Testing the Waters 2015, 11-15 October, Monte Verità, Ascona, Switzerland

Aim of the conference

The overarching aim of *Testing the Waters 2015* is to bring together scientists and stakeholders from all involved disciplines to integrate results and contribute to the solution of a complex, societal problem (trans-disciplinarity). To date, no in-depth comparison of different data sources was possible due to a lack of i) overlap in space and time or ii) commonly agreed protocols. Therefore, submissions related to truly trans-disciplinary projects, integrating results from wastewater studies and other epidemiological data, are particularly encouraged for theme 1 on targeted monitoring. Furthermore, scientific advances in individual disciplines are pertinent to refine components of wastewater-based drug epidemiology (inter-disciplinarity). These are covered with theme 2 on methodological improvements (back-calculation) and theme 3 on analytical chemistry. Legal and ethical aspects are addressed in theme 4. Altogether, this will contribute to filling current gaps and providing guidance on future applications, also beyond illicit drugs (theme 5). For the benefit of community-wide health assessment, the main objective is to disseminate recent advances and discuss new approaches in wastewater-based drug epidemiology (WBE). This will lead to a targeted cross-sectoral evaluation of recent research activities in this field.

Targeted audience

Drug use epidemiologists, analytical and environmental chemists, environmental engineers, pharmacologists, toxicologists, experts in forensics and stakeholders from public health sector, addiction and prevention institutions.

Number of participants

approx. 100 expected

Conference themes

Five distinct topics (see attached announcement and more details later in this document)

Supported by

Congressi Stefano Franscini, ETH Zurich, SCORE-COST and SEWPROF [other sponsors not contacted yet (see sponsoring package description for sponsoring options)]

Organized by

SCORE-COST, SEWPROF, EMCDDA, and Eawag

Vision: Integrating different drug monitoring tools as a basis for adequate prevention measures and expanding wastewater-based epidemiology to other public health aspects

Municipal wastewater contains excreted drug target residues (DTR, i.e. parent compounds and metabolites of illicit drugs), which directly reflect the consumption of entire communities. Owing to recent advances in analytical chemistry, DTR can now be quantified selectively and sensitively even in difficult matrices such as raw wastewater. Therefore, the emerging field of wastewater-based epidemiology (WBE) aims at quantifying drug consumption through wastewater analysis. Traditional methods to quantify actual consumption of illicit drugs rely on population surveys and targeted surveys among users. In addition indirect measures, like drug seizures and hospitalizations, can be included in triangulation efforts. The integration of wastewater studies with existing drug monitoring tools will improve the depiction of levels and trends in drug use and the detection of the diffusion of new drugs. Wastewater studies will, however, not be able to tell who the users are and thus it is difficult to base adequate prevention measures on such information.

An integration of traditional drug use monitoring tools with the wastewater tool should build on the strong aspects of each method (see table 1 on next page) and on the need of the society. Testing the Waters 2015 aims to contribute to the interesting challenge to develop good strategies for integration of monitoring methods for different societal needs. And, last but not least, theme 5 indicates the potential to expand wastewater-based epidemiology to public health aspects beyond illicit drugs.

Description of themes

Theme 1 Targeted (Inter)National Monitoring & Early Warning Systems

Responsible members of scientific committee Caleb Banta-Green; Christoph Ort; Malcolm Reid; Liesbeth Vandam; Guido Van Hal.

This topic will cover the integration of wastewater studies with existing drug monitoring tools. It has been demonstrated that wastewater analysis can increase our understanding of drug use patterns at local, national and international level. Integrated knowledge will also form the basis for adequate prevention measures. We will set the scene by presenting major drug trends and developments and identify where wastewater analysis can provide important complementary insights. Contributions are encouraged that demonstrate and discuss the usefulness of wastewater analysis complementary to traditional surveillance data (TSD) from existing drug surveillance systems (added value). A particular focus should be on integrative attempts that strive for combining TSD and WBE in concerted efforts in a single project. Furthermore, this topic welcomes studies that show WBE results from parts of the world where there are no standardized surveillance systems or no TSD exist in order to gather knowledge on the use of illicit drugs in these regions. Additionally, the emerging issue of an increasing number of synthetic new psycho-active substances will be covered in this topic. Wastewater-based epidemiology or pooled urinalysis can effectively contribute to an early warning system to detect these substances, which will be crucial to take prompt action to protect consumers' health.

Theme 2 Methodological Improvements in Wastewater-based Epidemiology

Responsible members of scientific committee Ellen Amundsen; Frederic Been; Lubertus Bijlsma; Adrian Covaci; Angela Me.

The primary focus of WBE to date was on a reliable quantification of DTR mass loads in wastewater. To work towards a realistic estimation of consumption, numerous factors need to be further improved. This involves refining methods and develop new approaches to determine the number of people that effectively contributed to a given wastewater sample. Most promising is the analysis of human biomarkers in wastewater. Furthermore, studies on excretion rates of existing and new DTR as well as studies on the transformation of DTR in sewers are required. Besides extended evidence on these physical and chemical parameters used for a basic "back-calculation", new mathematical models and statistical approaches (data triangulation) are being developed with the aim of being able to i) include information from other sources and ii) provide realistic uncertainty estimates of the final results. Therefore, Bayesian inference techniques have great potential in WBE. Meaningful contributions in this topic are expected to originate from groups that are heavily involved in projects that were set up in a trans-disciplinary manner from the very beginning.

Table 1. Aspects of traditional surveillance systems and wastewater-based epidemiology. One of the main goals is to suggest approaches on how to best combine pros of the two approaches and overcome individual cons.

Aspects	Traditional surveillance systems	Wastewater-based epidemiology
1. Size of investigated population (under-representation of certain groups)	⊖ Limited sample size (hundreds to thousands). No sample is representative for all drug users in the population. Population surveys and (local) targeted surveys among drug users have to be combined to estimate the population of drug users.	⊕ Entire population connected to a central sewer system (tens to hundreds thousands up to millions).
	⊕ Population samples can be spread over an entire country/region.	⊖ Covering non-metropolitan areas increases number of samples (small wastewater treatment plants).
2. Response rates	Decreasing	not applicable
3. Information on individuals' consumption habits	⊕ Prevalence over different time spans (7-day, 30-day, 12 months, life time)	⊖ completely lacking
	⊕ Gender, age, education, additional socio-economic information	
4. Self-report bias	⊖ Evaluation implies substantial additional effort: Validation of self-reported use can be assessed by blood, oral fluid and urine for last 24 hour/week use and hair samples for last/several month use. Quantity cannot be assessed by such methods.	not applicable
5. Total amount consumed by a large population	⊖ Methods so far use a quantity/frequency approach based on surveys (bottom up) or a market approach based on distribution from production areas to the market (top down). Both methods will be subject to bias and uncertainty. Extent of bias and uncertainty are difficult to quantify.	⊕ Can be calculated with realistic uncertainty estimates (good sampling and back-calculation procedures must be applied)
6. Time lag of results	Usually long (several months/half a year or longer). Better routines based on electronic questionnaires and production may decrease time lag.	Near real-time possible (if quality control can be guaranteed and results are not published in a peer-reviewed journal).
7. Dosage and purity	⊕ Limited information is available, but possible to expand (measure purity "on the scene", hire trend scouts).	⊖ Completely lacking, only total of "clean" drug of a community is measured
8. Environmental transformation of drug residues	not applicable	⊖ requires further research
9. Quantification of number of people (population-normalized drug loads)	not applicable	⊖ Quantification of commuters/tourists requires further research/application of existing methods.
10. Providing realistic estimates for uncertainty and bias	Traditional sampling survey theory yields uncertainty estimates for population surveys. Bias is usually difficult to assess. Assessment of uncertainty of combined surveys (general population and targeted surveys) can employ bootstrapping techniques.	⊕ feasible for various results on a daily/weekly basis (drug residue loads in sewers, consumption estimates)
		⊖ assessing longer periods (e.g. annual averages) requires new monitoring setups than currently is the norm
11. Total number of consumers (in specific region/period)	difficult to quantify due to point 1	difficult to quantify due to point 3
12. Frequency of data collection	relatively infrequent (1-3 years)	can be done on a daily basis
13. Follow consumers over time (cohort? study)	Longitudinal (cohort) studies are not uncommon, but they are costly and subject to drop out over time.	not possible
14. Ethical issues	Country- and context-dependent: In many surveys data must be made anonymous. With informed consent and a promise of secrecy from the researcher, data do not have to be anonymous. The interviewee can be contacted again or other information can be matched to the original data.	depends on setting Avoid too small areas of sampling(?)
15. Costs	dependent on type of survey and number of participants	dependent on number of samples and analytes

Theme 3 Advances in Analytical Chemistry

Responsible members of scientific committee Erik Emke; Felix Hernández; Barbara Kasprzyk-Hordern; Justice Tettey; Alexander van Nuijs.

The chemical and physical complexity of a wastewater sample is the reason why LC-MS/MS is the most widely applied technique, owing to its excellent sensitivity and selectivity. However, in the last couple of years, several research gaps and requirements were identified. These include: i) limited application of high resolution mass spectrometry (HRMS) to identify unknowns and perform retrospective analysis, ii) lack of fast, sensitive and reliable multi-residue analytical methods, iii) limited understanding of impacts of matrix components on the performance of mass spectrometry methods, iv) requirement for more effective sample preparation methods, v) need for new bio-analytical approaches to identify and quantify health biomarkers (see topic 5), vi) need for real-time and cost-effective measurements of biomarkers in wastewater through electrochemical or bio-analytical sensing. In this section relevant analytical advances will be discussed, including hybrid HRMS (utilizing QTOF and LTQ Orbitrap for target and non-target screening, and multi-residue quantification approaches), enantiomeric profiling (to distinguish consumed and disposed drugs or production waste) and sample preparation (large volume injection and on-line SPE). Developments in novel (bio-)analytical approaches for identification and quantification of health biomarkers including biosensors and OMICs techniques will be also presented.

Theme 4 Ethical and Legal Aspects

Responsible members of scientific committee Pim de Voogt; Paul Griffiths; Jeremy Prichard.

In most countries ethical aspects of conducting research are governed by professional codes or national legislation. No specific ethical guidelines currently exist for researchers analysing wastewater to detect illicit drugs or other drugs such as pharmaceuticals, alcohol or nicotine. Ethical issues most often arise when researchers collect data from individuals. Most of the existing ethical codes of con-duct and guidelines do not obviously apply to the conduct of WBE because it does not involve collecting data on individuals, as the intermingled urine of many thousands of people cannot be used to identify individual drug use. Relatively little attention has been paid to the ethics of WBE research in part because of its novelty and in part because it is not readily amenable to traditional approaches to research ethics. While most studies of WBE have concentrated on mapping indicators of population drug consumption, several studies have applied WBE in specific settings, such as prisons, schools and music festivals. In such cases WBE researchers have to deal with ethical issues related to drug use in identifiable groups, such as disadvantaged communities, prisoners and school students. Potential harms include the stigmatization of participants and, in the prison and school settings, austere policy responses to WBE data that impact negatively upon inmate-participants or students. Wastewater-based epidemiology cannot provide the type of evidence that is usually required in criminal proceedings or forensics because no data on individuals are collected. However, circumstantial evidence may be collected from WBE research, for example from enantiomeric profiling of DTR in wastewater that result from direct discharges into sewer; from parent drug/biomarker ratios that may reflect direct discharges; or from comparative analysis of raw materials (that may have been dumped or found at police raids) and synthesized products or from the analysis of synthesis intermediates to develop strategies to discover clandestine/illicit laboratories

Theme 5 Innovative Applications: Wastewater Analysis for Community-wide Health Assessment

Responsible members of scientific committee Sara Castiglioni; Pierre Esseiva; Kevin Thomas.

Thus far, WBE focused on the targeted analysis of well-established DTR to determine levels of illicit drug use. The near-real-time nature of WBE opens up possibilities of developing targeted analyses for new drugs, which are becoming available at unprecedented rates according to a recent EMCDDA report. With the advent of advanced analytical techniques (see topic 3), there is ample opportunity to develop screening procedures for new drugs (see topic 1) as they enter the market, as well as retrospectively analyze for these drugs in previously analyzed samples. Although conceptually simple – i.e. traces of almost everything we consume are excreted unchanged or as a mixture of metabolites in urine and feces ending up in sewers – it was only in 2011 that WBE was proposed to also reveal valuable insight into

aspects of public health other than illicit drug consumption. The range of excreted biomarkers of endogenous human metabolism is, therefore, broad and exhibits the clear potential to develop a series of innovative techniques as a solution to quantitatively assess patterns of factors related to lifestyle, health, nutrition, and environmental exposure within populations. Recently, the WBE approach has evolved to include legal drugs such as nicotine and alcohol. Another example are isoprostanes that have been proposed as potential biomarker to measure the collective and systemic oxidative stress response of an entire community as part of a wider measure of community health. Specific approaches to assess human exposure to environmental and food contaminants (such as pesticides and fungal toxins) are also under development. It is hypothesized that individual communities will show different patterns with respect to the levels of various biomarkers and this difference can be related to lifestyle (e.g. alcohol, tobacco and drug use), health, nutrition and environment within each community. The development of novel applications in this field is particularly relevant because it can provide objective and updated information of several different factors related to a specific population. Such information must be integrated with existing monitoring systems and data sources to establish knowledge that form the basis for adequate prevention measures.

Format

Due to the pronounced inter- and trans-disciplinary character of the topic it seems of utmost importance to create an opportunity for scientists – and other stakeholders – to attend the same (only) session to counteract the typically observed phenomenon of attending the (parallel) session one is most familiar with. This aspect will be further accounted for with time allocated for working groups. Furthermore, the schedule with starting these groups on Monday afternoon should stimulate informal discussion and provide sufficient time to prepare the second half day (synthesis, see program on next page). This shall foster truly trans-disciplinary projects, which is eminent to direct science and to demonstrate the benefit in real world applications. This was a clear conclusion of the organizers and participants of the only conference to date (EMCDDA, Lisbon, 2013) specializing in wastewater-based epidemiology (WBE).

The entire Wednesday is dedicated to presentations by early stage career researchers to present and get involved in scientific discussions. The best presentation will be awarded (sponsor maybe the Swiss Federal Office of Public Health). Furthermore, it seems important to emphasize the need to involve policy makers and stakeholders in the discussion. Another special feature is the Poster Flash session scheduled just before the lunch break. It provides an efficient way of giving selected posters a face. Authors will be given a two-minute time slot to advertise their poster. The time after lunch for a 2-hour poster session with all posters is ideal to counteract the “after lunch fatigue”. Usually posters stimulate discussions at least as strongly as presentations and, therefore, it seems important to dedicate a prominent space to posters on the first full day.

In summary, the suggested program, keynote speakers and targeted audience (expected participants) is perfectly suitable to i) exchange newest research outcomes, ii) identify and fill research gaps, iii) focus research directions, iv) facilitate inter-, trans-disciplinary and cross-sectoral thinking. This will enhance our understanding and our appreciation of potential benefits resulting from large-scale routine application WBE as a platform and an early-warning system for societal health and lifestyle assessment. Explicitly encouraging participation of early-stage career researchers is essential to enhance their networking and consequently increase the likelihood for a new generation to follow an academic career.

Tentative Programme

	SUNDAY 11 OCT 2015	MONDAY 12 OCT 2015	TUESDAY 13 OCT 2015	WEDNESDAY 14 OCT 2015	THURSDAY 15 OCT 2015
8:30-9:00		*Keynote 2*	*Keynote 4*	*Keynote 5*	*Keynote 8*
9:00-10:00		Oral 1-3	Oral 7-9	Oral 10-12	Oral 24-26
10:00-10:30		Break	Break	Break	Break
10:30-11:00		*Keynote 3*	**Working groups** (condense, synthesize and present)	*Keynote 6*	*Keynote 9*
11:00-12:00		Oral 4-6		Oral 13-15	Oral 27-29
12:00-12:30		Poster Flash 1-10 (moderated)		Discussion	Final discussion
12:30-14:00		Lunch	Lunch	Lunch	Lunch (opt.)
14:00-16:00	Registration	Poster Session	**Excursion**	*Keynote 7* Oral 16-19	
16:00-18:00	Welcome Reception	**Working groups** (discussion)		Oral 20-23 Discussion	
18:00-18:30		Break		Break	
18:30-20:00	Dinner (opt.)	Dinner	**Conference Dinner Isola Brissago**	Dinner and award ceremony for best presentation of the day (all young researchers)	
20:00-22:00	Introduction, *Keynote 1* and Discussion (prepared)	Reserve for 5 oral presentations			

⇒ **Summary:**
- **9** **Keynotes** 30' each, incl. questions; all 9 invitation-based
- **34** **Oral presentations** 20' each, incl. questions/speaker change; 6 invitation-based, up to 28 open submissions [14 for young researchers only (Wednesday)]
- **10** **Poster flash presentations** 2' each, moderated format, to kick-off the 2-hour poster session in the afternoon