Coalition Clean Baltic
FOR PROTECTION OF THE BALTIC SEA ENVIRONMENT

Pharmaceutical Pollution in the Baltic Sea Region

SUMMARY

October 2017

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Read the full report at www.ccb.se/Evidence2017/CCB_pharmaceuticals_report_2017.pdf

Life

NATUR VÅRDS VERKET

Swedish Agency for Marine and Water Management

Executive Summary

Hundreds of different active pharmaceutical compounds are being discovered in waterways around the world. A significant concern is increasing among various stakeholders about the potential harm for the human health and the environment.

The pharmaceuticals are released into the environment during production process with the wastewater discharge of pharmaceutical companies, with municipal wastewaters, where they appear as a result of natural excretion by humans, and in cases of improperly handled pharmaceuticals waste (flushing it into the sewage or discarding obsolete drugs into the household waste). Not all European citizens have information about how to dispose of unwanted or obsolete medicines safely, and often use toilet, sink and household waste as common disposal practices for pharmaceuticals.

Pharmaceuticals also enter the environment via agri- and aquacultural veterinary practices. Medicinal products can directly enter the environment through feed surplus, notably in the case of aquaculture (Figure 1).

Nowadays we have a large number of studies about presence of pharmaceuticals in all components of the environment, but the contribution of each source has not been evaluated sufficiently.

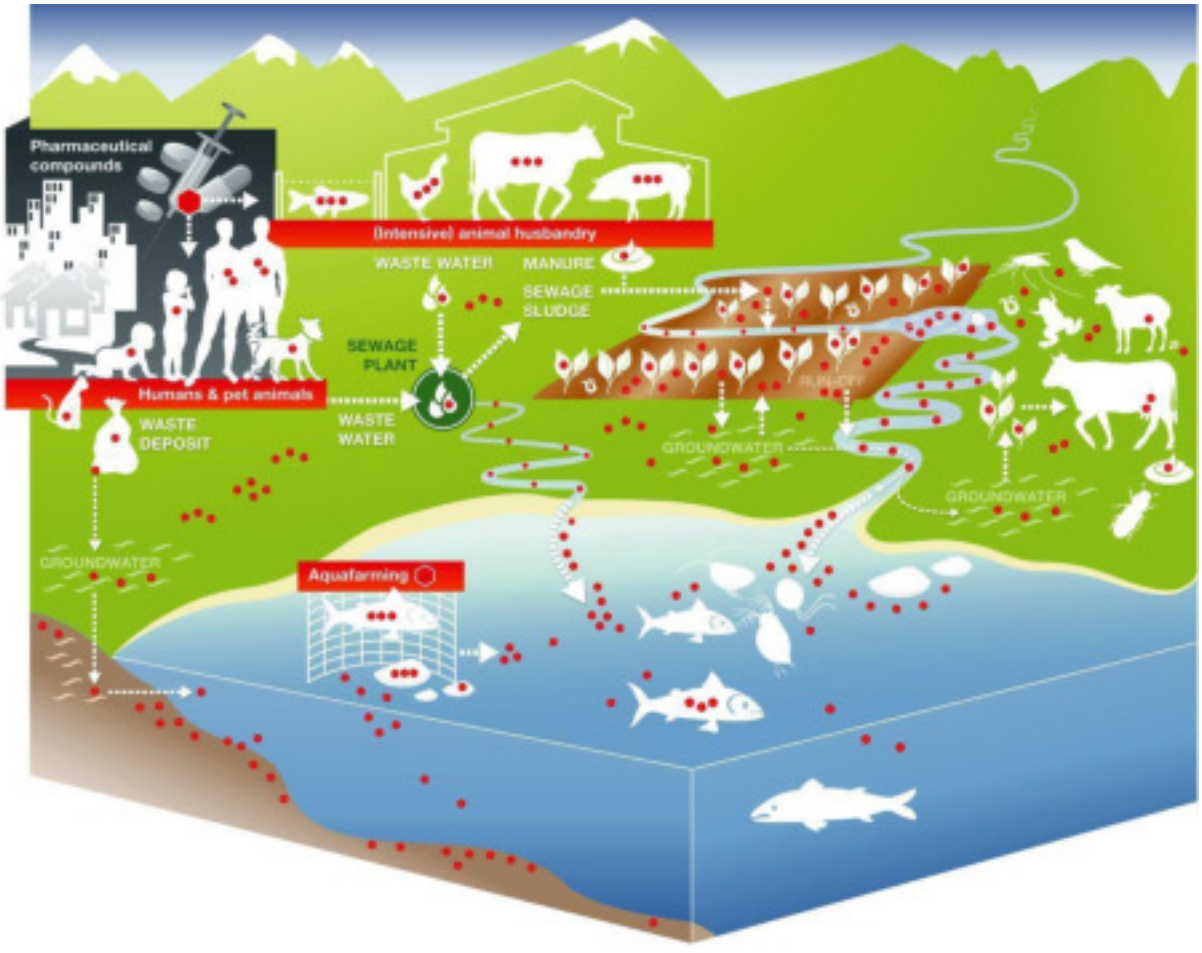

Figure 1. Routes of medicinal products in the Environment. Source: EMBO Reports 2014 (15)[1]

Pharmaceuticals leaving sewage treatment plants can end up in water for agricultural irrigation, and potentially in drinking water for human and animal consumption. Pharmaceuticals may also be retained as active compounds in the sludge phase with entry points into soil, groundwater and drinking water. The disposal of pharmaceutical waste, either by incineration or into landfill, or disposal down sinks or toilets that ends up in the sewerage system, creates entry points into ground water that may potentially enter drinking water. Through entry into drinking water pharmaceuticals may affect both the health of aquatic organisms and the health of humans.

Many studies show that the consumption phase is considered to be the biggest contributor to the emissions of medicinal products into the environment. Between 30 and 90% of orally administered dose is generally excreted as active substance in the urine of animals and humans. However, the nature and amount of medicinal residues mainly depend on the volumes and nature of the administered substances, their modes of administration, and metabolisation rates. E.g. only 9 out of 118 assessed pharmaceuticals were efficiently (> 95%) removed from wastewater during the treatment process and nearly half of the compounds were removed by <50%2. The report presents the analysis of medicines consumption in the Baltic Sea Region (BSR) countries.

In order to prevent the transfer of pharmaceuticals waste into the environment the EU has adopted Directive 2004/27/EC (relating to medicinal products for human use). This Directive introduces an obligation for the EU Member States to implement appropriate collection schemes for unused pharmaceutical products. However, it does not provide any guidelines on the implementation of the schemes and as a result significant differences exist between the Member States which is proved by a number of studies. Section 3 of the report presents information on the implementation of Waste Framework Directive in the Baltic countries, national legislation regulating the collection system in the BSR-countries and the description of the existing pharmaceuticals collection systems in each of the BSR-countries.

Better prescription practices and improved communication between doctors and patients can contribute to a reduction in the amount of unused medicines. Doctors control the duration and dosage of individual prescriptions, and are well positioned to help reduce the risk for the accumulation of unused pharmaceuticals that become waste and can end up in the environment.

Educational and informational campaigns may have a big impact in educating general public on how to dispose of unused medicines and on the risks of pharmaceuticals transfer into the environment. Lack of information on how to proceed with the disposal is one of the main reasons why people don`t use the collection schemes. Obviously, effective educational campaigns must go hand in hand with the well-functioning collection schemes. Information about the existing methods of informing the population about the problem of environmental pollution, medications and recommendations about information campaigns are contained in section 4 of the report.

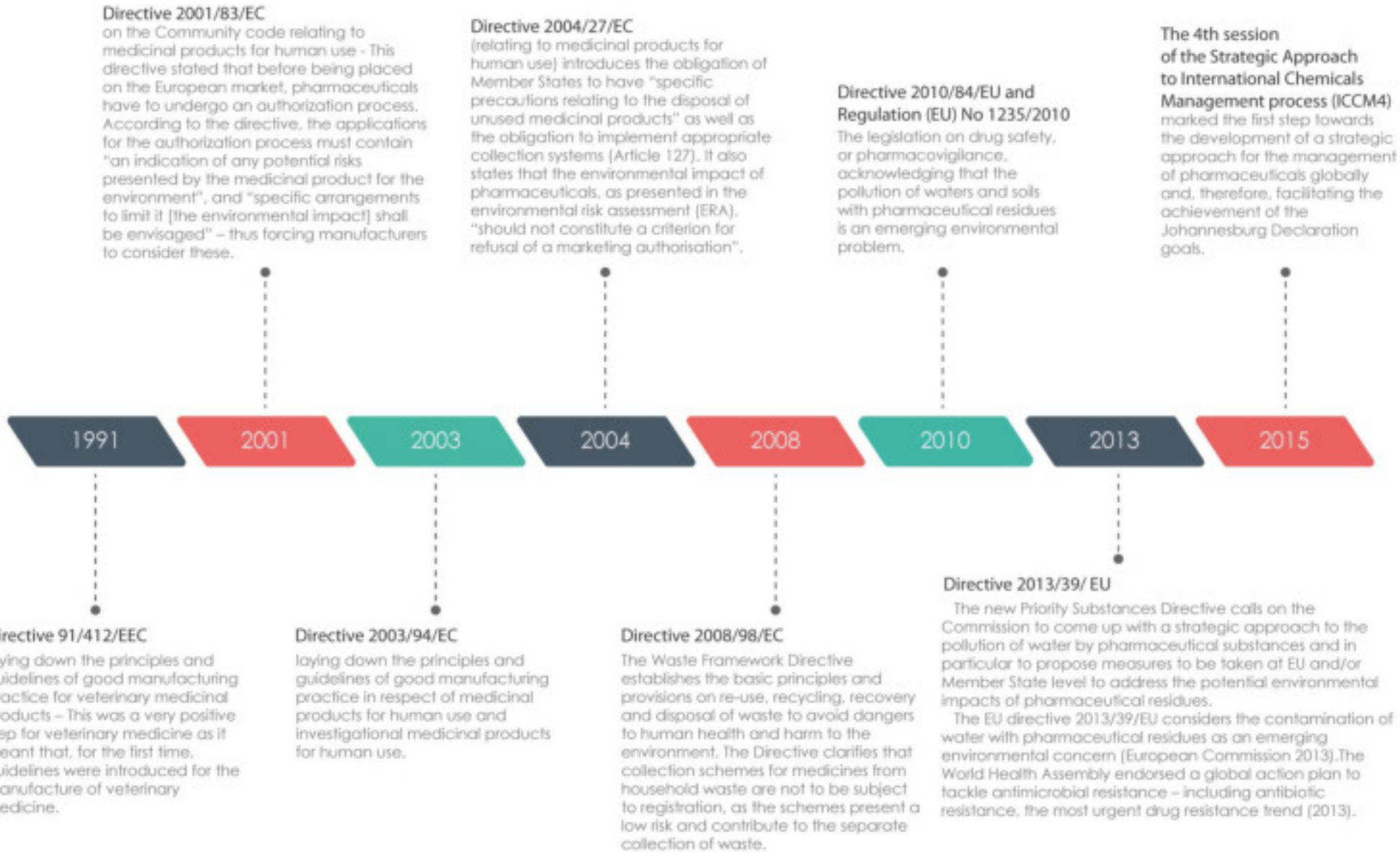

Figure 5: Timeline: development of the EU and international legislation on pharmaceuticals. Data source: www.saferpharma.org

Table 1. Pharmaceutical consumption in BSR countries in 2015, number of DDDs per 1,000 inhabitants and per day, Sources: compiled by the authors on the basis of national statistical reports

Groups of pharmaceuticals	DDD/1000 inhabitants/day									
	DK[16] (primary sector and hospital sector)	SE (only human and drugs prescribed by veterinarians are excluded)	FI[18] (amount of medicines sold by drug wholesalers to pharmacies and hospitals)	DE	EE[17]	LV[17]	LT[17]	PL	RU	UA
(A) Alimentary tract and metabolism:	**-**	**-**	**296.32**		**132.81**	**119.39**	**107.55**			
A02 (drugs for acid related disorders)	74.2	62.2	67.74		43.52	37.72	39.68			
(A02BC) Proton pump inhibitors are the most commonly used drugs:	65.1	-	63.15		39.8	35.19	28.42			
(A02BC01) omeprazole	19.1	-	12.29		26.26	25.37	19.25			
(A02BC02) pantoprazole	26.4	-	28.85		7.34	6.96	5.71			
(A02BC05) esomeprazole	2.3		13.41		6.20	2.59	1.19			
(A07) Antidiarrhealth, intestinal /antiinfective agents	6.6	-	12.83		3.67	3.27	3.38			
(A10) Antidiabetic drugs:	53.8	57.7	90.05		59.66	48.53	44.26			
(A10A) Insulins and analogues	18.6	27.4	31.7		15.93	11.72	12.44			
(B) Drugs affecting the blood and blood forming organs	**-**	**-**	**143.52**		**101.27**	**86.39**	**78.37**			
(B01) Antithrombotic agents	96.4	86.2	118.36		84.26	80.22	71.84			
(B01AC06) acetylsalicylic acid	57.5	-	77.55		14.5 (**but** combinations 48.62)	66.2	51.12			

(C) Cardiovascular agents:	**-**	**-**	**556.35**		**416.87**	**370.18**	**439.56**			
(C07) Beta blocking agents, selective	35.5	49,7	67.52		47.53	52.50	71.6			
(C07AB02) metoprolol			12.62		23.19	13.17	20.82			
(C07AB07) bisoprolol			37.79		1.37	18.64	0.15			
(C07AB12) nebivolol			1.47		19.28	11.66	37.17			
(C08) Calcium channel blockers		78.8	80.04		58.38	36.17	32.23			
(C08CA01) amlodipine			50.92		30.75	17.58	8.71			
(C09) Agents acting on the renin-angiotensin system	177.5	171.9	228.85		196.58	148.07	214.14			
(C09AA) Ace inhibitors, plain:	87.8	89.1	103.50		84.85	65.57	102.14			
(C09AA02) enalapril	35.1	-	24.53		13.97	16.84	7.66			
(C09AA05) ramipril	45.9		70.26		59.24	23.92	30.99			
(C10) Lipid modifying agents (incl. statins)	141.3	98.1	105.35		51.62	65.65	21.75			
(D) Dermatologicals	**-**	**-**	**2.93**		**1.76**	**0.45**	**0.62**			
(D07) corticosteroids, dermatological preparations	23.8 ml or g per 1000 inhabitants per day	-	-		-	-	-			
(G) Genito urinary system and sex hormones	**-**	**-**	**133.07**		**51.5**	**31.37**	**30.22**			
(G03) Sex hormones and modulators of the genital system	75.5	about 65	82.81		34.92	20.34	15.78			
(G03A) Hormonal contraceptives for systemic use (incl. ethinylestradiol)	60.3	-	-		27.99	11.82	11.94			
(G03C+G03F) Estrogens and Progestogens and estrogens in combinations	11.4	9.2	-		3.28	5.23	1.74			
(J) Antiinfectives for systemic use:	**-**	**-**	**21.71**		**19.4**	**18.43**	**21.47**			
(J01) Systemic antibacterials	18.2	10.9	19.82		14.04	15.91	19.86			
(J01A) Tetracyclines	1.6		4.11		1.53	2.32	1.41			
(J01C) beta-lactam antibacterials, penicillins	11.9	-	7.00		5.55	7.18	10.87			

(J01CA04) amoxicillin	1.0		3.25		2.61	4.62	7.82			
(L02) Endocrine therapy	7.5	-	7.21		4.61	3.34	4.86			
(M) Analgesics and drugs affecting the musculoskeletal system:	**-**	**-**	**99.12**		**79.02**	**73.22**	**68.46**			
(M01A) Anti-inflammatory and antirheumatic agents, non steroid	40.7	Painkillers: 59.7	78.47		68.63	62.25	60.92			
(M01AB) acetic acid derivatives and related substances	4.2	-	4.80		11.54	26.00	26.59			
(M01AB05) diclofenac	2.5	-	4.29		11.12	20.98	20.63			
(M01AE) propionic acid derivatives	28.4	-	58.59		36.18	25.51	18.50			
(M01AE01) ibuprofen	25.6	-	49.18		26.27	23.07	13.35			
(M01AE02) naproxen	2,2	-	6.21		1.56	1.57	2.17			
(N) Central nervous system agents:	**-**	**-**	**259.53**		**113.98**	**98.46**	**153.53**			
(N02) Analgesics	94.8	-	51.90		17.35	14.2	12.73			
(N02A) Opioids	23.3	15.7	15.56		4.79	3.78	2.11			
(N02B) other analgesics and antipyretics	68.4	Painkillers: 59.7	34.30		11.90	10.19	10.08			
(N02BA) salicylic acid derivatives (incl. acetylsalicylic acid)	3.2	-	2.19		1.97	4.97	1.39			
(N02BE) anilides (incl. paracetamol)	65.1	-	32.11		9.87	4.47	7.81			
(N03) Antiepileptics (incl. carbamazepine)	18.7	14.1	20.11		8.12	8.54	9.75			
(N05) Psycholeptics	42.2	-	78.91		43.95	32.30	62.51			
(N05A) Antipsychotics	13.9	8.1	21.80		8.66	10.60	13.21			
(N05AH) Diazepines, oxazepines, thiazepines and oxepines (incl. olanzapine and quetiapine)	7.0	-	13.62		4.55	3.05	5.8			
(N05B) Anxiolytics	8.3	13,8	21.64		14.64	14.74	41.01			
(N05C) hypnotics and sedatives	20.0	51,1	35.47		20.65	6.96	8.29			
(N06A) Antidepressants	77.0	91.0	68.15		24.79	12.28	27.86			
(N06AB04) citalopram	20.9	-	12.3		1.51	0.62	2.07			
(N06AB06) sertraline	17.1	-	7.18		3.02	0.89	5.13			
(R) Respiratory system	**-**	**-**	**162.65**		**82.65**	**65.43**	**70.46**			
(R01) nasal preparations	27.8	-	31.78		35.00	33.12	25.77			
(R01A) decongestants and other nasal preparations for topical use (incl. xylometazoline)	27.7	-	29.59		32.69	32.74	24.89			
(R01AD) corticosteroids	12.9	-	19.2		7.88	5.63	3.47			

(R03) Drugs for obstructive airway diseases	59.2	52.3	70.48		24.69	15.40	23.68			
(R03A) adrenergics, inhalants (incl. formoterol)	36.4	-	37.99		16.43	9.69	17.78			
(R03B) other drugs for obstructive airway diseases, inhalants	19.3	-	24.19		5.14	2.05	3.77			
(R06) Antihistamines for systemic use (incl. cetirizine)	34.8	30.5	70.5		14.32	8.21	10.53			

Consumption data analysed using ATC/DDD methodology shows that the following groups are the most widely used in all Baltic countries:

(C) Cardiovascular agents: on the first place – (C09) blood pressure lowering drugs (enalapril, ramipril) and (C10) statins. Finland is the leader.

(N) Central nervous system agents: on the first place – (N02) Analgesics (Denmark is the leader), (N03) Antiepileptics (in Sweden, Denmark and Finland 2 times more than in Latvia, Lithuania and Estonia), (N05) Psycholeptics (Finland is the leader), (N06A) Antidepressants (Sweden is the leader).

(B) Drugs affecting the blood and blood forming organs: on the first place – acetylsalicylic acid.

(A) Alimentary tract and metabolism: A02 (drugs for acid related disorders) (Sweden is the leader), on the first place – omeprazole, pantoprazole; (A10) Antidiabetic drugs (especially Insulins and analogues (Finland is the leader)).

(R) Respiratory system: R03 (drugs for obstructive airway diseases); (R06A) Antihistamines (in Sweden, Denmark and Finland 2-4 times more than in Latvia, Lithuania and Estonia); (R01) nasal preparations.

(G) Genito-urinary system and sex hormones and especially (G03A) Hormonal contraceptives for systemic use: in Sweden 3-10 times more, than in other countries.

(M) Analgesics and drugs affecting the musculoskeletal system especially painkillers diclofenac, propionic acid derivatives and ibuprofen.

Table 5. Description of collection system pharmaceuticals from population in BSR countries. Sources: own research

Country	Population, 1 mln people (BSR only)	Mandatory or voluntary (M/V)* collecting system	Collection points	Amounts of pharmaceutical waste collected	Disposal method	Financial support
Denmark	5,5	M	All pharmacies, municipalities' collecting systems recycling centers www.apoteket.dk	No data	Incineration Kommunekemi A/S Ekokem A/S http://www.ekokem.com	Local government
Sweden	9,1	M	All pharmacies, municipalities' collecting systems recycling centers www.sverigesapoteksforening.se/miljokampanj/ on-line pharmacies www.apotea.se/milj%C3%B6	In 2011: - About 800 tons public leftover pharmaceuticals returned to the pharmacies; - About 250 tons of public leftover pharmaceuticals incorrectly disposed via solid waste or sewers; - About 10 tons of public leftover pharmaceuticals received by the recycling centers or recycling stations	Incineration About 20 facilities in Sweden licensed for the destruction of medical wastes	Responsible authority - Swedish Medical Products Agency
Finland	5,3	V	Community pharmacies Mobile collecting points www.fimea.fi/web/en/for_public/correct-use-of-medicines/how-to-dispose-of-medicines	In 2006[24]: -185 tons pharmaceuticals returned to the pharmacies; - 33 tons incorrectly disposed via solid waste; - 28 tons incorrectly disposed via sewers.	Incineration Ekokem A/S	No data
Russia	10,2	V	Mobile collecting points (more than 2000 points over year), recycling centers (8 ps.)	About 4 tons every year	Incineration JSC «PTZ Spetstrans» http://strans.spb.ru/	Committee for nature use, environmental protection and ecological safety, foreign grants
Estonia	1,3	M	All pharmacies, Some hazardous waste collection points http://sam.ee/kolbmatute-ravimite-kaitlemine?group=7	In 2014[24]: About 89 tons of pharmaceutical waste collected	No data	Pharmacies pay for the disposal and neutralization

Latvia	2,3	V	Some pharmacies, hazardous waste collection points http://www.pharmawaste.lv	According to the information provided by PILS pharmacies (11 pharmacies in total), they collect only about 5-10 kilograms per year. EUROAPTIEKA pharmacies (40 pharmacies in total) have concluded an agreement with SIA BAO (a special hazardous waste management company) and according to the data provided on their website, they collect on average 10 kilograms of expired medications per month at each pharmacy in Riga and around 5 litres at each pharmacy in other areas.	Incineration JSC BAO ensures a full cycle of medical waste management service http://www.bao.lv	The pharmacies are carrying expenses for the disposal of medicines collected from the population
Lithania	3,4	M	All pharmacies	The records are kept, however there is no publicly available data.	Incineration UAB „Tekasta“ ensures a full cycle of medical waste management services	Local government
Poland	38,1	V	Some pharmacies, special hazardous waste collection points http://www.mz.gov.pl/leki/produkty-lecznicze/utylizacja-lekow http://www.bys.com.pl/ - Warsaw	A collection programme was launched in Krakow in 2007. In framework of the programme, special containers were installed in 60 out of 216 Krakow pharmacies. The total weight of collected unused and expired pharmaceuticals made 4,9 tons[25]	No data	No data
Germany	3,1	V	Some pharmacies, local recycling centers. Disposal of unused or expired medicines through general waste is the safest and recommended way in most areas[22]	The Altmedikamente initiative estimated that the take-back schemes operated by the REMEDICA and MEDIrecycling are treating 1 400 tons of approx.4 000 - 7 000 tons of pharmaceutical waste generated annually in Germany.	Incineration	No data
Belarus	4,0	Collection system NA	According to preliminary studies, in each family there is an average of 200 grams of expired pharmaceuticals			
Ukraine	1,8	Collection system NA	-			
	* Required by the EU directive 2008/98/EC, however the national legislation is missing in some countries. M – legal obligation of pharmacies to participate in take-back scheme, V – voluntary participation of pharmacies and other organizations					

VI. Conclusions and recommendations

Analyzing the received information, the authors of the report are convinced that the problem of getting medicines into the environment in the BSR-countries poses a significant threat. Pharmaceuticals leaving sewage treatment plants can end up in water for agricultural and landscape re-use. The disposal of pharmaceutical waste, either by incineration or into landfill, or disposal down sinks or toilets that ends up in the sewerage system, creates entry points into ground water that may potentially enter drinking water. Through entry into water pharmaceuticals may affect both the health of aquatic organisms and the health of humans. At present, all the ways of APIs entry into the environment, and subsequently into the Baltic Sea, have been identified. The key ones include: with the sewage at the manufacturing stage, with the hospitals and cities sewage at the consumption stage, with the waste at the disposal stage, and in process of livestock and fish farming. By now, none of the countries introduced mandatory requirement to the monitoring of APIs concentrations in the sewage waters.

Nowadays we have a large number of studies about the presence of pharmaceuticals in all components of the environment, but the contribution of each source has not been evaluated sufficiently. In this case, the transformation of APIs does not always mean that detoxification occurs, as there are examples where transformation products are more toxic and abundant than the parent compounds.

Many studies show that the overconsumption of pharmaceuticals is considered to be the biggest contributor to the emissions of medicinal products into the environment. One of the major issues is the existence of unused medicines due to the lack of compliance with the prescribed regime, and then storage for future use and the achievement of shelf life expiration.

It can easily be seen that some countries consume different amounts of medicines that belong to the same pharmaceutical group (Table 1). One of the goals pursued by the environmental classification is to assist health care professionals in choosing the medicines they are prescribing with regard to their environmental classification among other factors. This is one of the steps to prevent environmental pollution with pharmaceuticals that needs to be taken. The emphasis should be made on pollution prevention. One of this ways is “Green chemistry". It may lead to new drugs being designed to have the desired curative effects while minimizing adverse environmental impacts.

Medical institutions may serve as a good platform to inform the public about the environmental impact of pharmaceuticals, as well as about the safe ways to dispose of pharmaceutical waste. From the consumer/patient point of view, it would make sense for pharmaceutical products to be disposed of in standard locations, publicly accessible and supervised, such as pharmacies. This would also be easier to communicate to people. Collection in a pharmacy guarantees that no one could tamper with the medicines and that children and animals could not accidentally ingest them. Furthermore, pharmacies are an easy access point for most patients. Pharmacists can provide information and ensure that the collected waste meets the system's criteria. Ideally, consumers would receive information about how to safely dispose of unused pharmaceuticals at the point of purchase, including not only pharmacies but also other authorized selling points.

Statutory requirements for the pharmacies to participate in collecting pharmaceutical waste from the public are set in Denmark, Sweden, Estonia and Lithuania. Polish, Finnish and Latvian pharmacies take part in the scheme on a voluntary basis. In Germany, the

requirement for separate pharmaceutical waste collection applies only to several regions where household waste is not incinerated.

All municipalities, apart from those of Ukraine, Russia (except for St. Petersburg) and Belarus, state that pharmaceutical waste is hazardous and shall not be dumped with the household waste or flushed into the sewage system.

In all Baltic countries (except for Russia, Belarus and Ukraine) it is possible to get information about returning waste medicines to pharmacies or waste collection points directly from pharmacies.

European pharmaceutical manufacturers also accompany the medicines with the patient leaflets about the need to apply special disposal techniques rather than flush those into the sewage. Russian, Belarusian and Ukrainian manufacturers are not yet providing such information.

Recommendations for the system of collection improvement

a. To develop and implement measures to prevent drugs from entering the environment, it is necessary to create dialogue between pharmaceutical companies, the health sector and environmental organizations. This concerns the issues of determining the environmental characteristics of medicinal products, the introduction of methods for wastewater treatment, optimizing prescribing of medicines, and so on.

b. It is necessary to organize public and professionals awareness raising about the effects of human and veterinary pharmaceuticals on the environment, and ways to minimize it.

c. Creating clear and mandatory regulation on the collection and disposal of obsolete pharmaceuticals from population.

d. Analytical studies are needed to assess the current level of pollution and identify the "hot spots" of the environmental pollution by the pharmaceutical preparations in all regions of the BSR-countries.

e. It is necessary to point out the need to use the risk assessment of pharmaceuticals, and their metabolites in the environment when addressing the knowledge gaps. In addition, it is important to assess the risk of various metabolites and transformation products in the environment and to establish the threshold values for pharmaceuticals residues in different media.

f. Initiate the consistent accounting and reporting on the operation of the systems for pharmaceutical waste collection from the public. A detailed annual report considering the quantities of medicines collected from different age groups is currently available only from Sweden.

g. Classify pharmaceuticals as hazardous waste and promote chemical deactivation as a more environmentally sound option than incineration at high temperatures for the disposal of pharmaceuticals.

h. Develop a system for the pharmaceutical waste collection from the public via online pharmacies, in countries where they are. This practice contributing to a wider informational coverage of the population, especially those living in remote areas, exists today only in Sweden.

i. Consider revising, updating and developing relevant HELCOM Recommendations addressing safe collection and disposal of pharmaceutical residues

The contributions of different stakeholders to the management and mitigation of pharmaceuticals in the environment are summarized in Annex 3.

Coalition Clean Baltic
FOR PROTECTION OF THE BALTIC SEA ENVIRONMENT

CCB's Working Areas:

- Water Protection in Agriculture (AGRI)
- River Basin and Wastewater Management (RBWM)
- Fisheries and Aquaculture (F/AqC)
- Biodiversity and nature conservation (BNC)
- Hazardous substances and marine litter (HSML)
- Sustainable development in coastal and marine areas (SDCMA)
- Harmful installations and maritime transport (HIMT)

Coalition Clean Baltic is a network of environmental NGOs:

• Ecohome, Belarus • IPO Ecopartnership, Belarus • Danish Society for Nature Conservation • Estonian Green Movement • Finnish Association for Nature Conservation • Finnish Society for Nature & Environment • Bund für Umwelt und Naturschutz Deutschland, BUND • Environmental Protection Club of Latvia, VAK • Latvian Green Movement • Lithuanian Green Movement • Lithuanian Fund for Nature • Polish Ecological Club, PKE • Green Federation - GAJA, Szczecin, Poland • Friends of the Baltic, St Petersburg, Russia • Green World, St Petersburg, Russia • Swedish Society for Nature Conservation • The Western Center of the Ukrainian Branch of the World Laboratory

Swedish Agency for Marine and Water Management