



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

AUTHOR:	Evelyne TOURAUD
AFFILIATION:	ARMINES - Ecole des Mines d'Alès
ADDRESS:	Boulevard Saint-Michel, 60 F-75272 Paris Cedex 06, France.
TEL.:	+33-4.66.78.27.12
EMAIL:	evelyne.touraud@ema.fr
FURTHER AUTHORS:	Benoit ROIG

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Participants: Laurence Amalric, Damia Barcelo, Dagmara Buntner, James Clark, Mark Cronin, H el ene Darras, El ena Dominguez, Val eria 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, Beno t Roig, Louise Summerton, David Taylor, Thomas Ternes, Evelyne Touraud, Valentine Vierne, S ebastien Zabczynski. (Annex 2)

B. Roig opened the meeting and welcomed all the participants. He presented the coordination structure, Armines-EMA. Which corresponds to a common structure of Armines (non profit organisation for industry oriented research) located in Paris and Ecole des Mines d'Al es (EMA - engineer school) located in Ales. The administrative and financial aspects of the project will be taken in charge by the European Affair Department of Armines (contact Valentine Vierne: vierne@ensmp.fr) while all other aspects (organisation, management, scientific) will be dedicated to EMA (contact Benoit Roig: benoit.roig@ema.fr and Evelyne Touraud: evelyne.touraud@ema.fr).

B. Roig concluded by presenting the agenda of the day (Annex 1) and the other documents (technical annex, list of participants, timetable, deliverables list, and list of events) distributed to all the participants.

E Dominguez gave an overview of EU research policy in the area of pharmaceutical products in the environment. She began with the presentation of the main purposes and covered activities of FP6 supports actions. Then, she listed the previous and on going RTD activities in the frame of FP 5 and FP6 dealing with pharmaceutical products.

So, she presented the main topics, major outcomes and the European contribution for previous and on going projects:

- FP5 : SUSTAINABLE MANAGEMENT AND QUALITY OF WATER (1998-2002)
 - ✓ Research projects
 - **Poseidon** studied of the different water treatment technologies currently available (EC contribution : **1,4 M e**)
 - Major outcomes:*
 - a) ozonation for treated wastewater seems to be a very powerful tool for preventing PPCP contamination of receiving waters;
 - b) estrogens, the most potent endocrine disrupters, can be significantly removed either by common cascaded wastewater treatment with extended sludge age or by ozonation;
 - c) technology readily available for drinking water;
 - d) Recommendation of creation an ecological label as an incentive to industrialists.
 - **Rempharmawater** looked at the impact of a wide range of human medicines at the point of exit from sewage treatment plants (EC contribution : **1,1 M e**)
 - Major outcomes:*
 - a) The effectiveness of the treatment is highly variable with different results depending on the product, time spent at the plant, slurry activation, etc (carbamazepine not removed)

- b) Selected pharmaceuticals can have an impact on the environment (risk assessment using ecotoxicity data)
- c) Oxidative removal (advanced oxidation processes) of selected pharmaceuticals efficiently reduces their toxicity on algae
- d) Database Pharmafic (→ PharmaEcoBase): ecotoxicological data, physical and chemical properties, results of measurements, etc (Cemagref).

- **Eravmis** focused on the impact of veterinary antibiotics, with production running at over 5000 tonnes/year (EC contribution : **1,3 M€**)

Major outcomes:

- a) Three of the most widely groups of veterinary medicines pose a low risk to the environment and human health.
- b) The experimental and modelling approaches that have come out of the work should assist regulators and industry across Europe in more accurately and more effectively assessing the potential impacts of veterinary medicines on the environment.
- c) In instances where a risk does exist, the project has provided information on potential mitigation strategies.

✓ Preparatory, accompanying and support measures

- **Envirpharma**: European Conference devoted to the problem of human and veterinary pharmaceuticals in the environment (EC contribution : **0,17 M€**)
Conference was held in Lyon, France (14-16 April 2003), and dedicated to define the future new areas of investigation necessary to improve the environmental risk assessment of the pharmaceuticals, and their removal, and to prepare a network of excellence on this topic. 184 participants from 18 countries attended the conference.

- **Triton**: Scheme to provide training and assistance for research players for the assessment of the fate and removal pharmaceuticals and estrogenic compounds (PECs) released into the environment (EC contribution : **0,25 M€**)

Areas of training:

- a) The analysis of the occurrence and fate of PECs
- b) Environmental risk reduction technologies (water and waste water treatment and artificial ground water recharge)
- c) Environmental risk assessment and management.

- FP6 : SUSTAINABLE DEVELOPMENT, GLOBAL CHANGE AND ECOSYSTEMS (2002-2006)

✓ Research projects

- **Erapharm** : Environmental risk assessment of pharmaceuticals (EC contribution : **2,8 M€**)

Specific objectives:

- a) Investigate previously unstudied major exposure routes of pharmaceuticals into the terrestrial and aquatic environment
- b) Investigate factors and processes affecting the fate of pharmaceuticals in soils, sediments and surface water
- c) Further develop testing and modelling approaches for evaluating the fate of pharmaceuticals
- d) Develop a scenario-based exposure assessment system for pharmaceuticals

- e) Explore the use of bioassays for an initial hazard screening and mode-of-action classification
- f) Evaluate how information on pharmacodynamics and toxicodynamics in mammals can be used to guide the evaluation of potential sublethal effects in fish
- g) Modify and refine test methods in order to detect the effects of long-term, low-level exposure to pharmaceuticals
- h) Investigate whether and to what extent environmentally relevant concentrations of pharmaceuticals cause effects in the environment
- i) Develop pragmatic approaches for assessing transformation products
- j) Provide recommendations on how to improve current European environmental risk assessment procedures for pharmaceuticals.

➤ **Related projects:**

- **Reclaim water** : Water reclamation technologies for safe artificial groundwater recharge (EC contribution : **3,0 M€**)
- **Emco** : Reduction of environmental risk posed by emerging contaminants through advanced treatment of municipal and industrial wastes (EC contribution : **1,2 M€**)
- **Norman** : Network of reference laboratories for monitoring emerging pollutants (EC contribution : **1,9 M€**)
- **Aquabase** : Organic micropollutants in the aquatic environment : interdisciplinary concepts for assessment and removal (EC contribution : **1,33 M€**)

➤ **Specific support actions:**

- **Knappe:** Knowledge and need assessment on pharmaceutical products in environmental waters.

By the presentation of this state of the art, E. Dominguez warns Knappe partners not to duplicate work and informs that DG Research waits for Knappe results to orientate its politics in terms of research directions.

René P. Schwarzenbach *et al* reviewed the challenge of Micropollutants in Aquatic Systems:

- Tools to assess the impact of these pollutants on aquatic life and human health must be further developed and refined
- Cost-effective and appropriate remediation and water-treatment technologies must be explored and implemented
- Usage and disposal strategies, coupled with the search for environmentally more benign products and processes, should aim to minimize introduction of critical pollutants into the aquatic environment

Expert stakeholders' views on the management of human pharmaceuticals in the environment can be summarized as follows:

- Both human health and ecosystem health concern
- Ranked below some well-known water contaminants (nutrients, pesticides and metals) in terms of management actions
- Uncertainty surrounding scientific understanding of the impacts; research into chronic and sub-lethal effects, as well as mixture effects, should be a priority

- Most effective management strategies: Advanced wastewater treatment technology, education of medical professionals to reduce overprescription, pharmaceutical-return programs coupled with public education, requirements for all municipalities to have a minimum of secondary wastewater treatment.

In conclusion, E. Dominguez presented the first actions towards a better choice/use of pharmaceuticals in order to highlight environmental awareness:

- The Stockholm County Council, the provider of public healthcare in the Stockholm, Sweden region, has introduced a classification of pharmaceutical drugs according to their potential for accumulation in surface water and interference with aquatic life
- The classification utilizes producer-supplied data on biodegradation, bioaccumulation, and eco-toxicity. The purpose of the classification is to increase the awareness of patients, doctors, and producers that pharmaceuticals may have side effects outside the patient
- Doctors and patients may make a more multi-factorial selection of drug in cases where several therapeutically-equivalent alternatives are available.
- The program is evaluated by annual analyses of pharmaceuticals in regional surface water and sewage treatment plant effluents.

To the question of C. Mouvet concerning FP7 opening for new project, E. Dominguez answered that each year/2 years, new work programmes are published: research priority is opened for next workprogramme and Knappe results may contribute.

B. Roig presented KNAPPE objectives and organisation. He came back briefly on the context in which the project was proposed. This context is focused on the presence of pharmaceutical products in environmental water. It is admitted and demonstrated that pharmaceutical products used for human and animal healthcare enter the environment by different pathways (excretion, waste disposal ...). These products can be resistant, to water treatments, persistent and can be found in environmental waters but also in drinking water. Moreover, according to the evolution of practices in terms of consumption of drugs (both for humans and animals), environmental compartments are likely to be more and more contaminated, especially in environmental waters.

Even if the consequences of the presence of these compounds are always under discussion (better established for aquatic systems than for human health), this phenomenon increases the preoccupation for water resources managers and more generally the environmental community. The scientific community considers that this problematic cannot be limited to scientists but have to take into consideration people involved in the live cycle of pharmaceutical products (industrialists, doctors, pharmacists, patients, public community

On an other hand, a first overview of this global approach allows to highlight some interesting point such as (i) the weak awareness of medical actors in environmental behaviour; (ii) the different social and people attitude in terms of disposal, consumption, recycling across Europe or at national level; (iii) the different politic and regulatory strategies at national and international scale; (iv) a lot of published and available data (scientific publications, national and international programmes) but very few connected and integrated.

From these observations, KNAPPE project was proposed and aims to consider the whole life cycle of the pharmaceutical products, from their manufacture to their presence in environmental waters, taking into account the different available information, procedures, actions KNAPPE aims to integrate and interconnect them in order to identify the main pressure points and lacks in the management of these products in the environmental field. So,

KNAPPE will propose some priority actions allowing lowering the presence and the effects of pharmaceutical products.

These objectives will be reached only if all the actors involved in the life cycle of the pharmaceutical products take part in the discussions and debates. Thus, the project will include as participants representatives of the industry, of doctors, pharmacists, regulatory institutions, patients, and scientists.

KNAPPE project is a Specific Support Action, proposed in the frame of the 6th framework program (priority 1.1.6.3 "Global Change and sustainable development "Sub-priority "Global Change and Ecosystems). It is financed by the European DG Research (590 k€) and include 9 partners (BRGM, Cemagref, Armines EMA from France; CSIC from Spain, University of York, University of Portsmouth from UK; Ecologic, Federal Institute of Hydrology from Germany; University of Slaska from Poland).

KNAPPE is organised in 6 work packages. This working space is under the coordination of the Scientific Council (composed by WP leader and in charge of the coordination of the different tasks) and the Executive Committee (formed with WP leader +10 external experts and in charge of the orientation of the project). The coordinator manages the whole project and is in relation with the EU commission.

B. Roig concluded his presentation by the announcement of the different events planned inside the project and the need to join some of them, in order to better guarantee the presence of stakeholders.

In particular, an International Conference is planned at the middle of the project. This conference aims to complement the works performed in the project by giving an overview of the new developments (future trends) concerning the pharmaceutical problematic (treatment, control, regulation, industrial processes, social actions ...). This event has to be coordinated with other events already planned and then the date will be validated.

V. Vierne presented the administrative and financial management of Knappe project:

- Starting Date: February 1st, 2007 : the costs will be eligible from that date
- Total duration: 18 months EU funding
- EC Total Financial support: 593,136 €
- The contract should be signed within February
- No Consortium agreement.

Armines Paris is in charge of:

- Contract : Sending and collection of the Forms A for signature and transmission to the EC
- Day to day management : Armines makes the day to day management (meetings organisation, contact with the institutions, control of deliverables, milestones and project activities, etc)
- Finance: Distribution of the advance, collection of the forms C and the audit certificates.

C. Mouvet wondered if the presence of additional stakeholders was possible. B. Roig answered that, in the Executive Committee, the number of external members was reduced to 10. E. Dominguez added that the allocated funding is enough to invite till 25 stakeholders in the Executive Committee for taking part to discussions and going beyond Knappe results. B. Roig informed that it is possible to invite them to events organized within the project.

D. Loeffler presented the objectives of WP1 dedicated to occurrence of PPs in the aquatic environment:

- List of PPs most relevant for the exposure of the aquatic environment
- Identification of data gaps to design environmental monitoring strategies to allow for an ERA
- Propose environmental indicators to elucidate the contamination source
- Identify compounds of concern with regard to exposure and ecotoxicity (WP2, WP4).

An inventory of PPs in the aquatic environment will be made, taking into account data available on:

- Exposure of different water compartments (treated + raw wastewater, surface water, groundwater, coastal water and drinking water)
- Pharmacological properties of selected compounds (pharmacokinetics, formation of metabolites and excretion)
- Chemical and physicochemical properties
- Environmental fate (sorption and transformation)
- Consumption in different countries (France, UK, Poland, Spain, Germany)
- Medical tendencies concerning delivery and drug sales (France, UK, Poland, Spain, Germany).

The main deliverables are:

- D1.1 (Month 6): List of relevant PPs regarding properties, occurrence, fate and consumption in different European Countries
- D1.2 (Month 9): Proposal of an environmental indicators and classification system for environmental management
- D1.3 (Month 13): Conclusion and summary of the workshop.

Partners involved in WP1 are BfG (leader), Cemagref, Armines and BRGM from France, CSIC from Spain, UoP from UK and SUT from Poland. The tasks are shared out as follows:

- BfG:
 - Generation of data list templates and Establishment of the inventory list (March 1st)
 - Input of data including (August 1st):
 - Data on pharmacological, physicochemical properties, fate and exposure
 - Evaluation of national reports, Ph.D.-Theses, national scientific literature
 - National consumption data (from 2000-2007): drug prescriptions, usage in hospitals, non-prescriptive drug, diagnostics
 - Identify indicator substances and establish classification system (November 1st)
 - Organisation of the workshop together with WP 2 (middle February 2008).
- Cemagref:
 - Access to Repharmawater/ERAPharm – database
 - Contact to EU project Norman
- Armines, BRGM, CSIC, UoP, SUT
 - Input of data including:
 - Evaluation of national reports, Ph.D.-Theses, national scientific literature
 - Data on pharmacological, physicochemical properties, fate and exposure
 - National consumption data (from 2000-2007)
 - Drug prescriptions, usage in hospitals, non-prescriptive drug, diagnostics.

Concerning the joined workshop WP1/WP2, 75 participants (pharmaceutical industry and other stakeholders) are expected to attend and 2 international speakers will be invited.

At the end of the presentation, the discussion was about:

- the collection of data and the access to existing databases (V. Dulio)
- the selection criteria of PPs (occurrence, toxicity, use) (D. Taylor)
- what about illicite drugs? : yes if they are used in medicine. The concern is coming (D. Barcelo).

E. Dominguez stressed the fact that databases already exist and the problem is the accessibility to the data, especially for PPs consumption. Daily doses are available in Drugs Master Files. How elsewhere?

Concerning the future of databases, addition of received data in existing databases (for example, extension of Eraphram databases – T. Ternes); connection of databases should wait to know how accessible the data are.

S. Zabczynski presented the overall objective of WP2 dedicated to the assessment of the current water treatment processes and their limitations. The objective of this WP is to use present knowledge progress and existing review studies to put emphasis the causes and effects of deficient wastewater treatment efficiencies and open the discussion of the future evolution to limit them. The expected results are the analysis of data concerning existing treatment processes (and their limitations), data on novel treatment processes and an assessment of the future practices and new strategies.

More precisely, WP2 will present:

- delineation the factors that determine PPs susceptibility to conventional treatment processes used in sewage treatment plants (STPs) and for more advanced treatments,
- identification of varying removal rate with regard to regional specificities, identify groups of human pharmaceuticals according to their removal rates by current biological sewage treatments, and try to establish links with their physico-chemical properties,
- gathering of the chemico-physical properties of PPs and kinetic data concerning PPs biodegradation,
- updating knowledge concerning the metabolites and transformation products produced during treatment processes and their biological activity,
- assessment of the concentration of pharmaceuticals in sewage sludge and hence their potential contribution to the pollution of the environment for sludge reuse or disposal,
- comparison of the technologies in regard to PPs removal,
- possibilities to improve the existing technologies,
- suggestion of different strategies for PP treatment with identification of future requirements.

WP2 will consider the associated costs and benefits of effecting a change in treatment options according to local conditions and the fact that presently, there are no economic or legal incentives for water companies to remove pharmaceuticals from wastewater

Concerning the 2 days common workshop WP1/WP2, the main objective will be to inform and involve stakeholders, end-users and water managers and to discuss the outcome and practical consequences of the results:

- topic: origins, occurrence, exposure pathways, indicator substances, classification system and monitoring of PPs, future priorities for research and development,
- invited participants: EU Competent Authorities, industrialists (producers and users), water treatment industry, medical experts (clinicians, pharmacists, veterinarians),

students, researchers, PhD students in environment and health, NGO (WWF, Greenpeace...).

Politechnika Slaska, SUT, is WP2 leader (5,5PM). The other partners are Cemagref, (2.5 PM) CSIC (1.0 PM), BfG (1.0 PM)

At the end of the presentation, P. Michoux highlighted the need to know how many water get through big cities (equipped with wastewater treatment plant) and small villages (without treatment plant and control). PPs consumption is lowering in villages. At long term, the outcome is to have the efficient and cost effective treatment. Participation of WP3 actors is required to develop a strategy.

T. Dworak presented the overall objective of WP3, integrating social and economic issues. The key aim of WP3 is to develop cornerstones of an EU prevention action to limit PP discharge into the aquatic environment, which may endanger the chemical and biological status of Water Bodies.

He began by a rapid description of Ecologic institute:

- Private non-profit institute (Berlin/Brussels)
- Think tank for applied environmental research, policy analysis and consultancy
- Focus on practical/policy relevant results
- Work covers the entire spectrum of environmental issues
- Wide experience on EU water policy

The objectives of WP3 are:

- To assess existing framework in the EU and selected countries to prevent PP discharge
- To assess develop options on the future design of instruments (e.g. taxes, voluntary measures, regulations) to prevent PP discharge into water
- To link findings to the WFD CIS and other policy developments (GW Dir, Soil Strategy, CAP, Health).

WP3 can be split into 2 main parts:

- Part A. State of the art review of the existing Framework (e.g. environmental, health, agricultural policies)
- Part B. Develop cornerstones of an EU prevention action to limit the discharge of PP into water

WP3 deliverables are planned as follows:

- Month 11: Status-quo report on existing legislation, instruments and measures in EU, selected MS and Accession Countries (D3.1),
- Month 16: Proceedings of Expert Workshop on the design of instruments to limit PP discharges (D3.2),
- Month 18 Report on options for the future design of instruments to limit PP discharges into water (D3.3).

At this end of the presentation, E. Dominguez stressed that big gaps exist between research and incentive measures and wanted to know which research means are needed to set up policy (in other DG). B. Halling informed that dealing with law issue is sensitive. Does a drug showing environmental effects have to be banned?

B. Roig presented WP4 in this absence of A. Boxall and representatives of Cemagref. Prior to describe the content of this WP, B. Roig presented the WP leader. Dr Alistair BOXALL is head of the EcoChemistry Team. He has extensive expertise in the environmental fate, behaviour and effects veterinary medicines, biocides, industrial chemicals and human medicines. He participated to several international projects: ERAPHARM (environmental risk assessment of pharmaceuticals), ERAVMIS (env. risk ass. of veterinary medicines in slurry), Indirect human exposure to veterinary medicines (Defra), Effects of antifungal pharmaceuticals on soil (AstraZeneca), ... He was member of the organising committee of the EU conference ENVIRPHARMA and chaired the SCI conference on Pharmaceuticals in the Environment.

WP4 is dedicated to health and environment impacts/effects of PPs. The overall objective of this WP is to (i) review the data on the effects of PPs on aquatic and terrestrial organisms and humans; (ii) explore the significance of the reported effects in terms of environmental and human health; (iii) investigate PP transformation products and mixtures of PPs on ecosystem functioning and human health

The main tasks of the WP will be to (i) review the environmental impact and health effects of PPs in term of magnitude of exposure, potential risks, ecotoxicity assessment and toxicological significance, risks of mixtures, indirect effects, potential impact ...; (ii) to implement a classification (typology) taking into account environmental considerations with regard to ERA procedures. Indeed, pharmaceutical products are often presented according to their pharmacological classification that is not always relevant for an environmental consideration; (iii) organisation of a 2 day workshop, involving many stakeholders (regulators, industry, toxicology experts, doctors & vets) and allowing to discuss the compiled data and many of the key questions concerning the impacts of PPs on environmental and human health.

The WP will deliver a report on environmental impact and health effects of PPs (month 18), and a proposition of a typology of PPs with regard to ERA procedure (month 18).

E. Dominguez stressed that it was not acceptable that Cemagref, with 4 persons involved in Knappe, did not attend the kick off meeting. The coordinator has to inform this partner of this remark.

Concerning the organisation of the dedicated workshop, E. Dominguez indicate that, because of the availability of stakeholders, it will be better to join workshops of WP1, WP2 and WP4. T. Ternes agreed. From the stakeholders' point of view, it depends on who will attend and the common interests. DG Research has to be informed of modifications.

J. Clark presented WP5 dedicated to eco-pharmacostewardship and vigilance. He began with the presentation of the York Chemistry Centre and the objectives of Green Chemistry:

- The York Green Chemistry Centre is the first multidisciplinary academic organisation dedicated to creating genuinely sustainable supply chains for chemical and related products. 50 staff and graduates are working on various aspects of green and sustainable chemistry. A long-standing history of collaborations exists with the pharmaceutical industry,
- Green chemistry is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances. It consists in discovery and application of new chemistry/technology leading to prevention/reduction of environmental, health and safety impacts at source.

Then, he presented the overall objective of WP5:

- To review the role of eco-pharmacostewardship and vigilance throughout the lifecycle of PPs
- To further our understanding of how and where stewardship and vigilance schemes can be adopted to improve the overall sustainability of PPs
- To identify existing examples of good practice, study drivers for increased uptake and develop strategies for increased development of greener drugs

He stressed on eco-pharmacovigilance (do not confuse with pharmacovigilance) and described more in details the specific activities devoted to ecopharmacostewardship and pharmacovigilance and the role of partners involved in the WP:

- Ecopharmacostewardship :
 - Identify what stewardship approaches are available or could be developed to minimise the environmental impacts of PPs throughout their life cycle (UoY-CSL)
 - Investigate the adoption of benign-by-design clean synthesis methods and green production technology to design greener PPs (UoY- GCN)
 - Examine the use of Life Cycle Assessment (LCA) as a tool to assess sustainability implications of new and existing drugs (UoY-CGN)
 - Identify examples of greener drugs and identification of eco-compatibility criteria (UoY-CGN)
 - Examine the use of classification and labelling schemes (Ecologic)
 - Examine approaches to communicate methods of 'good practice' to manufacturers, prescribers and users of pharmaceuticals (Armines).
- Pharmacovigilance :
 - Identify the substances/scenarios that should be monitored (UoY-CSL, BRGM, UoP)
 - Establish how monitoring can be targeted (BfG, BRGM)
 - Identify appropriate post-authorisation monitoring methods (UoP, BRGM, Armines).

The main deliverables are 2 documents discussion on:

- Eco-pharmacostewardship (November 2007)
- Risk management and pharmacovigilance (December 2007)

The main milestone is the organisation of a 2 day stakeholder workshop involving regulators, industry, doctors, vets, NGOs and other relevant organisations (April 2008).

E. Dominguez said that one might face barriers to expand the proposed programme. J. Clark is aware of the difficulty and highlight the importance of this issue in the decision making process.

E. Touraud presented WP6 overview. WP6 is dedicated to the valorisation and the dissemination of KNAPPE knowledge and results and efforts have to be made in order to achieve the best use of these results and to optimize their transfer to the interested parties.

The first objective of WP6 is to expand and disseminate, as widely as possible, the present knowledge on the many dimensions of the topic of PPs in the environment. WP6 will foster communication and collaboration between scientists, regulators, stakeholders in order to identify priority actions and propose recommendations for lowering presence and impacts of PPs in the environment.

The dissemination strategy is based on:

- The implementation of KNAPPE web site (www.knappe-eu.org) : this web site which will be a dynamic « work in progress », its content being continually updated,
- The organisation of workshops to promote scientific dialogue and debates and international conferences to identify main pressures points and propose actions leading to best practices for limiting presence and impacts of PPs in the environment,
- Newsletters and information letter for widespread public communication in order to increase public awareness about PPs in the environment and the importance of the individual (user, consumer, professional communities...) to reduce the potential for environmental impact,
- Finally, a CD Rom compiling all the data, reports and recommendations will be distributed as widely as possible.

Growing number of people are involved in the topic of pharmaceuticals in the environment; in recent years, research and studies on PPs in the environment have increased, too. There is a need to highlight the most important questions and issues related to the presence of pharmaceuticals in the environment:

- Identify the concerns, the needs and the gaps related to occurrence, fate, transport, exposure, risk assessment, monitoring, engineering,
- Propose priority actions directed to environmental stewardship, pollution prevention, technologies, public awareness.

It will be achieved by fostering and promoting:

- Communication between scientists and regulators
- Inter-disciplinary discussions
- Brainstorming, exploration of new ideas
- Collaboration of all stakeholders and beneficiaries of the work.

Then, E. Touraud insisted on the fact that research has been fragmentary, resulting in a weak connection between the different data. She proposed to adopt inside Knappe project an integrated approach relying on the whole lifecycle of PPs from manufacture to exposure. This approach requires, as a first step, the collection of representative and reliable data. The second is to interconnect all these data in order to better understand the fate and behaviour of PPs since their manufacture. It would make it possible to identify the main pressure points along the life cycle PPs and to propose relevant actions aimed at reducing their occurrence and their impact on the aquatic environment.

Then, she presented a database of available information on the general chemistry and toxicology of potential environmental levels of pharmaceuticals (www.chbr.noaa.gov/peiar). This database, achieved by Centre for Coastal Environmental Health and Biomolecular Research, University of South Carolina, could be a interesting starting point for Knappe project.

Finally, she concluded by the fact that one needs to pass from a fragmentary and reductionist approach to a holistic understanding to design environmental stewardship programme. This requires the integration and opening out of all the communities. The synergies between all the actors, the knowledge sharing will lead to innovation.

Partners involved in WP6 are University of Portsmouth (2.5 PM), University of York (0.75 PM) and Cemagref (0.5 PM). The main milestones are the international conference which will be postponed in February 2008 and the final conference which will conclude the project and present to the whole community the main recommendations.

At the end of the presentation, R. Greenwood stressed on the need of at least 12 months to have everybody informed for an international conference.

In conclusion, the main highlighted points were:

- To avoid duplication of work and accede to current data bases,
- To identify what we need to know in order to better understand fate, behaviour, mode of action, effect of PPs....and how?
- To integrate stakeholders in all discussions, brainstorming inside meetings, workshops and conferences.
- To reorganise the planning of meetings: T. Ternes proposed to join workshops 1/2, 4 wit the international conference in February 2008. E. Dominguez noticed the relevance of this proposition.

ANNEX 1: AGENDA OF THE KICK OFF MEETING

08:30	<i>Welcome to Hotel Leopold – Registration</i>	
09:00	<i>OFFICIAL OPENING OF THE KICK OFF</i>	B. Roig
09:10	<i>KNAPPE: presentation and objectives</i> <ul style="list-style-type: none"> - EU research policy in the area of pharmaceutical products in the environment. - Presentation of the Project 	E. Dominguez B. Roig
9:45	<i>KNAPPE: management & activities</i> <ul style="list-style-type: none"> - Project administrative, financial and legal frame 	V. Vierne
10:00	Coffee Break	
10:30	<i>Work-Package Presentation (15 min per WP)</i> <ul style="list-style-type: none"> - WP1 - WP2 - WP3 - WP4 - WP5 - WP6 <i>Discussion</i>	T. Ternes S.Zabczynski T. Dworak A. Boxall J. Clark E. Touraud
12:30	Lunch	

ANNEX 2: LIST OF PARTICIPANTS

Name	Institution	E mail
AMALRIC Laurence	BRGM (F)	l.amalric@brgm.fr
BARCELO Damia	CSIC (E)	dbcqam@cid.csic.es
BUNTNER Dagmara	SUT (PL)	dagmara.buntner@polsl.pl
CLARK James	University of York (UK)	jhc1@york.ac.uk
CRONIN Mark	Liverpool John Moores University (UK)	M.T.Cronin@ljmu.ac.uk
DARRAS H�el�ene	SAUR (F)	hdarras@saur.fr
DOMINGUEZ Elena	European Commission (B)	elena.dominguez@cec.eu.int
DULIO Val�eria	Ineris (F)	Valeria.DULIO@ineris.fr
DWORAK Thomas	Ecologic (D)	dworak@ecologic.de
GOUY Daniel	Sanofi Aventis (F)	Daniel.Gouy@sanofi-aventis.com
GREENWOOD Richard	University of Portsmouth (UK)	richard.greenwood@port.ac.uk
GRESLE Anne	SAUR (F)	agresle@saur.fr
HALLING Bernd	IFAH (B)	b.halling@ifahsec.org
JOURNAL Romain	Sanofi Aventis (F)	Romain.Journal@sanofi-aventis.com
KAMPA Eleftheria	Ecologic (D)	kampa@ecologic.de
LOEFFLER Dirk	BfG (D)	Loeffler@bafg.de
MICHOUX Pascal	MSD (F)	pascal_michoux@merck.com
MOUVET Christophe	BRGM (F)	c.mouvet@brgm.fr
MURRAY Michael	ABPI (UK)	mmurray@abpi.org.uk
PETROVIC Mira	CSIC (E)	mpegam@cid.csic.es
RADULESCU Roxana	European Patients' Forum (B)	roxana.radulescu@eu-patient.eu
ROIG Benoit	Armines - Al�es (F)	benoit.roig@ema.fr
SUMMERTON Louise	University of York (UK)	ls25@york.ac.uk
TAYLOR David	AstraZeneca (UK) / EFPIA	David.Taylor4@astrazeneca.com
TERNES Thomas	BfG (D)	Ternes@bafg.de
TOURAUD Evelyne	Armines - Al�es (F)	evelyne.touraud@ema.fr
VIERNE Valentine	Armines - Paris (F)	vierne@ensmp.fr
ZABCZYNSKI S�ebastien	SUT (PL)	sebastian.zabczynski@polsl.pl

KNAPPE CONTRACTUAL PARTNERS

ANNEX 3: ORAL PRESENTATIONS