



Sixth
Framework
Programme

KNAPPE

Knowledge and Need Assessment on Pharmaceutical Products in Environmental Waters

Contract n° 036864

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The deliverable authors are responsible for the content

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Participants: Laurence Amalric, Damia Barcelo, Dagmara Buntner, James Clark, Mark Cronin, Hélène Darras, Eléna Dominguez, Valéria Dulio, Thomas Dworak, Daniel Gouy, Bernd Halling, Richard Greenwood, Anne Gresle, Romain Journal, Eleftheria Kampa, Dirk Loeffler, Pascal Michoux, Christophe Mouvet, Michael Murray, Mira Petrovic, Roxana Radulescu, Benoît Roig, Louise Summerton, David Taylor, Thomas Ternes, Evelyne Touraud, Valentine Vierne, Sébastien Zabczynski .

B. Roig specified that the first Executive Committee meeting was opened to all the participants of the kick off meeting in order to make all the partners aware of the role of this committee, to disseminate, as widely as possible, the stakeholders' positions and to promote dialogue and debates.

E. Touraud made a brief presentation of the Executive Committee composition and role. She stressed on the external experts role and took stock of currently involved institutions and first contacts:

- EFPIA, GCN, SCI, SAUR Group, Merck Share Dohme Group, Sanofi-Aventis Group, European Patients' Forum, IFAH attended the meeting,
- Following e mails exchanges, Richard Williams (SETAC), Christian Daugthon (EPA), Klaus Kümmerer (University Medical Center-Frieburg) support Knappe project,
- First contacts have been taken with Pharmaceutical Group of the European Union and Health and Environmental Alliance

Executive Committee members are requested to participate to the EC meetings (4 are planned) and Knappe workshops and conferences.

M. Cronin spoke to the name of SCI, the Society of Chemical Industry and SETAC, the Society of Environmental Toxicology and Chemistry. He defined the missions of these institutions and stressed on their interest towards Knappe project:

- The principal objective of SCI (www.soci.org) is to further the application of chemistry and related sciences for the public benefit". Approximately, 20,000 members across broad scientific disciplines, mainly in UK
- The main mission of SETAC (www.setac.org) is to support the development of principles and practices for protection, enhancement and management of sustainable environmental quality and ecosystem integrity." SETAC split into Geographical Units and Local Branches.

These 2 learned organisations could provide support to meetings, a place to publish and networks and communication platform.

The next Committee meeting of the SCI BioActive Sciences Group is planned for February 20th, 2007. The next possible SETAC-Europe meeting at which a KNAPPE session could be proposed is May 2008.

D. Taylor spoke to the name of European Federation of Pharmaceutical Industry Associations (EFPIA). He gave an overview of EFPIA organisation and priorities:

- EFPIA is a regional Trade Association : 30 National Trade Associations, 46 Member Companies
- EFPIA overall objective is to improve the competitiveness of the pharmaceutical industry in Europe by setting up a regulatory and political environment, which above all stimulates R&D and rewards innovation

- EFPIA Priorities :
 - to strengthen the EU science base
 - to speed up patient access to innovative therapies;
 - to improve the healthcare market environment in Europe;
 While emphasising industry's contribution to society through an effective communication strategy

He described the path to a new medicine (different steps) and illustrated with the case of AstraZeneca. EFPIA expectations from Knappe project can be resumed as follows:

- Realistic & Objective
 - Don't extrapolate from 'unknown' to 'unacceptable'
 - "zero emission" is not a solution acceptable to patients
- Holistic & Risk Based
 - A 'life cycle approach' is necessary
- Collaborative & Inclusive
 - EFPIA is very happy to collaborate with KNAPPE
 - EFPIA represents the R&D industry of Europe
- Constructive
 - This is no longer a 'new' issue
 - A substantial amount has been done since 1999

In conclusion, D. Taylor stressed on some essential points:

- Resources of all stakeholders are limited
 - Much is already known
 - We need to make progress, not repeat existing work
- We need to identify key research goals
 - We need to establish priorities
 - Some goals may take a long time to achieve
- Regulators & industry have similar goals.
 - To deliver continued improvements in patient benefit whilst minimising environmental impacts.

E. Dominguez asked about precaution principle. D. Taylor answered that it should be carefully applied and it always induces costs.

P. Michoux spoke on behalf of Merck Sharp & Dohme (Europe) Inc. as EMEA GSE Regulatory & Technical Director. Pharmaceuticals in the Environment (PIE) are a concern receiving a growing attention:

- Pharmaceuticals have been detected in aquatic environment,
- Human effects are well characterized; some environmental effects may be unknown.

MSD challenge is to deliver life improving and saving benefits while minimising impacts on the environment. It involves:

- Increases in ERA timescales
 - for Medicines that will not be a product
 - Additional studies should not delay product registration
- Consistency vs. Flexibility
 - Different approaches or National requirements
 - GLP validated testing laboratory capacity

P. Michoux outlined the expected benefits of Knappe project:

- Establish consistent understanding and communication of PIE issues across EU,
- Provide an industry point of view of managing the life cycle of PPs.

From MSD point of view, the benefits of a science-based approach, as proposed in Knappe project, could be to:

- Provide confidence to the communities, governments, and industry that the safety of pharmaceuticals in the environment is well understood
- Provide the data needed to prioritize issues requiring further investigation
- Understand and address concerns resulting from detection of pharmaceutical compounds in the environment
- Identify gaps in existing knowledge that require further investigation regarding the potential for impacts.

Knappe would allow providing consistent understanding and an industry point of view of managing the life cycle of PPs. New approaches to communicate risk are needed.

E. Dominguez asked the question if the new ERA regulation is appropriate. P. Michoux answered that the new ERA guideline is a significant progress; however he is not sure that the regulation perfectly fits with all future medicines such as gene therapy.

D. Barcelo said that there was a problem of validation in former data. Now, with the new instruments and inter-laboratory exercises, the quality of data should increase.

H. Darras spoke to the name of SAUR, one of the three leaders in the water and waste management industries in France. SAUR is involved in all steps of the water cycle, and is interested in all associated water processes. The Group is willing to know about the efficiency of treatments on PPs and metabolites and wondered about types of PPs to be analyzed and how. SAUR France is leader of a national research program concerning the impact of the secondary biological treatments on final membrane filtration (clogging, efficiency...) in a frame of water recycling (precodd 2006 – REEBiM).

Concerning pharmaceutical products, they are looking for global indicators dedicated to their occurrence, mainly in drinking water. H. Darras stressed on the fact that analysing all PPs in water could not be cost-effective for the consumers.

She indicated that there is no current visibility regarding the French regulation evolution.

D. Gouy spoke to the name of Sanofi Aventis and ERA in the Group. An interdisciplinary expert group, Ecoval, is devoted to ERA. Its missions are:

- To assume the Group's responsibility for the environment through the best possible knowledge of our products' impact.
- To meet external demands, in particular those linked to regulatory constraints, and to anticipate the inevitable evolution of these demands.

D. Gouy presented also the procedure for the elaboration of the marketing authorization dossier. This dossier includes an Environmental Risk Assessment for each product in phase 2 development.

D. Gouy asked about what level of drug can be accepted in the environment. Characteristics of drugs in environment have been compared with other chemicals: environmental exposure is partly correlated to Acceptable Daily Intake (ADI). Presence in water does not necessarily mean toxicity for human living or environment. In the frame of Knappe project, Sanofi Aventis expectations can be resumed as follows:

- Definition of the objective of Knappe considering that emission of drugs in the environment is inevitable
- Scientific, realistic and integrated approach considering all the information available to evaluate the real environmental or human risk
- Regard water exposure evaluation as a tool for risk assessment and not as a final goal
- Start from the physical, chemical, pharmacological, toxicological, ecotoxicological ... properties to evaluate an acceptable water exposure.

Moreover, Sanofi Aventis recommends avoiding:

- Postulating that drugs are toxic
- Applying zero exposure
- Increasing sensitivity of analytical methods without reasons
- Evaluating the risk by class but consider each drug case by case according to its properties
- Attempting to evaluate interactions at this stage

E. Dominguez asked if the Company willing to share the information with the public. D. Taylor said that it is public but not publicized. Doctors already know.

T. Dworak asked about patient/consumer responsibility as polluter. D. Taylor answered that it is not an issue for the moment. P. Michoux added that industry is not the only responsible as they are lot of interactions in the whole environmental cycle of pharmaceuticals. D. Taylor asked who will pay for the removal of PPs in environment. Drugs' price would increase.

B. Roig concluded the executive committee by highlighting the first identified expectations of stakeholders. Preliminary, he noticed the big effort of communication from industrialists but also some confidentiality concerning the access to data contained in the marketing authorization dossier.

- Industrialists highlighted the fact that this global approach shouldn't be restricted to Europe scale, but expand at a world wide level.

- They agree to improve environmental considerations during the manufacture of their products but insisted on the required balance between risk assessment and patient benefits

- Need for new and relevant information in order establish priority actions.

B. Roig noticed also some differences between manufacturer and water treatment manager, especially in terms of detection: pharmaceutical industries requiring drug by drug approaches, while water managers, approaches with the use of global indicators.

ANNEX 1: AGENDA OF THE EXECUTIVE COMMITTEE

	<i>EXECUTIVE COMMITTEE</i>	
14 :00	- Executive Committee presentation	E. Touraud
14 :15	- Stakeholders expectations	M. Cronin (SCI) D. Taylor (EFPIA), P. Michoux (Merck), A. Gresle (SAUR) D. Gouy (Sanofi Aventis)
15:45	- Discussion	
16:15	<i>Conclusion</i>	B. Roig
16 :30	END OF MEETING	

ANNEX 2: LIST OF PARTICIPANTS

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ANNEX 3: ORAL PRESENTATIONS