EFFICIENT TREATMENT OF PHARMACEUTICAL RESIDUE AT SOURCE - EPIC

Pharmaceuticals in environmental permits issued to Finnish pharmaceutical industry

Jukka Mehtonen
Finnish Environment Institute SYKE
Final seminar of EPIC, 17.5.2019

Needs

- API emissions from pharmaceutical industry commonly assumed to be negligible in the western countries, but information on emissions not been published
- information on policy instruments & measures to promote sustainable manufacture of APIs at different scale →
  - national level: enhancing environment permitting of pharmaceutical plants (no need for new legislation!)
  - EU & global level: emissions occurring during the production chain are out of the scope of both marketing authorization for medicinal products & Good Manufacturing Practices (GMP) on pharmaceutical plants
- Minimise waste and wastewater containing pharmaceutical residue & enhance its collection and treatment in the pharmaceutical plant before mixed and diluted with other waste water at the municipal waste water treatment plant (MWWTP)

Needs - main drivers

International, EU Water Framework Directive (WFD, 2000/60/EY):

- **EU Strategic Approach to Pharmaceuticals in the Environment -11.3.2019**
  - *Under WFD, consider specific pharmaceuticals, and groups of pharmaceuticals with similar effects, in the work supporting the regular review of substances posing a risk at Union level, and work with MSs on EQSs for pharmaceuticals posing a risk at national level*
  - *Ensure that the emission of pharmaceuticals to water is considered as a possible Key Environmental Issue when reviewing BAT Reference Docs under IED for relevant sectors*
  - Implementation of strategic approach in Finland is now about to start…
- Obliges member states to monitor pharmaceuticals on the Watch list (2018/840/EY); → may be nominated as Priority Substances and assigned legally binding EQSs and to be required emission reduction measures in the future

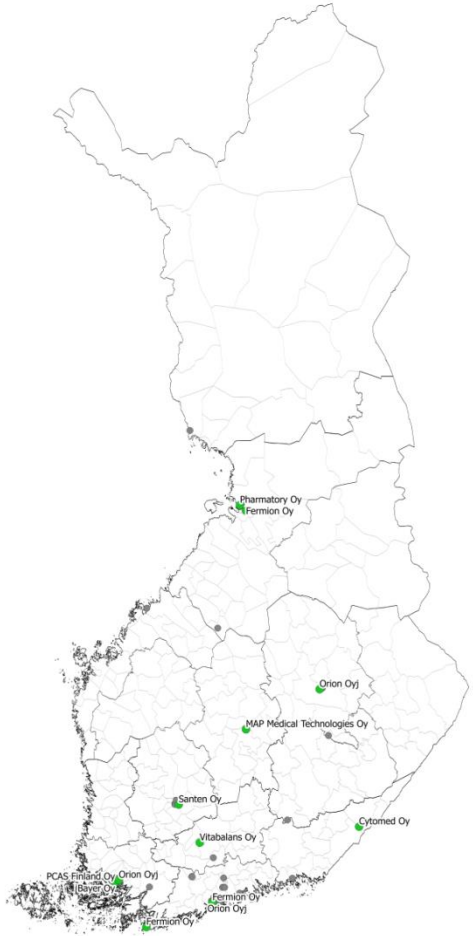
National: Finnish National Programme on Dangerous Chemicals (2017):

- Improve env. assessments of medicinal products for human and veterinary use by enhancing inter-agency cooperation

Approach

1. Screened the extent of pharmaceutical industry in Finland (EudraGMDP)
2. Selection of relevant pharmaceutical plants
3. Search of plants posing environment permits & evaluation of env. permits

- Objectives:
  - analyze how APIs are considered in environment permits of pharmaceutical plants in Finland
  - give recommendations on enhanced environmental permitting of pharmaceutical plants
- Focus: APIs in wastewater & solid waste



Approach - studied 13 pharmaceutical plants

- Environment permits were analyzed; all relevant information (incl. permit conditions) on e.g. emission & environment impact monitoring, wastewater, solid waste etc.

Yritys	Toimipiste	Luvan tiedot		Toiminta
		Diaarinumero	Voimaantulo	
Bayer Oy	Turku	LOS-2004-Y-1043-111	10.12.2009	Tuotanto, pakkaaminen, laadunvalvonta, maahantuonti
Cytomed Oy	Lappeenranta	ESAVI/4/04.08/2011	29.12.2011	Tuotanto, pakkaaminen, laadunvalvonta, maahantuonti
Fermion Oy	Espoo	ESAVI/267/04.08/2012	5.4.2016	Tuotanto, laadunvalvonta
	Hanko	ESAVI/211/04.08/2012	21.12.2016	Tuotanto, laadunvalvonta
	Oulu	PPO-2004-Y-398-111	6.6.2006	Tuotanto, laadunvalvonta
MAP Medical Technologies Oy	Tikkakoski	KSU-2004-Y-452/111	9.9.2005	Tuotanto, pakkaaminen, laadunvalvonta
Orion Oyj	Espoo	ESAVI/2010/04.08/2012	5.4.2016	Tuotanto, pakkaaminen, laadunvalvonta, maahantuonti
	Kuopio	PSA-2004-Y-265-111	11.4.2005	Tuotanto, pakkaaminen
	Turku	LOS-2004-Y-1038-111	29.1.2009	Tuotanto, pakkaaminen, laadunvalvonta, maahantuonti
PCAS Finland Oy	Turku	LOS-2004-Y-1060-111	29.1.2008	Tuotanto, laadunvalvonta
Pharmatory Oy	Oulu	PPO-2002-Y-76-111	11.6.2002	Tuotanto, laadunvalvonta
Santen Oy	Tampere	LSSAVI/193/04.0	22.11.20	Tuotanto, pakkaaminen,

Approach – Key findings

- Nearly all plants (12 / 13 plants) discharge waste waters into MWWTPs after pretreatment or after separating most harmful fractions

Permit conditions

- Solvents commonly considered
- APIs & their emissions seldom considered; 3/13 permits; most recent permits issued 2013–16
- Not common to have obligation to measure API concentrations in wastewater (2/13 permits) or ecotoxicity of wastewater (1/13)

→ seldom set permit conditions on monitoring of API emissions

- Although, Finnish environmental protection act (527/2014): *industrial operators must be aware of their environmental impacts (6 §) and limit emissions into environment and into sewer network to the lowest level possible (7 §)*

Benefits

- **MWWTPs** and supervisory and **permitting environmental authorities** are provided with information on benefits of enhanced application of legislation concerning environmental permits of pharmaceutical plants

- **MWWTPs** benefit from new knowledge on **the composition and load of pharmaceutical via wastewater from pharmaceutical plants**

- In the long perspective removing pharmaceutical residue at source **improves the quality of water and the reusability of WWTP sludge and allocates treatment costs to the source of origin**

Recommendations 1/4

1. Pharmaceutical plants must be aware of API emissions and impacts on MWWTPs & surface waters

- Emissions to sewer network should be estimated in a calculative way or via measuring or with their combination on those APIs handled in plant.
  - **Calculative way is primarily recommended to be used** based on information on e.g. production amounts and losses during manufacture
- Permit holder must estimate the significance of API emissions when performing **risk assessment at plant level** in cooperation with supervisory authorities
  - Risk assessment should cover the MWWTP but also the recipient waters. If risk found, necessary measures to decrease risks must be presented
- **Industrial wastewaters discharged to MWWTP are recommended to be tested with bioassays** in order to secure efficient MWWTP biological wastewater treatment processes
  - Active sludge nitrification & bacterial growth inhibition tests; especially during unnormal conditions

Recommendations 2/4

2. Recommendation on limit values for APIs & bioassays

- **Recommended to apply Svenskt Vatten´s (2012) or other justified limit values for active sludge nitrification inhibition tests**. If limit values are exceeded, the reason for inhibition should be found out.
- **The limit values for certain specific APIs are to be assessed and formulated**
  - Efficient MWWTP processes, high protection level of recipient waters and safe reuse of MWWTP sludge should be taken into account
  - Require smooth cooperation between permitting authority, operator (pharmaceutical plant) & MWWTP

Recommendations 3/4

3. Good practices for management of wastewater and waste from pharmaceutical industry

- Operator (pharmaceutical plant) is to be obliged to conclude an industrial wastewater agreement with MWWTP
- Wastewater and waste fractions containing significant amounts of APIs are to be collected separately and to be delivered to special hazardous waste treatment. Wastewater discharged into (municipal) sewer are to pretreated efficiently enough.
- The failed medicine batches are waste, which is not to be discharged into (municipal) sewer
- There should be no floor drains in process chemical and raw material storages with direct connection to into (municipal) sewer
- The use of hazardous chemicals (environment or human health) should be minimized in processes of pharmaceutical plants

Benefits – Recommendations 4/4

- Legislative base:
  - Finnish Environmental Protection Act (527/2014): 6 §, 19 §, 52 §, 53 §, 62 §, 67 §
  - Finnish Environmental Protection Degree (713/2014): 41 § & 42 §
  - Finnish Waste Act (646/2011): 15 §

- **The case-specific consideration and local conditions are to be taken into account when considering or applying these recommendations in the environment permitting of pharmaceutical plants in Finland**

Other conclusions

- The authorities should ensure that
  - relevant APIs are to be added into parameter selection of environmental administration data systems (e.g. YLVA). This is prerequisite for that operators can report results related to API emissions (incl. concentrations) in a electronic format to data systems.
  - more detailed information on Good Practices for treatment methods on API containing wastewater will be added into relevant EU BREFs (e.g. Organic Fine Chemicals) under IED (Industrial Emission Directive)
- The environmental aspects of pharmaceutical industry (e.g. API emissions) should be included into some international system (e.g. Good Manufacturing Practices, GMP) in order to gain maximal environmental benefit and not to set pharmaceutical companies in different parts of world to unequal position.
  - this global measure is to be promoted by EU

Collaboration

National

- Financiers / investors (steering group)
- Healthcare operators & related stakeholders: health institutions, hospitals, Finnish Medical Society Duodecim, Association of Finnish Pharmacies & SFL
- Pharmaceutical industry: Pharma Industry Finland (PIF), Pharmaceutical Information Centre & Orion Oy, KRKA Finland Oy
- Authorities: YM, ELY Centres, Regional State Administrative Agencies (AVIs)
- Finnish Water Utilities Association (FIWA), MWWTPs

Collaboration

International

- Pharmaceutical industry: International Pharmaceutical Federation (FIP), Swedish Association of Pharmaceutical Industry (LIF), European Federation of Pharmaceutical Industries and Associations (EFPIA)
- EU Commission – DG ENV
- Authorities:
  - EU Strategy for the Baltic Sea Region (EUSBSR) - Policy Area Hazards: Baltic Sea Pharmaceutical Platform for dialogue and knowledge exchange on pharmaceuticals in the environment between stakeholders
  - Swedish national knowledge centre on pharmaceuticals (under Swedish Medical Products Agency)
- Scientific community: Interreg projects CWPharma, HAZBREF and BEST

Further information

SYKE (firstname.lastname@ymparisto.fi)

- Lauri Äystö
- Jukka Mehtonen
- Heidi Ahkola
- Matti Leppänen
- Taina Nystén

Laki ja Vesi Oy

- Niina Vieno; (niina.vieno@lakijavesi.fi)

Helsingin yliopiston Farmasian tiedekunta & Generation Green –hankkeen koordinointiryhmä
(firstname.lastname@@helsinki.fi)

- Tiina Sikanen
- Jari Yli-Kauhaluoma

Thank you!

Jukka Mehtonen
jukka.mehtonen@ymparisto.fi