Contribution of vigilance data to the risk assessment of pesticides

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Background

- **Regulatory framework**
  - Several EU Regulations require the notification and/or collection and/or reporting of adverse events caused by pesticides in humans
  - Acute or chronic, in the general population or agricultural workers
  - Work-related, accidental, misuse, deliberate poisoning
- **Dir. EC 128/2009 on sustainable use of pesticides**
  - "Member States shall put in place systems for gathering information on pesticides acute incidents… operators, agricultural workers or persons living close to pesticide application areas"
  - "The Commission in cooperation with the MS shall develop… a strategic guidance document on monitoring and surveying of impacts of pesticide use on human health"
- **PPP and active substances: Reg. EC 1107/2009, 283/2013**
  - Submission of human data at the time of the re-approval process
  - Post-market monitoring: continuous follow-up process, detection of new/emerging risks

Public health surveillance systems

- **Two approaches**
  - Population level: epidemiological studies
  - Individual level: reports of case incidents
- **A few definitions**
  - Survey: single effort to measure and record something
  - Surveillance: repeated standardised surveys to detect trends in populations: absence or presence and distribution of a disease
  - Monitoring: intermittent analysis of routine measurements and observations: detection of changes in health status of a population
  - Vigilance: activities relating to the detection, assessment, understanding and prevention of adverse events. Combines surveillance and monitoring
- **Types of systems**
  - Active; passive; sentinel
  - Work-related disease surveillance systems; occupational disease registries
  - Non specific recording systems: Poison Control Centres (PCCs)
  - EU alerting system on chemical hazards: RASCHEM

Characteristics of collected data

- **Reporting mechanism**
  - Based on obligatory or voluntary notification (e.g. vigilance)
  - Reporters: occupational physicians or nurses, GPs, employers, workers
  - Review of clinical cases collected by non specific systems e.g. PCCs: general population, employers, workers, physicians,…
- **Data collected**
  - Worker's gender, date of birth, age, occupation and sector of professional activity, exposure, duration of exposure, diagnosis, symptoms, time of onset of symptoms, past medical history, level of imputability (case causality assessment)
  - Quality of data: data reviewed by experts
- **Dissemination of results**
  - Annual reports to the government; summary reports in scientific journals

Key limitations

- **Heterogeneity within MS**
  - Reporting scheme based on obligatory or voluntary notification
  - Schemes not specifically designed for pesticides: e.g. poor data on exposure; mixed exposures: PPPs, biocides, other chemicals
  - Voluntary reporting: not extensive
  - Lack of harmonisation: accuracy of information; exposure assessment; assessment of causal relationship between exposure and adverse effects
  - Accessibility of information: data not publicly available
- **Link with prevention**
  - Depending on policy-makers' and stakeholders' interest

→ **No unified reporting scheme in the EU**

Use of surveillance and vigilance data in the RA of pesticides: AS

- **Re-approval of AS process: section 5 of Reg 283/2013 – Mammalian toxicity**
  - **Chapter 5.9 "Medical data"**
    - Medical surveillance on manufacturing plant personnel
    - Direct observations: clinical cases, poisoning incidents
    - Epidemiological studies
  - **Other chapters: hazard identification for every endpoint**
    - Acute and short term toxicity, all routes
    - Skin, eye, respiratory irritation, sensitisation: occupational exposure
    - Genotoxicity: human material
    - ADME studies
      - biological measurements after acute exposure (clinical cases)
      - biomonitoring performed in the context of occupational surveillance

        → dose-response relationship; AOEL

Use of surveillance and vigilance data in the RA of pesticides: PPP

Re-registration process of PPPs

Application of all human data information compiled on the PPP which is in the re-registration process

- Identification of new/emerging hazards e.g. irritancy, sensitisation, other work-related troubles
- Identification of high risk situations e.g. worker re-entry after spraying, accidental splashing during opening of packaging or spilling during tank loading, …
- Detection of emerging health problems related to
  - Occupation, mode of application, …
  - Personal protective equipment (PPE)
  - Misuse

→ **Risk assessment**

→ **Risk management decisions: revision of the conditions of PPP authorisation**

An example: the Phyt'attitude network-France

- Established by the health and social insurance organisation for agricultural workers
- Based on a network of 35 regional centres for occupational medicine
- Voluntary reporting by occupational physicians or nurses, agricultural workers, farmers,…
- Free phone number

Phyt'attitude
Signalez-nous vos symptômes
N° Vert 0 800 887 887
APPEL GRATUIT

- Data collected
  - Name of PPPs, sector of activity, job, crop, task at the time of the incident, duration, wind speed and temperature, wearing of PPE
  - Signs and symptoms, past medical history, clinical course, treatment
  - Records are reviewed by a clinical toxicologist; setting of a level of imputability to each couple trouble-PPP (imputability scale derived from that used in pharmacovigilance) and a final imputability for the case

Proposals for improvement of case incidents reporting - national level

- Increase the reporting of acute and chronic incidents by setting up post-marketing surveillance programmes (occupational and general population)
- Develop surveillance networks with occupational health physicians
- Improve the collaboration between PCCs and regulatory authorities in order to collect information on all PPP poisonings
- Improve training regarding pesticide toxidromes in toxicology courses for medical and paramedical staff responsible for diagnostic decisions, data entry and management

Towards a unified vigilance scheme in the EU?

- Harmonisation of human incident data collection activities at the EU level
- Development of a valid method for assessing the weight/strength of the causal relationship ('imputability') for acute (and chronic) incidents
- Development of glossaries and a thesaurus to support harmonised reporting between EU Member States
- Coordination of the compilation of EU-wide databases
  - Harmonised data from Member States should be gathered at the EU level
  - Periodical examination of the data by the Commission/EFSA
  - Issue of a report focusing on the most relevant findings

→ Develop an EU-wide vigilance framework for pesticides

Towards pesticidovigilance?

Or

“pesticidosurveillance”?

“PPPvigilance”?

“PPPsurveillance”?

“phytopharmacovigilance”?

“…”

Thank you!