Evaluation report

Radiocontrast agents

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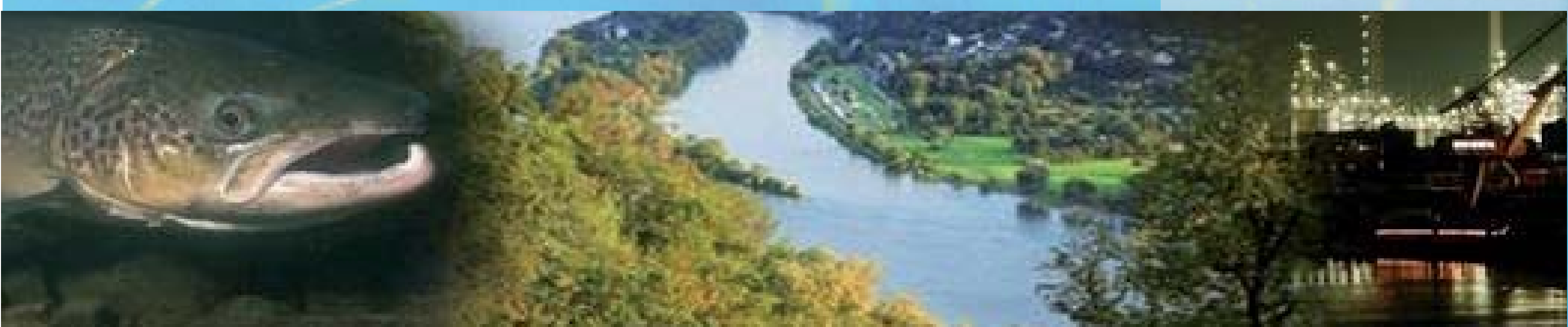

Within the strategy aimed at reducing micro-pollutant inputs originating from urban and industrial waste water, evaluation reports are being drafted for 10 groups of substances targeted at summarizing scientific and technical facts and at pointing out gaps of knowledge. Also, the evaluation reports present a variety of possible measures at the source (e.g. registration of substances, limitation of uses) and technical measures in crucial wastewater treatment plants (e.g. introducing a further treatment stage). The "Conclusions" of the evaluation reports list the most efficient measures to be further investigated into within a holistic ICPR strategy. However, these measures are no recommendations the ICPR addresses to its member states. Measures listed in this chapter will be integrated into a survey report of all measures in order to be able to take into account eventual synergetic effects of measures (effects of measures on different groups of substances) when proceeding with the final evaluation. Based on the final evaluation of all measures the ICPR will determine recommendations for the Member States

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1. Introduction

Radiocontrast agents are used for diagnostic purposes, as they absorb X-rays to a greater extent than human soft tissue and thus visualize these tissues. After their application they are largely unaltered when excreted and may get into wastewater.
This report exclusively concentrates on iodine based radiocontrast agents. It has been known for years, that iodine based radiocontrast agents are detected in all parts of the aquatic environment[1].
In comparison, we dispose of considerably less results for other radiocontrast agents[2]. In water bodies, the iodine based radiocontrast agents diatrizoic acid/diatrizoate, iopromide, iopamidol, iomeprol are those detected most often and in highest concentrations and are therefore used as indicator substances.
The quantities sold in Germany in 2001 range between 42,000 kg/year (iopamidol) and 83,000 kg/year (iomeprol) and correspond to an amount of 0.5 to 1.0 g/inhabitant; more recent figures concerning iopromid indicate distinctly increasing quantities.

As far as input pathways are concerned, a distinction must be made between those radiocontrast agents which are given as injection (syringe) or infusion and excreted with the urine (e.g. iomeprol, iopromide, iopamidol) on the one hand and those which are applied by way of the mouth or rectally (diatrizoic acid, ioxitalaminic acid) and excreted via the intestinal tract. Substances used for a diagnosis of the gastro-intestinal tract (diatrizoic acid/diatrizoate, ioxitalaminic acid) are ionic iodine based radiocontrast agents. Since 2000, in Germany only non-ionic iodine based radiocontrast agents (iopromid, iopamidol, iomeprol) are injected intravascularly (into veins and arteries). From a chemical point of view, they only differ with respect to the side chains and in their physico-chemical properties (osmolality, viscosity, hydrophilicity).

Due to the high consumption tending to increase, their solubility, polarity and stability it is not surprising that these substances are detected in surface waters, in groundwater (e.g. bank filtrate, groundwater recharge) and partly in drinking water. Therefore, during the evaluation of water quality, the group of radiocontrast agents must be taken into account. Contrary to pharmaceuticals used for therapeutic (curative) purposes they are however being developed as biological inactive substances. Therefore, so far it is being considered that they have little ecotoxicological effect. Nevertheless, waterworks are uneasy about the fact that these substances are frequently and increasingly detected in drinking water. In general, current treatment procedures do not permit to (completely) eliminate them. Furthermore, it is known that under certain environmental conditions, e.g. during biological wastewater treatment, bank filtration and ozone treatment a great number of organic iodine based transformation products develop, the characteristics and toxicity of which can so far not be assessed. So far, 46 transformation products due to microbiological reactions have been identified.

[1] (Ternes & Hirsch, 2000; Putschew & Jekel, 2006, Putschew et al., 2007).
[2] Magnetic Resonance Imaging e.g. uses chelates based on the toxic gadolinium ions. In this connection, further investigations on their occurrence in the water cycle and on environmental effects would be desirable.

2. Problem analysis

In surface waters, iodine based radiocontrast agents are continuously detected in concentrations ranging from 2- to 3-digit nanograms (ng) to some micrograms (µg) per litre. In the Rhine, concentrations continuously increase from the Upper Rhine to the estuary. In Basel, the average concentrations of most iodine based radiocontrast agents are below 0.1µg/l. On the Lower Rhine and in the Delta Rhine, concentrations are mostly around 0.2 and 0.5µg/l. The highest concentrations registered in the Rhine were about 1.3µg/l. Partly, concentrations are even higher in the tributaries (in Germany e.g. in the Emscher, Lippe, Ruhr, Sieg). (Depending on the substances, maximum values up to 10 or 30 µg/l).

Of the thirteen iodine based radiocontrast agents listed in the substance data sheet, the four above mentioned substances are detected in comparably high concentrations in the main stream of the Rhine and in its tributaries. As they also cover two different areas of application, they are apt to serve as indicator substances (substances representing the whole group of substances).
The highest concentrations are found in

- Those tributaries of the Rhine with a high share of (biologcially) treated urban wastewater or high population density; a higher density of hospitals in the catchment and high average age of the population, such as found in the Ruhr/Emscher area may potentiate the occurrence of these substances;
- In those tributaries or sections of the Rhine, along which production plants are located;
- In the Delta Rhine.

The following statements apply to water quality:

- Iodine based radiocontrast agents are found in the raw water of waterworks and are often also detected in drinking water. This is in particular true of the Lower Rhine and the Delta Rhine, as well as of some Rhine tributaries. As these substances are very polar, they are neither adsorbed during bank filtration, nor during active carbon filtration. Concentrations may partly be reduced during biological degradation processes and ozone treatment (ozone is a strong oxidizing agent). There is evidence that these processes develop numerous iodine based organic transformation products which are detected in drinking water.
- The average concentrations of some iodine based radiocontrast agents detected in the waters of the Rhine catchment partly lie distinctly above the IAWR target value of 0.1µg/l or above the target value for drinking water hygiene determined by the German Umweltbundesamt[3]. Also, the health guidance value (GOW) (1.0µg/l) of the Umweltbundesamt (UBA, 2008) for iodine based radiocontrast agents is partly exceeded[4]. However, the amounts of iodine based radiocontrast agents liable to be absorbed via drinking water are distinctly lower than the therapeutic doses applied.

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3 The range of the target value for drinking water hygiene for iodine based radiocontrast agents indicated by the UBA ((≤0,1 to <1,0 µg/l) is explained by the fact that, with respect to the possibility that toxicologically relevant transformation products develop from oxidative drinking water treatment, this target value must differ and, as a matter of precaution, must lie below the GOW_4 = 1,0 µg/l (UBA, 2008).

4 The GOW is considered to be a precautionary value for radiocontrast agents in drinking water and drinking water resources or in waters, from which raw water is taken for drinking water supply. It is a general precautionary value for verifiably non genotoxic substances for which data on toxicity by way of mouth, on immunotoxicity and on the potential to harm reproductive cells do not lead to a value below 1 µg/l (GOW_4) (see UBA, 2003). It equally applies to components of the sums of similarly acting substances.

- According to the German UBA there is no information of ecotoxicological relevance from which environmental quality standards may be derived. Therefore, neither environmental quality standards (EQS) nor proposals for EQS are available for iodine based radiocontrast agents.
- It is proved that the substances are not genotoxic (toxic for genetic material) and do not show any neuro-toxicological potential (toxic for nerves) or potential to harm reproductive cells.
- So far, no sub-chronic or chronic (life long) animal experiments have been carried through with iodine based radiocontrast agents and it has not been possible to calculate life long tolerable intake rates.

The radiocontrast agents considered are largely detected in the Rhine catchment area. Due to the existence of these substances and of mixtures which might contain these as well as other substances and transformation products, undesired effects and chronic or sub-chronic effects may develop which cannot be pointed out beforehand, e.g. during licensing procedures. In particular, drinking water production from direct intake, bank filtration or artificial groundwater recharge is made more complicated along the Lower Rhine and the Delta Rhine and some tributaries and the choice of further treatment measures (e.g. ozone treatment) is based on uncertainties. In order to improve water quality and to respect the interdiction of deterioration according to EU WFD (Art. 4, Par. 1 and Art. 7, Par. 3) cost-efficient measures are required to avoid a further water pollution with iodine based radiocontrast agents or to achieve a reduction of present concentrations.

3. Analysis of pathways

Unlike most pharmaceuticals for therapeutic purposes the application of these substances is practically speaking reduced to hospitals and X-ray practices and they are excreted within few hours (max. 24 hours) after their application. As far as patients are concerned, who will remain at hospital or in the X-ray practices for some hours after their examination, further possibilities exist with respect to reducing or avoiding the substances inputs into the water cycle than those existing for pharmaceuticals for therapeutic purposes.

Mostly, iodine based radiocontrast agents get into the municipal wastewater via the wastewater of hospitals, X-ray practices and households immediately after their application.
Via the combined sewer overflow, during rainfall, a small percentage (about 1 – 3 %) of municipal wastewater flows directly into surface waters. Also, wastewater from households not connected to the municipal sewer (about 1-2 %) is directly flowing into the surface waters. But more than 95 % of urban wastewater flows into wastewater treatment plants. Only a small or varying percentage (~ 8 %; see investigations into a wastewater treatment plant of the waterworks in Berlin, 2005, 2006) can today be eliminated with the help of biological treatment[5]. Thus, concentrations of iodine based

[5] In a pilot test in Lausanne (BAFU 2010, not yet published) average elimination (or transformation) rates between 20 and 40 % were determined for the different iodine based radiocontrast agents (table 1 in annex I). However, “elimination rates” for iopromide, iopamidol, iohexol and iomeprol depend on the age of the sludge (Ternes, orally). Ternes et al. did not observe any elimination or transformation of diatrizoic acid/diatrizoate, no matter, how old the sludge was. On the contrary, in the experimental station in Regensdorf (EAWAG/BAFU, 2009) a ~40 % (+/- 39%) a biological elimination rate was observed for diatrizoic acid/diatrizoate, while no biological elimination rate could be determined for the other iodine based radiocontrast agents. Presumably, this is due to the low sludge age. It is mainly observed that biological degradation always leads to stable products which may again reach the groundwater or drinking water and/or cause problems.

radiocontrast agents ranging between 0.02 and 165µg/l are found in the outlet of municipal wastewater plants. Wastewater plants receiving an increased share of wastewater from hospitals are liable to discharge concentrations ranging between 0.5 and > 100µg/l (ISA/RWTH Aachen, IWW Mülheim, 2008; EAWAG/BAFU, 2009).

In a more recent, comparative investigation of the LANUV NRW (11/2010, not published) verifiable (high) concentrations of iopamidol (3.8µg/l), iopromide (0.35µg/l) and iomeprol (2.6µg/l) were detected in the outlet of a smaller wastewater treatment plant not treating any hospital wastewater. The little diluted concentrations in wastewater from wastewater treatment plants may lead to high concentrations in small rivers. In the Hessian R. Winkelbach for example up to 100µg/l diatrizoic acid/diatrizoate have been measured[6].

Inputs due to direct discharges from industry (production plants) differ all depending on the substance and the wastewater treatment measures of the plants. In Northrhine-Westphalia (NRW), for 2005, the share of the iopromide loads originating from direct industrial inputs were estimated to a maximum of about 10 % (LANUV data; reference year 2005); for the other iodine based radiocontrast agents investigated into, the shares originating from direct inputs were negligible. All in all, the share is today estimated to be below 10 %.
Thus, municipal wastewater treatment plants are identified to be the main input pathway into surface waters. The sources of emission are above all hospitals and X-ray practices, in individual cases also production plants (direct or indirect discharge).
Due to the short retention time in the human body, the share emitted by households mainly depends on the time the patients spend at hospital. Municipal wastewater treatment plants receiving an above-average share of hospital wastewater thus have above-average concentrations and loads of iodine based radiocontrast agents (see ISA/RWTH Aachen, IWW Mülheim, 2008). A comparable close correlation between the number of inhabitants connected and the determined load as found for numerous pharmaceuticals applied for therapeutical purposes can thus not be supposed. This must be taken into account, when assessing models and measures and determining priority measures.

4. Possible measures

To minimize the input of radiocontrast agents, emission reduction measures can be taken at different levels:

- Measures at the source;
- Information of the public and of experts
- Decentralized measures
- Centralized measures in urban wastewater treatment plants;
- Review of monitoring programmes and systems of assessment

In the following, the potential measures are developed more in detail.

Measures at the source

- Reduce water pollution due to measures taken by the producers (pharmaceutical industry):
  - Enhanced environmental impact assessment during licensing
  - Binding further investigations on the environmental compatibility by the producer even after the product launch (pharmacovigilance): E.g. examination of the chronic/sub-chronic effect on aquatic organisms, on transformation products, on behaviour during drinking water production and treatment;
  - Development of biologically better degradable radiocontrast agents by producers

[6] Ternes and Hirsch, 2000

- Use of existing possibilities to recycle potential substances worth recovering (incineration with recovery of iodine), e.g. by separate wastewater collection, concentration and incineration of by-products. The by-products are incinerated in a rotary kiln, while the iodine is recovered. The process is already being applied by the Bayer-Schering works (Bergkamen) and thus immediately available for other plants. Due to high, resp. rising trade prices for iodine, the recovery of this substance pays (for the producers). Due to the comparatively low share of water pollution by radiocontrast agents from direct sources, the total effect of measures concerning direct industrial discharges will only be moderate to low (<1-10 %).
- Use of special wastewater treatment measures (e.g. for wastewater split flows; urine/bulk concentrate): According to literature, urine containing iopromide may successfully be treated by reductive dehalogenation (delamination of iodine) with iron; as compared to ozonisation, no organic transformation products will develop (-> mineralization) (Putschew et al., 2007).

Information of the public and of experts

The public and experts, in particular universities, the pharmaceutical industry and staff belonging to health care institutions – doctors, pharmacists, nursing staff as well as patients will be informed about the environmental relevance of radiocontrast agents and about their impact on drinking water treatment (product information) as well as about possibilities of recovering the agents and their environmental friendly disposal or the collection and treatment of wastewater.

Decentralized measures

Different solutions exist for directly discharging plants and decentralized measures may be taken in hospitals and X-ray practices. The following procedures have already been tested (pilot tests or in comparable applications) and may therefore be extensively applied at comparatively short notice and will be highly effective for the Rhine catchment:

<u>In hospitals/X-ray practices:</u>

Since patients excrete radiocontrast agents within less than 24 hours after their application, the quantities of these agents in municipal wastewater may be reduced by separately treating the collected urine.

- Measures in hospitals/X-ray practices:
  - Separate wastewater treatment or treatment of wastewater split flows (reductive dehalogenation is equally suitable) or
    Install urine collection points for the urine of patients treated and separate urine collection in toilets and concentration of urine (by nanofiltration) in hospitals. (This requires adequate information of the patients, in order to achieve acceptance and use of separate toilets or the urine collection system; acceptance of the system by doctors and hospital staff as well as by patients has proved to be good (Berlin Waterworks, 2006).
  - Additionally, it is recommended to install take-back systems or central collection points for concentrated urine (see below). The concentrated urine may e.g. be incinerated by the producer while recovering the iodine at the same time.
  - Installation of incinerating toilets in order to be able to innocuously dispose of radiocontrast agents contained in excrements (see below);
  - Urine collection bags may be used in hospitals and as „patient measure”. This measure would contribute to include outpatients (BAFU 2009).

Disposal of the two iodine based radiocontrast agents used for contrasting the intestinal tract (diatrizoic acid/diatrizoate, ioxitalaminic acid) and disposal of the iodine based radiocontrast agents contained in urine:

- A procedure exists, using a so-called “electrical incinerating toilet”. These devices which completely and innocuously dispose of all human excrements are widespread in Scandinavia. Within environmental protection they are there being used in houses and summer houses not connected to the sewerage system. They could equally be used in X-ray practices or in the X-ray hospital departments.
- This measure is immediately available and would completely and innocuously dispose of the excrements containing iodine based radiocontrast agents.
- Energy requirement: 1.0 -2.0 kWh per use of toilet (producer indication; Fritidstoa: förbränningsoaletter; www.fritidstoa.se).
- Use so far: Particularly common in Norway, in most houses standing on their own and leisure or fishing huts along the fjords.

The application of the system in hospitals seems to be new (DWA, under examination). Its use so far indicates acceptance and easy application of the system and compared to economies in wastewater treatment, the energy requirement is so far assessed to be moderate to low. (In this case, too, it is true that the achievable effect and cost-effectiveness of each individual case depends on the time patients normally spend in the hospital or X-ray practice after the diagnosis and which adaptations measures (organisational procedure, eventually construction measures) are required in each individual case.)

<u>During the preparation (hospital pharmacy) and during or after application:</u>

- Avoid residual quantities or separate disposal of residual quantities arising during the preparation or application. This requires information of doctors, of the pharmaceutical, medical, technical and nursing staff.

<u>Connected measures in the Rhine bordering countries (or e.g. per federal state):</u>

- Installation of central collecting points in each Rhine bordering country (or each federal state) with collection tanks for primary urine, nanofiltration plant producing concentrated urine and collection tank for concentrated, iodine-containing urine.
- As indicated above, the iodine-containing concentrated urine may be incinerated while recovering the iodine contained (this measure gives rise to no or extremely low disposal costs).

This measure is effective for iodine based radiocontrast agents applied by injection/infusion and excreted with urine, but not for those contained in excrements from the intestinal tract (amidotrizoe acid/diatrizoate, ioxitalaminic acid). The achievable effect for the first ones is assessed to be high (> 50 %) with little need of time (< 5 years) and, due to the possibility of substance recovery cost-effectiveness is assessed to be good. However, it is true that the achievable effect and cost-effectiveness of each individual case depends on the time patients normally spend in the hospital or X-ray practice after the diagnosis and which adaptation measures (organisational procedure, eventually construction measures) are required in each individual case.

<u>Treatment procedure for collected concentrates (in the producer's plant / centralized treatment / in the hospital):</u>
Wastewater split streams (e.g. of urine, collected concentrates) may be treated by mineralization of iodine based radiocontrast agents by ways of reductive dehalogenation (eliminating iodine) with elementary iron. According to literature and compared to ozonisation (and other procedures) no iodine-containing organic transformation products arise during this procedure and a high degree of elimination is achieved or achievable (> 90%; see Putschew et al., 2007). Furthermore, the iodine recovering procedure has already been successfully applied (Berlin Waterworks, 2006).

Also, nanofiltration (filtering procedure retaining particles of 10 to 1 nanometres) or reverse osmosis may be applied to wastewater split streams in order to remove iodine based radiocontrast agents.

<u>Decentralized measures concerning the targeted treatment of hospital wastewater:</u>
Within a pilot project of the district hospital Waldbröl (RWTH 2009) the elimination performance of further wastewater treatment stages were assessed for ozonisation (1,02 mg O_3/ mg DOC) and active carbon filtration (AF). For diatrizoate an average elimination of about 75 %, for iopamidol an average elimination of about 82 % were achieved by means of active carbon filtration. Ozonisation led to an average „elimination" (in this case degradation/transformation) of about 60 % for iopamidol, for diatrizoate it was not possible to determine any elimination (partly the influent concentration was below the effluent concentration).
During a comparison of variants carried through in the cantonal hospital in Liestal (BAFU 2009) it was investigated how micro-pollutants of this hospital may be eliminated most efficiently. In this connection, the substance iobitridol was chosen to represent the iodine based radiocontrast agents. The investigations concerned:

1. Measures in the wastewater treatment plant using
   a) ozonisation and
   b) powdered activated carbon;
2. A separate wastewater treatment plant for the cantonal hospital Liestal;
3. The equipment of the cantonal hospital Liestal with vacuum toilets and incinerating the vacuum toilet sludge or waste incineration plant;
4. Patient-based measures using urine collection bags.

These investigations showed that, for iodine based radiocontrast agents the measure taken at patient level was most successful. Its results concerning the eliminable load and with respect to its cost-effectiveness were better.
The cost-effectiveness of measures taken at a hospital level – separate wastewater treatment plant for the hospital or installation of vacuum toilets in the hospital – is comparable to that of measures taken in urban wastewater treatment plants. The disadvantage compared to „measures at patient level" (urine collection bag) is that they do not cover iodine based radiocontrast agents administered to outpatients.

Centralized measures in urban wastewater treatment plants
Although iodine based radiocontrast agents are largely (~90%) discharged into the waters by wastewater treatments plants, depending on the radiocontrast agent, further wastewater treatment measures (e.g. ozonisation, activated carbon) in (selected) wastewater treatment plants lead to a varying but not satisfactory reduction. However, further central measures may complete the possible decentralized measures and measures at the source.
The estimated 3,200 wastewater treatment plants in the Rhine catchment cover a total volume of at least 98 million population equivalents. 191 of these wastewater treatment plants (that is 6 % of all wastewater treatment plants) cover of a total volume of more than 100,000 population equivalents). These wastewater treatment plants dispose of more than half of the entire treatment capacity (54 %) in the Rhine catchment[7]. Extending these 191 wastewater treatment plants by the aforementioned further treatment measures might reduce the discharges of organic micro-pollutants originating from urban wastewater treatment by at least 30 %.

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[7] Report to the European Commission on the results of the survey according to Directive 2000/60/EC of the European Parliament and the Council of 23 October 2000 establishing a framework for Community action in the field of water policy (article 15(2), 1st indent); - Part A = Overriding Part); status: 18.03.05, Coordination Committee Rhine 2005 (CC 02-05d rev. 18.03.05).

Depending on the treatment procedure (activated carbon, ozonisation or a combination of both) and a substance-specific varying effect, the discharges of radiocontrast agents can only be partly reduced. In the most optimistic case, in the Rhine catchment, this would lead to a reduction of the load of iodine based radiocontrast agents of < 10 to a maximum of ~ 30 %; recent results of a pilot test in Lausanne (see table 1 in annex 1) show that a 10 to 14 % reduction could be achieved. However, it must be taken into consideration that ozonisation gives rise to transformation products, so that it is not possible to speak of an elimination (see above); as iodine based radiocontrast agents are highly polar, only fresh activated carbon can achieve a reduction (which is thus hardly cost-effective). Furthermore it must be taken into account that the emitted load of iodine based radiocontrast agents does not behave linear to the population equivalents, as these agents are only partly discharged by households. A major part is being discharged with hospital wastewater. Therefore, in order to efficiently reduce the discharge of iodine based radiocontrast agents, the selection of wastewater treatment plants must be modified, taking into account hospital wastewater.

All in all, this might reduce the pollution of the Lower Rhine and the Delta Rhine with organic trace components. However, it would neither be possible to achieve or respect the IAWR target value of 0.1µg/l nor the target value for drinking water hygiene for radiocontrast agents including transformation products and additive effects of substance mixtures with comparable effects determined by the German Umweltbundesamt. In particular, for radiocontrast agents, only measures at the source, at patient level or decentralized measures would make sense.
With respect to radiocontrast agents, centralized measures in wastewater treatment plants could however improve the protection of drinking water protection along the main stream of the Rhine, in particular along the Lower Rhine and in the Rhine delta as well as along some Rhine tributaries. When assessing cost-effectiveness, the positive effect simultaneously achieved for other substances/groups of substances (e.g. for other pharmaceuticals, biocides, etc.) must simultaneously be taken into account.

As far as effect and cost-effectiveness are concerned, we dispose of results of pilot tests with further wastewater treatment procedures in urban wastewater treatment plants and in one hospital wastewater treatment plant (see annex I). When identifying the most efficient required measures (see chapter 5), these results may already be taken into account.

Review of monitoring programmes and assessment systems
The analysis of available information indicates in the following with respect to the design of monitoring programmes and the further development of assessment systems:

1. No binding quality criteria are available aimed at assessing the ecological/chemical state and at protecting drinking water resources.
   If necessary, these should be derived at a suitable institutional level.
2. The assessment of the ecological and chemical status of waters by the EU Member States within the Water Framework Directive and that carried out within the Swiss law on water protection does not take into account the substances mentioned in this report.
3. The data available (monitoring data and knowledge about the correlations) concerning the iodine based radiocontrast agents mentioned in this report are already satisfactory. However, this is not true for information on chronic/sub-chronic effects of these substances and on their metabolites.
4. So far, no representative monitoring data are available for other (also non iodine based) radiocontrast agents and there is no systematic assessment of administered and emitted quantities, environmental relevance and toxicity.

5. Generally speaking, the following elements could be taken into account when reviewing the assessment systems:

- Assessment of the environmental relevance of the different substances/groups of substances through substance balances, simple model assessments, development and taking into account information resulting from discharge charts (here: hospitals, X-ray practices/surgeries, producers), eventual indications due to licensing procedures (EMEA), sales figures or consumed quantities; comparable methods to[8].
- Assessment of the environmental relevance by assessing or classifying substance characteristics such as structure-activity relationship.
- Results of new analytical research methods[9].

5. Conclusion

Summary of the most efficient measures to be further elaborated and examined.

- **Measures at the source** during product licensing and production in order to reduce water pollution due to extended environmental impact assessment (before and after licensing) of pharmaceuticals used for diagnosis, including their metabolites and transformation products; incentive systems to develop more environment friendly alternative products.
- **Information of the public and of experts** concerning the environmental relevance and effects of radiocontrast agents in the Rhine catchment on drinking water production; compulsory labelling of those radiocontrast agents which are found to have an effect on waters or drinking water or for which such an effect is expected; information on existing possibilities for good practice, disposal of, cleaning, recirculation and recovery; promising possibilities were in particular found for iodine based radiocontrast agents.
- **Decentralized measures:** Treatment of wastewater or wastewater split streams in production units or health institutions directly discharging into surface water bodies or indirectly discharging through wastewater treatment plants and contributing with a substantial part to the load in these wastewater treatment plants. According to present results, a large share of iodine based radiocontrast agents is being emitted in hospitals and X-ray practices (in individual cases depending on time the patient spends) or it might be specifically collected within the hours to come after application and treated separately. Therefore, as far as iodine based radiocontrast agents are concerned, particular priority is given to measures at the source, decentralized measures and “measures at patient level”. As far as iodine based radiocontrast agents are concerned, effective alternatives could be indicated which, in some cases, are already tested and prove to be cost-efficient (according to a preliminary assessment based on the possibility to recover iodine). The implementation of the most efficient required measures could be controlled by formulating minimum emission requirements or by creating incentive systems in the Rhine catchment states.
- **Centralized measures:** As far as iodine based radiocontrast agents are concerned, the possible reduction depends on the substance and the procedure is not considered to be very productive. It is estimated to < 10 to a maximum of 30 % (with respect to today’s discharges).
  The experience made in wastewater treatment plants in which further treatment procedures are used to remove micro-pollutants (e.g. ozonisation, activated carbon) must be collected and interpreted in order to be exploitable for future decisions.

8 E.g. Ort et al. (2009); Keller et al. (2007); Reemstma et al. (2006)

9 Singer, H., Huntscha, S., Hollender, J., Mazacek, J. 2008.

- **Adapt monitoring programmes:** Few representative data are available for metabolites of the radiocontrast agents and other (including non iodine based contrast) radiocontrast agents.
- **Adapt assessment systems:** Basic knowledge for the assessment of the radiocontrast agents mentioned in this report is good, this is however not true of other metabolites and other radiocontrast agents. So far, legislation has not taken into account radiocontrast agents. Assessment systems should be developed on an adequate institutional basis.

Annex I

Comparison of different wastewater treatment procedures in wastewater treatment plants

There are different results concerning the degradation/transformation of radiocontrast agents in wastewater by means of ozonisation. For the radiocontrast agent diatrizoate, the salt of the amidotrizoe acid, a 13 % "elimination" was achieved (TERNES ET AL., 2003). Another study stated a total degradation of only 10 % (FAHLENKAMP ET AL., 2006). However, non-ionic radiocontrast agents showed a distinctly better elimination (iopromid: 97 %, iopamidol: 50-60 %, iomeprol: 60 %) (FAHLENKAMP ET AL., 2006); Ternes et al. however only found an elimination of 0-36 % (TERNES ET AL., 2003). During the Poseidon project concerning the radiocontrast agents iopromid and iopamidol and using granulated active carbon in wastewater, an elimination of 50-90% was determined (TERNES ET AL., 2004); for diatrizoate, the elimination performance achieved varied between 10 and 50 %. During half-technical investigations in a wastewater treatment plant with an active carbon adsorption wave consisting of a fermenter and a sedimentation basin, distinct differences appeared: About 70 % of the non-ionic radiocontrast agents iomeprol, iopromide and iohexol were eliminated, hardly 50 % of iopamidol were eliminated and the ionic amidotrizoe acid was hardly eliminated (10 %) (METZGER ET AL., 2005, 2007 and 2007a, in: ISA/RWTH Aachen & IWW Mülheim, 2008).

During a recent, not yet published pilot test (BAFU, pilot test STEP Vidy Lausanne 2010) the average elimination rates of biological treatment, ozonisation and powdered activated carbon were determined for different iodine based radiocontrast agents and led to the following findings: (table 1)

Table 1: Results of the STEP pilot test

	Elimination Biology*		Elimination Ozonisation*		Elimination powdered activated carbon	
	Average	SD	Average	SD	Average	SD
Diatrizoate and iotalaminic acid**	**24%**	22%	**18%**	16%	**15%**	12%
Iohexol	**42%**	24%	**42%**	15%	**48%**	27%
Iomeprol	**28%**	24%	**44%**	13%	**50%**	25%
Iopamidole	**20%**	15%	**42%**	15%	**44%**	26%
Iopromide	**30%**	28%	**38%**	19%	**43%**	30%

* No real elimination, but a transformation of the iodine based radiocontrast agent

** Sum of diatrizoate and iotalaminic acid, as, within this study, not analytically distinguishable.

SD = Standard derivation

Apart from when using fresh powdered activated carbon, which may lead to "real" elimination, the different wastewater treatment procedures (biological treatment, membrane process, AF, ozonisation) always give rise to stable iodine-organic transformation products (see Kormos et al., 2010) which may get into the groundwater/drinking water or give rise to other problems. During the assessment of results, this must also be taken into account.

<u>Examination of the cost-effectiveness of the different procedures</u>

At present, cost-benefit analyses concerning the elimination of iodine based radiocontrast agents (and other substances) with further treatment procedures are being carried through in different wastewater treatment plants (hospital wastewater treatment plant Marienkirchen, Gelsenkrichen, urban wastewater treatment plant Bad Sassendorf, wastewater treatment plant Schwerte, wastewater treatment plant Hünxe; district hospital Waldbröl) in Northrhine-Westphalia (Mertsch, 2009, Teichgräber 2009). The results of these studies may be used for future decisions.

Annex II

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