1. Huize Aarde

Stichting Huize Aarde ("Home Earth") in Enschede, The Netherlands is founded in 1992 in order to strengthen social responsibility in research, policy, management, production and consumption.

The activities of this foundation focus on:



- a) design and application of new concepts, such as Green Healthcare, Green Hospitals, Green Chemistry and Green Pharmacy;
- b) development and introduction of new methods for an integrated approach to these issues;
- c) encouraging cooperation between groups, disciplines and sectors concerned.

The framework of these activities are objectives of the United Nations Agenda for Sustainable Development in the 21st Century (Agenda 21). From 2000 on Huize Aarde has worked for a more sustainability oriented healthcare.

2. The hazardous environmental cycle of pharmaceuticals and multi-resistant bacteria

During a treatment with antibiotics, humans and animals excrete these substances more or less transformed, together with intestinal bacteria that became resistant to the antibiotics. Conventional biological wastewater treatment plants remove the antibiotics only partially. According to several studies these plants reinforce the spreading of the antibiotic resistance by horizontal transfer of resistance genes between bacterial species. As a consequence, antibiotics and multi-resistant bacteria, including their plasmids with exchangeable resistance genes, are found in all environmental media on a global scale. Humans and animals come into contact with these contaminants via food, drinking water, air and swimming in contaminated water. To get a better picture of the risk that society runs by this environmental cycle, first of all, an

overview is required of all environmental routes of contact, see figure 1.

Many types of pharmaceuticals & multi-resistant bacteria from various sources

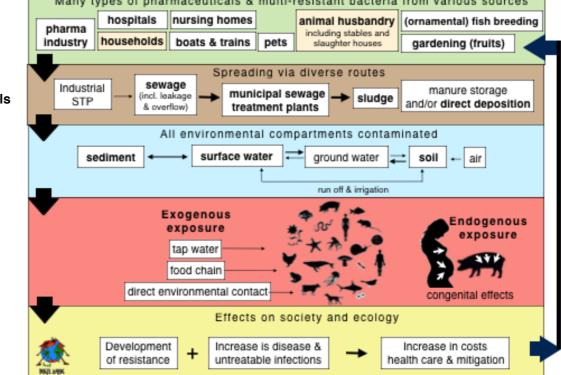


Figure 1. Environmental cycle of pharmaceuticals and resistant bacteria Exposure to emitted antibiotics and multi-resistant bacteria is widespread. Research by Radboud University Nijmegen, The Netherlands, reveals that across Europe adults and children are constantly exposed through drinking water and locally produced food to antibiotics, see figure 2a and 2b. This prolonged emission of antibiotics and multi-resistance to the environment, means that humans and animals are continuously exposed to existing and new resistance types (Gullberg E. et al. 2011).

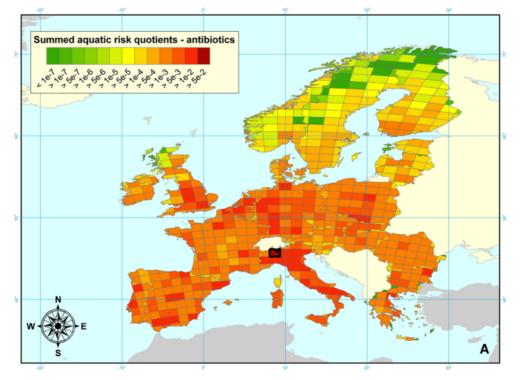
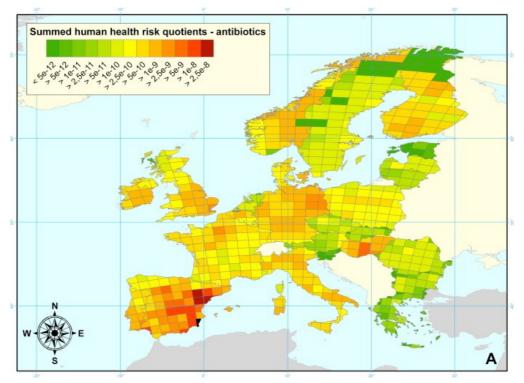




Figure 2b. Relative risk of antibiotics in locally produced food, Oldenkamp R. et al. 2013



The environmental cycle of and exposure to these chemical and biological contaminants will be strengthened by climate change (periods of prolonged droughts that concentrate the contamination) and by peaks in rainfall (causing regular flooding that disperse the contamination). Avoiding this contamination not only has health benefits. An added advantage of cleaner soil and water is favorable for agriculture; it also reduces costs for drinking water production; and is beneficial for (water)tourism.

2. Proposed actions

To introduce this issue in the Healthcare agenda, Huize Aarde designed the Green Healthcare Program. Within this Program three complementary hand-on approaches are developed: Hospitales Verde (Green Hospitals); MEDUWA (MEDicines Unwanted in WAter); and SOSPharmaH (Source Oriented Solutions for Pharma-pollution by Hospitals).

2.1. Green Healthcare Program

To avoid the hazardous environmental cycle of pharmaceuticals and multi-resistant bacteria and other precarious emissions from the healthcare practice, measures are required urgently. Being aware that, in general, campaigns have a short time impact, Huize Aarde: a) introduces broad concepts such as Green Healthcare; Green Chemistry and Green Pharmacy in healthcare institutes; b) develops projects that are part of existing institutional programs for quality management or socially responsible management; c) involve different actors of the water and medicine chain, as well as students from a number of universities, to promote regional and international collaboration in the search of effective and affordable measures.

2.1.1. Hospitales Verdes

Hospitales Verdes (Green Hospitals) is a collaboration between hospitals in South America (Venezuela and Colombia) and The Netherlands to encourage sustainability orientated management and to introduce measures to protect workers' safety as well as water, soil and air quality.

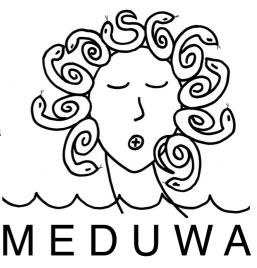




Figure 3. Exchange of experiences between Colombian, Venezuelan and Dutch hospitals, Maracaibo Venezuela 2001.

2.1.2. MEDUWA (MEDicines Unwanted in WAter)

At present, the EU INTERREG-VA-project MEDUWA-Vecht(e), a large cross-border German/Dutch consortium of universities, companies, governmental and non-governmental organizations, operates within a shared river basin to address a common problem. That is the environmental cycle of human and veterinary pharmaceuticals and multi-resistant bacteria (including their mobile plasmids) that are transferred via drinking water, food and air back to humans and animals.



This environmental cycling of chemical and biological contaminants is expected to be intensified by climate change. Putting a stop to this cycle not only brings benefits to the health of humans and animals. It makes the local meat producing based economy less vulnerable to increasingly critical consumers and more stringent international legislation. In addition, cleaner soil and water lowers drinking water production costs and is also beneficial for tourism, especially water recreation in the area.

The MEDUWA-coalition works on innovative and complementary activities that visualize, communicate and simulate proposed measures to prevent and mitigate this contamination, see diagram 1.

WP	product	prevention	mitigation	measuring	visualisation communication
1.1	Watershed info system				
1.2	Gray water footprint				
1.3	Risk assessment				
2.1	Automatic in-situ monitoring				
2.2	Wireless water monitoring				
2.3	Nanofiltration				
3	PAW oxidation				
4.1	Phytoremediation				
4.2	Herbal antibiotic replacement				
4.3	Algal antibibiotic replacement				
5	Wireless cattle monitoring				
6	Biopharmaceuticals				

Diagram 1. The seven activity classes of MEDUWA

Short description of the MEDUWA-activities:

- application of a GIS-tool to support decision makers for effective, evidence-based and affordable solutions, and for communication to the media. This tool visualizes emitted quantities, concentrations, and the spreading of resistant bacteria under different climate scenarios and measures;
- b) determination of the spreading of patterns of multi antibiotic resistant Extended Spectrum Beta-Lactamase (ESBL) and multi antibiotic resistant E. coli (ARE) through the whole water cycle (from households, hospitals, nursing homes and farms to drinking water);
- c) determination of the amount of water that is polluted with antibiotics and multi-resistant bacteria by in- and outward patients and livestock during treatment with antibiotics (Gray Water Footprint);
- d) assessment of the relative risks of contamination of water, soil, food and air by antibiotics and multi-resistant bacteria for humans (especially fetuses and children) and animals.
- e) development of a sensitive 24/7 continuos water monitoring;
- f) development of innovative methods of treatment: point-of-care plasma activated water treatment, nano-filtration of sewage and drinking water, and phytoremediation (cleaning with herbs of soil and water contaminated with antibiotics);
- g) development of preventive measures: automatic monitoring of livestock to avoid the use of antibiotics and other medicines, the development of bio-pharmaceuticals, and replacement of antibiotics with herbs and algae.

2.1.3. SOSPharmaH (Source Oriented Solutions for Pharma-pollution by Hospitals)

The project SOSPHarmaH is complementary to MEDUWA and aims at reducing the emission of pharmaceuticals like antibiotics and multi-resistant bacteria/viruses by in- and outward patients (> 90% of these emissions is excreted by outpatients).



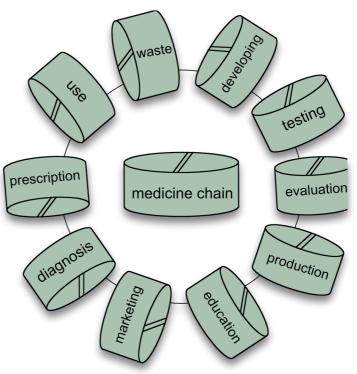
Because the hospital is an important link in the medicine chain, it can play an important role in socially responsible use of medicines. During the project, experts from various disciplines and institutions collaborate with hospitals in order to achieve a broad range of complementary behavioral and technical source oriented measures. From 2014 on the project has been running in University Medical Centre Utrecht (UMCU) under the name "Groene Farmacie" (Green Pharmacy). Main topics at the UMCU are: awareness raising; lowering wastage of medicines; monitoring of sewage; replacement of less environmentally friendly pharmaceuticals; adsorption of pharmaceuticals after toilet use.

3. Methodology

The methodology of Huize Aarde to lower emissions of pharmaceuticals such as antibiotics and multi-resistant bacteria is summarized as follows:

- a) To design projects, such as MEDUWA, SOSPharmaH and Green Hospitals, with common goals, e.g.: UN Agenda for Sustainable Development in the 21st Century (Agenda 21);
 Corporate Social Responsibility management (ISO 26000); EU Third health Program; FAO/ WHO/OIE, Global Action Plan Antibiotic Resistance.
- b) The setting up of an interdisciplinary and inter-sectoral network between research institutions, governmental and non-governmental organizations, as well as regional umbrella organisations and enterprises, each with a different role in the coalitions. In the case of pharma-pollution a chain approach is pursued where the entire medicine chain (from the developer, prescriber, user, to the water technologist) is involved to prevent the use of pharmaceuticals and/or to stop emissions (Green Pharmacy), see figure 3.

Figure 3. At different levels of the medicine chain actions are taken to avoid or lower emissions. This approach is called Green Pharmacy.



- c) For extensive communication use is made of existing communication channels of partners. GIS-tools are applied for communication to the public and to support decision making on effective and affordable measures. Also publications are prepared for journals.
- d) By giving room to project partners and their colleagues to formulate their own options for action, participants develop a feeling of ownership of the problem and its solution. This ownership guarantees structural and sustainable changes in managing the issue.

4. Results

4.1 Green Healthcare Program

The Province of Overijssel has chosen the Green Healthcare Program for being an exemplary project because of its interdisciplinary approach and its impact on policymaking. See the next link for a summary of the initiatives taken and the results achieved: <u>http://www.groenegezondheid.nl/</u> <u>link.php?title=pharmapollution_NL</u>

4.2. Hospitales Verdes (Green Hospitals)

For results see <u>http://www.groenegezondheid.nl/link.php?title=green_hospitals</u>. This initiative was nominated in 2006 by eight Dutch Ministries, as a good example of innovative international cooperation.

4.3. MEDUWA

If the mitigation measures listed under §2.1.2. (nano-filtration or plasma-activated treatment of sewage and drinking water; phytoremediation; automatic monitoring of livestock; replacement of antibiotics) are developed and applied in the whole watershed, contamination with pharmaceuticals and multi resistent bacteria will be lowered considerably.

Up till now MEDUWA has changed the role of regional water authorities from problem bearer into problem sharer, and changed the role of the health sector from problem maker into problem solver:

a) The regional water authority, Waterschap Vechtstromen (Almelo, NL) and the regional union of pharmacists (KNMP Oost NL) have gathered and compared data on medicine use and their environmental concentrations, to identify the most problematic molecules;

b) Waterschap Drents Overijsselse Delta (Zwolle, NL) together with a group of local physicians of the city of Meppel started a project to replace diclofenac by the less hazardous painkiller naproxen; c) The national union of regional water authorities (Unie van Waterschappen, The Hague) in consultation with Huize Aarde has incorporated the chain approach of Green Pharmacy in their strategy. Subsequently, the representative of EU national water authorities, EUREAU, has adopted the same strategy;

d) The approach, network and results of MEDUWA will be used in the EU INTERREG-VA EurHealth-1Health project (2016-2019) on infection prevention, of the University Medical Centre Groningen and their Dutch and German partners.

- e) Huize Aarde has been invited to present the MEDUWA-approach in the following events:
- Transnational Action Program on Emerging Substances (TAPES), Final Conference, Brussels 2015.
- Third International Conference on Sustainable Pharmacy, DBU Osnabrück, Germany, 2012.
- Seminar Medicines in Waste Water, Univ. Med. Centre Groningen, NL 2015.
- Kick-off conference of INTERREG projects EurHealth-1Health and Health-i-care, UMCG, 2016.

4.4. SOSPharmaH

The University Medical Centre Utrecht (UMCU) has adopted the SOSPharmaH approach, added its own sub-projects and is preparing other sub-projects. Also, the University hospitals UMC Groningen and Radboud UMC Nijmegen are preparing similar projects. Outside of Europe, the SOSPharmaH approach has drawn attention: in Colombia a number of university hospitals, and the Ministries of Health and of the Environment are preparing similar projects.

Leaflet of the project Green Pharmacy, Utrecht University Medical Centre, 2015

Houd medicijnen uit het milieu Medicijnen over of houdbaarheidsdatum verlopen? Lever ze in bij de apotheek of het gevaarlijk afvaldepot in uw gemeente	Project Groene Farmacie				
Spoel ze NOOIT door de gootsteen of het toilet!	Het project Groene farmacie is één van de vijf icoonprojecten van het UMC Utrecht om onze duurzaamheidsambitie concrect en zichtbaar te maken. Met het project Groene				
Want wist u dat: Mant wist u dat: Medicijnen veelal via de gebruiker in het rioolwater terecht komen, het overgrote deel via de huishoudens en een klein deel via de ziekenhuizen? De Nederlandse rioolwaterzulveringsinstallaties deze medicijnresten niet voldoende	Farmacie wil het UMC Utrecht bijdragen aan het beperken van de verontreiniging van water, lucht en voedsel door medicijnen. Dit doen we door: • Verspilling van medicijnen te voorkomen				
uit het afvalwater kunnen halen? Per jaar zo'n 25.000 kilo medicijnen in het oppervlakte water terecht komt en ook nog eens 65.000 kilo via de rivieren ons land binnen komt? De meeste medicijnen in het milieu slecht en onvoiledig afbreekbaar zijn wat negatieve gevolgen kan hebben voor het milieu en de gezondheid van mens en	 Bewustwording en betrokkenheid te vergroten Proeftuin te zijn voor pilots met zuiveringstechnieken Bij te dragen aan het toegankelijk maken van de beschikbare kennis en indien mogelijk te klezen voor minder schadelijke medicijnen. 				
dier? Sommige medicijnen zoals antibiotica in het milieu de resistentie van bacteriën kunnen vergroten? Er al sporen van medicijnen zijn aangetroffen in drinkwater en voedsel?	In dit project werkt het UMC Utrecht samen met de Universiteit Utrecht, Stichting Huize Aarde, Milieuplatform zorg, RVM, KWR Water Research Institute, Deltares, Hoogheemraadschap "De Stichtse Rijnlanden".				
In Nederland jaarlijks ruim vier miljard Euro aan medicijnen wordt uitgegeven, waarvan voor meer dan 100 miljoen Euro wordt weggegooid en van de helft van de niet gebruikte medicijnen onbekend is wat ermee gebeurt?	Wat doen we al?				
Een deel van de ongebruikte medicijnen onder bepaalde voorwaarden op verpleegafdelingen weer opnieuw uitgegeven kunnen worden waarmee grote milieuvoordelen en kostenbesparingen te behalen zijn?	Het UMC. Utrecht heeft sinds 2013 ruim drie miljoen Euro bespaard door een verbeterde uitgifte- en retoursystematiek van geneesmiddelen. Twee promovendi van het UMC Utrecht en de Sint Maartenskiliniek in Nijmegen, Niels Vileland en Charlotte Bekker onderzoeken het mogelijk opnieuw uitgeven van ongebruikte (dure) medicatie. Het UMC Utrecht wil een pilot gaan uitvoeren met absorptiemiddel in toiletpapier om te voorkomen dat medicijnen in het milieu komen.				
EUS UMC Utrecht	te voorkomen dat medicijnen in net milieu komen.				

5. Conclusions

After becoming aware of the complexity of the issue, the different sectors involved discovered that each sector is not in a position to solve the problem by itself. However, (semi-)governmental institutes that are responsible for giving effective solutions to issues like the dispersion of pharmaceuticals and multi-resistance in the environment are, unfortunately, restrained by short-term priorities.

During the development and implementation of MEDUWA and SOSPHarmaH, it is observed that the influence of a small NGO is important for the dissemination, scheduling, and handling of the issue. The independency and flexibility of a small NGO like Huize Aarde make it possible to bring together key people from various organisations of different sectors speedily, thereby sharing their knowledge, experience, responsibility, influence, and power of decision making with a common goal, the solution to the threat of the environmental cycle of harmful substances and multi-resistant bacteria.

6. Recommendations

- In order to solve social dilemmas such as the serious threat to health by antibiotics, a shared vision and more integration of policies on human and animal health and the environment are needed.
- The broad concepts of Green Healthcare, Green Chemistry and Green Pharmacy need more attention for an integrated management of the topic.
- More recognition and financial support of civil society in their effort for the transition to a sustainable society.

7. EU added value

Huize Aarde:

- · concretizes the objectives of the EU Health Programmes into hands-on projects;
- stimulates innovation in methods and techniques by the elaboration and introduction of the new concepts Green Health, Green Chemistry and Green Pharmacy;
- works on cross-sector and cross-border collaboration to integrate regional, national and international policies and programs;
- develops approaches that can be exported to other regions inside and outside the EU.