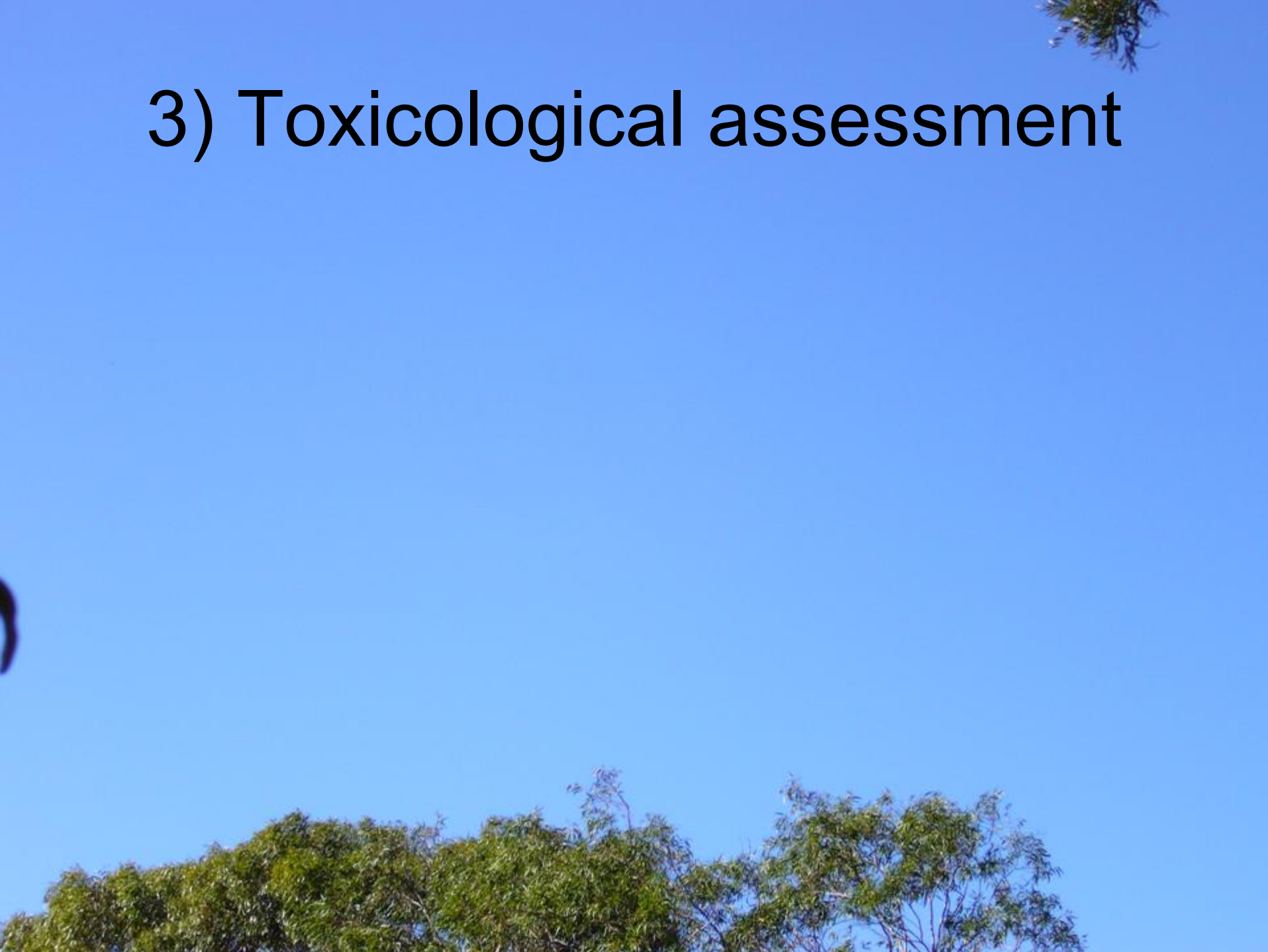


Evaluation process for Codex



GAP is Good Agricultural Practice

3) Toxicological assessment



Toxicological assessment

Purity of the test material

Metabolism in laboratory animals

Harmful effects

Dose response for lab animals

Multigeneration study

Development toxicity

Neurotoxicity

Mutagenicity – genetic damage

No data gaps?

Tox assessment (2)

- NOAEL – no observable adverse effect level
  - highest dose with no effect on the most sensitive animal species tested
  - mg/kg bw/day

Acceptable Daily Intake (ADI)

The daily intake which, after a lifetime of exposure at that level, is almost certain not to result in injury of any kind.

ADI = NOAEL ÷ safety factor (usually 100)

units: mg/kg bw/day

Acute Reference Dose (ARfD)

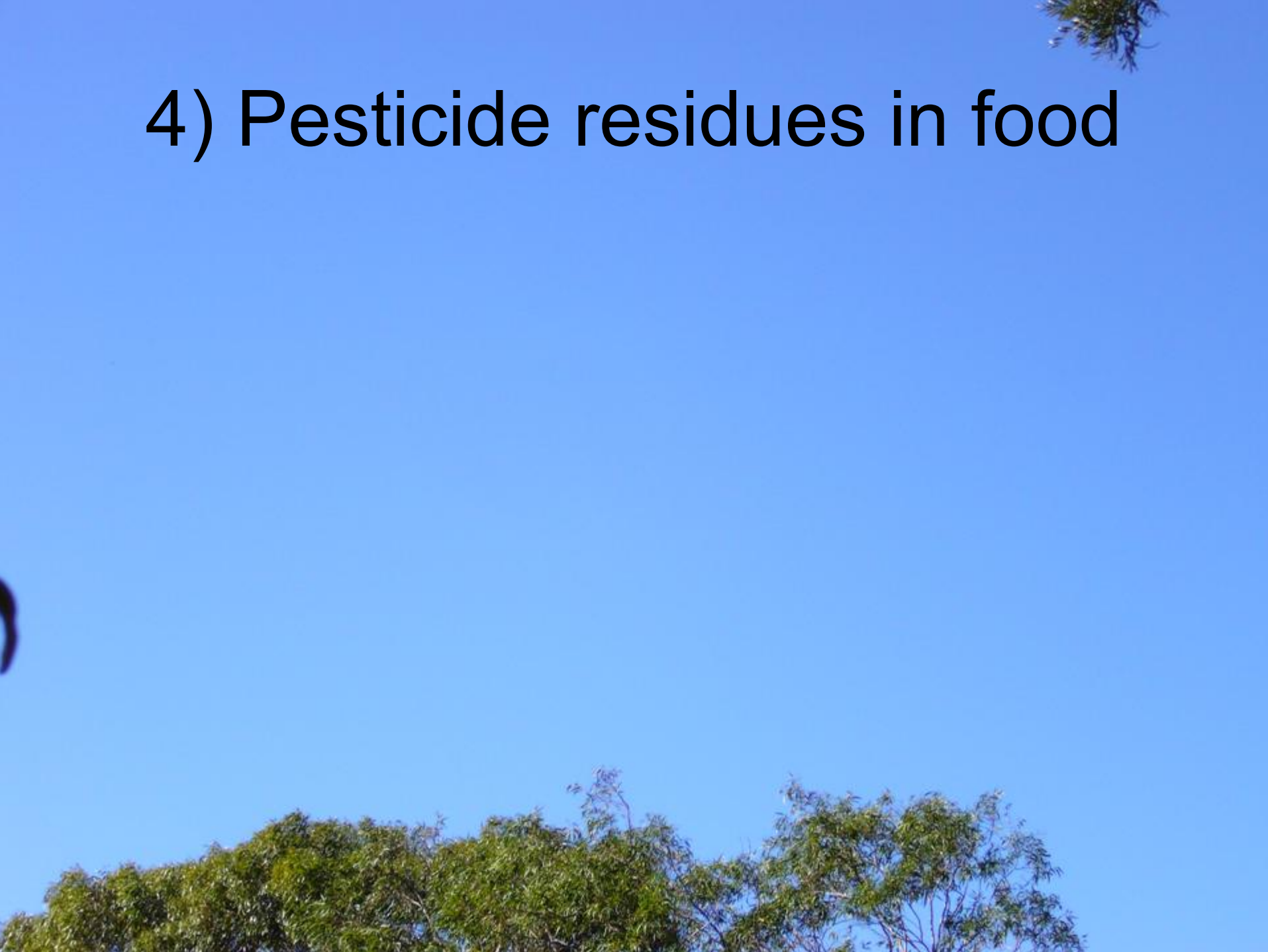
The amount of a substance in food and drinking-water, normally expressed on a body-weight basis, that can be ingested in a period of 24 hours or less, without appreciable health risk to the consumer, on the basis of all the known facts at the time of the evaluation.

- ARfD = NOAEL ÷ safety factor (usually 100)
- units: mg/kg bw

In summary:
the toxicology studies give us the ADI and the ARfD.

The idea for safety assessment is to ensure that consumers are not exposed to residue intakes that would exceed the ARfD in the short term or the ADI in the long term.

4) Pesticide residues in food



Pesticide residues

- metabolism
- analytical methods
- residue definition
- Good Agricultural Practice
- supervised residue trials
- food processing
- residues in milk, meat and eggs

Livestock metabolism

- Usually **lactating goat** and **laying hen**
- residue distribution in tissues, milk and eggs;
- metabolite identity;
- nature of the residue in tissues, milk and eggs; and
- residue fat solubility.

Plant metabolism

- nature of the metabolites (and photolysis products);
- plant metabolites not appearing in animals;
- composition of residue at normal harvest;
- surface or absorbed residue;
- foliar absorption;
- root absorption;
- translocation to seeds, fruits or other edible portion;
- absorption of soil metabolites; and
- differences in metabolism in transgenic crops.

Metabolism in soils and sediments

- persistence
- soil metabolites
- root crops
- seed treatments
- rice
- crop rotation – residues in following crops
- soil dissipation

Analytical methods

- Supervised trials and processing studies
  - include relevant metabolites
  - validation data
  - analytical recoveries 70-130%
  - LOQ (limit of quantification) – lowest concentration where recoveries shown to be acceptable
- Enforcement
  - apply to enforcement residue definition
  - prefer inclusion in multi-residue method

Freezer storage

- parent and relevant metabolites stable during storage intervals in the studies
- represent the range of substrates
- conditions and intervals where decline is more than 30% generally unacceptable

Residue definition

Enforcement

- Simple
- Cost of analysis
- Multiresidue methods
- A compound should not appear in more than one residue definition
- International agreement
- Express as parent compound
- Fat solubility

Dietary intake

- Include transformation products* if contributing to hazard
- Include transformation products if from multiple sources and contributing to hazard

*transformation products = metabolites, photolysis products and chemical degradation products.

Good Agricultural Practice

- JMPR accepts national registered uses as GAP
- Labels provide details of use

Supervised residue trials

- Cover range of conditions occurring in practice
- Accept data from trials that match registered uses (with allowances around application rate, pre-harvest interval, etc)
- Adequate number of trials
- Obtain maximum residue level, STMR, HR

- STMR. The supervised trials median residue (median in the set of trials, edible portion)
- HR. The highest residue in the set of trials in the edible portion
- Maximum residue level on commodity of trade – estimated by JMPR
- Maximum residue limit. JMPR recommends maximum residue level to CCPR as suitable for establishing MRL (maximum residue limit).

Food processing

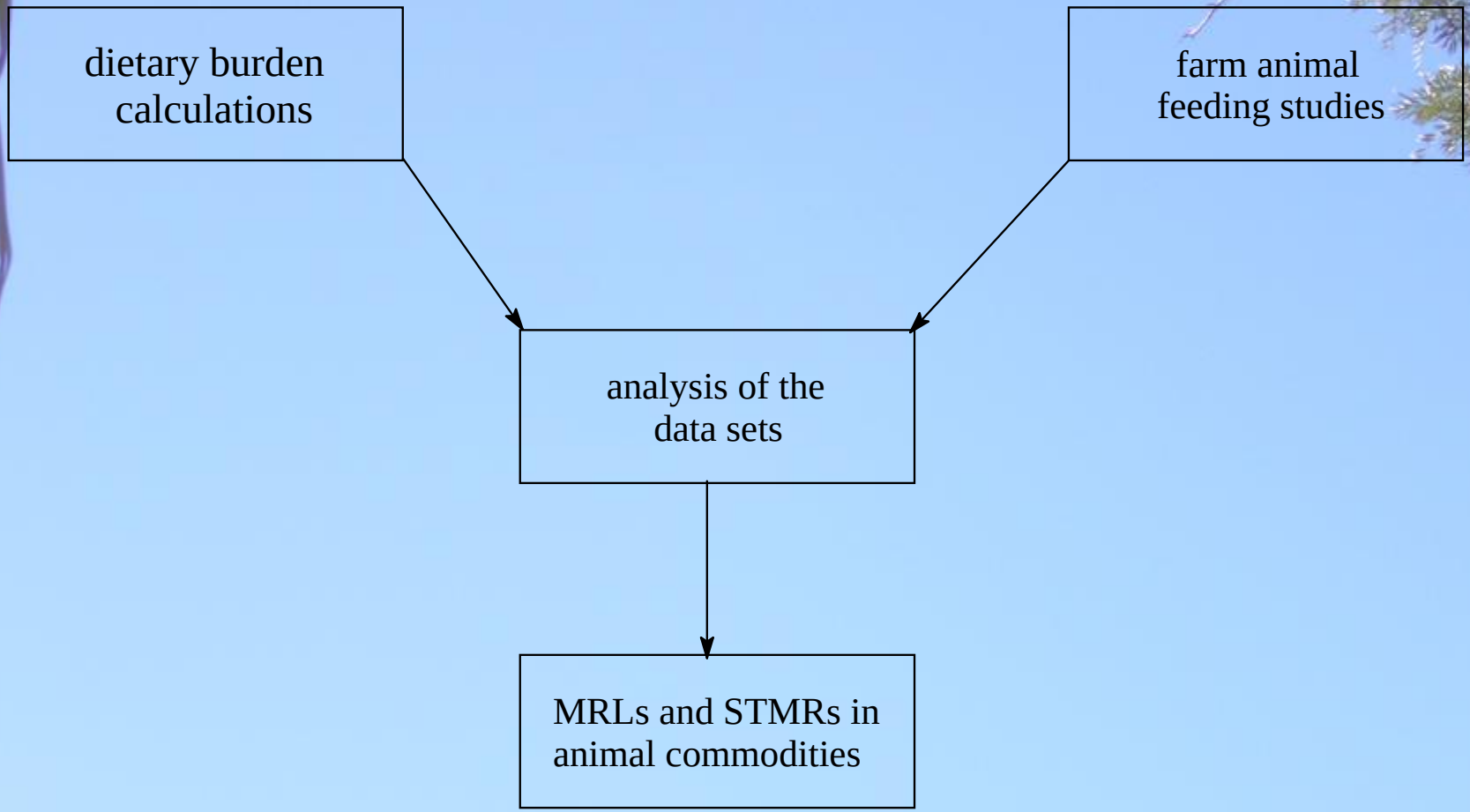
- Nature of the residue in processed commodities
- Change in residue levels from raw agricultural commodity to processed food commodity

$$\text{Processing factor} = \frac{\text{residue level in processed commodity}}{\text{residue level in raw commodity}}$$

Livestock feeding

- Find the levels of residue in animal tissues, milk and eggs from repeated daily dosing
- Dosing should reflect expected animal dietary burden of residues in feed
- Rate of depletion when dosing ceases

Livestock dietary burden + feeding studies
→ estimated residue levels in animal tissues, milk, eggs



Direct external animal treatment

- Use formulated product at recommended dose rate, method of application and timing
- Include the use likely to generate the highest residues
  - Uses on sheep: off-shears, short wool, long wool, plunge-dip, spray dip, jetting, pour-on, wound treatment.

5) Diets or food consumption

Diets or food consumption data

- **Chronic intake**
  - average diets
  - food balance sheets

http://www.who.int/foodsafety/chem/gems/en/index1.html

- **Short-term intake**
  - large-portion size
  - food unit weights

http://www.who.int/foodsafety/chem/gems/en/index2.html

Cluster diets 1

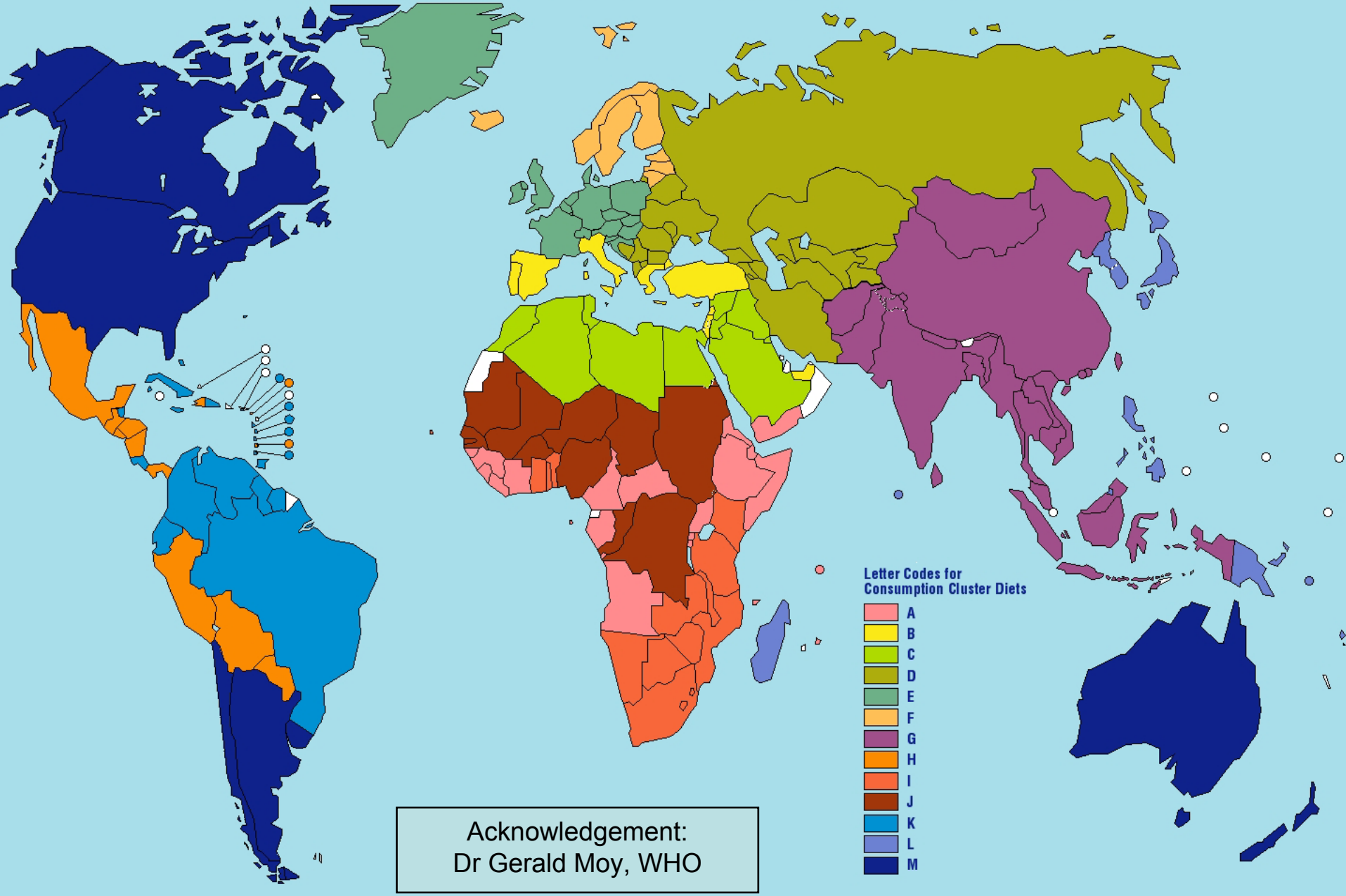
Thirteen GEMS/Food* Consumption Cluster Diets were introduced in 2006.

- based on average FAO Food Balance Sheet data for 1997-2001.
- Cluster G includes China, India and Indonesia

http://www.who.int/foodsafety/chem/gems/en/index1.html

**WHO Global Environment Monitoring System .*

GEMS/Food Consumption Cluster Diets – January 2006



Acknowledgement:
Dr Gerald Moy, WHO

WH

Cluster diets 2

Consumptions for raw commodities include the consumption of the derived processed commodities

- Example: the consumption of grapes includes the consumption of wine.

In the dietary exposure calculation when residue data are available for a processed commodity, the consumption of the processed commodity has to be subtracted from the raw commodity consumption.

Notes in the spreadsheets explain the calculation

- Example: 1.4 X wine consumption is subtracted from grapes consumption.

6) Dietary risk assessment

Dietary risk assessment - long term

Dietary intake of residue

= residue concentration X food consumption

Estimated daily intake for the pesticide

= sum of intakes for all foods where the residue occurs

Divide this value (mg/person) by body weight and compare with ADI

Dietary risk assessment - short term

High consumption of a food on one day

High residue (HR)

Residue level in first unit is ‘v’ times as high as HR.

v = 3 (default value)

Risk assessment

- Chronic
  - 13 GEMS/Food Consumption Cluster Diets
  - sum of exposures for each food commodity (STMR × food consumption)
  - compare with ADI
- Short-term
  - Each food separately
  - large portion × HR × variability factor (some)
  - compare each with ARfD

Recommendation to CCPR

- JMPR recommends the estimated maximum residue levels as MRLs (maximum residue limits) only if the risk assessment passes both the chronic and short-term intake hurdles.

7) Trade issues

MRLs are used for three purposes

1) As reference points to decide if pesticides have been misused under control-of-use regulations.
2) As trade standards.
3) As starting points for estimating consumer exposure.

Control-of-use MRLs are parochial - far from ideal for international trade

- When MRLs are used for control-of-use, with each country having its own pests, use patterns and use instructions, national MRLs are different from one country to another.
- Export food commodities, although meeting their own national MRLs, may not meet the importing country MRLs, leading to a trade dispute or incident (the imports are not allowed to be sold).
- Residues in food are presumed to be a consumer risk in each country until they have been fully evaluated and MRLs (or exemptions) established and the uses are registered.

Codex MRLs as trade standards

- Codex MRLs were introduced to deal with this situation.
- The SPS* agreement states that Codex standards and documents are taken to be the international consensus and can therefore be used as the presumptive levels in the event of a trade dispute.

**Sanitary and Phyto-Sanitary*

Conclusions

- There are many similarities in pesticide evaluation at the national and international levels.
- The international standards (Codex) rely on data and information from the national registration systems.
- Codex standards aim to protect the health of consumers and to serve as globally uniform standards for international trade.