VOLUME 2 NUMBER 10

The OPCW Science & Technology Monitor

A sampling of Science & Technology Relevant to the Chemical Weapons Convention

16 October 2015

In This Issue

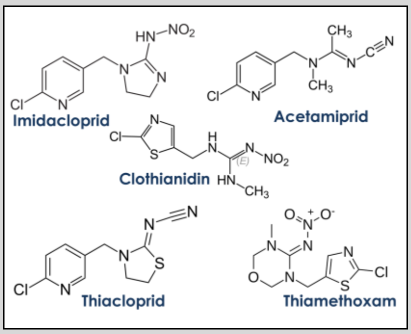
Featured content

From D. Endy, S. Galanie, C. D. Smolke. http://dx.doi.org/10.1101/024299

Fermentation of opiates

Image from Pixabay.

Genomics



Neonicotinoids

Welcome

Welcome to the *OPCW Science and Technology Monitor*, an occasional bulletin to provide updates on developments in science and technology across a broad spectrum of topics relevant to the CWC. Past issues are available from the Science and Technology section of the OPCW website.

We begin this issue with a round of applause for the 2015 Nobel Prize winners. In physics: Takaaki Kajita and Arthur B. McDonald "for the discovery of neutrino oscillations, which shows that neutrinos have mass". In physiology or medicine, a tale of anti-parasite drugs: William C. Campbell and Satoshi Ōmura "for their discoveries concerning a novel therapy against infections caused by roundworm parasites"; and Youyou Tu "for her discoveries concerning a novel therapy against Malaria". In chemistry: Tomas Lindahl, Paul Modrich and Aziz Sancar "for mechanistic studies of DNA repair". In economic sciences: Angus Deaton "for his analysis of consumption, poverty, and welfare". In literature: Svetlana Alexievich "for her polyphonic writings, a monument to suffering and courage in our time". Last but not least, the Nobel Prize of Peace was awarded to the Tunisian National Dialogue Quartet "for its decisive contribution to the building of a pluralistic democracy in Tunisia in the wake of the Jasmine Revolution of 2011". Congratulations to all!

The S&T Puzzle

Our periodic table puzzle finally ended the CTBTO winning streak! One of our own Industry Verification Officers accumulated 458 points by identifying CWC relevant examples of elements: H, C, N, O, F, Na, Si, P, S, Cl, Ti, Cr, Mn, Fe, Co, Ni, As, Mo, I and W. Puzzle statistics now stand at: VER 5, OSP 2, OCS 1, INS 1 and CTBTO 5.

In this edition of the puzzle, we ask you to identify differences between the images on the left. The first person to correctly list all of them wins the prize: a choice of requesting a featured topic or designing a puzzle or a hand selected beverage courtesy of the Science Policy Adviser.

A bonus prize if you can tell us which of our Office of Strategy & Policy colleagues is under the mask. Send answers by email.

Science Fun:

For this edition of Science Fun, we looked for commonality amongst neonicotinoids, fermentation, and genomes: we found a food that does not spoil and is produced on an economically viable scale by an insect (an insect adept at chemistry and whose genome tells us, originated in Asia; details here). The food is not the insect itself, but the honey it produces!

Honey is produced from plant nectar by honey bees. It contains carbohydrates (sugars), proteins, free amino acids, vitamins, minerals, anti-oxidants and other chemicals; the chemical composition reflects the type of nectar collected (DNA sequencing helps too). The geographical origin can be determined by the chemical composition and isotope ratio analysis (a technique used in chemical forensics) can identify adulterated samples.

Photograph from Pixapay.

Making honey is quite the effort: it requires flying more than 176,00 km and visiting more than 5.7 million flowers, just to make 1 kg of the stuff. Worker bees go off into the world and collect nectar from flowers and store it in a "honey stomach", where sugar (sucrose) in the nectar is enzymatically broken down into glucose and fructose. On returning to the hive, the worker bee regurgitates its payload and sends it off to a house bee. The house bee continues the enzymatic breakdown process started by the worker bee (by repeatedly drinking and regurgitating the nectar). Once suitably processed, the nectar is deposited into a honeycomb.

News and Updates

Recent reports and publications:

Briefing to States Parties by OPCW Scientific Advisory Board Chair from EC-80.

Evaluation of the Results of the 37th Official OPCW Laboratory Proficiency Test and Status of Laboratories Designated for the Analysis of Authentic Samples.

September 2015 issue of Dstl's *inSIGHT*.

Converging sciences – the extent of interdisciplinary research and why it matters.

How to avoid bias in research and other challenges in irreproducibility from *Nature*.

A look at editing mischief for contentious scientific topics on Wikipedia (details here).

2015 Global Innovation Index.

Verification handbook - a definitive guide for verifying digital content for emergency coverage.

Ambassadors on twitter and best practices for Ambassadorial tweeting.

Science, education and industry resources:

The Hague Ethical Guidelines provide a set of key elements related to the practice of chemistry under the norms of the CWC. These guidelines have also been translated into Spanish.

A 3D Printing Database.

Recipes for Biomedical & Life Sciences Researchers from Springer.

An app for counting elephants toenails to learn math!

The ESCom Package - Key process for the successful implementation of REACH.

A collection of A0 printable OPCW S&T related Posters is online: biomedical sample analysis, physicochemical properties of chemical agents, mechanism of action of nerve agents, mechanism of action of blister agents, mechanism of action of choking agents, mechanism of action of blood agents and WWI gas mask development timeline.

Some news from world of science and technology:

From the weeks of 9 – 15, 16 – 22, and 23 – 29 August; 30 August – 5 September; 6 – 12, 13 – 19 and 20 – 26 September; 27 September – 4 October; and 4 – 10 October in chemistry.

A dehydration process takes place to bring the water content of the honey below 18% (nectar can contain over 70% water); higher water content can actually allow yeast to ferment the honey. Bees accelerate the evaporation process by fanning with their wings. In the end, it takes several days to convert watery nectar to syrupy nectar, and here is one of the secrets behind honey not spoiling – low water content combined with low water activity (e.g. limited water available to support bacterial growth and the low water content promotes the dehydration of bacteria).

There is of course more to the story than simply limited water. Honey contains a number of acids (including gluconic acid, the result of enzymes acting on glucose) and typically has a pH around 4. The formation of gluconic acid will also produce hydrogen peroxide – a chemical that increases the antibacterial properties of honey! Did you know that honey has antimicrobial and antibiofilm applications? It has been used in traditional medicine for treating skin wound infections and disease; there are even commercially available anti-bacterial wound dressings. It turns out honey finds use in burn treatment, treatment of athlete's foot, as an anti-inflammitory and an anti-oxidant. Compounds found in honey even may have applications in chemotherapy (as well as mitigating side effects of chemotherapy agents). This would appear to indicate that honey is a microorganism free product, but alas some of the microrganisms in our world are quite resilient and can survive in honey (and they may not always be benign!).

As most of us probably don't think of honey as a medicinal substance; we are likely to be more familiar with its use in cooking and baking. Perhaps it could be thought of as a sweetener with medicinal

Fermentation

As a means of producing chemicals, fermentation has been used for centuries, the method is particularly valuable for producing protein based and other biopharmaceuticals. For those watching trends in modern chemical production, fermentation has attracted considerable attention in relation to the bioeconomy and a blurring distinction between certain industrial chemical and biological processes (as illustrated by the production of organic acids as platform chemicals).

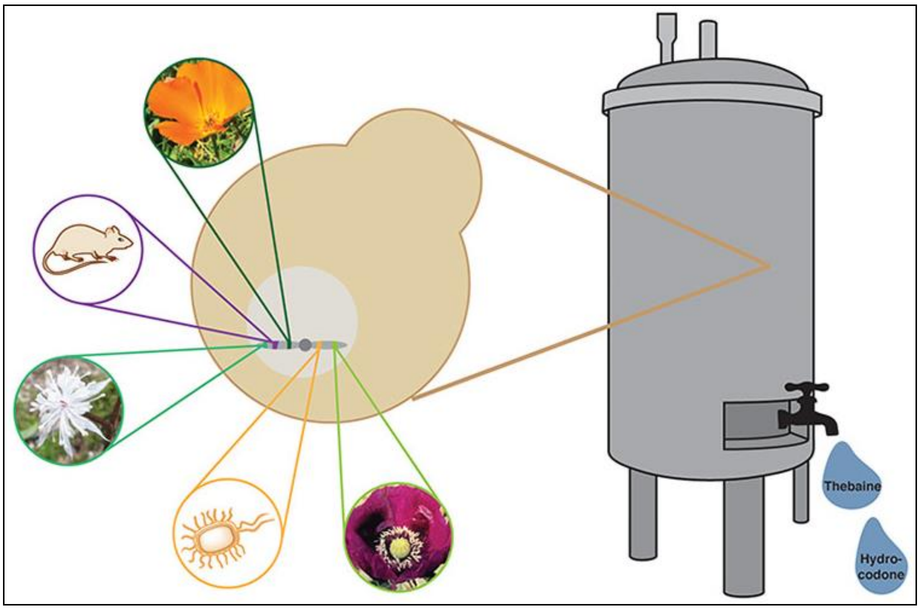


Image from Stanford News.
A bioengineering team engineered more than 20 genes from five different organisms into the genome of baker's yeast; the result: a yeast capable of converting glucose into hydrocodone.

Much has been written on large volume biobased chemical production, the engineering of microorganisms, complexity and limitations of metabolic engineering, and the adoption of biotechnology for chemical production. We have also been alerted to challenges facing industrial biotechnology for commodity chemical production resulting from low oil prices and oil price volatility. As oil prices stay low, the expense associated with some biobased processes to produce fuels (from algal biomass for example) requires co-production of additional biochemicals with economic value; requiring engineering microorganisms capable of accumulating multiple products and coculture systems. The use of fermentation to produce speciality and fine (bio)chemicals, such as flavours, fragrances, cosmetic ingredients and isoprenoids is an active area of growth. This is exemplified by the shift of synthetic biology based companies to these sectors; more information on the types of products emerging from synthetic biology companies can be found here). With this in mind, we take this opportunity to look at some recent developments in speciality (bio)chemicals arising from microbial fermentation processes.

The wealth of information resulting from breakthroughs in genomics has enabled a broad spectrum of metabolic engineering opportunities and approaches. Examples include producing and screening new forms of antibiotics (details here);

properties? Of course, the ability of honey to produce products for human consumption goes well beyond sweets, as demonstrated by its use in fermentation!

When thinking about all this honey, ask yourself how important it is to have the honey removed from the insect. If you are looking for sweet honey mixed with protein, perhaps the honey pot ant is a more desirable treat?

"HoneyAnt" photogtaph by Greg Hume at en.wikipedia..

Crowdsourcing:

The City of The Hague invites students and organisations to submit ideas to solve global challenges such as safety & security, energy, climate and food to The Hague Innovators Challenge 2016. Prizes worth 5,000 to 35,000 euros will be awarded to the best submissions.

The Humanitarian Innovation Fund is looking for a lightweight, portable, simple, efficient, and durable incinerator for medical waste. Must be suitable for use in humanitarian emergencies!

Reimagine CO_2 by converting emissions into high value products in the $20M NRG COSIA Carbon XPRIZE.

Do you have a world-changing invention that you would like to see in the pages of *Popular Science* Magazine? If yes, enter your creation in the 2016 Invention Awards

Need some tools to help with social innovation projects? Take a look at the DIY (Development

eliminating the need to milk poisonous snakes to produce anti-coagulants (details here); and "brewing" perfumes or silk proteins.

Recent examples with implication for pharmaceutical production include modifying yeast strains with genes from plants to enable production of opiates (details here) or cannabinoids (details here) starting from glucose. The prospect of yeast strains producing narcotics has received attention in the popular press and prompted calls for regulation. Suggestions were made that a home brewing kit might be used to produce drugs of abuse; however, in an attempt at home brewing pharmaceuticals, researchers failed to detect opiates in their ale.

The ale kit example reminds us that developing an engineered microbe based production process requires combinatorial approaches to metabolic engineering and high-throughput screening processes to identify strains capable of performing in desired process conditions and scales; highly automated microfluidic systems are an integral part of this work (details here). This can require screening millions of strains, as illustrated in a recent article about the company Amyris, Inc., in order to identify single digit numbers of strains capable of performing at commercial scale. Additionally, tolerances of the microbes to process conditions (thermally and in regard to toxicity of the metabolites being produced for example) must be considered; requiring suitable means of strain evolution.

Given the broad ranges of natural and unnatural chemical products obtainable through fermentation, the methodology is well suited for sustainable chemical production initiatives; as described in a recently published roadmap to accelerate the advanced manufacturing of chemicals.

Genomics

The Human Genome Project (HGP), one of biology's first "Big Science" projects, celebrated its twenty-fifth birthday last month; twenty-five years in which the field of genomics, the study of the complete set of DNA within a single cell or an organism, has seen enormous technological development. Genomics has opened up new possibilities for applications in healthcare, helped scientists identify the genes that make a person more attractive to mosquitos (the genes producing certain body odours), better understand the evolution of octopus cleverness (details here) and provided a means to study historical livestock by sequencing historical documents. With the "next generation sequencing" market expected to grow to over 27 billion USD by 2022, there will be continued investment and further discoveries to come.

Today, the amount of genomic data that is produced doubles every seven months; should this continue, expect there to be more genomic data in 2025 than astronomy, YouTube and Twitter data combined! Thus begging the question, should we replace the term "astronomical" with "genomical"? It is

Impact and You) Toolkit.

Upcoming S&T Related Events:

OPCW Calendar of Events October to December 2015.

19 - 23 October
International Conference on Global Emergency Preparedness and Response
Vienna, Austria.

31 October - 2 November 2015
The Port Hackathon
CERN

3 November
The 6th edition of the Intelligent Sensor Network Conference
High Tech Campus, Eindhoven, The Netherlands.

4 – 7 November
World Science Forum
Budapest, Hungary.

16 – 19 November 2015
Malta Conference
Rabat, Morocco.

18 – 21 November 2015
16th Asian Chemical Congress
Dhaka, Bangladesh.

22 – 27 November 2015
2nd African Conference on Research in Chemical Education (ACRICE)
University of Venda, Thohoyandou, South Africa.

23 – 25 November 2015
XIIIth International Symposium on Environment, Catalysis and Process Engineering (ECGP'13)
Hammamet, Tunisia.

30 November 2015
Emerging Technologies and the CWC: Autonomous Systems and Artificial Intelligence CSP-20 Side Event Organised by UNICRI, Hague Security Delta and OPCW
World Forum, The Hague, Netherlands.

genomics (combined with other "Omics" technologies) that are enabling the large scale metabolic engineering of microbes and expanding the potential of the fermentation based chemical production methods described in the previous feature.

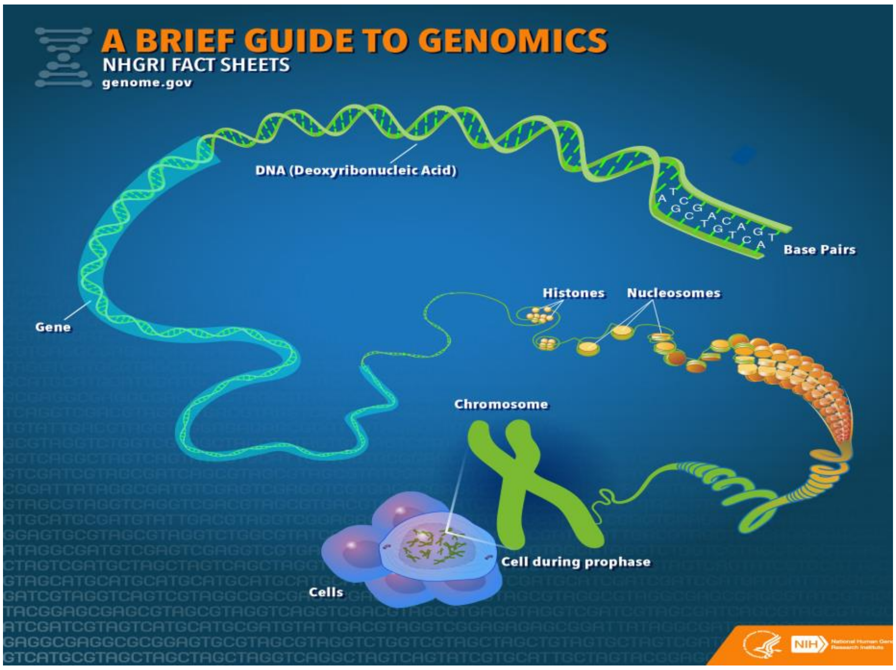


Image from the *National Human Genome Research Institute*.

DNA sequencing, effectively a chemical analysis of the building blocks of DNA (**A**denine, **G**uanine, **C**ytosine and **T**hymine) has become a powerful tool for studying biological systems. Examples of large scale studies include sequencing of entire human populations (including ancient populations using DNA extracted from archaeological samples) and large scale microbial mapping studies of urban areas (such as New York City; see also erratum). The actual cost of sequencing has dropped to the point that companies can now charge1000 USD for the sequencing of a complete human genome! In the case of large scale industrial metabolic engineering, high-throughput methods have been (and continue to be) developed.

The tools employed for DNA sequencing continue to advance and miniaturized devices are commercially available. Nanopore sequencers for example, have been used in real-time analysis of salmonella outbreaks in a hospital, viral pathogen detection in clinical samples and in West Africa for rapid Ebola testing.

Sequencing microbial populations in wounds or the eyes of individuals (the ocular microbiome); or in areas where bacteria thrive such as an athletic facility (details here) are three examples of how sequencing can provide information that helps to prevent the spread of infection.

Of relevance to the world of safety and security, sequencing can be used to rapidly detect pathogens, elucidate the origin and transmission of viral outbreaks (Ebola), to detect foodborne illnesses and for precision emergency medical treatment.

Data handling and informatics is a key aspect of the use of

2 December 2015
"Science for Diplomats":
Chemical Forensics.
CSP-20 Side Event
World Forum, The Hague,
Netherlands.

14 – 18 December 2015
Biological Weapons Convention
Meeting of States Parties.
Geneva, Switzerland.

15 – 20 December 2015
Pacifichem 2015.
Honolulu, Hawaii
United States of America

2 – 4 February 2016
The Unmanned Systems Expo (TUSE)
The World Forum, The Hague
The Netherlands.

6 – 10 March 2016
Pittconn 2016
Atlanta, GA
United States of America

13 – 17 March 2016
251st American Chemical Society National Meeting & Exposition
San Diego, CA
United States of America

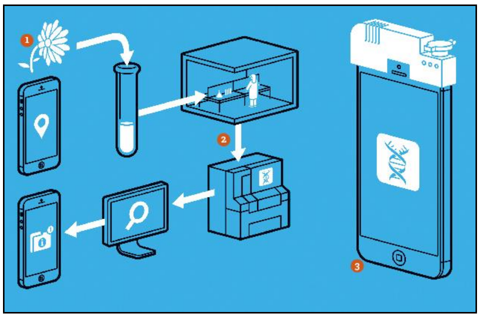
6 – 8 April 2016
XXI IUPAC CHEMRAWN Conference
Solid Urban Waste Management
Rome, Italy.

21 July 2016
2016 Spring ConfChem
Science, Disarmament, and Diplomacy in Chemical Education: The Example of the Organisation for the Prohibition of Chemical Weapons.

15 – 20 August 2016
24th IUPAC International Conference on Chemistry Education (ICCE 2016)
Kuching, Sarawak.
Malaysia.

4 – 7 September 2016
52nd Congress of the European Societies of Toxicology (EUROTOX2016)
Istanbul, Turkey

sequencing technologies. Detection and identification of pathogens requires matching data to reference sequences in databases, in this respect the data used in analysis is not limited to genomic data. For example, organisms that produced a detected protein sequence can potentially be identified by recognising the DNA sequence required to express that protein (and genomic data can be validated by comparison to proteome data, a technique used in proteogenomics). A pitfall to this type of analytical approach is the need for databases free of "contaminated" sequence information. These proteogenomic approaches are valuable tools for the study of toxins and other natural products.



Can DNA be sequenced by iPhone? (Apps already exist!). *Image from* United Hemisphere.

We are very familiar with how chemistry influences biology, to further illustrate this phenomena consider a new set of nucleobases created by chemists (**Z**, 6-amino-5-nitro-2(1*H*)-pyridone and **P**, 2-amino-imidazo[1,2-*a*]-1,3,5-triazin-4(8*H*)one) and how much additional information a 6-nucleotide based genome would contain!

Without adding new nucleobases, there is plenty of sequencing work to be done as our biosphere already contains enough DNA to fill an estimated one billion standard shipping containers (details here). Just in case we do run out of samples, the work won't stop as arrangements are already being made to bring sequencing to the stars!

Neonicotinoids

Since their introduction in the 1990's, neonicotinoids have become the most widely used class of agricultural insecticides in the world; imidacloprid, clothianidin, acetamiprid, thiacloprid and thiamethoxam represent the most common of these compounds. These insecticides have received much attention due to concerns of their effect on bee colonies. Hundreds of scientific studies have been carried out to address this issue: providing evidence that can both support claims and raise uncertainties. Further complicating this issue is an observation that bees may actually prefer neonicotinoid-laced nectar!

Neonicotinoids are systemic, being taken up by the plants and transported to leaves, flowers, roots, stems, pollen and nectar. The insecticide remains active in the plant for weeks, protecting the crop throughout a growing season. The insecticides are often applied as seed coatings, with large scale use on crops such as maize, soy and cotton. The insecticides also find use in

Contact Us:

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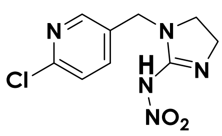
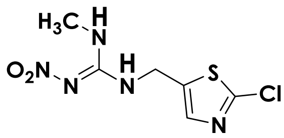
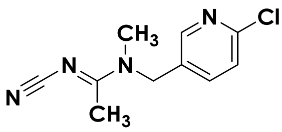
the treatment of turf, as foliar sprays in orchards, in soil treatment of trees and potted plants, and in a range of greenhouse crops.



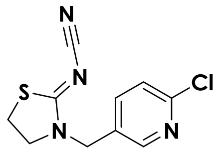
Imidacloprid



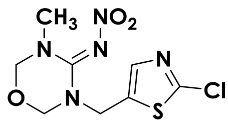
Clothianidin



Acetamiprid



Thiacloprid



Thiamethoxam

Neonicotinoids selectively target the nicotinic acetylcholine receptor in insects. The compounds bind to this receptor, stimulating nerve excitation which leads to paralysis and death. While mammals also have nicotinic acetylcholine receptors, structural differences between the insect and mammalian receptors (creating selectivity for the types of chemicals they bind) result in toxicity to insects but not mammals. Examples of neonicotinoid toxicity to other invertebrates (aquatic invertebrates and earthworms) have also been reported Reports of acute human poisoning from neonicotinoid exposure are rare; however, concerns about potential health impacts to humans from neonicotinoid metabolites is an area of current research.

With such wide scale use of neonicotinoids, understanding environmental risk and fate (including under varying soil conditions); persistence and concentrations in farm soil (including farms employing conservation practices); and the residual levels in the crops themselves are important. Available studies include soil applied insecticides in irrigated agricultural systems, and the use of insecticide mixtures. Neonicotinoid residues from agricultural activities have been detected in streams and other surface waters (global reviews and regionally focused studies are available), prairie wetlands, wild flowers, snow melt and soil dust. All of these studies remind us of the importance of analytical chemistry and sampling and analysis for pesticides.

The presence of neonicotinoids and their breakdown products in the environment raises the potential for direct and in-direct (food chain) effects in wildlife ecosystems (an active area of research especially in regard to the concerns on neonicotinoid impact on pollinators). Bioremediation of neonicotinoid contamination is possible and photocatylictic and oxidation-based methods for neonicotinoid degradation have also been tested.

As environmental effects of neonicotinoids and possible impacts on benign insect populations continue to spark debate, scientists continue to explore alternative chemistry that may have use in pest control. Recent studies have identified candidate chemicals that include terpenes (details here), butyl anthranilate (a compound found in fruit, details here) and spider venom.

Science & Technology at the Biological Weapons Convention Meeting of Experts

The Biological Weapons Convention (BWC) Meeting of Experts was held from 10 – 14 August 2015. Under the advances in science and technology standing agenda item, papers were submitted by Iran (statement here), Switzerland (on convergence and on reviewing developments), the United Kingdom (on response to infectious disease outbreaks – statement here and on production and delivery - statement here) and the United States (on production and delivery, and tacit knowledge).

The Chair of the OPCW Scientific Advisory Board (SAB) presented the work of the SAB in plenary and in an S&T side event. Switzerland (on CRISPR/CAS9) and the Georgia Institute of Technology (on vaccines) provided additional S&T presentations; and statements on science and technology were delivered by The Inter Academy Panel (IAP), India, The Netherlands and Russia (in Russian). The S&T side event featured contributions from Biosecure, IAP, and the Research Group for Biological Arms Control (who also presented a poster).

Additional side events with science and technology dimensions were held on microbial forensics (supporting and use in attribution analysis) and the UN Secretary-General's Mechanism (training and analysis network). Of relevance to sampling and analysis from the poster session: a description of real-time detection of biological aerosols from the Swedish Defense Research Agency.

Biosecurity education featured prominently in the Meeting of Experts. A side event on safeguarding science included presentations on biosecurity textbooks (also in the poster session), the gain-of-function debate, biosecurity in Denmark and contributions to biosecurity from scientific organisations. In a second side-event organised by the Netherlands, biosecurity awareness raising to students, professionals and the synthetic biology community was discussed along with biosecurity self-assessment.

An advance meeting report is available.

As the BWC prepares for its 8th Review Conference in 2016, assessment of bioweapons threats and advances in science and technology with BWC implications are receiving significant attention. A pertinent question: can BWC governance keep pace with technological change? To help move these assessments forward, a symposium (with participation from scientific experts) was held from 13-15 September in Warsaw. A report of this symposium is forthcoming.

2015 BWC Meeting of Experts. Photo by Filippa Lentzos

BWC Trends Symposium (Polish Academy of Sciences)

Did You Know?

Brazilian wasp (*Polybia paulista*) venom can selectively kill cancer cells?