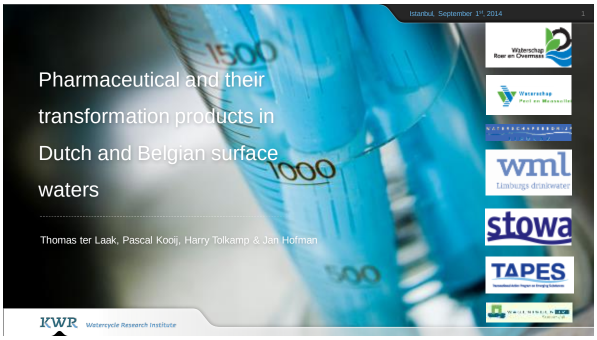
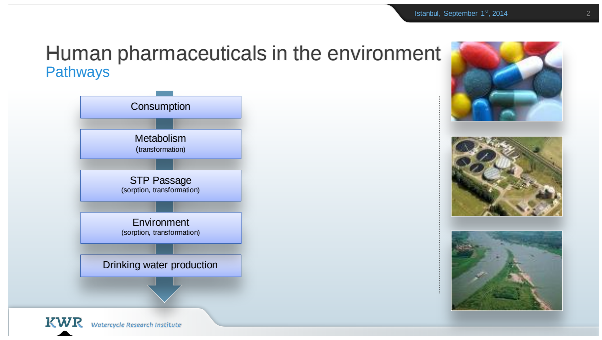
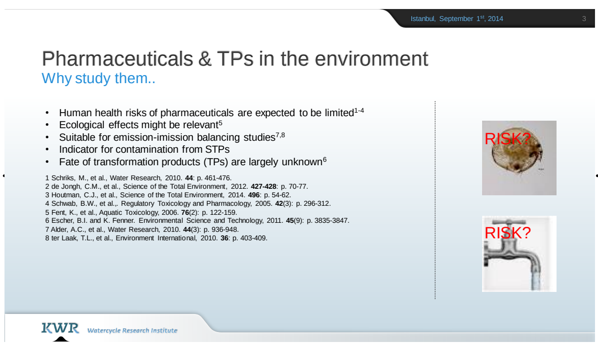
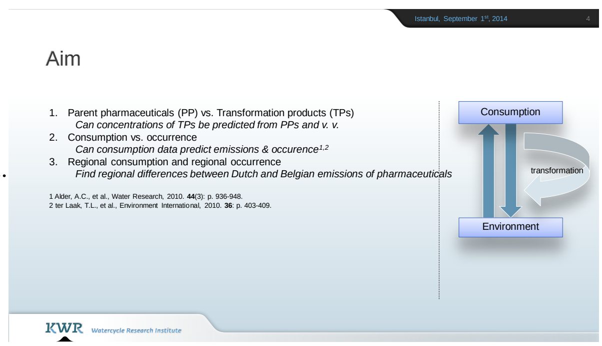
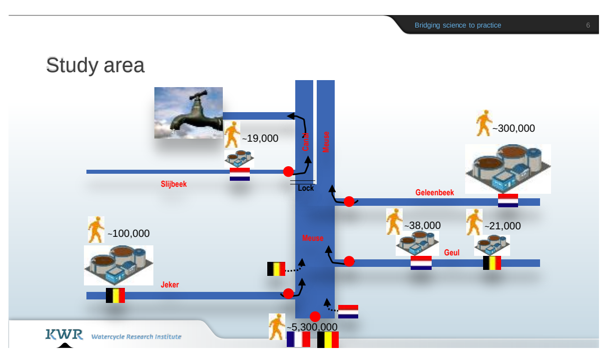

Istanbul, September 1st, 2014
1
Pharmaceutical and their transformation products in Dutch and Belgian surface waters
Thomas ter Laak, Pascal Kooij, Harry Tolkamp & Jan Hofman
wml
Limburgs drinkwater
stowa
TAPES
KWR Watercycle Research Institute


Istanbul, September 1st, 2014
2
Human pharmaceuticals in the environment
Pathways
Consumption
Metabolism
(transformation)
STP Passage
(sorption, transformation)
Environment
(sorption, transformation)
Drinking water production
KWR Watercycle Research Institute


Istanbul, September 1st, 2014
3
Pharmaceuticals & TPs in the environment
Why study them..
• Human health risks of pharmaceuticals are expected to be limited1-4
• Ecological effects might be relevant5
• Suitable for emission-imission balancing studies7,8
• Indicator for contamination from STPs
• Fate of transformation products (TPs) are largely unknown6
1 Schriks, M., et al., Water Research, 2010. 44: p. 461-476.
2 de Jongh, C.M., et al., Science of the Total Environment, 2012. 427-428: p. 70-77.
3 Houtman, C.J., et al., Science of the Total Environment, 2014. 496: p. 54-62.
4 Schwab, B.W., et al.,. Regulatory Toxicology and Pharmacology, 2005. 42(3): p. 296-312.
5 Fent, K., et al., Aquatic Toxicology, 2006. 76(2): p. 122-159.
6 Escher, B.I. and K. Fenner. Environmental Science and Technology, 2011. 45(9): p. 3835-3847.
7 Alder, A.C., et al., Water Research, 2010. 44(3): p. 936-948.
8 ter Laak, T.L., et al., Environment International, 2010. 36: p. 403-409.
RISK?
RISK?
KWR Watercycle Research Institute


Istanbul, September 1st, 2014
4
Aim
1. Parent pharmaceuticals (PP) vs. Transformation products (TPs)
Can concentrations of TPs be predicted from PPs and v. v.
2. Consumption vs. occurrence
Can consumption data predict emissions & occurence1,2
3. Regional consumption and regional occurrence
Find regional differences between Dutch and Belgian emissions of pharmaceuticals
1 Alder, A.C., et al., Water Research, 2010. 44(3): p. 936-948.
2 ter Laak, T.L., et al., Environment International, 2010. 36: p. 403-409.
Consumption
transformation
Environment
KWR Watercycle Research Institute


Istanbul, September 1st, 2014
5
Study area
Streams in the Meuse catchment at the Dutch-Belgian border
Belgium
Germany
Netherlands
KWR Watercycle Research Institute

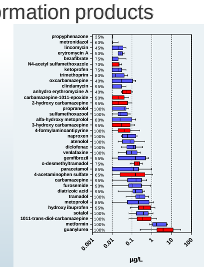

Bridging science to practice
6
Study area
~19,000
~300,000
Slijbeek
Lock
Geleenbeek
~100,000
~38,000
~21,000
Geul
Jeker
~5,300,000
KWR Watercycle Research Institute

Pharmaceuticals and transformation products

Both pharmaceuticals and TPs found

45 pharmaceuticals and 18 TPs measured,
24 pharmaceuticals and 13 TPs observed

1. Guanyl urea (50 %)
2. Metformine (21 %)
3. 10-11 trans diol carbamazepine (4%)
4. Hydroxy ibuprofen (4%)
5. Sotalol (3%)
6. Metoprolol (2%)
7. Tramadol (2%)
8. Diatrizoic acid (2%)
9. Furosemide (1%)
10. Carbamazepine (1%)
11. Other (10%)



CONCENTRATION RANGES OBSERVED IN ALL SAMPLES

Pharmaceutical and transformation products

Numerous pharmaceuticals and TPs exceed the TTC

45 pharmaceuticals and 18 TPs measured,
24 pharmaceuticals and 13 TPs observed

1. Guanyl urea (50 %)
2. Metformine (21 %)
3. 10-11 trans diol carbamazepine (4%)
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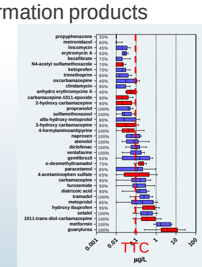
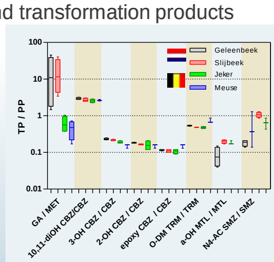


CONCENTRATION RANGES OBSERVED IN ALL SAMPLES

Ratios of pharmaceutical and transformation products

- Ratio of metformin (MET) and guanlyurea (GA) is variable
  - significant difference between Dutch and Belgian fed streams
- Ratio of carbamazepine (CBZ), tramadol (TRM), metoprolol (MTL) and sulfamethoxazole (SMX) and TPs are rather stable
  - predictions of one from the other are possible



TRANSFORMATION PRODUCT / PARENT RATIOS IN DIFFERENT STREAMS

Ratios of pharmaceutical and transformation products

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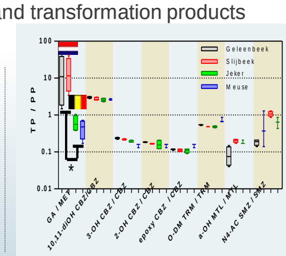


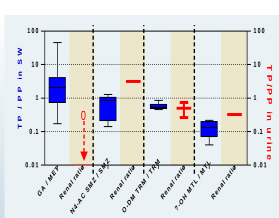
TRANSFORMATION PRODUCT / PARENT RATIOS IN DIFFERENT STREAMS

Ratios of TP and parent pharmaceutical (PP)

Metformine, sufamethoxazole, tramadol and metoprolol

- Guanlyurea-metformin ratio (GA/MET) is variable. GA is not formed in the human body[1]
- TP-sulfamethoxazole ratio (N4-AC SMZ/SMZ) in SW differs from renal ratio[2]
- TP-tramadol ratio (O-DM TRM/TRM) SW corresponds with renal ratio[3-5]
- TP-metoprolol ratio (A-OH MTL/MTL) (slightly) differs from renal ratio[6]

1 KNMP. *Informatorium Medicamentorium*. 2006.
2 Lienert, et al., Environmental Science and Technology, 2007. **41**(12): p. 4471-4478.
3 Chitil, L., et al., Journal of Chromatography B, 2009. **877**: p. 1937-1942.
4 Ardakani Y. H. and R.M. R., DARU, 2009. **17**: p. 245-255.
5 Lintz, W., et al., *Biotransformation of tramadol in man and animal*. 1981. **31**(11): p. 1932-1943.
6 Tu, Z.G. and L.L. Zhao, Acta Pharmacologica Sinica, 1995. **16**(4): p. 325-329.



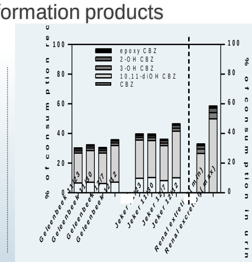
TRANSFORMATION PRODUCT VS. RENAL CLEARANCE

Pharmaceutical and transformation products

Carbamazepine

Ratio of carbamazepine (CBZ) and TPs in SW are stable and correspond to renal ratios[1]

1 Eichelbaum, M., et al., Clinical Pharmacokinetics, 1985. **10**(1): p. 80-90.

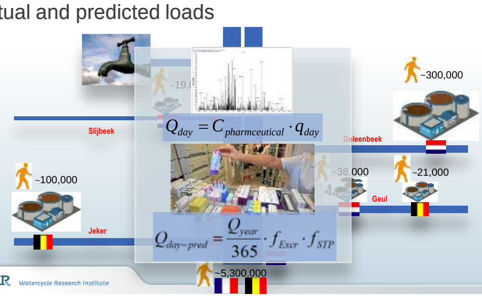


CARBAMAZEPINE AND TPS IN SW VS. RENAL CLEARANCE

Pharmaceutical and transformation products

Pharmaceutical and human metabolite persistent in STP & environment	Pharmaceutical and/or human metabolite less persistent in STP & environment	No human metabolite, pharmaceutical well degradable in STP (and environment?)
Stable ratio in SW similar to human excretion ratio	Less stable ratios in SW, diverging from human excretion ratio	Very variable ratios within and between streams ?STPs
E.g. carbamazepine, tramadol	E.g. sulfamethoxazole, metoprolol	E.g. metformine
Predictions of concentrations from PP to TP and *vice versa* are accurate	Predictions of concentrations from PP to TP and *vice versa* are less accurate Research on driving factors of deviation and transformation in STP are necessary	Predictions of concentrations from PP to TP and *vice versa* are inaccurate Research on driving factors of transformation in STP are necessary

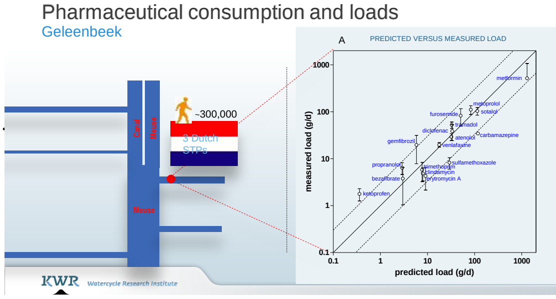
Actual and predicted loads



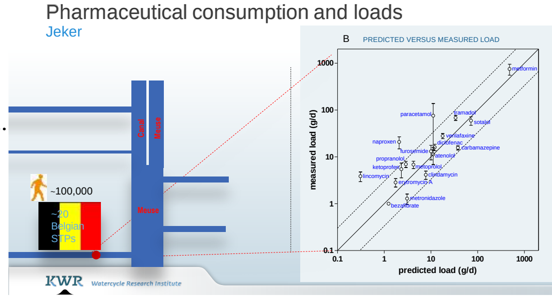
$$Q_{day} = C_{pharmceutical} \cdot q_{day}$$

$$Q_{day-pred} = \frac{Q_{year}}{365} \cdot f_{Excr} \cdot f_{STP}$$

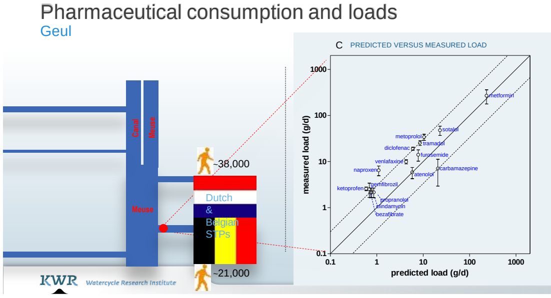
Pharmaceutical consumption and loads
Geleenbeek



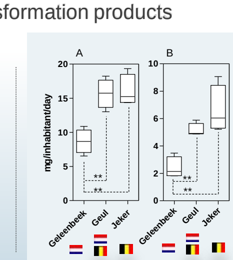
Pharmaceutical consumption and loads
Jeker



Pharmaceutical consumption and loads
Geul



Pharmaceutical and transformation products
Dutch vs Belgian *per capita* loads

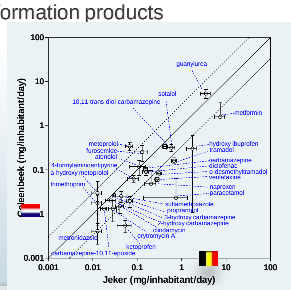


PER CAPITA LOADS IN DIFFERENT STREAMS WITH (A) AND WITHOUT (B) METFORMIN AND GUANYLUREA

Pharmaceutical and transformation products

Dutch vs Belgian *per capita* loads

PER CAPITA LOADS FROM NL & BE



Conclusions

- Concentrations TPs similar to pharmaceuticals
- TP/PP ratios often allow predictions
- Regional consumption can be used to predict emissions
- PP/TP ratios are often stable and partially explained by renal clearance
- B and NL different loads & composition
- Driving factors of transformation in STP (and environment) requires additional research

More information?

Thomas.ter.laak@kwrwater.nl

ter Laak, T., et al., *Different compositions of pharmaceuticals in Dutch and Belgian surface waters explained by consumption patterns and treatment efficiency.* Environmental Science and Pollution Research, 2014. **in press**.

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