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Drug residues in aquatic environments Needs and tools for monitoring and risk evaluation

A colloquium organised by Onema under the dual aegis of the ministries of health and ecology.

Monitoring drug residues in our aquatic environments and evaluating the risk for the environment and human health was at the core of the seminar organised by Onema on 25-26 May in Paris. Nearly 80 health and environment specialists came to share their expertise. The objective? Set down the basics for a joint effort programme to increase knowledge and contribute in developing the national inter-ministerial plan on drug residues in water.

For two days, researchers, stakeholders in water policy, experts from the health and environmental agencies as well as from the drug and water treatment industries met in Paris to take stock of the situation and needs in terms of monitoring and evaluating the risks associated with the presence of drug residues in aquatic environments. This seminar, organised by Onema, under the dual aegis of the health and ecology ministries, benefited from the strong involvement of the French scientific council on water and aquatic environments.

The challenges in acquiring knowledge on a European scale are substantial: this entails identifying the drugs and the aquatic compartments to be investigated in order to develop coherent monitoring strategies. This also involves developing suitable modelling tools and suitable ecotoxicological tests in order to assess the risks linked to the presence of these molecules in the environment. Such efforts are already underway in Great Britain, Germany and Sweden via the national environmental agencies.

Aquatic environment contamination is frequent but low

In France, an analysis of about thirty studies conducted over the last ten years within the framework of the national health and environment plan confirms the presence, as trace contamination (nanogrammes per litre), of drug residues – hormones, antibiotics, anti-inflammatory drugs, antineoplastics… – in the great majority of the natural aquatic compartments, especially in surface water but also in groundwater. What is the source contamination of these environments? Primarily, household wastewater, as water treatment plants do not often provide an effective barrier in eliminating these residues. In particular, small hydrosystems are potentially vulnerable due to the low dilution of the discharges and less-advanced wastewater treatment systems.

It is still however difficult to establish a diagnostic as the data is limited and it cannot always be extrapolated: 25% of the studies address only ten pharmaceutical molecules, little data exists on the presence of degradation products for these compounds as well as concerning veterinary drugs. There is also a lack of studies on the presence of these substances in the sludge from treatment plants, the soils and sediments.

Drug residue, present as trace contamination in aquatic environments.

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Wastewater, a source of contamination for aquatic environments.

Report from **Anne Morin,** coordinator of the «Water quality» programmes, department of chronic risks - Ineris - Aquaref Coordinator.

Prioritising the substances to monitor: this requires sharing information

In order to prioritise the substances to be monitored in aquatic environments, the criteria to be taken into account are of three types: the physical-chemical (solubility, persistence…), toxicological and ecotoxicological properties of the substances and how many tonnes are placed in the market, as well as their presence in the environment. And this, regardless of the target taken into account, the environment or humans, and regardless of the classification method selected.

Although the concentration of the substances in the environment can be modelled, sufficient monitoring data has to be available in order to validate the models that are developed. The lack of such data for the emerging substances makes difficult their inclusion in the current exercise of revising the list of priority substances for the Water Framework Directive.

In order to overcome this problem, the European network NORMAN is attempting to collect the information stemming from campaigns carried out in the environment by various teams in the member states of the European Union. In parallel, the data collected in France has to be gathered and, ultimately, a harmonised format for collecting this data has to be imposed so that it can be used by the greatest number, for health or environmental reasons. Sharing the results of existing programmes has to be organised at the national level in order to best serve the various objectives: the national health and environment plan, the drug residues plan, the national substances in aquatic environments plan.

There is still a lack of monitoring tools and methods

The physical-chemical analytical methods available today reveal their limits when used to assess exposure and toxicity at a low dose. As such, interpreting the results in terms of the presence or absence of drug residue in aquatic environments is highly dependent on the performance of the analytical method. That is why experts insist on the need to standardise the methods used by the analytical laboratories.

Are these substances with a low dose toxic for aquatic ecosystems? Except for the case with hormones, for which the environmental impact has been demonstrated (feminisation of fresh water fish), scientists are raising the question. It has been possible to demonstrate effects in the laboratory for other drug residues but the results are yet to be validated in the field. However, there is a lack in methods and tools for assessing this toxicity in situ. Experts particularly deplore the absence of tests for the chronic and enhanced effects of mixtures of substances at low concentration. Biomarkers could open up interesting perspectives here.

Evaluating the environmental and health risks

Scientists now agree on the fact that the ecological risk linked to the discharge of drug residues into water is much more significant than the health risk. Yet the stakes in studying the presence of drug residues in aquatic environments are shared by the health and ecology sectors: this involves proving objective elements that make it possible to accurately evaluate the levels of health and environmental risks in order to apply suitable management policies.


Michel Bramard - Onema

Launching of a study on site in order to understand the environmental pathways of drugs.


Madeleine Carrouée - Onema

Standardise the physical-chemical analytical methods for monitoring drugs in aquatic environments.

Report from **Yves Levi,** Public health and environment

For a rigorous,

Evaluating the risks linked to mixtures of emerging pollutants that are present in very low concentrations in the aquatic environments, especially those associated with residues from the many chemical families of drugs, is an absolute necessity in order to advisedly invest in the best-suited water management tools. The proven presence of the danger throughout the entire water use cycle requires developing a combined and ambitious approach for evaluating the risks. It will involve the acquisition of data pertaining to exposures – stability of the molecules, flow modelling, identifying major sources, defining priority

That is why, while taking the specificities of the two approaches into account, the efforts concerning knowledge on the presence and on the effects must today be conducted straight on and in a coordinated fashion, through cooperation between the health and environmental sectors.

Already, researchers are expressing the desire to be able to access the toxicological and pharmaceutical data provided by the pharmaceutical companies when filing for marketing authorisation (AMM) of new drugs. This would make it possible to save time in analysing the risks and avoid repeating tests that have already been carried out.

Toward an interdisciplinary programme for monitoring residues

All throughout these two days, Onema collected proposals that were made in order to improve knowledge. Recommendations were as such formulated after the seminar and presented to the National Scientific Board on Water and Aquatic Environments. With its partners, Onema has produced a strategic document in order to contribute in developing the «Knowledge» section of the future national plan on drug residues in water. It is promoting the organisation of an interdisciplinary programme for monitoring residues in the aquatic environment, including short-term operational objectives as well as research and development efforts to be implemented in order to improve the evaluation of the risks. Collective scientific expertise could be set up in order to structure some of these orientations.

Rapid mobilisation after the seminar

At the end of this seminar, involvement was organised quickly. Reflective work has already begun between Onema, the ministry of ecology and the water agencies to launch a national effort to acquire additional data. This action is particular aimed at launching a study campaign on pilot sites in order to better understand the transfer of certain priority molecules and thus know the impact of the drugs in the environment.

The sites will be distributed across the territory and selected to be representative of the pressures exerted – husbandry, fish farming, urbanism (hospitals, chemical/pharmaceutical industries) – and of the various aquatic environments – surface water, groundwater, coastal and estuary environments. These sites will make it possible to experiment with innovative analytical or biological technologies, and to increase the predictive capacity of the flow of drug residues into aquatic environments.


Little data exists on the presence of veterinary drugs. Michel Bramard - Onema


Report from **Jean-François Munoz,** Hydrology study and research laboratory, ANSES (French Agency for Food, Environmental and Occupational Health & Safety).

Controlling the quality of analytical methods and tools

The health and environmental regulatory monitoring system on the quality of water is based on a technical and accredited organisation that makes it possible to reach a high level of confidence in the data obtained. Validating the methods per matrix type (either water, suspended matter, or sediments, etc.), as well as performing standardisation and inter-laboratory tests, are required in order to demonstrate the performance expected from a laboratory.

The teachings from the inter-comparison tests between laboratories make it possible to reinforce the current study and research programmes, and also favor the standardisation approach for laboratories with a perspective on change in terms of monitoring. Entailing so-called emerging compounds, i.e. those that do not belong to the regulatory parameters pertaining to quality, such as drug residues, the existing experience does not yet make it possible to have any certainty (or minimal uncertainty) as to the best method for a matrix under consideration and with the best performance.

In order to assess these emerging issues well, it is indeed the entire process, from taking the sample to qualifying the compounds identified, that must be made reliable. Using techniques with increasingly higher levels of performance in order to detect traces and ultra-traces, controlling operating quality within each laboratory forms the framework of trust that is absolutely indispensable.

Laboratory, Université Paris Sud 11 – School of Pharmacy.

objective and verifiable assessment of the risks

target molecules, etc. – as well as developing knowledge on the complex mechanisms of the biological effects – ecotoxicology, ecology, health risk – of these mixtures at low doses. These actions are carried out in the middle and long term according to the complexity of the questions raised and the availability of exploratory tools. In order to change behaviours concerning the use of human and veterinary drugs or to justify a very expensive technological leap in treatment plants, the analysis of the risks must be very rigorous, objective and verifiable. It must combine scientific skills from many disciplines - ecology, microbiology, toxicology, analytical chemistry, process engineering, soft sciences, etc. The concern for drug residues in the environment indeed illustrates the major need to rigorously and objectively establish the prevention policies for the contamination of resources and improving the methods of treatment in order to reduce the mixtures of emerging micro-pollutants: drugs, plasticizers, hydrocarbons, flame retardants, persistent organic pollutants, etc.

Recommendations from the seminar

At the close of the seminar, the experts formulated recommendations in order to contribute to the development of the future national plan on drug residues in the water.

Improve the knowledge on substances in water

- issue and develop the criteria to quickly define the substances to be monitored with priority;
- select a representative sample of the study sites;
- optimise and intercalibrate the analytical techniques and methods;
- initiate targeted analytical campaigns in order to supplement existing knowledge;
- know and control the contamination of water resources used for the production of drinking water;
- examine the valorisation of innovating techniques to monitor and analyse substances;
- document the national groundwater and marine environments.

Needs in research

- develop tools for simulating the transfer of drug residues;
- develop chronic effect tests that are the most representative of the modes of action of the pharmaceutical compounds and of the receiving environments (mesocosms, mixtures of substances in low concentrations, bioaccumulation, enhancement of the effects linked to chronic exposure);
- develop biological indicators that make it possible to diagnose the presence in the environment of these pharmaceutical residues and to assess their effects;
- define toxicological thresholds;
- develop bioanalytical tools;
- study the possible relation between the presence of antibiotic residues and the appearance of an antibioresistance;
- study the effects on aquatic organisms of nanoparticles used in drugs;
- improve knowledge on the yield from eliminating drug residues at the drinking water production and treatment plants. Develop new elimination technologies;
- involve researchers in the social sciences, especially in the study of the acceptability of the risks.

Other major topics to be taken into account

- the presence and the impact of pharmaceutical product residues in the marine environment;
- antineoplastics and progestins;
- the impact on water, and on groundwater in particular, of spreading sludge and manure/liquid manure;
- taking into account sediments and groundwater, especially in the perspective of long-term monitoring.


Guillaume Czerw

A colloquium organised into three workshops:

- national framework: state of the situation and identifying needs in terms of monitoring
- existing means and optimising exploratory monitoring
- outlook for monitoring tools and risk evaluation

On 23 November 2009, the ministries in charge of health and ecology set up the national steering committee in charge of developing and monitoring the future national plan on drug residues on water.

For more information:
http://www.onema.fr/Residus-de-medicaments

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