Deliverable 6.1

Results of the Stakeholder Consultation on Requirements for a Possible Environmental Risk and Hazard Classification System for Pharmaceuticals

PHARMAS PROJECT (FP7, DG Research) -
Ecological and human health risk assessments of antibiotics and anti-cancer drugs found in the environment

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In cooperation with:

IVL – Swedish Environmental Research Institute

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1. Introduction

The issue of Pharmaceuticals in the Environment (PIE) has gained in prominence over the last two decades. In many countries, trace amounts of a significant number of these compounds have been found in environmental waters, as well as, typically in smaller concentrations, in the drinking water supply. Potentially, then, this issue can be of both environmental and human health relevance. However, the concentrations measured are very low, leading many stakeholders to question the existence of a problem. More significantly, there are numerous and very large knowledge gaps on the different aspects of this topic, which get in the way of providing conclusive answers to the different concerns – such as the actual environmental risk and human health risk in a certain region – arising from it. The scientific work packages of the PHARMAS project (www.pharmas-eu.org) address a number of these knowledge gaps in science.

This work package (WP6) follows a different objective: it sets out to evaluate, and suggest a prototype, for one of the possible approaches suggested to help address this issue, namely an **EU-wide web-based risk and hazard classification system for pharmaceuticals**. Recognising the importance of incorporating stakeholders' needs and views for any such system to be relevant and find uptake, the WP's first activity was a stakeholder interview process. The interviews' main aims were to identify the stakeholders' information requirements from such a system, and their evaluation of such a system's use and possible impacts.

This report presents the results of this interview process. Further deliverables of this WP will use these results to 1) evaluate the possible impact of such a system, and 2) to design a prototype version of it.

The background

Some of the issues and perspectives of stakeholders require a certain level of background knowledge on the topic - sometimes detailed. Figure 1 summarises the main pathways that human pharmaceutical products (PPs) follow from their production to their arrival in environmental waters and drinking water. Natural processes (such as biodegradation through bacteria in the environment) and man-made processes (such as wastewater treatment and drinking water treatment) can reduce the load and/or transform the compounds.

The pathways (the figure's arrows) also give an indication where efforts can be made to reduce the amount of PPs that eventually reach environmental waters and drinking water. In the case of a risk and hazard classification system that would be taken up by doctors, pharmacists, and patients, the system could imply a shift towards greener prescription, which would imply less input of dangerous PPs into the system (see Chapter 2 for a more thorough discussion). Side-effects of such a system could be increased awareness of the issue with authorities and broader public, which would help reduce overmedication and improper disposal, and create incentives for the production of "greener" drugs (green pharmacy, benign-by-design). Other approaches focus not on reducing input but on reducing the amount in the output, e.g. addressing hospital effluents or wastewater treatment practices.

Human PPs' presence in the environment is mainly restricted to the water cycle;[1] water and sediments, and the life in these media, are the potentially affected. However, practices such as fertilization of agricultural fields with sewage sludge or use of treated wastewater for irrigation spread the presence of PPs to other environmental media, such as soils and groundwater. The latter are also often affected by residues of veterinary products present in the manure or liquid slurry often

[1] An exception are medicines disposed of in landfills, and thus possibly leached into soil and groundwater.

used for fertilization. Several of these products are identical or very similar to human PPs in mode of action and in environmental effects, prompting some calls of interviewees to handle both groups of substances jointly.

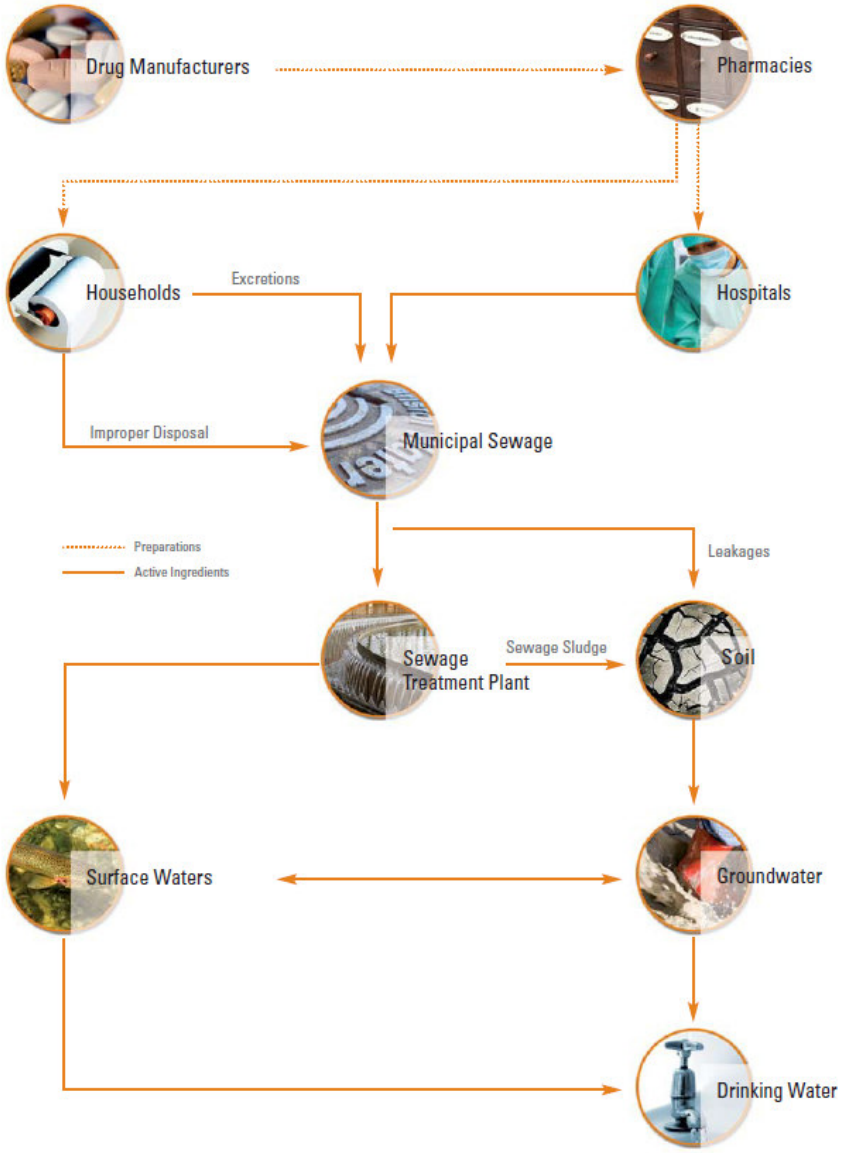

Figure 1: How do pharmaceuticals reach the environment? (taken from START report, "Pharmaceuticals for Human Use: Options of Action for Reducing the Contamination of Water Bodies"[2], P. 14).

The methodology

The interviews' subject was a possible EU-wide environmental risk and hazard classification system for pharmaceuticals. The questions focused on:

- the stakeholders' attitude towards such a possible system,

[2] http://www.start-project.de/downloads/start_Practical_Guide.pdf

- their evaluation of its use and of possible impacts,
- their information requirements from such a system,
- their own use of such a system (e.g. in their decision-making processes),
- their opinions on the characteristics and design it should have, and
- their risk perceptions on the issue of pharmaceuticals in the environment.

The interviews were in-depth and qualitative in nature, with extensive explorative follow-up questioning aiming to grasp the background for stakeholders' positions on the subject.

The explorative character was also necessary in view of the fact that **the characteristics and functions of the system** were **purposefully left open**. The system was only defined as "an EU-wide environmental risk and hazard classification system for pharmaceuticals", providing information on the topic. This approach was chosen so as to not influence stakeholders' opinions by suggesting certain functions or characteristics, but rather to discern what kind of information system would be helpful for their purposes. These positive sides were offset by a discussion sometimes hampered by the purpose and function of the system not being clear enough for the interviewee.[3]

The following stakeholder groups were identified for the purposes of this process:

• Environmental authorities (including River Basin Organisations) / Chemical authorities	**6 interviewees**
• Pharmaceutical industry	**3 interviewees**
• Drinking water / Wastewater companies	**2 interviewees**
• Authorities responsible for Drinking Water	**2 interviewees**
• Research organizations (different relevant disciplines)	**5 interviewees**
• Medicines Authorities	**3 interviewees**
• Medical association	**2 interviewees**
• Pharmacies / Pharmacy Associations	**1 interviewee**
• Consumer NGOs	**1 interviewee**
• Environmental NGOs	**2 interviewees**
• Public Health authorities	**1 interviewee**
• Pharmaceutical Waste/Recycling Companies	**1 interviewee**

Annex 1 provides more detailed information on the interview process, interview characteristics, geographical spread, and the questionnaire. Annex 2 provides the summaries of all interviews performed.

The report

The review of stakeholders' requirements of such an information system on PIE showed **two main concepts** of what such an information system should contain, and what it should deliver. Chapter 2 presents an outline of these two approaches, which we have termed **"knowledge base"** and **"decision support system for doctors / pharmacists / patients"**.

(In the rest of the report, **"information system"** or **"system"** will be used as the general term, whereas **"knowledge base"** and **"decision support system for doctors / pharmacists / patients"** will be used when referring to the specific concepts.)

[3] When the stakeholder had problems conceptualising such a system, the example of the Swedish classification system that is part of fass.se was provided. However, it was made clear that this was not to be understood as a model, but rather as an example of one possible approach to the subject. An interview question on system usability also referred to fass.se.

In front of the background of these different concepts for an information system, Chapter 3 presents the main results of this activity, by summarizing and analyzing interviewees' responses. Most relevant are interviewees' information requirements on the issue of PIE, and their opinions on the organization and structure of such a system.

Chapter 4 aims to go beyond the factual interviewee answers, to outline some issues, positions and interests of the different stakeholder groups regarding an information system on PIE (as derived from their statements). This chapter addresses the fact that the positions on an information system are informed by interviewees' views on the information currently available (e.g. appropriateness, sufficiency, quality), which differs between interviewees of different stakeholder groups.

Chapter 5 concludes this report, with a small number of recommendations and a discussion of some key aspects relevant for establishing any kind of information system on PIE.

Disclaimer: This report aims to present in an unbiased fashion stakeholders' positions on this topic, and discuss some issues based on stakeholder replies. The anonymised opinions are presented as opinions of representatives of organizations belonging to a particular stakeholder group. **These should not be taken as necessarily representative of, or as widespread opinions within, a particular stakeholder group**, but rather as existing opinions provided by representatives of individual organizations. The statements contained in this study are derived from a total of 29 stakeholder interviews4 and as such are limited in their validity.

2. Two approaches for an information system on pharmaceuticals in the environment

The interview questionnaire purposefully left open the possible characteristics and functions of the system, with the aim of not influencing stakeholders' answers regarding their requirements and uses of such a system.

An important finding of the interview process is that interviewees' requirements on the characteristics of an information system on PIE can be grouped under two concepts: **"knowledge base"** and **"decision support system (DSS) for doctors / pharmacists / patients"**. This chapter provides an outline of these concepts, and of their functions and rationales. This should serve as background for understanding stakeholder answers provided in Chapter 3.

Interviews showed that there is a very strong stakeholder requirement for a knowledge base on PIE. A large majority of the interviewees see a strong requirement for more available data on the issue (also in view of the knowledge gaps on the topic), as well as describing huge problems in finding out about, and accessing, that information that is available. The majority of stakeholders interviewed have extensive information requirements, which go significantly beyond that provided by a DSS for doctors/pharmacists/patients (see Chapter 3, Questions 3 and 4). In addition, there is a strong interest in raw data, and many interviewees expressed interest in developing their own tools based on the information in the system. Only some stakeholders expressed interest in a system that provides its own classification of environmental risk and hazard.

However, a **decision support system (DSS) for doctors / pharmacists / patients** that could inform and possibly influence purchasing behavior was also given support and was widely considered as a

[4] Two stakeholders were not interviewed directly, but only provided answers in written.

valuable initiative. Most interviewees considered this approach to have potential for positive environmental impact.

It is important to highlight that **these concepts do not exclude each other, nor do they have to be independent of each other**. Several stakeholders suggested the need for a system that covers both approaches. In addition, there is in principle no clear dividing line between a DSS for doctors/pharmacists/patients which makes available extensive and detailed background information for experts (e.g. in view of transparency), and a knowledge base approach. As the name suggests, a reliable knowledge base can work as a basis for different decision-making tools, which select, summarise and present information according to their own specific purposes. One of these possible tools would be a decision support system for doctors / pharmacists / patients.

The strength of interviewee support for a knowledge base, in comparison to the DSS for doctors/pharmacists/patients, is probably due to the latter only being of direct practical use for comparatively few stakeholder groups interviewed (doctors, pharmacists, health authorities). Most other stakeholders interviewed had more extensive information requirements.

The following sections present some main characteristics of these concepts, as derived from the stakeholder interviews.

2.1 Knowledge base/Database on PPs in the environment

Characteristics

Many interviewees expressed the need for a system to that would **collect practically all relevant information on pharmaceuticals in the environment (PIE)**. The information should aim to be as comprehensive as possible, and cover properties intrinsic to the pharmaceutical product (e.g. chemical and physical properties, including persistence, biodegradability and toxicity), information related to its occurrence in the environment (e.g. predicted environmental concentration, predicted no-effects concentrations, further ecotoxicological information, measured concentration for substances in water and soil), as well as further information (e.g. data on sales volumes for active compounds, behaviour in drinking water and wastewater treatment plants, human toxicological information). Many stakeholders required information for both the active substance as such and its metabolites (see Tables 1 and 2).

The different stakeholders had differing “cut-off” points for what information is relevant for their field and which would be off topic. For instance, whereas information on side-effects of pharmaceutical compounds was typically not considered relevant for their purposes by experts on drinking water and for drinking and wastewater companies, this point was considered relevant for scientists working on ecotoxicological risk studies. Notwithstanding these differences, stakeholders concurred the system providing a one-point source of very comprehensive information on the subject, and it should be continuously updated as new information becomes available.

Function

The knowledge base was not seen as having in itself a concrete function, such as a role in the selection of certain decisions/actions. The direct effects would be limited to information sharing, improved access to information (increasing possibility of knowledge), increased transparency, and increased awareness on the topic. The indirect effects of such an approach do not make possible to estimate how it would perform in concrete.

However, many actors saw this as a means for them to develop their own tools and decision-support systems, of relevance for their day-to-day work (see Chapter 5.1 "The case for a knowledge-base approach").

Positive environmental impacts of the improvement in available knowledge would result from faster recognition of environmental issues, and thus faster reactions (with the corresponding cost savings). Work on environmental quality would be improved and sped up. A knowledge base would also have economic impacts: by avoiding duplication of work a knowledge base would save costs and resources, and lower the cost of action (because of the costliness of producing data).

A further possibility seen for this system (as for a decision support system for doctors/pharmacists/patients) is the communication of environmental information on pharmaceuticals in the environment. Many stakeholders see the issue as misrepresented and overdramatized in the media, and are in favour of making high quality information available to provide a real basis for specialist or public discussions on the environmental hazard and risk associated with pharmaceuticals. Achieving more transparency was also mentioned as a goal in itself by interviewees belonging to the pharmaceutical industry.

Rationale for the system

The issue of PIE is comparatively new; in addition to its intrinsic complexity, it covers many different spheres and is relevant for various different regulatory perspectives. The information that has become available over the years is piecemeal, dispersed, and some of it fraught with uncertainties. A system that pools available information into one data reservoir is seen as highly valuable, in that it would increase the amount of information that stakeholders can access on a particular subject, e.g. environmental fate of a particular metabolite. Both lack of knowledge of available data and tools and access to this data is considered a bottleneck for work on the topic.

Stakeholders interested in this system are those that are most interested in or affected by the information gaps on this topic. Scientists of different fields (ecotoxicology, drinking water toxicology, quality of environmental waters), practitioners (drinking and wastewater companies), and regulators (drinking water and environmental authorities) tended to belong to this group (see Chapter 4).

Systems of this kind have been implemented for other emerging environmental issues, where information typically has many gaps, is widely dispersed, and there is little knowledge of parallel efforts. Directorate-General for the Environment of the EU Commission has commissioned its Joint Research Centre for such a system on endocrine disruptors, which shall also provide access to additional resources such as other databases and tools.[5] Such systems have also been used as a means for increasing transparency of information on a contentious or a possibly contentious topic. Both rationales (addressing data fragmentation and dispersion, and increasing transparency) are behind the call for a national database of public information on shale gas (related to the environmentally contentious gas extraction method termed "hydraulic fracturing" or "fracking"), performed a few weeks ago by the US Department of Energy's Advisory Board Subcommittee.[6]

[5] See http://ihcp.jrc.ec.europa.eu/our_activities/cons-prod-nutrition/endocrine_disrupters/eas_database/intro/?searchterm=None, accessed on 15/09/2011.

[6] Part of the consensus-based recommendations published by the board on August 11, 2011; see article "Secretary of Energy Advisory Board Subcommittee Releases Shale Gas Recommendations", http://energy.gov/articles/secretary-energy-advisory-board-subcommittee-releases-shale-gas-recommendations, accessed on 15/09/11.

From the risk communication tool perspective, these kind of systems have been linked with behaviour change on the part of patients; increased awareness could mean for instance that patients take pains to dispose their old and unused medication adequately.

2.2 Decision support system for doctors / pharmacists / patients

Characteristics

Interviewees envisaged this system as providing information on the environmental performance of different substances/products, by providing environmental risk and hazard information for PPs. This information could be used to compare between different, otherwise equivalent alternatives; environmental performance could thus be a criteria when choosing pharmaceuticals. The information contained in the system would thus be more or less limited to a) information on intrinsic chemical properties of the substance, e.g. that defining the hazard of the chemical, and b) information related to the risk posed by the substance in the environment, usually based on estimations of the concentration at which the compound could be found in environmental waters.[7]

This information would be presented at different levels of complexity, targeting different user groups (similar to what is currently done in the environmental section of Fass.se). Prescribers / pharmacists would have access to a concise summary of the main relevant characteristics of the substance's environmental risk and hazard. A more detailed level would present the background information behind the summaries. This section is seen as quite technical and doctors / pharmacists would only seldomly access it, but it would serve the purpose of transparency, as well as being of possible interest for scientists.

There is no broad consensus on a third, more simple section for the general public. Whereas some stakeholders envisage a level which presents information very succinctly, with the help of graphic elements such as pictogrammes or a streetlight or point system, others do not see the benefit of addressing this group. In the words of one interviewee of this opinion: *"The issue is too complex for straightforward decision making by the broader public."*

Function

Most stakeholders proposing this system see it as allowing to bring in environmental considerations into the decision of which compound should be chosen by the doctor/pharmacist/health board. Thus, the proponents hope, environmental criteria would join the main criteria, therapeutical value and cost, in deciding the purchase. Whereas there is very widespread consensus among stakeholders that therapeutical value definitely comes first, the idea is that if in a situation in which two medicines have equivalent therapeutical value the one that is less harmful for the environment could be chosen. The system should provide decision support to prescribers / pharmacists for this purpose, ideally allowing them to easily compare between different substances. The importance of simplicity and being tailored for the needs of its users was often highlighted.

A further possibility seen for this system (as for a knowledge base approach) is the communication of environmental information on pharmaceuticals in the environment. Many stakeholders see the issue as misrepresented and overdramatized in the media, and are in favour of making high quality information available to provide a real basis for specialist or public discussions on the environmental

[7] This information would be along the lines of that generated in the Environmental Risk Assessment (ERA) performed for new pharmaceuticals seeking approval under EU Directive 2004/27/EC.

hazard and risk associated with pharmaceuticals. Achieving more transparency was also mentioned as a goal in itself by interviewees belonging to the pharmaceutical industry.

Finally, some stakeholders see this system as being able to deliver on both fronts, on the one hand affecting prescription and purchasing decisions, and on the other providing different groups with increased information on the topic.

Rationale for the system

The stakeholders that support this approach see it as a way of influencing different behavior routines, which would result in environmental benefits.

Various benefits were associated with a system that provides input in the decision making process of medicine selection. In the short term, the system could influence prescription or sales decisions in favour of the more environmentally friendly alternative, thus contributing to reduce the impact of PIE. In the medium and long term, an additional benefit could arise if the system creates incentives for pharmaceutical companies to produce medicine with a lower environmental impact. A further benefit would be increased awareness and behavior change of patients (e.g. in their disposal of old and unused medicines).

For a system whose effect is limited to the provision of information, increased awareness and related effects such as improved disposal of old and unused medicines were seen as the benefits. Increased transparency would help prevent trust issues with the broader public.

Possible additional functions

A handful of interviewees, professionally close to processes of large-scale purchasing of PPs in their Member States, were interested in incorporating additional environmental information, beyond that of the medicine in itself, into such a decision support system. They highlighted their interest in incorporating into such a system information related to product Life-Cycle Analysis, Ecological Footprint, and Corporate Social Responsibility. This information would be helpful for greening procurement initiatives. Public purchasers of PPs would already have started to use this approach in their purchases of pharmaceutical products, but would be using information related to the environmental performance of whole companies rather than that of individual products.

3. Stakeholder needs and opinions on an information system on PIE

This Chapter summarises and analyses stakeholders' interview answers on a question by question basis. In doing this, it aims to provide a detailed overview of interviewees':

- attitudes towards, and evaluation of possible impact, of an information system on PIE,
- information requirements on the subject of PIE for their work,
- views on which pharmaceutical products should be included and their possible prioritization when populating the system with data,
- opinions on how such a system should be organized and structured,
- opinions and attitudes on the severity of the issue of PIE.

This information could help inform future discussion on the possible characteristics of an information system on PIE. (More detailed information is provided in individual interview summaries found in Annex 2.)

Q.1 Opinion on the need and use of an EU-wide environmental risk and hazard classification system for pharmaceuticals

All 29 interviewees responded that they would approve of the existence of an EU–wide environmental risk and hazard classification system. Seven interviewees expressed a strong interest for such a project, qualifying it as potentially *very important*, *necessary*, or *very useful*.

Eighteen of the 29 interviewees answered *yes* to the question *Would you use the classification system in your work*? Four stakeholders specifically stated that they would not use it. The first belongs to the environmental authorities group and answered *no* because such a system does not relate to his precise field of work, which is focused on chemicals. Two interviewees from the environmental NGOs group answered *no* explaining that pharmaceuticals are currently not a priority topic within their organizations. Finally, the fourth stakeholder belongs to the pharmaceutical waste/recycling group. He reported that the use of such a system would not be possible according to current procedures approved by the environmental authorities.

Q.2 Impact of a web-based classification system

Summary:

- **Environmental impact**

Most stakeholders foresee a positive environmental impact, however many condition this impact on the system's ability to engage doctors

- **Economic impact**
  - Many, but not all, interviewees respond to foresee an economic impact. Diverging comments were collected concerning:
    - Impact on pharmaceutical companies
    - Impact on the economy in general (including health systems)
- **Health/Behavior impact**
  - Opinion is mitigated on the system's ability to change doctors' prescription patterns
  - Interviewees often mentioned that human health is the foremost priority, hence takes precedence over environmental concerns
  - Diverging opinions were collected concerning the system's impact on the general public and on disposal behaviors

Environmental impact

Twenty-one stakeholders responded to foresee an environmental impact. Many condition this impact on the existence of ''greener'' alternatives with the same therapeutic effects, and on the ability to reach doctors and change prescription behaviors. Some suggested that the environmental impact would be in the ability to better identify risks and hence orient action. One stakeholder stated that it is hard to assess whether the system would have an impact because environmental effects of pharmaceuticals have been inadequately recorded so far. One stakeholder commented that the question of impact is hard to assess without knowing what the system will do. No stakeholder responded not to foresee an impact.

Economic impact

Fifteen stakeholders responded to expect the system to have an economic impact; three stakeholders responded they do not. Eight interviewees did not have any comments on the economic impact. It was mentioned that increasingly environmental conscious public buyers and patients could put pressure on companies to produce more environmentally friendly products.

Impact on pharmaceutical companies→ Five stakeholders have specified to foresee a positive economic impact for the industry. Reasons stated for this include: opportunities to develop new products and gain a competitive advantage, reduced costs for developing internal information systems, lower costs to produce environmental assessments for approval.

Three stakeholders specified to foresee a negative economic impact for the industry. One interviewee mentioned that this could lead to an increase in production costs. One stakeholder mentioned that such a system could increase competition amongst producers to deliver more environmentally friendly substances (seen as a negative impact). It was also mentioned that care should be taken to prevent such a system from becoming a disadvantage for European companies who compete with companies in countries where such environmental concerns do not affect decision making.

Impact on health care systems→ One stakeholder pointed out that the information system would benefit health care systems because such a system is part of a primary prevention approach to reduce chronic health problems. Primary prevention approaches would help reduce health care costs and thus benefitting health care systems.

Economic impact (economy as a whole)→ One (Swedish) stakeholder mentioned that the economic impact of the Swedish system, on the national level, is close to none. One interviewee commented that perhaps ''some medicines (will) end up being more expensive as a result of their being more environmentally friendly, so implying increased costs, but when one considers the economic benefits of reduced pollution the economic impact of such a system would be in my opinion at least cost neutral''.

Medical/behavior impact

Impact on medical profession → Ten stakeholders mentioned to anticipate seeing doctors changing their prescription patterns as a result of having access to the classification system. Three stakeholders stated not to foresee this kind of change. One stakeholder mentioned that while today price governs the decision making process, in the future perhaps environmental classification could affect the process. On three occasions, stakeholders mentioned that doctors are extremely solicited and have little time to visit such a system. Another mentioned that he thought doctors were already able to prescribe the more environmentally friendly alternative.

The conflict between environmental concerns associated to a substance and its therapeutic efficacy was raised seven times. Often, the stakeholders recalled that human health is the priority. One stakeholder suggested that a campaign which targets the medical profession would be helpful in promoting the use of the system. One stakeholder from Sweden stated that at the national level prescription behavior is influenced by the access to data on the environmental part of Fass.se. Two stakeholders proposed that the topic be integrated early on in the education process and informational events should be offered to help doctors become aware of the problem.

Impact on general public → Three stakeholders stated that the system could help promote change in **consumer behaviour**. One stakeholder mentioned patients could begin to ask for more environmentally friendly products, while two stakeholders do not agree with this statement. Two stakeholders mentioned the public would not be interested in accessing such a system, one of them implied it would be too complex for straightforward decision-making by the broader public. One stakeholder had the concern that the system could raise issues for the public in terms of following the therapy prescribed by their doctors. Another stakeholder stated that ''consumer demand for

environmentally friendly medicines will hardly change - at most for those consumers that are already environmentally conscious''.

Five interviewees mentioned to anticipate the system to have a positive impact on the safe **disposal** of pharmaceutical waste. Two stakeholders mentioned the importance of setting up of a **labeling scheme**. An issue, mentioned on two occasions, is the importance of the existence of an **effective take back scheme** in European Member States. One stakeholder commented it ''would take a considerable communication effort to make consumers be proactive and engage with the issue''. Another stakeholder mentioned disposal issues should be handled independently from an environmental classification.

Q.3 Information needs on pharmaceuticals in the environment

Question 3 asked interviewees what are their needs (or their organization's needs) on pharmaceuticals in the environment; Table 1 summarises interviewees' responses. This **open question** aimed to capture the foremost information requirements that stakeholders think of on the issue of PIE. (Question 4 proceeded to ask in more detail, and checking against a list of possible data). The information requirements listed in Table 1 are stakeholders' own words (with minor adjustments), and can thus be vague and have overlaps with other entries in the same table.

The results show strong interest in different kinds of strictly environmental information, such as different types of ecotoxicological data, environmental fate and pathways, and data on environmental effects. Strong interest also exists for sales and consumption data.

The highest amount of data requirements are reported by the actors related to drinking water (both operators and authorities) and by research institutions.

Table 1 Summary of interviewee answers to Question 3 (information needs on PPs in the environment)

Stakeholder group	Environmental authorities						Pharmaceutical industry			Water Utilities and Associations	Drinking Water Authorities	Research institutions						Medicinal products authorities			Medical associations		Pharma. Assoc.	Consumer NGOs	Environmental NGO		Public Health Systems	Pharma. Waste Companies
Information requirements																												
SH number	1	2	3	4	5	6[1]	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22[2]	23[2]	24	25	26[3]	27	28	29
Ecotoxicological data			X		X							X	X	X		X			X	X							X	X	
Chronic ecotoxicity data / chronic effects	X				X							X	X	X		X	X												
Acute data / acute effects												X	X	X															
Bioaccumulation and persistence data														X															
Data on environmental effects				X				X			X									X									
Data for risk assessment / risk assessment results		X							X[4]										X	X								X	
Exposure relevance														X															
How loads are distributed amongst sources											X																		
Human toxicology data											X																	X	
Aquatic toxicity																									X				
Degradation			X																						X				
Cummulative effects																											X		
Endocrine properties																											X		
Hazard																											X[5]		
Consumption data												X		X	X			X											
Sales figures			X[6]												X														

Amounts excreted by body																			X											
Details on older generic pharmaceuticals							X[7]												X		X									
Information in Fass.se								X																X						
Life Cycle Analysis information		X																												
Env. info on manufacturing process (footprinting)																								X						
Behaviour in drinking and / or wastewater treatment										X		X																		
Easy guidelines for WWTP operators																		X[8]												
Environmental concentrations										X				X															X	
Fate of molecules in environment										X							X											X		
Chemical transformation cascades (transformation products)											X																			
Distribution of pollutant loads among sources											X																			
Entry pathways and inventory of emissions											X																	X		
Metabolite data												X																		
Behaviour and effects in soils															X						X									
Mode of action												X								X										

1 This expert works in the field of chemicals (excluding pharmaceuticals), and thus has no direct information requirements for work purposes.
2 Did not answer the question
3 Only answered question four
4 For authorization
5 System should also provide information on the complete product, not only on active ingredients, but also on excipients
6 National and perhaps regional
7 The question does not apply directly as this stakeholder group generates ''environmental and effects data for al active ingredients'' for regulatory submissions. Data on generic pharmaceuticals would allow them to a robust environmental analysis. They are interested in ''any data that can underpin the environmental impact assessment not just data for regulatory submissions''.
8 For example a substance should not be found in concentrations higher than 0,1 µg/l in drinking water

Q.4 Detailed information requirement profiles of interviewed stakeholders on pharmaceuticals in the environment

Summary:

- **Information needs**
  - There are widespread information requirements for the following data sets:
    - physico-chemical data,
    - toxicity and ecotoxicity data,
    - behavior in the environment (fate, degradation),
    - information related to sales and volumes of pharmaceuticals in the environment,
    - behavior in drinking water and wastewater treatment plants,
    - environmental measurements (e.g. measured data for pharmaceuticals in rivers).
  - The strongest information requirements are actors related to drinking water (water utilities and their associations, drinking water authorities), research organizations, and environmental NGOs. Environmental authorities do not report as many information requirements. Actors related to the health system have comparatively minimal information requirements. The pharmaceutical industry interviewees expressed some requirements from such a system.
  - Interviewees had many comments as to how sales figures could be a useful tool
- **Level of detail**
  - Many interviewees need highly detailed information and raw data
  - Some interviewees only require to have access to more general information and data that will ease decision making
- **How the information should be prepared**
  - Interviewees repeatedly state to prefer tables over charts, however charts were said to be useful in specific cases and/or for specific types of users

Question 4 collected interviewees' requirements against a list of possible data on PPs in the environment; please refer to Table 2 for the results. Interviewees were urged to suggest additional possibilities, not on the questionnaire list, of information useful for their purposes (highlighted as such on table). Additionally, interviewees were asked which level of detail the system should offer, and how it should be prepared.

Information requirements

The **strongest information requirements** are associated with:

- physico-chemical data,
- toxicity and ecotoxicity data,
- behavior in the environment (fate, degradation),
- information related to sales and volumes of pharmaceuticals in the environment,
- behavior in drinking water and wastewater treatment plants,
- environmental measurements (e.g. measured data for pharmaceuticals in rivers).

This kind of information awakes broad interest among the different stakeholder groups.

The results in Table 2 show **clear differences in the information requirements** between different groups. By far those with the **strongest information requirements** are **actors related to drinking water** (water utilities and their associations, drinking water authorities), **research organizations, and**

environmental NGOs. Surprisingly, **environmental authorities do not report as many information requirements**[8]. This could be due to their not having interest in information related to human effects and human toxicology (e.g. side-effects, pharmacokinetic and pharmacodynamic entries, mammalian toxicology entries, routes of administration); they seem to focus on more strictly environmental requirements. In contrast, institutions related to drinking water could also be interested in determining the human health effects of exposure to trace concentrations of pharmaceuticals in drinking water. Regarding environmental NGOs, it is possible that their sense of mission encompasses aspects beyond those strictly environmental of the Environmental authorities, to include issues that impinge on human health.

In contrast, there are **practically no requirements** listed for interviewees belonging to **medical associations and pharmacists**. This is probably due to the detailed data entries in the questionnaire. Interviewees of these groups expressed in the interviews interest in clear and simple environmental information, that would provide clear guidance for their prescription decisions. In other sections of the interviews, stakeholders of these two groups expressly stated information requirements similar to the information provided for doctors in Fass.se (but with additional requirements such as product comparability and more user-friendliness).

The pharmaceutical industry interviewees expressed some interest in information on PIE (see Table 2 but also Chapter 4.3). The apparently not as strong information requirements could be related to the fact that, although the interviewees would appreciate the support that additional scientific data would provide their work, it would not play a crucial role, nor affect the fact that the industry is responsible for generating its own environmental data.

Level of detail/aggregation

Seven stakeholders explicitly stated they would like to see an information system that delivers a **high level of details**; this is especially true for stakeholders from research organizations. It was mentioned that being able to view the full reports with exact results and testing conditions is important. It was mentioned on more than one occasion that data should be available on the regional and national scale, and if possible local. Additionally, the following comments were collected:

- It would be nice to have the aggregated information (…), and if you see there is a problem it is good to have more detailed information, like footnotes or appendices with details.
- We need the type of concrete numbers that are generally prepared in the data sheets for industrial chemicals or pesticides.
- We want the full reports to see if tests were done properly and the results well interpreted.
- We need the data to be as accurate as possible (several decimals)
- Info should be available for everyone but labeled (this for doctors, this for scientists)

Four stakeholders replied they **do not need a high level of detail**. One Swedish stakeholder stated that: ''the requirements put forward, both from prescribers and pharmaceutical committees, is that the system should be simplified in comparison with the current system" (referring to Fass.se). One stakeholder mentioned the information should be presented as simply as possible, but without suppressing important information. Another stakeholder answered that summaries would be sufficient, but detailed information on sales figures and behavior in WWTP are needed.

How should the information be prepared?

[8] However, Stakeholders 2 and 6 did not provide any information on this question, thus not allowing for strong conclusions.

A unanimous preference is that for tables of figures over charts. The importance of being able to access the **raw data** was mentioned on many occasions. Additionally, the following comments were received:

- "I think more people who are looking for data on exposure, fate, degradation, ecotoxicity would want a table of numbers. A lot of key data will be single values or ranges of values, so it would be a dull but worthy table. In some other cases if you are able to provide info on routes of uptake then things like graphics, pie charts would be useful."
- "For our purposes (environmental NGO), information could be kept more general as well as presented graphically, showing e.g. the development over time, so that an impression of the development of the subject is provided. However the in depth information has to be available for everyone."
- "Data should be presented in the form of data sheets as they are produced in REACH."

Three stakeholders specifically mentioned the use of charts would be beneficial. One stated that automatically generated charts would be useful to drinking water companies who need a clear and easy way to identify if there is an issue or not. Another stakeholder mentioned that charts along with a simple point system could be useful for consumers. Six stakeholders referred to the importance of having different formats and levels of information to target different user groups. Finally two stakeholders commented that the ''important thing is that information can be retrieved quickly''.

Table 2 Information needs on pharmaceuticals in the environment (Question 4)

Staholder group / Information requirements	Environmental authorities						Pharmaceutical industry			Water Utilities and Associations		Drinking Water Authorities		Research institutions					Medicinal products authorities			Medical associat-ions		Pharma. Assoc.	Consu-mer NGOs	Environm-ental NGO		Public Health Sys-tems	Pharma Waste Comp-anies
SH number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18[1]	19	20	21	22	23	24	25	26	27	28	29
Physico-chemical	X		X	X				X	X	X	X	X	X	X	X	X	X	X	X	X					X	X	X		
Ecotoxicological	X		X	X	X[2]					X[3]	X	X	X	X	X	X	X	X[4]	X	X				X	X	X	X	X	
Stability and biodegradation -feature	X		X	X				X		X	X	X	X	X	X	X	X	X	X	X					X	X	X			
Pharmacokinetic			(X)								X	X	X	X	X	(X)	X			X							X		
Excretion data	X		X							X	X	X	X	X	X	X	X	X	X	X						X	X		
Routes of administration			X							X		X	X	X	X	X	X	X		X						X	X		
Pharmacodynamic			(X)								X	X	X	X	X	X	X			X							X		
Side effects			(X)										X	X	X		X	X		X						X	X		
Mammalian toxicology data	(X)		X								X		X	X	X		X	X		X					X	X	X		
Sales data	X[5]		X	X	X		6	X		X	X	X	X[7]	X	X	X[8]		X	9	X[10]						X	X[11]	(X)	
Behavior in drinking water and wastewater treatment	X		X	X			X	X		X	X	X	X[12]	X	X	X	X	X	(X)	X				X[13]	X	X	X		
Behavior in drinking TP				X	X					X	X	X	X	X	X	X	X	X	(X)	X					X	X	X	X	
Water flows / quality in EU river basins	X		X	X			X				X[15]	X	X	X	X	X[16]	X	X		X					X	X[16]	X	(X)	
Management of PP wastes	(X)[18]		X	19	X					X	X	(X)	X	X	X	X		X	(X)						X		X		
Additional requirements (beyond the list)																													
PEC/PNEC			X					X																					
Bioaccumulation								X						X															
Exposure														X										X					
Environmental risk information		X		X													X[20]		X	X				X		X			

Consumer data															X[21]																
Health effects of the smallest dose				X									X																		
Combination effects					X														X												
Metabolites / transformation products														X				X	X												
Uses for drug																				X											
Effects data (carcinogenic, mutagenic, reproduction toxic)													X	X																	
Aquatic toxicity														X																	
Upcoming PPs															X																
Behavior / effects / measurements in soil																X													X		
Chronic data					X								X								X								X		
Environmental fate infromation								X																					X		
Any scientific information underpinning ERAs							X																								

(X): the information would be useful, but is not a priority fort he interviewee

1 There are pharmaceuticals that are chemically related and have similar behaviors, so not necessarily info on all compounds but enough to make assumptions on similar chemicals

2 Even teratogenic effects

3 That is the key data

4 For drinking water, this is the most important thing

5 If we could first understand how it would be useful

6 That is business confidential information so it might be hard to get, at the moment we have a way of getting that through the IMS system, but I am sure most companies would be reluctant to make this available.

7 Per capita and per region

8 First priority

9 We do not use sales data because they cannot be verified

10 Every agency has sales figures (in Portugal) but we do not have data for OTCs

11 Because this is sensitive information that companies probably would not want to provide, the approach used with pesticides could be implemented: provide a figure that gives the order of magnitude of sales. For instance, if a company places 3,5 tones of a certain pesticide on the market, it would declare that it places between 1 and 10 tones of the product on the market. We would clearly prefer the exact data, but this would be a possible compromise solution

12 Data on the behavior of pharmaceuticals in drinking water and wastewater treatment plants should be collected in the authorization process of the pharmaceutical, not later on, when the substance found in sewage water.

13 Behavior in wwtp is very important. Even more important for my work is data for behavior in drinking water plants, for instance information on which new products, possibly dangerous, derive from pharmaceuticals in the ozonation process

15 It is very important for us to know in which concentration these pollutants occur, and their impact on aquatic life

16 Including groundwater

17 It doesn't mean that measurements should be made for all rivers. This would be helpful to provide an overview of the issue, e.g. these substances are problematic in these regions, and these others are not.

18 What would be useful is to take ten key widely used pharmaceuticals and see what proportion of total input to the environment comes from various sources
19 Issues concerning waste disposal could be addressed separately not to overload the system
20 The approach for a more accurate environmental classification of APIs should be done integrated in a risk assessment report. It is particularly important to keep in mind that a classification system must have a scientific basis not just in environmental occurrence and exposure, but also in pharmacological / toxicological measurable effects, having significant outcomes from medicinal product (for instance: neurobehavioral, immunological, endocrine homeostasis alterations)
21 Data on why consumption values are as they are (regional differences in disease prevalence

Q.5 Use of the classification system in interviewed stakeholders' work

Summary

- **Purpose of use**
  - Different stakeholder groups identified various different uses of the system. Most commonly cited uses are
    - As a general data source for work (use in ongoing work, to answer questions, etc.)
    - Help for external communication (with the public, with authorities, media.)
    - To help understand risks (to the environment, to human health)
    - Help identify priority areas (identify risks, actions to take, etc.)
    - To help giving good recommendations (to practitioners, prescribers, authorities, public, etc.)
- **Would the system influence decision making**
  - Some interviewed stakeholders replied that the system would influence their decision making. Others replied it would only be used as a data source.
- **Support of the system**
  - The vast majority of interviewees replied that their organization would support the system. Some interviewees identified particular stakeholder groups or organizations as potential strong proponents/opponents of the system.

Question 5 asked interviewees for which purposes they would use the classification system.

Purposes of use

Uses identified by interviewees from **environmental authorities**:

- to understand risks to the environment
- to give good recommendations to prescribers and inform them on environmental impacts of pharmaceuticals
- to inform practitioners in the health care sector
- to identify whether there is a need to set EQSs within the EU WFD
- to develop EQS and define the need for action
- to explain poor biology in a water body (good biology being a key criteria for compliance with the Water Framework Directive)
- to evaluate environmental risks of generic drugs
- to use it in ongoing work on micropollutants
- when confronted with questions concerning acute pollution
- to answer questions concerning improved water techniques
- when confronted with questions concerning measurements of pollutant concentration in river
- for enquiries from the press
- used to assess if there are risks to human health (also identified by the public health stakeholder)

Uses identified by interviewees working for **pharmaceutical companies**:

- for external communication on risks
- eventually, companies could use it to make decisions on which pharmaceuticals to take through to the market based upon perceived risk (he specified, however, that currently companies are not considering this). However, one stakeholder responded that the system

would not be very relevant for his organization on an everyday basis, as the company already possesses an internal classification system and all pertinent information on its products.
- as data source for work (twice, e.g. helping guide the testing procedures)
- providing information on generic pharmaceuticals (companies producing the latter were bought up by the interviewee's company; information on substances is poor).

Uses identified by interviewees from **research organizations/universities**

- to look for exposure relevance and the eco toxicological relevance, to identify mutagenic carcinogenic or reproduction toxic substances
- to identify regions where you can expect a risk associated to a certain substance
- in advising ministry on priorities for action
- in advising on EQS settings
- to prioritize active substances
- throughout the course of studies

Uses identified by interviewees from **water and wastewater companies/authorities**

- In environmental fate studies
- To research individual substances, it is very hard for our members (e.g. wwtp operators) to understand the toxicological information
- as a compass to orient us when we find a compound in drinking water: is there a risk and how to minimize is, can this be addressed in the treatment process
- to develop criteria for drinking water relevance
- when developing recommendations (for government agencies)
- to be transparent when dealing with city council

Uses identified by interviewees from **consumer NGOs**:

- as a general information source to provide general information to consumers on the issue.
- at the most to address occasional, highly specific questions posed by consumers.

Additionally, the following uses were identified:

- to see if identified substances pass drinking water barriers (identified by authorities responsible for drinking water)
- in putting recommendations on labeling and disposal (identified by medical pharmaceutical authority)
- by scientists to look at reports and see what methodologies are performed in testing (identified by the pharmaceutical authority)
- as a support when evaluating ERA received (identified by stakeholder from the medicine board group)

Influence of the system on decision making

One stakeholder from the **pharmaceutical association** group stated it could influence the selection of goods for the pharmacy. Both stakeholders from the **medical association** group stated that the system could influence the selection of pharmaceutical by the doctor. One stakeholder (from the **environmental authorities group**) stated the system would influence in prioritizing substances and actions to be taken. Two stakeholders from the **water and wastewater company/authority** group stated that 1) any sort of logical decision making scheme would benefit from the system, 2) it would only influence how input is provided to national agencies in charge of authorization and for establishing the needs for tests that will help determine a possible toxicological potential. Another stakeholder of the same group stated the system could be very important to be able to think about what measures should be taken (at the treatment plant).

Seven stakeholders responded their work would not be influenced by the system. The following reasons were stated: it would only used as data source, one interviewee works with chemicals (not pharmaceuticals), one interviewee works in evaluating ERA and environmental impact does not impinge on licensing, one stakeholder (from the public health agency) stated they do not perform themselves the risk assessments, the stakeholder from the waste recycling group stated that according to actual procedures approved by environmental authorities he could not use the system, the two stakeholders from the environmental NGO group stated that pharmaceuticals are currently not a topic of priority, lastly the stakeholder from the consumer NGO stated that none of their guidance fields would be directly affected by an environmental classification.

Support of the system

Only two stakeholders explicitly stated their organization would not support such a system. One stakeholder from the research organization/university group responded they would not support a numerical classification; it is judged too simplistic and could not be used for risk assessment. The stakeholder from the pharmaceutical waste/recycling group reported their support would depend on the specific procedures concerning the implementation of the system. Another stakeholder, from the environmental authorities, conditioned his support on the EU-wide system being different then the Swedish system (stating that the latter is designed specifically for the Swedish context). Two stakeholders from the pharmaceutical industry stressed the point that their company would support such a system, and that it has been engaged in the topic, making information available for the public for a long time.

Four stakeholders specifically stated they do not expect any organization to be against such a system. The following organizations were identified by stakeholders as **strong proponents of the system**:

- In Sweden, Pharmaceutical committees
- Pharmaceutical industry (identified by environmental authorities group)
- All water boards as well as environmental institutes (identified by drinking water authority)
- All organizations working on water quality (identified by drinking water authority)
- Drinking water companies (identified by drinking water authority)
- Wastewater treatment facilities (identified by environmental NGO)
- Scientists and environmental scientists (identified by environmental authorities from the drinking water perspective)
- Physician associations (medical association stakeholder)
- Environmental authorities

The following groups were identified by interviewees as potential **opponents to the system**:

- The pharmaceutical industry was identified 6 times as a potential opponent of the system. Once by the pharmaceutical industry itself pointing to some pharmaceutical companies which are not addressing the problem in a transparent fashion (mentioning generic medicines). Other stakeholders explain this resistance as due to: the industry's dislike of regulation, the fact that the industry would not benefit from the system, the implications of making consumer sensitive data available to the wider public, the possibility to distort competition arising from changes to prescription practices, and because they will have to provide the data which implies more resources. One stakeholder, from the medical association group, did mention that the pharmaceutical industry would support the project in spite of the higher work load it could imply.
- Government agencies were mentioned on two occasions. One stakeholder suggested that they do not want to be the ones ending up with the burden of collecting the information and paying for the system.
- Doctors were mentioned by three stakeholders. One stated that resistance would have to do with implementation, not fundamental resistance. Another commented that doctors ''live

well off the pharmaceutical industry and may have the apprehension that the system could affect their income in some way.''

- Twice, stakeholders mentioned ministry of health, or organizations working in public health stating their primarily interest are in human health and would rather avoid the complications of including environmental concerns into their work.

Q.6 Main characteristics of a classification system for adequate results

Summary

➢ **Sources of information**

Three different opinions were collected, the first of which was most popular amongst interviewees:

- ❖ The largest part of information comes from the industry and is complemented by literature
- ❖ The industry as the only source of information
- ❖ (Peer-reviewed) literature as the only source of information

➢ **Quality**

The importance of having good quality data is a shared concern amongst stakeholders. Opinions collected can be divided as follows:

- ❖ An external revision body must be set up
  - ▪ And systematically revise submitted data (the majority of stakeholders share this view)
  - ▪ Revise data on a case to case basis
- ❖ No revision is required (laboratory standards will ensure quality of data)
- ❖ Minimum quality standards must be set (quality criteria)

➢ **Language**

- ❖ Most stakeholders see a system where parts of the information are available in English while other parts (to ensure uptake by users) are available in the national language.

➢ **Categories of Pharmaceuticals to be included**

- ❖ The majority of interviewees agree to say that all pharmaceuticals should be covered
- ❖ Other interviewees suggest to focus on: widely used pharmaceuticals, those representing a high or hazard, or specific categories
- ❖ Some comments were collected on how exceptions should or should NOT be made for certain substances
- ❖ Interviewees unanimously agree that both over the counter and prescribed drugs should be included

➢ **Different opinions were collected on the categories of PPs to focus on in a first phase, the most common ones were:**

- ❖ High volume PPs
- ❖ Hormones and endocrine disruptors
- ❖ Antibiotics
- ❖ Cytostatics

Question six asked stakeholders to comment on what characteristics the system should exhibit to ensure it works adequately. This question allowed for a discussion on: what the origin of the data should be and how to guarantee its quality, what categories of pharmaceuticals should be included (Table 3), and which pharmaceuticals to focus on in a first phase (Table 4). Comments collected are summarized in this box.

Sources of information

The vast majority of stakeholders are of the opinion that information sources for the classification system should include the industry and literature. Fourteen stakeholders explicitly stated the **largest share of information should come from the industry**, seeing as they already are producing it for their ERA, and could be **complemented using other sources**. Additionally, the following comments were collected:

- For new products, data should be provided by the company that is placing them on the market. For products produced by multiple companies, there would have to be a sieve type of organization from which data and cost could be distributed in proportion to share of the market (statement from a pharmaceutical company).
- There could be other sources (than industry), but you have to consider what is practically possible.
- The industry shouldn't provide all the information because they have vested interests.
- The amount of work is huge if you put this only on the authorities.
- I think it is better if it is public; the collection of money has to be independent from the evaluation agency.
- There are plenty of data in public literature. There is a big controversy about using public literature: industry says it is impossible to use this source of info because, as opposed to the industry, it is not subjected to high standards. I think it is unfair and this issue should be solved in a transparent manner.
- The way it's done at Fass.se is good (data provided by industry and reviewed by an independent body). However, there have been isolated problems (…) especially where the available data are not identical everywhere and when the criteria are not very clear. This will probably not change easily, especially concerning old medications for which data is simply not available.

Only two interviewees referred to **pharmaceutical companies as being the only source of information** for the system. Only three stakeholders referred to **literature as the only source of information**, one of which explained that ''industrial studies (who follow standard tests) do not include, in most cases, all en points''. A second interviewee stressed the point that **only peer–reviewed data** can guarantee quality data, grey literature is not enough, and that one should be able to assess the sources.

Two interviewees explicitly stated it will probably **not be possible to use the industry as a source of information**; the first referred to the fact that industry holds a patent on the information rendering it impossible to use it, the other supposed that the industry will simply not be giving the information.

Quality

Almost every interviewed stakeholder referred during the interview to **the importance of having good quality data**. The issue **of neutrality, transparency, validity, and completeness** of the data were mentioned in some way in many occasions. The most recurring suggestion (12 times) is that of having an **external revision body**. However, one interviewee commented that ''external revision seems more or less impossible, because then you need all the experts looking at all the data''. Another (from an environmental authority) judged that ''an independent body for inspection is not necessary; **the standards that apply to the laboratories [GLP] will ensure the validity of the data''**.

One stakeholder said revision should occur ''only for individual cases, when there are issues, so as to keep the taxpayers' expenditures as small as possible''. Two stakeholders explicitly stated the industry can be trusted and that ''there is onus for the industry to be upfront''.

Others referred to setting up **minimum quality standards** (2) or **quality criteria** such as the Klimisch score (4), a quality label or a peer reviewed system. The issue of cyclically updating the data was mentioned on a few occasions. Additionally, the following comments were received:

- It is most important that the data is correct, you do not know how it can be manipulated. (…) Data should be updated as soon as new info is available because if you are going to influence people's choice your info has to be as accurate as possible.
- Of course the information will come from the industry and it can be trusted but it should still be evaluated. Other sources should be used to see if there are inconsistencies
- Quality of info is established by current regulatory systems (EMEA for ERA). There should be a strong emphasis on data being generated in accordance to good laboratory practices, in accordance to OECD guidelines or equivalent guidelines.
- The data would need to have undergone some sort of quality insurance by people who know what they are doing, who have seen the original research and can confirm that the conclusions are reasonable
- There are a lot of studies of different quality in research. To deal with this it is important to have good experts that will agree on which info has an adequate quality and which does not. This process must also be transparent
- Quality data is crucial, if people do not trust you, you have already lost the battle
- From the point of view of neutrality you could combine some sort of revision, I suspect no company would be against a neutral organization was set up to review the ERA of products
- Achieving neutrality is difficult. I have the impression that this is not always the case at Fass.se. A neutral position is good for minimizing mistakes and for raising questions that allow for improvements or, at least, reveal problems.
- You have to have an independent body in charge of putting together the request for data and then controlling the gathered data.
- There should be sanctions if the information provided by the industry is not correct
- Information should be ranked according to the quality of their sources.
- The way it has been done in Sweden is not appropriate. The data are not checked by the licensing authorities but rather only by a board that does not even review the data but only checks them for consistency.

The few comments collected on who should assume responsibility for such a system suggest that, in general, interviewees feel more comfortable with a system that would be managed by an official independent body, but that would not exclude the industry's participation.

Language

The few comments received concerning language acknowledged the difficulty of dealing with questions of language within the EU. Most suggested that, while some technical information can be made available in English, information for doctors, pharmacists, and the broader public should be available in the national language to maximize usability and uptake. Style was mentioned only once in that it should be simple as to be accessible to all target groups. Other statements collected include:

- It is difficult to correctly translate technical issues in every language; it's even more difficult for laypersons to then interpret this technical terminology. It should be very carefully agreed upon which interpretations should be included, in what languages and how they should sound, such as is done in level 1 or 2 in Fass.se. When in doubt, perhaps English should be

chosen as the original language and translations of the highest possible quality made in other languages from the English version.

- We would need an adequate translation as well as an accompanying manual or glossary as to how the system is used.

Table 3 Categories of pharmaceuticals that should be included in the system (questions 6b, 6d)

Stakeholder group / Information requirements	Environmental authorities						Pharmaceutical industry			Water Utilities and Associations		Drinking Water Authorities		Research institutions					Medicinal products authorities			Medical associations		Pharma. Assoc.	Consumer NGOs	Environmental NGO		Public Health Systems	Pharma Waste Companies
SH number	1[1]	2	3	4	5[2]	6[3]	7	8	9	10	11	12	13	14	15	16[2]	17	18[4]	19	20	21	22	23[2]	24	25	26[5]	27	28	29
All human PPs (marketed in EU)		X	X	X			X	X	X	X				X	X			X	X		X	X		X			X[6]	X	
Veterinary products							(X)					X				(X)	(X)								X	X			
Anticancer, antibiotics	X																												X
Widely used + hazardous + high risk			X			X						X								X					X				
Drugs of abuse																		X											
Cumulative subs., those not eliminated in disposal processes, toxic ones, endocrine disruptors, antibiotics and cytostatics																							X						
All PPs that have an effect on the neural system																		X[7]											
PPs over certain per capita consumption treshold													X												X				
Only relevant PPs											X																		
Exceptions for PPs which qualify for exemption		X					X[8]	X[9]																	X[10]				
Prescribed vs OTCs																													
Both	X	X	X		X		X	X	X	X	X	X		X	X		X	X		X		X		X		X[11]		X	X
First prescribed, if resources also OTC																							X						

1 In his research, the interviewee identified ibuprofen and propanalone, as well as a few antibiotics
2 Did not answer the question
3 Discussion on risk vs hazard
4 I think it is strange to have a lit, some pharmaceuticals that are widely used do not present any risk for human health
5 Interviewee replied that it is hard to answer without knowing more about the system
6 Because toxicologists are highlighting more and more the low dose effects of chemicals
7 Because it can be expected that they have an effect on the environment
8 There are guidelines for pharmaceuticals qualifying for exception from ERA you should take that into account eg. G low volume or orphan drugs, but in general most pharmaceuticals should be included
9 Allowing exceptions for vitamins, proteins, where a general assessment could be done
10 Orphan drugs can be ignored because they are sold in very little quantities
11 Information should be targeted at the prescriber and it should be communicated to the consumer on packaging, using a simple text.

(x) Indicates that the interviewee has referred to the importance of creating a system for veterinary substances, but that he does not necessarily wish to see this integrated with a system for human pharmaceuticals

Table 4 Priority drugs to focus on in a first phase (question 6c)

Stakeholder group / Information requirements	Environmental authorities						Pharmaceutical industry			Water Utilities and Associations		Drinking Water Authorities		Research institutions					Medicinal products authorities			Medical associations		Pharma. Assoc.	Consumer NGOs	Environmental NGO		Public Health Systems	Pharma Waste Companies
SH number	1	2	3	4	5	6 [1]	7	8	9	10	11	12	13	14	15	16 [1]	17	18	19	20	21	22	23	24	25	26	27	28	29
High volume PPs (sales and consumption)	X	X	X	X			X						X [2]	X	X		X	X [3]		X [4]		X [5]			X		X		
PPs with evidence of highest presence / highest exposure in env.				X										X															
PPs known to have environmental effects															X									X		X	X		
PPs with a risk characterization (PEC/PNEC) ≥ 1							X																						
PPs that trigger Phase 2 in EMA evaluation																					X [6]								
Stable compounds			X																										
Based on PBT characteristics					X		X																						
Based on high toxicity			X												X														
With a relevant mode of action					X									X															
Hospital drugs																													X
Sex hormones, endocrine disruptors, and other hormones		X [7]			X		X	X	X		X												X	X		X	X	X	
Antibiotics		X		X							X	X	X					X				X	X		X		X	X	
Lipid lowering					X																	X							
Cardio vascular medicines																	X					X							
Cytostatic drugs				X					X		X									X		X	X		X				
X-ray contrast agents				X	X																								

Anti-psychotics					X																									
Antimicrobial																				X										
Central nervous system drugs																	X													
Pain killers													X														X			
Anti-rheumatics											X																			
No group in particular								X	X [8]	X [9]									X											
Medicines with similarities to POP																											X			
Virostatics																											X			

1 Did not answer the question
2 Data should be provided for pharmaceuticals that are over a certain per capita consumption threshold, others can be neglected
3 It would be worth it to look at consumption data and identify drugs that are highly consumed and then look at excretion data and then make a list of the chemicals that you are expecting to find in the water, instead of looking at what someone else found and always measure the same pharmaceuticals
4 If a drug is widely used we should try to see if it is found in the environment
5 Cancer drugs are important but they are only distributed in hospitals and they have their own sewage system
6 But that impinges on exposure levels
7 Especially oestrogens and estrogenic substances
8 I dont't believe there are any good arguments for a prioritization
9 According to our analyses, there is no particular category to prioritize over another

Q.7 Usability and structure of the system

Summary

- **Tiered approach**
  An approach where different levels of information is made available to the different groups of stakeholders that would benefit from the system was well received by interviewees, although different opinions were collected on:
  - The level of interest and hence the relevance of addressing the general public
  - Having an open vs. restricted access system
- **Reccuring suggestions**
  - The system should contain a good search engine
  - Having an environmental label assigned to pharmaceuticals (this grading scheme is perceived as most useful for the public and for doctors scheme)
  - The system, if it is to be used by doctors, must be designed with their time constraints in mind
  - It should be easy to compare groups of substances or individual compounds side by side
- **Evaluation of Fass.se**
  - Most interviewees are familiar with Fass.se but do not use it
  - The interviewees were able to comment on the structure of the system had divided opinions:
    - The information is useful and well presented
    - It contains many data gaps
  - It is not easy to retrieve information from

Question 7 provided the opportunity to discuss structural elements of the system to maximize its usability and to evaluate users' evaluation of the Swedish information database for pharmaceuticals (Fass.se).

Structure of the system

The following comments and suggestions on how a possible information system should be structured were collected.

One stakeholder stated the importance to define what the system is designed to deliver prior to thinking of how it should be constructed. One stakeholder stated the system should be designed with the support of those who will use it and perhaps with people who are used to building health records.

Eighteen stakeholders stated the **"tiered" or level approach** was interesting or useful. Amongst these, the following comments were collected:

- Data has to be aligned and presented according to the needs of the user, info should be compartmentalized according to end user requirements (perhaps using tabs)
- One stakeholder described the target groups and information made available to them as follows: environmental specialists (info on EQS, limits, eco tox data), doctors (info on healing effects, and environmental characteristics), consumers (by means of a simple traffic light

system being able to identify environmentally friendly medication, they should not encounter info on healing effects)

- On two occasions, it was mentioned that the general public might not use such a system (one stakeholder suggested they would not understand it)
- One stakeholder asked whether all types of users would really use this information or if we should focus on one group that will really benefit from it
- One stakeholder suggested the general public should have restricted access, industry and research have similar access, and groups performing risk assessments have complete access.
- Three stakeholders explicitly expressed that having an open access system is important. Two stakeholders explicitly contradicted this view. One of which specified that while some data could be public, data belonging to the company would not.
- Eight stakeholders referred to the necessity of having a useful search engine. One of them mentioned the search box in REACH. It was mentioned that the system should be searchable on the basis of substance (drug and trade name) and attributes.

One stakeholder from the medical association commented that because it is not always possible to consult such a system, leaflets containing info on the most relevant pharmaceuticals should be prepared for doctors to be able to refer to them more easily. Another stakeholder suggested that to ease decision making, a simple risk or no risk flag could be implemented: a label, comparable the energy label, on how environmentally friendly a product (which would be an aggregate value of values contained in the database).

Other comments received include: a modern design should be used, it should be very intuitive, it should indicate how recent the data is, the classification should be available in a printed version, it could be interesting to publish a yearly report, it should be connected with relevant database such as TOXNET.

Evaluation of structure of Fass.se

Only three interviewees reported not to be familiar with Fass.se, but only six interviewees reported to be familiar enough with Fass.se to provide comments on the usability of the system. Four of them expressed positive comments on its structure: the first reported to like the way the system is built, the second claimed that all the information it includes is useful, the third stated the display is *not bad* and the information is presented in a useful format (for environmental authorities, remains to see if it is useful for doctors and patients), the fourth replied it is well designed from the point of view of experts. The following criticisms were received:

- Language is a barrier (most information is only available in Swedish)
- It contains many data gaps
- It is not *too* user friendly, the location of data is not terribly intuitive (one stakeholder reported that many of his colleagues share this opinion)
- The search for medicines is not practical (the user has to click to go see results on the next page) it would be better if they appeared on one page and cone could simply scroll down.
- It is cumbersome because you can only search by the substance and not by ingredient groups
- It lacks interconnectedness: it does not allow to compare data for different pharmaceuticals
- It is not appreciated because it is difficult to retrieve information from
- Navigation is awkward (e.g. it does not have a filter which retains ingredients for which environmental data are available)
- It assumes that 100% of what is consumed enters receiving water, which is not accurate (identified by interviewee of the pharmaceutical industry group)

Q.8 Perception of risk posed by Pharmaceuticals in the environment

Summary

- **Perceptions on risk**
  - Stakeholders express different levels of concern on the risk for human and for the environment.
  - Interviewees express a concern for a few key substances
  - The importance of putting pharmaceuticals in perspective with other chemicals is a recurring comment
  - The need for more research is a recurring comment
  - Several stakeholders feel that actions should be taken now rather than later
- **Media attention**
  - Most interviewees agree that the issue of pharmaceuticals in the environment is often sensationalized
  - Interviewees have different levels of satisfaction with the way the media addresses the issue
  - Interviewees present diverging opinions on informing the public
  - Interviewees present diverging opinions on the relevance of discussing this issue in the media
- **Efforts to address the issue**
  - Most interviewed stakeholders agree that efforts to address the problem are justified, although interviewees' ranking of the issue in terms of priority varies

Question 8 asked interviewees to share their perception on the risk posed by pharmaceuticals in the environment as well as on the media attention paid to the issue and the efforts to address it.

Perception of risk posed by PPs

Only one stakeholder reported to have **no informed opinion** on the issue. Five stakeholders have explicitly expressed **the issue should be taken seriously** and followed, one of which has ranked it as a high priority. A few stakeholders expressed **concern about a small number of particular substances** including: steroidal estrogenes, estradiol, diclofenac, antibiotics. One stakeholder referred specifically to the potential risks of antibiotic resistance. Six stakeholders insisted on the importance **of putting pharmaceuticals in perspective with other chemicals** that we use, implying that pharmaceuticals do not represent a high risk when compared to pesticides. One stakeholder commented that 'it would be interesting to (…) compare the risks of pharmaceuticals to risks associated to other types of chemicals (creating) a scale'' which would help decision makers to better understand the risk. Two stakeholders expressed that the **precautionary principle** should apply. Another mentioned that, in practice, the application of the precautionary principle is difficult. One stakeholder reported that while there is currently no evidence of failures to achieve good ecological status in his country's water bodies due to pharmaceuticals, there are cases where there are non-identified causes of failures (bad biology), where pharmaceuticals could be responsible. Another stakeholder commented that while toxic and ecotoxic effects are important we should do more in preventing pharmacologic effects (when the pharmaceutical exerts is effect in the aquatic environment, which occurs at much lower concentrations compared to ecotoxicological effects). The risk of teratogenic effects (which can occur at extremely low concentrations) is also an issue.

One stakeholder has explicitly expressed that based on current scientific knowledge there is **no significant risk**. Two stakeholders described the **risk to humans** as being low; two stakeholders

described the **risk to the environment** as low; and three stakeholders do not see a **risk from drinking water.**

One stakeholder from the pharmaceutical industry specified that ''there is only one pharmaceutical that has a deleterious effect on environment (diclofenac)'' and agreed that if there is sufficient exposure pharmaceuticals can have impacts on certain species. However, he denoted that diclofenac is ''a very atypical exposure scenario''; when pharmaceuticals are found in the environment they are found at very low concentrations. He mentioned that other pharmaceuticals have been attributed environmental effects, but it is not as clear. He also mentioned that the issue of antibiotic resistance is a real one but, again, it is not clear if it is an environmental one, and that data to this regard has yet to be generated. The same stakeholder concluded that there is no evidence to indicate risk to human health and that the issue should not divert regulators from the real risks (bacteria, lead, arsenic, viral, etc). Another stakeholder considers the risk to human health to be extremely low. All three interviewees from the pharmaceutical industry stated that pharmaceuticals should be put in perspective with other chemicals which also impact the environment. Two stakeholders stated that the issue of pharmaceuticals in the environment should be taken seriously. One stakeholder explicitly expressed that the issue should be taken seriously and that both risks and hazards should be investigated. All three interviewees from the industry expressed that more research is needed to address the issue, especially concerning environmental impacts.

Finally three stakeholders (two from the environmental authorities group and one from the environmental NGO) denoted that the current pollution **situation is not comparable to what was observed decades ago**; much improvement was achieved. The risks associated to other chemicals has decreased over the last 30 years which means that constant background of chemical pollution is becoming more and more important.

Many stakeholders implied in their comments the **need for more research**. Six stakeholders explicitly reported this need. Two stakeholders pointed out the importance of planning for the future; ''it is not because we have no clear major sign that things are going wrong that we cannot start planning for the future and secure the process which enable us to manage the situation, or start improving legislation''; ''we (drinking water utilities) have to address today problems that will become relevant in 50 to 100 years''. Three stakeholders reported more research is needed on studying the impact on the environment (including resistance, mixtures, aquatic effects, long term exposure at low concentration, and human health effects of the smallest dose). One stakeholder stated that ''environmental impacts have received too little attention and we don't even know anything about health risks''.

Media attention

The most recurrent comment concerning how the media treats the issue of pharmaceuticals in the environment is that it is sensationalized. Two stakeholders qualified it as generally sensationalized while eight qualified it as sometimes sensationalized. From this group, three stakeholders mentioned the media pick up on the results of research made possible by increasingly sensitive analytical methods which allow detecting very small concentrations which are not necessarily significant for human health. Two stakeholders commented that members of the media might not have all the knowledge to understand what they are writing about. One stakeholder disapproved of the imbalance in print media between the amount of space available for the pharmaceutical industry to promote their new products and the attention paid to discussing to possible risks associated to these medicines. One stakeholder stressed the point that the question of public information needs to be carefully addressed. One stakeholder commented that while ''media attention focuses on risks to human health it is hard to find environmental arguments in the coverage, however this is an environmental issue, we don't see an acute risk for human health caused by pharmaceuticals in drinking water''. Finally, two stakeholders mentioned there are other environmental issues that are

more relevant which the media needs to address. Lastly, one stakeholder commented that ''the media and the public pay too much attention to the subject, the authorities too little''.

Four stakeholders explicitly expressed to have no problem with the way media is handling the issue. Five stakeholders expressed that they were satisfied with the attention paid by the media. The importance of informing the public about possible environmental effects of medication was mentioned on one occasion. One stakeholder specified hat restricting the discussion to pharmaceuticals would be wrong; we use thousands of chemicals. One stakeholder stated he would like to see the media creating more awareness amongst doctors and the public. Two stakeholders commented that media attention is a good thing which allows us to make progress. Finally one stakeholder reported to not be aware of any incidence of media attention being paid to the issue.

Efforts to address problem

Twelve stakeholders find that the efforts to address the problem of pharmaceuticals in the environment to be justified. Amongst these the following comments were collected

- Research is essential
- Efforts to tackle this problem without interest groups are important. A more socially broad approach acts as a particular motivation to participate in the various projects.
- Pharmaceuticals should make the list of priority substances of the Water Framework Directive.
- It is not a priority
- Efforts are sometimes duplicated. What conclusions we will draw from the efforts is still very open.
- Efforts should not just focus on pharmaceuticals, it is important to have a broad view.
- Efforts are made to address industrial chemicals, so it is only consequent to also address medicines
- More can be done

One stakeholder commented that the production of medication should be more closely followed. While efforts made in the western world are numerous, the challenge is to go to less developed countries.

4. Beyond interview questions: Stakeholder issues and positions regarding an information system on PIE

The issue of pharmaceuticals in the environment (PIE), which are among the compounds known as "emerging contaminants", is an emerging environmental pollution issue, with, at least in a theoretical future, potential impact on human health. As with any environmental pollution issue,[9] different aspects of the issue are contentious and are associated with (also future) actors' interests, responsibilities, obligations, and expenditures. Stakeholder opinions on an information system on PIE and on information requirements are not independent of their involvement in the issue and on its political aspects.

This chapter presents stakeholder issues and opinions on an information system on PIE that go beyond their concrete questionnaire answers. **The aim is to outline, in the interviewees' own words, some of the issues on their agendas.** The rationale for this chapter is that the establishment of an information system for PIE will have to acknowledge, or somehow else deal with, these positions in order to find acceptance and uptake. On another front, acknowledgement of

[9] In spite of the differing opinions on the severity of the problem, or even on its existence; see Ch. 3, Question 8.

stakeholders' positions is even more necessary if stakeholders are to be moved to share information in such a system.

Disclaimer: This chapter does not claim to provide a comprehensive mapping of stakeholder groups' interests and positions, but rather present some individual points gathered from the stakeholder interviews. It should be kept in mind that interviewees presented at all time the **position of their individual organizations** (and sometimes personal opinions, duly highlighted); as such, **their opinions should not be taken to necessarily represent a wide-held view among similar organizations**, but rather **an existing opinion within this stakeholder group, possibly shared by other group members**. The limited number of interviews, both in total and per stakeholder group, should also be kept in mind when evaluating this data.

Finally, we believe that the groups defined cover all actors with a significant stake in the issue, but do not guarantee comprehensiveness.

4.1 General Comments

Practically all stakeholders interviewed acknowledge significant **knowledge gaps** on the issue of PIE;[10] many of these stakeholders are interested in this information for their work (see Chapters 2 and 3). The gaps concern both the behaviour, fate, and impact of PPs in the environment, and data related to the effects of the continuous intake of trace amounts of PPs on human health. Some of the gaps most frequently mentioned are:

- Behaviour in drinking and wastewater treatment plants, and in sewage sludge,
- Chronic toxicity data (long-term exposure),
- Data for "old" substances (which do not have an Environmental Risk Assessment and thus lack most data),
- Sales / consumption data.
- Share of pollutant load deriving from landfills (i.e. medicines disposed of in domestic waste) vs. that which reaches the environment via wastewater.

This data situation has two very significant consequences. On the one hand, **the knowledge gaps allow for uncertainty in the significance of the problem, and thus different interpretations of the importance of the issue** of PPs in the environment, and of the related issue of its presence in drinking water. This influences the second consequence, namely that **requirements for information are linked to the question of who would be responsible for making this "missing" information available**, as well as who would make the resources available for this process.

Some of the information required is existent, like more detailed information on the ERA tests and sales data for PPs. (However, this is private information, and some of it is considered business-confidential.) Other data, like ERA assessments for "old" substances or chronic toxicity data is usually not available. To generate this kind of information, a significant amount of resources and effort would be necessary.

[10] The amount of information available of course varies according to the active substance considered.

4.2 Environmental Authorities (including RBOs) / Chemicals Agencies

The extensive and detailed information needs of environmental authorities' representatives interviewed correspond to those of a **knowledge base system**.

Interviewees frequently mentioned that the lack of data, particularly chronic ecotoxicological data, is a problem for their evaluating environmental impact and risk associated to PIE. In the words of one interviewee:

> *"It is quite clear to us that if there are any risks to the environment they are likely to be chronic [i.e. due to long-term] and not acute [i.e. due to short-term] exposure. There are major data gaps. […] The dilemma is like the chicken and egg situation: without reliable chronic toxicity data we cannot assess whether there is a risk or not, but it is only when we have evidence that there is a risk that we can justify going on and collecting this data. […] In the face of uncertainty we make a judgment based in large part on instinct and precedent." (Stakeholder 1)*

Sales and consumption data, and information on the behavior in wastewater plants, were also repeatedly mentioned as data requirements.

Two interviewees of this group imply in their statements that changes are required to the registration process, so that the pharmaceutical industry makes more information available.

> *"Maybe the registration process for pharmaceuticals should be improved to include information on the environmental hazard associated with the substance." (Stakeholder 2)*

> *"The question this project might raise is, if there is a strongly held view that there is a lack of useful toxicity data: who are the best people to generate it? In most of the chemical groups it would be the suppliers, the industry." (Stakeholder 1)*

The information uses mentioned by interviewees of this group were establishing Environmental Quality Standards (according to the WFD), prioritizing PPs for in-depth evaluation and monitoring (same use identified by water operators and drinking water authorities), and risk evaluation of generic ("old") pharmaceuticals for which there is no data (same use identified by pharmaceutical companies). There was strong support for the establishment of an information system in interviewees of this group.

4.3 Pharmaceutical Industry

A common position in the interviews of this stakeholder group was that the issue of PPs in the environment is not insignificant, but much less important than the attention it is currently being given: a result of media overdramatizing and public opinion overreacting to the issue (particularly to the related, human health issue of trace amounts of PPs in drinking water).

Interviewees of this group (as well as drinking water interviewees) expressed the wish to see the issue relativised and compared with other environmental issues (e.g. current-day risk due to pesticides, historical risk due to DDT) so as to place the risk of PPs into context. There is a strong preference for an evaluation based on risk rather than hazard.

"If a classification system is adopted, the classification system must be based upon risk and not hazard. We were very insistent on this on the Fass.se system. If you base a system purely on hazard it misleads the consumer or the person making the decision. The system should be based upon risk as a principle." (Stakeholder 7).

Interviewees often stated that in principle there is openness to providing available information and increasing transparency. Two of the 3 interviewees mentioned that their companies have been freely publishing available environmental information on their products for years.

"(Making information available to the public) ... is a critical part of our contract with society, making information transparent and ethical is part of being a pharmaceutical company." (Stakeholder 7)

However, the issue of resources is not a minor point:

"(...) such a system requires a lot of resources to provide the information, to classify the materials (...). For companies to do this they have to see that the process is delivering changes and benefit." (Stakeholder 7)

Two main purposes of the system were identified by industry interviewees as beneficial. On the one hand, an information system could work as a risk communication tool for the broader public. On the other hand, the system would support the environmental risk evaluation processes: existing information could help refine risk assessment with real data that could replace the "very precautionary" assumptions of the risk assessment, and data would also assist in the environmental risk assessment performed for new products. Counting with information for similar compounds could guide the industry in their testing, possibly avoiding performing some unnecessary tests, and thus save money. (Medical products authorities also identified this as an aspect entailing economic benefits for industry.)

"The one aspect that this system could be used in is communication of risk to people using our products outside of our company (consumers, doctors, pharmacists)." (Stakeholder 7)

"(Q: For which purposes would you use the system?) A: Especially as a data source in my own work on environmental risk evaluation. In this type of work, it's very important and helpful to have access to data on active ingredients that are not in-house (e.g. old medications or generic drugs)." (Stakeholder 9)

4.4 Drinking water / Wastewater companies

Water operators interviewed favoured a **knowledge base system** for their work, but viewing positively the potential of a decision support system for doctors/pharmacists/patients to reduce the input of PPs into the environment.

From the wastewater perspective, water operators are very wary of being given the responsibility (and the financial burden) for implementing further treatment measures that will reduce the amount of PPs in the effluents of wastewater treatment plants.

"In my country we are seeing that local politicians are placing pressure on wastewater operators to take further measures [to reduce input of PPs in the environment], although there is absolutely no legal basis for this." (Stakeholder 11)

From the drinking water perspective, interviewees of this group coincided in seeing the real issue as an environmental one, with PPs in drinking water as yet of no real importance. However, data gaps should be closed and both foresight and precaution should be guiding actions.

> *"According to the information available at this stage: there is no need to worry. [...] That doesn't mean the question should not be further investigated and that no one should consider schemes to ensure we stay on the safe side. It is not because we have no clear major sign that things are going wrong that we cannot start planning for the future and secure the process which will enable us to manage the situation. It is not because there is no striking evidence of impacts to human health that we should not keep our eyes open and start improving the legislation." (Stakeholder 10)*

One change suggested to the legislation referred to the incorporation of information on treatability in drinking water plants in the authorization process, and this information influencing how a product is placed on the market (also identified by drinking water authorities). A further legislation change could refer to a fact criticized by interviewees of this group: that the regulation relevant to pharmaceuticals requires for less information on environmental fate than that for other pollutants such as industrial chemicals.

> *"When it comes to pharmaceuticals health is a paramount priority, I support that view, but it doesn't mean that it should preclude laboratories analyzing dossiers to have all the data regarding the environmental fate. That is also a good way to encourage stewardship. […] There is no reason why there should be exceptions [i.e. pharmaceuticals being treated differently to other chemicals] even though it is in the name of public health protection, because in the end we are talking about health protection here too." (Stakeholder 10)*

The uses of an information system were to provide quick guidance on molecules found in water, and provide basis for decision-making, such as how to minimize the risk associated with the molecule.

4.5 Authorities responsible for Drinking Water

Interviewees of this group shared with those of water utilities an interest in a **knowledge base approach**, the judgement that there is currently no real risk for human health deriving from PPs in drinking water, and the strong interest in focusing now on the problem rather than postponing the issue. The perspective can be said to be even more precautionary than that of water utilities' representatives interviewed:

> *"We who are responsible for drinking water supply have to address today problems that will become relevant in 50 or 100 years. Other authorities, such as Medical Product Agencies, don't see it this way, they say "What is the problem, we are miles away from measurements that are health relevant, there's no need for measures." But we have to work with a lot of foresight. That's why we really want to avoid any pollution that is avoidable, and not compare it to effects [on health, before making a decision]. We don't want to start doing something when the effects are already there. That is our concept of precaution." (Stakeholder 13)*

(In addition to those of water utilities, interviewees belonging to environmental and consumer NGOs also had a very strong focus on precaution.)

Both interviewees of this group highlighted the need for knowledge on the behavior of PPs in drinking water treatment, and one expressed the wish for legislation changes that would consider this information in the product authorization process, and influence its placement on the market (as did one interviewee of drinking / wastewater companies).

4.6 Research Organisations

The answers of interviewed scientists who work on PIE show a clear preference for a **knowledge base approach**, addressing the knowledge gaps and the dispersed data on the topic.

Research questions and information needs were very similar to those of interviewees belonging to environmental authorities, such as identifying risk and non-risk substances, setting priorities for taking action, advising on the setting of Environmental Quality Standards or on emission levels for authorities who issue permits. Sales / consumption data requirements were highlighted by most interviewees.

Of particular relevance for this group was the need for data to be very detailed and accurately documented, with exact information on methods, procedures, etc. Transparency and reproducibility of data were key issues; industry data was evaluated as having problems in this sense.

> *"If you have an industrial study in most of the cases it is done following good laboratory practices (GLP), according to OECD standards, so a very valid study. But in most of the cases there is no access to the main results. This makes it difficult to evaluate the whole study. You have the endpoints, and the security that it is done by GLP studies, but not all endpoints are covered by the standard tests. So you have to complement those datasets if possible. In most of the cases it is not possible for pharmaceuticals to do this because this information is confidential. It is more restricted for pharmaceuticals than for pesticides. There [with pesticides] you have your own draft risk assessment reports and from registration the data becomes available. There you have more data available. That's the problem. In the case of pharmaceuticals the main source of information is publicly available literature." (Stakeholder 14)*

Depending on the exact study topic of the interviewee, strong interest was expressed regarding available information of effects of PPs on bacteria, soils, and information related to veterinary drugs.

4.7 Medicines Authorities

Strictly speaking, these authorities do not have information requirements, because they receive by definition the environmental information they require from the pharmaceutical companies when these submit a product for approval.

However, interviewees of this group did express interest in a **knowledge base** system compiling information on the topic. Such a system could help provide risk / no risk information, help minimize exposure, and support recommendations on labeling and on waste disposal.

Interviewees also recognize the potential of the system to assist the industry in the assessment stage, thus reducing the need for some tests and saving resources. Counting with information for similar compounds could guide the industry in their testing, possibly avoiding performing some unnecessary tests, and thus save money. (Industry interviewees also recognized this potential.)

4.8 Medical Associations

The interest of interviewees of this group was limited to a **decision support system for doctors/pharmacists/patients**; no additional information needs or uses were identified in the

interviews. (The only other interviewee groups with this exclusive focus were pharmacists, and pharmaceutical waste / recycling companies.)

Uses of the system identified were prevention of environmental pollution (with ensuing positive health effects and reduced economic burden on the health care system), and helping support a change towards a medicine based less on pharmaceuticals and more on prevention and life-style changes.

(The medical associations interviewed were environmentally very engaged; as such they possibly do not provide a representative view of the interests of all doctors in the system.)

4.9 Pharmacies / Pharmacy Associations

The single interviewee belonging to this group saw such an information system as limited to providing **decision support for doctors/pharmacists/patients** (similar to medical associations and pharmaceutical waste / recycling companies).

The interviewee expressed an interest in including information beyond environmental risk and hazard of PPs, from a Corporate Social Responsibility perspective, to influence procurement processes (as did the public health stakeholder interviewed, and one interviewee belonging to the environmental authorities group). He highlighted the need of political will to include environmental aspects in the decision-making process in order to affect prescription and usage patterns.

4.10 Consumer NGOs

The single interviewee was supportive of an **extensive knowledge base system**, to be used as a database for environmental counseling of consumers and for addressing consumer queries. A strong focus was placed on the importance of drinking water issues for consumers; the system should contain information relevant, such as transformation products of PPs in drinking water treatment (e.g. ozonation). As other interviewees with a focus on drinking water issues, the interviewee emphasized the need for equal precautionary treatment between other pollutants, such as industrial chemicals, and pharmaceuticals.

> *"It is good to address this problem along the lines of the precautionary principle. Efforts are made regarding all possible industrial chemicals, so it is only consequent to also address medicines." (Stakeholder 25)*

The interviewee expressed very strong interest in including veterinary drugs in the system, due to the high amounts used in animal husbandry and because of the relevance consumers (intake of veterinary drugs via food).

4.11 Environmental NGOs

Both interviewees supported a **knowledge base system**; one of them envisaged a **decision support system for doctors/pharmacists/patients** working on the basis of the knowledge base system.

Interviewees suggested wide information requirements for such a system. A double approach was suggested by one interviewee: a system which collects both prospective information (based on estimations; valid for some of the information in the pharmaceuticals Environmental Risk Assessments) and retrospective information (data measured in the environment).

Environmental NGO interviewees were to varying degrees critical of information deriving from industry.

> *"We advocate the use of peer-reviewed data for such an information system. We do not believe that Good Laboratory Practice is enough to guarantee objective results, when the laboratory is e.g. paid for by the organisation submitting the application. The requirement for peer-reviewed data is also part of the pesticides directive." (Stakeholder 27)*

4.12 Public Health Systems

The single interviewee of this group works in a department with a health risk perspective on the topic; positions and interests are comparable to those of drinking water authorities. The interviewee's requirements are in line with a knowledge base approach.

The interest in the system would be for it to provide the information required for assessing environmental and health risks.

> *"It could be useful to have a database where we could find any data we need in order to assess in the best way the environmental and health risks of a defined substance. We need toxicological data, ecotoxicological data, list of characteristics of each substance." (Stakeholder 28)*

4.13 Pharmaceutical Waste/Recycling

A single interviewee of this stakeholder group provided answers to the questionnaire. It cannot be determined conclusively which kind of system (knowledge base or DSS for doctors/…) the interviewee would favour.

A key statement is that risk assessments of PPs in the environment being made available would completely change the operational procedures of the interviewee's company.

5. Concluding comments: Key issues for an information system on PIE

The preceding chapters aimed to provide an outline of two different approaches to an information system on PIE (Chapter 2), map interview opinions and requirements from such a system (Chapter 3), and point out some positions and issues of actors on the topic (Chapter 4). This information can be used for designing and developing an information system on PIE.

This chapter summarises and concludes with a set of key recommendations derived from interview results, and a discussion of the following key issues for an information system on PIE:

- The case for a knowledge base approach
- The case for a decision support system for doctors/pharmacists/patients
- Classification of PPs and the issue of risk vs. hazard
- Resources required
- Data availability issues

Key recommendations

- In order that the information made available can be given more possible uses and actions (and thus have impact), an information system on PIE should not make information available in a format that only suits specific, restricted purposes (such as informing prescription practices), but also take care of being useful for the purposes of further stakeholders. We recommend that an information system on PIE **be not exclusively a decision support system for doctors/pharmacists/practitioners**, but also **have elements of a knowledge base approach**. The stronger the knowledge base component of such an information system, the higher the chances for interesting present and future uses for the information and for positive impacts on the environment (see 5.1).
- To achieve the purposes exposed in the previous recommendation, **data should not only be complex** and aggregated. **Simple, "raw" data should also be made available**, so as to fulfill the requirements of stakeholder groups beyond the medical system. Chapter 3, particularly Questions 3 and 4, give indications of the kind of data that is most widely required by different stakeholder groups. Question 6 gives information on the preferred prioritization of stakeholders.
- Taking the perspective of the environment, and **in view of the data and knowledge gaps** on the topic and of the **importance of precaution in the water cycle**, **a more ambitious approach to an information system on PIE seems preferable**. An ambitious information system on PIE would however require a certain level of resources (particularly expert manpower, see 5.4).
- Interviews show that an **independent body** in charge of an information system on PIE has strong support among stakeholders, and is seen as **key to generate trust in the system**. Due to the high complexity of this information and the possibility of errors affecting this trust, data should not just be reviewed for internal consistency, but **should be extensively proofed and compared with other available data** (see **Chapter 3, Question 6**, for further discussion).

The following boxes presents a more detailed discussion of several key aspects for a possible information system on PIE.

5.1 The case for a knowledge base approach[11]

A **strong argument for a knowledge base** approach is the **wide variety of uses and purposes** it could serve. A **further argument** is the **strong pull from stakeholder side** for such a system, which would help ensure its uptake and its being put to relevant use, with

[11] As discussed in Chapter 2, there is in principle no clear dividing line, or the need for separation, between a knowledge base approach and a decision support approach for doctors/pharmacists/patients.

possibly eventual environmental benefits deriving from some of its multiple uses. Such a system's main purpose would be to provide information; it could (but would not have to) provide a **classification** of pharmaceuticals.

On the one hand, the **availability of information in itself** serves various purposes. It would help for instance researchers and authorities in their work, improving results, reducing costs, and increasing the speed to action. It would also increase transparency on the topic, and serve communication purposes (this point is also valid for other, less comprehensive approaches). Increased transparency also serves to avoid the loss of public trust on emerging environmental issues.[12]

On the other hand, a knowledge base approach **allows for information to serve further purposes**, defined by stakeholders. Several interviewees suggested different tools that they would develop. Frequently mentioned was a tool that would help find and prioritise PPs of more relevance for their work, e.g. PPs possibly affecting environmental quality of waters in a river basin, or for predicting drinking water relevance of a certain substance (the possibility of a substance being present in drinking water). Other interviewees mentioned decision support systems (including one for doctors/patients/pharmacists, but also e.g. for water operators) as possibilities; others were less specific: the knowledge base approach would be "the starting point for additional, intelligent things." Stakeholders would help carry this process.

> *"It is either stakeholders or pressure groups that will use the material to put the focus on specific issues." (Stakeholder 10)*

For such a system to provide this variety of uses, information in it would have to be very detailed, reliable, and provide "raw" data. This is in line with most stakeholders' data requirements (see Chapter 3, Question 6, for further discussion).

Information of these characteristics is also seen as central to be able to have **uses in the future**; experience would show that the uses of this kind of information change over time. Simple information is preferable to complex, aggregated information:

> *"If you look historically at our system [talking about REACH], the hazard classification and hazard information in the form of labelling and safety data sheets was just information to users, but now, twenty years later, it is being used in different kinds of downstream regulations as basis for further risk reduction measures. […] So the uses of the information changes with time, there will be more and more uses if the basic information is high quality, accurate, and simple." (Stakeholder 6)*

An **argument against a knowledge base approach** would be its not having a clear role or function of its own, and thus no direct practical impact on changing practices or behaviours. This also means that it would be very hard, it at all possible, to measure the impact of such a system, for instance in the form of (environmental) benefits vs. costs.

[12] Cf. German Advisory Council for the Environment, Precautionary Strategies for Managing Nanomaterials: Summary for Policy Makers. http://www.umweltrat.de/SharedDocs/Downloads/EN/02_Special_Reports/2011_09_Precautionary_Strategies_for_managing_Nanomaterials_KFE.pdf?__blob=publicationFile

5.2 The case for a decision support system for doctors/pharmacists/patients[13]

Although a decision support system (DSS) for doctors/pharmacists/patients would not satisfy the information requirements of most stakeholders, a **large majority of interviewees** would welcome the existence of such a system and **consider it as having potential for positive environmental impacts** (see Chapter 3, Questions 1 and 2). Depending on the amount of detailed information it includes and the characteristics of this information, it could to a certain extent also assist other stakeholder groups in their information requirements on PIE.

The **main use** for such a system would be to influence prescription and sales practices by doctors and pharmacists (and possibly organizations such as health boards). To achieve this aim, several hurdles must be taken. Particularly doctors are seen as a professional group under high requirements; any system would have to carefully consider their practices and be tailored very specifically to their requirements. The importance of achieving **acceptance** in the professional communities was highlighted repeatedly; one interviewee (of the medical profession) highlighted the need to adapt the system so that it is incorporated into current (national) medical practices and information systems. Several interviewees highlighted the importance of training in the system, and of including doctors in its design, for it to be successful. To achieve acceptance, the importance of **simplicity**, **convenience of use (speedy access)**, and **direct comparability** (i.e. at "one glance") between different substances of the same group were emphasised. Some selected quotes:

> *"I think that the user of the system would like to see that someone else does the thinking for them, that the information good/bad for the environment is given." (Stakeholder 2)*

> *"Doctors and pharmacists must be able to use it. They need information on the healing effects, and they need the ability to quickly and directly compare the therapeutic efficacy and environmental characteristics at their fingertips." (Stakeholder 5)*

Potential of the system to be taken up in **green procurement** activities was highlighted by interviewees more involved in their countries' health systems. However, the existence of **political will** is seen as important to achieve changes in procurement practices.

> *"Today lowest price wins. In future, perhaps the environmental classification could affect the [procurement] process. […] In order to affect prescription and usage patterns political will to include environmental aspects in the decision making process for pharmaceutical benefits is important. The existence of a sound and accepted classification system would serve as a good basis to make this happen." (Stakeholder 24)*

Further uses for this kind of system would relate to its function as information tool, providing information on the environmental behavior of pharmaceuticals to the broader public, and increasing transparency. Increased transparency also serves to avoid the loss of public trust on emerging environmental issues.[14] Industry representatives interviewed were positive about the benefits of such a system in this respect.

An **argument against this approach** is that it has one main practical purpose, and success hinges on being able to reach doctors and influence their prescribing behavior (which is not

[13] As discussed in Chapter 2, there is in principle no clear dividing line, or the need for separation, between a knowledge base approach and a decision support approach for doctors/pharmacists/patients.

[14] Cf. German Advisory Council for the Environment, Precautionary Strategies for Managing Nanomaterials: Summary for Policy Makers. http://www.umweltrat.de/SharedDocs/Downloads/EN/02_Special_Reports/2011_09_Precautionary_Strategies_for_managing_Nanomaterials_KFE.pdf?__blob=publicationFile

considered easy by interviewees). If the system fails to achieve effects in this its main purpose, it will fail to have a noticeable impact. This makes a strong case for a combined approach: a DSS approach that also makes available additional information which fits the information requirements of other stakeholder groups. This would increase the chances of the system finding uptake and use, and thus of having impact.

5.3 Classification of PPs and the issue of risk vs. hazard

Whereas a decision support system for doctors/pharmacists/patients has to be based on a classification of the environmental risk and hazard of pharmaceuticals, in theory at least a knowledge base approach would not necessarily require such a classification: the provision of "raw" information would indeed serve the purposes of many stakeholder groups. However, if broader groups beyond the scientific and technical are going to be targeted, so as to affect behavior or practices such as prescription, procurement, or disposal, classification seems unavoidable. This is also the case when providing information, e.g. risk communication and increasing public awareness.

The issue of if environmental risk (based on the (estimated) effects on the environment) or hazard (based on the intrinsic chemical properties of the substance) should be the principle for classifying and comparing products is quite contentious, and there are good arguments on both sides. Pharmaceutical industry representatives and some representatives of public authorities were in favour of a risk-based approach, arguing that it provides a far more accurate picture of the actual effects (or lack of them) of the product in the environment. These actors argued that hazard information could scare consumers; they could overreact and stop taking a medicine for environmental reasons, when they actually require it for their health. Environmental NGO representatives and a chemicals agency interviewee strongly favoured a hazard-based approach, because it is simpler, allows for direct comparison between products, and is based on real data rather than on assumptions (such as estimations for sale volumes and dilution factors in rivers) that are regionally highly specific and may show significant changes in time. A further argument for the use of hazard is that the environmental information of a pharmaceutical product would be the same around the world, facilitating global trade, as well as communication on the topic.

The point has been intensively debated in other processes, such as regulations addressing industrial chemicals, pesticides, and biocides, and the negotiations for the environmental section of Fass.se (on pharmaceuticals). This experience should be used to inform any debate on this point.

5.4 Resources required

(This point **does not consider** the question of resources required for generating additional information on PIE, e.g. those needed to address data gaps.)

The issue of the resources required to establish and maintain such a system is a function of the ambitiousness of the goals, and of the institutional setup. Taking interviewees answers as a basis, significant resources will be required for a system to provide results (independently

of its type).

A decision-support system for doctors/pharmacists/patients, although with the comparatively minor data requirements and thus review costs, would have to invest very significant efforts to reach doctors and pharmacists and achieve uptake. Several interviewees highlighted how hard it is to reach doctors, a group continuously being addressed by many different actors. One interviewee mentioned that his country's public health authorities could be moved to finance such a campaign.

Independently of the type of approach, most interviewees saw the requirement for a third-party organization in charge of such a system. If information sources in addition to industry should be considered (very often considered crucial for trust and credibility by interviewees), significant manpower needs to be in place to collect the information, evaluate it (e.g. according to its reliability, with a system analogous to the Klimish system), and highlight issues and problems with it. Contradictory information (e.g. industry results and research results in disagreement) would need to be addressed. A few interviewees were critical of the Fass.se system, in that the data review process would not be as thorough as required (others were supportive of this structure). The more comprehensive an information system on PIE would aim to be, the higher the manpower required in this sense. A possible structure that could reduce the resources required would be a Wikipedia approach, with e.g. researchers incorporating available data, but this approach would also require intensive and very qualified revision.

Public authorities with an environmental mandate could contribute resources: one interviewee of this group suggested that her organization would provide resources to such a system, whereas another one of this group made clear that in his organization there would be little willingness to pay.

5.5 Data availability issues

Data availability is a sore point in the issue of PIE. Whereas basically all interviewees agreed with the principle that health aspects have priority over environmental considerations, several criticized the fact that the requirements for new environmental data generated for pharmaceuticals are less stringent than those for other chemicals, e.g. not covering chronic data. One interviewee also criticized that, on top of lesser requirements, the level of detail of the information that is made public is less than that for e.g. pesticides. Several interviewees suggested that regulatory efforts should address these perceived issues. Whereas several stakeholders consulted saw the onus of generating more information (e.g. chronic ecotoxicity data) on the industry, there were also voices calling for public financing for research that closes data gaps, such as behavior of PPs in drinking water and wastewater treatment plants.

The research-based pharmaceutical industry representatives interviewed were critical of the current regulations in that they put the burden (and the cost) of Environmental Risk Assessments for new products at their feet. Producers of generic pharmaceuticals, however, would not have to make this information available, although they would produce large volumes of PPs that end up in the environment. The research-based industry

Regarding the data gaps with "old" pharmaceuticals, typically manufactured by various companies, several interviewees suggested these gaps could be closed using a system that shares the costs of the ERAs according to the market share. One interviewee suggested that a minimal tax on generics producers would generate sufficient resources to address some data

gaps and fund research for greener pharmaceuticals.

An initiative to establish an information system on PIE would require consultations with stakeholders. The possibility of making additional information available could also be explored. Particularly if there is buy-in and agreement from all stakeholders on the characteristics of the information system, additional information would serve the purpose of increased transparency and good risk communication, goals with wide support among the stakeholder groups.

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6. Annex 1: Details of interview process

Stakeholder groups

The following stakeholder groups were identified for the purposes of this interview process. We believe that the groups defined cover all actors with a significant stake in the issue, but do not guarantee comprehensiveness.

1. Environmental authorities (including River Basin Organisations) / Chemical authorities
2. Pharmaceutical industry
3. Drinking water / Wastewater companies
4. Authorities responsible for Drinking Water
5. Research organizations (different relevant disciplines)
6. Medicines Authorities
7. Medical associations
8. Pharmacies / Pharmacy Associations
9. Consumer NGOs (as representatives of the broader public)
10. Environmental NGOs
11. Public Health authorities
12. Pharmaceutical Waste/Recycling Companies

Identification and contact with stakeholders / Geographical spread

Based on internet research and suggestions from project partners and the project's advisory board, a list of possible interviewees was prepared. Interview requests were mostly done via email. The original aim of having a more balanced geographical spread over the EU was not possible due to a low response rate from southern and eastern European countries. Due to this, there are more interviewees from northern and western Europe, with a bias towards interviewees coming from Germany and Sweden (the home countries of the three institutes performing the interviews).

The following list provides the countries of provenience of the 29 stakeholders interviewed. Interviewees belonging to international organizations or authorities (e.g. pharmaceutical companies and EU authorities) are listed under "International".

1. International 3 interviewees
2. France 2 interviewees
3. Germany 8 interviewees
4. Ireland 1 interviewee
5. Netherlands 3 interviewees
6. Portugal 3 interviewees
7. Spain 1 interviewee
8. Sweden 5 interviewees
9. Switzerland 2 interviewees
10. United Kingdom 1 interviewee

Interview numbers and type of stakeholders

The following list classifies interview partners according to the kind of organization they belong to.

1. Environmental authorities (including River Basin Organisations) / Chemical authorities 6 interviewees
2. Pharmaceutical industry 3 interviewees
3. Drinking water / Wastewater companies 2 interviewees
4. Authorities responsible for Drinking Water 2 interviewees
5. Research organizations (different relevant disciplines) 5 interviewees
6. Medicines Authorities 3 interviewees
7. Medical association 2 interviewees
8. Pharmacies / Pharmacy Associations 1 interviewee
9. Consumer NGOs 1 interviewee
10. Environmental NGOs 2 interviewees
11. Public Health authorities 1 interviewee
12. Pharmaceutical Waste/Recycling Companies 1 interviewee

A total of 29 interview questionnaires were answered. 27 were phone or personal interviews, whereas 2 questionnaires were completed by interviewees and sent back via email.

Interview Questionnaire:

The following pages present the interview questionnaire, with an introductory text for interviewees. Comments marked in red were for the interviewer. In most cases a version (without interviewer comments) was sent to interviewees via email a couple of days before the phone interview, for preparation purposes.

Questionnaire for PHARMAS interviews

Introduction to subject :

Scientific knowledge of trace amounts of pharmaceutical products (PPs) in the water environment goes back to the 1960s, but it only gained increasing attention – both scientific and from the broader public – during the 1990s and particularly the previous decade. Two issues have been focused on. On the one hand, attention has centred on the danger that PPs and their metabolites pose for wildlife, such as the effects of oestrogen compounds on snail and fish. And on the other hand the focus has been on the problem of human exposure to PPs, e.g. via tap water, and the long-term effects such exposure could have.

To the best of current scientific knowledge, it appears that most pharmaceuticals do not pose a threat to the environment, but a small number do; none appear likely to pose a significant threat to human health via environmental exposure. These conclusions are supported by the most recent and detailed human health risk assessment (Cunningham et al., 2009). The real situation, however, is that there are many more uncertainties than certainties, which leaves the public and the press still unconvinced that drinking water containing a tiny quantity of a pharmaceutical is completely harmless.

The EU-funded PHARMAS project aims to address some of these knowledge gaps in the science of PPs in the environment, focusing on two groups of pharmaceutical compounds. In addition to the scientific focus, the project has a second focus on the possibility of establishing an environmental risk and hazard classification scheme for PPs. Both for decision makers, and also for the general public, it is important to make this science easily understandable and available.

This scheme would communicate the risk and hazards of specific pharmaceutical compounds in the water environment. It would address both the broader public as well as a variety of stakeholders that are involved in the matter. For this reason, interviews are being conducted with representatives of the following stakeholder groups:

- European and national public health care system
- Medicinal / Pharmaceutical authorities
- Medical associations (practitioners)
- Pharmacies and pharmacy associations / Pharmacists and professional associations
- Pharmaceutical industry
- Environmental agencies (incl. selected River Basin Organisations) / Chemicals Agencies
- Environmental NGOs
- Patient organisations and consumer NGOs
- Pharmaceutical waste and recycling companies
- Water and wastewater companies / utilities
- Research organisations / Universities / Relevant scientific societies

This interview aims to elicit the requirements of different stakeholders on the implementation of an EU-wide risk and hazard classification system for pharmaceutical products (PPs) in the environment. It does this for pharmaceuticals in general. The duration of the interview is something around 1 hour.

Date	
Name of Interviewer	
Name of Interviewee	
Title of Interviewee	
Department / Organisation	
Contact details (phone, email)	

Questions:

1. (5 min) What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals? *(Wait for spontaneous answer.)*
    a. Would you approve of the existence of such a system?
    b. Would you be interested in using it yourself?
    c. For which purposes would you use this system?
2. (5 min) What would the impact of such a web-based classification system be?
    a. Environmentally?
    b. Economically?
    c. Medically?
    d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)
3. (5 min) What are your (or your organisation's) needs for information on PPs in the environment? *(Wait for spontaneous answer)*
4. (10 min) Getting into more detail…

- precisely which information (which data) would you require?

  OPEN CHECK-LIST: can cover points from following list or additional ones:

  - *characteristics of compound, e.g.*
    - *physico-chemical entries*
    - *ecotoxicological entries*
    - *stability and biodegradation-feature entries*
    - *pharmacokinetic entries*
    - *excretion data entries*
    - *entries on routes of administration*
    - *pharmacodynamic entries*
    - *entries on side effects*
    - *entries on mammalian toxicology data*
  - *sales figures, e.g.*
    - *current and retrospective sales data from interviewee's country / European countries.*
  - *information on behavior in wastewater treatment plants*
    - *WWTP-specific entries*
  - *information related to water flows / water quality in European river basins*
  - *information related to management of pharmaceutical wastes*

- *entries on occupational advices for the management of pharmaceutical wastes (valid e.g. for cytostatics because of their mutagenic properties)*

- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

5. (5 min) How would you use this classification system in your work? (Wait for spontaneous answer.)

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

6. (5 min) What should the main characteristics of a classification system be to ensure the system works adequately? *(Wait for spontaneous answer.)*

a. origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.
b. Which categories of PPs should it cover? *(Wait for spontaneous answer.)*
c. Any priority drugs to focus on in a first phase (e.g. antibiotics?)?
d. Should both prescribed and OTC (over the counter) drugs be covered?

7. (5 min) What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

a. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)
b. What changes would you like to see in the system?
a. What are the shortcomings of the system? *(Wait for spontaneous answer.)*
    i. re. information
    ii. re. functioning
    iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

a. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

8. (3 min) What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?
b. Are the efforts for addressing the problem justified?

9. (2 min) Do you have any other comments? (If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)

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7. Annex 2: Interview Summaries

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 1

Stakeholder Group: Environmental authorities (including RBOs*) / Chemical authorities

*RBOs: River Basin Organisations, authorities in charge of implementing the Water Framework Directive

Date	12.08.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Interviewee works on setting Environmental Quality Standards (EQS) and permitting discharges into the environment.
Type of organisation	Environmental Agency of a European Member State

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

There is a difference between classification system and prioritization, do you mean some way of identifying priority risks? If your intention was to produce a dossier for every pharmaceutical or major pharmaceutical in use across Europe that would be an enormous undertaking. Would I approve yes, would I make the case for the environmental agency resourcing it probably no. Is it a sufficient priority for us to invest our limited resources, no there are more pressing issues. It is sort of a willingness to pay question.

b. Would you be interested in using it yourself?

Yes

c. For which purposes would you use this system?

I would use it probably in terms of identifying whether we need to set EQSs for any of these substances. One might use them also to understand risks to the environment. The question we ask is: is good biological status put at risk by these pharmaceuticals. If we found poor biology in certain locations we might say ok let's go look if we find these pharmaceuticals. Trying to explain poor biology [trying to find the reasons, possibly chemical, for poor results in the biological monitoring required as part of the Water Framework Directive].

2. What would the impact of such a web-based classification system be?

As far as I am concerned the impact would be environmental.

a. Environmentally?

To identify risks

b. Economically?

c. Medically?

With biologically active substances, we have to be realistic about the chances of building in that sort of design feature into specialist substances (talking about green chemistry) because whatever you do to the molecule might affect its efficacy. For those reasons I would think a little bit more about disposal practices.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

No I do not think there would be an environmental effect from the consumer side of things. If I went to the doctor and he said I will give you this drug although it is not the best drug but it has less environmental impact, I would be a bit disappointed.

There is an issue about safe disposal. If the major source was the practice of flushing unused pharmaceuticals down the toilet and that posed a risk to the environment, well that ought to be relatively easy to overcome.

3. What are your (or your organisation's) needs for information on PPs in the environment?

Chronic ecotoxicity data

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Pharmacodynamic entries: *probably no.*

Pharmacokinetic entries: *probably no*

Excretion data: *yes.*

Routes of administration: *probably no.*

Side effects: *I don't know.*

Mammalian toxicology: *possibly.*

Sales data: *yes.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes.*

Management of pharmaceutical waste: *yes, but not crucial information.*

- at which level of detail / (level of aggregation?)

I suppose if you were to ask the critical bits of information they would be environmental fate, fate in sewage treatment, chronic ecotoxicity. I would want to know those in quite a bit of detail. The other things I am not sure about. If you were to do a proper risk assessment then you would need quite detailed information on many perhaps all of these parameters.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

I think most people, if they are looking for data on exposure, fate, degradation, ecotoxicity, they would want a table of numbers expressed. In some other cases if you are able to provide information on routes of uptake then things like graphics, pie charts would be very useful. Pie charts would be ideal to present likely sources to the environment. Personally the more information you can put together as figures, graphs and graphics, the better. But a lot of the key data will be single values or perhaps ranges of values so it would be a rather dull but very worthy table.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

Explaining poor biology [trying to find the reasons, possibly chemical, for poor results in the biological monitoring required as part of the Water Framework Directive]. Helping to set up EQSs. Understanding risk to the environment, that one is quite useful in terms of diagnosing causes of poor biology. That is an important activity that currently we cannot always do very well.

We are doing some work at the moment on sewage treatment effluents, quite detailed analyses. We are looking for things that we would usually not be looking for. In our routine regulatory activities it is the other way around, where we are led by biology.

- Would your organization favour such a classification system? Why / why not?

Yes, it is hard not to favor such a system.

- Which organizations in your country would be pro / against such a system? Why / why not?

I cannot imagine anyone saying we do not want to see a useful database of environmental information. The question is how much would we be prepared to invest in that. Water companies, organizations who are responsible for providing potable drinking water might be, research organizations would be, some in the UK who have an active interest in emerging contaminants would be for this kind of system. I do not think anybody would feel that this is a bad idea. The only question is if the data input are unreliable and that more harm can be done than good by making it available.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

The industry is generating the data to provide to the EMA for the authorization procedure. The question this project might raise is, if there is a strongly held view that there is a lack of useful toxicity data, who are the best people to generate it. In most of the chemical groups it would be the suppliers, the industry. I do not think anybody is withholding data, I think it just doesn't exist. The industry is happy to get involved but they probably believe there is no issue so therefore are not inclined to address it.

The data could come from anywhere. I do not think we should put a bar on information. What matters is that we set minimum quality criteria. The data would need to have undergone some sort of quality insurance by people who know what they are doing, that have seen the original research and can confirm that the conclusions are reasonable. There are existing schemes for this within REACH and EQS settings (klimish criteria).

- Which categories of PPs should it cover?

  That is a really critical question because it asks where should we put limited resources. You mentioned antibiotics and anticancer drugs. It is hard to know. In our own studies we identified ibuprofen and propanalone (none of which are antibiotics or anticancer). I think we identified a few antibiotics.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Rather than taking particular classes I would rather be led by environmental exposure or high volume substances first.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Yes, well there might be more OTC around than prescribed.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

a. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

b. What changes would you like to see in the system?

c. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

I suppose I would come to this system knowing which substance I am interested in, so I would want it to be searchable on the basis of substance. I would probably know what features about that substance I am most interested in, so I would come to it with a shoping list of attributes I am interested in, so I would want it to be searchable in that way.

I am not certain members of the general public would use the system. Perhaps some might want to know what is the most widely used pharmaceutical in Europe, or which is the most toxic and ask if we are monitoring it. Which is not wrong, and it is part of our job.

8. What is your perception of the risk posed by PPs in the environment?

In the face of uncertainty we make a judgment based in large part on instinct and precedent and our feeling is that this is not a high priority risk to the natural environment, but it is not irrelevant either. We wish to maintain some sort of watching brief. A major driver for all of this is regulatory imperatives and there aren't any at the moment. If there were, that would definitely drive action.

a. Is the media attention justified?

I am not aware that there is an inappropriate level of interest in pharmaceuticals. Personally I do not think there should be more coverage. I think the press will pick up on risks to human health primarily, there has been a lot of press in recent years about sex reversal in fish. Research has shown that much of that has been justified. I think where the press would take a keen interest would be in risk to health through drinking water.

b. Are the efforts for addressing the problem justified?

In the environment agency we have chosen a level of involvement that is not very high, we are happy for others to pursue that. Because we are not terribly active in this field we are very happy for others to take up the reign. I don't think this varies amongst member states, I can't see why it would be a priority in Spain or elsewhere. You cannot do everything, and priorities are driven by practicality. The WFD is what drives most of our work and the main chemical that is identified as causing failures are more traditional pollutants or nutrients, sediments and metals. We have no evidence that pharmaceuticals are responsible for failure [to comply with good environmental status]. But there are cases where there are non identified causes of failures; that is not to say pharmaceuticals are responsible, but they could be.

There are a small number of substances where I think concern is justified (sterol estrogens, estradiol, possibly diclofenac, anti-anflamatories). They stand out and they are taking seriously. They stand out above the others as to say there is generally not a high level of concern about the large number of other pharmaceuticals. I do want to drive attention to those because I think they are significantly different.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 2

Stakeholder Group: Environmental authorities (including RBOs*) / Chemical authorities

*RBOs: River Basin Organisations, authorities in charge of implementing the Water Framework Directive

Date	2011-06-20
Name of Interviewer	Jörgen Magnér, IVL
Type of Interviewee	former Environmental Director
Type of organisation	City Council

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

Principally yes, since a work on how to update the Swedish system are undertaken at the moment. The update process involve the the same stakeholders that were involved in the first classification, but do also include eg SEMCo (The Swedish Environmental Management Council, the government's expert body on environmental and other sustainable procurement), TLV (The Dental and Pharmaceutical Benefits Agency, a government agency whose remit is to determine whether a pharmaceutical product or dental care procedure shall be subsidized by the state) and NEPI (network on pharmaceutical epidemiology), a slightly enlarged group working with the issue. The aim is to further develop an environmental classification system with input from the experiences from the first Swedish system. It is a Swedish system designed to be used in Sweden. If and how an EU-wide system would be used would depend on how it differ from the Swedish system.

b. Would you be interested in using it yourself?

Same answer as for the previous question. It will depend on the variables the system contain and how these relate to the coming updated Swedish system.

c. For which purposes would you use this system?

In order to give good recommendations to prescribers, and also to inform prescribers and other personel in the medical sector regarding environmental impacts of pharmaceuticals.

2. What would the impact of such a web-based classification system be?

Hopefully it would result in a shift towards the prescription of pharmaceuticals with less environmental impact.

a. Environmentally?

b. Economically?

c. Medically?

I do not think it would result in any large medical impacts.... but viewed in a larger context in which a more rational use of pharmaceuticals is aimed at, eg a more rational prescription for elderly, it could certainly result both environmental and economic impacts, as well as improved medical effect.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

It depend on what the system looks like. The consumers can only handle unused drugs in one way and it is to return them to the pharmacy. To what extent a classification system would affect this behaviour is hard to tell.

3. What are your (or your organisation's) needs for information on PPs in the environment?

Large of course, since the information availabe often is incomplete or contradictory. Data is incomplete since data enough for a risk assessment often is lacking. The requirement for an environmental risk assessment did not exist before 2004. The demand for environmental information did not excist at all until approx 1995 so it is not suprising that there are data gaps for older pharmaceuticals. Further, the information provided for the same substance often differ between different producers.

4. Getting into more detail…

- precisely which information (which data) would you require?

To keep it simple I would like it to include a LCA (life cycle assessment) including the entire chain from the raw material to the use or disposal of the product.

Consumption of raw material and energy consumption form a LCA perspective, and also an environmental risk assessment.

- at which level of detail / (level of aggregation?)

The requirements put forward, both from prescribers and pharmaceutical committees and also TLV, is that the system should be simplified in comparison with the current system. I think that the user of the system would like to see that someone else do the thinking for them, that the information good/bad for the environment is given, or a number according to given scale. I think the user would like to hand over the details to those who conduct the evaluation.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

It should be very easy for the prescribers and other users. When choosing a pharmaceutical the information should be easily assessed without detailed knowledge. I can imagine a binary system, ok/not ok from an environmental perspective, or some kind of scale with a cut-off point, eg below 3 at a scale from 1-5 is not ok.

5. How would you use this classification system in your work?

To inform prescribers and practitioners in the health care sector on how the system is built and how they can use it. For educational purposes.

- How would it support / influence your decision-making processes?

It is the expectation that such a system would be that easy to understand that it can be routinely used. A EU-wide system would put more pressure towards the producers compared to a Swedish system.

- Would your organization favour such a classification system? Why / why not?

Same answer as previously.

- Which organizations in your country would be pro / against such a system? Why / why not?

The pharmaceutical committees would definitely be pro. LIF (Swedish trade association for the research-based pharmaceutical industry) is positive. But it depends on how the system is built. TLV has some specific requirements. If used by TLV it would be a powerful mechanism that would affect sales and prescriptions. But for TLV to do so, it should not only be easy to understand, but also robust from a legal point of view. If a classification results in a lower reimbursement, sales of that pharmaceutical will decrease. The producer would then try to start a legal process claiming weaknesses in the grounds for such a decision. Thus, the system should be indisputable and legally correct.

The County Administrative Boards should be positive. There should not be any organisations against it, but TLV have some specific requirements.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

The most important characteristics is that it is correct from a scientific point of view and that it is easy to understand for the user.

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  The primary data need to be provided by the producer. It is the same situation as they provide all data from clinical trials for the approval of the pharmaceutical. But then some organisation should evaluate the data provided, and maybe make estimates based on it. That should primarily be the Medical Products Agency or the equivalent European organisation.

- Which categories of PPs should it cover?

  All pharmaceuticals for which EMA evaluate risk today. But they have made exemptions for some pharmaceuticals such as vitamins and electrolytes today.. and this should be given some more thought. Proteins and peptides are exempted and with reference to this some producers have refrained to give information for some peptide like antibiotics... this was probably not the intention of EMA. The intention was that natural products should be exempted.... Some limitations to the exemptions should probably be made.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Yes, antibiotics and steroid hormones, especially oestrogens and estrogenic substances, but as a second priority high volume pharmaceuticals sold in many tonnes each year.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Absolutely. Over the counter drugs are sold in high volumes, and include eg diclofenac that is troubling.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

It should be easy to assess and of course easy to understand. It should also give information on how recent data it includes... if it is updated... it should probably be regurlarly... date for this should be given.

*In case they are **familiar** with fass.se*:

d. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

Well, it does not give the possibility to compare data for different pharmaceuticals, that is a major weakness. The possibility to make comparisons should be included in such a system.

e. What changes would you like to see in the system?

f. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

   v.

8. What is your perception of the risk posed by PPs in the environment?

I see two levels of risk... the increasing level of resistance but also the pharmacologic effects of the pharmaceuticals.... Toxic and ecotoxic effects are also of importance to some extent, eg caused by diclofenac, developmental effects, estrogenic effects etc... But it is the pharmacologic effects when the pharmaceutical exerts its effect in the aquatic environment, certainly at concentrations much lower compared to when exotoxiciological effects occur... It should be guarded especially against these pharmacologic effects.

There is one additiontal issue.... the risk of teratogenic effects. Even the extremely low concentrations of pharmaceuticals present today, piccogramme/l levels, these concentrations (not specifically pharmaceuticals) is enough to induce teratogenic effects.

a. Is the media attention justified?

I do not find the media to be that awake at the moment. Media used to be, but now they mostly just note that pharmaceuticals can be found in the environment.

b. Are the efforts for addressing the problem justified?

Yes, absolutely.

Additional comments: *I have one additional comment and that is that the pharmaceutical industry has been very successful in their lobbying, especially in Brussels, preventing European agencies from addressing these issues. In Sweden the introduction of a classification system has gone well and from the industry side Sweden has been viewed as a test market. I believe they think it necessary to continue this work internationally. But I also know that during the work in the Commission with an assignment from the Parliament concerning environmental effects of pharmaceuticals, industry has initially been very negative.*

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 3

Stakeholder Group: Environmental authorities (including RBOs*) / Chemical authorities

*RBOs: River Basin Organisations, authorities in charge of implementing the Water Framework Directive

Date	28.07.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Interviewee works on setting Environmental Quality Standards (EQS) for environmental waters.
Type of organisation	National office for the environment

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

I think it is very important to have an EU wide system, it would be even better to have a global system to deal with the risk and hazard associated to pharmaceuticals in the environment. Maybe the registration process for pharmaceuticals should be improved to include information on the environmental hazard associated with the substance. Human hazards for human health are well investigated.

b. Would you be interested in using it yourself?

Yes.

c. For which purposes would you use this system?

If it is a system to develop quality standard, where you define the need for action, I would use the system. Before you define quality standards you have to carry out an analysis of the situation. If you find new substances in the watercourses, you must investigate whether or not they are problematic. This does not require the use of quality standards but rather the PNEC values. For a ministry, which must remain neutral, it is very important to have a harmonized system for defining PNEC; science does not offer one clearly defined way. PNEC values along with the risk assessment coefficients are provided for a substance as part of the registration process and these are often not publicly available. The PNEC values for the registration process are derived from standardized OECD test systems. If you investigate the risks associated with a substance in watercourses, you must take a look at a broader number of possible effects. For example, in the WFD the PNECs are derived from the GLP procedure with OECD standards, but they also take into account research studies which are not standardized but do fulfill certain standards. In registration you have to be much stricter. Assessing environmental risk requires to consider multiple possible effects. Quality standards for water courses are not comparable with PNECs you derive in the registration process. You have to go a bit further if it is about safety of water bodies. If a certain substance is found not to be a problem for daphnia one cannot infer that it will not be a problem for any other living organism; there also exist sub lethal effects, hystopathological effects, sexual effects on fish, etc. There is no standardized OECD tests that can assess these problems. That is why there are different types of classification systems.

If you only have one national expert classifying all research studies, you do not get the same end result as when you have 10 EU experts working together. A lot of discussion is necessary.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

If a government is dealing with environmental problems this will provide them with another decision-making tool. The same goes for engineering companies who have to investigate or assess an effect.

b. Economically?

It is difficult to say, it is not really my field, in the same direction as I said before, it may be easier to investigate problems and save people the trouble of developing their own system, maybe there would be less uncertainty, I think the effect would be minor.

If you do something isolated for my country you will get criticized, it is important to have a harmonized system (also because of competition issues, level playing field for pharmaceutical companies). The company image could be damaged and the company would not be happy to lose the share of market; that is why it is important to create an EU wide system.

c. Medically?

If it is a system to assess risk for human health it can have a medical impact. If you can identify harmful substances or processes, for example at the work place, which can harm human health via their mishandling.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

Maybe the normal daily user is not accessing the web based classification system, but rather the personnel with a certain education.

3. What are your (or your organisation's) needs for information on PPs in the environment?

Mainly the sales figures: which compound is sold in which quantity? On a national level, we demand that companies provide an estimate of their sales. It would be very good to have the actual sales on a national and perhaps a regional level.

Another thing that is important for us is the information with which we can investigate: fate (biodegradability), the ecotoxicological assessment data about PNEC, important metabolites (biological metabolites from wwt, or human metabolites, in soils). It is important to know which portion of the substance is entering the water courses and in which form (metabolite or parent compound).

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Pharmacodynamic entries: *possibly.*

Pharmacokinetic entries: *possibly*

Excretion data: *yes.*

Routes of administration: *yes.*

Side effects: *possibly.*

Mammalian toxicology: *yes.*

Sales data: *yes.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes. To have a prioritization of all the compounds that are used. You cannot investigate all pharmaceuticals that are registered in the EU, you need a list of the most important ones. For us, in my country, when we experience a problem it is good to know that other countries also have this problem.*

Management of pharmaceutical waste: *yes, then you can investigate whether you can optimize treatment.*

- at which level of detail / (level of aggregation?)

It is nice to have information even on the regional scale, not just national. For example information on the level of watersheds for my country. This allows to make more appropriate predictions (particularly thinking of the sales figures). I think it would be nice to have the aggregated information as a rough screening but then if you see there is a problem it is good to have the more detailed information. Like the footnotes or appendices with details.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

It is very good to have data presented in figures, so you can easily see here is e.g. Germany and here is my country and quickly compare. It is good to have all characteristics in one table. The info must be easily visible and easily accessible, without needing to read a lot of text.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

My interest would be the ecotoxicological data, PNEC, and a way to access the background info that lead to this PNEC. Maybe it would be helpful to have the transfer coefficient. So you can say ok, you use 100%, then 10% is excreted and from this only 1% enters the water body. When you have the data you can calculate the risk for any type of river.

- Would your organization favour such a classification system? Why / why not?

Yes

- Which organizations in your country would be pro / against such a system? Why / why not?

I would say most of the organizations would support such a system.

In the pharmaceutical field there are many diverging interests. You need to find a consensus about the problem, possibly that can be the job of such a system. Establish consensus on what the risk is and how you present it.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

Users should be able to follow all the different information that has been aggregated to produce a final value and come to a certain conclusion. If somebody is suspicious, he should be able to access critical points or aspects of a procedure. It is important to be able to access the original study behind ecotoxicological data.

It is very important to have expert systems. As I said before, for the quality standards, there are a lot of studies of different quality in research, these contain important information but you cannot take all of these studies 1 to 1 to derive standards. To deal with this it is important to have good experts that will agree on which info has an adequate quality and which doesn't. This process must also be transparent.

It is always good to have an independent authority in the field if you want to have a safe system. I am not against certain interests, but it has to be balanced. Especially in smaller countries it is impossible to have independent experts. On the EU level it would be possible I guess.

- Which categories of PPs should it cover?

It is important you get the most toxic, the most widely used, used in high amounts and those that are stable. Maybe I would add the ones that are biologically active, but that is another way to define it. Antibiotics: it is not a bad idea to include them but there might be others as well that have a similar importance.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  I have nothing against a system that would include every pharmaceutical, but I would start with those [mentioned in the previous point]. Perhaps not every pharmaceutical needs to end up in a classification system. There must be a criterion to establish which ones make the list or not. It is always good when these criteria allow to identify the most problematic substances. The criterion should be based on the characteristics of the substance and not to the label or the use of the substance.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Possibly it should be both.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

g. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

h. What changes would you like to see in the system?

i. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

I think there should be different levels of info. It would be best if it were like a database from which you can search for substance groups, or a specific substance and use a scroll down list to see the most toxic and the most widely used or whatever. When you first enter the system it is good to have the aggregated info and if you are interested you can click to access the details. For most of the people the aggregated info is enough for their daily work. In principle anybody should be able to access any type of information. Open access is important but should be complemented by a good hierarchy in the information.

We live in a democracy, it is always good when risks are communicated in a simple but transparent way. Anyone should be able to inform itself and discuss this issue. It would be good to have a good web based system that explains the problem and gives good well established information.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

I think the problem is quite well recognized in my country. Sometimes the media can overdramatize, but it is important to inform the public about the problem. The situation from some decades ago is not comparable to today's situation. Water quality has strongly improved in the last decades; problems with pharmaceuticals are not comparable to the problems we had in the past. There are some regional problems where we have a high population density and a high use of pharmaceuticals and a high portion of treated wastewater in surface water. This can affect drinking water or ecosystems, but treatment systems can be optimized to resolve the issue. In my country the problem has always been communicated in this way, and it is quite a neutral discussion.

It is correct for the media to inform the public, but to restrict the talk to pharmaceuticals only would be wrong. We use thousands of substances in different ways in our daily lives, and benefit from these; we should be aware that our daily life affects the environment, not just through the use of pharmaceuticals. If we want to have this quality of life in 10 or 20 years we cannot band all these substances that provide medical benefits. It is important to have the discussion on whether people want to invest on various measures to treat the water.

b. Are the efforts for addressing the problem justified?

I think they are, but one should not solely focus on pharmaceuticals. It is important to have a broad view. It would be wrong to say that pharmaceuticals are biologically active and therefore are problematic for the environment; there are many biologically active substances that are not pharmaceuticals. There are certain situations where you have substances from wastewater in drinking water, but it is important to tell people it is not harmful for human health (referring the presence of pharmaceuticals in drinking water).

The problem of persistent substances is very old. Some very problematic substances have been replaced and the problem was solved. Now it is really something different. We have developed analytical methods that allow us to measures compounds in very low concentrations so the problem is shifting. In my country in the 60s and 70s there were big problems with water quality related to nutrients and input of specific substances from industry and this has been resolved. The problems we encounter today are not as dramatic. It is important t when communicating the problem that there has been development. Industry has implemented many measures. It is a good question to know how far you want to go in terms of water treatment.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 4

Stakeholder Group: Environmental authorities (including RBOs*) / Chemical authorities

*RBOs: River Basin Organisations, authorities in charge of implementing the Water Framework Directive

Date	22.06.2011
Name of Interviewer	Dr. Florian Keil, ISOE
Type of Interviewee	Dr., expert in Ecotoxicology.
Type of organisation	Environmental Agency of a large European MS.

Questions:

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

Yes, an environmental classification for human pharmaceuticals is necessary, and we are advocating for an EU-wide implementation (we have always supported this).

b. Would you be interested in using it yourself?

Yes, not only personally when visiting the doctor or buying medication, but also in my related work at my countries Environmental Agency. The agency would also advertise and disseminate such a system.

c. For which purposes would you use this system?

If the underlying data are of good quality and have been reviewed by an independent institution, we could use it to assist us in evaluating the environmental risk of generic drugs.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

Difficult to say, because environmental effects have been recorded inadequately so far. Of course, we hope that easily degradable products are preferred in taking/prescribing medicines, so that positive environmental effects can be achieved. Necessary for this of course is that the requisite environmentally friendly product alternatives are available.

b. Economically?

If, in the future, patients pay more attention to whether they are taking environmentally friendly medications, then there will be more pressure on the pharmaceutical industry to produce corresponding products (i.e. "Green Pharmacy"); It seems that Sweden has already may positive developments in this area.

c. Medically?

Difficult to say: the doctor must first make a decision with the patient in mind, i.e. s/he must first decide whether the environmentally friendlier alternative drug is even an option for the patient. Positive effects are also conceivable relating to the increased occurrence of antibiotic resistance.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

The introduction of an environmental classification will be difficult because, in practice, doctors already have to take a number of factors into account. This raises the question of whether doctors even have the time to use an environmental classification. In principle, the topic should be integrated early on in the education process and informational events should be offered to help doctors become aware of the problem.

3. What are your (or your organisation's) needs for information on PPs in the environment?

[See question 4]

4. Getting into more detail…

- precisely which information (which data) would you require?

  All the data that we require for the approval process, i.e. physico-chemical data, data on environmental effects (aquatic/terrestrial), data on degradability in water treatment plants and in the environment, as well as consumer data. In addition, it would also make sense to have data on substance behaviour in the treatment of drinking water and data on water quality. To what extent drinking water relevance should be a criterion is difficult to answer, because it depends mostly on which raw water sources are used. Additionally, robust data on the health effects of the smallest doses would be needed. Disposal instructions should be included; however, we must take care not to overload the system. Issues concerning waste disposal could also be addressed separately.

- at which level of detail / (level of aggregation?)

  As simply as possible, but without suppressing important information.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

  Similarly to the four-level model used in Sweden; alternatively, a traffic-light system could also be considered. The important thing is being able to retrieve important information quickly!

5. How would you use this classification system in your work?

We can imagine contributing to its creation and maintenance and could make especially good use of it if the data were also fed in from other sources.

- How would it support / influence your decision-making processes?

  An environmental classification could help us in prioritising substances, i.e. in answering the question "What do we need to pay attention to in the future?" If there is enough robust data, the system could also help us in the approval process of generic drugs or the sustainable evaluation of old medications (for the approval of which no environmental evaluation is required).

- Would your organization favour such a classification system? Why / why not?

  [See question 1]

- Which organizations in your country would be pro / against such a system? Why / why not?

  In Sweden, the pharamceutical industry is also contributing to the system; however, it is conceivable that it will in part not be in support of the release of consumer sensitive data, for instance, within an environmental classification. Doctors associations could also refuse due to the extra work burden that could possibly arise. Environmental groups would certainly welcome its implementation. It is unclear how the health insurance companies will react, however, since they would have to enter into new negotiations with producers if the demand for environmentally friendly drugs were increased, especially concerning generic drugs. Its implementation should therefore be accompanied by a dialogue in order to align the different positions of the various interest groups with one another. If the pharmaceutical industry is opposed to this, the implementation will be difficult however.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

a. origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

The data must be valid and comprehensible and must be checked by an independent party. The data must be comprehensive and must cover all areas. The language used must be simple, so as to include all target groups. The way it has been done in Sweden is not appropriate, since the data are not checked by the licensing authorities but rather only by a board that doesn't even review the data but only checks them for consistency. In addition, there are only data on acute environmental effects and none from chronic tests, i.e. they are not state of the art. Therefore, a neutral supervisory body is needed to recommend whether a record can be accepted into the system (similarly to how the EMA does it).

b. Which categories of PPs should it cover?

All that are on the market.

c. Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

Yes, one should begin with any drugs for which there is already evidence of their presence in the environment as well as any drugs that have high consumption rates. Besides these, problematic substances such as chemotherapeutical agents, antibiotics and x-ray contrast agents should be classified first.

d. Should both prescribed and OTC (over the counter) drugs be covered?

Yes, all drugs that have ever been approved. If the data are presented in a brochure, only the most common ones should be included (but all should be presented in the web-version).

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

The display on fass.se is actually not bad (the language is of course a problem – Swedish!). For us, it's useful in this form; whether doctors or patients can use it is another question, however. For that, it probably needs to be simpler. For instance, there ought to be a screen directly into which you can type in the drug or ingredient and the type of information that you need. The presentation is definitely dependent on what you are using the system for; it should therefore be tailored to specific groups. A possible structure could be that I first indicate what type of user I am, than I indicate the drug or ingredient name, and then immediately get an overview with the most important information (i.e. the traffic light or something similar). If I want to dig deeper, I can go from there. To sum up: precede from simple to more complex information and offer different levels of information. The system ought to offer an aid in decision making, i.e. the opportunity to compare the environmental properties of different drug ingredients.

8. What is your perception of the risk posed by PPs in the environment?

This issue has to be differentiated more accurately whether we're talking about environmental or health risks! So far, environmental risks have been given to little attention; we don't even know anything about health risks. With respect to chemotherapeutic drugs, for example, we need to look more closely at possible effects of the smallest of doses. Hormonal effects in the aquatic environment are proven. It is unclear, however, whether we should expect effects in humans from this. Generally, more caution and more research on health risks are needed.

a. Is the media attention justified?

Yes, because we haven't paid enough attention to it in the past. Too little is known about the problem among doctors and the public. There is a lack of awareness!

b. Are the efforts for addressing the problem justified?

More can always be done! The topic has been well received among scientists and is currently being increasingly discussed. But we should not lose sight of medications for too long because consumption will increase in the future. Additionally, the production of medications should be more closely followed. In general, the precautionary principle should be applied, since drugs are designed so that they have effects in small quantities.

9. Do you have any other comments? (If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)

Not at the moment. If I do, I will send them to you!

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 5

Stakeholder Group: Environmental authorities (including RBOs*) / Chemical authorities

*RBOs: River Basin Organisations, authorities in charge of implementing the Water Framework Directive

Date	23.08.2011
Name of Interviewer	Dr. Florian Keil, ISOE
Type of Interviewee	Dr., in charge of environmental water quality issues.
Type of organisation	Authority responsible for water quality for a section of one of the largest European rivers (international). Responsibilities are those of River Basin Organisations (RBO).

Questions:

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

Yes, without restrictions!

b. Would you be interested in using it yourself?

Yes, both directly and indirectly.

c. For which purposes would you use this system?

The International Commission for the Protection of the Rhine (IKRS) deals with micro-pollutants in its own working group, the results of which are incorporated into my work. That is, I use them for assessing material loads in the area I am responsible for (the Rhine and its tributaries) and rely on them. For this working group, a classification would be extremely helpful, since they have had to develop everything themselves so far. In this sense, I would thus use the classification system indirectly.

I could use it directly if I were confronted with questions concerning acute pollution. In that case, I could use it to quickly obtain reliable information.

Additionally, a classification would be an important building block for developing new environmental quality standards within the EU Water Framework Directive; in this process too, however, I am only indirectly involved. Nevertheless, it plays an important role in my work.

2. What would the impact of such a web-based classification system be?

I think it would have an effect on how doctors prescribe medicine, how we dispose of medicine and would bring about a more responsible use of medications. In this way, it could actually lead to less water pollution. Of this I am convinced.

But, the opposite is also possible – if a medical ingredient or drug receives a "particularly environmentally friendly" seal of approval, there is the risk that consumers get the impression that they can just flush it down the toilet with good conscience.

My feeling is that doctors are already heavily burdened with regulations. Thus, a classification could prove to be yet an additional burden on them. The opposite could of course be the case if doctors say

that they finally have a reliable aid in the decision making process at hand and feel thereby relieved as they are confronted more and more with environmental questions. I ascribe to this view.

3. What are your (or your organisation's) needs for information on PPs in the environment?

In particular, I need eco-toxicological data, since these are the basis for the derivation of environmental quality standards in the context of the the EU Water Framework Directive.

4. Getting into more detail…

- precisely which information (which data) would you require?

  For this, I need not only acute data, but also data on long-term effects – even teratogenic effects – such basic information on each active ingredient. But to really be able to assess water quality, I need actually need information on combination effects, since, generally speaking, water bodies are polluted by multiple pollutants.

  We also have to be able to decide which substances are important. The consensus has been that the important ones are those that appear frequently, i.e. those with high consumption rates. Thus, data on this would be very helpful. On the other hand, we could be making a mistake because precisely those substances that have low consumption rates could be particularly critical for water protection. Sales figures should only assist in gaining an initial prioritisation; in principle, we need some sort of index that balances dangerousness and consumption rate, thereby enabling a differentiated prioritisation.

  Information on water quality should not be included: due to the great heterogeneity and diversity of the relevant water bodies, the system cannot handle that. In addition, those responsible for drink water quality will not be willing to feed in the respective data. But, information should be given – key word "web-based" – where relevant information on water quality can be found for those interested.

  Including the relevance of drinking water would be useful; however, it is not clear to me how and whether one could implement this in practice. How drinking water is treated varies greatly depending on the region and country. Thus, a uniform display would therefore be problematic. Drinking water on the Rhein is somewhat different than on the Po or the Rhone. In addition, I don't know of any drug ingredients that are relevant for my countries' drinking water or water utilities (except x-ray contrasting agents). This may be the case for other countries, but it would be disastrous to assume this as the standard in a uniform system.

  Instructions on proper disposal should absolutely be included in the classification.

- at which level of detail / (level of aggregation?)

  We need the type of concrete numbers that are generally prepared in the data sheets for industrial chemicals or pesticides. For consumers on the other hand, a traffic light system, or something similar, would suffice.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

  In the form of data sheets as they are produced within REACH – with all the information such as CAS-No., trade name, preparations, eco-toxicology, water solubility, etc. – for assessing the findings in the water bodies, this would be very helpful.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

  As a part of my work at the IKRS, which is involved in EU processes, I have to answer questions concerning prioritisation and improved wastewater treatment techniques to extract specific substances. In this sense, a classification would influence such decision-making processes indirectly.

  As someone who sits on the bank of a river and is confronted with measurements that I then must evaluate, a classification would directly influence my decisions and assessments. But also for inquiries from the press, a classification would be directly useful, so that reliable information on topics that I do not deal with on a day-to-day basis would be quickly available.

- Would your organization favour such a classification system? Why / why not?

Yes, my organisation would support that without restrictions! It would facilitate its own work considerably – both the on-site work as well as the committee work.

- Which organizations in your country would be pro / against such a system? Why / why not?

  Everyone for whom such a system implies extra work, especially the pharmaceutical industry! There will definitely be an argument like "health benefits vs. environmental benefits" and related resistance. There could be resistance for the abovementioned reasons even among doctors. These instances of resistance, however, have to do with the implementation. I do not think there will be resistance on a fundamental level.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

I need information on two levels: Firstly, I would need a simple enough system such as a traffic light with five or six levels to enable a speedy assessment. Secondly, I need detailed information in the form of data sheets for specific drug ingredients (possibly processed according to trade names as well, which then lead me to the drug ingredients). I need this for my work on a daily basis. The whole thing should be web-based, and the data sheets available as PDF-downloads. In addition, I need a database in which I can search according to ingredient and trade name.

a. origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

The sources must be transparent: for instance, the original literature for the ecotox-data should be given. Based on my experience, however, an independent body for inspection is not needed. The standards that apply to the industry laboratories will also be evident here and will ensure the validity of the data. In addition, the industry itself has a great interest in providing clean data, since the damage to its reputation would be enormous, should some sort of fraud be discovered. This is also the case for the data that are requested for the drug approval process. In this process as well, we rely mostly on the industry's data – why should that be different for environmental data?

As for the language, English would suffice as far as the technical information (data sheets) is concerned. But for doctors, pharmacists or consumers, the information should be provided in the respective country's language.

b. Which categories of PPs should it cover?

Instead of answering this question, I'll make a suggestion for sorting: first according to indication, second according to effects and third according to chemical properties (e.g. analogous to pesticides).

At least at first, we should not exclude any medication groups per se.

c. Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

For us on the Rhine, lipid-lowering agents, anti-psychotics, x-ray contrasting agents and hormones are especially interesting.

d. Should both prescribed and OTC (over the counter) drugs be covered?

Yes!

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

I am not familiar with fass.se.

*In case they are **not familiar** with fass.se*:

i. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

The classification should definitely be available in a printed version as well. In practice, this makes sense to have as a support, since access is often faster.

The system must be able to serve three different target groups. The first is the environmental specialists, who need information on environmental quality standards or limits, and, when they have these, need easily accessible ecotox-data. For this, searching by drug ingredient and trade name must be possible. Secondly, doctors and pharmacists must be able to use it. They need information on the healing effects, and they need the ability to quickly and directly compare the therapeutic efficacy and environmental characteristics at their fingertips. Thirdly, consumers must be able to go to the doctor and request that the doctor prescribe an environmentally friendly medication by means of a simple traffic light system. (However, consumers should not encounter information on healing effects). These three informational levels must be offered by the classification in any case.

8. What is your perception of the risk posed by PPs in the environment?

We still don't know enough. There really are only "spotlight" findings. However, I am a strong advocate of the precautionary principle. Thus, I assume that a risk exists simply due to our lack of knowledge. A classification could help us to come up with new, substantiated estimates – perhaps even to the conclusion that the risk is actually not that big! Thus, a real risk exists – for the environment, but less for humans!

a. Is the media attention justified?

Yes, in my personal experience, the media's interest has always been appropriate. The media has also been willing to deal with uncertainties. The media should keep at it because then the necessity of saying something about the environmental effects of medications becomes clearer. The fact that press sensationalises the issue probably cannot be avoided.

b. Are the efforts for addressing the problem justified?

Yes, even though sometimes a lot of duplication of effort. I am pleased with what is being done on the different levels. What conclusions we will draw from the efforts is still very open. However, if a classification system is not implemented, I would have to revise my opinion that the current efforts are justified and sufficient. In addition, there is absolutely a need for more research on the environmental effects of medications!

9. Do you have any other comments? (If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)

No.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 6

Stakeholder Group: Environmental authorities (including RBOs*) / Chemical authorities

*RBOs: River Basin Organisations, authorities in charge of implementing the Water Framework Directive

Date	09/09/2011
Name of Interviewer	Rodrigo Vidaurre
Type of Interviewee	Ecotoxicologist, involved in classification, labeling and safety data sheets for chemical products, UN-GHS and EU-CLP and REACH, legislation and guidance documents.
Type of organisation	Chemicals Agency of a European MS.

This interviewee's work is not directly related to pharmaceuticals in the environment (PIE), so there are no answers provided to questions 3, 4, 5, parts of 6, and 7.

I have been heavily involved in the classification, labeling and safety data sheets for chemical products in terms of what is being put on the market in general. I have been involved in developing the system taking what we had at the EU brought up to the UN level, in the development of the globally harmonized system of classification and labeling of chemicals (GHS) (substances and mixtures).

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

I see a great need for it. The way we are all using these quite extensively and we do find them in the environment as well, several of these active ingredients.

a. Would you approve of the existence of such a system?

Yes.

b. Would you be interested in using it yourself?

I doesn't really relate to my work. Not in my position.

c. For which purposes would you use this system?

See b.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

It could have an impact on the way these chemicals are being used. In this sense it could have an impact on the environment.

b. Economically?

That would depend on the data requirements. If there are requirements for doing new tests just so as to fulfill these assessments, then yes, it would have an economic impact. If it is based on available information it would have a smaller impact.

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

Doctors could take this classification system into consideration when prescribing. It could also have an impact on individuals' choices and how they dispose of pharmaceuticals.

3. What are your (or your organisation's) needs for information on PPs in the environment?

4. Getting into more detail…

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

6. What should the main characteristics of a classification system be to ensure the system works adequately?

Principle of classification (risk vs. hazard): *If you build a risk based information system, it is a balance of having it accurate but not too complicated so it will be used. To have a correct risk assessment is quite difficult, it requires a lot of information. When we talk about having something more simple in terms of intrinsic properties (hazard), the user could easily compare two different products for his or hers use. This is easier: it is an easier message to say "this is more hazardous".*

The "how" it is being used is the next step. If it is low risk: well, it may be a low risk today, because of current uses, but if you don't give the information that this is a very hazardous product you can find that there are more uses (and misuse) to it and the risk will change. Also, if you have a medicine which doesn't say anything about its hazard, it just says "for the way it is meant to be used there is no risk", the consumer may think that it is safe to flush down the toilet because there is no environmental risk associated with this medicine. The message that would be given in this case is wrong, if we do not at least mention the hazard associated to the intrinsic properties.(We sometimes talk about the potential high risk due to intrinsic hazardous properties),

Another advantage of including hazard is that the chemical then is labeled the same around the world, facilitating global trade.

On the other hand, if you would just follow a hazard approach maybe the companies would begin to make less strong medicines to avoid being classified as being hazardous. The number of pills you would have to take would perhaps double and hence there would be no positive effect on the environment.

I'm a not saying that it is a bad approach to do risk assessments. For certain priorities (high volume and/or highly hazardous) chemicals this may be worthwhile. But if you just build on risk assessment, you might make it too complicated.

The decision to make a risk assessment could be triggered by the hazard information. If it is more hazardous then in addition you could make a risk assessment (which ideally would take also production into account).

You need a lot of information to do an accurate ERA. It is a balance. I am not sure how difficult it will be to find a balance for risk assessment; for hazard assessment it is much easier, there is already a globally harmonized system (GHS) that then I think should be used.

When you say classification of pharmaceuticals I think it would be unfortunate then to just talk about classified if you do not mean hazard classification. This because the term classification in relation to chemicals is strongly connected with hazard classification and hazard information in the form of labelling and safety data sheets. If risked based, I think that should at least be stated when you say classified, e.g. "Risk based classification" or "Risk and hazard classification".

Evolution of information use: *I think if you look historically at our system, the hazard classification and hazard information in the form of labelling and safety data sheets was just information to users, but now, twenty years later, it is being used in different kinds of downstream regulations as basis for further risk reduction measures.*

ECHA is building a classification and labelling inventory (a databases also as a public version) just to get the picture of how chemical substances are being classified and labeled on the market. That will be used even further.

So the uses of the information changes with time, there will be more and more uses if the basic information is high quality, accurate, and simple (e.g. hazard based). I feel that the starting point would be intrinsic properties, and then to build from that.

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  I do not know the number of substances we are talking about it, but the amount of work related to products may be huge if you put this only on the authorities. The information should be gathered by the companies. The question then is who will do this hazard (and possibly also risk) assessment. If it is to be done by the authorities then other information sources could be used and it could be that the authorities would do part of the work (for prioritised ***substances****), but the hazard classification of the* ***products (preperations/mixtures)*** *should initially be done by the companies themselves and enforced by the authorities.*

- Which categories of PPs should it cover?

  In addition to widely used chemicals we should include substances that are known to be hazardous or of high risk. Even if they are not widely used, they should clearly be included in the system.

  It is important to find something that will be acceptable from a regulatory standpoint for the companies so it will be used. It is no use to have a list of chemicals where only a few percent have this information. That is also why I think that the starting point may be hazard information, it is easier to generate than risk assessment, but that could be in addition to hazard for prioritised substances.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?
- Should both prescribed and OTC (over the counter) drugs be covered?

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

In case they are ***familiar*** *with fass.se*:

j. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

k. What changes would you like to see in the system?

l. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

In case they are ***not familiar*** *with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

I think the issue is definitely big enough to address it now. I think it is a major step forward to define some system. The question is how to make it useful so it will actually be used, and not too complicated. We know that these substances are ending up in the environment and it does have an impact. Many of the medicines used by the public are used quite widely; knowing that, I think this is a high priority issue.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 7

Stakeholder Group: Pharmaceutical industry

Date	12/07/2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Two representatives of the department in charge of hazard assessment (including under its responsibilities the Environmental Risk Assessments of pharmaceuticals)
Type of organisation	Large international R&D pharmaceutical company, belonging to top 10 in both sales and revenues.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

The question of what the need is depends on what the intended goal and the intended audience are. You can't design a system before you have decided you understand what the system is designed for.

We are very aware of the fass system, we have contributed a lot of information. In principle we support such a system but we think that before the European wide system is developed there should be some lessons learned from the fass system. Has it delivered benefits? Such a system requires a lot of resources to provide the information. For companies to do this they have to see that the process is delivering changes and benefit. We have the CLP system for chemicals which provides simple information: this system has been validated, but fass has not.

Making information available for the public is a critical part of our contract with society. We believe that making information transparent and ethical is part of being a pharmaceutical company. We have published for quite a few years now the environmental information we have on our products. In practice we are very supportive of making data available, the one question mark we would have is whether a classification system per se is needed.

b. Would you be interested in using it yourself?

It is not relevant for internal classifications, we already classify our pharmaceuticals internally so our staff handles it appropriately. We also have discharge limits. The one aspect that this system could be used in is communication of risk to people using our products outside of our company: our consumers, doctors, pharmacists, same target audience as possibly intended by fass.

c. For which purposes would you use this system?

See b.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

b. Economically?

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

It's a difficult question to ask, because it assumes a classification system in place to give an opinion.

I assume that there would be an appetite, society would demand pharmaceuticals with a better environmental risk profile, but that assumes that for any given medical condition there are a number of equivalent medicines that are also comparable. That might not happen very often. Environmentally there could be a case for such a system if you had a number of drug substances with the same clinical efficacy, maybe the same cost, and the same side-effect profile, and the system would then allow the doctor, patient, or pharmacy, to choose the medicine with the best environmental profile. We believe clinical efficacy, side effects profile, and benefit for patient should come first.

3. What are your (or your organisation's) needs for information on PPs in the environment?

This question is not really relevant for us, we generate a significant amount of environmental and effects data for all of our active ingredients.

4. Getting into more detail…

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

Again, these questions are broadly irrelevant because we generate a lot of our own data. But occasionally for generic products, or other products, which we haven't developed but we buy in, where there may be data deficit. An issue we have with this material is that they come with a poor data set for environmental risk and hazard, what we would like to have a greater deal of detail of environmental hazard information, which we would use for our risk assessments.

I am interested in any scientific data that can underpin the assessment, not just data for regulatory submissions (standard fate and effects data) but any data that could inform the environmental impact of a pharmaceutical would be useful, genomic data, etc.

***Information on behaviour in wastewater treatment plants:** This is a data gap in research. This information is very important for real world refinement of risk: measured concentration of pharmaceuticals in the aquatic and terrestrial environment would be very useful for refining risk assessment. The estimation of predicted environmental concentration that one uses in ERA is very precautionary.*

***Information on sales figures:** That is business confidential information. I am sure most pharmaceutical companies would be reluctant to make this information publicly available. This information could be used by the company that is volunteering the classification (in the calculations for the risk assessment), but we do not want that number to be available to the public. However, the conclusion of the risk assessment that uses this number would be available to the public.*

***Information related to water flow and water quality in European rivers:** Yes, as background information, if somebody would collect and make this information available so that academics, industry could access it.*

We are very interested in pursuing good science regarding the environmental impact of our pharmaceuticals. To a scientist any data is potentially useful, so we would welcome the availability of data to which currently we do not have access, as a general principle.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

There is the potential that maybe, if you had the environmental information on pharmaceuticals, a company could make decisions on which pharmaceuticals to take through to market (this is a very futuristic view of the market, no company is in a position to do this right now) based upon perceived risk there may be commercial benefits, or benefits to the environment that could be delivered by choosing one candidate from our pipeline rather than another. That is one potential use, but a very horizon-type issue, that no pharmaceutical company is addressing at the moment.

The other area where the classification system could be used is communication to our users and customers.

We do not know of any significant organizations that would resist on the system if it was shown to be of true value.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

For transparency and having a levelled playing field, it would be better to have a common system that all companies follows, possibly administered by a third party that has no vested interest.

Regarding predicting environmental concentration: we believe we need a European-wide system, we would not want to have a system giving different risk quotients per region of the EU, that would be too difficult to administer.

If a classification system is adopted, the classification system must be based upon risk and not hazard. We were very insistent on this on the fass system. If you base a system purely on hazard it misleads the consumer or the person making the decision. The system should be based upon risk as a principle.

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  Origin of information: for new products data should be provided by company that is placing the product on the market. For active ingredients for which there are multiple products from multiple companies there would have to be a sieve type of organization which shares data and cost could be distributed according to proportion to share of the market.

  Quality of information is established by current regulatory systems, particularly EMEA for environmental risk assessment. In the first order there should be a strong emphasis on data being generated in accordance to Good Laboratory Practice in accordance to OECD guidelines or equivalent guidelines. And then subsequently if that data is not available, literature data should be admissible and be evaluated according to a Klimish score, a means to evaluate the quality of data in literature. Lastly a system such as read across from other substances that are structurally similar, and use the possibility of extrapolating environmental risk profiles from that kind of proposal. But we would emphases data should be available in a GLP OECD format would be the most desirable. From the point of view of neutrality, you could combine some sort of external revision, I suspect no company would be against a neutral organization similar to the EMEA which was regarded as neutral was set up to review the environmental risk assessment of products. As for language, it is difficult because there are so many within the EU, but if you want to effect the end user (doctor, user) in needs to be in a language they will understand.

- Which categories of PPs should it cover?

  In principle all of them. Currently there are guidelines for pharmaceuticals qualifying for exemption from environmental risk assessment so you should take that into account, e.g. low volume or orphan drugs, this should be taken into account, there will always be exemptions. But in general most pharmaceuticals should be included.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Assuming a need for prioritisation: a possible priority would be substances with PEC/PNEC greater then 1, pharmaceuticals with a risk characterization greater than one, therefore "risk to the environment has not been excluded". It is also not unusual to have PBT. Endocrine disruptors could be a category. And high volume pharmaceuticals. Some of them have no data associated with them.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Both should be covered, from an environmental perspective there is no difference. As a matter of fact OTCs from an environmental exposure perspective contribute far more than prescribed drugs, because of the higher volume of the pharmaceutically active ingredient.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

a. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

b. What changes would you like to see in the system?

c. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

Targeting different levels of information to different users, aligning data with the needs of users, is a principle to be embraced, simple for patient, more detailed for scientist. However fass is not too user friendly, the location of data is not terribly intuitive. There is a lot of work to be done on presenting the data. Maybe information could be presented under three different tabs: patient, prescriber, expert user. A useful search engine is a first criteria.

8. What is your perception of the risk posed by PPs in the environment?

d. Is the media attention justified?

e. Are the efforts for addressing the problem justified?

As far as we know there is only one pharmaceutical that has a deleterious effect on the environment (dichlophenac: impact on vultures in India). So indeed given the exposure pharmaceuticals can have impacts on certain species. But exposure has to emphasised here. There are other pharmaceuticals to which environmental effects have been attributed but there are confounding factors. One of them is ethylene-estradiol: it has been demonstrated it produces feminisation of fish in laboratories. However, there is a number of other natural and man-made synthetic chemicals that also have this effect. The cause and effect haven't been demonstrated conclusively.

Recent media attention has been on human health aspect of PPs in drinking water. We believe this is very sensationalized and does not bare any resemblance to absolute risk. A recent report by WHO on pharmaceuticals in drinking water agrees with most of the published information, that it is not a significant risk. From a human-health side the attention is not justified.

Another issue well known even to the public is the issue of antibiotic resistance. That is definitely the kind of thing that is happening, it is not clear if it's an environmental issueAnother issue is that antibiotics used veterinarily probably dwarf the use of antibiotics by humans.

From our perspectives we would ask that pharmaceuticals for humans and for animals should be kept separate, also reflecting the regulations. In principle, of course, we believe that such a system should also exist for veterinary drugs, but definitely kept unique.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 8

Stakeholder Group: Pharmaceutical industry

Date	28.06.2011
Name of Interviewer	Jörgen Magnér, IVL
Type of Interviewee	Project manager
Type of organisation	National association of research-based pharmaceutical industry of a European MS

Questions:

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

b. Would you be interested in using it yourself?

Answer:

1. Yes, why not. There have been attempts to lobby for this in Europe but it has not succeeded. It might as well exist on an EU level. They have as much need for it. However, it will miss out on the local aspect. It feels more complex and perhaps a slightly worse picture would emerge at the EU level. You will lose the local aspect. It becomes harder to take national decisions based on EU data. It is a future challenge.

a. Yes.

b. Yes, maybe then we would take the information and use it at fass.se

2. What would the impact of such a web-based classification system be?

a. Environmentally?

b. Economically?

c. Medically?

d. Regarding behavior routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

Answer:

2. If there will be consequences, I assume they are the same as in Sweden, but larger, on a broader level, with more countries.

a. It would be great and it would increase awareness at an European level. An increased pressure would emerge regarding other problems with drugs as an emission etc.

b. For the manufacturers, it's easier to just have a global common system, instead of a lots of national databases.

c. The manufactures that are at high risk would then have an impact throughout Europe, which would facilitate decisions regarding companies that have larger effects. This could affect patients as well.

d. Mainly, it would increase awareness in more countries. It would also increase the awareness of having good systems in order to take back unused drugs. Maybe today it is just a safety issue. Maybe we would start thinking of it more as an environmental issue, which it also is.

3. What are your (or your organization's) needs for information on PPs in the environment?

Answer:
3. We as an organization, first and foremost, because we are a company that provides information on drugs, we need to get hold of the information to be able to distribute it. We also have a need to obtain information about a drug's effects on the environment. What are the problems, what can we do? This type of information is required.

4. Getting into more detail…

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

Answer:

4a. I would like it to be just as fass.se, with a PEC / PNEC assessment, biodegradability tests and results. Bioaccumulative ability of the compound. Physical and chemical properties such as solubility. But in principle, it only needs to contain the same information as fass.se, which is sufficient to assess the substance. Then it depends on whether it will be substance-based or based on specific products. Even sales figures should be presented. This is presented as a PEC-value at fass.se, where sale must be reflected. Information of the fate in the environment is also important. Does it end up in the sludge or does it passing through with the receiving water and also how it can be degraded.

In the case of an EU system, you may want to know how treatment plants, etc. look like in the rest of the countries. It becomes more complex in Europe in terms of calculating PEC-value of all water in Europe.

b. As accurately as possible. But it is based on a model so it cannot be exact. You may not need to calculate with several decimals. On a European level the uncertainty becomes very large.

c. There are things to improve on fass.se. It should be standardized forms and less based on texts. Preferably divided field which could end up in a database directly. The presentation of the information: There is no European fass.se so it will become a specific page. Maybe if it will have all the data in fields in a database so it can generate tables and bar charts directly and so that there is standardized in such a way that they can becomes automated. It would have been nice.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?
- Would your organization favor such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

Answer:
5. We could, if we like the system, trying to build it into fass.se and show it to the public in an accessible way.

a. Yes, It would affect the decisions we make regarding the Swedish system, and we also have to take a decision if we are going to present a European system. The control located within the Swedish working group could not be maintained. We would probably have less to say.

b. Yes, we would do but it depends on how it should be structured. There could be systems that we might not think is a good model. But in principle we would support it.

c. I think there are many who would be for such a system. If you take those involved with the Swedish environmental classification system, for example, Swedish Pharmacy Association (Läkemedelsverket) would probably support it. Stockholm County Council (Stockholm läns landsting) would like to support it while they have their own systems that they care about, i.e. "Indexing". The Swedish MPA (Läkemedelsverket) would support it. Depending on how it would be. But if it would be designed in a good way no one would be against it. We would be against if it was designed, in our opinion, in an incorrect way.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

a. Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

b. Which categories of PPs should it cover?

c. Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

d. Should both prescribed and OTC (over the counter) drugs be covered?

Answer:

6. That it is up to date, reviewed and complete i.e. that it is not missing so much data. So above all, these three criteria.

a. Providing the information regarding the pharmaceutical must the manufactory companies do. Although that there could be opportunities to retrieve data from other researchers outside the pharmaceutical companies. If there is some form of third-party review, the objectivity can be maintained to a high extent.

b. All human pharmaceuticals. OTC (over the counter), prescribed and all the different ATC groups. However, allowing exceptions for vitamins and proteins, where a general assessment could be done.

c. The first phase is not so important. However, hormones and sex hormones are important even if it is not important at the beginning. At first, little problem can appear but the system will solve itself throughout the progress. It is not so important to take the ones with the greatest impact first. The important is that the outcome of the information is useful.

d. Yes.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

a. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

b. What changes would you like to see in the system?

c. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

iv. Would you address the different levels of depth of information?

Answer:

7a. There is hardly any distinction between advanced users and the general public. Since the introduction of the environmental directory, all phrases regarding environmental risks, persistence and bioaccumulation are visible. However, there is more information for the advanced user to access, which is not displayed at first for the public user. We have requirements that there would be a web service so that you can transport information to fass.se from the EU database. Yes, we like the system today. There are things to improve but it is good.

b. More standardized background information.

c. Hard to compare substances. It is the big problem. That it is a disuniformity in the background information.

i.

ii.

iii. More database like format from the beginning.

iv. We would like to show all the details and all levels. But we would also continue to have the background data hidden, to not confuse anyone, and keep it clickable if anyone is interested.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

Answer:
8. That it should be taken seriously. That we should study them as much as possible and to make decisions that are good for all parties. To be able to put it in to perspective with other environmentally hazardous products / items. Sometimes it may be present at a very low amount and may not be so dangerous. It is important to investigate for both the risk and hazard.

a. Media is not always 100% familiar in what they write about. However, I think it is justified that they write about as much as they understand. But sometimes it is put out of proportion. Thus, not all times.

b. Yes, absolutely. I think so. We work according to what we know and of course we should make an effort.

9. Do you have any other comments? (If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)

Answer:
9. No, not really.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 9

Stakeholder Group: Pharmaceutical Industry

Date	23.06.2011
Name of Interviewer	Dr. Florian Keil, ISOE
Type of Interviewee	Dr., Environmental Risk Assessor.
Type of organisation	Large international R&D pharmaceutical company, belonging to top 10 in both sales and revenues (2008 data).

Questions:

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

    a. Would you approve of the existence of such a system?

Such a system could be helpful. However, we have to be aware of the fact that pharmaceutical companies such as mine are moving in the direction of personalised medicine. Because of this, the question of the therapeutic comparability of active ingredients will become more central. The therapeutic comparability, however, is the basis for prescribing and choosing a more environmentally friendly alternative active ingredient by means of a classification system.

    b. Would you be interested in using it yourself?

Yes.

    c. For which purposes would you use this system?

Especially as a data source in my own work on environmental risk evaluation. In this type of work, it's very important/helpful to have access to data on active ingredients that are not in-house (e.g. old medications or generic drugs).

2. What would the impact of such a web-based classification system be?

    a. Environmentally?

It could have positive environmental effects if substances with lower environmental risk are prescribed more. But again here there is the possibility of conflict between the therapeutic efficacy and suitability of a substance.

    b. Economically?

I don't see any problems economically. The economic problems lie more in the efforts to achieve overall cost reductions in the health system. In Sweden we learned that it is generally generic brands that come into question when the cheapest medication must always be prescribed. This, however, hurts the pharmaceutical companies that perform research.

    c. Medically?

I don't see any fundamental problems in this area either; at worst, if in certain active ingredient groups there are only few active ingredients left on the market with possible unfavourable environmental effects, it could possibly lead to conflicts between individual stakeholders.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

A classification system could definitely change the way doctors prescribe medicines; we've seen first indications of this in Sweden. Responsible patients could also begin to request environmentally friendly medications more, but those who would do so are probably few, since an informed decision in this area requires a great deal of knowledge. Proper disposal of old medications should be viewed and solved independently of an environmental classification.

3. What are your (or your organisation's) needs for information on PPs in the environment?

As a specialist in the environmental risk evaluation of medications, of course all data that is relevant for authorisation or is necessary for the obligatory environmental risk evaluation.

4. Getting into more detail…

- precisely which information (which data) would you require?

  To many substances still lack basic data on physico-chemical properties (this is also especially true for fass.se). In order to use a classification system for my work (see above), this data is essential.

- at which level of detail / (level of aggregation?)

  Since I am a specialist, I need very detailed data!

- how should the information be prepared and presented (figures, graphs, level of convenience)?

  Different formats are needed for different target groups. Thus, a classification system should offer several different levels that cover the topic to varying degrees of depth.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

  Since I would only use it as a data source for my work, it would have no influence on my decision-making process.

- Would your organization favour such a classification system? Why / why not?

  My <u>personal</u> impression is that my company would have nothing against the introduction of an environmental classification. The company has been actively engaged in the topic for years already: for example, it is participating in fass.se, has published data sheets on its active ingredients on the internet as well as a position paper on the topic of medications in the environment.

- Which organizations in your country would be pro / against such a system? Why / why not?

  There could be companies that aren't as open in their attitude towards this problem; manufacturers of generic medicines could be among such companies, because they often have no interest in generating these types of data. As I see it, it would be good if, by introducing an EU-wide environmental classification, the generic manufacturers, in particular, were made to take more responsibility to deal with this problem. Apart from these, I can't imagine that anyone else would be against it, because it's not about combating certain substances but finding optimal treatment, while also taking environmental impacts into account, when alternatives exist.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

a. origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

The way it's done at fass.se, i.e. where the data is provided by the industry and viewed by an independent body like the IVL, is good. However, there have been isolated problems which have shown that we can't structure such a system strictly to the last detail – especially where the data available are not identical everywhere and where the criteria are not always very sharp. That's the just in the nature of the matter, which probably won't change easily, especially concerning old medications, for which the data is simply not available. Ensuring

adequate data quality is increasing, however, and I generally consider such a qualification of data possible (when disclosing references). Achieving neutrality is a difficult issue. I have the impression that this is not always the case at fass.se. In general, it's probably the case that we will simply have to find our way at first; that will definitely take a couple of years of constructive discussion. Nevertheless, a neutral position is good for minimising mistakes and for raising questions that allow for improvements or at least reveal problems. Something like that can help the system (analogous to Peer Review).

As far as language is concerned, it is difficult to correctly translate technical issues in every language; it's even more difficult for laypersons to then interpret this technical terminology. Thus, it should be very carefully agreed upon which interpretations should be included, in what languages and how precisely they should be formulated – such as is done in Level 1 or 2 of fass.se. When in doubt, perhaps English should be chosen as the original language and translations of the highest possible quality made into other languages from it. However, it will definitely be necessary to translate it into all European languages, especially with a view to practical users such as doctors. For this we would need an adequate translation as well as an accompanying manual or glossary as to how the system is used.

b. Which categories of PPs should it cover?

All of them.

c. Any priority drugs to focus on in a first phase (e.g. antibiotics)?

I don't believe there are any good arguments for a prioritisation. You must take each active ingredient individually, though you can of course start with the "usual suspects" such as cytostatics. But then you also have to remember that there can also be critical substances elsewhere. One must not generalise! The only exception: hormone disrupting substances – we know that these consistently have effects even in small concentrations.

d. Should both prescribed and OTC (over the counter) drugs be covered?

Yes, absolutely. Generic medications, which constitute a majority of OTC medications, come into play here again. "Risks of Scale" play a role as well: due to the high consumption rates, there can be high MECs and/or PECs, which can create problems even if the medications are not actually as environmentally toxic.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

It is fundamental that the system be risk-based! We know that a few of our medications are not uncontroversial, but, on the other hand, the consumption rates are so small that the risk – determined on the basis of the PEC-PNEC comparison – is also very small. Nevertheless, parameters such as biodegradability, bioaccumulation and toxicity should also be part of the system as a basis for risk evaluation. Additionally, direct comparison of active ingredients with regards to, for instance, their environmental properties would be desirable (but always secondary to the priority of adequate medical therapy).

Fass.se is cumbersome because you can only search by individual substance and not by ingredient groups, from which one could receive a list of the individual substances. Fass.se is a highly structured database! The system is lacking interconnectedness, which, however, could be easily built in since the data are there! As it is, you have to fight your way through, click by click, until you come to the actually interesting data, including the environmental data. The navigation on fass.se is too awkward: for instance, it doesn't have a filter that retrieves only those ingredients for which environmental data are available. For an EU-wide system, improvements would be necessary to be able to offer a more user-friendly databank.

The system should be tailored according to the needs of various target groups (tiered system). Due to its ability to constantly stay up-to-date, a website is both important and indispensable. In addition, printed materials should also be available for specific target groups, for example the glossary that could be used to train doctors.

8. What is your perception of the risk posed by PPs in the environment?

In general, I consider the risk for humans to be extremely low. After all, we're talking about substances that generally have already gone through humans; therefore, an accumulation is very unlikely. All scholarly publications that I have seen in the past years have showed an extremely low risk for humans.

Concerning the environment, it is more difficult, since we have much less toxicological data. This is especially true for old medications. Generally, I suspect that the risk lies somewhere between low and very low. But I do also suspect that there are also individual substances – hormone disrupting agents, perhaps certain chemotherapeutic substances, antibiotics, psychiatric medications and those substances that interfere with metabolism – of which the risks have not been determined or for which, depending on exposure (risk management!), we must assume that local risks do exist. But generally, the biological knowledge base is missing.

a. Is the media attention justified?

The media should strive for more in-depth coverage; often, the depictions are too superficial or even sensationalist. Due to the continuing widespread lack of knowledge on this topic, a serious handling of this topic is however both justified and desirable.

b. Are the efforts for addressing the problem justified?

There's actually a greater need for these efforts, especially in basic research. The efforts to tackle this problem beyond interest groups are also important. For me, a more socially broad approach acts as particular motivation to participate in the various projects These issues can only be tackled together with the other involved actors.

9. Do you have any other comments? (If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)

Solving this problem requires an integrated approach. Pharmaceutical residues in the environment should be viewed interdisciplinarily as one aspect of water as a resource. In so doing, more comprehensive approaches to tackling the problem could be developed.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 10

Stakeholder Group: Drinking water / Wastewater companies

Date	29/08/2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Deputy technical manager of institutional relations (in charge of drinking water matters).
Type of organisation	Large water service operator. (Also involved in national and European associations of water operators.)

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

Yes, there is a need.

b. Would you be interested in using it yourself?

Yes.

c. For which purposes would you use this system?

In our day to day work, depending on how it works. Any sort of logical decision-making scheme would benefit from a system like that. We need a compass to orient us when we find a compound in the drinking water. At the moment whenever we do, we do all sorts of analysis within our laboratories. We get results from all kinds of labs. Every now and then they put an arrow on a specific substance which would have potential effects. This is where there is the need for a decision criterion: whether or not this is an issue to be dealt with, (either by environmental protection or drinking water treatment, with a preference on environmental protection) or if there is nothing wrong with the molecule.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

b. Economically?

c. Medically?

It is hard to comment when I do not know what the system does, but in theory it would definitely have an economic impact, certainly on users like us, or other users of pharmaceuticals (farmers, public). Potentially it could have an impact on all three areas (health, economic and environmental).

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

There is a lot to be done on the issue of guiding consumers on how to dispose of pharmaceuticals. In my country there is certainly a need to do it better, and certainly many countries can increase their performance on this issue. But a lot of the input to the environment is from excretion which cannot be tackled through better disposal but rather marketing (referring to green by design, it should be considered in research). Regarding

prescription routines, I think it would depend on the country and on individual practices. The culture and local uses will make for widely differing prescribing behaviours.

3. What are your (or your organisation's) needs for information on PPs in the environment?

Basically two needs. The first one is the fate of the molecules in the environment; this kind of information is hard to find and not shared. Data of environmental concentration measurements in different river basin managements would also be interesting.

Another key information we need to know, and the decision making bodies regarding the approval of a pharmaceutical should be aware of, is the treatability in drinking water plants. At the moment it is not at all considered (and only poorly considered in the marketing of pesticides) although it is an important criteria. The most important criteria in this sense, by far, relates to environmental fate in the environment, biodegradation. You can assume that half of the EU population gets water from groundwater resources and these are protected physically against solid pollution; against soluble pollution the only protection is biodegradation. If that is not possible, the second thing to consider is oxidation processes and adsorption on carbon.

When it comes to pharmaceuticals health is a paramount priority, I support that view but it doesn't mean that it should preclude laboratories analyzing dossiers to have all the data regarding the environmental fate. That is also a good way to encourage stewardship. If the molecule is very good at fighting a particular disease that is great but there may be a need to make that molecule available only to hospitals and not to the broader public. The ''how'' it will be put into the market matters.

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes*

Ecotoxicological entries: *yes, key data.*

Excretion data: *yes, excellent criteria.*

Routes of administration: *yes*

Pharmacodynamic entries: *probably beyond what a water plant operator needs.*

Side effects: *not for us, but you have to differentiate what is a good criteria for decision making. I think this could be used extensively by operators in their dialogue with public health officials.*

Mammalian toxicology: *no, operators could have difficulty interpreting this data.*

Management of pharmaceutical waste: *I think that is of interest for anyone.*

Behavior in drinking water and wastewater treatment process: *yes, with wastewater it is the same as in the drinking water. Once you know biodegradability, adsorption capacity, and oxidation capacity you have the bulk of it. Also the potential to be used as fertilizer is important.*

Sales data: *it is a tough question. In theory it could be useful, in practice I am not sure how it could be used. When it comes to pharmaceuticals it is a very critical thing; for pesticides I would have a different opinion. Sales data for pharmaceuticals can be a criteria for a decision making body for authorization but I am not sure that operators would be well positioned to make a good use of that.*

- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

Simplified information only to a certain extent. Something which is usable, e.g. according to a given sludge contact time. It can be relatively simple, but we need something that will allow us to determine whether a

treatment is likely to have a significant impact or not. That should be given in the form of straight forward data. From country to country design criteria are not the same.

I need the raw data, no graphs.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?

The idea is to determine, when one finds a set of molecules, if there is nothing terribly wrong with it, because if there is then it is a case for banning the use of the molecule in the watershed, how we can minimize risks. If it is detected in the environment and thought to represent acceptable risks, it is a preoccupation to have that left in the environment and from there in the drinking water. The idea is how can we best minimize the risk with the calculation we just touched upon a second ago. How we use that: the question is if this is amenable to a slight change in the treatment speed or whether we need another treatment scheme. That is the sort of decision we need to make.

This is why transparency of the data is important, because the operator is almost never the ultimate decision maker. It is for us to prepare the dossier and say look with the treatment as it is at the moment we are not able to get rid of this pollutant and there is a need to have a broader approach. That is to be negotiated with the city council. We need a great deal of transparency about this data.

- Which organizations in your country would be pro / against such a system? Why / why not?

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

As long as there is a bit of control the options can be diverse. It could come from the pharmaceutical industry. But we certainly cannot rely on the industry to determine what sort of control they have to be submitted to.

If analyses have to be carried out I don't see that it can only be done by a research lab. They also depend on all kinds of research schemes, I have doubts they would be absolutely independent of any pressure.

You have to have independent organisms in charge of putting together the request for data and then controlling the gathered data. There is really a need for a supervising body. I would see that as a supra national state, an EU body.

- Which categories of PPs should it cover?
- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

According to the analyses we have seen lately, there is no particular category to prioritized over the other.

- Should both prescribed and OTC (over the counter) drugs be covered?

Both should be covered, without making a difference.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

m. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

n. What changes would you like to see in the system?

o. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

Different levels of information sounds like a good idea. I do not think it is useless to address the general public; we have to work with the principle that information should be shared with the public. There shouldn't be any restrictions regarding public access. The only thing is how that should be designed so that those who are susceptible of making a professional use of the system have access to the information in a useful way.

When it comes to the public, they will be advised by someone who has the authority to do that. The public alone will not be making any decision. It is either stakeholders or pressure groups that will use the material to put the focus on specific issues. No one should be restricted access to the data.

There is no reason why there should be exceptions [referring to differences between regulations for pharmaceuticals and for other chemicals] *even though it is in the name of public health protection, because in the end we are talking about health protection here too.*

8. What is your perception of the risk posed by PPs in the environment?

p. Is the media attention justified?

q. Are the efforts for addressing the problem justified?

My personal perception is yes it is justified. Just like in any other fields, there is excess in the way media report things, caricatures sometimes done by the media to make a buzz. We can debate about how the media is doing their job of informing the public on this issue. But I would say that per se the media attention is a good thing. Otherwise we would not be making progress.

According to the information available at this stage: there is no need to worry. I don't see where pharmaceutical residues, even though they are there, would be a problem for human health. That doesn't mean the question should not be further investigated and that no one should consider schemes to ensure we stay on the safe side. It is not because we have no clear major sign that things are going wrong that we cannot start planning for the future and secure the process which will enable us to manage the situation. It is not because there is no striking evidence of impacts to human health that we should not keep our eyes open and start improving the legislation.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 11

Stakeholder Group: Drinking water / Wastewater companies

Date	02/09/11
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Head of department in charge of wastewater and protection of environmental waters.
Type of organisation	National association of water utilities of a large European MS.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

This is a very meaningful initiative, which would allow to have an overview of the problem. A system that brings together the relevant substances and appraises their risk would be from our perspective a very helpful tool. I envisage a database which collects all kinds of relevant information on this topic.

a. Would you approve of the existence of such a system?

Yes.

b. Would you be interested in using it yourself?

Yes.

c. For which purposes would you use this system?

We could use this system to research individual substances. It is very hard for our members, e.g. operators of a wastewater plant, to understand the toxicological information. It would be very good if we would have a tool which our members could find information what kind of substance is this, how is it characterised, what are the risks ... all information that could be interesting and useful.

It would also be interesting for us as an association, for our communication with the political sphere, e.g. when developing recommendations.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

As I understand the system, it would be a system that provides information, and not classification. But a system that provides classification could be based on this information system. An information system could serve as basis for an environmental label; this would give the possibility of taking measures that address the pollution input. An indirect measure, addressing prescription and consumer behaviour.

It would however take a considerable communication effort to make consumers be proactive and engage with the issue.

b. Economically?

It could be beneficial for the pharmaceutical industry, a competitive advantage for them if they produce environmentally more friendly substances.

The industry could have problems with environmental information being made available, they could feel disparaged. However, an information system is not an environmental label, so I can't think of an actor who would have problems with the system.

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

It is a very controversial point if doctors' behaviour can be influenced with such a system. Consumers wouldn't be easily affected; they would require information on the packaging, e.g. for liquid medicines "Do not in any case dispose of in toilets."

3. What are your (or your organisation's) needs for information on PPs in the environment?

Data that is scientifically based and that has been validated. Data to entry pathways, a resilient inventory of emissions, how pollutant loads are distributed among sources, so that we can make mass balance studies.

Chemical transformation cascades: how is a medicine degraded and which other compounds arise (potentially more dangerous than the original substance). Transformation products are nowadays not captured, and they can arise e.g. in the drinking water process due to ozonation. (I see responsibility of public bodies (national research ministries, EU Commission) to produce research on this topic, on which too little is known.)

Although the issue is an environmental issue, and not really one of human health (see answer 8), we would like the system to incorporate information on human toxicology as well as environmental information.

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Pharmacodynamic entries: *yes.*

Pharmacokinetic entries: *yes.*

Excretion data: *yes.*

Routes of administration: *no.*

Side effects: *no.*

Mammalian toxicology: *yes.*

Sales data: *yes, both past and present, it would be interesting to analyse trends.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes, it is important for us to know in which concentration these pollutants occur, and their impact on aquatic life.*

Management of pharmaceutical waste: *yes.*

- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

Raw data is of more use, in some cases aggregated is helpful.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

  Such an information tool would be very important to be able to think about measures: where should these be taken, where do they make more sense. It would be a very important tool for basing our decisions. This both at treatment plant level as at political level, when producing recommendations.

- Would your organization favour such a classification system? Why / why not?

  Yes, very much, for the reasons mentioned above.

- Which organizations in your country would be pro / against such a system? Why / why not?

  My country's Environmental Agency would probably also have strong interest. The pharmaceutical industry may be less interested in such a system.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

Such a system requires continuous maintenance; an official, independent body should be charged with this, such as the European Environmental Agency, in my opinion. I would be less in favour of the system being managed by the industry.

From our perspective we would like to have medicines grouped according to their type, and count with main parameters and sum parameters for these groups. It is hard for us to work with individual substances. This is

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  Industry should provide the data. The process should be cooperative. The data should definitely not be produced by the authorities. A body such as an Environmental Agency could be in charge of such a system, and the industry association would have to commit to regularly deliver data. An Environmental Agency would also be in a good position to take up additional data, such as results of independent research, and bring all data together.

- Which categories of PPs should it cover?

  Not all, only relevant PPs should be covered. Definitely antibiotics, cytostatics, and estrogen compounds. Then anti-rheumatics.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  See previous point.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Both. OTC are very important, huge volumes and not much good data on them, they are a real "black box".

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

a. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)
b. What changes would you like to see in the system?
c. What are the shortcomings of the system?
    i. re. information
    ii. re. functioning
    iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

A differentiation should be made between experts, intermediate users such as water treatment plant operators, and consumers.

8. What is your perception of the risk posed by PPs in the environment?

The risk perception of PIE is exaggerated in comparison to that related to other compounds, e.g. pesticides, biocides, industrial chemicals. We would like to see the risk of PIE relativised, also in relation to other sources of pharmaceuticals: we see extensive debates on tiny amounts of pharmaceuticals in drinking water, when consumers take up much higher amounts in their food, or via other products.

a. Is the media attention justified?

The media attention focuses on the risk to human health; it is hard to find environmental arguments in media coverage. The discussion always centres on "poisonous" or problematic substances in drinking water. However, this is an environmental issue, we don't see an acute risk for human health caused by pharmaceuticals in drinking water.

b. Are the efforts for addressing the problem justified?

Yes.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 12

Stakeholder Group: Authorities responsible for Drinking Water

Date	23.06.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Drinking water expert in a National Institute for Public Health
Type of organisation	National Institute, working for government ministries of a European Member State.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

I would be interested, but not just for pharmaceuticals, for all pollutants that can be present in the drinking water.

a. Would you approve of the existence of such a system?

Yes

b. Would you be interested in using it yourself?

Yes

c. For which purposes would you use this system?

We often have questions and go to our toxicological experts who in turn do literature review and give us a response. That works for us, but a classification would be helpful. To try to answer the questions: are there health risks involved, or ecological risks, we are mostly interested in human health risks (when drinking water) or are these substances able to pass treatment.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

I guess if you had this data you could at an early stage identify if there are health/ecological risk involved with certain pharmaceuticals that are released in the environment. So earlier risk assessment. Also better prediction of which substances will pass drinking water treatment.

b. Economically?

If it makes it easier to identify problem substances, the medical industry could get more problems seeing that there is more info about harmful effects, it could trigger societal discussions.

c. Medically?

No because human health is the first priority.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

If there is an equivalent alternative that is less harmful for the ecology, the system could have an influence. You can also think of other remediation actions, like extra treatments for the water, but I do not think it will change

doctors' behavior, other than disposal methods. They will always prescribe the medicines. Consumer behavior can be changed.

3. What are your (or your organisation's) needs for information on PPs in the environment?

Acute and chronic toxicity, degradation in sewage and drinking water treatment plant, use (meaning amount of use, kg, to be able to identify point sources - if we know upstream which amounts are used, we can predict what we will find in the treatment plant, to define your remediation measures you need to know where they come from), hydrophilic, hydrophobic compounds, so we are able to identify which compounds would end up passing through the treatment phases.

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Pharmacodynamic entries: *yes, as far as its relevant to determine the amount that leaves the human body and is degraded through a wwtp.*

Pharmacokinetic entries: *yes, as far as its relevant to determine the amount that leaves the human body and is degraded through a wwtp.*

Excretion data: *yes.*

Routes of administration: *yes.*

Side effects: *no.*

Mammalian toxicology: *no.*

Sales data: *yes.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes.*

Management of pharmaceutical waste: *yes, but not crucial information.*

- at which level of detail / (level of aggregation?)

Summaries would be sufficient, but I would require detailed information on sales figures and on behaviour of PPs in drinking water and in wastewater treatment plants.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

I think for those more crucial information I would prefer raw data, it's nice to have figures too, but I would need to be able to access the raw data

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

It would help to identify where certain pollutants come from, and then to think of possible emission reduction strategies and to assess health risks and potential problematic substances.

- Would your organization favour such a classification system? Why / why not?

Yes

- Which organizations in your country would be pro / against such a system? Why / why not?

  All water boards would be in favor as well as environmental institutes. The ministry of human health might not be in favor because they are primarily interested in human health and when you address environmental aspects they expect all kinds of problem. The pharmaceutical industry would not be interested, because they would not benefit from it.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  I do not think the pharmaceutical industry should run this system. However, they should be involved.

- Which categories of PPs should it cover?

  I would start with the most critical pharmaceuticals.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Antibiotics, other crucial ones.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Over the counter should be covered, also veterinarian use, especially for antibiotics.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

d. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

e. What changes would you like to see in the system?

f. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

I would say for experts to use it, the info must be downloadable, it could be interesting to present a yearly report with an overview of everything. For me it is difficult to answer this question

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

Pharmaceuticals in general is really broad, I think some antibiotics use can be of concern so from this point of view it is justified but other substances are the object of too much attention when you compare their effect to that of pesticides. So yes sometimes, I think there is too much media attention paid to pharmaceuticals, veterinarian use is also just as important as human use.

b. Are the efforts for addressing the problem justified?

Additional comments: *In the WFD there is a lot of attention paid to ecological problems, but drinking water is not discussed as much. When substances are admitted to the market, we should look at how these substances are easy to remove from drinking water. For drinking water companies this is a very important issue.*

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 13

Stakeholder Group: Authorities responsible for Drinking Water

Date	15/06/11
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Head of the Toxicology Department for Drinking and Bathing Water.
Type of organisation	Environmental Agency of a large European MS.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

It would be very positive for my work. We could use this kind of information to develop criteria for drinking water relevance. On the basis of substance or metabolite properties we could evaluate the potential for the substance to make its way into drinking water.

a. Would you approve of the existence of such a system?

Yes.

b. Would you be interested in using it yourself?

Not directly. The drinking water relevance criteria we could develop should be used in the authorisation process, to influence the authorisation and the way the product is placed on the market.

c. For which purposes would you use this system?

See b.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

Positive impacts minor in the short term, definitely there the middle and long term, if the system is really implemented and the number of relevant pollutants is reduced.

b. Economically?

c. Medically?

The freedom to choose one's medicine should not be restricted. Only the selection between substances that will produce a certain result should be influenced. This means that products that are more easily biodegrabable should be favoured. This favouring of environmentally more neutral products should take place both during the authorisation process and when prescribing (doctors) and selling (pharmacies).

Old, less environmentally neutral compounds should be replaced with time by better alternatives. They also could be charged with a small fee to support independent research into new compounds and formulations with improved environmental characteristics.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

Behaviour routines should be changed (see c). Physicochemical criteria used should to incorporate drinking water relevance. I miss them at a prominent place in the current Swedish system

3. What are your (or your organisation's) needs for information on PPs in the environment?

Toxicological data for humans, or the statement that this data is not available. Acute data, chronic data, specific and unspecific mechanism of action, reliable informations on carcinogenic potential, length of animal tests, transferability of data to humans, short-running tests if long-running tests are not available. Different toxicity studies, including not yet standardized ones. Suspected or proved mode of action for side effects. Data should also valuable for very low exposure. All this would not be necessary for all pharmaceuticals, but mainly for those 20 or 30 that have been or can be expected to be found in my MS in drinking water (more or less the same that are found in drinking water in the EU).

In addition as many ecotoxicological, physico-chemical and QSAR-data as feasible on those single environmental metabolites representing more than 10% turnover of the parent compound.

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Excretion data: *yes.*

Routes of administration: *yes*

Side effects: *yes.*

Pharmacodynamic entries: *yes.*

Pharmacokinetic entries: *yes.*

Mammalian toxicology: *yes (see 3 for additional information requirements on toxicology).*

Sales data: *yes. Per capita use, per region, ideal for our purposes.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes, to understand how something has made its way to where it was found, e.g. accidents or bad disposal.*

Management of pharmaceutical waste: *yes.*

The system shouldn't stop users from taking medicine. This is why the information shouldn't be provided on the medicine packaging.

- at which level of detail / (level of aggregation?)

Data should be provided at regional level for environmental data (measurements) and sales data.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

A simple information level for consumers, with graphs and a point system. More detailed information should be provided in peer-reviewed dossiers, summarizing e.g. the toxicological evaluation. And those who want more detailed information should be lead to the sources, even if they are not publicly available: he or she should know, where he can ask for this information.

Information should be available for everyone, but labeled according to relevance: this is of more relevance for doctors, this for pharmacists, for consumers, for scientists.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

  It would only influence how I provide input to the agencies in charge of authorization in my country, and for establishing the needs for tests that will help determine a possible toxic potential.

  I would also take a look at human toxicological information, to see if there is a need for a recommendation for our national Toxicological Threshold of Concern for a substance in drinking water.

- Would your organization favour such a classification system? Why / why not?

  Yes.

- Which organizations in your country would be pro / against such a system? Why / why not?

  I would believe that Environmental Agencies would be positive, as well as health agencies such as those in charge to assess risks to health from environmental contamination.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  Data should be provided by the industry. Type of information source and its quality should also be provided, e.g. type of journal in which data was published, national or international, peer-reviewed or not. Problem with industry data is that it is private data, and thus not publicly verifiable. Also grey literature, bringing this data together.

- Which categories of PPs should it cover?

  Data should be provided in form of an "exposure potential" for pharmaceuticals that are over a certain per capita consumption threshold and at the same time with a minimum of relevance for raw water sources. Pharmaceuticals that are below a critical "exposure potential" can be neglected.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Pain killers and antibiotics, because of the high per-capita consumption figures, of gentoxic and neuroactive compounds.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Both.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

r. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

s. What changes would you like to see in the system?

t. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

I would recommend three levels. Information for doctors / pharmacists should be comparable, maybe with a point system, with qualitative information. More detailed information would be available at a further level. The third level should contain all the information.

Some thought should be given to the authorities that are entrusted with the system. They should be public authorities, but possibly a combination of a Medicines Authority and an Environmental Authority. A medicines authority shouldn't be left in charge of this system on its own, nor should an environmental authority: there would be too many conflicts. If both are in charge, conflicts could be resolved without fights being carried out in public.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

The public and media pay too much attention to this issue, the authorities too little. We who are responsible for drinking water supply have to address today problems that will become relevant in 50 or 100 years. Other authorities, such as Medical Product Agencies, don't see it this way, but we have to work with a lot of foresight. That's why we really want to avoid any pollution that is avoidable, and not compare it to effects [on health]. We don't want to start doing something only once the effects are or might be already there.

Consumers have to understand that in densely populated urban areas there is no possibility of perfectly clean drinking water, we are all responsible for producing contamination, and we all want to take the best possible medicine. But it is possible to have drinking water that is as clean as possible, with pollution levels far below health thresholds.

b. Are the efforts for addressing the problem justified?

Yes - on a long term scale. There are no "acute" problems with drinking water.

Additional comments: *Data on the behaviour of pharmaceuticals in drinking water and wastewater treatment plants should be collected in the authorization process of the pharmaceutical, not later on, when the substance found in sewage water.*

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 14

Stakeholder Group: Research organisations

Date	17/06/2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Risk assessor for micropollutants.
Type of organisation	National ecotoxicology centre.

In my country more than 40% of exposure-relevant micropollutants are pharmaceuticals from point sources. My task is to derive proposals for Environmental Quality Standards for these substances. Therefore I have to work with effect data sets of these substances and data evaluation. The prioritization was made according to the exposure relevance or to specific toxicity. Currently we have made hazard assessments of 22 pharmaceuticals.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

There is a clear need regarding the high exposure relevance in surface water and wastewater. Such a system can lead to identification of risks and non-risks. I think Sweden has made a very good progress on this issue in 2009, they proposed a classification system for more than 60 pharmaceuticals. They have a simple classification system, very easy to use and also interesting for non eco-toxicologists. But a more detailed system is still necessary for hazard assessors.

a. Would you approve of the existence of such a system?

Yes.

b. Would you be interested in using it yourself?

Yes, data from official and recognized partners could be directly used, but an additional data check is necessary. So we would prefer a database with the original references or at least independently checked endpoints.

c. For which purposes would you use this system?

To gain an overview for the exposure and the eco-toxicological relevance, effect data for aquatic organisms. Additionally persistence criteria would be also fine, studies on bioaccumulation would also be interesting. The classical PBT assessment,; even more interesting would be the identification of carcinogenic, mutagenic or reproduction toxic and hormonally active substances. In most of the cases this is not the case for pharmaceuticals, because they are designed against adverse effects but if you look at non target organisms unexpected mode of action can occur.

Regarding the ecotoxicological data we calculate according to the TGD for EQS Environmental Quality Standards. One main problem is the data availability for pharmaceuticals: it's not easily available, and many gaps exist. Now for some substances we have very good data sets, but for others, like for all the metabolites, there is still a need to improve data availability. Some of these data exist, e.g. for new substances according to EMEA 2006, but they are confidential and not usable for prospective and retrospective risk assessments. There is the main safety gap for the newer pharmaceuticals. For the older pharmaceuticals we have from time to time enough reliable and relevant ecotoxicity studies, but for the newer pharmaceuticals the data are confidential.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

Yes, If it's a good database then it would have an positive environmental impact. The current problem of several risk assessment institution is to share their knowledge in an efficient way. If all the work goes in one database and it becomes available this could also lead to a more harmonized risk management procedure. I expect there would be an environmental impact, if it's well known and well managed. That is another key problem; it takes a lot of manpower to establish the system and to maintain the highest level of knowledge.

b. Economically?

I don't think the economic impact would be strong. It could give the pharmaceutical industry information which environmental risks are expected and to develop new products. I think it would be a chance to improve the environmental characteristics for these active substances on a long run, but the critical knowledge has to become available first.

c. Medically?

Hopefully there would be an impact, but doctors also need to have the time to look at the database and need a very easy risk classification system. I could imagine they would look for these factors additionally and not only for human health, but also for aquatic risk. If they know several pharmaceuticals with similar positive effect they could decide for this one with the lower environmental impact. But again, doctors have to work a lot and are also influenced by industry, by the prices and by what they can spend for patients. My answer is hopefully, rather than a clear yes.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

If there would be an easy labeling scheme people would have a chance to think about how they want to manage their medicines. Currently some people dispose of them via the toilet. If clear information and knowledge about increasing aquatic effects would be available I think more people would bring the substances back to the pharmacy or look for another way to dispose of old substances.

3. What are your (or your organisation's) needs for information on PPs in the environment?

We work together with other analytical departments within the institute to investigate the exposure relevance. We need also analytical data to see what is in the environment and to see which substance we have to evaluate. It is also useful if you do not have analytical data to check the consumption data. There are very old pharmaceuticals which have still a very high consumption. For some new ones there are no analytical methods yet developed and info on how much of these substances are on the market is not available. From time to time we also buy these data to make an environmental risk assessment, via flow analysis for substances because analyses are also expensive. This allows, for some substances, a wide survey for exposure relevance and we are currently coordinating some multinational flow analysis projects for micropollutants.

On the other hand we work together with international departments for hazard asseesments to allow a maximum of data and knowledge exchange for a more reliable hazard assessment. In general all institutions need a better data availability for effect data, bioaccumulation and persistence data for many pharmaceuticals.

Only the combination of reliable exposure assessment and hazard assessment leads to the possibility of a reliable risk assessment.

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Excretion data: *yes.*

Routes of administration: *yes*

Side effects: *yes.*

Pharmacodynamic entries: *yes.*

Pharmacokinetic entries: *yes.*

Mammalian toxicology: *yes.*

Sales data: *yes. That is helpful if you do not have analytical data to predict environmental concentration with models.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes.*

Management of pharmaceutical waste: *yes.*

Also more information about metabolites, and about hormonally active, immunotoxic, carcinogenic, mutanogenic or reproductive toxicity effects. Also from the human health sector: from time to time this is interesting for secondary poisoning characteristics. If you have a very specific mode of action and a substance that bioaccumulates then you have the risk of indirect toxification via the food chain.

- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

5. How would you use this classification system in your work?

There are two clearly different concepts for a system. The first is an easy information for the public where is a high need of a very simple classification system.

On the other hand for a proper assessment you need directly the original data in a database approach. This data could be used for a prioritization of substances and allows own classifications. If the database is well maintained it could grow and become better. There is a problem of data availability for most of substances and the chance to reduce a lot of redundant work between hazard assessors in collecting and validating data..

Some projects like ERAPHARM lead to very useable database tools which are not used and maintained anymore, like the pharmacoecobase, but they still provide relevant information for the classification of pharmaceuticals.

- How would it support / influence your decision-making processes?

  It would help with the calculation of predicted environmental concentration and predicted no effect concentration, which would lead to an indication that we could expect a risk for a substance. With both information we are able to look at which region there will be a tolerable or intolerable risk for aquatic organisms. .With analytical data and EQS (Environmental Quality Standards) a risk evaluation is possible.

- Would your organization favour such a classification system? Why / why not?

  Yes.

- Which organizations in your country would be pro / against such a system? Why / why not?

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

If you have an industrial study in most of the cases it is done following good laboratory practices (GLP), according to OECD standards, so a very valid study. But in most of the cases there is no access to the main results. This makes it difficult to evaluate the whole study. You have the endpoints, and the security that it is done by GLP studies, but not all relevant endpoints are covered by the standard tests. So you have to complement those datasets if possible by public available studies with reliable and relevant effect data. The registration data for pharmaceuticals is more restricted than for pesticides. In pesticide registrations you have your draft risk assessment reports and DA; finally the data becomes available and you have a better data set. In the case of pharmaceuticals the main source of information is public available literature.

Second point is a need of a person who is able to make a validity and relevance check of the study, according to a guideline document like the TGD for EQS. If everyone had the possibility to bring information into the system it would be dangerous,there is the need of an experienced person to manage the quality of data. The language could be also a problem: English would make it easier to accept the information [from the different sources contributing to it].

- Which categories of PPs should it cover?

  All of them!

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Drugs with high use, exposure relevant drugs, drugs with a very relevant and specific mode of action.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Yes for both but it makes a big difference for the environment if it's a prescribed or over the counter drug. In regions where you have a high drug available over the counter, as opposed to prescribed in other regions, we observe higher concentrations. It is necessary to inform the people about the use and disposal.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

u. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

v. What changes would you like to see in the system?

w. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

It would be helpful to have different information levels. One possibility would be to have one information system for doctors, and one for the environment.

We need a system with a structure that makes it easy to find information. I was really inspired by the ERAPHARM database. You get an overview of which info is available for a substance of your choice. I would prefer a database over a webpage approach.

Regarding manpower, at the moment it's a big problem in the exercise of deriving new quality standards for the WFD. The possibilities to gain from sharing information are increasing. If it is possible to establish a system out of this cooperation, together with stakeholders, and allow to generate a database which would have continuous maintenance that would be a fine solution. The current version of fass.se is insufficient to find the available data in an efficient way, but it is clearly better than nothing.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

Yes, pharmaceuticals are bioactive and relatively exposure relevant substances with sometimes unexpected risks for the aquatic environment.

b. Are the efforts for addressing the problem justified?

Yes, there should be an increase of risk evaluations and perceptions between human benefits and aquatic risks in a prospective and retrospective way. At the current status for the registration of human pharmaceuticals there is no chance to reduce this risks and also the concept of pharmacovigilance has to be established for human pharmaceuticals and not only for veterinary use.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 15

Stakeholder Group: Research organisations

Date	17.06.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Scientist, working on Environmental Risk Assessment of medicines, biocides, pesticides.
Type of organisation	Research institute for his country's Ministries of Environment and Public Health

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

I think it's very useful to have a system. The data behind the classification is the most crucial aspect. Classification is always useful if you want to prioritize your focus, nobody will dispute that, but the quality of the focus depends on the quality of the data.

I think what you should have in mind a specific user group and provide this group with guidance on how to navigate the tool. There should be some incentives to make the good choice. For example there could be a very simple tool to allow calculating the environmental burden of the product they use. They can see the different results for various alternatives. But there needs to be a bigger context in which people's awareness is raised and changes in behavior are being promoted and incentivized.

b. Would you be interested in using it yourself?

Yes.

c. For which purposes would you use this system?

I would use it for giving advice on priority setting. A system like that would lower the cost of action. It is costly to produce data. But I would say don't bother informing the broader public, which might sound strange from an environmental perspective. I do not have the data to prove that, but people who are concerned about environment and health may think something like the following: ''pharmaceuticals are toxic any way, even for yourself so I don't like to take medicine''. If additionally you inform them of the potential risks to fish I can imagine these groups refusing all together to take medicines and trying to discourage others to do so. You can imagine that this can lead to bad consequences for patients in need.

2. What would the impact of such a web-based classification system be?

The success of the system will depend on there being enough discriminatory power; do you classify chemicals differently, will you inform people on other choices they have. There probably will be differences between pharmaceuticals but the question is does the medical professional really have alternatives to choose from given the treatment required for a certain case.

a. Environmentally?

From an environmental perspective, I think it would help because it saves a lot of work, helps those who are responsible for environmental quality to do a better job. It could give wastewater treatment plant managers the necessary information to justify the need for additional treatment for example.

b. Economically?

Yes, if you put that broadly there has to be a driver to impact that. Of course if you decide that you need to lower the burden on the wastewater treatment, it will have a major impact on the industry. Cause they will have to invest more to clean their water. There has to be more incentives on awareness of healthy living to trigger economic activity, which will be for a large part subsidized. The classification system would merely be instrumental to this, a benchmark to justify your efforts and to check your performance. The classification doesn't provide the driver. The data in there showing risks and potential for improvement should inform decision makers to then take action.

c. Medically?

We have very low medicine consumption levels in my country, one of the lowest prescription rates of antibiotics in all of Europe. Some researchers say that we are so economic on pharmaceuticals that it might be harmful in terms of public health (suggesting there is not much to be gained in reducing pharmaceutical use.) But we do have many animals and they consume a lot of pharmaceuticals. The impact would be on the environment in my country, not a medical impact or behavior routine.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

These issues are too complex for the broader public for them to be able to weight the pros and cons on their own and potentially take bad decisions. The issue is too complex for straightforward decision making by the broader public. I think it is simple and straight forward, but you should not leave the decision to the individual. Patients can get involved because it is their health, but the decision is the doctor's. The doctor can choose between alternative medicines at the treatment stage. I think that professionals are pretty much interested, but I do not think that patients will have an impact on decision making, it will just raise issues for them in following the prescribed therapy. That is my concern.

3. What are your (or your organisation's) needs for information on PPs in the environment?

We need data on what people use, which medicine and where, so that we can correlate use and exposure. I am much more interested in understanding why you will find high concentrations somewhere, then just knowing the concentration. We want the why.

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Pharmacodynamic entries: *yes.*

Pharmacokinetic entries: *yes.*

Excretion data: *yes.*

Routes of administration: *yes.*

Side effects: *yes.*

Mammalian toxicology: *yes.*

Sales data: *yes.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes.*

Management of pharmaceutical waste: *yes.*

Additionally, I would like to have data that focuses on established use of medicine, why the use is as it is (regional differences in prevalence of diseases), new and upcoming pharmaceuticals, what can be expected.

- at which level of detail / (level of aggregation?)

I need a high level of detailed information. I need to know test conditions (ph, temperature, kocs, composition of sediments etc). We would love to have all the study reports, that would be the easiest, or if we can't have that, we need elaborate tables with all the endpoints

- how should the information be prepared and presented (figures, graphs, level of convenience)?

I want tables.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

  Advise ministry on certain priorities for taking action. The data, not the classification, can be used for advising on environmental quality standards either for EQS settings of companies or water boards who need to issue permits. They sometimes have the problem of needing to set standards for companies producing medicine. The data is a good place to get an indication of how to proceed.

- Would your organization favour such a classification system? Why / why not?

  Yes

- Which organizations in your country would be pro / against such a system? Why / why not?

  Those working on water quality will support this. I even think that the organization that is there to provide info to consumers is interested in this issue, because it is about information. If people are against it it's usually in the field of public health, because they have other problems to deal with. Industry is not really against it as such, but the question remains do we really have a problem, where is the urgency for action, do we need to do all this effort. Will there be discriminative power and will there be alternatives to choose from. Let's assume there is urgency, will you be able to use the data, I guess you don't know until you have tried it. People can be reluctant to use classification. I think those who are already convinced that attention should be paid to medicines in the environment would like classifications in general because they do not like to deal with tons of chemicals in one boat; they wish to focus their efforts on most important chemicals. Those priorities will not be set solely by a classification system itself, they will need other information.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  Quality data is of course crucial, if people do not trust you, you have already lost the battle. You need transparence, high quality data, you need to be clear on what quality means; where is the data from, who assessed it. If you talk about data, which are crucial, there are plenty data in public literature, not just in industry, there is a big controversy about using public literature. Industry is saying it is not straightforward to use this source at the same level as GLP-Data, because they need to comply with high standards and this literature does not comply with standards. I think there is a need for more guidance how the different sources of information can be used and this is an issue that should be solved in a transparent manner. If not you may get stuck only using industry literature and having no way to explain to the public that there are more data and you don't know how to use it.

- Which categories of PPs should it cover?

All of them should be included, because if you don't include them all then you have already classified them somewhat.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Those who are being emitted the most, but ok it's also about potency, and we also know that certain drugs are really persistent and are used quite a lot and will always be there. Antibiotics from an environmental perspective are really not important, cancer drugs are equally unimportant, but maybe from a drinking water perspective there are of concern, it's difficult to balance that.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Both

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

x. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

y. What changes would you like to see in the system?

z. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

I would like to be able to look at the data, but be able to access more than that and post comments (Wikipedia peer review concept). It takes a lot of organization but will help build trust. Now on how to use data, you talked about internet based. You would need a search function that works as well as google. Sometimes a search function is not really working, you can only enter the chemical name and it will find it, but if you misspell nothing happens. We need flexibility in searching for information, it's expensive but very important.

I do not see an issue in the fact that most of the data would be from the industry. For registration purposes the company needs original research; they cannot just refer to databases or assessments made elsewhere. So it is clear that the endpoints of the research do not have economic value. Even if they will be made publicly available, they cannot be used by another company. We have seen companies that would hand in an ERA using values from other sources (endpoints from other sources). But that should not be possible, that is very important. We need a system where those who own the data can rely on review done by qualified people and that ideally goes into a system of peer review. Once the endpoints are out they should be in a wiki kind of environment. It still happens that we discover mistakes.

The industry should be on board at a high level, but also to make participation more obligatory government has to be involved. It should be organized at a pretty high level of authority.

There should be different levels of aggregation of information, not necessarily arranged in different screens, or you circumvent all the aggregate level data by going directly to the database to find what you need. Also some professionals would like to have data per compound, so selection should be made easy. Policy makers care not for the hazard profile of a chemical but rather want to know if things have changed as a result of their policy.

(considering man power to build the system) I would think that you need 80 hours to make a small monograph per compound. Then you still need more people looking at it. You can add another 20-100 hours per compound. Quite a bit of work, and very expensive.

8. What is your perception of the risk posed by PPs in the environment?

Actual risk is rather low. The risks associated to other chemicals has decreased over the last 30 years, which means that constant background of chemical pollution is becoming more and more important. I think it is good to understand how a situation is, how much ecological stress these residues cause, in the end that may be the difference between a healthy water body and reaching your targets or not.

a. Is the media attention justified?

I think it is justified, media attention resurges cyclically, attention is good. It helps in the broader perspective of controlling and managing chemicals in society in a better way. It may be that you pick up a project like this and in the end you say well that was much about nothing, or you will have learned a lot, so next time something emerges we are ready. That mechanism is essential.

b. Are the efforts for addressing the problem justified?

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 16

Stakeholder Group: Research organisations

Date	08.07.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Scientist in research unit focusing on the monitoring of residuals from pharmaceutical products in the different environmental compartments.
Type of organisation	National Centre for Research on Environmental Health

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

I am very interested such an idea. The knowledge gaps are numerous and need to be addressed. When you are doing a research project you need to balance what you want/can do with the resources you have. For researchers, the classification will help us focus our research on the most relevant substances: persistent, having an effect on the environment, etc.

a. Would you approve of the existence of such a system?

Yes.

b. Would you be interested in using it yourself?

Yes.

c. For which purposes would you use this system?

The advantage of the system would be to offer a database of information. I would use the system in the first phase of my projects, but also at the end, to compare my measured concentrations with the ones that are associated with a certain risk. But to do this I am currently always lacking information.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

One must evaluate the risks to see if the measured concentrations are dangerous or not. This is particularly important when you want to reuse wastewater (or sludge).

b. Economically?

I am not sure what the economic impact on the pharmaceutical industry would be. If you have a homogeneous and trustworthy system you could potentially lower your costs for authorization. I see a big impact on the scientific community, also on the environment in link with science and the possibility of changing behaviours. It is not so clear to me what the economic impact would be.

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

See b. In my country there were a lot of campaigns on the use of antibiotics, because people self medicated. It is very important that the doctor prescribes responsibly and that the patient abides by the doctor's

recommendations. Information is important for people to manage pharmaceuticals responsibly (consumption and disposal).

3. What are your (or your organisation's) needs for information on PPs in the environment?

I need ecotoxicological data on chronic effects, long term effects and most of all behavior and effects in soils. I need information to model the outcome of different scenarios. Most importantly, standardized ecotoxicity data. Perhaps also methods for analysis to characterize and quantify different environmental matrices. If it were something more simple, like a system that just classifies pharmaceuticals and presents typical information (which is provided for the authorization process): that would also be very useful for me and save me a lot of work.

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Excretion data: *yes.*

Routes of administration: *yes*

Side effects: *no.*

Pharmacodynamic entries: *yes.*

Pharmacokinetic entries: *yes, but not as much.*

Mammalian toxicology: *no.*

Sales data: *yes. First on the list!!*

Behavior in drinking water and wastewater treatment plants: *yes, in second position.*

Water quality data for European rivers: *yes.*

Management of pharmaceutical waste: *yes.*

In addition to surface waters, soil measurements and groundwater measurements should be performed.

- at which level of detail / (level of aggregation?)

Exact results would be important for me. In every step of your research you will need detailed information, produced in a homogenous way, from quality studies, and validated methods.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

At my level I need the raw data.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

I would base my studies on the system. Not only for prioritizing active substances but also throughout the study. For example, the physico-chemical properties are important when it comes to the sampling procedures, to identify and quantify the substances. I would use it throughout the whole process and at the end I would be able to assess if my measured concentrations represent a risk or not.

- Would your organization favour such a classification system? Why / why not?

  Yes

- Which organizations in your country would be pro / against such a system? Why / why not?

  You will need a lot of cooperation for your project; information sharing, review, etc. Politically some organizations might be reluctant to share their data, depending on the ministry you contact. I do not think you will encounter anyone that tells you they would not use the data however. The ministry of health and public policy: they would use this information.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.
- Which categories of PPs should it cover?
- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?
- Should both prescribed and OTC (over the counter) drugs be covered?

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

aa. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

bb. What changes would you like to see in the system?

cc. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

I can't really say, I have a hard time evaluating because it depends on why you want to use it. The system should be very intuitive. You will need a lot of people to manage the system, it will be a lot of work.

We must find the way to involve industry, they have the information

The different levels of information:

- *the public should have only restricted access. People do not know how to handle this information and you do not want to raise fear.*
- *industry and research should have a similar access*
- *level for groups which perform risk assessments with complete access.*

I think that the people who will use the system can work very well in English. I would facilitate certain things if it were translated, it would raise the level of users for example in my country.

8. What is your perception of the risk posed by PPs in the environment?

Yesterday, I was watching the news and a doctor was saying that pharmaceuticals were detected in drinking water, but at concentrations that presented no threat to human health. But then if I think of all of the pharmaceuticals we consume I begin to panic. In my country, the age at which the female population gets their first menstruation is getting younger and younger and this is due to them being exposed to endocrine disruptors, not just other types of organic contaminants, but pharmaceuticals and hormones we use as pharmaceuticals and personal care products.

a. Is the media attention justified?

Personally, the media scares me, there is no journalist in my country who has received proper training to be able to communicate this type of information, they only scare people.

b. Are the efforts for addressing the problem justified?

I think it is justified, I was at a meeting on contaminants and priority substances, and obviously pharmaceuticals are not included, but there are some which should make this list.

Additional comments: *I think that the focus of your project is very well chosen, however pharmaceuticals for veterinary use are also important active substances (a lot of which are the same ones as used for humans, with changes to the routes of administration and quantities). In my country, pharmaceuticals for veterinary uses are just as important as those for human use.*

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 17

Stakeholder Group: Research organisations*

*The questionnaire was filled in directly by stakeholder. No interview was held.

Date	30.06.2011
Name of Interviewer	
Type of Interviewee	Scientist.
Type of organisation	Pharmacy Faculty, University of a European Member State.

Questions:

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

b. Would you be interested in using it yourself?

c. For which purposes would you use this system?

The EU-wide environmental risk and hazard classification system for pharmaceuticals will be very important to assess the pharmaceuticals. However, such a numerical system, as has been performed by SE seems to be too simplistic and could not be used for a risk assessment exercise.

Please see the comments below mentioned.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

b. Economically?

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

Please see the comments below mentioned.

3. What are your (or your organisation's) needs for information on PPs in the environment?

Data from environmental fate and chronical effects of Active Pharmaceutical Ingredients, which will form the basis for the hazard classification.

4. Getting into more detail…

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

A scientific report should be performed for each pharmaceutical group (concerning the similar mode of action), i.e., similar to the approach has been done for veterinary residues.

Please see the comments below mentioned.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

We do not support a numerical classification. Each numerical classification should be integrated in a scientific assessment report in which should be integrate not only the ecotoxicological parameters of the active ingredient but also the its pharmaceutical quality and pharmacological properties.

Please see the comments below mentioned.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

a. origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

b. Which categories of PPs should it cover?

c. Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

d. Should both prescribed and OTC (over the counter) drugs be covered?

Please see the comments below mentioned.

The most used medicinal products, for instance for the cardiovascular and central nervous system. The both prescribed and OTC drugs should be covered. We would like to highlight that some medicinal products for central nervous system are OTCs.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

a. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

b. What changes would you like to see in the system?

c. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

Please see the comments below mentioned.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

From our research work it is evident that a wide spectrum of pharmaceuticals therapeutic classes can occur in the environment. However an important issue is to know about the subtle effects / impact of APIs in the environment.

Please see the comments below mentioned.

9. Do you have any other comments? (If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)

Comments:

For a better usage of environmental classification of pharmaceuticals, we do not agree with a numerical classification similar to Swedish classification of 2011 which has already been subject to some criticism. So we recommend:

The approach for a more accurate environmental classification of APIs should be done integrated in a risk assessment report. It is particularly important to keep in mind that a classification system must have a scientific basis not just in environmental occurrence and exposure, but also in pharmacological / toxicological measurable effects, having significant outcomes from medicinal product (for instance: neurobehavioral, immunological, endocrine homeostasis alterations)

This should include the following information for each API:

1. *Pharmaceutical properties, pharmacodynamic (mode of action), pharmacokinetic and toxicology*
2. *Fate and effects in environment.*
3. *Risk assessment*
4. *Finally, based on risk assessment results, the classification can be done. The classification should be supported by a risk assessment results*

Based in our professional experience in particular, in this area, we note that the stakeholders need to have access to more detailed information which could be consulted in the above mentioned assessment reports for each API.

There is a lot of work that need to be done in Europe and research should be made in a comparable way in order to establish European standards.

So, we are interested to continue these studies necessary to establish the basis for EU regulation.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 18

Stakeholder Group: Research organisations*

*This interviewee belongs to a research organisation that is financed by the water and wastewater utilities of his country.

Date	18/07/2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Scientist. Main research topic is fate of chemicals (including pharmaceuticals) in the environment.
Type of organisation	Research organisation that is (partly) funded and owned by the water companies of his Member State.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

What I know is that there is no real system, or no standard system, for pharmaceuticals and that is an important issue. From a drinking water (DW) company perspective: They continuously have questions on what are target values, specially re. human health, how to classify the risk of these chemicals, since there are no target values for these chemicals. Although for instance GWRC (Global Water Research Coalition) said there is no real human health risk from pharmaceuticals, they need these values. For them it's very important to have a classification and target values.

a. Would you approve of the existence of such a system?

b. Would you be interested in using it yourself?

c. For which purposes would you use this system?

2. What would the impact of such a web-based classification system be?

a. Environmentally?

b. Economically?

The economic impact would be for the pharmaceutical companies. From the drinking water company perspective one question is: is it a health risk for humans? The answer is no, at least in Europe. Some companies say ok that is fine, but public opinion brings in another element that might require the company to go beyond requirements in trying to eliminate these compounds. Perhaps as information becomes available, incentive would be provided through shift in public opinion for drinking water companies to implement better treatment systems. The drinking water companies of my country are very proud that people do not drink bottled water here. There is no financial push, it is mostly pride based.

c. Medically?

Looking at the Swedish situation, I know that doctors sometimes make different decisions than they usually would because they have access to this data. I guess doctors, hospitals, pharmacists can have a huge impact on the use of pharmaceuticals, and access to this data can trigger it.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

I do not think that the public can have such an impact. Considering doctors I would say yes, consuming consumers not so much

3. What are your (or your organisation's) needs for information on PPs in the environment?

Drinking water companies use for pesticides, to take an example, a limit of 0.1 microgramme/l. Information that would provide such quick and easy guidelines would be most appropriate and very useful for drinking water companies. For scientists, more science is interesting, we would want something that goes beyond general knowledge and that is precise for each compound.

4. Getting into more detail…

It is difficult in Europe to find consumption data on pharmaceuticals, every country has its data organized in a different fashion. Finding recent data is important to figure out the load that is entering the environment. So one requirement: consumption data. A second one: excretion. This information is usually published in pharmacist handbooks but questionable. Next question is how much is going through the wastewater treatment plant, so we need a factor for that. Also extra information on metabolites and transformation products. I also usually am missing information on issues like more hydrophobic pharmaceuticals which are often acetylated (to make them more soluble in water and excreted), in the wwtp bacteria can eat off this group again and you transfer it back to the parent compound and looking at the literature there is little known about it. From a pharmacological perspective there must be some knowledge, so connecting both would be interesting. Speaking for the water companies, especially on human healt,h they continuously have questions on target values to classify risk of chemicals. Although the GWRC (global water research coalition) said that there is no significant human health risk associated to pharmaceuticals, they need these values.

- precisely which information (which data) would you require?

Physico chemical entries: *yes, very important.*

Ecotoxicological entries*: yes, very important.*

Stability and biodegradation: *yes.*

Mammalian toxicology: *yes.*

Side effects: *yes*

Excretion data: *yes.*

Routes of administration: *yes*

Sales data: *yes. It is difficult to find consumption data. For international waters you need to gain info from numerous countries, this is especially strenuous.*

The producers should state how much of a particular active ingredient they produce and how it's spread in the community. I think they have some issues with that, because it's a competitive context. But there is also another issue; we often focus on pharmaceuticals that are commonly used while we have very little information concerning new pharmaceuticals that have been recently developed. We have no data on their occurrence and consumption. If a pharmaceutical is produced at a high rate, there should be a mention of it in such a system.

Restrospective and recent sales are both are important. Recent: if you are looking at the sales of the last month, these substances are probably in the river, its important to know seasonal variations. It is interesting to know old sales info for river bank infiltration, sales for 80s and 90s is relevant in these cases to get info on what kind of water you are extracting.

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes, very important.*

Management of pharmaceutical waste: *yes, very important.*

Also extra information on metabolites and transformation products.

- at which level of detail / (level of aggregation?)

As a scientist I like to look at the raw data, not averaged out values, especially because there can be some difference in time.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

Maybe if you have a leveled approach, aggregated data and then you click to access data behind it (accessing the excel sheet behind the data). The drinking companies want graphs and clear easy ways to identify if there is an issue or not.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

As I do a lot of fate studies on chemicals, I would probably use it a lot to look up consumption data and degradation. Those are things that I currently turn to literature to find. It would be interesting to have it all organized in one place. I could find information quicker, and make decisions faster, it could make my decision making process more efficient, faster.

- Would your organization favour such a classification system? Why / why not?

Absolutely, just to have more easily available data, we are always looking at what is in water, we are interested to know where it's coming from, who is making it, etc.

- Which organizations in your country would be pro / against such a system? Why / why not?

National organisations for public health and for the environment would be very happy to use it, drinking water companies will be happy with it, all kinds of scientists in environmental science would use it. Pharmaceuticals companies would not be happy because they would have to prepare the data. If my country's government has to pay for it, they will not enjoy that, especially with the current administration.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

The origin depends on what kind of information you want, part of it should come from the pharmaceutical companies themselves, but you also need journal information. The quality is more or less guarded by the peer review. I do not know how you can control the quality, maybe a label, peer reviewed, not peer reviewed. External revision seems more or less impossible, because then you need all the experts looking at all the data. You could put into place something like Wikipedia: if someone finds something completely different then what he sees in the database, he can contact the person responsible for the database.

In the end, as a scientist, you need to make the decision [on the quality of the data for your work] yourself.

- Which categories of PPs should it cover?

For human health issues I would say that all pharmaceuticals that have some sort of effect on the neural system are quite important, because you might expect some effects in the environment. Some pharmaceuticals that are widely used do not present any human health issues although they occur a lot in the environment.

I think everything should be covered, even drugs of abuse, which of course there is no prediction data on. Practically speaking they are also pharmaceuticals. I am in favor of a system that considers all the compounds.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

Antibiotics would be one priority. Basis for priority should be consumption data.

One specific drug that is highly used, at least in my country, is metformin (antidiabetic). It is not really looked at, it is difficult to analyze chemically (not with standard methods) so it is not in current monitoring campaigns. So it would be worth it to look at consumption data and identify drugs that are highly consumed and then look at excretion data and they make a list of the chemicals that you are expecting to find in the water, instead looking at what someone else found and always measure the same pharmaceuticals. There are probably other pharmaceuticals that are interesting but we don't look at them.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Yes, because a prescribed drug is an OTC drug in another country. The only difference might be that with OTC is not easy to affect consumption, because you need to address the public and not the doctor.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

dd. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

ee. What changes would you like to see in the system?

ff. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

It should be possible to search according to individual chemicals: you have one chemical and all the information you can find on it listed in a table. It should also be possible to have the cross connection between similar pharmaceuticals: horizontal connections to other chemicals and metabolites and vertical ways of looking at the data for one pharmaceutical.

Different levels of complexity, and having access to all the knowledge that is available would be interesting. I think that having different levels of information is quite important, you do not want to bother everybody with 5 pages of information for one chemical.

Data should be available to everyone, I do not see why scientists should have more rights than a non-scientists.

Perhaps, it would be interesting for doctors to offer some sort of value, something comparable to an energy label on a light bulb, that grades the pharmaceutical on how environmentally friendly it is. It would be an aggregate of other values that need to be discussed.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

Considering drinking water, I do not really see there is a risk. I recently did a small desktop study on antibiotics and indirect risks of bacteria and I think, compared to water, the food chain contains far higher loads of these chemicals. As for the environment, especially with these huge mixtures and all the information we do not know: there can be some issues, especially for pharmaceuticals like antibiotics, you can build resistance. There can be

subtle effects that have large impacts, but we cannot predict them. Just adding biologically active chemicals in the system is always risky.

Putting them in perspective with pesticides would be interesting.

Additional comments: *It is difficult to put in perspective a risk associated to a chemical, it would be interesting to do this: compare the risks of pharmaceuticals to risks associated to other types of chemicals. In this way you can get a scale. For a decision-maker, it can be hard to understand the risk: this could help.*

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 19

Stakeholder Group: Medicinal Authorities

Date	28.06.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Scientific Administrator, Non-clinical
Type of organisation	Medicines Agency

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

Without seeing the tool it is difficult to answer this question, but what is important is the quality of the data which would support the system. The data must be reliable.

b. Would you be interested in using it yourself?

It would be easier for me to comment on the system if I knew your exact objectives for it.

c. For which purposes would you use this system?

If there is a requirement or recommendation for a system. It is the scientific committee that would look at how it should work and be used; in this sense it is hard for me to speak for all the members of the committee.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

It could help to protect the environment, by helping us to understand better the eco-toxicity of some substances.

b. Economically?

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

Economically, medically and regarding the behavior of prescribers: it is not what we focus on, so I cannot really answer these aspects.

3. What are your (or your organisation's) needs for information on PPs in the environment?

We would want all information that can help us in the evaluation of the risk, based on eco-toxicity studies which are required in our legislation.

4. Getting into more detail…

- precisely which information (which data) would you require?

Information required for the Environmental Risk Assessments.

Excretion data: *yes, this is by principle the basis of environmental exposure following the use of medicines. As the ERA is a stepwise approach only parent compound is considered for the ERA evaluation by default. Metabolites are usually not studied unless concern.*

In addition:

Behavior in drinking water and wastewater treatment plants, management of pharmaceutical waste*. Recommendations on waste would be based on the outcome of risk assessment. If a risk is identified precautions to minimize exposure would be required (this was done in the case of an authorised estrogen patch).*

Information on metabolites: *Not routinely required unless concern.*

Sales data: *No. As sales figures cannot be assessed they are not requested,In the stepwise approach of the guideline the first step is a default exposure which can be refined if justified by independent literature data e.g. epidemiological studies, prevalence of a disease..*

- at which level of detail / (level of aggregation?)

Full reports are required to allow a proper evaluation of the results.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

The information should be as clear as possible, good structure, graph, etc. We need both good data and interpretation, because an external reviewer should be able to understand how the conclusion was reached in the report. Following evaluation, the reviewer may or may not agree.on the interpretation.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

  It will not influence the decision-making process. The data on which the classification is based shod be compared with the data previously evaluated to ensure consistency.

- Would your organization favour such a classification system? Why / why not?

  If the classification is consistent with the outcome of the evaluation it might strengthen it. How to use the system will be up to the Scientific Committee to decide.

- Which organizations in your country would be pro / against such a system? Why / why not?

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  The regulatory system is aimed at requiring data of the highest scientific level and reliable.

  Any information missing in our system, should be first evaluated before being approved by the Scientific Committee

- Which categories of PPs should it cover?

  All products should be treated the same way so you have a way to compare. So not only include the ''good products'' leaving out the ''bad ones'', but covering everything on the market.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?
- Should both prescribed and OTC (over the counter) drugs be covered?

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

gg. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

hh. What changes would you like to see in the system?

ii. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

Offering different levels of information is good. Information should be quickly understandable for the public, while more specialized groups will be interested in more details: details of studies, results. The highest level depends on how you want to use the system. Most important: reliable data. The final objective of the classification system should be to provide clear information for everyone.

The data should be checked, and if there is need for additional tests, these should be conducted where need be. The legislation contains enough guidance for pharmaceutical tests. We publish summaries of our assessments on our website including details of studies performed for the environment risk assessment. This is in line with the policy of transparency.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

It is a topic that is increasingly of interest, it's important to identify environmental risks as pollution will tend to increase with our population and the increase use of medicine, so it's necessary to take measures to minimize these risks

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 20

Stakeholder Group: Medicines Authorities

Date	20.07.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Risk assessor for the authorisation of human medicinal products.
Type of organisation	Medicines Agency

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?
   a. Would you approve of the existence of such a system?
   b. Would you be interested in using it yourself?
   c. For which purposes would you use this system?

   It is important to assess pharmaceuticals. We would want this to be a numerical system, based on risk assessment where we have access to the data. So not only the end numbers, but the scientific assessment reports. We need transparency.

2. What would the impact of such a web-based classification system be?
   a. Environmentally?

   For my country, the impact would be important on the broader public. The scientists I do not know really. The broader public will be interested. In my country we have a very good system for the collection of unwanted pharmaceuticals.

   b. Economically?
   c. Medically?
   d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

   The consumers definitely, the doctors I do not know. I do not think they look at environmental impacts, they only seek to treat the patient, but changing user's behavior is important and achieving that would be great.

3. What are your (or your organisation's) needs for information on PPs in the environment?

   Mode of action, quality, chemical properties, pharmacodynamic properties, pharmacokinetic, ecotoxicologic results, risk assessment results

4. Getting into more detail…

   Physico chemical entries: *yes.*

   Ecotoxicological entries*: yes.*

   Stability and biodegradation: *yes.*

   Pharmacodynamic entries: *yes.*

Pharmacokinetic entries: *yes*

Excretion data: *yes.*

Routes of administration: *yes.*

Side effects: *possibly.*

Mammalian toxicology: *yes.*

Sales data: *(yes). Every agency has sales figures, and that is public information in my country. However, we do not have numbers for the OTCs: OTCs and other substances can be problematic however, but every year we have statistical studies about this.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes, that will be interesting for the ecopharmacovigilancy.*

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

5. How would you use this classification system in your work?

I can only use the numbers, the raw data, and if I have an assessment report.

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  Quality data is the crucial part. The problem is also that we cannot take information provided by the industry, because they have a patent. Perhaps they can help.

- Which categories of PPs should it cover?

  OTCs, antimicrobial are important, and anti cancer drugs, because they are really toxic. The most prescribed drugs, the most used, should be included. These are similar in most countries I think.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  I tried to make a prioritization here (see above). The first point is if the drug is widely used, we should first try to see if they have been found in the environment.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Yes, and they should be treated the same way.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

jj. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

kk. What changes would you like to see in the system?

ll. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

The Swedish system I know about, I tried to retrieve info from it, which is difficult. But in any case, I do not like the system, I need more background information.

I need more information, for example I looked for papers and they do not have the chronic ecotoxicology, they are based on acute toxicology, there are a lot of gaps on acute toxicology and yet they produce results... There are a lot of scientific gaps there. For example for the risk hazard quotient they take the classification from acute studies and not from chronic studies. Scientific gaps is a major problem. I think it is difficult to deal with the information provided by the fass system. I never take it. The classification doesn't hold true.

8. What is your perception of the risk posed by PPs in the environment?

At first I didn't think we would find any pharmaceutical products in the environment, but I have been proven wrong.

a. Is the media attention justified?

The media attention is sporadic, now we do not hear about these issues anymore as there are more pressing needs in my country at the moment.

b. Are the efforts for addressing the problem justified?

Yes.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 21

Stakeholder Group: Medicines authorities

Date	26.08.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Preclinical assessor at a national medicines board. In charge of evaluating Environmental Risk Assessments.
Type of organisation	National medicines authority.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

I suppose because it does not affect the license of the drug it will never be an absolute requirement. From a personal point of view I think it does need to be there. Probably companies are yearning to become more environmentally friendly, in terms of maintaining their company image. But because it does not affect their license then in reality there is no necessity for them to comply. It is probably nice to have, but not necessary.

a. Would you approve of the existence of such a system?

Yes.

b. Would you be interested in using it yourself?

Again I suppose in terms of getting a knowledge of what is there and insisting on the inclusion of that generic wording in to the product label it might be useful (clear messages on the package that there is risk for the environment if item is disposed of in the wrong way). But again because it does not impinge on the license I suppose it is just a nice to know, not need to know.

c. For which purposes would you use this system?

See b.

2. What would the impact of such a web-based classification system be?

I do not think it would have much impact.

a. Environmentally?

b. Economically?

I suppose economically it could help, I assume it would be an open based system so it could help the industry seeing classes of drugs and pharmaceuticals even before they go to make an application to see if there is a need for them to do anything before submitting their dossier. Rather than going and doing a full on assessment they could refer to it. But I am not sure how that would be considered by regulatory authorities. It could have a negative impact I suppose it would depend on is there other products out there that can be more environmentally friendly. But again this could help companies to reduce their impact.

It would help industry, if they have a new compound similar to one in the system it will give them information straight away. It could help them justify the lack of need to do an Environmental Risk Assessment. To give them an idea of what potentially is or is not a risk.

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

I would like to think so but in reality I think doctors will go for the best drug and what costs less. You are looking at members states in terms of what is covered, that will all play into it. Whether a pharmaceutical is environmentally friendly or not would be down the list of practicalities that a practitioner would consider.

Some doctors might use this system, it will depend on if there are campaigns to raise awareness. I would think to a degree they will think about it but I do not think it will influence their prescribing methods. If there were to use a system like this you will need to do a lot of campaigning to get them aware of it.

I do think people are environmentally friendly. They are looking for environmentally friendly products. In terms of educating the general population on safe disposal, it might help. Whether or not they specifically use the database I am not sure.

3. What are your (or your organisation's) needs for information on PPs in the environment?

My organization does not have specific information needs, but considering the question from a more abstract perspective: effects on microorganisms, sediment effects. In our guideline there are various areas that need to be looked at.

4. Getting into more detail…

See 3.

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

I think it could be used as a support because it will not affect the license but it might affect the labeling. It might be useful in that process. We have an environmental protection agency, they do not look at, it we had a GMO product they would look at that in terms of notification. They might find it useful. I can't think of organizations that would be against it in the government sector. I do not see why anyone else would have a problem with it, because it will not affect licensing.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

I suppose you would look at peer reviewed journals, I do not suppose the pharmaceutical industry is going to be giving you this information. Anything that has been validated.

However, if industry data is available, you have to trust industry. In all our assessments we use their data. I think there is onus for the industry to be upfront and we would take them at face value and trust them. I think you would have to have the same approach.

- Which categories of PPs should it cover?
- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

I would think probably everything that requires a phase 2 [in the ERA], so if you can't find it you would assume that there is no risk attached. But then again that impinges on the exposure level.

- Should both prescribed and OTC (over the counter) drugs be covered?

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

mm. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

nn. What changes would you like to see in the system?

oo. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

I would just like to know if a pharmaceutical is a risk hazard or not, cause then we would put in back to the company. We would need a very simple risk or no risk system.

Regarding the different levels of information: I suppose it's who you are pitching it to, we would not have the expertise or the time to go into too many details. Perhaps it can be extended for people who need to know what is exactly this risk.

Regarding the general public: I think they would be interested, but I do not know to what extent they would understand.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

I think people are not aware of their actions in disposing of their unwanted medicines. I am not aware in terms of the environmental impact that it is causing. What kind of study has been carried out in my country on water or whatever? I am sure they are there but I am not aware of them. I am more aware of regulation. I would suspect that the general population would not be aware at all. I never see any media attention paid to this issue in my country. I suppose if I read the studies that talk about the risks being important then I would say yes we should discuss this more, but until then I would not see the need for more media attention.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 22

Stakeholder Group: Medical association

Date	30.08.2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Dr., President of medical association
Type of organisation	Medical association of a European MS of doctors concerned for the environment.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

b. Would you be interested in using it yourself?

c. For which purposes would you use this system?

I haven't worked with patients since 1997, but Fass has always been there and you look at in when you need. But the computerized health record (patient record) system is connected to Fass, which means that as a general practitioner you do not have to go into Fass so often. You have medicines that you use often and under certain circumstances you need the Fass.

It is very important that things be connected, the WISE list and the patient record system. And the WISE list must be connected to the environmental information.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

I think they managed to reduce the prescription of certain antibiotics [with the use of the Swedish classification system]. These antibiotics should have been phased out a long time ago and I do not understand why we are still using them. There is so much discussion about the resistance problems. Resistance concerning both human health and the environment. Doctors think of people not the environment. It takes a long time before you see the effect on the environment. I think there were residues in the water that were lowered after they repeated their investigation, so there might have been some impact but I think it is too early to see.

b. Economically?

The economic impact here is close to none. There is no change because they made the WISE list: If there is a big difference in cost then the economy comes first, before the environment, so it has not had much effect on the economic situation.

c. Medically?

I do not know if the patterns of prescription have changed. Total amount of medicine should be reduced, we should use more of non pharmacologic methods, and those should be paid by the county. We consume more and more pharmaceuticals. Drugs are easily available in the shops today and it encourages people to consume more. It is an attitude, you cure yourself by taking pills, not by other ways.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

No I do not think it can impact the general public on safe disposal of pharmaceuticals. They have no idea, or very few do, about the environment. They are supposed to go to the pharmacies to drop off all unwanted drugs. Today, most people do so.

3. What are your (or your organisation's) needs for information on PPs in the environment?

4. Getting into more detail…

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

No information provided re questions 3 and 4.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

We are particularly proud of this system, the ones who know about it are proud. The industry is also positive, which is very good, they look forward and see that they will gain something from this. Some organizations might not be interested but they are not against it.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

I suppose there should be additional information from other sources (than industry). But you have to consider what is practically possible. The industry has this information because they are supposed to give it to the EU. You have to start there and maybe it can be developed later if you have a lot of resources. Then you have to control, see if other researchers that are not attached to the industry have other results, but this takes time and resources. But who will do this?

- Which categories of PPs should it cover?
- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

Yes cancer medicines are very important because they are very active, but they are not prescribed a lot. The amount of drugs is important.

Antibiotics are very important of course, cancer drugs because they are very active. But they are distributed only in hospitals and they have their own sewage system.

Lipid lowerers and cardio vascular medicines are two very big groups, as well as pain killers..

- Should both prescribed and OTC (over the counter) drugs be covered?

Both. No difference should be made.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

pp. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

qq. What changes would you like to see in the system?

rr. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

I think you also have to work with lists of environmental classification (leaflets). You have to do something like that because it is not always possible to go on the website fass.se. I don't know if other countries do this. I don't know what the possibilities are in other countries.

Doctors have to be much more involved, it is difficult to reach doctors.

Shortcomings: Before we joined EU, Fass was controlled by an authority. That meant that they decided the subtitles, what kind of information should be where etc etc. Today, the companies decide what to write or not to write. It happens that one medicines say "yes, environmental effects" because they did some studies. The same generic, but from another company, says "no environmental effects" because they did not do that kind of studies.

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

***General comments:** It is very important to include medical organizations. Do not forget that family practitioners prescribe the big amounts of medicines, not the hospital, only 10% or something comes from the hospital and the rest is from primary health care. It is important to cooperate with the family practitioners. To make it easy to use you have to cooperate with those who are supposed to use it. The web masters must cooperate with the people who are going to use it, they need to know how doctors will think. You have to use people who are used to building health records.*

Doctors need simple things, because they have so many other complicated things to think about.

You should do it based on groups of chemical substances, the doctor will know what they are meant for. The system should tell which penicillin, which beta-blocker, etc. is the best one from an environmental point of view. Company name, generic name, group. There should be many ways of searching the sytem.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

If you look at the media, you see an imbalance. The pharmaceutical companies get a lot of marketing space to promote their new products. They have press releases from an early stage to promote their new products. We also do not talk about the fact that medicines are toxic, for us and the environment, and that they might come back to us.

But the use of antibiotics in my country has gone down. We have had campaigns directed towards different groups, the doctors, the pharmacies, and the public. When the message reaches people, people are educated and do not demand antibiotics so much, they will try other methods. Often that can be done, but not always. These campaigns were financed by the state. The government now thinks that everybody is responsible for their own health, and can make choices individually. However, they have realized that this can be a big problem. The doctors are quite conscious about it, they took the initiative a long time ago to work using less antibiotics. Cultures differ, in my country we are used to state campaigns, perhaps this is not the case in other countries.

b. Are the efforts for addressing the problem justified?

Yes.

Additional comments: *Pharmaceutical companies that look into the future see what the future challenges are. Sooner or later this question will be there, it is better to take the initiative and make something good of it now.*

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PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 23

Stakeholder Group: Medical association

Date	17.05.2011
Name of Interviewer	Konrad Götz, ISOE
Type of Interviewee	Doctor. Board member of a medical association.
Type of organisation	Medical association of a European MS of doctors concerned for the environment.

Questions:

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

b. Would you be interested in using it yourself?

There is definitely a need for a classification system and he would be willing to use it himself. However as a practicing physician, he needs the system to be quickly accessible during consultations. It needs to have a clear structure and be precise (see question 6).

2. What would the impact of such a web-based classification system be?

a. Environmentally?

b. Economically?

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

A classification system would benefit the environment, especially concerning additive and cumulative effects, which are still widely unknown.

There is a share of around 4-9% of the population, which shows increased sensitivity towards even the smallest doses of any kind of pollutants in the environment. Limit values do not apply to them and their medical conditions are often interpreted as psychosomatic or psychiatric issues.

Economically the system would benefit health care systems because it would reduce chronicle health problems. Our health care systems treat acute health problems at high costs which cannot be covered anymore unless primary prevention is extended. A classification system is part of such a primary prevention approach which aims at reducing the general exposure to any kind of environmental pollution. Primary prevention is crucial to keep health care costs controllable.

3. What are your (or your organisation's) needs for information on PPs in the environment?

4. Getting into more detail…

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

It would support choosing between alternative compounds the one which is environmentally most favorable i.e. has the best aggregated score. The level with more detailed data might be used for further information, if required.

- Would your organization favour such a classification system? Why / why not?
- Which organizations in your country would be pro / against such a system? Why / why not?

The pharmaceutical industry would probably oppose the system because they are against any kind of regimentation.

Pharmacists would be required to provide more information, when selling the same products. Their professional associations will probably support the system but for the individual pharmacists the system means more effort. However with over-the-counter medication the system also results in a stronger consulting role for pharmacists.

Physicians might be more of an obstacle than pharmacists, but it depends on the training they receive. Still there are differences. Surgeons, psychiatrists and dentists will probably be more reluctant than internists. Especially dentists often prescribe antibiotics without much consideration and more according to what they have in stock than what is appropriate.

Professional associations of physicians will probably be supportive; especially the state chambers of physicians because due their responsibility for professional trainings it would provide them with a more important role. Still it might be necessary to present them a first concept to get them on board.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

a. origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

The system should be in the respective national language, so that it can be easily used and understood and as a requirement for legal certainty. At the same time it should be in English as well to guarantee comparability.

The data can be provided by the pharmaceutical industry but according to predefined homogenous standards and under revision of an independent scientific institution on national or European level.

It should be available on the computer any time. The system needs to be updated regularly but not via online updates as computers with patient information are usually not connected to the internet for data protection reasons.

For practitioners the systems needs to be quickly and easily accessible during consultations. It needs to be clearly structured and precisely defined. He suggests a two tiered system with some kind of aggregated score (for example from 1 to 5) for quick information. This score should be based on various parameters being summed up to a single digit. On the second level, information on the various parameters should be available for further information.

Information should be presented in numbers and diagrams to be easily accessible.

It is crucial – he stresses that several times – that practitioners receive training on the system. He suggests that the training is focused on the approximately 50 compounds that the practitioner uses

regularly. Besides this training, there also needs to be some kind of control scheme to ensure compliance. Without training, incentives and control schemes the system will not have any use because practitioners are reluctant to invest any effort and time, which is already scarce anyway.

The system should be made available to the public and patients, however only the more detailed information. The aggregated score should be reserved for physicians and their assistants, who should receive some training at this level as well.

b. Which categories of PPs should it cover?

Cumulative compounds, substances which are not eliminated in disposal processes, toxic substances, endocrine substances, antibiotics and cytostatics.

c. Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

Antibiotics, cytostatics and endocrine compounds should be given priority.

d. Should both prescribed and OTC (over the counter) drugs be covered?

OTC medication should be covered but only in second place and depending on the financial means available.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

In case they are familiar with fass.se:

a. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)
b. What changes would you like to see in the system?
c. What are the shortcomings of the system?
    i. re. information
    ii. re. functioning
    iii. How could these be overcome?
    iv. Would you address the different levels of depth of information?

The language discrepancy makes it impossible to assess the system, but it requires too much clicking to get to the information. There needs to be some kind of quick information.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?
b. Are the efforts for addressing the problem justified?

9. Do you have any other comments? (If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)

The system needs to be computer-based, due to the amount of information and the need for regular updating. However for up to 5 to 10 years, it might be necessary to publish the information in hard copy as well because there is group of older physicians, who are not too confident using the computer.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 24

Stakeholder Group: Pharmacies / Pharmacy Associations

Date	15/6/2011
Name of Interviewer	Jörgen Magnér, IVL
Type of Interviewee	Director of Quality, Pharmacy Association
Type of organisation	National Pharmacy Association of a European MS.

Questions:

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

I think it would be very good. I participated in making in the classification used in Fass. There was a lot of work to include all the global companies. But we managed to obtain a good model that is now greatly appreciated in Europe. The various classifications in Europe leads to us talking past each other, it is not good. This is a great pro with a joint European system. It can be difficult to develop, at first we did not think that it would be manageable to develop the national system... but it works if you set your mind to it.

a. Would you approve of the existence of such a system?
b. Would you be interested in using it yourself?
c. For which purposes would you use this system?

a) In the pharmacy industry, absolutely. We also get questions from customers about this.

b) Yes, we have a duty of provision on all prescription drugs where we have very little leeway. But in everything we sell ourselves (our "self choice") we would like to use it as we have noticed is in demand among customers. Many customers want to make an active choice and it would be easier for them.

c) It could influence the selection of goods of the pharmacy, depending on how they choose to market themselves. We choose what products we want to sell. We are not only interested in the environmental risk of the active ingredient but also consider other perspectives, more of CSR perspective... manufacture, composition of package etc...

2. What would the impact of such a web-based classification system be?

a. Environmentally?
b. Economically?
c. Medically?
d. Regardingbehaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

If one makes such a system with good summaries, it would help. There are treatments that are quite equvivalent. Two medications that work equally (eg ß-blockers) might not have the same environmental effect. It would be good to see how they affect the environment. If they differ this may be taken into account when prescribed.

Contracts are controlled to some extent by environmental classification. Today lowest price wins and in the future, perhaps the environmental classification could affect the process.

The best treatment for the patient will always apply.

In the case of Sweden, we have high knowledge of how any unused drugs should be taken care of (left to the pharmacy). I do not think it will be affected so much for the Swedish part. Existing drug prescription may be changed. Today quite large volumes are prescribed at a time. Swedish drug preferential says you may prescribe up to 90 days usage of drugs, but practice is to prescribe at least for 90 days and this is not the intention. This means that much is not being used which gives an unnecessary environmental but also economic burden on our society.

3. What are your(or your organisation's) needs for information on PPs in the environment?

I think the classification at Fass provides a good base. What is lacking today is above all the information about products being manufactured with good manufacturing practice and from a positive environmental standpoint.

4. Getting into more detail…

1. precisely which information (which data) would you require?
2. at which level of detail / (level of aggregation?)
3. how should the information be prepared and presented (figures, graphs, level of convenience)?

a) We find the information given at fass.se to be good. We would like information on both how harmful a pharmaceutical may be, but also the environmental risks... this risk includes the exposure... which is already covered at fass.se today. However, it would be good with better compilations to be able to look at groups of pharmaceuticals. This is lacking today.

b) In the contact with patients at the pharmacy, it is important to never point out the customer/patient as an environmental villain. The patient need the treatment and should thus be able to have the best treatment. I do not think that details of ecotoxicity data ever will be discussed at the pharmacy. These data are however important and can be used in more detailed discussions with prescribers.

c) It should be made easier to present groups of pharmaceuticals in order to be able to point out differences between different pharmaceuticals (eg to compare different beta-blockers). This need to be made simple in the classification system. It is important to be able to find those pharmaceuticals that differ in classification. Most pharmaceuticals will probably pose an insignificant risk, it is important to easily be able to find those that stick out, eg with regard to PEC/PNEC-ratio.

5. How would you use this classification system in your work?

b) How would it support / influence your decision-making processes?

c) Would your organization favour such a classification system? Why / why not?

d) Which organizations in your country would be pro / against such a system? Why / why not?

To be able to answer customer questions but also for the „self choice" sortiment at the pharmacy.

a) It could be one factor affecting the sortiment sold.

b) Yes, it is always good with a common standard. The plethora of other environmental classifications present today is trublesome. A common EU-standard for pharmaceuticals would be favourable.

c) I don´t know whom that would be against such classification. The subject has matured among most stakeholders. We would also like to see that the enironmental effects caused by the production processes included in the

classification. This could maybe cause producers of generics to be against the classification, since it would cause an increased pressure on those companies if they do not manage to reach the requirements.... Governmental Agencies might be a little conservative... TLV might find it complicated to include the classification in the decision process and this is required in order to affect prescribed pharmaceuticals.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

a. Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

b. Which categories of PPs should it cover?

c. Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

d. Should both prescribed and OTC (over the counter) drugs be covered?

a) Data must be provided by the pharmaceutical companies since they are the ones that have it.

b) All eventually. In the ideal case all would be classified.

c) Maybe start with those already known to cause environmental effects. Pharmaceuticlas that may be endocrine disrupters etc.

d) It is not possible to make that sort of boundaries. Many substances are both prescribed and sold over the counter, eg paracetamol, and this can not be separated. There are groups of pharmaceuticals exempted from risk assessment according to EU and this could maybe be followed. These are also often preparations that are on the borderline between beeing pharmaceuticals and not..eg herbal preseparations and vitamins sold as supplements. Substances known to be easily degraded could maybe be exempted... however that is a classification in it self.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

c. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

d. What changes would you like to see in the system?

c. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

There is a need to make it easy to make compilations of groups of pharmaceuticals in order to evaluate them. Eg if we evaluate and make decisions on our sortiment for pain relief sold over the counter we need to be able to easily overview this group.

a) It has worked relatively well. But there are areas for which people lack education, both physicians and and pharmacists, and this is needed. But there is now a training at fass.se.

b) The possibility to make compilations on pharmaceutical groups in order to compare different pharmaceuticals used for similar or the same treatments.

c) The problem is older substances, who should be responsible for providing data... There is data available for all newer substances... but for older substances, maybe with only one original producer but many companies manufacturing generics, data is missing. If patents are lacking it may be complicated to decide whom that should provide the data. This may become a major problem in the development of a classification system at EU level. It does not seem reasonable that all companies should carry through the necessary studies, but there are no system today on how to share the costs for these. This issue needs to be solved. Older pharmaceuticals are often sold in large volumes and it is thus important that data are provided for these substances.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

a) Some of the headings seen in papers may be somewhat exaggerated. The development of analytical methods make it possible to detect concentrations almost at „homeopathic levels". The problem should of course be taken seriously but the reporting could be more balanced. We know that many of the substances are stable and they are biologically active, so they should be given some attention and followed up.

b) Yes

9. Do you have any other comments?(If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)

In order to affect prescription and usage patterns political will to include environmental aspects in the decision making process for pharmaceutical benefits is important. The existance of a sound and accepted classification system would serve as a good basis to make this happen.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 25

Stakeholder Group: Consumer NGOs

Date	28.06.2011
Name of Interviewer	Dr. Florian Keil, ISOE
Type of Interviewee	Expert on the environment / resource use
Type of organisation	Large consumer NGO of a European MS

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

a. Would you approve of the existence of such a system?

Yes, absolutely, because from a consumer perspective trace pollution in drinking water is a recurrent subject, and in the case of pharmaceutical products there is strong concern within the public.

b. Would you be interested in using it yourself?

Yes.

c. For which purposes would you use this system?

As a consumer NGO we wouldn't use it directly, but rather as an information source, so as to provide general information to consumers on the issue. In all probability consumers wouldn't use such an environmental classification themselves. I would personally use it as a database. One could also imagine using the system in the environmental counselling of our consumer NGO association. However, as said, the environmental counsellors would probably not use it directly in their work.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

Working with the assumption that price differences would not be too significant, it would be imaginable that pharmacists in future would also consider environmental aspects when providing guidance. In this way products that are more environmentally friendly would find more sales and the wished-for environmental effect would be achieved.

b. Economically?

Pharmaceutical companies will have to try to offer products that are more environmentally friendly. However, this will probably be more of an impulse for innovation than a source of economic losses.

c. Medically?

I don't see any effects in this regard, because regardless of the existence of a classification system, it must still be possible to prescribe a medicine if it is less environmentally friendly but therapeutically more adequate.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

Consumer demand for environmentally friendly medicines will hardly change – at the most for those consumers that are already environmentally conscious. This is why it is crucial that doctors and pharmacists use such a

system when prescribing and counselling consumers on their purchase – there is definitely more leverage here. Acceptance for such a system could be generated if it is included early on in the training of these professions.

3. What are your (or your organisation's) needs for information on PPs in the environment?

Primarily data regarding aquatic toxicity (standard tests) and degradation data.

4. Getting into more detail…

- precisely which information (which data) would you require?

As a consumer organisation we don't require data on the medicinal side of things (for instance pharmacokinetic or side effect data), because we don't provide such kind of counseling. Our focus is on the environment: in our counseling we would refer to the existence of an environmental classification scheme for pharmaceuticals. Sales or use data would probably not be very relevant in this counseling context.

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Pharmacodynamic entries: *no.*

Pharmacokinetic entries: *no.*

Excretion data: *no.*

Routes of administration: *no.*

Side effects: *no.*

Mammalian toxicology: *yes.*

Sales data: *no.*

Behavior in drinking water and wastewater treatment plants: *yes. Data for behaviour in wastewater treatment plants very important. Even more important, of crucial importance for my work, is data for behaviour in drinking water plants, for instance information on which new products, possibly dangerous, derive from pharmaceuticals in the ozonation process.*

Water quality data for European rivers: *yes. This information would be helpful additional information, particularly if water quality data from water providers would be included in such a database.*

Management of pharmaceutical waste: *yes. Information on correct disposal of pharmaceuticals should be taken up in such a system. It is also a task of consumer NGOs to provide information on this kind of topic.*

- at which level of detail / (level of aggregation?)

The way this issue is addressed in the Swedish system is very good for experts, because one can access the detailed data. However, in addition to the area with expert information, it is necessary to have comparatively undetailed data for doctors, pharmacists, and consumers. At this level there should be something like a 3-step system (a substance is "harmless", "neutral" or "bad" for the environment). A clear orientation which will guide action is required at this level. One should also give the location of this information some thought: if they were to be placed on the packaging consumers could be unsettled and would not buy or intake a medicine.

- how should the information be prepared and presented (figures, graphs, level of convenience)?

See above. The system should have different information levels.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

It would have no influence on my decision-making processes. None of our guidance fields would be directly affected by an environmental classification. At the most, I could use the database to help address occasional, highly specific questions posed to us by consumers.

- Would your organization favour such a classification system? Why / why not?

  Yes, as explained in the answer to 1.

- Which organizations in your country would be pro / against such a system? Why / why not?

  I could imagine that the pharmaceutical industry could, depending on the circumstances, reject such a system, if it would fear distortion of competition arising from changes to prescription practices. Doctors may also possibly reject the system, because they live well off the pharmaceutical industry and may have the apprehension that the system could affect their income in some way. Environmental associations would surely be for it. In total I would see more actors supporting it than actors against it. However, if the pharmaceutical industry opposes such a system, its implementation and adoption will definitely be hard.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  The pharmaceutical industry should provide the data; this falls within the responsibility of producers. The disclosure of data should be addressed in some form of regulation. An independent body would be desirable to revise data, but only individual cases, when there are issues, so as to keep the taxpayers' expenditures as small as possible.

  English would be fine for the detailed information, which will be read by the experts. If the system should be used by normal citizens, then it most definitely has to be available in the national languages. Otherwise it will hardly find acceptance.

- Which categories of PPs should it cover?

  Those with high volume sales. Also veterinary products, because it is in this field that the big volumes are used (e.g. antibiotics in animal husbandry).

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Medicines with similarities to POP (persistent organic pollutants) compounds, medicines containing chloride and fluoride. Possibly base-analogue cytostatics and also virostatics, that, as I believe, do not degrade too easily. The so-called "orphan drugs" can probably be ignored, because they are only sold in very small quantities. Also herbal medicines can be ignored, because in most cases they degrade easily. However, for these drugs a screening should be done, to see if there are not possibly individual substances that are problematic.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Both. It is important to include OTC because here the big quantities are sold.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

ss. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

tt. What changes would you like to see in the system?

uu. What are the shortcomings of the system?

  i. re. information

  ii. re. functioning

  iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

Fass.se is well designed from the point of view of experts. However, for some substances I miss the environmental information – why are they not available for all substances? For consumers, the decisive information should be summarized much more strongly (e.g. using pictogrammes or smileys).

The search for medicines in the system is also not practical: the alphabetic search only provides me with 10 substances per page, and I have to click my way through to find the ones after that. This isn't very practical: it would be better if they would all appear on one page and one could simply scroll down as far as one needs to.

It would also be helpful, in my opinion, if a system such as fass.se would be connected with relevant databases such as TOXNET.

The direct comparison between different compounds would be important and helpful, but possibly also complex and problematic if it were to manage all categories, i.e. also covering therapeutical aspects.

8. What is your perception of the risk posed by PPs in the environment?

My perception is that PIE is a problem for the environment, which is however not yet extremely relevant for drinking water. In the case of drinking water, other compounds are currently more of an issue (e.g. pesticides or antimicrobials in cleaning and disinfection fluids).

a. Is the media attention justified?

In principle yes, even though it is sometimes the case, particularly when reporting on drinking water issues, that journalists are looking for the scandal. A critical and factual coverage is, however, good and important, particularly because drinking water is a foodstuff, from which all of us depend.

b. Are the efforts for addressing the problem justified?

Yes, most definitely. It is good to address this problem along the lines of the precautionary principle. Efforts are made regarding all possible industrial chemicals, so it is only consequent to also address medicines.

Additional comments: *Veterinary products should definitely also be addressed, because it is in this field that the really big volumes are used!!!*

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 26

Stakeholder Group: Environmental NGOs

Date	20/09/11
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Water expert
Type of organisation	Association of environmental NGOs of major EU Member State. Active both at national and European level.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

PIE (pharmaceuticals in the environment) are an issue, as can be seen that some of them are on the list being evaluated as Priority Substances according to the Water Framework Directive. One particularly worrying issue is endocrine disruptors.

I would strongly welcome such a system. I would also welcome if the environmental information be made relevant in the approval of

a. Would you approve of the existence of such a system?

Yes.

b. Would you be interested in using it yourself?

Not personally, unless we in future decide to place a focus on the subject. (I believe it the subject is already a problem, but am not sure I will eventually work on it.) However, I think it would be helpful for authorities, pharmacists, doctors.

c. For which purposes would you use this system?

See b.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

If the system is taken up in the doctors' decision process of prescription, and if there is the possibility of choosing the more environmentally friendly option between medicines that are otherwise equivalent, and if the system is user-friendly: I see good potential for such a system.

b. Economically?

It could be that some medicines end up being more expensive as a result of their being more environmentally friendly, so implying increased costs, but when one considers the economic benefits of reduced pollution the economic impact of such a system would be in my opinion at least cost neutral.

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

Yes (see a.). Main target group of system should be doctors and pharmacists, patients should be secondarily. Consumer disposal can be affected, however this depends on the possibility of good existing take-back schemes. This is not the case in my MS at the moment. Otherwise consumers don't have the possibility of changing their behaviour routines.

3. What are your (or your organisation's) needs for information on PPs in the environment?

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Mammalian toxicology: *yes. Everything related to human toxicology should be very well researched.*

Side effects: *already available.*

Excretion data: *yes.*

Routes of administration: *yes*

Sales data: *yes, very important to know volume of input into environment, at least regarding order of magnitude.*

Behavior in drinking water and wastewater treatment plants: *yes. Information on behaviour in wastewater treatment plants is more interesting than for drinking water. This is a point where changes can be effected re. the input of PPs into the environment.*

Water quality data for European rivers: *yes, in principle these could be collected. But this doesn't mean that measurements should be made for all rivers. This would be helpful to obtain an overview of the issue, e.g. these substances are problematic in these regions, and these others are not.*

Management of pharmaceutical waste: *yes. The system could have information on the disposal systems in different EU countries, as well as on the correct management procedures of pharmaceutical waste.*

Also need for data on research questions such as pathways of PPs, and which environmental compartments and organisms are most affected.

- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

For our own purposes, information could be kept more general, as well as presented graphically, showing e.g. the development over time, so that an impression of the development of the subject is provided.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

  The system wouldn't affect our decision-making processes yet (see 1b.).

- Would your organization favour such a classification system? Why / why not?

  Yes, we would favour it.

- Which organizations in your country would be pro / against such a system? Why / why not?

  I can imagine that wastewater providers would be particularly interested in this information. I don't know re. doctors, but I believe they should be interested in additional information. I can imagine that the industry would

be against it, if they don't find a way to make it profitable for them for instance by designing greener drugs that can have a price.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  Industry should provide the data basis. However, they shouldn't provide all the information, because they have a vested interest. There should be a public body in charge of this issue, it shouldn't be in private hands. There should be checks, as well as sanctions if the information provided by the industry is not correct. There are instances of information provided by industry producing useful environmental data sets, but there has to be control and effective sanctions.

- Which categories of PPs should it cover?
- To answerThis should be related to the benefits such a system, and the resources
- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  In the first place those pharmaceuticals that are considered priority substances according to the Water Framework Directive, then those substances that were previously listed as "dangerous substances". The REACH approach should be followed then, so that new compounds are taken up, and that prioritization is made according to certain criteria, e.g. substances for which environmental impact has been demonstrated, such as endocrine disruptors.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Yes. Information would be targeted at the prescriber in the one case, in the other it should communicate to consumer on packaging, using a simple system.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

vv. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

ww. What changes would you like to see in the system?

xx. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

System should make comparison of pharmaceuticals possible, at one glance (and not provide an avalanche of numbers hidden in reports).

8. What is your perception of the risk posed by PPs in the environment?

From a water perspective: there have been strong improvements in the water quality of water bodies since 1990; current pollution levels are acceptable. But this means that the relative importance of the issue of PIE has increased, I believe it will continue to increase in the future.The biological activity of these substances is relevant for aquatic wildlife.

yy. Is the media attention justified?

It is important that the public and the media focus on these issues. Only in this way can the will to address a problem be developed. Popular media typically exaggerates and creates alarms, but there are other media that can profit from a good data basis.

zz. Are the efforts for addressing the problem justified?

Yes. Additional efforts should be made to determine the extent of the problem and increase knowledge, but there is enough knowledge of the problem to start taking measures to reduce the input into the environment.

Additional comments: *Veterinary products should also be evaluated. It is also important to evaluate all substances that are part of a medicine, and not only the active substance. Therapeutical value should be the first criteria for the purchase decision of medicines.*

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 27

Stakeholder Group: Environmental NGOs

Date	26/09/11
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Expert on chemical pollution, specialising in biocides and pesticides.
Type of organisation	Environmental NGO of a major European MS, active both at national and EU level.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

We always advocate for transparency. Transparency also allows for future development of relevant regulations. We believe there is not enough preoccupation with the environmental effects of pharmaceuticals at the regulatory level. In front of this background we welcome a system which collects and provides information on PIE (pharmaceuticals in the environment), which would also provide a basis for future evaluation of the issue.

a. Would you approve of the existence of such a system?

Yes

b. Would you be interested in using it yourself?

If related topics would become an issue for us, for instance if the issue of endocrine disruptors in environmental waters is taken up by us, or antibiotic resistance. This depends on our decision which issues we will focus on.

c. For which purposes would you use this system?

See b.

2. What would the impact of such a web-based classification system be?

a. Environmentally?

Such a pooling of information can be positive for the regulatory authorities in charge of authorisation (yes or no, or restrictions on applications) thus producing positive environmental effects. Also positive for environmental authorities, in charge of monitoring. Problematic products could be monitored after their authorisation, and this information system could help the authorities.

b. Economically?

c. Medically?

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

For the system to have the capacity to change consumer behaviour, there has to be the possibility to give back unused medicines at pharmacies. This is not the case in my MS.

If doctors are to be reached, a website will not be enough: a lot of outreach will be necessary. I would imagine that there is the potential of doctors and patients changing their behaviour somewhat, with positive consequences for the environment.

3. What are your (or your organisation's) needs for information on PPs in the environment?

Interesting information would be information on environmental pathways, measured or modeled, environmental fate. Hazard information also of interest. Endocrine properties. Toxicological information: development tox, neurotox. Cumulative problems: different sources or different product types that work cumulatively in the environment. As well as classical information: carcinogenity, antibiotic resistance...

Information should be as wide as possible. The system should also incorporate as widely as possible the information derived from studies. There are some interesting systems for pesticides; however, they only include information derived in the authorisation process. We would like to see a system which incorporates additional information to that generated for official purposes.

4. Getting into more detail…

- precisely which information (which data) would you require?

Physico chemical entries: *yes.*

Ecotoxicological entries*: yes.*

Stability and biodegradation: *yes.*

Excretion data: *yes.*

Routes of administration: *yes*

Side effects: *yes.*

Pharmacodynamic entries: *yes.*

Pharmacokinetic entries: *yes.*

Mammalian toxicology: *yes.*

Sales data: *yes. Because this is sensitive information that companies probably would not want to provide, the approach used with pesticides could be implemented: Provide a figure that gives the order of magnitude of sales. For instance, if a company places 3,5 tonnes of a certain pesticide on the market, it would declare that it places between 1 and 10 tonnes of the product on the market. We would clearly prefer the exact data, but this would be a possible compromise solution.*

Behavior in drinking water and wastewater treatment plants: *yes.*

Water quality data for European rivers: *yes, very interesting to count with monitoring data, also for sediments.*

Management of pharmaceutical waste: *yes.*

In general I think a double approach is necessary: Both prospective information (judgment on environmental behaviour, environmental fate, etc., on the basis of substance's properties) as well as retrospective information (real measured data) should be incorporated into such a database.

- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

The day-to-day user should be provided with simple information, cumulative information, possibly providing an evaluation of the substance. This should help to inform the patient, to help him in his decision. However, the in-depth information has to be available, and for everyone.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?

  See 1.

- Would your organization favour such a classification system? Why / why not?

  See 1.

- Which organizations in your country would be pro / against such a system? Why / why not?

  Organisations that are in favour of increased transparency would be in favour of such a system.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  We advocate the use of peer-reviewed data for such an information system. We do not believe that Good Laboratory Practice is enough to guarantee objective results, when the laboratory is e.g. paid for by the organisation submitting the application. The requirement for peer-reviewed data is also part of the pesticides directive (2009/128/EC). Grey literature (reports and such) is not enough, we require peer-reviewed literature.

  In the case of pesticides, the authorities in charge of authorisation produce a summary report and give their decision. However, the original information, the studies are not made public, we cannot access this. This is from our perspective a problem. For an information system, we believe that information taken up should be information that is well referenced and coming from sources that can be accessed. And it should not be only information provided by the producers, but also information from neutral sources. This is a crucial point, it is a matter of having trust in such a system.

  A possibility would be to rank the information according to the quality of their source. It is very important for us to have information on the quality of the data. This could be done according to a criteria catalogue, in the development of which different interest groups should be involved. This catalogue should be open to the public. The system should be reviewed every couple of years.

  In the case of chemicals, pesticides, and biocides, the agency in charge of authorisation is obliged to make public the environmental data. I do not know enough about the system for pharmaceuticals, but if this obligation does not exist (or if the obligation is less stringent) this obligation should be implemented.

  Detailed information could be provided in English, information targeted at doctors / patients should be in all European languages.

- Which categories of PPs should it cover?

  It should cover all drugs, because toxicologists are highlighting more and more the "low doses effects" of chemicals.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  First efforts should focus on substance groups known to be problematic: antibiotics, substances which can create resistances, and hormonally active substances. Production volume should also be a key criterion for prioritising.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Both groups. System should also include dietary supplement products, e.g. vitamins.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

aaa. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

bbb. What changes would you like to see in the system?

ccc. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

ddd. System should be searchable according to active substance, but also searchable according to products. It should make comparison between different substances easy.

System should be searchable both by name of active substances and name of product.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

I think this is a major problem, if one considers it in conjunction with the problem of veterinary drugs in the environment, and due to activities such as fish farming, for instance. These are cumulative effects: the input of human pharmaceuticals into the environment is a relevant problem. Regulatory efforts should be made, and risk reduction measures should be implemented. A key risk reduction measure is increasing transparency and making more information available, so that decisions can be taken on a wider data basis. This allows for better decisions at all levels, from the regulatory level all the way down to the user level.

Additional comments: *System should also provide information on the complete product, not only on active ingredients, but also on excipients. Some pesticide databases could serve as models for this system, e.g. Pesticide Footprint website, http://www.eu-footprint.org/ppdb.html.*

Environmental NGOs and consumer NGOs would be responsible for producing recommendations; this would be beyond the scope of such an information system. Tools would also be developed by other stakeholders, people related to water monitoring, people from water utilities.

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 28

Stakeholder Group: Public Health

Date	28/06/2011
Name of Interviewer	Rodrigo Vidaurre, Ecologic Institute
Type of Interviewee	Responsible for the environmental risks to water for drinking and recreational purposes, in department in charge of prevention of environmental risk and food. In charge of the national action plan on pharmaceuticals in water, in cooperation with the Ministry of Environment.
Type of organisation	Health Ministry of a European Member State.

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?

I am not sure. It's not necessary according to me, but we think it could be helpful to make a better assessment of environmental risks and health risks of the pharmaceuticals in water. This classification system could be a good tool to collect and make a database on environmental and ecotoxicological data of PPs.

Another requirement would be that the classification system be an European one, but it would be even better if it were a world-wide one.

a. Would you approve of the existence of such a system?

Yes.

b. Would you be interested in using it yourself?

Yes.

c. For which purposes would you use this system?

For the purpose of risk evaluation (however, we do not do risk evaluations on our own, we rely on the national health agencies).

2. What would the impact of such a web-based classification system be?

a. Environmentally?

The system could be helpful to identify primary substances that need to be evaluated more in depth.

b. Economically?

The public purchaser has begun to use this kind of criteria with the companies they deal with, not with the product. Also there is definitely a new trend towards providing information to the consumer. Consumers could eventually select their drugs according first to their needs, but also to their environmental impacts. That would generate an economic impact amongst pharmaceutical companies, to remain competitive and develop ecological drugs.

Such an environmental labelling could be a disadvantage for European products, when compared to e.g. Indian products that do not make available such information. We have to be careful this does not become a disadvantage for European companies

c. Medically?

It could be helpful to orient research projects, to develop less toxic medicines. It could be helpful for public hospitals and public network, the purchaser has to use different criteria to select medicine. Most of the time for a disease you have alternatives, one of the criteria could be the ecological footprint.

d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

It could be used for the indication of health professional and vets in order to guide them towards better professional practices, to help them select the less contaminating medicine.

3. What are your (or your organisation's) needs for information on PPs in the environment?

It could be useful to have a database where we could find any data we need in order to assess in the best way the environmental and health risks of a defined substance. We need toxicological data, eco tox data, list of characteristics of each substances, exposure concentration.

It could be helpful to pilot the project to follow the evolution of new knowledge on drugs and to identify what drugs should be priority. For example, we could follow the evolution of two drugs and year by year and perhaps realize that it is not a problem, and another drug that we had not identified as problematic turns out to be.

4. Getting into more detail…

- precisely which information (which data) would you require?
- at which level of detail / (level of aggregation?)
- how should the information be prepared and presented (figures, graphs, level of convenience)?

Information on the behavior in wtp (for drinking and wastewater) could be useful information. It is hard to believe that data on sales could be available. Sales figures at national level would not be so useful for modelling but rather more in focusing research (ecotox caracteristics e.g.) on priority substances. If you work with models (IT model process to simulate the fate of substances in waters), you have to work on a limited area and so you need to know the concentration of drug in that particular area, the local sales are at the right level.

Concerning data on water flows and water quality, would there be continuous surveys of the status, something more systematic may not be necessary. We are aware of the presence of pharmaceuticals in the environment and we know their level of concentration. So before implementing a continuous monitoring, I would prefer having some relevant data or proof that we need to monitor some particular substances. Anyways this info would be more or less useful to us.

5. How would you use this classification system in your work?

- How would it support / influence your decision-making processes?
- Would your organization favour such a classification system? Why / why not?

  Which organizations in your country would be pro / against such a system? Why / why not?

We would not be the ones to make the most use of it. It would be more useful to the national agencies than us who are dedicated to policies. It could be useful to doctors. I have a hard time imagining how we could make a good use of such a database on a regular basis.

It could provide assistance to the national agencies in doing risk assessments. We could implement stricter policy measures if needed to limit the presence of the most dangerous PP residues. I think that the system could provide a better and wider information and that would allow me to identify the substances that pose a risk.

6. What should the main characteristics of a classification system be to ensure the system works adequately?

- Origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

  The origin of the information has to be known and certified. Information must be scientific, factual and neutral. It must be transparent. If opinions are present they are to be presented as such. I think it's better if it is managed by a public service, the way to collect the money has to be independent from the evaluation agency (referring to the Swedish system). We could use information on the environmental consequences with the level of proof, level of evidence to demonstrate the reported effects.

- Which categories of PPs should it cover?

  All drugs should be addressed.

- Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

  Perhaps antibiotics and hormones. All drugs should be addressed, but to progress step by step we would start with those.

- Should both prescribed and OTC (over the counter) drugs be covered?

  Yes, they are both interesting, and there are more and more products that are available over the counter.

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

eee. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

fff. What changes would you like to see in the system?

ggg. What are the shortcomings of the system?

i. re. information

ii. re. functioning

iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

Some data could be public, but other data belongs to the company and we would only be able to get restricted access. There should be at least two levels of access, professional and general population, and access reserved to advanced users like academics.

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

b. Are the efforts for addressing the problem justified?

I think the media are more interested than the general population. I am not sure that population is very upset by the presence of PPs in the drinking water, except maybe for hormones. But we should make efforts to address the problem. We have to address carefully the question of public information.

We do not know a lot on the health risks associated to the presence of PPs in water. We do not know a lot about long term exposure at low concentrations. A long term risk assessment is needed: but on short term we can drink the water even if trace amounts are present. Organic pollutants and chemical pollutants are maybe of higher concern.

We have to find a way to inform the population, or special groups of population such as NGOs or citizen groups who could be afraid of the risks. Media publications can frighten the public more than anything. We have to

address this issue because we do not know the long term risks and we have a duty to educate the general public. The first step seems to make clear enough to everyone notions as hazard or risk, uncertainty principle. We did a small survey and found that the Germans were the first ones to start educating the general public, because they were the first ones to detect the presence of pharmaceuticals in the environment. Netherlands, Luxembourg, Germany and Italy are the most advanced on the issue, not because the problem is bigger there but because they are more vigilant and began before other countries.

Additional comments: *I think the EU community is moving towards a better environmental assessment of pharmaceutical products. The recently modified European directive on pharmacovigilance mentioned specifically a paragraph on the environmental impact of PPs and the need for assessment.*

PHARMAS project: Interviews WP6.1

Summary Interview Stakeholder No. 29

Stakeholder Group: Pharmaceutical Waste/Recycling Companies*

*The questionnaire was filled in directly by stakeholder. No interview was held.

Date	26.08.2011
Name of Interviewer	
Type of Interviewee	Dr., General manager
Type of organisation	Company specialised in takeback of pharmaceutical waste in a European MS

Questions:

1. What is your opinion on the need for an EU-wide environmental risk and hazard classification system for pharmaceuticals?
    a. Would you approve of the existence of such a system?

    YES

    b. Would you be interested in using it yourself?

    NOT POSSIBLE ACCORDING WITH ACTUAL PROCEDURES APPROVED BY ENVIRONMENTAL AUTHORITIES

    c. For which purposes would you use this system?
2. What would the impact of such a web-based classification system be?
    a. Environmentally?

    YES

    b. Economically?

    c. Medically?

    d. Regarding behaviour routines? (e.g. consumer disposal of unused pharmaceuticals, behavior of doctors prescribing)

    YES
3. What are your (or your organisation's) needs for information on PPs in the environment?

    AT MOMENT THE UNIC INFORMATION IS PROVIDED BASED ON PACKAGING WASTE MATERIAL AND USED DRUGS COLLECTED BY MY COMPANY
4. Getting into more detail…
    - precisely which information (which data) would you require?
    - at which level of detail / (level of aggregation?)
    - how should the information be prepared and presented (figures, graphs, level of convenience)?
5. How would you use this classification system in your work?
    - How would it support / influence your decision-making processes?

RISK ASSESSEMENT OF PP FOUND IN THE ENVIRONMENT WOULD CHANGE COMPLETELY THE OPERACIONAL PROCEDURES OF PHARMACEUTICAL COMPANIES AND MY OWN COMPANY

- Would your organization favour such a classification system? Why / why not?

  DEPENDING OF THE SPECIFIC PROCEDURES CONCERNING THE IMPLEMENTATION OF THE SYSTEM.

- Which organizations in your country would be pro / against such a system? Why / why not?

  PHARMACEUTICAL COMPANIES ARE MORE CONCERNED BECAUSE THE SYSTEM WILL OBLIGE THEM TO CRETE NEW RULES FOR PRODUCTION AND MONETORING RISK ASSESSEMENT

6. What should the main characteristics of a classification system be to ensure the system works adequately?

a. origin of information (who provides data), guaranteeing adequate quality of information, neutrality, external revision, language.

THOSE POINTS ARE THE KEY ISSUE FOR A SYSTEM OPERATING PROPERLY

b. Which categories of PPs should it cover?

ANTI CANCER DRUGS

ANTIBIOTICS

c. Any priority drugs to focus on in a first phase (e.g. antibiotics?)?

HOSPITAL DRUGS

d. Should both prescribed and OTC (over the counter) drugs be covered?

NOT IMPORTANT

7. What would your requirements of a web-based classification system be, e.g. in terms of usability?

*In case they are **familiar** with fass.se*:

a. Do you like the way the system is built? (e.g. regarding your own needs, regarding the different levels of information between broad public and advanced users)

b. What changes would you like to see in the system?

c. What are the shortcomings of the system?

   i. re. information

   ii. re. functioning

   iii. How could these be overcome?

*In case they are **not familiar** with fass.se*:

   iv. In your opinion, what should the main characteristics of the system be? (E.g. what kind of structure (architecture) should the system have? Should there be different levels of information, and if yes: for which kind of users and which kind of knowledge?)

8. What is your perception of the risk posed by PPs in the environment?

a. Is the media attention justified?

NO. OTHER ENVIRONMENTAL ISSUS ARE MUCH MORE RELEVANTS.

RISK ASSESSEMENT CAN BE A TOOL TO PROVE IT

b. Are the efforts for addressing the problem justified?

NOT A TOP PRIORITY

9. Do you have any other comments? (If you think of additional comments after the end of this interview (e.g. later on today or tomorrow), please send them to us via email!!!)