Integration of epidemiology studies in pesticide risk assessment

Scientific conference on the use of epidemiological findings in regulatory pesticide risk assessment
EFSA – Parma - 21/11/2017
Martin Dermine – Pesticide Action Network Europe

Very clear requests from the legislator...

- Reg. 1107/2009: Art. 4(1): An active substance shall be approved in accordance with Annex II if it may be expected, **in the light of current scientific and technical knowledge** (...) that active substance meet the requirements provided for in paragraphs 2 and 3

- Not properly implemented : current work from academic world exceptionally taken on board

- “Epidemiological studies are of particular value and must be submitted” according to the Scientific Opinion on epidemiological studies (2017)

Very clear requests from the legislator...

- Reg 1107/2009: Art. 8(5): **Scientific peer-reviewed open literature**, as determined by the Authority, on the active substance and its relevant metabolites dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of the dossier shall be added by the applicant to the dossier

- EFSA has an important discretion on how far it decides to include peer-reviewed science

EFSA 2011 Guidance Document on inclusion of peer reviewed science in R.A.

- Draft did not include classifications (e.g. Klimisch rating)
- PPPR panel requested to include it
- "Systematic review" was transformed to "Nearly systematic rejection" because of classification tools.
- "*It must be emphasised that compliance with good laboratory practice (GLP) standards should not be considered as a guarantee of reliability. Study reliability must be judged solely on the basis of the accuracy and reproducibility of the facts reported*".

Classification loophole is massively used by industry in its literature review

- “Missed and Dismissed report” (PAN Europe, 2014): For a sample of 9 pesticides, **only 23%** of 453 major toxicity studies were identified by industry, while **100% (of the 23%) was dismissed**, using the controversial Klimisch/BASF method.
- = No systematic review of peer reviewed science
- EFSA nor (Rapporteur) Member States complained...

Current pesticide R.A./R.M. insufficient to protect people...

Fruit and vegetable intake and their pesticide residues in relation to semen quality among men from a fertility clinic

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Chiu *et al.* 2015

Association Between Pesticide Residue Intake From Consumption of Fruits and Vegetables and Pregnancy Outcomes Among Women Undergoing Infertility Treatment With Assisted Reproductive Technology

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Chiu *et al.* 2017

Current pesticide R.A./R.M. insufficient to protect people...

Instituts thématiques

Inserm

Institut national de la santé et de la recherche médicale

Paris, June 12, 2013

Press release

Pesticides and their effect on health

An Inserm group of experts

Since the eighties, epidemiological research has been looking into how pesticides are involved in several pathologies in persons who are exposed to these substances in the course of their work, in particular cancerous pathologies, neurological pathologies and reproductive disorders. These investigations have highlighted the potential effects of even low levels of exposure during the sensitive periods of development (in utero and during childhood).

In this context, the DGS (Direction Générale de la santé – the public health authority)

INSERM 2013

Prenatal exposure to the organophosphate pesticide chlorpyrifos and childhood tremor

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Rauh *et al.* 2015

OECD protocol studies present major weaknesses

- Regulatory testings are narrow-focussed (reproductive toxicity, carcinogenicity...)
- OECD tests very insensitive and not testing real doses comparable to exposure
- Many OECD protocols are decades old and miss relevant endpoints (endocrine disruption, immunotoxicity, developmental neurotoxicity, etc.)
- Carried out by industry itself (major conflict of interest, source of bias and fraud)

EFSA disregards epidemiology studies

- Actual exposure to pesticides and its consequences need to be considered as priority
- Studies showing serious clinical effects are considered of weak evidence in EFSA's opinion, despite reflecting real life situations
- The discrepancy between IARC and EFSA's approaches on glyphosate carcinogenicity brought publicity on this issue
- EFSA's 2015-meeting on epidemiology studies reported 'multiple limitations' and the need for 'standardisation'
- Standardising = weakening R.A.
- 'Klimisch' for epidemiology?
- Studies should be ranked based on their quality, not according to classification schemes

Need for a fair, open and balanced approach

- EFSA should have the same level of criticism for OECD regulatory studies as for peer-reviewed studies
- Conflict of interest of the authors/funders could also be part of the classification?
- “Monsanto-papers” give a flavour of the attempts of industry to get to obtain a desired outcome

EFSA 2017 scientific opinion on the use of epidemiological studies in R.A. (1)

- Standardisation eases work from risk assessors
- Standardisation = simplification = ticking boxes
- Standardisation = security
- Long range of conditions proposed (precise quantitative exposure assessment, random sampling, no chemical-specific exposure collected, control of confounders, a plausible mechanism is provided, etc.): 100% dismissal?

EFSA 2017 scientific opinion on the use of epidemiological studies in R.A. (2)

- Adverse Outcome Pathways: under research currently not to be included in the R.A.
- Biological relevance should be considered as a confirmatory tool
- AOP = simplification = reversing precautionary principle
- Repeated correlations = precautionary principle
- Use of AOP will increase the dismissal of studies

Conclusions

- Reg. 1107/2009 indicates that all available data have to be taken into account
- Such a scientific opinion might lead to dismissing numerous valuable studies
- Epidemiology studies should ‘correct’ the weaknesses of the current R.A. Process
- Scientific excellence ≠ ticking boxes
- Diversity in science is a richness we have to favour
- Monocultures are weak and ill

Conclusions

- This scientific opinion should be reviewed by independent experts in epidemiology
- Epidemiology studies should prevail for regulatory decisions (real-life)
- If correlation between a pesticide and health/environmental impact: immediate ban. Humans ≠ guinea pigs
- EFSA's primary goals diserve excellence in science