

Pesticide assessment

Project Coordinator, **Ir Jacob van Klaveren**, explains the work and directions of the ACROPOLIS initiative, as it develops a Europe-wide standard for pesticide risk assessment

The Euro-barometer show pesticides as one of the principal worries of EU consumers regarding food safety. Given this consumer concern over exposure to agrochemicals, how urgent is the economic case for improving risk assessment strategies?

Pesticide residues on foods are one of the principal worries of EU consumers when it comes to the risks associated with their food. As this worry is increasingly linked to the incidence of multiple residues, the development of methodologies to account for these residues and their effects could alleviate consumer concerns. This is particularly relevant for fresh produce, as consumers often associate pesticide residues with unprocessed products such as fruit and vegetables. Confidence in the safety of fruit and vegetables must not be eroded given the overwhelming health benefits of a diet rich in fruit and vegetables.

Until now, cumulative risk assessment has not been part of risk management and consequently it is not known whether there is a risk or not. The lack of a methodology in itself is the principal worry of consumer groups.

The research of ACROPOLIS contributes to the development of a methodology to ensure that the missing aspects in the risk assessment of pesticides can be addressed in future risk management. This will increase trust of the consumer in the safety regulation of pesticides. Greenpeace is a consumer group and a member of the Scientific Advisory Board of ACROPOLIS. Their concerns regarding current risk assessment can be expressed on this board and they might address their opinions and wishes for future developments in pesticide risk assessment.

In general, it is not to be expected that the new methodologies will identify more risk related to public health, since the current standard setting methodology uses the precautionary principle. However, it is often unknown how much precaution has been built into the risk assessment, because the current approach fails to separate and visualise variability, uncertainty and safety factors. ACROPOLIS will build upon this approach to visualise the three different elements.

Are there any achievements you would like to highlight from the project since its inception earlier this year?

Our partners have started to make their food consumption data compatible with the

probabilistic models to calculate exposure assessment. This was according to the agreement made in the ACROPOLIS proposal. France and Belgium have added consumption databases to this platform because they are convinced that ACROPOLIS is a promising tool for risk assessment at the national level in the nearby future. This was not planned as part of the initial ACROPOLIS project and can be regarded as a successful extension of the approach.

You aim to organise stakeholder conventions as part of the project. How do you envisage the interaction of commercial, government and consumer groups? How will the project facilitate and manage these relationships?

Stakeholder conventions will be an important and challenging part of the ACROPOLIS project. For new methodologies to be accepted, it always takes time; they can be hampered by a lack of understanding or by disagreement. It is therefore important to better understand the attitudes of institutes or persons responsible or linked to pesticide risk assessment. Consumer groups, non-governmental organisations, retailers, regulators, quality managers of multiple food suppliers, producers and the pesticide industry will be interviewed regarding their attitude towards cumulative and aggregate exposure. Information will be collected through expert in-depth interviews with stakeholders or their representatives. Besides assessing potential opportunities, threats, strengths and weaknesses from the stakeholders' perspective, the level of understanding of different concepts of cumulative risk assessment, including probabilistic methodologies and perceived information needs, will also be explored. This will be reported and will form the basis for the first stakeholder meeting and for further quantitative assessment of attitudes.

The aim of the stakeholder conferences is to raise understanding of the concepts of cumulative and aggregate exposure assessment methods including probabilistic modelling. It will not interfere with policy decisions on the acceptance of cumulative and aggregate exposure assessment by the European community, nor will it interfere with the risk management issues (eg. cut-off criteria). This is a responsibility of agencies such as EFSA or DG Sanco.



Chemical check

The impact of pesticides on food safety is of serious concern to European policy makers and the general public. With this in mind, the **ACROPOLIS** project is developing new measures, tests and tools for the industry and regulators to prove that pesticide use is safe

WHEN AUTHORISING NEW pesticides for the European marketplace, producers have to perform toxicology and field trial studies to prove that the product can be used safely without resulting in unacceptable residue levels. However, according to recent European law, assessment of cumulative and aggregate exposure needs to be developed as soon as possible to estimate safe maximum residue limits that take into account the 'cumulative and synergistic effects of pesticides' (as stated in Regulation (EC) No. 396/2005). The Europe-based project ACROPOLIS (Aggregate and Cumulative Risk Of Pesticides: an On-Line Integrated Strategy) is developing a scientifically sound but accessible framework to address this need in the future. The team's work will fill the gap in the methodology as mentioned in the law, and industry might have improved guidelines helping them in future investments.

BUILDING CONSENSUS

Creating a new pesticide is an expensive business, as Ir Jacob van Klaveren, Project Coordinator and Head of the Department of Databases and Exposure Assessment of the National Institute for Public Health and the Environment, is well aware: "Development of a new active substance is a significant investment with an estimated 10 year development time," he asserts. Without an agreed methodology, the process could be more costly, lengthy and investment more difficult: "A lack of consensus on the methodology and a limited access to models and data might hamper clear investment strategies," warns van Klaveren. Furthermore, the lack of a lucid framework for the industry could prove an obstacle to the introduction of new pesticides; "An inability to

accurately predict that a product is registrable early in development," he says, "will hamper efforts and investments".

There are three major limitations to current risk assessment models that ACROPOLIS can improve upon. Firstly, current methods only address one food item at a time when a pesticide may occur on a variety of food stuffs. Secondly, several pesticides also share a common toxicological effect but the possible cumulative effect within the human body is not considered. Lastly, pesticide exposure can occur through a number of sources, including food, dermal exposure, inhalation during spraying or using pesticide within the home in the form of consumer products. ACROPOLIS aims to introduce a comprehensive method that will solve these problems. Working towards this is a consortium of 11 different participants from universities and regulatory bodies. Van Klaveren is convinced that close collaboration is crucial, in order to ensure the project outcomes are effective: "Different partners with ACROPOLIS have already agreed upon a common modelling approach to guarantee a uniform, efficient and integrated platform useful for all stakeholders," he states. "The positive approach between partners has been in place since the beginning of the project, which reflects the enthusiasm and consensus among the partners responsible for model development."

IMPROVING ASSESSMENT

The overarching objective of ACROPOLIS is to improve risk assessment strategies in Europe. The team have divided this into five specific aims:

- Improved cumulative exposure assessment and

INTELLIGENCE

ACROPOLIS

AGGREGATE AND CUMULATIVE RISK OF PESTICIDES: AN ON-LINE INTEGRATED STRATEGY

OBJECTIVES

The project will develop a framework for cumulative and aggregate risk assessment of pesticides that is scientifically sound and accessible for all actors involved in the European risk assessment and risk management.

PARTNERS

- **National Institute for Public Health and the Environment**, The Netherlands
- **The Food and Environment Research Agency**, UK
- **University of Milano**, Italy
- **National Research Institute for Food and Nutrition**, Italy
- **Institute for Risk Assessment Sciences - Utrecht University**, The Netherlands
- **Health and Safety Executive - Chemicals Regulation Directorate**, UK
- **National Institute of Public Health**, Czech Republic
- **Freshfel Europe**, Belgium
- **National Food Administration**, Sweden
- **Ghent University**, Belgium
- **Wageningen University and Research Centre**, The Netherlands

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JACOB VAN KLAVEREN studied Human Nutrition at Wageningen University. He became an advisor for the national government and international bodies such as WHO, EFSA and the European Commission on various food safety issues. He is currently head of the Databases and Exposure Assessment Department at the Dutch National Institute for Public Health and the Environment.



Acropolis aims to improve understanding of risk assessment of pesticide use in foods

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cumulative hazard assessment methodology

- The development of new models for aggregated exposure assessment addressing different routes of exposure
- Setting up new toxicological testing for identifying possible synergistic effects and developing a strategy for refinement of cumulative assessment groups
- Integrating cumulative and aggregate risk models into a web-based tool (including accessible data for all stakeholders)
- Improving the understanding of cumulative risk assessment methodology of stakeholders

ACROPOLIS's new toxicology testing is a crucial part of the project's strategy. Initial classification of pesticides under the European Food Safety Authority (EFSA) will be based on the chemical structure, the mechanism of pesticide action, the general mode or mechanism of mammalian toxicity, or the particular toxic effect. Refinement then comes through a detailed evaluation of available toxicology data for each substance to identify those causing a common toxic effect. The next step in the refinement requires the determination of the toxic mode/mechanism of action by which each substance causes the defined common toxic effect.

ACROPOLIS is currently exploring the use of *in vitro* testing, with a view to assessing the method for use in the final framework, as van Klaveren explains: "*In vitro* testing might prove to be useful instruments to exclude or include a pesticide in a common assessment group". The *in vitro* testing will use conazole fungicides that are widely used in Europe. The ACROPOLIS researchers are testing different conazoles: "The first step of this project will be a check of several

conazoles to identify those able to induce the toxic effect," illustrates van Klaveren. "If an effect is not measured, the tested pesticide will be excluded from the common assessment group." In addition, tests will look at the combined effect of conazoles by exposing the *in vitro* cells to a mixture of conazoles. If the team's *in vitro* tests are successful then further tests of this kind may prove useful in future refinements within the cumulative risk assessment strategy.

USING THE WEB

The web-based tools are already being implemented for the safety assessment of single pesticides. Currently the web interface is based on Monte Carlo Risk Assessment (MCRA) software available via the web (www.mcra.rivm.nl). It is made up of models addressing acute and chronic risks of pesticides and many other kinds of chemical: "The current models address both short-term exposure to acute toxic pesticides as well as long-term exposure to chronic toxic pesticides," explains van Klaveren, who is confident about the next steps for the ACROPOLIS team. During the next year, the project's cumulative exposure models will be made available via the MCRA programme, with data made available to stakeholders as well as the extension of models addressing uncertainty. The second half of the ACROPOLIS project will integrate Bench Mark Dose Modelling and exposure modelling. Dissemination will come through stakeholder conventions. Training will be provided to industry on how to use the models for the preparation of dossiers relevant for authorisation of new pesticides as well as training for Regulators and EFSA to check the correctness of the calculations submitted to them.

MEETING EUROPE'S NEEDS

Despite encouraging progress to date, there are some challenges ahead for ACROPOLIS. There is very little information available regarding the internal distribution and metabolism of pesticides within the body, and the project's *in vitro* tests do not take into account possible metabolism or distribution. The team will produce a literature review to investigate internal dose monitoring to try and solve this; indeed, the future looks bright for ACROPOLIS. Relatively little is known about different exposure routes. For example, a pesticide can be ingested via food, via dermal contact or via inhalation using pesticides in the field or inside the home. Farmers' behavioural patterns, such as the frequency they use protective clothing, might be better understood in future European projects to fill gaps and hopefully this can be linked to ACROPOLIS models." It seems that in the near future, ACROPOLIS will be able to meet Europe's need for aggregate exposure assessment more fully. The ACROPOLIS team will bring together the leading models in all relevant exposure routes.

The overarching objective of ACROPOLIS is to improve risk assessment strategies in Europe

