MODALITIES AND PROTOCOL FOR FIXATION OF MRLs IN MILK AND MILK PRODUCTS INCLUDING RISK ASSESSMENT

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What is a residue?
How it comes in milk?
Establishing MRLs
  • Risk Assessment (RA)
  • Protocol for RA Steps
  • Modalities
  • National
    – Harmonization with Codex
    – Challenges
    – Further action
WHAT IS A RESIDUE?

• Undesirable chemical
• **Intentional use**
  – Ongoing
  – Past
• Enters food
• Contaminant *(unintentional presence)*
• Examples
  – Plants : Pesticides - Excludes fertilizers, plant nutrients, feed additives
  – Animals : Veterinary drugs
• Parent compound, metabolite, toxic impurity
HOW DOES IT COME IN MILK?

Major Routes

Pesticides
- Sprays for storage
  - Agricultural crops
    - Contaminated feed, fodder, water
      - Ectoparasite control
        - Milk producing animals
          - Stability/solubility/degradation
            - Soil Manure
              - Milk
                - Milk products

Veterinary drugs
ESTABLISHING MRLs: RISK ASSESSMENT

• Risk = \( f \) (Hazard x Exposure)

• Risk assessment
  – Hazard identification
  – Hazard characterization
  – Exposure assessment
  – Risk characterization
# ESTABLISHING MRLs: RISK ASSESSMENT

<table>
<thead>
<tr>
<th>Hazard Identification</th>
<th>HI</th>
</tr>
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<tbody>
<tr>
<td>Registered for use</td>
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<tr>
<td>Data availability (FAO manual on the submission and evaluation of residue data for the estimation of maximum residue levels in foods and feed, 2002)</td>
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<tr>
<td>Results in residue in food</td>
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<table>
<thead>
<tr>
<th>Hazard Characterization</th>
<th>HC</th>
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<tbody>
<tr>
<td>Data adequacy assessment</td>
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<tr>
<td>Health-based guidance value (ADI/ARfD)</td>
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<table>
<thead>
<tr>
<th>Exposure Assessment</th>
<th>EA</th>
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<tr>
<td>Chronic/Long term: GEMS/National diets data x STMR (Pesticides)</td>
<td></td>
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<tr>
<td>Theoretical food basket x STMR (VD)</td>
<td></td>
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<tr>
<td>Acute/Short term: Large portion x HR (Pesticides)</td>
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<table>
<thead>
<tr>
<th>Risk Characterization</th>
<th>RC</th>
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<tr>
<td>Comparison of exposure with health-based guidance value</td>
<td></td>
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<tr>
<td>Recommendations</td>
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</table>
RISK ASSESSMENT: PROTOCOL

Investigations with laboratory animals

Subchronical and chronical effects

No effect level

Safety Factor → E.g. 10x10

Health-based guidance value (e.g. ADI)

Teratogenicity
Carcinogenicity
Mutagenicity
Immunopathology etc.

Body weight

e.g. \( \text{ADI}_{BW} \)

Health-based guidance value (e.g. ADI)

Safety Factor

Subchronical and chronical effects

No effect level
HEALTH-BASED GUIDANCE VALUE

• A numerical value derived by dividing a point of departure (e.g. no-observed-adverse-effect level) by a composite uncertainty factor to determine a concentration that can be ingested over a defined time period (e.g. lifetime or 24 hours) without appreciable health risk.

• ADI=Acceptable Daily Intake: The daily dosage of a chemical which, during an entire lifetime, appears to be without appreciable health risk

• ARfD=Acute Reference Dose: The estimate of the amount of a substance that can be ingested in a period of 24 hours or less without appreciable health risk.
RISK ASSESSMENT: PROTOCOL

PESTICIDES

Metabolism & distribution studies

Field trials & GAP

Residues for risk assessment

Marker ("enforcement") residue

STMR; HR

MRL

Intake assessment (regional/national diets)

Intake ≤ ADI; ARfD

Recommend MRL

Intake > ADI; ARfD

Recommend MRL,
state if ADI or ARfD is exceeded

EA

RC
RISK ASSESSMENT: PROTOCOL

VETERINARY DRUGS

Metabolism & distribution studies → Marker residue ← Total residue

Field trials & GPVD → Depletion curve & confidence interval → Median residue

1. estimate

ADI

2. estimate

Intake ≤ ADI
accept MRL; option to adjust MRL

Intake > ADI
adjust MRL or MRL not recommended

FAO/WHO EHC 240
REFINING EXPOSURE ESTIMATE

Screening method → Point estimate → Probabilistic method

Improved food consumption data quality

Regional diets → Model diets → Household diets → Individual diets

Methods used for estimating exposure → As consumed levels → Total diet studies

Monitored levels → Reported use levels → Maximum levels in standards

Improved chemical concentration data quality

Least time consuming, fewer data required and least cost → Most time consuming, more data required and greatest cost

FAO/WHO EHC 240
<table>
<thead>
<tr>
<th>Pesticide</th>
<th>ADI(mg/kg body Weight)</th>
<th>ADI per person (mg/per person of 50 kg) (ADI*50)</th>
<th>Food Commodity</th>
<th>Residue generated under supervised trials mg/Kg</th>
<th>Waiting period (days)</th>
<th>Food Consumption (g/person)</th>
<th>TMDI (mg/person/day)(Col 3xCol 5/1000)</th>
<th>ΣTMDI (mg/person/day)</th>
<th>% ADI</th>
<th>Codex MRL</th>
<th>Proposed MRLs mg/kg</th>
<th>Methodology</th>
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<tr>
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<td>Milk and milk products</td>
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<td>0.2</td>
<td>GC-MS</td>
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**STMR**

**MRL**
ESTABLISHING MRLs: RELATED MODALITIES

General
• Scientific uncertainties/variability
• Residue definition
• Food/commodity definition/description
• Prevailing residue levels
• Banned chemicals (Negative List)
• Non-registered chemicals and import
• EMRLs (Pesticides)
• Antimicrobial resistance (Antimicrobials)
• Analytical methods
• Periodic review
ESTABLISHING MRLs: RELATED MODALITIES

Milk

• Susceptible population: Milk consumed by children
• Biological filtration by animal
• Withdrawal period (Veterinary drugs)
• Partitioning of residue (Pesticides)
  – Identify as ‘fat soluble’: MRL applies to whole milk
    (For a "milk product" with a fat content less than 2%, the MRL applied should be half those specified for milk. The MRL for "milk products" with a fat content of 2% or more should be 25 times the maximum residue limit specified for milk, expressed on a fat basis.)
  – Establish MRL for milk and fat separately
NATIONAL: HARMONIZATION WITH CODEX

PESTICIDES

MRL / Tolerance Limits of Insecticides (Includes Herbicides, Fungicides, etc) in various commodities

- Registered under Insecticides Act, 1968
  - MRL fixed under FSSR
    - MRL retained as such unless there is a concern or new data available for modification appropriately.
  - MRLs not fixed under FSSR
    - Codex MRL exists
      - Codex MRL is at LOQ
        - Adopt as such
      - Codex MRL above LOQ
        - Perform risk assessment taking Codex Value
        - Exposure within acceptable range - Adopt Codex MRL
        - If within acceptable range, the Codex MRL will be accepted.
    - No Codex MRL
      - Monitoring data made available (e.g. through ICAR system)
      - MRL using OECD calculator and perform risk assessment
      - Exposure not within acceptable range - the refinement for risk assessment to be conducted
      - Exposure not within acceptable range
        - If not within acceptable range -
          - Write to CIB&RC to delete label claim on specific commodities.
          - Default ** Tolerance Limit of 0.01 mg/kg will apply.
          - Default Tolerance Limit subject to review on the basis of availability of relevant data.

- Not Registered under Insecticides Act, 1968
  - Default ** Tolerance limit of 0.01 mg/kg

- Banned under Insecticides Act, 1968
  - Monitoring data indicates residues at LOQ^2
  - Monitoring data indicates residues above LOQ^2
    - E-MRL of 0.01 mg/kg
    - E-MRL based on monitoring data to be fixed using OECD calculator. On the basis of continuous monitoring data E-MRL to be reviewed after 5 years until it attains LOQ.

FSSAI

‘HARMONIZATION’ IS NOT SIMPLE ‘ADOPTION’
ESTABLISHING MRLs: CHALLENGES

- Data availability and adequacy
- Availability of expertise
- Functional separation in the roles of risk manager and risk assessor
- Documentation and follow-up actions
- Assessing cost vs. level of accuracy
ESTABLISHING MRLs: FURTHER ACTIONS

• Collaborate with relevant institutions for planned data generation/sharing
• Training to develop expertise
• Emphasis: Effective documentation of risk assessment/management activities
• Sustained follow-up to address data gaps and uncertainties identified
• Periodic review
THANK YOU
IMPLICATIONS

• Health hazards to consumers
  
  • **Adverse effects**: toxicity, teratogenicity, carcinogenicity, mutagenicity etc.
  
  • **Microbiological risks**: favouring resistant or pathogenic microorganisms in the intestine, development of drug resistant strains
  
  • **Immunopathological effects**: allergies

• Technological problems to food processor – culture failures
IMPLICATIONS

• Proper use - beneficial

• Excessive / improper use - presence in food in unsafe amounts

Safe food - primary concern
### RESIDUE LEVEL VS. LIMIT

#### Level
- Amount of chemical (pesticide) estimated to be present in food with attendant uncertainties
- Relevant good practices (GAP)
- Comparison with health-based guidance value like ‘Acceptable Daily Intake (ADI)’

#### Limit
- Amount of chemical (pesticide or veterinary drug) allowed to be legally present in food
- Relevant good practices (GAP, GPVD)
- Foods complying with ‘limit’ are toxicologically acceptable

<table>
<thead>
<tr>
<th>Level</th>
<th>Limit</th>
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<tbody>
<tr>
<td>(Risk Assessment)</td>
<td>(Risk Management)</td>
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The chart illustrates the distinction between residue levels and limits, highlighting the process of risk assessment and risk management in the context of pesticide residue management.
PESTICIDES AND ITS RESIDUE

**Pesticide** means any substance intended for preventing, destroying, attracting, repelling, or controlling any pest including unwanted species of plants or animals during the production, storage, transport, distribution and processing of food, agricultural commodities, or animal feeds or which may be administered to animals for the control of ectoparasites. The term includes substances intended for use as a plant growth regulator, defoliant, desiccant, fruit thinning agent, or sprouting inhibitor and substances applied to crops either before or after harvest to protect the commodity from deterioration during storage and transport. The term normally excludes fertilizers, plant and animal nutrients, food additives, and animal drugs.
PESTICIDES AND ITS RESIDUE

• **Pesticide Residue** means any specified substance in food, agricultural commodities, or animal feed resulting from the use of a pesticide. The term includes any derivatives of a pesticide, such as conversion products, metabolites, reaction products, and impurities considered to be of toxicological significance.
VETERINARY DRUG AND ITS RESIDUE

• **Veterinary Drug** means any substance applied or administered to any food producing animal, such as meat or milk producing animals, poultry, fish or bees, whether used for therapeutic, prophylactic or diagnostic purposes or for modification of physiological functions or behaviour.
Residues of Veterinary Drugs include the parent compounds and/or their metabolites in any edible portion of the animal product, and include residues of associated impurities of the veterinary drug concerned.