“Chain approach to reduce pharmaceutical residues in water”

Abstract

The improvement of ambient water quality and the production of safe drinking water are the two main drivers for action on pharmaceutical residues in the Netherlands. An estimated total of 140 tonnes of pharmaceutical residues are discharged via sewage treatment plants into Dutch waters annually.

The issue of pharmaceutical residues is a ‘wicked problem’. Wicked problems are not easy to define and don’t have clear-cut solutions. They are characterised by scientific uncertainties, many stakeholders with different values and interests, and institutional complexity. Water pollution caused by pharmaceutical residues has all these characteristics. Wicked problems are best tackled via a multi-stakeholder approach.

From the beginning of 2016, a small project team led by the Ministry of Infrastructure and Water Management started designing the “pharmaceutical chain approach”, by undertaking an analysis of the whole pharmaceutical chain and the stakeholders concerned. As a next step, the ‘rules of the game’ (e.g. the prerequisites for the programme) were set:

- Patients must keep access to the medicines they need; medicines shall not be banned.
- All actions taken in the pharmaceutical chain should have a pragmatic approach and should be aimed at solving problems; measures for the sake of appearances will be avoided.
- All stakeholders act where they can, within acceptable costs.
- Stakeholders don’t wait for other stakeholders to take the first step.

Once the prerequisites of the programme were clear, possible measures were explored together with the stakeholders. By the end of 2016, a set of 17 possible measures to reduce, or mitigate the impacts of, pharmaceutical residues in water had been identified for further investigation. For each step in the pharmaceutical chain, measures have been proposed and evaluated. These steps are clustered in ‘development and authorisation’, ‘prescription and use’, and ‘waste and sewage treatment’.

Measures at the front end of the pharmaceutical chain will certainly help reduce the amount of individual medicines discharged to water. However, it was concluded that those measures cannot completely solve the problem. Measures at the back end of the chain – within the sewage treatment plants – will remain necessary. Measures at the source or end-of-pipe are two sides of the same coin and action at both ends of the pharmaceutical chain should be undertaken in parallel.

Since the start of the pharmaceutical chain approach programme in 2016, it has stirred up the topic in the Netherlands. As a result, the two ‘worlds apart’ of water and health care sectors have met, and are getting to understand each other’s position. However, the problem is not solved yet. As described above, the issue of pharmaceutical residues in water is a ‘wicked problem’ that won’t be tackled with one easy-to-execute-measure.

The challenge for the next years will be to take measures at all relevant places and levels, and to keep the attention, energy and enthusiasm that all stakeholders have shown. The focus should be on those measures that will have significant impact. Energy and funds should not be dedicated to measures that later turn out to be of little significance. This would not only be a waste of energy and public money, but will also lead to loss of support with the stakeholders.

A similar pragmatic approach in other European countries and at EU level would be welcomed, since the substances are discharged by people in all EU water sheds and the pharmaceutical chain does not end at the Dutch borders.

This paper is an excerpt from a case study, written for the OECD workshop on Contaminants of Emerging Concern in 2018.

Water quality in the Netherlands and pharmaceuticals

There are two main drivers for further improving the water quality in the Netherlands: aquatic ecology and the production of safe drinking water.

A driver for action: Aquatic ecology

Policy on water quality started in the Netherlands in the early 1970s, with the adoption of the 'Wet Verontreiniging Oppervlaktewateren' (WVO – Act on pollution of surface waters). At that time, many waters in the Netherlands were coloured black, suffering from a lack of oxygen due to the lack of wastewater treatment at cities and industries. During the decades to follow, many sewage treatment plants (STPs) and wastewater treatment plants at industrial sites (WWTPs) were built. By the 1990s, the problems with lack of oxygen were tackled, but concentrations of nutrients remained high, changing the colour from black to green. At present, still several waters are eutrophicated, but more and more waters are getting clear instead of green, and species of fish and macroinvertebrates have returned that haven't been observed for many decades. The species returning – especially the more sensitive ones – bring higher demands regarding concentrations of micro-pollutants. This calls for action to reduce concentrations of these compounds.

A driver for action: Safe drinking water

Another driver for action lies in the production of safe drinking water. Since methods for analysing substances in water improve, more and more substances are being detected, both in drinking water and in its sources. At the same time, consumers expect their drinking water to be absolutely free of contamination, even the smallest amounts. This gives a continuous pressure on drinking water companies to further reduce the amount of unnatural substances in their product. While, with the ageing population, the amount of used medicines will increase, and thus the amount of residues entering the water system also increases. Combined with the growing fluctuations in river discharge due to climatic changes, public and political concerns regarding pharmaceutical residues (and other CECs) in water are rising.

Pharmaceutical residues: analysis of impacts, pathways and sources

From the beginning of this century, several reports have been published that picture the presence and effects of pharmaceutical residues in the aquatic ecosystem. In 2002, the Dutch LOES-report (Landelijk Onderzoek oEstrogene Stoffen – Estrogens and xeno-estrogens in the aquatic environment of the Netherlands, Vethaak 2002) described the endocrine disruption caused by domestic sewage discharges. In later years, the findings were confirmed by other studies, both national and international, such as the BOI IS report on the environmental risks of medicinal products (Mudgal, 2013). Scientific interest in this topic is still increasing. In 2016, the RIVM (the Dutch National institute for public health and the environment, Moermond 2016) confirmed in a study reviewing national and international findings, that pharmaceutical residues form a risk for the Dutch aquatic environment. Pharmaceutical residues may cause tissue damage, endocrine disruption and behavioural effects in organisms, and pose risks for the production of drinking water.

Almost all pharmaceutical residues in sewage water originate from medicines that have been taken by patients and are being excreted in the toilet. Only a minor part reaches the sewage system after being washed down the sink or toilet. Several studies show that about 90% of the total pharmaceutical load originates from households, while only 10% is discharged from hospitals and nursing homes (e.g. Mudgal, 2013). RIVM (Moermond, 2016) found that at least 140 tonnes of pharmaceutical residues are discharged via STPs into the Dutch waters every year. In addition, approximately 30 tonnes of x-ray contrast media are discharged by STPs each year.

Water quality and pharmaceuticals: A 'wicked problem'

The issue of pharmaceutical residues is defined as a 'wicked problem' by the University of Utrecht (Hartmann 2015). Wicked problems are not easy to define and don't have clear-cut solutions. They are characterised by scientific uncertainties, many stakeholders with different values and interests, and institutional complexity. Water pollution caused by pharmaceutical residues has all these characteristics. Although several reports and articles have been published on the impacts of pharmaceutical residues on aquatic ecosystems and drinking water production, there still are

questions regarding the severity of the problem. Many stakeholders are involved, ranging from producers and the health care sector, to the water and drinking water sectors, on an international, national, as well as on a local level. The actors all have their own vision on the problem, have different interests, and could play different roles in possible solutions. The issue touches upon several policy areas that are fostered by different governmental institutions (both national and international) which illustrates the institutional complexity.

Although the perception of the problem differs among stakeholders, each one of them has an interest to meet. It was recommended for a 'wicked problem' like the pharmaceutics case, to design an approach together with the stakeholders in terms of interest, and to avoid discussions about the differences in problem definition. Although each stakeholder has a role to fulfil, the most important role lies with the ministry of Infrastructure and the Environment: this ministry should take the lead in facing the issue of pharmaceutical residues in water.

Policy response

From the beginning of 2016, a small project team led by the Ministry of Infrastructure and Water Management started designing the pharmaceutical chain approach. The project team consisted of representatives from the Union of Regional Water Authorities, the Association of Drinking Water Companies, the Ministry of Health, Welfare and Sport, and research institutes. The Ministry of Agriculture, Nature and Food Quality was closely involved because of veterinary pharmaceuticals[1].

The chain approach is a multi-stakeholder programme that worked along five steps:

1. form a small project team with each stakeholder represented;
2. make an analysis of the whole chain and involve the stakeholders in this analysis;
3. agree on the 'rules of the game' (prerequisites for action);
4. explore possible actions;
5. choose promising measures and make an implementation plan (current status).

Analysis of the pharmaceutical chain

The team started with getting an overview of the stakeholders involved and exploring their interests. For IenM, this meant setting off on an expedition to the unknown territories of health care. It quickly became clear that stakeholders were unfamiliar with each other's worlds, and viewpoints existed that would not help in tackling the problem. This inventory phase ended with picturing the pharmaceutical chain (below, figure 1).

[1] This paper focusses on medicines for human use, since during the process it turned out that for veterinary pharmaceuticals, stakeholders are different and thus a different approach should be taken.

Figure 1: the pharmaceutical chain – including stakeholders involved (visualisation by JAM visual thinking[2])

The picture shows the pharmaceutical chain with its actors on the arrow, surrounded by the stakeholders. The pharmaceuticals itself are pictured in orange.

The pharmaceutical chain starts (bottom left in the picture) with the development of medicines at research institutes and pharmaceutical companies. In this process, many substances are being reviewed, and after 10-15 years, a new medicine might be ready for registration. In the second step (far left), a marketing authorisation is applied for; a process in which the medicine is thoroughly assessed by the authorising authority, both for effectiveness and safety. Once the marketing authorisation of a medicine is approved, it can be produced and distributed. In the next step (middle of the chain), the patient gets the medicine, either at the hospital, at the pharmacy by prescription of a doctor, or at the pharmacy or drugstore without a prescription ('over the counter' medicines). Pharmaceutical residues leave the patient's body in its original form or as metabolites, and end up in the sewer system. This is the most important route to the aquatic environment. A small part of the medicines remains unused or gets outdated and is thrown away in the garbage bin or collected at the pharmacy. An even smaller part gets washed down the drain (fluid medicines) and also finds its way to the sewer. In the last part of the pharmaceutical chain (right side), sewage is treated at the STP, where on average 65% of the medicines are removed. As stated before, in the Netherlands at least 140 tonnes of pharmaceutical residues are discharged to the environment after this step. When producing drinking water, very small amounts of medicines pass the filtration process and end up in drinking water (NB: as a rule of thumb, one has to drink the equivalent of Olympic pools to reach the medicine amounts of individual pills[3]).

Rules of the game

The pharmaceutical chain picture was discussed in the Working Group on Medicines – in which stakeholders from the whole chain are represented – after which the working group agreed upon the basic prerequisites for any possible action:

- Patients must keep access to the medicines they need; medicines will not be banned.
- All actions taken in the pharmaceutical chain should have a pragmatic approach and should be aimed at solving problems; measures for the sake of appearances will be avoided.
- All stakeholders act where they can, within cost constraints.
- Stakeholders don't wait for other stakeholders to take the first step.

[2] www.jamvisualthinking.com

[3] An Olympic pool contains 2.500 m3. Pharmaceutical residues are found in Dutch drinking water in the range of 10-50 ng/l (Moermond, 2016). So, in order to reach a dose of 100 mg one has to drink at least 8 pools.

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Possible measures in the pharmaceutical chain

Once the rules of the game had been set, possible measures were explored together with the stakeholders. By the end of 2016, a set of 17 possible measures (Table 1) had been identified for further development. For each step in the pharmaceutical chain, measures have been proposed and evaluated. These steps for intervention are clustered in 'development and authorisation', 'prescription and use', and 'waste and sewage treatment' (see figure 2 below). At this moment, the 17 measures are being further developed. The effectivity of individual measures and the cost-benefits are being evaluated. In this paper, we will discuss a number of arguments that were used in the evaluation and give a few examples of promising measures.

Table 1: First inventory of possible measures to reduce medicine residues in freshwater. NB: several measures were dropped after evaluation.

Possible measure	Intervention point in the pharmaceutical chain	Sector responsible
Identify pharmaceuticals that have negative environmental effects	Environmental effects	Water authorities and drinking water sector
Identify effects of veterinary pharmaceuticals in water	Environmental effects	Water authorities
Quantify emissions of veterinary pharmaceuticals to surface water and groundwater	Environmental effects	Several (new chain)
Development of 'green medicines' that have less environmental impact	Development & authorisation	Pharmaceutical companies and research institutions
Management system for environmental risks of medicines (Eco Pharmaco Stewardship)	Development & authorisation	Pharmaceutical companies
Access to (environmental) data on active ingredients	Development & authorisation	Pharmaceutical companies, authorising agencies, (international) authorities
Identify pairs of pharmaceuticals with same medic effect, but different environmental impact	Prescription & use	Several; lead by Ministry of Water Management
Prevention and adequate use of pharmaceuticals	Prescription & use	Ministry of Health
Identify possible measures in the phase of 'prescription and use'	Prescription & use	Health care sector and water sector together
Collection of surplus pharmaceuticals	Waste & sewage treatment	Municipalities and chemists
Development of improved treatment of sewage at STP's, including overview of existing innovative treatment and overview of costs	Waste & sewage treatment	Water authorities and research institutions
Identify STP's with highest impact on aquatic ecology and drinking water sources	Waste & sewage treatment	Water authorities
Start pilots with improved treatment at existing STP's	Waste & sewage treatment	Water authorities and research institutions
Develop communication instrument to explain the pharmaceutical chain	Cross cutting issues	Ministry of Water Management
Develop communication strategy and execute	Cross cutting issues	Lead by Ministry of Water Management
Learn from the best practices abroad	Cross cutting issues	Lead by Ministry of Water Management
Put issue on international agenda (e.g. river basin commissions of Rhine and Meuse, European Commission, others)	Cross cutting issues	Lead by Ministry of Water Management

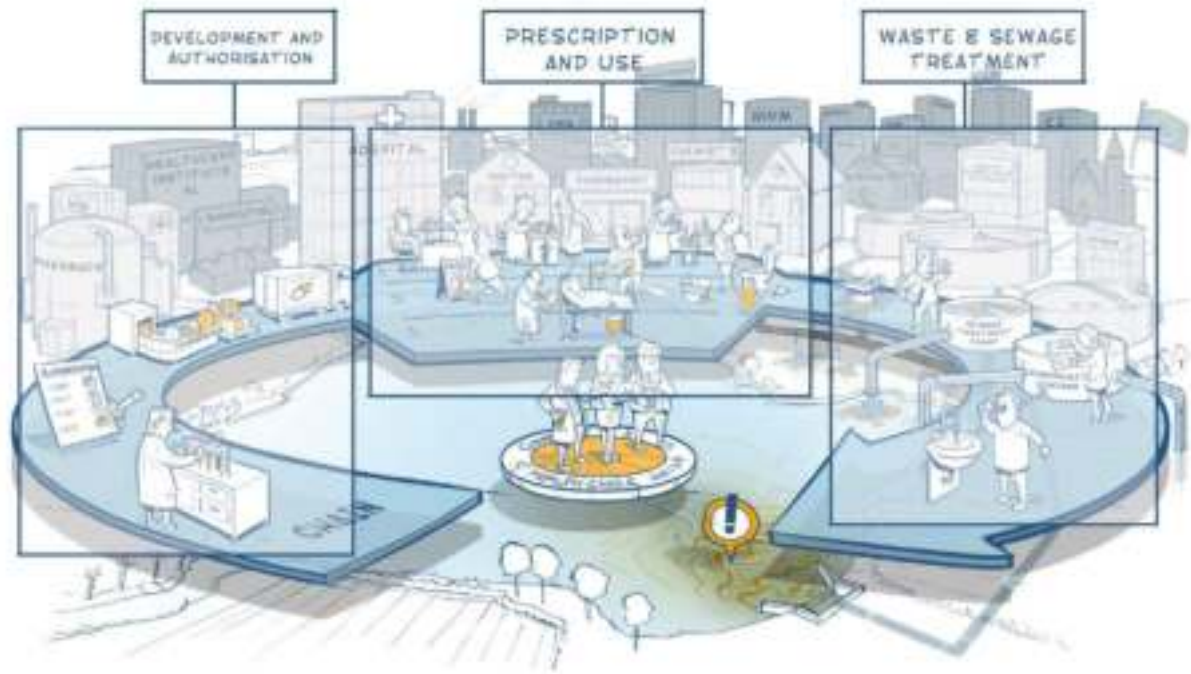

Figure 2: clustering of possible intervention points in the pharmaceutical chain (JAM visual thinking)

On November 16th 2016, the set was part of the formal declaration on the Dutch Delta-approach for Water Quality and Fresh Water Supply. This declaration was developed in order to boost Dutch water quality policies (not limited to pharmaceutical residues) and was signed by the minister of IenM together with representatives of regional and local authorities, and stakeholders from agriculture, health care, drinking water, environmental and nature conservation NGOs, and research institutes. Amongst them were ten stakeholders from the health care sector and pharmaceutical industry.

Measures at the source vs. end-of-pipe measures

The first question when discussing measures in the pharmaceutical chain, is whether the initiative for action should lie within the health care sector (at the source), or within the water sector (end-of-pipe). Underlying issues regard the question who is responsible for the problem and it's solution, and who should pay for those solutions.

In the process of developing the pharmaceutical chain approach, the Dutch health care sector showed that they already do a lot to make efficient use of medicines, although not for environmental arguments, but because of patient's health and reducing costs of the public health care system. The Ministry of Health, Welfare and Sport runs several programmes to improve the health of Dutch citizens in general, to improve the cost-efficiency of the public health system, and to reduce the risk of antibiotic resistance. The effect of these programmes is that – compared to other European countries – Dutch doctors prescribe relatively few medicines, and the Netherlands is front runner globally when it comes to low prescription of antibiotics.

Despite of this, in the phase of 'prescription and use' still two other measures were identified that could further reduce the medicine load to water. The first promising measure is that doctors and chemists should be better informed about the negative effects of washing down medicines through the sink. It turned out that people in the health care sector think that washing away surplus medicines, is an environmental friendly way of disposal. Since good ways of disposing medical waste already exist (e.g. protocols in hospitals to dispose of solid waste), this measure is relatively easy to implement. The second measure would be to prevent x-ray contrast media from getting discharged via the toilet. These substances are used in high dosages, they are inert and very mobile. This makes them hard to remove from drinking water sources. A pilot project in a Dutch hospital showed that patients are often willing to use disposable urine-bags during the time it takes for the contrast media to leave their body (typically within one day).

In the phase of 'development and authorisation', it was concluded that better assessment of potential environmental effects of medicines could help the water sector (both water managers and drinking water companies) to better monitor the effects in water. At this moment they often don't know which substances to analyse. Although the possibility of developing 'green medicines'[4], or more readily degradable medicines, is often mentioned, the expectations for this measure remains relatively low. This is on one hand because the development time is long (10-15 years), on the other hand because medicines often are designed to be non-biodegradable (or slowly biodegradable) by nature, in order to obtain steady concentrations in the human body, that forms a hostile environment to alien substances like medicines.

Although measures at the front end of the pharmaceutical chain will help reduce the amount of individual medicines discharged to water, it is concluded that those measures cannot completely solve the problem. Measures at the end of the chain – within the STPs – will remain necessary due to the necessity of medicines for human health and wellbeing. Although this might be a logical conclusion, water authorities managing STPs have the fear that such a conclusion would lead to the unrestrained discharge of medicines and other pollutants to the sewer. The example of 'wastewater policies' in the Rotterdam harbour might however solve this dilemma. In Rotterdam, an industrial complex hosted several chemical plants that all had their own wastewater treatment system, while the complex itself had its own treatment plant via which all wastewater was discharged into the river. This central treatment plant regularly malfunctioned because of discharges from one of the other systems, and, as a result, regularly discharged heavily polluted water into the river. To solve this, it was agreed to perform the treatment of wastewater according to the following principles:

1. Substances unique to one (or a few) individual plant(s) are to be treated at that particular plant(s). There, the substance concentrations are high because they are not diluted, which makes treatment easier and cheaper.
2. Substances discharged by the majority of the plants, are to be treated at the central treatment plant. In this way, only one treatment plant has to be equipped with the specific treatment method.
3. Every plant avoids discharges where possible. For example, in the past it was common use to wash away spills, leading to peaks in the discharges. From now on, such spills are to be absorbed with absorbing media first, and then to be removed with the dry waste. This means less peaks and less operational costs for the wastewater treatment systems as a whole.

Applying this method of reasoning to the medicine case, would lead to a situation where:

- the use and discharge of medicines is reduced as much as possible, e.g. via the measures described above,
- the major dischargers of medicines treat their own sewage with specific methods, e.g. separate treatment for hospitals,
- the many discharges of households is being treated centrally at the STP with an extra purification step.

In this way, source-directed and end-of-pipe measures can be implemented at the same time.

Currently, the Dutch regional water authorities are performing a hotspot analysis to evaluate which STPs might deserve an extra purification step from the viewpoint of aquatic ecology and production of drinking water. It is expected that this will be limited to a relatively small number of treatment plants, because of the size of the STP, the size of the surface water system they discharge into, or the location of drinking water intake points.

Programme outcomes

Since the start of the programme in 2016, the pharmaceutical chain approach has stirred up the topic in the Netherlands. As a result, the two 'worlds apart' of water and health care sectors have met, and are getting to understand each other's position. However, the problem is not solved yet. As described above, the issue of pharmaceutical residues in water is a 'wicked problem' that won't be tackled with one easy-to-execute-measure.

[4] The term 'green medicines' refers to pharmaceuticals with little or no environmental impact, and often is actually meant 'readily degradable medicines'

The challenge for the next years will be to take measures at all relevant places and levels, and to retain the attention, energy and enthusiasm that all stakeholders have expressed so far. The focus should be on those measures that will have significant impact. Energy and funds should not be dedicated to measures that later turn out to be of little significance. This would not only be a waste of energy and public money, but will also lead to loss of support with the stakeholders.

A similar pragmatic approach in other European countries and at EU level would be welcomed, since the substances are discharged by people in all EU water sheds and the pharmaceutical chain does not end at the Dutch borders. Operating in isolation would be just 'banging one's head against a brick wall', which could lead to an unwanted increase in the use of medicines.

Literature:

Hartmann, D. et al, Rapport 'Geneesmiddelen in het milieu' – visies van stakeholders in kaart gebracht. (*Pharmaceuticals in the environment – visions of stakeholders being mapped*) Young Innovators League, Utrecht University, 2015.

Moermond et al., Geneesmiddelen en Waterkwaliteit. (*Pharmaceuticals and water quality*) RIVM, Bilthoven, 2016.
http://www.rivm.nl/Documenten_en_publicaties/Wetenschappelijk/Rapporten/2016/oktober/Geneesmiddelen_en_waterkwaliteit

Mudgal, S. et al, Study on the environmental risks of medicinal products FINAL REPORT. BIO Intelligence Service, December 2013

Vethaak, A.D. et al, Estrogens and xeno-estrogens in the aquatic environment of the Netherlands Occurrence,Potency and Biological Effects. RIZA/RIKZ-report no. 2002.001, February 2002.

Abbreviations:

BOGIN	Dutch generic and Biosimilar medicines association
CBG	Medicines evalutation board
CEC	Chemicals of emerging concern
EZ	Ministry of economic affairs
IenM	Ministry of infrastructure and the environment (name until October '17)
IenW	Ministry of infrastructure and water management (name since October '17)
IVM	Institute for Rational Use of Medicine
KNMP	Royal Dutch Pharmacists Association
NHG	Dutch College of General Practitioners
RIVM	National institute for public health and the environment
STP	Sewage treatment plant
Vewin	Association of drinking water companies in the Netherlands
VIG	Association Innovative Medicines
VNG	Association of Netherlands Municipalities
VWS	Ministry of health, welfare and sport
WVO	Act on pollution of surface waters
WWTP	Wastewater treatment plant