

PROJECT REPORT

Nordic Biopreparedness Forum
-An initiative to strengthen laboratory preparedness
for high-consequence biological agents



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SAMMANFATTNING

Den här rapporten sammanfattar arbetet som genomförts åren 2014-2016 med att initiera ett nätverk, Nordic Biopreparedness Forum, mellan de nordiska länderna inom området beredskapsdiagnostik för en stärkt gemensam förmåga. Målet var att etablera ett samarbete mellan myndigheter och institut som ansvarar för folkhälsa, veterinärmedicin, livsmedelssäkerhet samt försvarsforskning och försvarsmedicin. Alla dessa parter har intresse i att kunna utföra analyser av olika provtyper (t ex patientprover från djur och människor, mat, vatten och miljö- prov) vid förekomst av allvarlig smitta eller vid misstanke om kontaminering med högpatogeta biologiska agens.

I fokus ligger den laborativa förmågan, kapaciteten och beredskapen för att kunna genomföra analyser för att påvisa mikroorganismer som orsakar allvarlig sjukdom och måste hanteras på säkerhetslaboratorium av skyddsnivå 3. Under initieringsarbetet har workshops genomförts där deltagare från Danmark, Finland, Island, Norge och Sverige tillsammans har diskuterat och beslutat form och omfattning för det gemensamma nätverket. Dessa möten har också inneburit byggande av kontaktnät och kunskapsutbyte, med seminarier för att dela lärdomar och erfarenheter från olika sjukdomsutbrott, nya metoder och tekniker samt strategier för kvalitetssäkring. Under 2015-2016 har Nordic Biopreparedness Forum formaliserats. En kommitté har tillsatts med medlemmar från de flesta av de deltagande länderna som tillsammans med nätverkets medlemmar beslutar om gemensam verksamhet utifrån ambitionsnivå och resurser. Föreslagna framtida aktiviteter är: utbyte av referensmaterial, personalutbyte för att lära av varandra inom området beredskapsdiagnostik, gemensam metodutveckling samt ringtest för att utvärdera analysförmågan för högpatogeta agens vid de deltagande myndighetslaboratorierna. Alla dessa aktiviteter är tämligen resurskrävande, varför det är en stor vinst om de kan genomföras i samarbete och på så sätt också komma flera aktörer till nytta.

ABSTRACT

This report describes the initiation of the Nordic Biopreparedness Forum (NBF) in 2014-2016. This is a forum between the Nordic countries in the area of preparedness diagnostics for enhanced joint capability. The aim was to establish collaboration between agencies and institutes for public health, veterinary medicine, food safety and defence research. These actors share an interest in analysis of samples (e.g., clinical samples from animals and humans, food, water, and environmental samples) in case of severe disease or suspected contamination with high-consequence biological agents. The forum focus is the laboratory capability, capacity and preparedness for detection of microorganisms that cause severe disease and which are therefore handled at laboratories of biosafety level 3 (BSL3). During the initiation of the NBF, workshops were organised where participants from Denmark, Finland, Iceland, Norway and Sweden discussed and decided the form and scope of the forum. These meetings facilitated networking and exchange of knowledge, with seminars to share information and experiences from different disease outbreaks, new methods and techniques for analysis, as well as strategies for quality assurance. In 2015-2016 the NBF was formalised. A committee with representatives from the participating countries was appointed that, together with the other forum members, decides upon joint future activities depending on the ambition level and resources. Suggested future activities include: exchange of reference material, staff exchange to learn from each other through working side-by-side, joint method development, and organisation of proficiency testing to evaluate the capability to analyse sample for high-consequence agents at the participating laboratories. All these activities are resource demanding. Therefore, it is valuable to be able to carry them out in collaboration, so that they can benefit several participating agencies and institutes.

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SCOPE OF THE FBD

The overall aim of the Forum for Biopreparedness Diagnostics (FBD) is to strengthen the capability and capacity to identify microbial high consequence agents (i.e. agents that require biosafety level 3 laboratories) in various sample types and enable the authorities to share the sample load during crisis. To achieve this, the FBD strives to harmonise methods, equipment and quality assurance to ensure that results emanating from the participating authorities are comparable. The multisectoral laboratory network enables diagnostic work applied to different sample types e.g. tissue (human and animal), food, feed, drinking water and environmental samples. FBD is a collaborative effort of four Swedish governmental agencies: the National Food Agency (NFA), the National Veterinary Institute (SVA), the Swedish Defense Research Agency (FOI) and the Public Health Agency of Sweden (PHAS).

FBDS ARBETE

Det övergripande målet med Forum för beredskapsdiagnostik (FBD) är att skapa och förbättra förutsättningar för ett mer effektivt utnyttjande av landets samlade kapacitet och kompetens för diagnostik av biologiska riskklass 3 agens (det vill säga patogener som kräver skyddsnivå 3 laboratorier). Genom sådan samordning ska myndighetslaboratorierna kunna utföra jämförbar och kvalitetssäkrad diagnostik med god kapacitet och uthållighet i händelse av storskalig spridning av allvarlig smitta. Forum för beredskapsdiagnostik (FBD) är ett samarbete mellan fyra svenska myndigheter: Livsmedelsverket, Statens Veterinärmedicinska Anstalt (SVA), Totalförsvarets forskningsinstitut (FOI) och Folkhälsomyndigheten (FOHM), som tillsammans täcker kompetensområdena humanmedicin, veterinärmedicin, foder, livsmedel inklusive dricksvatten, miljöprover samt expertis med avseende på miljöprovtagning och bioforensisk analys.

1. GLOSSARY OF TERMS AND ABBREVIATIONS

Table 1 glossary of terms and abbreviations

Biopreparedness	A state of readiness for potential future public and animal health or other emergencies caused by disease or dissemination of pathogenic biological agents.
Biosafety	The application of knowledge, techniques and equipment to prevent exposure of laboratory personnel and the environment to potentially infectious agents or other biohazards. Biosafety defines the containment conditions under which infectious agents can be safely manipulated.
Biosecurity	Measures that are taken to stop the spread or introduction of harmful organisms to human, animal and plant life.
BSL2	Biosafety Level 2. This biosafety level is applied to facilities and routines (e.g. use of personal protection equipment and decontamination practices) for work with pathogenic microorganisms of moderate hazard to staff or environment.
BSL3	Biosafety Level 3. This biosafety level is applied to facilities where biological agents are handled that cause severe and potentially lethal disease, infect in low doses and can spread via air.
High-consequence agents	Disease-causing microorganisms that require handling at BSL3, according to the work environment authority, and that are likely to cause severe disease or death, for example anthrax, tularaemia, plague and Q-fever.
BUOS	The Centre of Expertise for Biological Threats, Finland
CBB	The Centre for Biosecurity and Biopreparedness ¹ , Denmark
DEMA	The Danish Emergency Management Agency ²
DTU	The Technical University of Denmark ³
DTU Food	The Technical University of Denmark National Food Institute ⁴
DTU Vet	The Technical University of Denmark National Veterinary Institute ⁵
DVFA	The Danish Veterinary and Food Administration ⁶

¹ <https://www.biosikring.dk>

² <http://brs.dk>

³ <http://www.dtu.dk>

⁴ <http://www.food.dtu.dk>

⁵ <http://www.vet.dtu.dk>

⁶ <https://www.foedevarestyrelsen.dk>

Table 1 glossary of terms and abbreviations

Evira	The Finnish Food Safety Authority ⁷
FBD	The Forum for Biopreparedness Diagnostics, Sweden
FDF	The Finnish Defence Forces ⁸
FFI	The Norwegian Defence Research Establishment ⁹
FOI	The Swedish Defence Research Agency ¹⁰
Keldur	The Institute for Experimental Pathology and University of Iceland ¹¹
Landspítali	Landspítali - The National University Hospital of Iceland ¹²
MAST	The Icelandic Food and Veterinary Authority ¹³
Matis	Icelandic Food and Biotech R&D ¹⁴
NBDN	The Norwegian Network for Biopreparedness Diagnostics, Norway
NBF	The Nordic Biopreparedness Forum, the collaboration described in this report.
NBN	The Nordic Biosafety Network ¹⁵
NFA	The National Food Agency, Sweden ¹⁶
NFSA	The Norwegian Food Safety Authority ¹⁷
NIPH	The Norwegian Institute of Public Health ¹⁸ , Norway
NMDD	The Nordic Working Group for Microbiology & Animal Health and Welfare ¹⁹
Nofima	A Norwegian institute for applied research within the fields of fisheries, aquaculture and food research in Europe ²⁰
NVI	The Norwegian Veterinary Institute ²¹
PHAS	The Public Health Agency of Sweden ²²
SLAM	Standardisation of laboratory analytical methods, a joint project funded from EU's 7th framework programme ²³ .
SSI	Statens Serum institut, Denmark ²⁴
SVA	The National Veterinary Institute ²⁵ , Sweden
THL	The National Institute for Health and Welfare, Finland ²⁶

⁷ <https://www.evira.fi>⁸ <http://puolustusvoimat.fi>⁹ <http://www.ffi.no>¹⁰ <http://www.foi.se>¹¹ <http://keldur.is>¹² <http://www.landspitali.is>¹³ <http://www.mast.is>¹⁴ <http://www.matis.is>¹⁵ <https://www.folkhalsomyndigheten.se/nordic-biosafety-network>¹⁶ <http://www.livsmedelsverket.se>¹⁷ <http://www.mattilsynet.no>¹⁸ <http://www.fhi.no>¹⁹ <http://www.norden.org> (search for: NMDD)²⁰ <https://nofima.no>²¹ <http://www.vetinst.no>²² <https://www.folkhalsomyndigheten.se>²³ http://cordis.europa.eu/project/rcn/103191_en.html²⁴ <http://www.ssi.dk>²⁵ <http://www.sva.se>²⁶ <https://www.thl.fi>

2. AIM

The aim of the initiative in this report was to establish a Nordic collaboration between agencies and institutes that handle agents causing severe infectious disease. In particular, the collaboration focuses on laboratory preparedness for analysis of samples containing high-consequence agents requiring diagnostics at biosafety level 3 (BSL3). These matters are of concern to several sectors: public health, veterinary medicine, defence research and food safety (figure 1).

Regional collaboration is a valuable means to enhance preparedness for handling outbreaks or other events involving high-consequence agents²⁷. The focus of this collaboration is strengthening laboratory capability to detect and identify these microorganisms; however, exchange of knowledge and experiences from the whole chain of analysis – including preparedness strategies for unusual and severe disease – will support diagnostic preparedness overall.

AIM FOR AN INTER-SECTORIAL NORDIC COLLABORATION IN LABORATORY BIOPREPAREDNESS:

- A forum with defined structure and plan for joint activities and future aims is established in 2016
- The forum includes the Nordic countries Denmark, Finland, Iceland, Norway and Sweden, with participants from the sectors: public health, veterinary medicine, defence research and food safety.

²⁷ http://cordis.europa.eu/project/rcn/103191_en.html Project within the EU 7th framework programme; Standardisation of laboratory analytical methods SLAM.



Figure 1. The biopreparedness collaboration encompasses four sectors: public health, veterinary medicine (animal health), defence research and food safety. The panels show examples of activities and possible sample types for analyses performed within the different sectors. All staff wears personal protection equipment for biosafety level 3.

Top left panel (public health) shows a patient blood sample and laboratory personnel reading the results of a Gram staining to characterise bacteria in a sample.

Top right panel (veterinary medicine); when staff operates on location ²⁸ (e.g. collecting samples during an outbreak investigation) they usually wear disposable personal protection equipment as shown in the photography. The pig ²⁹ represents one of their possible patients. Materials analysed by the veterinary laboratories include animal, feed, and environmental samples from, e.g., outbreak sites.

Bottom left panel (defence research) illustrates one of the sample types analysed within this sector – white powder that is sometimes used in hoaxes and scares to suggest spread of e.g., anthrax.

Bottom right panel (food safety) shows personnel reading culture plates and two examples of food matrices: beef and drinking water.

²⁸ Photography: SVA

²⁹ Photography: Bengt Ekberg, SVA.

3. BACKGROUND

3.1 CONSIDERING A NORDIC BIOPREPAREDNESS COLLABORATION

High-consequence microorganisms that cause severe diseases in humans and animals, such as anthrax, plague and brucellosis, are relatively rare in the Nordic countries. However, this may change due to globalization. People travel more than ever, animal trade is extensive, and many consumers are used to having food from the whole world on their tables. As a result, microorganisms and disease may also move more freely. What is rare today in the Nordic countries could therefore be a different issue tomorrow. Furthermore, the natural spread of disease is accompanied by the more malign aspects of biothreats, where current political instability makes terrorism part of our everyday news. Hence, there is a need for preparedness to analyse and handle highly pathogenic agents, even if the current prevalence of these agents is low.

In the Nordic countries some highly pathogenic agents are endemic, like *Francisella tularensis* (tularemia) and *Bacillus anthracis* (anthrax). Others are found in neighbouring countries in Europe. One such example is *Brucella* which causes disease in many species of domesticated animals such as sheep, pigs and cattle and infects humans in contact with these animals or by ingestion of unpasteurised dairy products. These bacterial agents have all been discussed and deemed important while establishing the network. Several institutes have also expressed a need for collaboration regarding diagnostics of highly contagious viruses, which is a possible future expansion of the network's scope.

Preparedness diagnostics is costly to sustain since it requires special laboratories, strict routines and trained staff to perform the diagnostics correctly, to prevent spread of the disease, and to diminish risk for infection of the personnel.

In Sweden, the national cross-sectorial Forum for Biopreparedness Diagnostics (FBD) was initiated in 2007 by four governmental agencies responsible for food safety, defence research and animal and public health and in need of diagnostics for high-consequence pathogens. The aim of the FBD is to strengthen diagnostic capability and capacity for high-consequence agents in Sweden. This has been a fruitful, cost-beneficial collaboration for the participating authorities with respect to training exercises, method development and quality assurance³⁰.

Therefore, an idea was formulated in 2013 to initiate and extend a Nordic forum to include Denmark, Finland, Iceland, Norway and Sweden. A project was approved for funding in 2014-2016 by the Swedish Civil Contingencies Agency.

³⁰ Report from the Swedish Civil Contingencies Agency (in Swedish): Nyttan av nätverk Utvärdering 2015 av anslag 2:4 Krisberedskap. (2016) Publ. No MSB938. ISBN 978-91-7383-616-6

3.2 CHALLENGES WITH DIAGNOSTICS AT BIOSAFETY LEVEL 3

Working with high-consequence agents puts special demands on the laboratories, routines, and not least the staff. Biosafety level 3 (BSL3) laboratories (figure 2) are shielded from the surroundings by pressure and air locks to ensure that the microorganisms stay within the facility. Another preventive measure is heat treatment or other decontamination methods of everything that is to be taken out from the laboratory. Hence, working in these facilities is time consuming and often straining for the staff. An exchange of experiences and best practices between colleagues is valuable in order to improve biosafety routines and methods.

Although tularaemia is quite common in some Nordic countries, most of the, high-consequence species are rare. Subsequently, analysis for these agents is rarely used, but has to be in place in a security facility upon demand. This calls for a strategy to uphold ability through regular practice and training.

Another difficulty is the lack of international standard methods for analysis of these microorganisms. Hence, a variety of in-house methods are established, and each laboratory has to decide on the level of quality assurance, a highly necessary but time-consuming work. The laboratories often have little access to samples that are naturally contaminated with these agents, e.g. patient samples from actual outbreaks or contaminated environmental samples. Hence, for most of the high-consequence agents it is not possible to evaluate the performance of the methods of analysis on “real” samples. It is therefore necessary that the laboratories participate in proficiency tests or use other means of quality assurance to confirm sufficient performance of each method.



Figure 2. The two photographs illustrate differences in personal protective equipment in BSL2 (left) and BSL3 (right) laboratories. In the BSL2 laboratory, the staff wears lab coat. Gloves are only worn upon risk for contamination (of hands or sample). In contrast, the BSL3 staff wears a ventilated respirator powered by batteries in the belt, covering lab coat and soft boots, double disposable nitrile gloves, disposable sleeve protectors and apron. All work with the pathogenic microorganisms is performed within a safety cabinet.

3.3 CURRENT NORDIC COLLABORATIONS FOR ENHANCED BIOSAFETY, BIOSECURITY AND PREPAREDNESS

There is a tradition of collaboration between the Nordic countries, not least on issues related to infectious disease. Within each sector (public health, veterinary medicine, defence research/medicine and food safety) networks and forums help us with our everyday work and elevate the output compared to what can be achieved by a single country.

3.3.1 Sectorial division within each country

In Norway, the Norwegian Defence Research Establishment (FFI), the Norwegian Institute for Public Health (NIPH) and the National Veterinary Institute (NVI) have the capacity to diagnose high-consequence pathogens. The FFI has worked extensively with sample preparation and has the ability to analyse various environmental samples. Clinical human samples are the responsibility of NIPH, and animal samples are handled by the NVI. The National Food Safety Authority collaborates with the NVI, where the latter would perform the analysis in the event of food-borne infection with these agents.

In Finland, highly pathogenic agents related to public health and military medicine are handled by the National Institute for Health and Welfare (THL) and the Finnish Defence Forces (FDF); that together run the Centre of Expertise for Biological Threats (BUOS) in Helsinki (see below). The Finnish Food Safety Authority (Evira) is a merger of the former National Food Administration, the Research Institute of Veterinary Medicine and Food, as well as the Control Centre for Plant Production. Hence it covers the whole food production chain from farm to fork. Evira manages feed, food and animal samples upon disease or suspected transmission of infectious agents.

In Denmark, the DTU Veterinary Institute, the DTU Food Institute, Statens Serum Institut (SSI) and the Centre for Biosecurity and Biopreparedness (CBB) have the national responsibility for analysis of highly pathogenic agents. Animal samples are analysed at the DTU Veterinary Institute and human samples at SSI. Samples with suspected highly pathogenic contamination of food and water are sent for analysis to the DTU Veterinary Institute.

In Iceland, the Institute of Experimental Pathology handles animal samples upon suspicion of highly pathogenic agents. Human samples are analysed at the National Hospital, Landspítali, while the Icelandic Food and Biotech R & D (Matis) analyses samples of food, water and environment. The agencies in Iceland collaborate extensively with agencies and institutes in other countries in the area of microbiological analysis.

In Sweden, the National Veterinary Institute (SVA), the Public Health Agency of Sweden (PHAS) and the Swedish Defence Research Agency (FOI) have the capacity and facilities for diagnosis of high-consequence agents. The National Food Safety Agency (NFA) cooperates with the SVA to analyse food and drinking water samples at the BSL3 laboratory.

Overall, the Nordic countries are well prepared for analysis of samples containing high-consequence agents, in terms of laboratory facilities, analytical capability and staff. The organisation between countries varies, but in general governmental agencies or institutes in different sectors share the responsibility for analysis of high-consequence biological agents.

Networks are listed below that specifically focus on work with high-consequence agents or are connected to biosafety and biosecurity issues, not least in BSL3 settings.

3.3.2 National networks

Centre of Expertise for Biological Threats (BUOS) in Finland

One example of cooperation in Finland for combating outbreaks of communicable diseases is the Centre of Expertise for Biological Threats (BUOS). It is run jointly by the Finnish Defence Forces and the National Institute for Health and Welfare since 2005. This centre operates as a national expert organisation for biological threat prevention and preparedness and is actively involved in international cooperation. The centre also provides support and capacity building regarding rare, unexpected biological threat events^{31,32}.

Forum for Biopreparedness Diagnostics (FBD) in Sweden

The diseases caused by high-consequence agents are a concern for several sectors; therefore, the FBD network was initiated in 2007 in Sweden. This network joins four agencies: the Public Health Agency, the National Veterinary Agency, the National Food Agency and the Defence Research Institute. It has since received funding from the Swedish Civil Contingencies Agency to strengthen and harmonise the national BSL3 capability.

The overall aim of the FBD is to strengthen national preparedness for the analysis and handling of an outbreak or other event involving high-consequence agents in Sweden. The diagnostic capacity has increased over the past decade through sharing existing methods and laboratory safety routines, as well as by performing joint method development, proficiency tests and exercises.

Norwegian Network for Biopreparedness Diagnostics (NBDN) in Norway

During the initial contacts between Swedish and Norwegian agencies in 2013 and 2014, a network similar to the FBD was initiated in Norway 2014. The Norwegian Network for Biopreparedness Diagnostics (Norsk Beredskapsdiagnostisk Nettverk, NBDN) includes the Norwegian Veterinary Institute, Defence Research Establishment, and the Institute of Public Health. The formation of NBDN has contributed to a closer collaboration between the Norwegian agencies with a strengthened national preparedness for handling potential outbreaks with high-consequence pathogens in Norway.

Swedish Laboratory for Food Safety and Biopreparedness

The Swedish Laboratory for Food Safety and Biopreparedness was established during 2004-2013 with funding from the Swedish Civil Contingencies Agency, and is a collaboration between the National Food Agency and the National Veterinary Institute. These two agencies share responsibility to ensure safe food and feed, and hence have a mutual interest in developing and sustaining diagnostic preparedness in case of contamination of the food production chain. This joint effort focuses on method development, staff training and upholding capability and preparedness for sample preparation and molecular detection of bacterial high consequence agents in food, feed, drinking water and clinical animal samples.

³¹ https://www.sintef.no/globalassets/project/fobis/ws5/nikkari_fdf.pdf

³² http://stm.fi/en/artikkeli/-/asset_publisher/cooperation-in-combating-global-biohazards

3.3.3 Nordic networks and ongoing collaborations in connection to the NBF

Nordic biosafety network, NBN

The Nordic Biosafety Network was formalized in 2005, largely upon an expressed wish for collaboration from the Nordic biosafety community. The scope of the NBN is all matters relating to laboratory biosafety and biosecurity. The network has members from national agencies and institutes, hospitals, academia and industry. Annual meetings are arranged with alternating host countries; between meetings the contact is upheld via an online forum.

This network has been an inspiration for initiation of the forum described in this report, the Nordic Biopreparedness Forum (NBF). While the NBN covers questions of laboratory biosecurity and biosafety – for example, personal protection equipment and decontamination – it does not focus on the actual analyses and diagnostics that are the core of the NBF. Hence, the NBN and the new network will have partly overlapping, but not identical, member communities. The progress of the NBF initiative was presented at NBN meetings in Stockholm in 2014 and Helsinki in 2015. There was also a joint discussion at the Helsinki meeting to find benefits of collaboration between the networks and instances where overlaps should be avoided.

The Nordic Working Group for Microbiology & Animal Health and Welfare (NMDD)

The Nordic Working Group for Microbiology & Animal Health and Welfare (NMDD) was established in 2007 and is a working group under the Nordic Council of Ministers. NMDD focuses on microbiology including antimicrobial resistance, animal health and welfare, in the food chain. This working group has the task of stimulating collaboration between authorities responsible for food safety in the Nordic countries. The aim of establishing the Nordic Biopreparedness Forum was presented to NMDD in 2015, and in 2016 the joint workshop in Oslo received funding from the NMDD to support the collaboration in the field of high-consequence agents.

4. THE NORDIC BIOPREPAREDNESS FORUM: FROM IDEA TO FORMALIZED NETWORK



Figure 3. Timeline describing the evolution of NBF from idea to formalized collaboration.

The idea of establishing a Nordic network for BSL3 laboratory preparedness stems from the experience of the benefits from the FBD and from the results of the EU-project Standardisation of laboratory analytical methods, SLAM³³. In SLAM it was recognized that the level of laboratory preparedness varied widely between countries and that upholding a broad ability for handling rare/never events with hazardous agents is resource demanding. It was suggested that regional collaborations would strengthen the overall ability to handle outbreaks or other events with harmful substances. (SLAM covers not only infectious disease but also chemical and radiological/nuclear agents.) Due to the long history of cooperation between the Nordic countries, it was a short leap of mind to consider this region as a basis for a laboratory biopreparedness network.

³³ http://cordis.europa.eu/project/rcn/103191_en.html

Phase 1 – First contact - visiting colleagues in neighbouring countries

In 2014, the FBD project group contacted colleagues in the neighbouring Nordic countries with the intention of visiting and initiating a dialogue about current levels of preparedness, diagnostic ability, experience of working with high-consequence agents, gaps and needs, and, of course, the proposed collaboration. These meetings and the participating agencies/institutes are summarized in table 2. During the meetings, there was often an opportunity to visit the BSL3 facility at the host agency, and hence learn about routines, technical solutions and the kind of work that is performed in these labs.

Table 2: Meetings with sister agencies and institutes, 2013-2014

Date	Year	Place	Participating representatives
10 December	2013	Nofima, Ås, Norway.	Norway: Nofima, NVI, FFI, NIPH. Sweden: FOI, PHAS, NFA, SVA.
4 February	2014	SVA, Uppsala, Sweden	Norway: Nofima, NVI, FFI, NIPH. Sweden: FOI, PHAS, NFA, SVA.
22 May		DTU Veterinary Institute, Copenhagen, Denmark.	Denmark: DTU Food, DTU Vet, SSI. Sweden: FOI, PHAS, NFA, SVA.
2 October		Evira, Helsinki, Finland	Finland: Evira. Sweden: FOI, PHAS, NFA, SVA.
3 October		BUOS, Helsinki, Finland	Finland: THL, FDF. Sweden: FOI, PHAS, NFA, SVA.
4 November		Keldur, Reykjavik, Iceland	Iceland: Keldur, National hospital dpt Virology. Sweden: PHAS, NFA, SVA.
4 November		National hospital, Reykjavik, Iceland	Iceland: Keldur, National hospital dpt Virology and dpt Bacteriology, Head of surveillance and outbreak investigation, Chief Epidemiologist office. Sweden: PHAS, NFA, SVA
5 November		National hospital dpt of Virology, Reykjavik, Iceland	Iceland: National hospital dpt of Virology. Sweden: PHAS, NFA, SVA.
5 November		Matís, Reykjavik, Iceland	Iceland: Matís, Keldur. Sweden: PHAS, NFA, SVA.

From the visits, meetings and other contacts, it was clear that the interest and also possibility to participate in a future collaboration varied between countries and institutes. Several of the contacted institutes agreed that collaboration on BSL3 laboratory Biopreparedness would be useful since there is a limited number of professionals working with these questions in each country. Connecting them would be a valuable basis for exchange of knowledge.

A spin-off effect of the meetings was that they brought experts together in the countries that were visited by the FBD representatives. In Norway, FFI, NIPH and NVI formed a national network (the NBDN, mentioned above) similar to FBD to strengthen the laboratory ability and preparedness.

After the meetings needs and ideas for a future collaboration were summarized, a list of contacts compiled, and the question to join in the making of a network was sent out.

In the initial phase, the focus was on identifying common needs to maintain and strengthen the diagnostic ability for these high-consequence agents and to form a network to support each other in this field.

A joint aim was formulated: To strengthen the Nordic biopreparedness by sharing knowledge and experiences from outbreaks, and to improve current methods and strategies for quality assurance. The planned work would rationalize and strengthen the biopreparedness diagnostic capability and quality within each country, and in the Nordic area overall.

Phase 2 - Joint workshops and decisions

Two initial workshops were held in Sweden in order to bring together professionals working with high-consequence pathogens in different sectors. The workshops included seminars for knowledge exchange and discussion of a possible network.

The first bilateral workshop, with 34 participants from Sweden and Norway, was held at the Swedish National Veterinary Institute in Uppsala on August 28-29, 2014. Group discussions on GAP-analyses and beneficial areas of exchange were interspersed with presentations on topics including current outbreaks of highly pathogenic disease in humans and animals, decontamination, and new technologies for sampling and analysis.



Figure 4. Group discussion at the bilateral workshop between Norway and Sweden, held at SVA in Uppsala in August 2014.

The second workshop was held at the Public Health Agency of Sweden in Solna on May 7-8, 2015, with 33 participants from all Nordic countries except Iceland. Unfortunately, there was a general strike in Iceland, so participants from the Icelandic National Hospital, Landspítali, were unable to attend. Similar points were discussed as in the previous workshop. Presentations were given on: biopreparedness diagnostics summarized for each country; field work at the ongoing EBOLA outbreak; and new diagnostics for EBOLA, African swine fever; and activities and capability at the Centre for Biosafety and Biosecurity in Denmark.

The Norwegian network NBDN then arranged an extensive and appreciated **third workshop** at the Norwegian Institute of Public Health in Oslo on March 15, 2016, with 48 participants from all of the Nordic countries. The presentations in the workshop covered several areas, for example microbial forensics, bioinformatics, plans for a new BSL3 laboratory, MERS-CoV, Lyssa virus, an EU-project (EMERGE ³⁴), and a presentation of the joint proficiency test held in 2015. In addition an invited speaker from the UK presented experiences from the London Olympics from a biopreparedness view. During the workshop there were also group discussions mainly concerning the future of the NBF.

The workshops concluded that diagnostics of high-consequence pathogens is a potential area for closer collaboration between agencies within in the Nordic region. However, grand ideas can be costly and it is important (not least in the beginning) to find a realistic level of collaboration.

³⁴ <http://www.emergeproject.eu/>

JOINT ACTIVITIES SUGGESTED BY THE WORKSHOPS:

1. Annual meeting as a minimum level of collaboration

It was agreed, in order to keep it simple, that a yearly workshop would be a straightforward way of initiating a network.

Workshop aims would be to:

- Exchange knowledge and experience, in connection with BSL3 diagnostics and management of unusual outbreaks.
- Build a network for staff working with diagnostics at BSL3 facilities.
- Evaluate results from joint proficiency tests.

Ideas for organization of workshop:

- Alternate the host country as main organizer of the annual meeting.
- The network committee would contribute to planning for the meeting.
- The meetings would have varying themes, for example strategies to handle samples, speed versus sensitivity, gaps and needs, chain of analysis, current events/outbreaks.

2. Proficiency tests

Joint proficiency tests for high-consequence pathogens were of interest for many of the agencies. This was to be discussed further to establish if it would be a part of the network activities.

Suggestion: It is costly to organize proficiency tests. At the workshop it was proposed that agencies participating in proficiency tests should also contribute by organizing them, on a rotary schedule.

3. Exchange of knowledge and possibly material

A benefit of the network would be getting to know each other, learning "who does what". Hence, knowledge exchange could be initiated on an ad hoc basis, out of interest and could occur via everyday means of communication (e-mail, phone) at yearly meetings or possibly by laboratory visits and training. Interesting areas included: methods and techniques, risk assessments, routines and handling, expertise concerning specific agents, etc. The sharing of reference material and strains could be of interest and worth looking into.

Phase 3 – Formalisation and future

At the joint workshop in 2015, it was decided that the network should be maintained through a committee with two members from each participating country. Currently (2016), the committee consists of one or two representatives from each country except Iceland. The committee has decided that contact information for network participants is to be kept simple i.e., as a list of names, affiliations and e-mail addresses that the committee or other network members can use for communication. Further, the committee has composed a letter of intent describing the scope and aims for the network (see appendix 1).

Table 3: Nordic agencies and institutes and their connection to the Nordic Biopreparedness Forum (NBF).

Country	Forum partners	Associated partnership/ Kept in information loop regarding e.g., upcoming workshops.	Informed of the initiation of the forum
Denmark	DTU National Veterinary Institute, Statens Serum Institute (SSI), and the Centre for Biosecurity and Biopreparedness (CBB)	DTU National Food Institute	The Danish Emergency Management Agency (DEMA) and the Danish Veterinary and Food Administration (DVFA)
Finland	The National Institute for Health and Welfare (THL)	Finnish Defence Forces and Evira	
Iceland		Landspítali The National University Hospital of Iceland and Keldur Institute for Experimental Pathology and University of Iceland	The Icelandic Food and Veterinary Authority (MAST) and Icelandic Food and Biotech R&D (Matis)
Norway	The Norwegian Institute of Public Health (NIPH), the Norwegian Defence Research Establishment (FFI), and the Norwegian Veterinary Institute (NVI)		The Norwegian Food Safety authority (NFSA)
Sweden	The National Food Agency (NFA), the National Veterinary Institute (SVA), the Swedish Defense Research Agency (FOI), and the Public Health Agency Sweden (PHAS)		

5. ONGOING AND FUTURE NETWORK ACTIVITIES

5.1 WORKSHOPS

The workshops described above represent an important step towards a formalised network. Bringing together professionals from agencies in the Nordic countries to share experience, knowledge and discuss benefits of future collaboration has been invaluable in getting the forum to the point where we are now. At the workshop in Sweden 2015 it was decided that annual meetings should be a minimum level of network activity, preferably with alternating host country. The committee had a pre-workshop meeting on March 14, 2016 in Oslo and decided that the 2017 workshop will be held in Denmark and hosted by the DTU.

5.2 LABORATORY PROFICIENCY TESTS

There are few or no international proficiency tests available for the high-consequence pathogens in matrices from the different sectors. Proficiency tests are used in order to compare the sensitivity and specificity of the methods and equipment at the participating authorities, and to assure good performance of the staff that handles this type of samples. Thus, evaluation of the result is a crucially important part of these tests. During the evaluation, test results are discussed and exchange of methods and routines can be performed, aiming to give more robust and optimized capability for each participating laboratory.

The Swedish Forum for Biopreparedness Diagnostics (FBD) organized a proficiency test in the autumn of 2014, and the institutes in Norway were invited to participate. The proficiency test consisted of ten inactivated, unknown bacterial samples of which five were to be analysed as fast as possible (time-test). The sample types were milk, serum and water. All included participants in Sweden and Norway (listed as Forum partners in table 3) participated in the proficiency test³⁵.

In 2015, the Veterinary Institute in Norway arranged a similar proficiency test in which the Swedish agencies and institutes (as listed in table 3) participated. The proficiency test consisted of ten inactivated, unknown bacterial samples of which four were to be analysed as fast as possible. The results were presented and discussed at the joint workshop in Oslo in March 2016.

In September 2016, FBD arranged yet another proficiency test with five samples and participating institutes and agencies from Sweden and Norway³⁵.

5.3 EXCHANGE OF INFORMATION AND MATERIAL

During the visits to the different Nordic countries and in the joint workshops, personnel with shared interests were brought together. As a result there has been exchange of information and laboratory resources such as MALDI-TOF spectra and isolated bacterial strains of unusual species. (These are valuable as reference materials for obtaining good diagnostic quality.) Hence, connections to other professionals in the neighbouring countries increase the possibility to receive important information and materials that thereby increase the overall capability and quality of BSL3 diagnostics.

³⁵ Boskani, Flink, Frosth, Bereczky and Granberg (2016). Quality Assurance of Biosafety Level 3 laboratories. FBD 2016/17 in Swedish Forum for Biopreparedness Diagnostics report series. MSB1042 ISBN: 978-91-7383-694-4.

6. DISCUSSION AND CONCLUSIONS

Since infections caused by high-consequence agents are uncommon in the Nordic countries, there are a limited number of experts with experience to recognize these diseases (medical public health or veterinary staff). The demand for diagnostics is low, but at the same time, relatively resource demanding since high containment laboratories and trained staff are needed to uphold the ability in case of an event. Since the situation is similar in all the Nordic countries, Sweden initiated a project in 2014 to explore the possibility and interest for extending the network to sister authorities in all the Nordic countries. How much resources should be allocated to maintain this diagnostic preparedness? This question has been solved in different ways in the Nordic countries, resulting in varying levels of preparedness concerning the laboratory facilities, which methods can be employed, and the staff. Hence there is a gain from a joint discussion on laboratory preparedness in a broader, Nordic, perspective rather than as isolated countries.

6.1 CURRENT STATUS OF THE NORDIC BIOPREPAREDNESS FORUM

During 2015-2016, the NBF has been formalised through the appointment of a committee that has composed a description of the forum including background, aims and activities, and organisation (see appendix 1). Much of the information below was brought forward in this description.

The committee strives for two to three representatives from each country. Currently there is one representative from Finland, two each from Denmark, Norway and Sweden and none from Iceland. The communication and decision making within the committee is upheld via e-mail and phone meetings. The committee renewal cycle follows the calendar year and chairmanship is rotated between countries yearly, starting with Sweden.

At the joint workshops and committee meetings, the participants of the Nordic Biopreparedness forum (NBF) have the aim of strengthening the biopreparedness diagnostic capability and quality in the Nordic countries, thereby improving the ability of the Nordic Countries to react to natural outbreaks as well as bioterror incidents involving high-consequence infectious biological agents.

This is to be obtained through information exchange, common training and proficiency tests, exchanges of staff and reference materials, and standardization of analytical methods and protocols.

The NBF focuses on activities that address the above-mentioned unique challenges faced by the Nordic Countries in the biopreparedness area, and which are not or inadequately addressed by other international biopreparedness and biosafety initiatives (including current EU-funded projects).

NBFs activities thus comply with the Haga declaration of 2009³⁶ which aims to increase Nordic co-operation to prevent, reduce and manage the consequences of major accidents and disasters.

Upholding this type of cross-sectorial forum between nations is largely based on personal contacts despite a given network structure. It is therefore crucial that the participating authorities prioritise the activities within the forum and ensure that the personnel involved are both dedicated to the task and given time to carry out the work. On the other hand, redundancy is also important. Ideally, several personnel from each institute and country should be involved so that there are no information gaps or slow-downs if key-persons change jobs or priorities.

6.2 FUTURE PERSPECTIVES

Upholding sufficient preparedness for high-consequence agents – a resource demanding diagnostics, in case of rare or unlikely events – is a major challenge in all the Nordic countries. The smaller a population, the harder it is to convince director generals, stakeholders and politicians that the preparedness is needed. Through collaboration, some of the costs can be shared and thereby reduce the total sum of investments needed in the long run. Costs for method development, quality assurance and implementation of modern equipment are some examples where sharing knowledge can reduce costs for the participating authorities.

To strengthen the biopreparedness diagnostics capability for high-consequence agents in the Nordic region, a network is valuable and highly needed. Maintaining such a network is not costly, but some funding is still needed for arranging yearly workshops. Funding from the Nordic Council was approved for arranging the 2016 workshop. Appreciated activities within the network, such as arranging and sending proficiency tests by which our quality can be measured and improved, is difficult to fund on the limited government budgets. Joint proficiency tests on a European or Global level are sometimes possible and for the coming few years the EU-funded project EMERGE could give the opportunity to participate in proficiency tests during 2016- 2018.

It is important to continue the dialogue regarding future directions. Should the authorities strive for specialised laboratories or uphold a broad panel of diagnostic methods at each location? The level of preparedness is based on risk assessment and threat analyses, but unexpected events will continue to surprise us. Scalability and flexibility are therefore needed, and a regional forum or network is invaluable when an unexpected event occurs.

³⁶ [https://www.msb.se/Upload/Om%20MSB/Internationellt/Deklaration%20Haga-deklarationen%20slutlig%20\(4\)%5b1%5d.pdf](https://www.msb.se/Upload/Om%20MSB/Internationellt/Deklaration%20Haga-deklarationen%20slutlig%20(4)%5b1%5d.pdf)

Link to the Haga declaration (in Swedish), an agreement between Nordic ministers responsible for public crisis preparedness and emergency and rescue services for increased cooperation. One of the areas of collaboration suggested by the agreement is preparedness for chemical, biological, radiological and nuclear agents (CBRN) and the ability to prevent, detect and handle events with CBRN-agents through education and training activities, research and development of technology and equipment as well as cooperation in emergency situations.

APPENDIX 1 – GENERAL DESCRIPTION OF THE NBF, COMPILED BY THE NETWORK COMMITTEE

NORDIC BIOPREPAREDNESS FORUM (NBF)

Background:

The global mobility and transport of humans, animals and foodstuffs increases the risk of spread of infectious high-consequence pathogens to the Nordic Countries. Climate changes and global political threats are additional risks. The Nordic countries may therefore not continue in their positions as “outposts” regarding outbreaks of exotic high-risk threat agents. They are forced to increase their preparedness against these agents in the region. Upholding and improving the diagnostic laboratory preparedness for these rare diseases – most of which do not occur naturally in the Nordic countries – is resource demanding and the number of BSL3-facilities and staff working in this field is low. In many cases, there are no standardized methods and so in-house solutions are applied. Furthermore, in the Nordic countries, biopreparedness is handled according to the sector principle, i.e., different authorities have responsibility for certain sample types or agents. Bringing together representatives from the public health, veterinary medicine, food safety and biodefense sectors in connection with BSL3 diagnostics in the Nordic countries is therefore clearly needed.

In recognition of these unique challenges faced by the Nordic Countries in this area, the Nordic Biopreparedness Forum was established in May 2015 by microbiological, medical and molecular experts representing national agencies from the Nordic Countries (Denmark, Finland, Iceland, Norway and Sweden).

Aim and activities of the NBF:

The aim of the NBF is to strengthen the biopreparedness diagnostic capability and quality in the Nordic countries, thereby improving the ability of the Nordic countries to react to natural outbreaks as well as bioterror incidents involving high-consequence infectious biological agents (i.e., agents that require highly specialized biosafety level 3 laboratories and trained personnel).

This is obtained through information exchange, common training and proficiency tests, exchanges of staff and reference materials and standardisation of analytical methods and protocols.

The NBF focuses on activities that address the above-mentioned unique challenges faced by the Nordic countries in the biopreparedness area, and which are not or inadequately addressed by other international biopreparedness and biosafety initiatives (including current EU-funded projects).

NBFs activities thus comply with the Haga-declaration of 2009 which aims to increase Nordic co-operation to prevent, reduce and manage the consequences of major accidents and disasters.

Organisation:

The activities of the NBF are coordinated by a steering committee, comprising up to three representatives from each country.

The committee renewal cycle follows the calendar year (January till December), and chairmanship is rotated between countries; i.e., every December, participating countries nominate or reconfirm their committee members, and the next country takes over the chairmanship.

APPENDIX 1 – GENERAL DESCRIPTION OF THE NBF, COMPILED BY THE NETWORK COMMITTEE

The composition of the current committee acting till December 2016 is:

Sweden (chair in 2016):

- National Food Agency
- Totalförsvarets forskningsinstitut, FOI (Swedish Defense Research Agency).

Denmark:

- Veterinærinstituttet, Bakteriologi, Patologi og Parasitologi, DTU VET, (National Veterinary Institute).
- Mikrobiologi & Infektionskontrol, Statens Serum Institut, SSI (Bacteriology Reference Laboratory, National Institute for Health Data and Disease Control / SSI).
- Center for Biosikring og Bioberedskab, CBB (Centre for Biosecurity and Biopreparedness, National Institute for Health Data and Disease Control / SSI).

Finland:

- Terveystieteiden tutkimuskeskus, THL (Department of Infectious Diseases, National Institute for Health and Welfare, THL).

Norway:

- Forsvarets forskningsinstitutt, FFI (Norwegian Defence Research Establishment).
- Norwegian Institute of Public Health
- Folkehelseinstituttet, FHI (Norwegian Institute of Public Health).

Iceland: pending.

Current activities:

Annual workshop:

- A yearly one-day workshop is held for experts from the Nordic countries, and is open to all interested parties.
- Topics include, for example, lessons learned from recent incidents and outbreaks, laboratory method development, quality control of laboratory methods, and updates on other international biopreparedness initiatives.
- The annual workshop provides the main opportunity for the steering committee to report on its work, and receive feedback from Nordic experts and agencies.
- Finally, but not least importantly, the workshop provides opportunities for informal networking and knowledge sharing between Nordic experts.
- The 2017 workshop will take place at the Danish National Veterinary Institute, in March. The workshop will be advertised by early September 2016, and the program will be available by early December 2016.

Proficiency tests (laboratory proficiency trial):

- A questionnaire to map the participating laboratories requirements for a proficiency test was distributed by the steering committee in May. Pending the results, proficiency tests will be organized in 2017 or 2018.

Networking:

- The Nordic Biopreparedness Forum collaborate with the Nordic council (funded the NBF workshop 2016), EU-funded project EMERGE and the Nordic Biosafety Network.

