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Dear readers,

After the Physics division (Fukushima) and the Chemistry division (Syria) were involved in international events, our biologists were also confronted with a crisis of global dimensions: the outbreak of the Ebola epidemic in West Africa placed great stress on the public health systems of the affected countries. But even Europe and the USA were tested, considering that almost as many nurses were infected as Ebola patients treated. This clearly indicates the necessity of information campaigns and training options. We were involved in the on-site diagnostics in Guinea within the context of the European Mobile Laboratory (page 14).

Particularly in demand are research laboratory capacities that satisfy the highest bio-safety requirements. Our biosafety laboratory, in service since the beginning of 2014 – meets the highest safety standards and is the only facility in Switzerland that is equipped to safely handle highly infectious pathogens like the Ebola virus. One of the international research projects we are involved in is a vaccination candidate against Ebola (VSV-ZEBOV). We are examining how effectively vaccine-generated antibodies are able to inactivate the virus, by using samples from persons participating in a study by Geneva University Hospitals.

Crises relevant to civil protection increasingly tend to be of global dimensions. Our experts must be capable to form networks both nationally and internationally. For this purpose, we are establishin new research partnerships. Every year we provide academic internships in Spiez for several Ph.D. and M.Sc. students from a variety of scientific disciplines. We seek to continue and extend our close collaboration with universities and polytechnics.

As a focus of our international activities, we started in October 2014 a new workshop series, Spiez CONVERGENCE. Experts discussed the implications of the growing convergence of chemistry and biology for arms control. The conference report was compiled in cooperation with the Centre for Security Studies of the ETH Zurich (page 22).

In the nuclear field, arms control has almost no hope of succeeding without trans-national cooperation. From 5 November until 9 December 2014 the Comprehensive Test Ban Treaty Organisation (CTBTO) conducted in Jordan its most extensive field exercise to date involving the investigation of a possible violation of the treaty. An expert from our Physics division was involved in the “on-site inspection”. Such an inspection would serve as a last option for verifying a suspected incident, such as an underground nuclear test, should the monitoring system have failed to unambiguously identify a violation of the treaty (page 6).

Dr. Marc Cadisch
Director SPIEZ LABORATORY

The Comprehensive Nuclear-Test-Ban Treaty Organization (CTBTO) conducted a large field exercise in Jordan

Thanks to international experience, we continuously incorporate new developments into our scientific-technical expertise and are therefore able to optimise our services on behalf of Switzerland's civil protection. Thus, we accepted the mandate for operating the National Reference Centre for Tick Transmitted Diseases (NRZK). It provides confirmatory or reference diagnostics for tick-transmitted pathogens in human samples. Furthermore since 2014 we have been operating, on behalf of the Federal Office of Public Health, the National Reference Centre for Anthrax (NANT), which is responsible for monitoring highly pathogenic bacteria.

As Federal Institute for NBC Protection, we are obliged to constantly improve the quality and performance of our measuring instruments and methods, in order to be able to respond to new challenges: For identifying toxic chemicals, we introduced the method of high-resolution mass spectrometry (page 30). When it is suspected that humans have been exposed to a chemical warfare agent, biomedical samples can be analysed and tested for the presence of certain substances. One of the Ph.D. theses we supervised, examined what marker substances might be involved and how they could be synthesised in order to use them as reference chemicals (page 26).

Our scientific-technical expertise is applied in an inter-disciplinary fashion and the resulting synergies strengthen our activities in environmental analytics. We regularly support analytical missions of the UN Environment Programme. In 2014, we tested the efficacy of modern bullet trap systems in underground shooting ranges in Switzerland. If such systems are insufficiently insulated they can severely contaminate the environment with heavy metals (page 10).

Effective NBC protection is only possible if we recognise threat situations and risks early on, anticipatingly develop our expertise and provide essential up-to-date equipment. In this way we will be able to respond to a crisis quickly and flexibly. Without the engagement and creativity of competent experts this would be impossible. I wish to express my cordial thanks here to the staff of Spiez Laboratory for their great commitment.

CTBTO: Integrated Field Exercise in Jordan

Dr. Christoph Wirz

The Comprehensive Test Ban Treaty Organisation (CTBTO) is establishing a control regime that is able to check on compliance with the Comprehensive Test Ban Treaty (CTBT). On-site inspections form part of this regime, in order to establish definitely, whether a suspicious incident really is related to a nuclear explosion. At the end of 2014 in Jordan, the CTBTO carried out its most extensive inspection exercise to date, the "Integrated Field Exercise IFE14". The exercise has shown that today nuclear weapon tests can no longer be kept a secret.

The CTBT bans all nuclear explosions, whether for military or for peaceful purposes. The treaty was opened for signature in 1996 at the UN in New York; however, it has not yet entered into force. The CTBT specifies 44 nuclear-capable countries that must ratify the treaty to bring it into force. The ratifications of the USA, China, Israel, Iran, Egypt, India, Pakistan and North Korea are still lacking. Nevertheless, already today, the Vienna based CTBTO maintains a world-wide monitoring network to ensure compliance with the treaty, and is capable of detecting nuclear weapon tests. The network consists of monitoring stations spread across the globe to measure seismic shock waves, sound waves in both water and air and to detect radionuclides in the air. In addition, when the treaty is in force, an "on-site inspection" (OSI) can be demanded by a member state if non-compliance is suspected, in order to definitely determine whether an underground nuclear test has been carried out. From 3 November to 9 December 2014, the CTBTO organised a major field exercise in Jordan, the "Integrated Field Exercise IFE14". A chronologically compressed on-site inspection was practised that made use of 15 of the altogether 17 inspection techniques foreseen in the treaty. Spiez Laboratory uses its expertise to assist in verifying compliance with the test ban treaty and was involved in the IFE14 exercise with a radionuclide expert.

Organisation of the exercise

Jordan hosted the IFE14, providing an area of about 1000 km² (see map) as well as administrative und material support. In a genuine inspection, where the CTBTO would "merely" be concerned with the actual investigation, the Integrated Field Exercise also entailed additional

tasks: More than 250 people were involved in the exercise. Participants were assigned to teams and had to assume various roles:

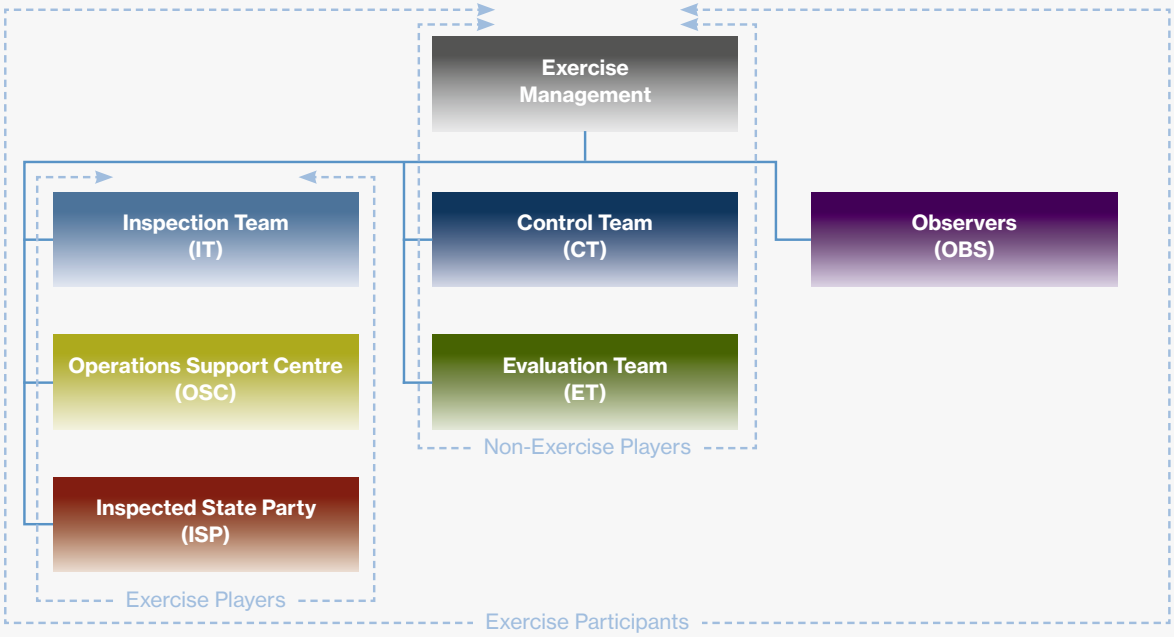
- Exercise Management assessed the safety of the exercise layout and decided what safety precautions were necessary. They were also in charge of logistics and material transport as well as the point of contact with Jordan, the host nation.
- The main participants in the exercise were the Inspection Team (IT) supported by the Operations Support Centre in Vienna and as "opponent" the Inspected State Party (ISP).
- The Control Team construed a fictional but technically realistic scenario and ensured that the agenda was followed as planned during the exercise.
- The Evaluation Team observed the individual teams, collected the suggestions of participants and evaluated these.

Initial phase

The inspectors convened in Vienna and arrived as team at Amman airport on 7 November 2014, where they were received by members of the Inspected State Party team. After receiving the inspection mandate and the "initial inspection plan", safety instructions followed. Negotiations were made about the location and organisation of the operations base, about the logistical support as well as the detailed plans for the first days of the inspection. In parallel, the 150 tons of inspection equipment were checked. It included items such as measuring instruments, sensors, communications equipment, generators, tents, etc., that were transported in especially designed freight containers. These containers served in the field as weather protected storage rooms and as shelters where instruments could be serviced. According to the treaty the inspected state party has the right to check all the equipment and to reject anything not listed in the mandate. The time allotted to such activities in the treaty is limited. On 9 November, the transfer was made to the actual inspection area, where the Base of Operations was also assembled.

The exercise was conducted in an inspection area of up to 1,000 km² on the banks of the Dead Sea - some 100 km southwest of Amman.

Measuring the earth's magnetic field



Organisational structure of the Integrated Field Exercise 2014

Inspection phase

From 11 November to 4 December, various field teams, always escorted by representatives of the ISP were deployed each day. They installed measuring devices, brought back data and samples to the Base of Operations. The samples were measured in the laboratory later and the data evaluated and interpreted. The escorts from the ISP had to ensure that, both in the field and the laboratory, no measurements were made other than those determined beforehand and that these were carried out correctly.

The inspection phase consisted of two parts, the "initial period" and the "continuation period". According to the treaty, not all measuring methods are permitted during the initial period. Here only slightly intrusive methods may be applied to reduce the inspection area to a few "polygons of interest".

Overflights are extremely important at the beginning of the inspection to photograph the entire area and to visually search for suspicious structures and to examine unnatural changes in terrain. During later flights, radioactivity could be measured from the air. Seismic sensors were installed throughout the entire inspection area. They serve to localise tremors, so called aftershocks, which can occur up to two weeks after a nuclear explosion.

Monitoring radioactivity is important during every phase. During the initial phase, downwind samples of dust and air are collected and then tested for radioactive nuclides in the laboratory. In addition, the field teams measure gamma radiation at each mission location. Two different types of instruments are used here for measuring. One device serves to measure the dose rate. It is easy to use and very sensitive. If the dose rate is elevated, other devices are used that can reveal what nuclides have caused the increased dose rate.

This initial period ends with the "Progress Inspection Report", which is sent to the CTBTO centre in Vienna and on the basis of which the Executive Council decides whether the inspection is to be continued. In the IFE14 exercise, this initial phase lasted for 13 days. As expected, the field exercise continued and during the "continuation period" more intrusive techniques could be applied. In this case, the inspectors' focus of interest was on two large quarries. There, techniques such as ground penetrating radar, magnetic and electromagnetic field mapping, resistivity DC and active seismic methods were applied. These techniques serve to detect underground constructions, cables and pipelines, but can also be used to obtain information on geological details such as folds or faults in layers of rock. Geological data serve to find the best locations for "subsoil gas sampling". For this technique a 5 to 10 metre hole is drilled into the ground, a tube is inserted and the hole opening sealed off with cement. Afterwards gas that the ground contains can be slowly drawn out into a balloon. The gas is

To localise tremors, seismic sensors were installed throughout the entire inspection area

then transferred to pressure flasks and measured in the laboratory. If measurements reveal the presence of certain radioactive noble gases, this is proof of an underground nuclear test in the closer vicinity.

Post inspection phase

After the inspection, the inspection team compiles the "Preliminary Findings Document". This report should contain facts only and no assumptions or any allegations of guilt. As with a genuine on-site inspection, the IFE14 exercise led to tough negotiations on how individual issues were worded in the report, before both sides were able to sign the document. The report was then sent to Vienna where in the case of a real inspection, the CTBTO Executive Council would have to decide whether the treaty had been violated or not.

Altogether the IFE14 exercise was outstandingly well prepared and directed by the Control Team and Exercise Management. Jordan provided the CTBTO with an ideal area that provided many challenges for the exercise. The techniques applied functioned well. Within an area of 1000 square kilometres it was possible to pin down a suspect region of 300 square metres. One was able to reliably measure the radionuclides that had been added to the samples. The IFE14 exercise constituted an important step forward with regard to possible entry into force of the treaty. The exercise has shown that the control mechanisms for ensuring compliance with the treaty would function well.

The exercise required 150 tons of inspection-equipment

Gamma measurement on-site

Subsoil-Gas-Sampling to measure various radioactive noble gases

Sustained protection of the environment at shooting ranges with man-made bullet trap systems

Alfred Jakob

Poorly insulated man-made bullet trap systems at shooting ranges can over the years lead to health-threatening concentrations of heavy metals in the environment. For this reason, insulation requirements for such installations are nowadays extremely high. The environment analysis group of Spiez Laboratory has both the expertise and the measuring procedures to test the insulation of modern bullet trap systems through live fire in underground shooting tunnels where airborne dust concentration is measured.

Lead and various lead compounds were used in a variety of applications in the past. The serious health risks associated with these heavy metals were rarely examined and often unknown. Consequently, e.g. lead piping was used for drinking water. Pigments for colouring and enamel contained lead compounds such as lead chromate. The use of highly toxic lead tetraethyl as antiknock additive in petrol for gasoline engines is well known. Also lead accumulators in car batteries are prevalent all over the world. Soldering tin used in printed circuit boards and electronics may contain lead too.

Today, it is known that lead is a toxic heavy metal that can lead to severe chronic poisoning, even when absorbed by humans in small doses of a few milligrams over weeks and months. Current research shows that the intake of lead severely damages the nervous system, impairs kidney function and the cardiovascular system. Typical lead poisoning symptoms are anaemia and retarded mental and physical development in children.

Leaded petrol is no longer used in Switzerland since January 2000. The toxic antiknock petrol additive tetraethyl was prohibited in the entire EU in 2005. International guidelines (RoHS regulations: “Reduction of Hazardous Substances”) to reduce dangerous substances in electronic devices are in force today. Since 2005, lead-containing electric or electronic devices are no longer allowed to be sold in Switzerland and the EU. This is to prevent toxic heavy metals from being disposed of in waste and contaminating ground water. In food ordinances the safety limits for lead are downsized regularly.

Man-made bullet trap system

Warning poster

Approximately 4000 shooting ranges in Switzerland are listed in the registry of contaminated areas. The bullet traps of these installations are heavily contaminated with lead and every year more lead accumulates in the bullet traps.

Large amounts of lead are processed and incorporated into bullets of differing calibre. Ammunition lead is not pure lead but a lead-antimony alloy containing 2–5 % antimony. Its toxicity is comparable to that of arsenic and consequently highly poisonous. In many shooting ranges the projectile is collected in natural earth bullet traps. As the rounds contain approx. 90 % ammunition lead, this results over the years during which the range is in use, to extreme local contamination of the soil. Under the influence of weather the projectiles in the ground corrode. Antimony compounds form, some water soluble, which are mobilised through precipitation and consequently can put drinking water at risk. Today, the bullet traps are fenced off as a safety precaution to prevent humans and animals from being directly poisoned. Bullet traps located in ground water preservation zones have to be remediated.

The Environmental Protection Act lays down that harmful effects on the environment must be prevented or limited at an early stage. That means that continued firing into earth bullet traps violates this precautionary concept. Due to severe soil contamination with heavy metals and the possible endangering of humans and the environment, owners of shooting ranges are obliged to upgrade their bullet traps. To prevent renewed contamination of the ground after clean-up, man-made bullet traps are integrated into the range.

Today, various man-made bullet traps are in use that reliably and sustainedly prevent further environmental contamination when correctly integrated and under emission-free operation.

Slightly deformed rounds from a granulated bullet trap

Severely fragmented and pulverised rounds from a lamella bullet trap

This bullet trap works on the principle that the rounds are collected in a box that serves as a bullet trap positioned behind the target plate. The projectile penetrates the front plate of the bullet trap (usually a thick plastic plate) and is decelerated within the bullet trap box.

Deceleration of the projectile within the bullet trap can be either elastic or non-elastic. In the former case, the projectile is either not or only slightly deformed and exposure of the projectile core is prevented. Such deceleration is achieved with soft materials such as rubber granulate. When the projectile is decelerated by the non-elastic method e.g. through steel lamella, it is significantly shattered and the some of its core is reduced to powder.

It is obvious that bullet traps which are not fully insulated contaminate the environment with heavy metals. So insulation requirements are high, in particular for lamella bullet traps. In constructing the bullet trap, the manufacturer must meet the fire technical safety requirements as well as comply with environmental legislation.

The environmental requirements comprise of the following points:

- Heavy metal emissions comply with legal restrictions throughout the bullet trap's entire service life
- Emission free maintenance of the bullet trap
- Disposal and recycling of heavy metals from ammunition
- Disposal of contaminated materials

Spiez Laboratory is very experienced in airborne dust measurements and possesses the corresponding instruments required. The air in the vicinity of the bullet trap is collected with an air sampling device and airborne dust is fully extracted with a filter. The chemical analysis of the filter provides direct information on the concentrations of air pollutants, such as heavy metals.

Man-made bullet trap systems can be tested by Spiez Laboratory through legally compliant measurement of emissions. By firing in an underground shooting tunnel and subsequently measuring the airborne dust, bullet trap systems can be reliably tested for lead emissions. Because disturbing wind effects are excluded in the shooting tunnel, reproducible test results can be obtained. The Environmental Analysis group of Spiez Laboratory has years of experience in these tests and is able to conduct these according to an accredited procedure.

Operation of the airborne dust sampler in the field

Air filters loaded with different amounts of dust

Ebola-Diagnostic with the European Mobile Laboratory in Guinea

Jasmine Portmann

Since March 2014 European scientist teams have been on a field mission in Guinea with a mobile laboratory, to investigate suspected Ebola cases and to strengthen the local laboratory capacity. Spiez Laboratory was involved in the mobile laboratory mission in the area of the epidemic with a lab-technician and was thus able to provide support in Ebola diagnostic in the framework of a mission by the World Health Organisation (WHO) and "Doctors Without Borders". The main task of the mobile lab was to investigate suspected cases for Ebola infection.

In the current epidemic, the highly pathogenic Ebola fever virus found its first victim in a small village in the West-African Republic of Guinea: a two-year old from a village in the Guéckédou district was first infected by the virus at the end of 2013. (N Engl J Med 2014;371:1418-25). On 2 December 2013, the child complained of abdominal cramps. Subsequently the child developed fever, bloody faeces and vomiting. Four days later, it died of the disease. In the following days and weeks, its three-year old sister, its mother, grandmother and a nurse suffered the same fate. People who had looked after the sick child, who had been present at the mourning services and had had physical contact with the deceased, carried the virus into their families and the nearby settlements.

The disease spread very rapidly: Already after twelve weeks, the area where cases occurred encompassed several ten thousand square kilometres – the Index patient and its relatives did not live in a remote area, but at an important traffic hub. Furthermore it was only realised relatively late that the disease in question was indeed Ebola. Several doctors first assumed that it was a case of Lassa-fever– a relatively frequent, but less lethal viral infection. Not before 10 March 2014, i.e. well over three months after the first casualty, did the regional health services and hospitals inform the Ministry of Health of the Republic of Guinea about a strange and highly lethal disease associated with fever, vomiting and diarrhoea. Finally, the government confirmed the outbreak of Ebola on 19 March 2014.

Medical station of “Doctors Without Borders” in Guéckédou

Family of filoviruses

Genus	Species	Virus name	Lethality
Cuevavirus	Lloviu cueva virus	Lloviu virus	?
Ebolavirus	Bundibugyo ebolavirus	Bundibugyo virus	25–50 %
	Reston ebolavirus	Reston virus	0 %
	Sudan ebolavirus	Sudan virus	30–60 %
	Taï Forest ebolavirus	Taï Forest virus	0 %
	Zaire ebolavirus	Zaire virus	60–90 %
Marburgvirus	Marburg marburgvirus	Marburg virus	25–80 %

The Ebola virus belongs to the filoviridae family. Due to its clinical progression, the Ebola virus is regarded as one of the viruses that can cause haemorrhagic fever (VHF). Among the five virus species of Ebola three have caused greater epidemics among humans (Zaire, Sudan, Bundibugyo). The outbreak in west Africa can be traced to the Zaire line.

Shortly after this confirmation, the European Mobile Laboratory Project (EMLab) of the WHO’s Global Outbreak Alert and Response Network (GOARN) was requested to provide on-site support. The EMLab has three mobile lab units which are stationed in Munich, Tanzania and Nigeria for immediate deployment. Devices for analysis and consumables are stored in 15 transport containers that can be transported by commercial airlines. These mobile laboratories for diagnostics are able to carry out a variety of methods to detect highly pathogen microorganisms. The EMLab is staffed by European lab specialists who work with highly pathogen viruses and bacteria. It cooperates on location with the health authorities, the WHO and “Doctors Without Borders”. It is financed by the EU, and coordinated by the Bernhard-Nocht-Institute for Tropical Medicine in Hamburg.

After only three days of preparation of, the first members of the EMLab travelled on 26 March 2014 to Guéckédou to fight the outbreak of Ebola. Guéckédou is a small town in the South of Guinea that has grown to about a quarter of a million inhabitants since the civil wars. The region around Guéckédou proved to be one of the areas in Guinea most severely affected by the epidemic.

“Doctors Without Borders” had already established a medical station on location to clinically diagnose and treat Ebola patients. The EMLab was able to make use this infrastructure and assemble its laboratory in a tent. Which allowed the team to begin testing patient samples quite quickly. This enabled reliable laboratory diagnosis of the disease, which was one of the basic prerequisites for taking effective measures to overcome the crisis: The confirmation of the Ebola virus and its analysis in the lab provide information for conclusively retracing the path of infection and thus deciding what further steps have to be taken to limit the outbreak.

A lab technician from the Virology group of Spiez Laboratory was part of the third EMLab team that was deployed in May 2014 to Guinea:

The mobile labs can be packed into 10 to 15 robust, dust and water tight boxes weighing 30 kg each for air or road transport

At the location of operation the laboratory is adjusted to existing infrastructure. A minimum surface area of 20 m² is required.

The Ebola pathogen is transferred with the body fluids of infected animals and humans. Ebola viruses are only infectious for a short time outside the host body, but can be transmitted by contaminated objects. Danger of infection exists as soon as the patient suffers from symptoms of the disease such as fever, vomiting, diarrhoea. To date, there is no evidence for transmission by air.

The incubation period is 2–21 days. The basic reproductive rate R0 shows how many people are infected on average by each infected person. For Ebola R0 is around 2. So the average sick person infects up to two other persons. Depending on the type of Ebola involved, 50 to 90 percent of those infected die.

five members from Germany, Italy, Slovenia and Switzerland flew from Munich via Paris to Conakry the capital of Guinea. They were received there by the WHO and went through various safety briefings. They continued their journey with a small plane to the forest province of Guinea, in the middle of the crisis region.

The team moved into its lodgings at the only hotel in Guéckédou, where all the other WHO staff (lab staff, epidemiologists, logisticians) were housed. For work, the team was ferried with WHO vehicles through the small town over bumpy roads to the medical station of "Doctors Without Borders" some ten minutes away. Every morning the medical staff of the station, observing the strictest safety regulations, took blood samples from new patients or from in-house patients to check their progress. Work at the laboratory began at eight o'clock in the morning and lasted as long as it took.

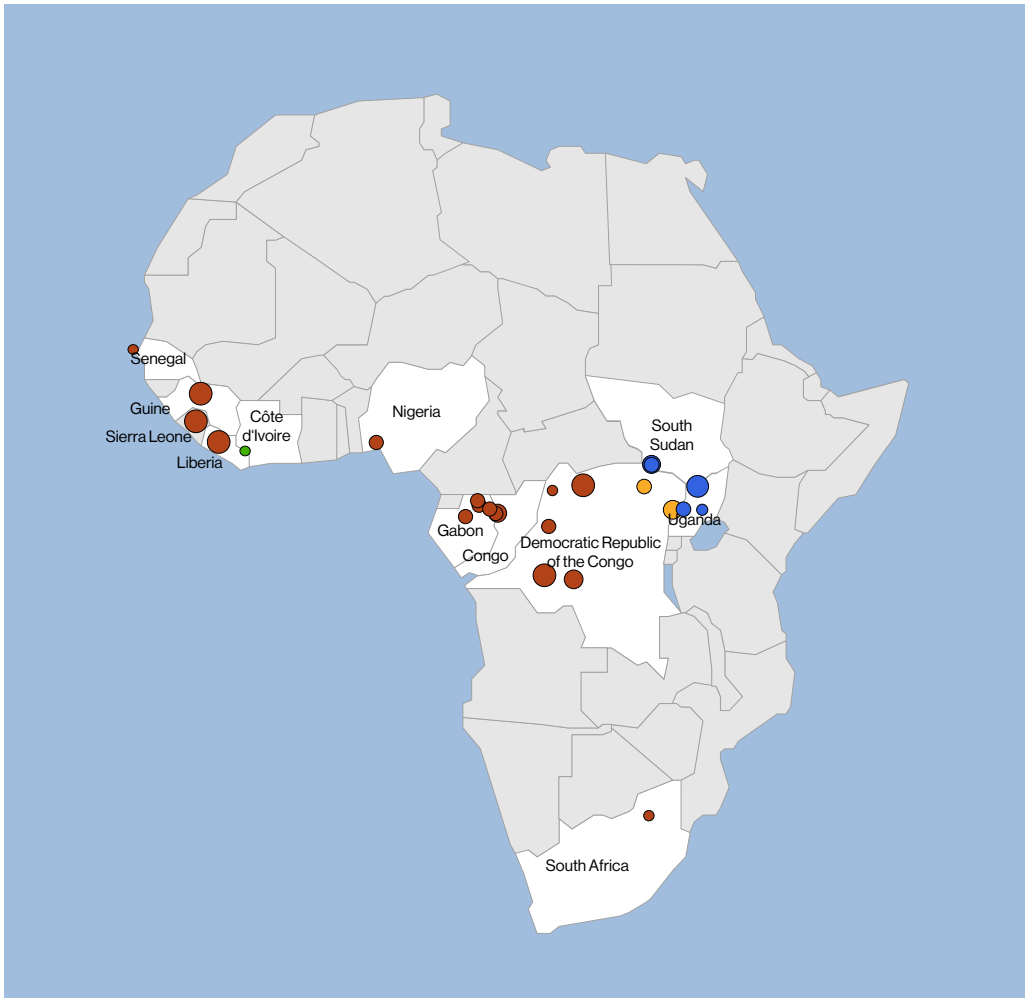
The samples were safely packed at the isolation ward and brought to the laboratory. There patient information was checked first, then the samples were given a lab number and entered into a database. Afterwards, the mobile staff members cautiously transferred the samples one-by-one into the glove box, where a constant under-pressure is maintained by a ventilation system. In this safe environment the samples could be chemically inactivated.

Together with the differential diagnosis, the team also carried out an additional rapid test for malaria in the glove box. The glovebox-procedure was the most time consuming step in the process and also physically the most demanding one, as every sample had to be processed separately. On days with a particularly high influx of patients, about 15 samples could be processed during the morning hours.

Outside the glove box the genetic information i.e. the ribonucleic acid (RNA) of the virus was extracted from the inactivated sample with a commercial kit. With the use of a molecular biological detection method, the polymerase chain reaction (PCR), it was possible to confirm or exclude the presence of the Ebola virus RNA in a given patient sample. The EMLab evaluated the results of the analysis and communicated these to the treating physicians of "Doctors Without Borders".

Late in the afternoon, a further batch of samples that had come in during the day could be processed. These analyses occupied the team often until late into the evening. This sometimes proved to be quite a challenge as additional electricity was required at night, which sometimes put a strain on the generators.

Samples often had to be tested in between in order to obtain a result as quickly as possible, for instance in emergency cases involving children, pregnant women or patients in very critical condition. Occasionally, the EMLab team also received samples from the Red Cross funeral team that ensured the observation of safety precautions during funerals. When the cause of death was unclear, the Red Cross members first took a swab sample from the oral mucosa and sent the sample for analysis to the mobile laboratory. The procedure from sampling to lab result took about four hours. These lab results were of great importance for the physicians of "Doctors Without Borders",



Among the five virus species of Ebola three have caused greater epidemics among humans (Zaire, Sudan, Bundibugyo). The outbreak in west Africa can be traced to the Zaire line. (Map CDC)

Ebolavirus outbreaks by species and size, 1976 – 2014

Species:
- *Zeire ebolavirus*
- *Sudan ebolavirus*
- *Tai Forest ebolavirus*
- *Bundibugyo ebolavirus*

Number of cases:
- *1–10*
- *11–100*
- *101–300*
- *Greater than 300 reported cases*

left:
Glove box for chemical inactivation of patient samples and for differential diagnosis

right:
Management of equipment poses particular challenges

as depending on the outcome of this analysis, further measures had to be taken quickly.

During the entire operation, a nine-year-old girl accompanied the EM Lab team. Ten relatives of the sick child had died of Ebola. The girl, however fought tirelessly for the best part of three weeks against the disease and kept the entire medical station on the go with her loud voice. On her final day before leaving, the EM Lab team tested the girl for Ebola and the result was negative for the third time. She had already been without fever for almost a week and had no symptoms of the viral infection any more. The result was loudly and effusively celebrated by all involved. The mother, the girl's only surviving relative was at last able to take her daughter into her arms. A defining and lovely experience to conclude the mission.

Afterwards the EMLab continued to operate on location in both Guinea and Sierra Leone, and part of the time in Nigeria und Liberia too. The EMLab teams are relieved every four weeks. Although staffing the teams and the resupply of consumer goods is a logistic challenge, the EMLab will remain on location until the epidemic is overcome.

Genome based analysis of the Swiss Francisella tularensis holarctica population

Dr. Matthias Wittwer

Since 2014, the Biology division of Spiez Laboratory has assumed two reference functions on behalf of the Federal Office of Public Health (FOPH): the National Reference Centre for Tick-transmitted Diseases (NRZK) and the National Reference Centre for Anthrax (NANT), which is in charge of reference diagnostics and monitoring of highly pathogenic, bioterrorism-relevant bacterial germs (including F. tularensis). Due to their bioterrorist relevance and the clinical importance of tick transmission in Switzerland, F. tularensis is thematically relevant to both reference functions. The Biology division has therefore made the description of the structure of the Swiss F. tularensis population one of its research emphases. The focus is on the significance of ticks as vectors from animal to human and on epidemiological issues.

Tularemia, also called rabbit fever, is an infectious disease caused by Francisella tularensis and can manifest itself in various forms of disease. In its natural infection cycle the disease infects wild mammals; with mice, hares and rats being affected most frequently. The highly infectious pathogen is transferred by hematophagous insects (mosquitos, ticks) or through direct contact with infected animals und can survive for three months in the environment (ground, water). Two main types of the germ are known: Type A (subspecies tularensis) is the more virulent (more severe symptoms) strain and occurs mainly in North America. Type B (subspecies holarctica) causes a more mild disease and is prevalent throughout the entire northern hemisphere.

Due to the extremely low dose required for infection (10–50 germs) and the high mortality rate of air transmitted infection, F. tularensis is included in the Category A list of potential B weapon agents together with anthrax and plague.

Sampling

To obtain a more detailed understanding of tick-associated diseases, Spiez Laboratory began in 2009 to collect samples of ticks from all over Switzerland in collaboration with

NBC Defence Lab 1. On the basis of this investigation, it was possible to define six regions where there is an increased prevalence of F. tularensis holarctica (Figure 1).

Well over 100 000 ticks have been analysed since. Of these, only 0.01 ‰ proved to be positive for F. tularensis holarctica. In collaboration with the Robert Koch Institute in Berlin it was possible to cultivate and isolate F. tularensis from positive tick lysates for the first time. The successful cultivation has confirmed the role of ticks as vectors and is prerequisite for the subsequent phylogenetic typing with "next generation sequencing" methods described below. To determine the epidemiological connection between tick isolates and human infections more precisely, the genomes of 20 F. tularensis holarctica strains were sequenced (9 human- and 11 tick isolates from 4 different geographic regions).

Molecular epidemiology

Over the past thirty years, classification of organisms according to their genetic information has become an indispensable principle in molecular biology. The first methods to be developed in this field were based on enzymatic digestion of the entire genome; length and number of ensuing fragments allow conclusions regarding the identity of the organism. As these methods permit only a limited taxonomic resolution, new procedures were established as time went on which were based on deciphering (sequencing) the genome. The precision of genome based classification has continually increased due to the perfection of genome sequencing technologies. This development culminated in the availability of "next generation sequencing" devices that make it possible to decipher the entire genome of an organism for few hundred francs. Only the maximum resolution achieved from knowing the entire genome sequence enables us to subdivide bacteria such as F. tularensis, whose genetic information hardly changes over generations, into epidemiologically and forensically relevant subpopulations. Procedures like next generation sequencing which allow the description of the entire genome of an organism, open new ave-

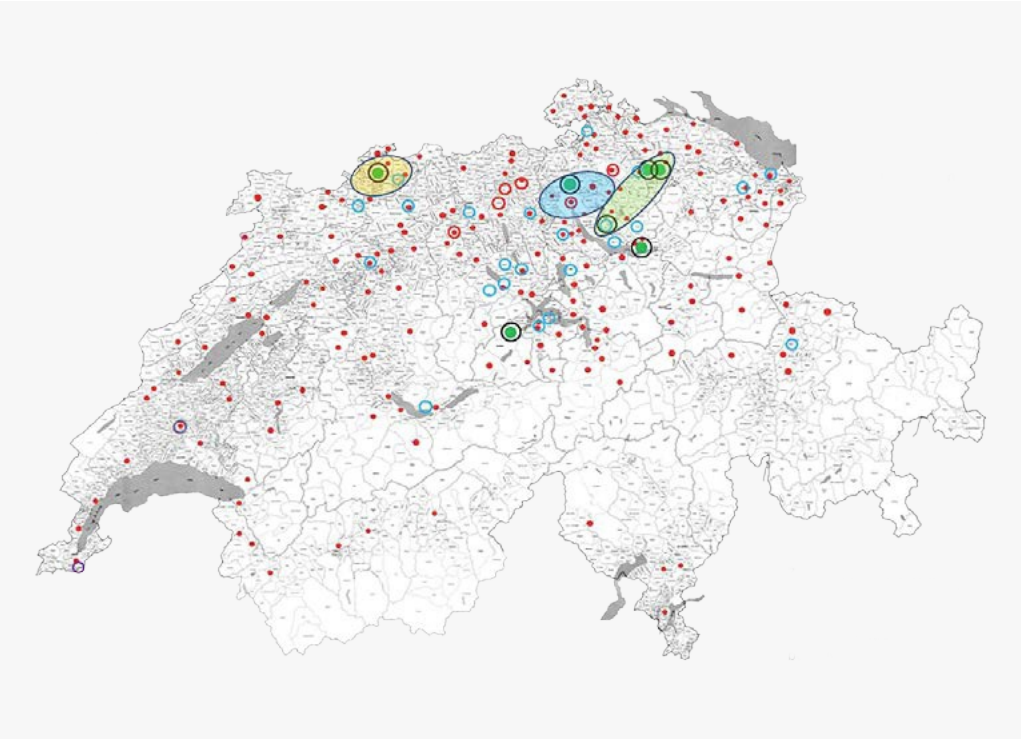


Figure 1: Overview of the tick sampling locations of 2009 and 2012. The highlighted areas indicate regions of markedly higher prevalence of F. tularensis in ticks and of human infections. The regions with a higher prevalence are situated noticeably in northern and central Switzerland.

- *Region B*
- *Region Z*
- *Region S*

- *Tick sampling locations in 2009*
- *F. tularensis positive in 2009*
- *Tick sampling in 2012*
- *Reported cases of human infections*

nues into forensic epidemiology for the Biology division and provide the basis for further developing and optimising existing methods in molecular biology.

Describing the extent of kinship between different organisms by comparing whole genomes gives rise to new phylogenetic issues. It is still unclear how the loss (deletion) or insertion of long DNA sections can be translated into a measure for relational similarity. For this reason genome based phylogenetic analysis is limited to “single nucleotide polymorphism” (SNP). This method focuses on differences in the DNA sequence that are caused by the substitution of a single nucleotide and are passed on from generation to generation. The Limitation to SNPs also has the advantage that analysing demands less computing capacity from IT infrastructure.

Results

As expected, SNP-based genome comparison allows the allocation of the majority (18/20) of the isolates to the “Franco-Iberian” strain FTNF002-00. This strain occurs primarily in France, Italy and Spain and is also prevalent in Switzerland. Two human isolates indicate a closer kinship to the north-European B.13 strain that is dominant in Scandinavia, Germany and in east-European countries.

As far as kinship extent within the 20 sequenced isolates is concerned, it stands out that the geographic origin of tick isolates is reflected in the similarity of their genomes. Such micro-geographic differentiation of F. tularensis is unexpected considering the low mutation rate of the genome and underlines the potential of the method.

The high degree of kinship between tick and human isolates (Fig.2: Region B and Region Z) confirms the role of ticks as a zoonotic vector.

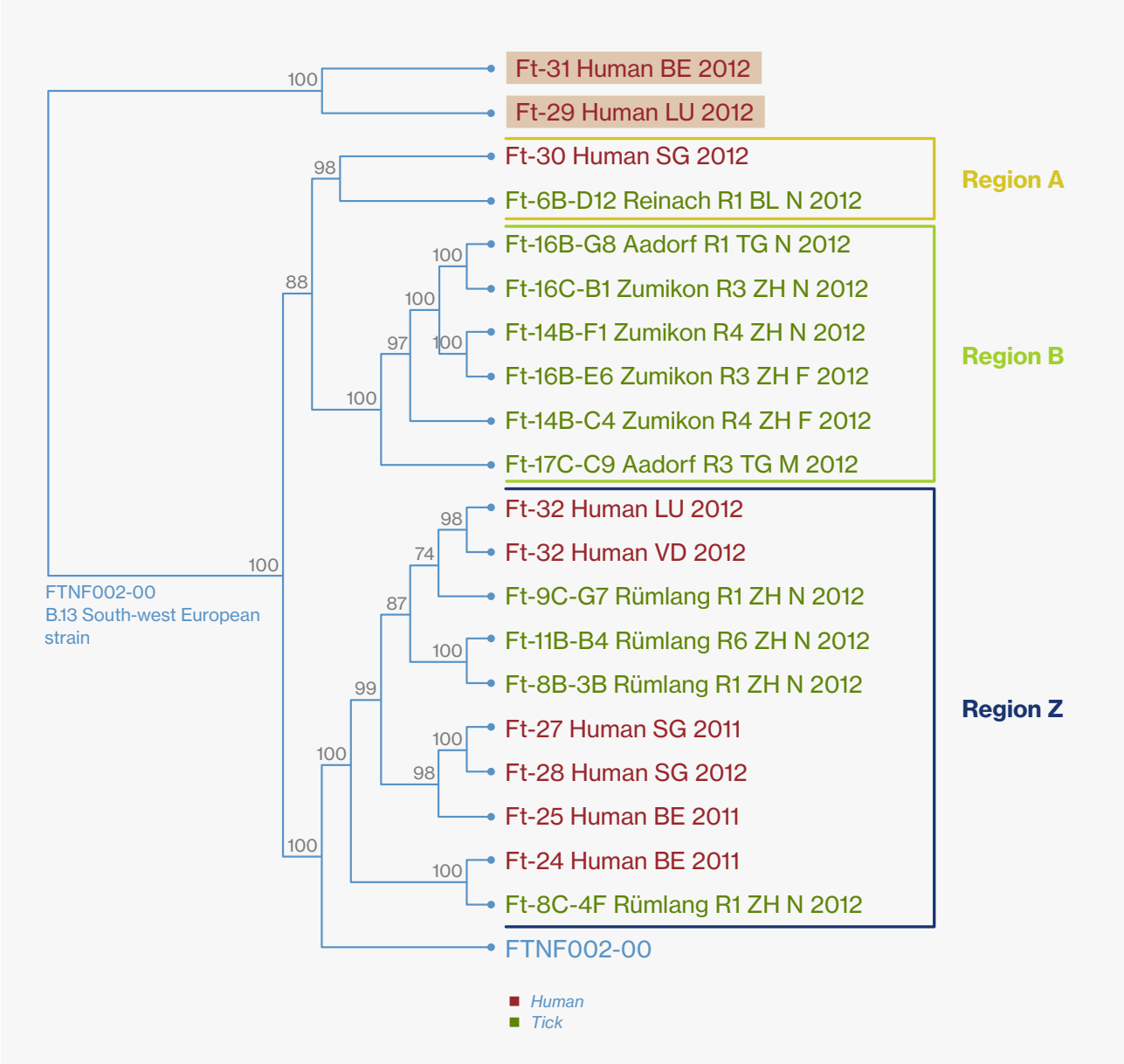
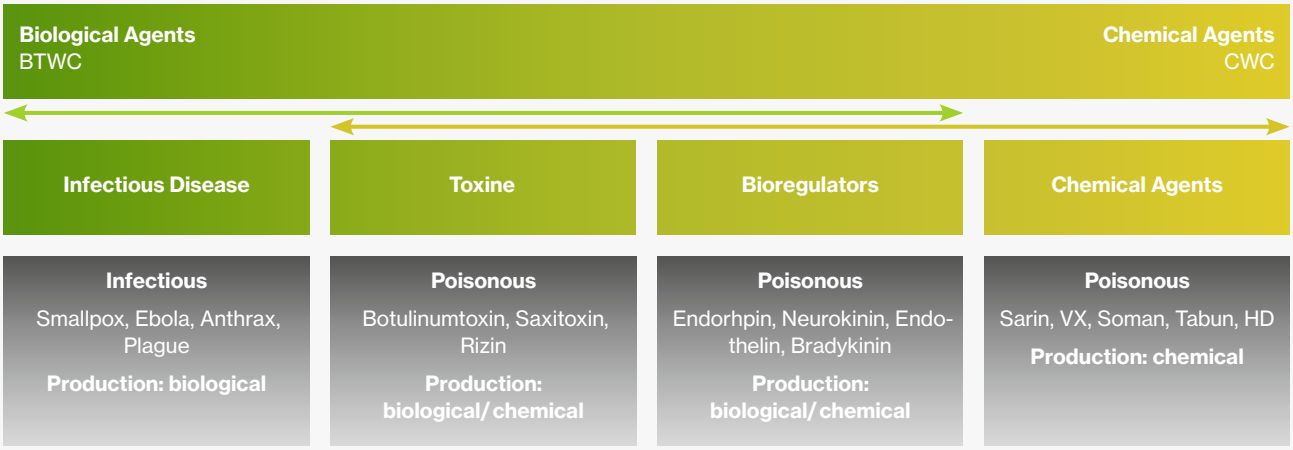


Figure 2: Presentation of genome-based extent of kinship of isolated F. tularensis strains from infected ticks and humans. The majority of isolates can be assigned to the south-west European FTNF002-00 strain. The B.13 strain which occurs more frequently in north-eastern Europe was isolated from two patients. Regional grouping of isolates can be perceived at a lower kinship level. The occurrence of ticks and human isolates within the same group indicates transfer of the pathogen from tick to human.

Biological / chemical Agents



Spiez CONVERGENCE

Stefan Mogl, Dr. Cédric Invernizzi, Dr. Beat Schmidt

Spiez CONVERGENCE is a new workshop series organised by Spiez Laboratory, the Swiss Federal Institute for NBC-Protection. The series is dedicated to inform participants about advances in chemical and biological sciences, and serve as a forum for discussion. This process is intended to identify developments in chemistry and biology which may at some point have implications for the Biological Weapons Convention (BWC) or the Chemical Weapons Convention (CWC), and which therefore may warrant further study. With this series, Spiez Laboratory supported by International Relations Defence, the Federal Department for Foreign Affairs and the Center for Security Studies of the ETHZ is contributing to a science and technology review for the arms control treaties.

The BWC and the CWC are arms control treaties strongly linked to developments in science and technology. The increasing overlap between chemical and biological sciences – generally referred to as convergence in chemistry and biology, or short "Convergence" – has been noted by the treaties' States Parties in recent conference reports, and they recommended exploring its potential implications. "Convergence" describes an integrative and collaborative approach in the life sciences that brings together theoretical concepts, experimental techniques as well as knowledge of different (science and engineering) disciplines at the crossroads of chemistry and biology.

This first Spiez CONVERGENCE brought together experts from academia, industry and policy making. It started with an introduction to the concept of "Convergence" from the perspectives of the CWC, the BWC and from an Non-Governmental Organisation, followed by summaries of previous reviews conducted on the subject by the Organisation for the Prohibition of Chemical Weapons' Scientific Advisory Board (OPCW SAB) as well as by the Biochemical Security 2030 project (Bath University, UK). The scientific and technical presentations dealt with the subjects of "chemistry making biology and biology making chemistry" and "enabling technologies". Expert speakers gave presentations on the following subjects:

- Directed Evolution of Enzymes for Industrial Use: using advanced computational methods and directed evolution to tailor enzymes which address a specific industrial need

- Genome Editing: presentation of various gene modification tools commonly used in the field of synthetic biology

- Holistic Characterization of Organisms: history and current technology capabilities that allow for rational approaches in terms of modifying organisms and gathering information about the cellular machinery

- Industrial Biology: engineering yeast to produce artemisinin, a potent anti-malarial drug, and how the engineering process of yeast has been automated to optimize time to market for other chemicals produced by means of exploiting this metabolic pathway

- Generating Data for Systems Biology: methods for generating data for systems biology, including through genomics, transcriptomics, proteomics, and metabolomics, and examples of how that data is currently used

- CRISPR/Cas for Genome Editing: using a bacterial defence mechanism known as CRISPR/Cas as a genome editing tool, from the basics of how the system changes DNA to how scientists have begun applying the tool in their research

- Between Biology and Chemistry, Toxins and the Relevance of Convergence: overview of toxins – poisonous products of an organism which are incapable of reproducing themselves – and how they highlight the convergence between chemistry and biology due to their nature and coverage by both the CWC and BWC

- Biological Circuits and Biobricks in Systems Biology: biological circuits, computers and memory in systems biology, and how multigene systems can mimic or affect metabolic pathways, thus enabling more sophisticated and precise manipulation of a living entity

- Antibody-Drug Conjugates and the Specific Delivery of Cytotoxic Payloads: today's industrial production of Antibody-Drug Conjugates (ADCs) for the targeted delivery and release of cytotoxic payloads to cancer cells

- Applications of Nanoparticles in Biology: surface-coated nanoparticles that perform functions common in biology but, by mimicking folded biomolecules in a way that they exhibit the coexistence of regularly arranged hydrophobic and hydrophilic structures on a length scale on the surface

- Current and Future Impact of Additive Manufacturing (3D Printing) on Biology and Chemistry: the concept of 3D printing to fabricate components via various approaches to layered material deposition

- Computing: Designing and Engineering of Biological Systems by Means of Computer Modelling and Programming Language: the practice of combining computational methods with various engineering approaches in biology

General Findings

The separation between biology and chemistry – as established in the BWC and CWC treaty regimes – has never been as pronounced in the chemical and biological sciences, thus an overlap between the disciplines is not a new development. However, certain scientific advances in this overlap continue to blur the boundaries between what constitutes biology and chemistry even further. This is reflected for example in how chemicals will be produced in the future: by traditional chemical methods, with the help of biological catalysts such as enzymes, or through the specially designed metabolic process of a self-replicating organism or an organism-like system. Drivers for pursuing a particular method of production will include economic, environmental as well as other considerations. Organisms known in nature will be engineered to exhibit altered or new functions. Or their genetic functions may be reduced to a minimum "chassis" type organism, which can serve as building block for the design of new biological systems. Alternatively, organism-like systems with specific functionality may be chemically built from scratch.

How far and at what speed such advances will progress depends largely on developments in other disciplines acting as enabling technologies. These include data computation and management of large databases, nanotechnology, robotics, systems automation and many others. The resulting scientific and technological advances will open up new areas of appli-

cation of chemistry and biology in society. The impact will largely be beneficial. But "Convergence" also creates new opportunities and possible risks for chemical and biological arms control.

Applications of "Convergence" will assist in developing new means of protection against toxic chemicals and infectious diseases: methods for their detection, diagnostics and identification, pre- or post-exposure medical treatment and countermeasures as well as decontamination. But "Convergence" will also permit the production of known toxic chemicals, including toxins, by different new methods, and it may lead to novel toxic chemicals. Scientific advances will permit the engineering of known organisms that cause infectious diseases, in order to change how the disease progresses or can be treated. It will become possible to design and create new organisms based on the study of existing ones, which in turn may cause new forms or types of infectious diseases. "Convergence" may enable new methods for distributing or administering toxic chemicals, or provide the necessary expertise to design new vectors or systems for the distribution of infectious organisms and their specific targeting. It is important to emphasise in this context, that advances in science and technology cannot simply transform themselves and mutate into weapons. Application of "Convergence" to weapons development requires a weapons program. The development of a weapon using a new biological or chemical agent requires a managerial decision followed by a development and scale-up program, a testing phase and a doctrine for its use. How would such a program look like at state level? It would most certainly be very different from chemical weapons programs of the past.

"Convergence" may simplify certain technical procedures and at the same time reduce the necessary level of tacit knowledge required for weapons programs. It therefore might open up new opportunities for sub-State actors trying to develop or acquire some form of a biochemical weapon. These types of risks however, are often overstated. The relative gains sub-State actors could reap from these technological advances remain unclear – especially if compared to the capabilities they already possess. Furthermore, the challenges of weaponisation still remain considerable.

Toxic chemicals and infectious organisms will remain prohibited as weapons through the provisions of the CWC and the BWC. But the impact that "Convergence" has on the provisions of the two regimes needs to be kept under review to avoid opening new gaps. Furthermore, new technical opportunities created by "Convergence" might weaken the commitment of States to continue adhering to the regimes. But this is a question of political will. What are the forces that drive scientific progress and its practical application in society? Technology development follows directions that are determined by a desired outcome. That fact remains

even if the intermediate steps are not as yet clearly understood. It is not likely – but also not impossible – that decisions could be made for deliberate small-scale breakout attempts from a regime.

Existing mechanisms for reviewing advances in science and technology to detect and assess key developments vary between the CWC and the BWC. The OPCW SAB meets once or twice a year to discuss a standing agenda, and every five years it undertakes more substantive reviews for the CWC Review Conference. This process is likely to capture some developments, most likely the ones affecting the chemical industry and those related to the protection against chemical weapons. The review process at the BWC is based on annual meetings of national experts, but shows little focus. It is currently not suited to evaluate and assess how "Convergence" may affect the treaty.

Today the life sciences are advancing at an unprecedented pace. The amount of data and knowledge acquired should lead to non-linear progress in the future. Speakers from academia and industry convincingly showed in their presentations how the rate of progress in their domains is clearly outpacing treaty review cycles. Therefore, advances in the life sciences, in related technologies and industrial application require constant monitoring. Given the pace and complexity of current scientific and technological advances, today's review mechanisms, even if executed in best faith, may lack sufficient breadth, depth and quality of expertise to provide dependable results.

Outlook

Spiez CONVERGENCE cannot develop specific policy recommendations for the arms-control regimes and does not intend to do so. It also does not issue a consensus report. It is dedicated to assist its participants and readers with their own science and technology assessments, and to trigger, if possible, further discussions in other fora.

The workshop series Spiez CONVERGENCE will continue and the second edition is scheduled for September 2016.

The full report of Spiez CONVERGENCE is available online – www.spiezconvergence.com

UN chemical weapons experts visit a centre for victims close to Damascus

Synthetic approach for investigating bioadducts between nerve agents and proteins

Julien Ducry, Dr. Christophe Curty

The synthesis of degradation products of chemical warfare agents and their metabolites is well known, our understanding of bioadduct formation is incomplete in many ways. A procedure for synthesising bioadducts has been developed at Spiez Laboratory, in cooperation with the University of Fribourg, Switzerland. This work focuses on the formation of bioadducts between neurotoxic organophosphates and proteins. It provides a library of reference substances for establishing analytical methods such as the preparation of samples and instrumental techniques.

Syria. Ghouta. August 2013. More than a thousand people were killed in a chemical warfare agent attack, after which environmental and biomedical samples were taken on site under UN mandate. Analyses of rocket fragments, tissue, soil and other materials including blood and urine samples of the victims irrevocably confirmed the use of the nerve agent sarin [1]. The analyses of the biomedical samples, which consisted mainly of blood and urine, proved how important they are in order to confirm the use of chemical warfare agents. They ideally complement the analyses of environmental samples, and by monitoring biological markers allow to determine whether a person has been poisoned. In addition to the medical diagnostics, such studies provide information on how the chemical agent interacts with the human body and furthers our understanding of toxicokinetics, and allows the development of new therapeutic procedures.

Any method used to verify exposure to chemical warfare agents enhances the verification regime of the Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction [2]. The Organisation for the Prohibition of Chemical Weapons maintains a network of designated laboratories, including Spiez Laboratory, for the identification of intact agents or their degradation products in environmental samples. A similar network for bio-

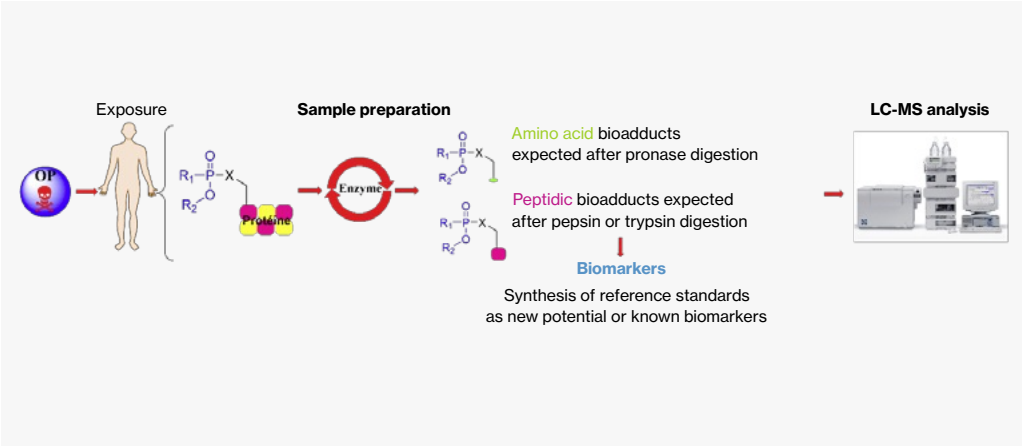
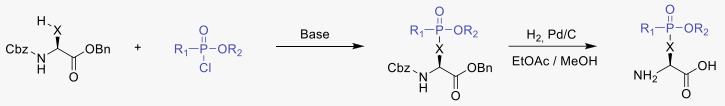


Figure 1: From the poisoning to the analysis of bioadducts

medical samples is being developed. Currently, only few laboratories worldwide are capable of conducting such analyses.

Chemical warfare agents have a relatively short lifetime in the human body. They are rapidly hydrolysed, metabolised or form "bioadducts" with nucleophilic sites of macromolecules, such as proteins and DNA. Chemical warfare agents and their degradation products can be identified in biomedical samples only for a very short time after exposure, and metabolites for two to three weeks thereafter. Bioadducts, however, can be detected for several months and thus provide a more consistent basis for diagnostic and monitoring activities, such as forensic medical investigations.
While the synthesis of degradation products of chemical warfare agents and their metabolites is well known, our understanding of bioadduct formation is incomplete in many ways. Until now, the majority of bioadducts were identified by using radioactive derivatives in in-vivo or in-vitro studies. A procedure for synthesising bioadducts has been developed in cooperation with the group from Professor Bochet, Chemical Department of the University of Fribourg, Switzerland. This doctoral thesis in organic chemistry focuses mainly on the formation of bioadducts between neurotoxic organophosphates and proteins (Figure 1). A systematic study has been made on the reactivity between various amino acids and the main chemical warfare agents G, V and GA-like. Simulants were used in order to reduce the toxicity of the individual compounds. It must be said that this approach provides identical compounds to those potentially formed during intoxication with nerve agents. Thus, initially protected amino acids were phosphylated at the reactive sites of their lateral chains. After removal of the protecting groups, these intermediates yielded the desired compounds corresponding to the amino acids phosphylated by the main nerve agents GA (tabun), GB (sarin), GD (soman), GF (cyclosarin), VX, RVX (Russian VX) and CVX (Chinese VX) (Table 1). Adaptation of the protecting groups has allowed the use of phosphylated amino acids in solid phase peptide synthesis, which has provided reference phosphylated peptide sequences (Table 2).
The developed procedures have produced the desired compounds with good yields and high purities after purification by Flash chromatography. Finally, the stability of synthesised bioadducts was investigated in various environments to assess their lifetime under physiological conditions and which ones could be used for preparing samples (Table 3).

This synthetic approach has clearly shown that in addition to bioadducts already isolated from in-vivo and in-vitro experiments, new compounds should be considered as biomarkers. It has also provided a library of reference substances for establishing analytical methods. Currently, an application for the rapid detection of nerve agent intoxication is being developed, based on fluorescence and using synthesised bioadducts.



Ser X = CH_2O, Tyr X = $CH_2C_6H_4O$, Thr X = $CH(CH_3)O$, Lys X = $(CH_2)_4NH$, Cys X = CH_2S[a], Trp X = $CH_2(C_8H_5N)$, Arg X = $(CH_2)_3NHC(NH)_2$

Entry	Methylphosphono-chlorydate	Amino Acid	Product 1	Base	Time	Yield	Product 2	Time	Yield
1-7	Simi-VX	1 = Ser		DABCO	180	**93**		60	**61**
		2 = Tyr		DABCO	o. n.	**98**		45	**96**
		3 = Thr		DABCO	o. n.	**90**		30	**98**
		4 = Lys		Et_3N	60	**91**		120	**81**
		5 = Cys		DMAP	300	**75**		2 jours	**68**
		6 = Trp		tBuOK	120	**35**		240	**77**
		7 = Arg		Et_3N	120	**34**		120	**98**
8-14	Simi-Sarin (GB)	8 = Ser		DABCO	o. n.	**57**		45	**96**
		9 = Tyr		DABCO	180	**79**		30	**89**
		10 = Thr		DABCO	2 jours	**48**		60	**96**
		11 = Lys		Cs_2CO_3	60	**78**		240	**95**
		12 = Cys		DMAP	300	**89**		450	**88**
		13 = Trp		tBuOK	120	**49**		240	**93**
		14 = Arg		Et_3N	120	**53**		180	**73**
15-21	Simi-Soman (GD)	15 = Ser		Et_3N/DMAP	o. n.	**91**		30	**44**
		16 = Tyr		Et_3N/DMAP	210	**79**		60	**85**
		17 = Thr		Et_3N/DMAP	o. n.	**80**		45	**65**
		18 = Lys		Cs_2CO_3	60	**82**		150	**98**
		19 = Cys		DMAP	240	**72**		2 jours	**65**
		20 = Trp		tBuOK	120	**34**		240	**83**
		21 =Arg		Et_3N	120	**34**		300	**51**
22-28	Simi-cyclosarin (GF)	22 = Ser		DABCO/DMAP	o. n.	**72**		60	**97**
		23 = Tyr		Et_3N/DMAP	240	**83**		60	**89**
		24= Thr		Et_3N/DMAP	o. n.	**88**		60	**87**
		25 = Lys		Cs_2CO_3	60	**71**		150	**92**
		26 = Cys		DMAP	240	**77**		o.n.	**76**
		27 = Trp		tBuOK	120	**33**		240	**85**
		28 = Arg		Et_3N	120	**40**		o.n.	**62**
29-35	Simi-chinese VX	29 = Ser		DABCO/DMAP	120	**90**		45	**98**
		30 = Tyr		DABCO/DMAP	o. n.	**82**		45	**99**
		31 = Thr		DABCO/DMAP	o. n.	**90**		30	**99**
		32 = Lys		Cs_2CO_3	60	**94**		135	**94**
		33 = Cys		DMAP	240	**72**		420	**81**
		34 = Trp		tBuOK	120	**44**		240	**59**
		35 = Arg		Et_3N	120	**27**		300	**82**
36-42	Simi- russian VX	36 = Ser		DABCO/DMAP	o. n.	**87**		30	**97**
		37 = Tyr		DABCO/DMAP	2 jours	**77**		45	**96**
		38 = Thr		DABCO/DMAP	o. n.	**86**		30	**98**
		39 = Lys		Cs_2CO_3	60	**83**		120	**51**
		40 = Cys		DMAP	240	**76**		330	**83**
		41 = Trp		tBuOK	120	**7**		150	**54**
		42 = Arg		Et_3N	120	**27**		300	**82**
43-49	Simi-tabun (GA)	43 = Ser		DABCO/DMAP	480	**57**		60	**qualitatif**[c]
		44 =Tyr		Et_3N/DMAP	o. n.	**92**		120	**99**
		45 = Thr		DABCO/DMAP	o. n.	**0**		n. a.	**n. a.**
		46 = Lys		Cs_2CO_3	60	**79**		120	**89**
		47 = Cys		DMAP	360	**61**		420	**9**
		48 = Trp		tBuOK	120	**36**		240	**81**
		49 = Arg		NaH	120	**22**		120	**92**

[a] Boc group and tert-butyl ester were used (hydrogenolysis does not work with Cys). These were cleaved with TFA/DCM (1:1)
[b] Isolated yields
[c] unstable product

Table 1:
Synthesis of bioadducts

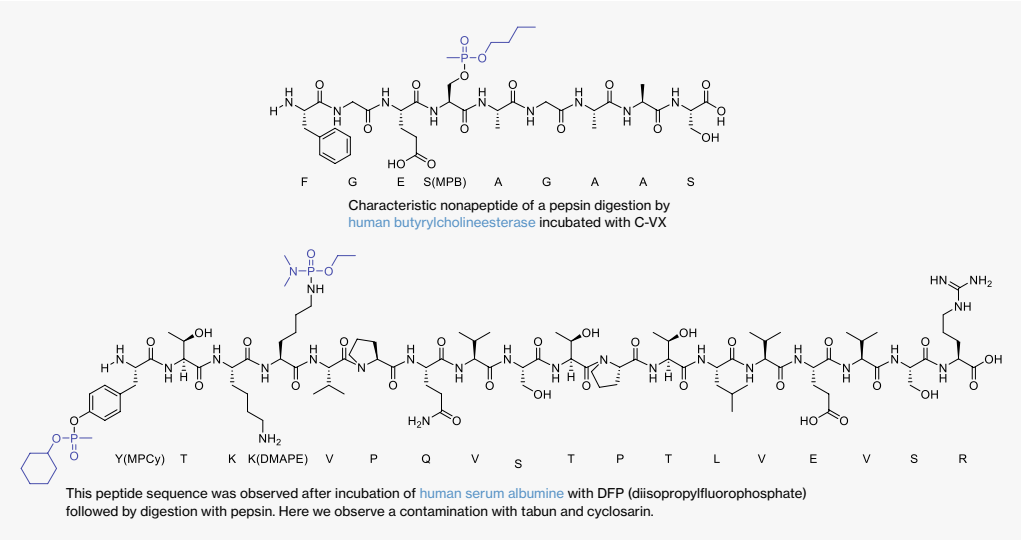


Table 2:
Examples of synthesised polypeptides

half-life ($t_{1/2}$) ≥ 60 days ; 11 ≤ $t_{1/2}$ ≤ 60 days ; $t_{1/2}$ ≤ 10 days

Bioadducts	D_2O (neat) pH 5-6, 25 °C	D_2O + HCl pH < 1, 25 °C	D_2O + NaOH pH > 14, 25 °C	Synthetic urine pH 7, 37 °C	Trizma Buffer pH 7.4, 37 °C
H-Ser(MPIP)-OH					
H-Cys(MPIP)-OH	pH 3				
H-Trp(MPIP)-OH					
H-Lys(MPIP)-OH					
H-Tyr(MPIP)-OH					
H-Thr(MPIP)-OH					
H-Arg(MPIP)-OH					
H-His(MPE)-OH		n/a (unstable compounds)			
H-Asp(MPE)-OH					
H-Asn(MPE)-OH					
MPE-Gly-OH					
MPE-Pro-OH	pH 2			n/a	pH 7, 25 °C

Table 3:
Stability of bioadducts in relation to the medium

References

[1] UN Mission to Investigate Allegations to the Use of Chemical Weapons in the Syrian Arab Republic – Report on Allegations of the Use of Chemical Weapons in the Ghouta Area of Damascus on 21 August 2013, UNO, 2013.

[2] Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction, OCPW, updated version 2005.

Application of High-Resolution Mass Spectrometry for Verification Analysis

Andreas Schorer, Dr. Martin Schär, Dr. Peter Siegenthaler

The unique properties of high-resolution mass spectrometry (HRMS) offer exciting possibilities for the verification analysis at Spiez Laboratory. HRMS allows the elucidation of molecular formulas of unknown chemicals, thus facilitating their identification. In addition, chemicals relevant to the Chemical Weapons Convention (CWC) can be detected in suspect samples based solely on their chemical composition. Relevant molecular formulas can be collected in a library and used for efficient and fast screening. HRMS has already proven its power to identify unknown chemicals in important analytical tasks and Proficiency Tests organised by the Organisation for the Prohibition of Chemical Weapons (OPCW).

As a Designated Laboratory, the Analytical Chemistry Branch of Spiez Laboratory supports the Organisation for the Prohibition of Chemical Weapons (OPCW) with the implementation of the Chemical Weapons Convention (CWC). Mass spectrometry is one of the key techniques for the detection and identification of CWC-related chemicals in suspect samples. Among mass spectrometers, high-resolution instruments stand out due to their unique capability to determine the molecular mass of a chemical with high accuracy. In recent years two high-resolution mass spectrometers, a QTof LC-MS and a QTof GC-MS could be procured. They have become important tools for identifying unknown chemicals during diverse analytical tasks and OPCW Proficiency Tests.

High-resolution Mass Spectrometry

Mass spectrometry is an analytical technique to determine the molecular mass of atoms and chemicals. The chemical to be tested is transferred into the gas phase and charged (ionised). By employing magnetic and electric fields the ions are then accelerated in the mass spectrometer, separated by their mass-to-charge ratios (m/z) and eventually detected. The resulting mass spectrum is digitally recorded for analysis. The molecular mass is a unique and characteristic property of each chemical and thus indispensable for the unambiguous identification of unknown chemicals. Mass spectrometry has thus

left:
QTof GC-MS System
Agilent 7200

right:
QTof LC-MS System
Bruker maXis plus

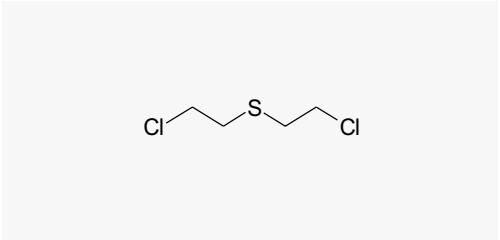


Figure 1: Chemical structure of „Mustard Gas“ (HD) with the molecular formula $C_4H_8Cl_2S$

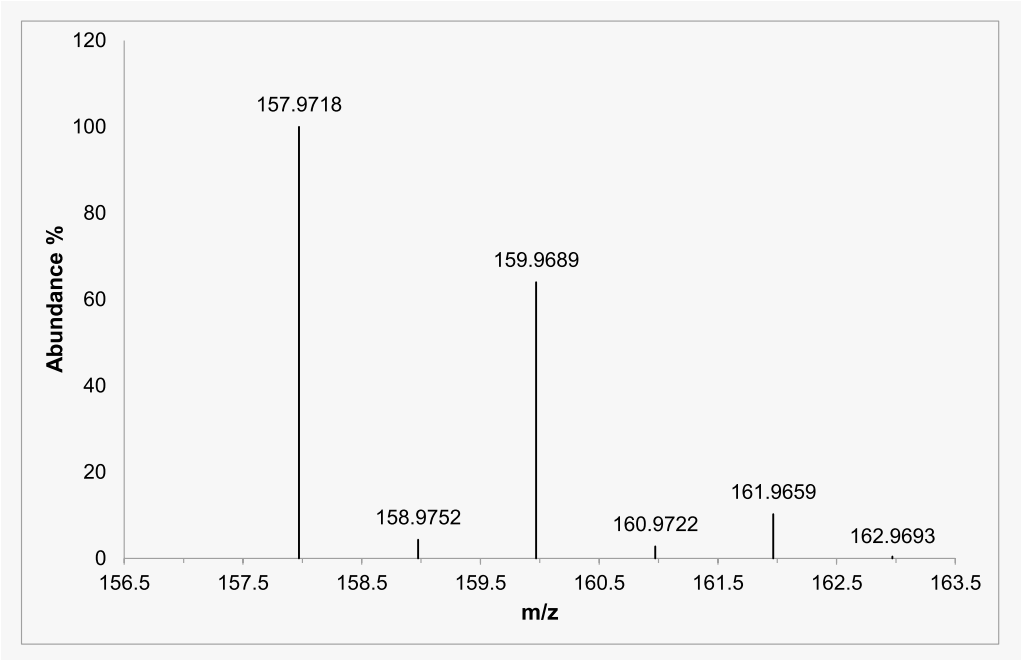


Figure 2: Theoretical isotopic abundance of the molecular ion of HD

become increasingly critical for solving analytical and biochemical problems – a fact that has greatly accelerated the development of the technique in recent years.

The following parameters define the basic performance of a mass spectrometer:

- mass accuracy
- resolution, i.e. the capability to distinguish two adjacent peaks in a mass spectrum
- scan speed, i.e. the speed with which mass spectra can be acquired

The resolution of a mass spectrometer can be defined as the ratio m/Δm, whereas m designates the m/z value and Δm the width at half the peak height of a spectrometric signal. Resolutions above 10 000 are called high-resolution. However there is no firm definition for the term “high-resolution”. In the past, only the complex and expensive Fourier Transform instruments (FTMS) or double focusing spectrometers were available for high-resolution mass spectrometry. With the appearance of the Orbitrap® instruments [1] by Thermo Fisher Scientific in 2005 and the enormous improvement of the time-of-flight technology (Tof-MS), an array of high-resolution instruments are now at hand for those laboratories which rely on mass spectrometry.

The power of a high-resolution QTof GC-MS system can best be illustrated by comparing a HRMS-measurement of the chemical warfare agent Mustard Gas (HD, figure 1) with a measurement made on a conventional, unit-resolution mass spectrometer.

Figure 2 shows the theoretical isotopic abundance of the molecular ion of HD. The chlorine and sulfur atoms are responsible for the characteristic pattern.

If HD is measured with a conventional unit-resolution and a high-resolution mass spectrometer the figure 3 mass spectra are obtained.

It becomes obvious that the spectrum measured with the unit-resolution instrument reflects the theoretical isotopic abundance of HD only marginally. In contrast, the high-resolution mass spectrum is almost identical to the theoretical isotope pattern. Using the data from the high-resolution spectrum, the molecular mass of HD can be computed with high accuracy up to several digits after the comma. From the

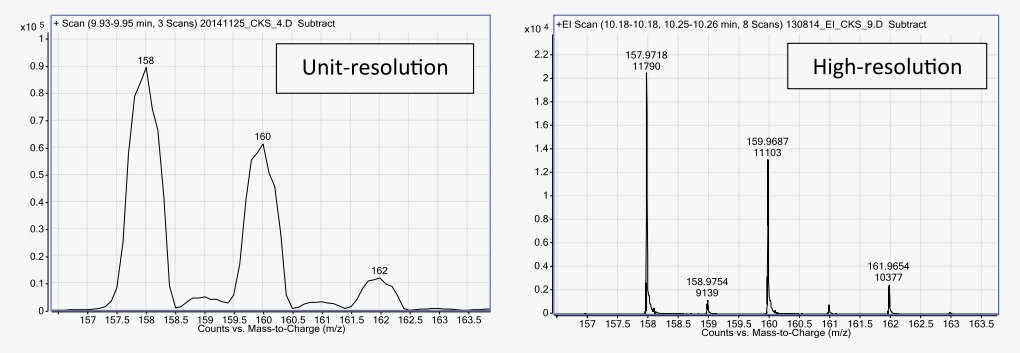


Figure 3: Mustard Gas (HD): GC-quadrupole-MS measurement with conventional unit-resolution (left, resolution ≈ 230) and high-resolution QTof GC-MS measurement (right, resolution ≈ 12 000)

	Without isotope abundance information					2% isotopic abundance accuracy	5% isotopic abundance accuracy
Molecular Mass [Da]	10 ppm	5 ppm	3 ppm	1 ppm	0.1 ppm	3 ppm	5 ppm
150	2	1	1	1	1	1	1
200	3	2	2	1	1	1	2
300	24	11	7	2	1	1	5
400	78	37	23	7	1	2	14
500	266	115	64	21	2	3	33
600	505	257	155	50	5	5	36
700	1046	538	321	108	10	6	82
800	1964	973	599	200	20	4	136
900	3447	1712	1045	345	32	13	153

Table 1. Dependence of the number of possible molecular formulas on mass accuracy and on the isotopic abundance accuracy [2]

data obtained with the conventional unit-resolution instrument only the nominal mass can be derived.

What are the advantages of high-resolution mass spectrometry for chemical analysis?
The elucidation of the molecular formula is essential to identify unknown chemicals. However, even with highest mass accuracy, in most cases the exact mass alone is insufficient for an unambiguous determination of the molecular formula. If the isotopic abundance is considered, the number of possible molecular formulas for a measured molecular mass can be significantly reduced, which is shown in table 1.

In general, with increasing mass accuracy the number of possible molecular formulas is reduced. But for masses above 500 Dalton (Da), the resulting number of possible molecular formulas remains too high to deduce the actual formula, also with a very high mass accuracy of 0.1 ppm. In combination with accurate isotopic abundance however, the possibilities of molecular formulas drop to a reasonable number, from which the actual molecular formula can be derived. As most of the molecular masses of CWC-related chemicals are below 400 Da (highlighted in red) a mass accuracy of 3 ppm and an accuracy of the isotopic abundance of 2 % should be sufficient to reduce the number of possible molecular formulas to as low as 2.

Screening for CWC-related chemicals using liquid chromatography coupled with high-resolution mass spectrometry (LC-HRMS)
Besides the determination of molecular formulas of unknown chemicals, high-resolution mass spectrometry in combination with liquid chromatography is very helpful when screening for CWC-related chemicals in suspect samples.

With conventional mass spectrometers, Multiple Reaction Monitoring (MRM) is commonly used for screening. MRM requires specific optimisation of instrument parameters with reference chemicals. Screening with a high-resolution mass spectrometer is (more) straightforward: Applying a very narrow mass window, LC-HRMS data are screened for theoretical m/z values of interesting chemicals. This screening method is not dependent on the availability of reference chemicals – only the theoretical m/z values of interest have to be known, and they can be stored in a screening library. In contrast to MRM, a LC-HRMS measurement collects the mass spectrometric information of every single chemical in the sample. Thus, further retrospective analysis of any kind can be carried out later.

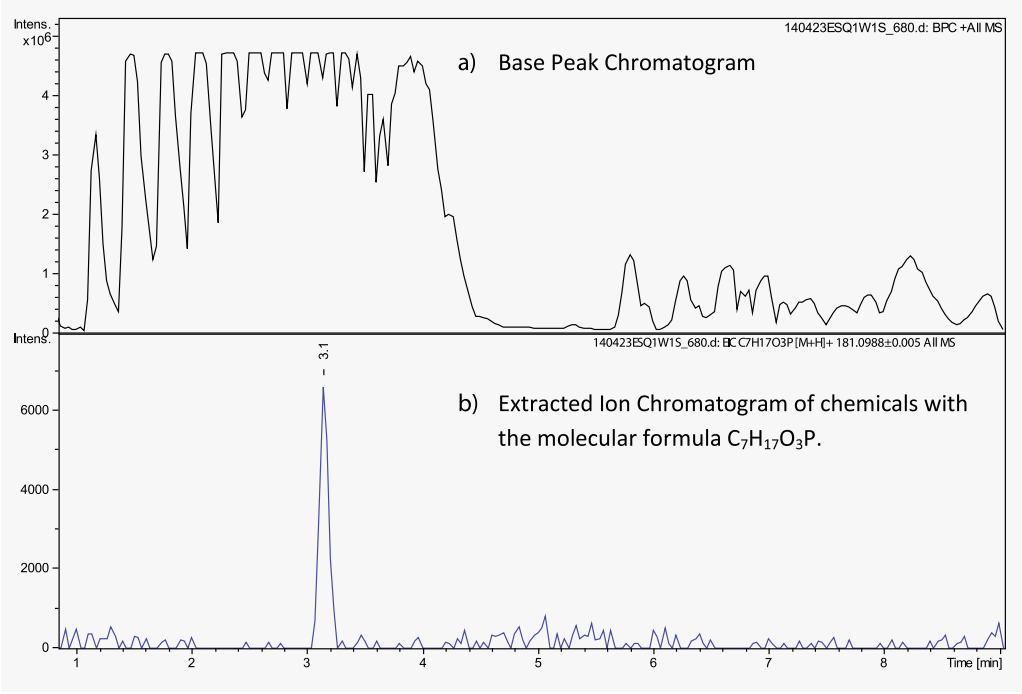


Figure 4. LC-HRMS screening of a sample from an OPCW Proficiency Test.
a) Base Peak Chromatogram
b) Extracted Ion Chromatogram of chemicals with the molecular formula $C_7H_{17}O_3P$

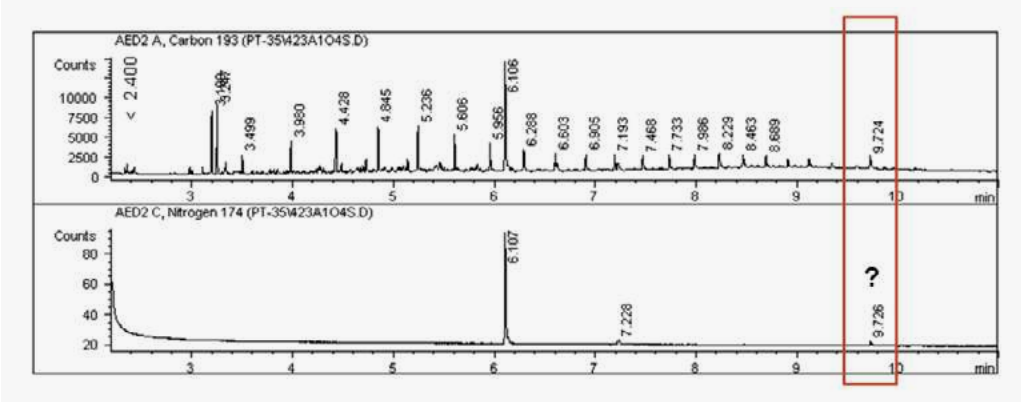


Figure 5. Measurement with GC-AED: the upper chromatogram shows the carbon-trace, while the lower shows the nitrogen-trace with three nitrogen-containing chemicals

The Analytical Chemistry Branch at Spiez Laboratory maintains for verification analysis an LC-HRMS screening library containing hundreds of molecular formulas.

The following section illustrates the screening process for a sample from an OPCW Proficiency Test (PT) using HRMS.

Chromatogram a) in figure 4 shows a high number of intense and partly saturated signals, which originate mostly from the complex sample matrix. If CWC-related chemicals were present, they could be masked by the intense background signals and therefore not be identified.

For that reason, the LC-HRMS data have to be screened for potentially relevant chemicals. As an example, a search for typical degradation products of nerve agents (alkylphosphonic acids and their alkyl esters) with the common molecular formula for the protonated ion $C_nH_{2n+4}O_3P$ is carried out. After browsing the LC-HRMS data with a narrow m/z-window of ±0.005 for chemicals with the generic molecular formula $C_7H_{17}O_3P$, a signal at 3.1 minutes is detected as shown in Figure 4 b).

The use of a narrow m/z-window is solely possible with HRMS, which leads to a very high selectivity. The Extracted Ion Chromatogram b) only shows ions with m/z values that fall into the narrow m/z-window. The m/z values of background chemicals do not “fit” into the narrow window and are “filtered out”.

Identification of unknown chemicals using GC-HRMS

The following example from an OPCW Proficiency Test illustrates how HRMS in combination with Gas Chromatography (GC) supports the identification of unknown chemicals.
A sample was measured with a GC system coupled with an element specific atomic emission detector (GC-AED). 3 Nitrogen-containing chemicals are found, which could be CWC-related and thus have to be identified (figure 5 lower chromatogram).

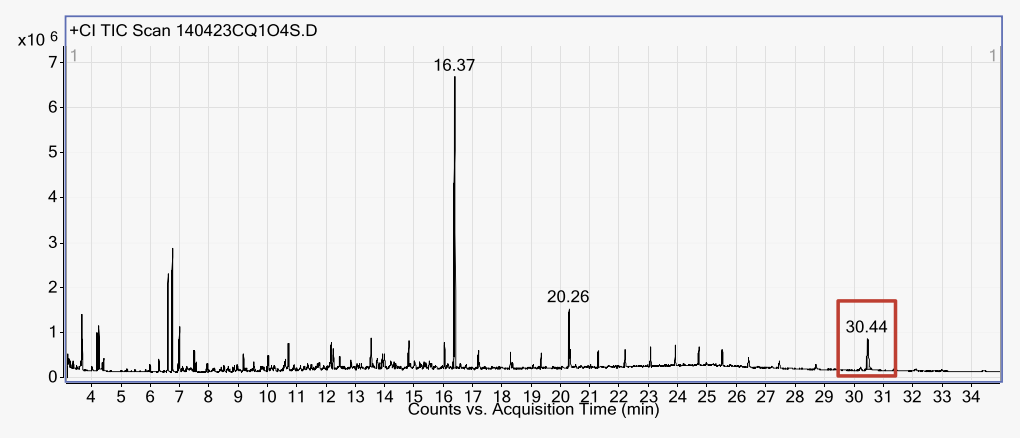


Figure 6: QTof GC-MS chromatogram of the sample from the OPCW Proficiency Test

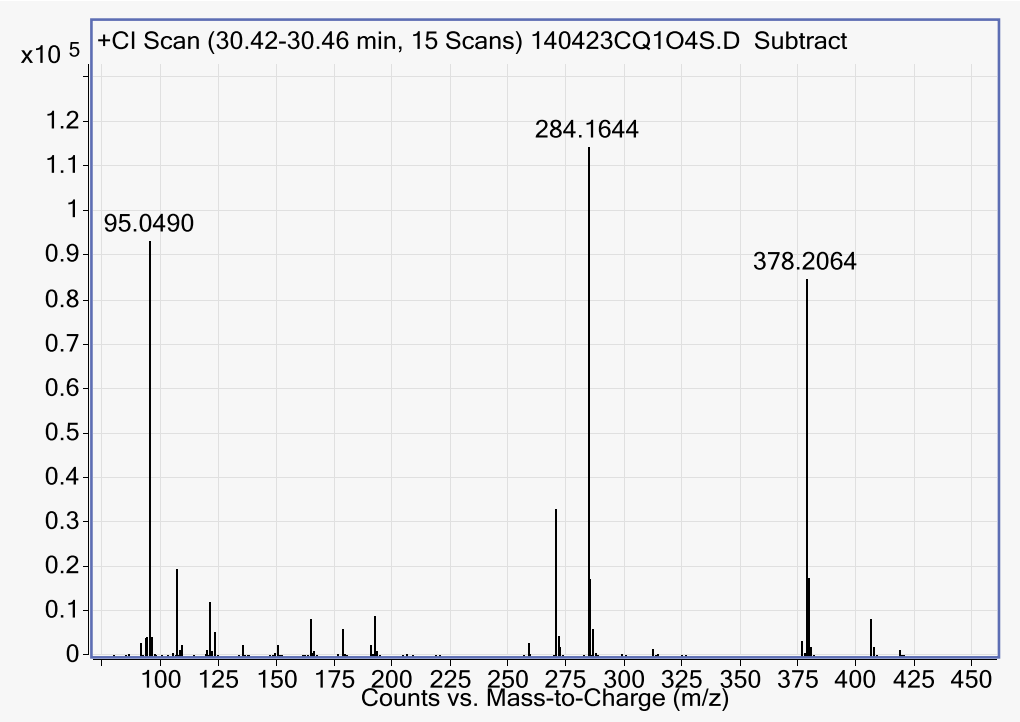


Figure 7: High-resolution mass spectrum of the unknown chemical

Using the available unit-resolution spectral libraries two of the three N-containing chemicals can be identified. For the identity of the third chemical (highlighted in red) no hint is found. A GC-AED analysis shows that this chemical contains nitrogen, hydrogen and carbon but no other elements. In order to identify this chemical HRMS comes into play.

Figure 6 shows the Total Ion Chromatogram of a QTof GC-MS measurement of the unknown N-containing chemical with a peak highlighted at 30.44 minutes.

The high-resolution mass spectrum of the unknown chemical at 30.44 minutes is given in figure 7.

This spectrum reveals the protonated molecular ion at m/z 378.2064 as well as two main fragments at m/z 284.1644 and m/z 95.0490. Based on these m/z values and the isotopic abundance, possible molecular formulas can be computed using dedicated software. The software calculates a scoring value for each proposal as indicator for the accuracy of the match between theoretical data and measured values. Figure 8 shows a hit list with proposed molecular formulas for the unknown nitrogen-containing chemical.

A chemical with the molecular formula $C_{24}H_{27}NO_3$ has reached the highest score, and several structures can be deduced from this molecular formula. Therefore, to elucidate the structure of this chemical, further information has to be taken into account. This includes the m/z values of the fragments as well as additional information obtained with other analytical methods.

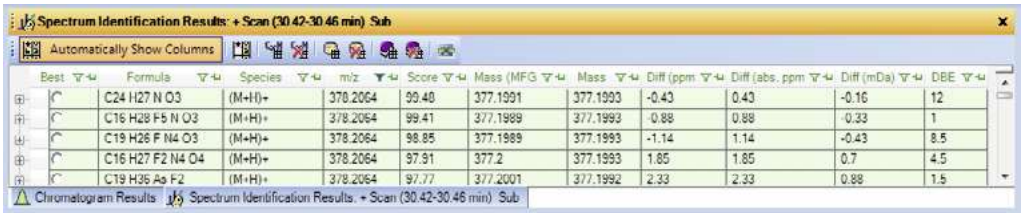


Figure 8: List of computed possible molecular formulas for the unknown chemical

Based on all the information the following structure could be proposed (figure 9).

Finally, the identity of the chemical was confirmed with a measurement of the corresponding reference chemical that was synthesised at Spiez Laboratory.

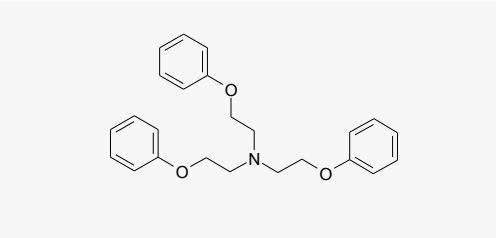


Figure 9: Structure of the unknown chemical tris(2-phenoxyethyl)amine

Description of the HRMS-systems of the Analytical Chemistry Branch

	QTof GC-MS System Agilent 7200	QTof LC-MS System Bruker maXis plus
Coupled with	Gas chromatography	Liquid chromatography
Tof MS resolution	> 13000 @ m/z 272	60000 «Full Sensitivity Resolution»
Tof mass accuracy	< 5 ppm @ m/z 272 (typical < 2 ppm)	0.6 ppm RMS Error (typical 1 ppm)
Sensitivity	1 pg Octafluoronaphthalene S/N > 2000:1 (EI MS splitless)	1pg Reserpine S/N > 100:1 RMS (Full Scan MS-mode)
Quad mass range	m/z 20–1050 (0.7–4.0 Da FWHM)	Up to m/z 3000
Tof mass range	m/z 20–1700	m/z 50–20000
Scan speed	1–50 spectra/sec	Up to 30 spectra/sec
Tof flight path length	2 m (reflectron)	≈ 4 m (reflectron)

Literature

[1] Hu Q, Noll RJ, Li H, Makarov A, Hardman M, Graham Cooks R. The Orbitrap: a new mass spectrometer, J. Mass Spectrom. 2005, 40: 430-443.

[2] Kind T, Fiehn O. Metabolomic database annotations via query of elemental compositions: Mass accuracy is insufficient even at less than 1ppm, BMC Bioinformatics 2006, 7: 234-243.

FOCP Director Benno Bühlman opens the 7th National NBC Pprotection conference in Bern

7th National NBC Protection conference

Pia Feuz, Dr. César Metzger, Dr. Giuseppe Testa

Aside from conveying basic expertise and procuring adequate equipment, good precautionary NBC measures also require deliberate cooperation and networking. Faithful to the motto of "know the protagonists during a crisis" the NBC Protection conference under the hospices of the Federal Commission for NBC Protection (ComNBC) provides a platform for sharing expertise and cultivating contacts. The National NBC Protection and Coordination Office looks back on a successful event with exciting topics.

The new director of the Federal Office for Civil Protection FOCP, Benno Bühlmann opened the conference by affirming his commitment to national NBC protection. In the future, the FOCP will engage itself more intensely in this field and develop and consolidate cooperation with the cantons.

Ambassador Manuel Bessler (Swiss Agency for Development and Cooperation SDC) started the conference with his presentation on the necessity of NBC protection from the perspective and experience of missions abroad by the Swiss Humanitarian Aid organisation (SHA). Disasters abroad show that operations always require the competent expert consultation of NBC specialists – whether for giving advice to those affected on location or to protect one's own teams. For such consultation the SHA depends on the voluntary support of cantonal and federal specialists.

Challenges in NBC-protection

The changes in society, the technical possibilities and growing population density pose new challenges for civil protection. These also include how to deal with cyber threats, dual-use goods or precursors of explosives. Consultations during the conference showed that NBC protection is directly related to a number of these new challenges, which makes preventive and precautionary measures necessary. The presentation on commercial substances that can be used to manufacture explosives attracted particular attention. In today's information age it is easy to obtain relevant construction instructions which increases the threat situation. Further contributions addressed the legislation on radiation protection, dispersion modelling for nuclear emergency protection, collaboration with the Network of Chemistry Experts

The National NBCN Protection Board

Many players of civil protection are involved in dealing with incidents related to the safety of the population. Emergency organisations such as police, fire brigade, ambulance and rescue services but also civil defence, technical services and the military collaborate closely at the operational level. To ensure efficient cooperation and that resources can be deployed effectively, strategic coordination is needed at the national level. At the federal level the Federal NBCN Crisis Management Board and the federal offices provide for these tasks. At the cantonal level we have bodies such as the Intergovernmental Conference for the Military, Civil Protection and Fire Services (RK MZF) or those of the Cantonal NBC Coordination Platform (KPABC).

The National NBCN Protection Board (in office since April 2014) ensures the link between the Confederation and the cantons and is responsible for monitoring measures relating to N, B, C, and natural disasters. It convenes four times a year and is chaired by the head of the National NBCN Protection and Coordination Office. It consists of a balanced mix of federal and cantonal representatives. “Master plans” or the basic NBC documents and the document on how national NBCN prevention is organised provide the foundation for the Board’s work. Although the Board is not in itself authorised to impose precautionary measures, the formulation of general recommendations can still be effective. Furthermore its recommendations are usually widely accepted by both Confederation and cantons due to the Board’s balanced constitution.

First projects

In collaboration with the Coordinated Medical Services, the Board participated in 2014 in evaluating the operational concept of “Decontamination of persons in damage, transit and hospitalisation areas upon NBC incidents”, which is to be published in 2015. Another central task is disseminating relevant information on civil protection: In relation to precautionary measures for dealing with potential Ebola-infections in Switzerland, the Board took actions in order to facilitate the efficent exchange of procedures for first reponders among the cantons (in particular those on disinfection and handling of waste). Under the lead of the National NBCN Protection and Coordination Office these instructions are processed for inter-cantonal exchange and stored on an intranet-based platform.

and the issue of multi-resistant germs (MRG). The conference's wide range of expert presentations was appreciated by the participants.

Medical NBC protection

Development in civilisation such as the increasing closeness of densely populated areas to industrial plants and traffic routes or the possibility of terrorist attacks entail risks for large sections of the population. Together with the Office for Coordinated Medical Services the conference presented a block of topics relating to medical NBC protection. Apart from presenting both a training programme and the logistics for what is called a decontamination hospital, the focus was on two presentations on a concept for a radioactivity consultation centre (should an incident occur). During the general emergency exercise of 2013, Switzerland ran a consultation centre and gained preliminary experience with this facility. LTC Dr. med. Michael Kassirer presented the Israeli concept for a consultation centre and reported on the findings his country has made. Dr. Kassirer was able to impressively explain the great importance of psychological care for "well-worried" persons (deeply concerned persons not affected healthwise). Not attending to these people would make it considerably more difficult to run the consultation centre. Depending on the type of incident, the Israeli concept aims at uninjured persons preliminarily decontaminating themselves – if possible – in their own homes by showering and changing their clothes. Later, these people would pack their potentially contaminated clothes into plastic bags and take them along to the consultation centre for further examination. This could prevent the consultation centre from being overtaxed during the acute phase of a radiological incident. The importance of international exchange for learning from already tested concepts was evident. The conference's programme was augmented with a special presentation on the Ebola epidemic in western Africa. The Federal Office of Public Health FOPH reported on the current situation in Africa and the dramatic increase in infections. The international community underrated the danger of an Ebola epidemic. Spreading of the virus in Switzerland was, however, considered to be highly unlikely for cultural and customary hygiene reasons. The Swiss health system is capable of isolating individual patients and treating them in the best possible way.

Promotion of women: an opportunity for NBC protection

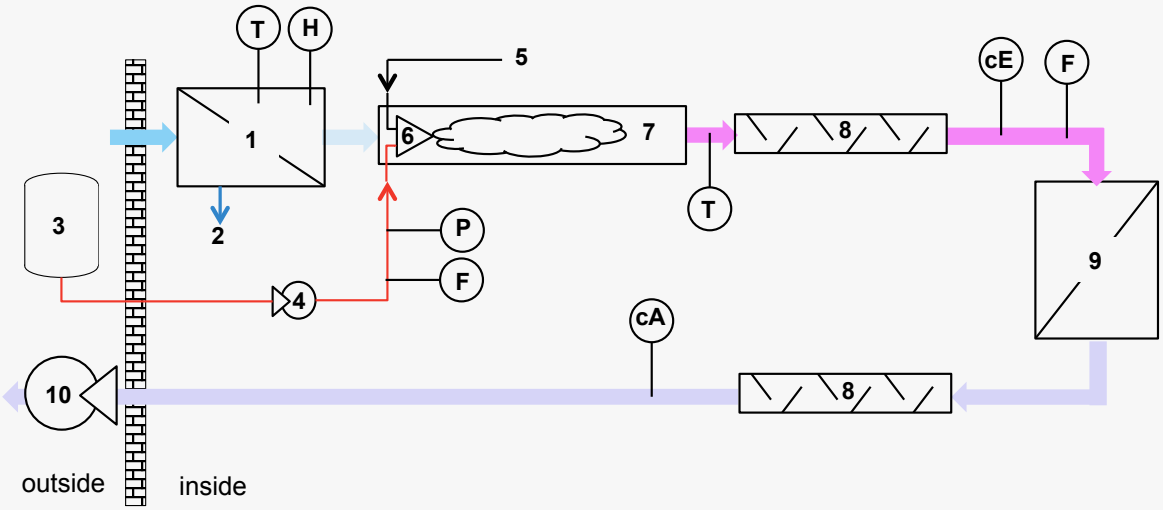
NBC protection is a field that focuses on science and operations. For several reasons the proportion of women involved in this field is quite small. To discuss this politically delicate subject in greater detail, it was possible to engage among other participants, Dr. Brigitte Rindlisbacher, Secretary General of the DDPS, and Dr. Sylvie Durrer, Director of the Federal Office for Gender Equality. The Head of the National NBC Protection Secretariat believes that the deliberate promotion of women is an opportunity to further improve and gain greater acceptance of civil protection in Switzerland.

Conclusion

Altogether 138 people attended the conference, of which 20 were women. The majority of feedbacks gave a positive picture: More than 95 % of those participating in the survey graded the conference as good to very good. The National NBC Protection Secretariat is preparing a similarly broad programme for the next conference from 1–2 September 2015.

Title of presentation	Speaker
Opening	Dr. Giuseppe Testa, Head of National NBC Protection Secretariat
Welcoming speech by the new director the FOCP	Benno Bühlmann, Director of the FOCP
Humanitarian aid and NBC protection	Manuel Bessler, Delegate for Humanitarian Aid and Head of the Swiss Humanitarian Aid Unit
NBC protection challenges	
Revision of Radiological Protection Ordinance	Dr. Sébastien Baechler, Head of Radiological Protection Division, FOPH
Cyber threats – Swiss situation report	Pascal Lamia, Federal IT delegate, FDF
Customs inspections relating to dual-use goods	Serge Gumy, Head of Tax Assessment Division, Federal Customs Administration
Danger from precursors for making improvised explosive devices	Dr. Balthasar Jung, Head of Explosives Analysis Team, Scientific Research Department, Zürich
Promotion of women: an opportunity for NBC protection	
Opening presentation	Dr. Sylvie Durrer, Director of the Federal Office for Gender Equality
Information from the DDPS	Sabine Lehner, Delegate for Equal Opportunities DDPS Marc Siegenthaler, Head of Personnel DDPS
Closing words	Dr. Brigitte Rindlisbacher, Secretary General DDPS
Medical NBC protection	
Advanced Hazmat Life Support (AHLS) course	PD Dr. Mathias Zürcher, Vice President SGNOR
Antidotes and logistic implementation in the decontamination hospitals	Dr. Dorothee Heer, AFLO
Consultation Centre for Radioactivity BsR	David Bürge, Canton of Aargau
Consultation Centre in Israel	LTC Michael Kassirer, MD, Israel Defence Forces Medical Corps
Current experience and work in NBC protection	
Dispersion modelling for nuclear emergency protection	Dr. Cyrill von Arx, ENSI
Network of Chemistry Experts – tasks and collaboration	Line Girardin, NEOC
Multi-resistant germs (AMR)	Prof. Dr. Gabriela Pfyffer, ComNBC
Special presentation on EBOLA	Dr. Patrick Mathys, FOPH
Closing words	Dr. Giuseppe Testa, Head of National NBC Protection Secretariat

GROFISPA: Basic Scheme



A new sorption test rig for large filters

Andres Wittwer

The NBC Protection Branch has further developed a test procedure to check the gas sorption performance of large NBC filters by means of modelling in an economical, safe, ecological and occupationally hazard-free manner. Cyclohexane has proved to be a suitable new test agent. The change required a complete reconstruction of the test facility.

The ability of a filter to retain gases is commonly termed as sorption performance or gas absorption capacity. In order to test this, a defined airflow with test gas is passed through the test filter to determine the exposure time until the filter is exhausted and test gas breaks through, i.e. until its concentration behind the filter rises in the clean air.

It is indispensable for development and quality assurance that filters for respiratory protection are tested with those gaseous air contaminants against which they must provide protection. In Spiez Laboratory, smaller filters for individual protection, typically used in a gas mask, can be tested against almost all relevant gaseous air contaminants. For reasons of safety and expenditure these tests, most of them carried out with highly toxic chemicals, are limited to laboratory scale, where airflows of up to 100 litres per minute containing well-defined contaminants are generated, and no more than a few grams of test agent are needed. To test NBC filters for collective protection facilities (filtered shelters) up to a hundredfold of these test air volumes and quantities have to be handled. With highly toxic chemicals the expenditure for such tests in terms of safety precautions and costs is too high. Therefore, Spiez Laboratory has adopted a two-step test procedure:

1. The quality of the sorbent (activated carbon granulate), i.e. its sorption performance is tested on a model with warfare agents or other highly toxic substances at laboratory scale. The test model must correspond to the real filter as regards sorbent quality and dimension (thickness of sorption layer and airflow velocity or duration of contact).

2. Checking, whether the sorbent layer in the large filter has at least the same absorption capacity as that in the filter model. This is to

Components:
1 Air dryer unit
2 Condensed water
3 Test agent tank
4 Test agent pump
5 Compressed air
6 Spray nozzle
7 Evaporator tube
8 Mixing tube
9 Gas filter test object
10 exhaust fan

Sensors:
T Air temperature
H Air humidity
F Flow rate
P Pressure
cE upstream concentration
cA downstream concentration

Test air channel:
Outside air
Dry air
Test air before filter
Test air after filter
Liquid test agent

ensure that the sorbent in the real filter is properly filled in (no “weak spots” in the sorption layer). This further ensures that the sorbent can be fully exploited (i.e. the sorption performance tested at laboratory scale also applies to the complete filter.)

This comparative test requires a high test concentration for a short test time and large amounts of the test agent are applied. Basically, any gas with good adsorption properties is suitable, which makes it possible to use an environmentally friendly, occupationally hazard-free and cost effective test agent.

The above defined two-step test procedure for large filters has been successfully applied for decades, in which for the sorption comparison test 1,1,1-trichloroethane was used until 1990 and trichloroethylene thereafter. Because they are poorly inflammable, these highly chlorinated hydrocarbons posed a low risk of fire or explosion. Furthermore, they could easily be measured by former detection methods. However, these compounds are increasingly recognised as environmental and occupational hazards. Today, we are obliged to replace them if this is technically feasible. The following criteria were used to evaluate the suitability of alternative test agents:

- adsorption properties
- volatility
- compatibility with health and environment
- detectability of low concentrations
- flammability and explosiveness
- cost
- experimental results

The evaluation clearly showed that any compound that puts neither the environment nor occupational health at risk has the disadvantage of being substantially inflammable and explosive. After safety risk assessment and experimental verification, the two compounds propane and cyclohexane were selected as final candidates.

Test Agent	Advantages	Disadvantages
Propane	• Low consumption • Simple addition into the airflow • Moderate risk of fire and explosion • Filter regeneration possible after test (non-destructive testing!)	• Poor reproducibility, thus poor discrimination potential • Regeneration too elaborate
Cyclohexane	• Test agent approved for several testing standards • High reproducibility, thus good discrimination potential • Good correlation with existing results	• Evaporation necessary for addition into airflow • Substantial risk of fire and explosion

Sectional view of a big filter:

The arrow indicates sorption bed depth and flow direction

Sorption bed data:
Volume: ≥ 66 L
Air flow rate: 150 m³/h
Bed depth: 157 mm
Flow velocity: 99 mm/s

The test procedure has been adapted for cyclohexane on the basis of its evaluation results. In fundamentally redesigning the test procedure and completely reconstructing the test facility the following objectives were pursued:

- elimination of environmental and occupational health hazard
- Integration of fire and explosion precautions[1]
- general improvement of occupational safety and efficiency (beforehand, several partly heavy modules had to be mounted for each test assignment)
- general renewal of outdated installations

1 The past method of injection and slow evaporation into a gas reservoir cabinet of 50 m³ was no longer an option with an inflammable gas depot of more than 1 kg. Now, the storage tank for the test agent is located outside the building. Apart from the handling of highly inflammable liquid cyclohexane, the formation of explosive air-vapour mixtures must also be taken into account (target value for test concentration = 45 % of lower explosion limit [LEL]) along with the flammability and dust explosion property of activated carbon loaded with cyclohexane.

Laboratory test tube (sorption bed model):

The arrow indicates sorption bed depth and flow direction

Sorption bed data:
Volume: ≥ 0.43 L
Air flow rate: 0.98 m³/h
Bed depth: 152 mm
Flow velocity: 96 mm/s

- improvement of reliability and significance of the test procedure[2]

- adjusting to market needs (the altered procedure allows testing according to several more recent standards. Obsolete Swiss standards can be updated).

Basic engineering for the new test facility was prepared by Spiez Laboratory. The fundamental requirements for realising the project and a prerequisite for obtaining an operational permit, were a risk analysis and a corresponding fire and explosion prevention concept, including proof of implementation. Such a facility can only enter into service after such a safety declaration has been confirmed.

2 Previously, ambient air was used for the test airflow without any humidity control. The rather moderate impact of air humidity on the uptake of the former test agent was compensated for by simultaneously testing the model sample in parallel. However this compensation was incomplete because the small model warmed considerably less than the big filter (relatively better dissipation of sorption heat).
With the new test rig, a greater impact on the uptake of the new test agent is largely eliminated by keeping relative air humidity below 30 %. Thereby parallel model testing with each filter is no longer necessary.
Furthermore, instead of comparing break-through times, the comparison will be based on the uptake of the test agent determined by weighing. This will eliminate the direct influence of deviations from set airflow rate and test concentration on the test result.

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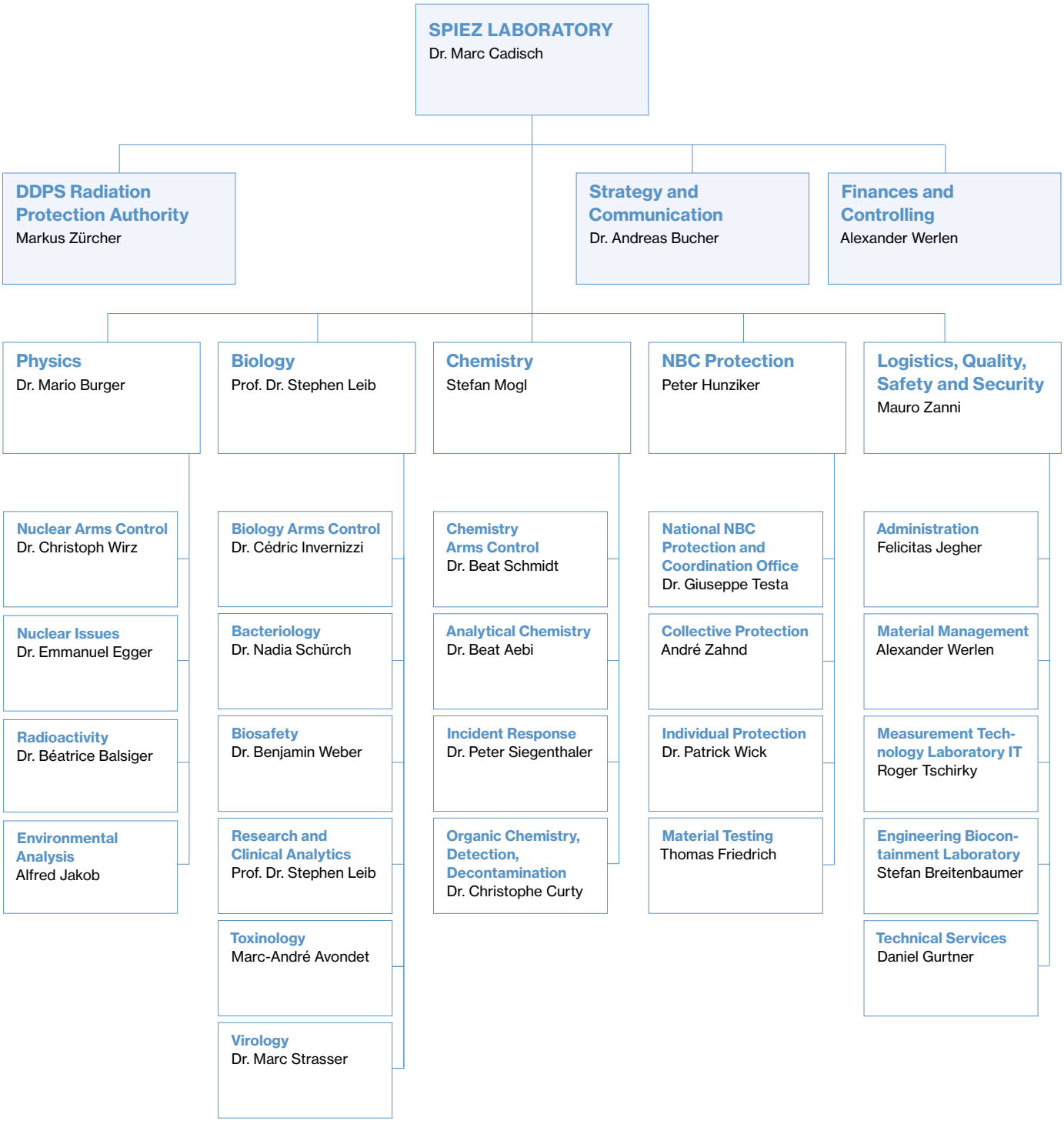
Organisation



Accredited activities

ISO/IEC 17025 accredited laboratories

STS 0019	Testing laboratory for the analysis of samples for chemical warfare agents and related compounds
STS 0022	Testing laboratory for adsorbents and respiratory protection filters
STS 0028	Testing laboratory for the determination of radionuclide concentration
STS 0036	Testing laboratory for polymers and rubber, and for the protection performance of polymers, rubber and textiles against chemical warfare agents
STS 0054	Testing laboratory for the detection of biological agents
STS 0055	Testing laboratory for NBC protection material, shelter equipment and shelter installations
STS 0101	Testing laboratory for the determination of main and trace elements and selected air-pollutants

Round Robin tests October 2013 – September 2014

Accredited laboratory		Quantity	Type and partner
STS 019	Chemical anaysis/verification	1	35. Official OPCW Proficiency Test
STS 022	Sorbent	–	
STS 028	Radionuclides	4	ALMERA gamma ray spectra (3) ALMERA PT gamma- und radiochemistry (various methods and matrices, 6 samples), RV IRA/BAG (1 food sample, gamma), RV REIMEP-22 (1 sample age determination uranium)
STS 036	Plastics and rubber	8	Round robin series, Kunststoffinstitut Lüdenscheid
STS 054	Biological toxins	3	
	Medical biochemistry	–	–
	Diagnostics of bacteria- Drinking water	6	HPA Water Microbiology External Quality Assessment Schemes
STS 055	Ventilation	0	
	Air blast effects	0	
	Ground shock effects	0	
STS 101	Major and trace elements	5	“International Soil-Analytical Exchange“ ISE, University Wageningen WEPAL “Potable Water“, ielab, Alicante
	Air pollutants	2	“Stack Emission”, ielab

Presentations

Our scientists attend and actively contribute to conferences and offer their input to training courses dealing with NBC protection issues. Below are some of the presentations, given by our specialists during 2014.

Date	Subject
12.01.2014	Andreas Zaugg: Microwaves, Microreactors – the New Synthesis Technologies for the Preparation of S1 Chemicals, S-1 Users Forum, Madrid
16.01.2014	Dr. Cédric Invernizzi: The Dual Use Dilemma in the Life Sciences, IVI, Mittelhäusern
27.02.2014	Andreas Schorer: Identification of Unknowns – First Experiences with the Agilent 7200 GC/Q-TOF System, Agilent Technologies MS User Meeting, Zürich
07.04.2014	Stefan Mogl: Gap Analysis on Verification Methodology, SAB TWG Verification, Den Haag
22.04.2015	Dr. Marc Cadisch, Spiez Laboratory – Swiss Science and Technology for NBC-Protection, Swiss Pharma Science Day, Berne
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28.05.2014	Dr. Andreas Bucher: ABCN Referenzszenarien, ENSI Informationsforum Betriebssicherheit von Oberflächenanlagen, Brugg
08.07.2014	Dr. Peter Siegenthaler: OPCW Proficiency Testing at Spiez Laboratory, DSO National Laboratories, Singapore
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14.07.2014	Dr. Peter Siegenthaler: Analysis of Environmental Samples in Support of a United Nations Investigation of Alleged Use of Chemical Weapons: Experiences & Lessons Learnt, OPCW Headquarters, The Hague
31.07.2014	Dr. Cédric Invernizzi: Immunology: Key Concepts for the BWC, Meeting of Experts, Universität Genf, Genf
28.08.2014	Christian Müller: Quantitative SEB ELISA, EQuATox-Meeting, Stockholm
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04.09.2014	Dr. Rahel Gäumann: Vorkommen, Verbreitung und wichtigste durch Zecken übertragene Krankheiten, Bürgerspital, Solothurn
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10.10.2014	Dr. Giuseppe Testa: Protection en cas d'urgence aux environs des installations nucléaires, Zusatzkurs Sachkundige/r Strahlenschutz, Schwarzenburg
21.10.2014	Marc Stauffer: Metallspurenanalytik in Fliessgewässern, armasuisse, Berne
23.10.2014	Stefan Mogl: Convergence in Chemistry and Biology: Implications for the CWC, ETH, Zürich
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23.10.2014	Dr. Patrick Wick: Verwendung geeigneter PSA beim Umgang mit KKF Anlagen, Eidg. Herbstkonferenz der Schiessoffiziere, Hölstein BL
21.11.2014	Dr. César Metzger: Biologische Gefährdungen/Bedrohungen (Ebola), Medic-Instruktoren der Kapo Bern, Berne
02.12.2014	Stefan Mogl: Spiez CONVERGENCE, CWÜ Staatenkonferenz, Den Haag
04.12.2014	Dr. Beat Schmidt: Weaponisation of CNS Acting Chemicals for Law Enforcement, CWÜ Staatenkonferenz, The Hague
16.12.2014	Dr. Martin Schär: Analytische Strategie, ETH, Zürich

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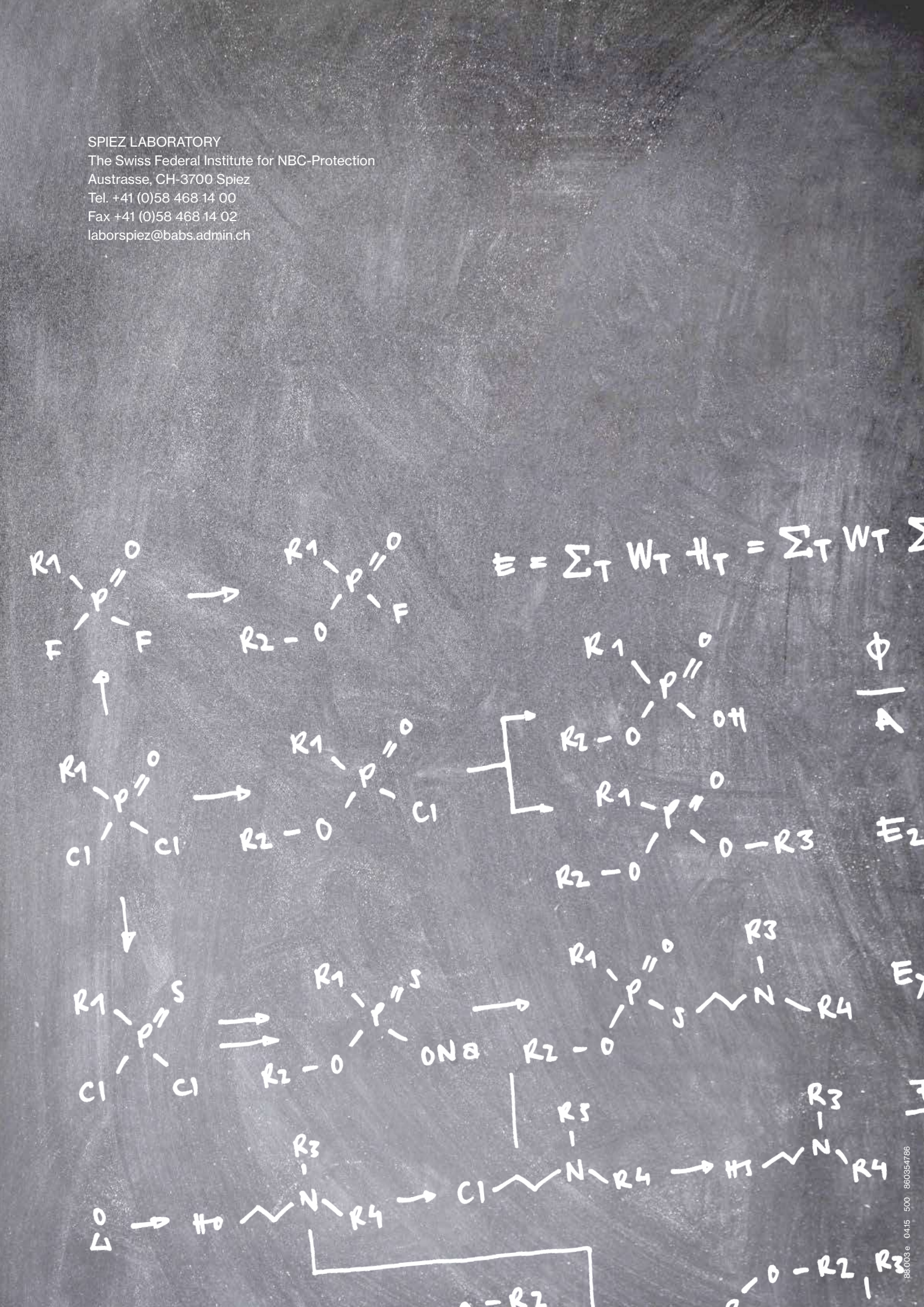

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