ERAPHARM: A EUROPEAN PROJECT ON ENVIRONMENTAL RISK ASSESSMENT OF PHARMACEUTICALS

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Introduction

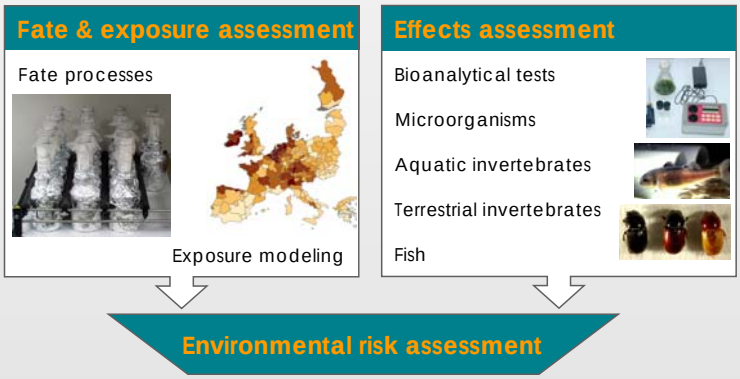
Within a process of international harmonization, guidance on the environmental risk assessment (ERA) of veterinary pharmaceuticals has been established (CVMP/VICH 2000, 2004). A European guideline on the ERA of human pharmaceuticals is being discussed (EMEA/CHMP 2005). However, there are still a number of uncertainties concerning the assessment of specific exposure pathways and potential environmental effects of pharmaceuticals. The overall aim of the EU-funded research project 'Environmental risk assessment of pharmaceuticals' (ERAPharm) is to advance the existing knowledge and to contribute to the improvement of procedures for environmental risk assessment of human and veterinary pharmaceuticals.

Two terrestrial field studies will be conducted within ERAPharm for investigating fate and effects of the parasiticide ivermectin:

(1) in North Europe (York, U.K.)

(2) in South Europe (Madrid, Spain)

Objectives



- To investigate factors and processes affecting the fate of pharmaceuticals
- To further develop testing and modeling approaches for evaluating fate
- To develop a system for scenario-based exposure assessments
- To explore the use of bioassays for initial hazard screening and mode-of-action classification
- To evaluate how information on pharmaco- and toxicodynamics in mammals can be used to target fish testing
- To adapt test methods for detecting possible effects of pharmaceuticals
- To investigate if environmentally relevant concentrations of pharmaceuticals cause effects in bacteria, invertebrates and fish
- To develop pragmatic approaches for assessing transformation products
- To provide recommendations on how to improve current European environmental risk assessment procedures for pharmaceuticals

Partners

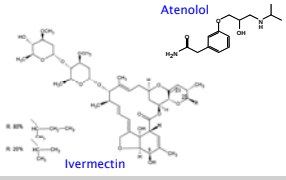
- ECT Oekotoxikologie GmbH, DE (co-ordinating partner)
- AstraZeneca UK Ltd., GB
- Brunel University, GB
- Federal Institute of Hydrology (BfG), DE
- Centre National du Machinisme Agricole du Génie Rural des Eaux et des Forêts (Cemagref), FR
- University of York, GB
- The Danish University of Pharmaceutical Sciences, DK
- Swiss Federal Institute for Environmental Science and Technology (Eawag), CH
- Geotechnisches Institut AG, CH
- Utrecht University, NL
- Instituto Nacional de Investigación y Tecnologia Agraria y Alimentaria, ES
- National Environmental Research Institute, DK
- Umweltbundesamt, DE
- Canadian Water Network, CA

Current state

- Methods for detecting the selected pharmaceuticals in water, sediment, soil, manure and sludge have been developed and adapted. First fate studies were performed on the laboratory and semi-field scale.
- European regions exhibiting a high risk for loss of veterinary pharmaceuticals from soils to surface water have been identified.
- The β-blockers atenolol, propranolol, metoprolol and sotalol were screened using a mode-of-action based set of bioassays.
- Microcosm experiments for investigating the effects of antibiotics on structure and function of microbial communities with special emphasis on the spread of genetically encoded resistance are being started.
- Effects of ivermectin and other pharmaceuticals on terrestrial invertebrates and plants have been studied using laboratory and semi-field tests.
- Long-term studies were carried out to investigate the effects of atenolol on pelagic invertebrates and those of ivermectin on benthic invertebrates.
- Long-term fish studies with atenolol are being started. Work has begun to characterize the β1- and β2-adrenergic receptor in the fathead minnow.
- Initial work on the environmental risk assessment of the two case study compounds, atenolol and ivermectin, has been carried out.

Case studies

Risk assessments will be performed for one human pharmaceutical, the β-blocker atenolol, and one veterinary pharmaceutical, the parasiticide ivermectin, using the approaches developed within ERAPharm in comparison to current regulatory approaches.



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CVMP/VICH (2004). VICH-GL 38. Environmental impact assessment for veterinary medicinal products. Phase II guidance (CVMP/VICH/790/03-final).

EMEA/CHMP (2005). Guideline on the environmental risk assessment of medicinal products for human use (CHMP/SWP/4447/00 draft).

Photos: AstraZeneca, BfG, Eawag, ECT.

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