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Pandemic Risk and Emergency Management

D2.2 Analysis of risk assessment and surveillance: current systems, practices, technologies and research needs

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1 Introduction

1.1 Risk assessment and surveillance

1.1.1 Risk assessment

WHO defines risk assessment as a systematic process for gathering, assessing and documenting information to assign a level of risk. It provides the basis for taking action to manage and reduce the negative consequences of acute public health risks." [1] Risk assessments are based on the knowledge at hand in a given moment in time and are often carried out under time constraints. As a situation and knowledge evolves, risk assessments may need to be repeated and the assessment may change.

1.1.2 Surveillance

Surveillance is the collection, collation and analysis of data to guide public health actions. Surveillance of infectious diseases monitors the impact of a disease in a population. These data provide information for outbreak detection and management, measurement of the effectiveness of interventions, as well as indications of resource needs.

For surveillance to function properly it has to be carried out on an ongoing basis to ensure baseline data are available and trends can be followed. Surveillance differs from 'studies' in that it has a stronger focus on continuity and ease of data collection over completeness of data, and that there is defined direct use of the data.

Surveillance can be indicator-based or event-based. Indicator-based surveillance is defined by WHO as: "The routine collection of pre-defined information about diseases using case definitions (e.g. weekly surveillance of cases of acute flaccid paralysis). There are often predetermined outbreak thresholds for alert and response" [1]. Event-based surveillance is defined by WHO as: "The organized and rapid capture of information about events that are a potential risk to public health" [1].

1.2 Task description

Surveillance that provides relevant information based on epidemiological and microbiological data and other measurable indicators is essential to guide public health action in a pandemic. This requires structured methods for collecting data, analysing data and supplying it to decision-makers in an understandable format. These surveillance systems need to work together both in peace-time and in crisis situations; a good understanding of the responsibilities and mandates of different actors and how they interact is therefore required.

As part of PANDEM work package (WP) 2, systems, practices and technologies for risk assessment and surveillance were investigated and analysed in the EU at both national and EU level. The work included case studies of three EU member states and the United States (US) to demonstrate examples of good surveillance practice as well as gaps. A workshop was held in Brussels at month 6 where experts and users in the risk assessment and surveillance field reviewed good practice and provided valuable input to the identification of current gaps and needs. The resulting report will provide information for the gap analysis to be performed in WP 5.

1.2.1 Experiences from the international level

In this work package, we collected insights on gaps and strengths regarding outbreak detection and investigation, risk assessment and surveillance, from Member State level using structured interviews built around scenarios. Such insights, i.e., knowledge about gaps and strengths, has previously been gained also on the international level after the occurrence of actual events. Most recent examples of such post-event evaluations are from the H1N1 influenza pandemic (2009) and the Ebola outbreak in West Africa (2013-2016): the WHO compiled lessons learned and formulated recommendations for good practice in pandemic preparedness [2] and the European Commission also arranged meetings to gather and document the lessons learned, see for instance the ECDC report *The 2009 A(H1N1) pandemic in Europe – A review of the experience* [3]. Regarding Ebola, the EU held a conference in Luxembourg in 2015 from which the main conclusions were gathered in an informative report [4].

1.3 Methodology

The results from the previous deliverable *(D2.1 Threat analysis and scenarios*) was incorporated, where possible, in the planning and execution of the work.

Four national surveillance systems were evaluated - Ireland, England, Sweden, and the USA, which were chosen on the basis of access to national level data and range of countries with regard to size, structure and location. There is a risk that these four national surveillance systems represent countries characterized by a higher level of preparedness than the average. Therefore, it is not evident that the results of this evaluation can be generalized without further adjustments.

Interviewees were asked for information on their infectious disease surveillance systems. The information received was supplemented by searching the web sites of the national agencies for up-to-date information on the surveillance systems and links provided by these webpages. Key aspects of the surveillance systems were then compiled by country in a separate table (Annex 1). The focus was on a) notifiable disease surveillance, in particular for two diseases (pandemic influenza and smallpox) included in scenarios developed by WP2 (D2.1) as well as for an unknown disease and influenza in general; b) availability of surveillance systems at different levels of healthcare; and c) influenza surveillance, as it is a challenge and often encompasses several different levels of disease severity.

1.3.1 Case studies

Five in-depth interviews with national senior experts in four countries were conducted to acquire the information needed for the case studies. One expert from Sweden, two experts from Ireland, two experts from England and one from the US, were interviewed. The aim of the interviews was to identify these senior experts' view of good practice, systems, and technologies for risk assessment and surveillance, research questions and innovation needs with a focus on the respective national aspect.

The interviews were conducted via Skype and recorded to ensure all relevant information is included in the final manuscript. The interviews took approximately two hours each. Participants gave verbal consent for recording of the interview. Interviewees have been anonymized.

Three scenarios developed in WP2 (D2.1) were used to structure the interview: (1) a pandemic of an unknown disease, (2) a new influenza pandemic, and (3) a deliberate release of smallpox. Our manuscript of scenarios describing a new influenza pandemic and a deliberate release of smallpox were distributed before the interview to guide the interviewees.

The interviews followed the overall structure of a questionnaire (Annex 2) that centred on (i) current good practice, (ii) improvements needs, and (iii) research questions and innovations needed in the following three fields: outbreak detection, outbreak investigation, risk assessment and surveillance. For the surveillance section we focused on four aspects of which three had been identified by the European Commission project FLURESP and used in WP2 (D2.1): clinical attack rate, hospital admission rate, and case

fatality rate[1], as well as proportion of severe cases. We also included a few questions regarding collaboration between veterinary and public health agencies.

An overview of the surveillance system in the four countries in included in Annex 1.

1.3.2 Workshop

An expert workshop was held in Brussels in February 2016 to identify current good practice, tools, systems for threat analysis, risk assessment and surveillance; and to identify gaps that can be addressed with currently available solutions and research and innovations needed. Experts were chosen to ensure representation from a broad range of areas and input from institutions with national, EU and global mandates. Experts from Belgium, Germany, Ireland, Luxembourg, Romania, Sweden, the European Centre for Disease Prevention and Control, European Commission, and WHO participated in the session. Before the sessions all participants were supplied with a short version of the pandemic influenza outbreak scenario, to focus and concretize the discussions structured in two dimensions: time (preparedness phase/detection phase/pandemic phase) and geography (global/European/national). During the workshop the participants were divided into three groups. All groups discussed the following themes, in turns, with dedicated session leaders: “surveillance/information management and logistics”, “governance and communications” and “training and diagnostics”. The aim of this workshop was to identify and highlight current threats, current practices, tools and systems, and concurrent gaps that could be identified and translated into needs for research and innovations. The workshop is described in more detail, together with the main outcomes in the project report, D5.1.

1.3.3 Conclusion

Based on the case studies and the workshop, a set of key issues on current good practice and innovations needed were identified and summarized by the authors of this report at the Public Health Agency of Sweden.

[1] Napoli C, Fabiani M, Rizzo C, Barral M, Oxford J, Cohen JM, Niddam L, Goryński P, Pistol A, Lionis C, Briand S, Nicoll A, Penttinen P, Gauci C, Bounekkar A, Bonnevay S, Beresniak A. Assessment of human influenza pandemic scenarios in Europe. Euro Surveill. 2015;20(7):pii=21038

2 Case study from Sweden

2.1 Outbreak detection

Question 1. On a national level, how would the surveillance system in Sweden detect an outbreak? What examples of good practice, improvements and innovations on outbreak detection are you aware of?

2.1.1 Current good practice

2.1.1.1 Unknown disease

- In Sweden there is a close connection between local authorities (county medical officers) and hospitals so that an unusually high level of any kind of disease is easily communicated.

- In Sweden there is a very strong and developed infectious disease clinics system, so the patients with an unknown disease would be clustered together much more than in most other countries and would therefore probably be identified/discovered earlier than if they were more dispersed.

- There is good collaboration between veterinarian institutions and the public health agency. In Sweden there is a zoonotic council, with a broad membership, that is in charge of strategic issues. There is also a zoonotic preparedness group that deals with zoonotic outbreaks, with members from the public health agency, veterinarian laboratory agency and the food agency. In addition, there is a national influenza pandemic group that, when relevant, includes the veterinary side. The agency has the joint leadership with the veterinary side for the coordination in the antimicrobial resistance area. Both the zoonotic council and the coordination of work on antimicrobial resistance are regulated by law.

- There is no regular exchange of data between the public health agency and the veterinarian institutions, however there is good collaboration and data exchange when required, as previously demonstrated during the H5N1 influenza events.

2.1.1.2 Influenza

- All cases of laboratory diagnosed influenza are mandatorily reportable, so if it is laboratory detectable, the cluster would be detected with the systems Sweden has in place.

- Sweden has a running system that monitors the web search patterns and telephone calls to health information centres. This system is a very useful tool for flu detection and is more likely sustainable and able to detect new variations on

illnesses. Other syndromic surveillance systems need more resources and would probably not get the acceptance from the hospitals.

- The present system is reasonably cost-effective.

2.1.1.3 Smallpox

- Smallpox is a mandatorily reportable disease, so once it is known that there has been a release of the disease there are surveillance systems for it. The risk is that as it is unusual, in the early stages it may be misdiagnosed, but there is not much that can be done to avoid it.

2.1.2 Improvement needs or challenges

2.1.2.1 Unknown disease

- The running surveillance systems in Sweden would probably not detect an unknown disease. Even if there is a paragraph in the communicable diseases law saying that unusual occurrences should be reported, reports of this kind are very rare.

2.1.2.2 Influenza

- There are things that can be improved, but it is a question of cost-effectiveness: How much resources would need to be invested for the detection of a new influenza pandemic which happens every 30 years?

2.1.2.3 Smallpox

- It is very difficult to know how systems would react to a really deep crisis. The detection of the disease would depend on the hospitals and if they would prioritize reporting data when the clinicians might be overwhelmed by cases and worried patients. Systems would most likely not be very resilient in a real deep crisis situation and they have never been tested for that.

2.1.3 Innovation and research needs

2.1.3.1 Unknown disease

- Develop further instructions or governances to the hospital systems on the reporting of unusual occurrence of diseases, giving better instructions on how the current reporting paragraph can be used, and increase awareness on the possibility and responsibility of reporting unusual occurrences of diseases.

- Develop a user-friendly information technology (IT) platform for the reporting of unusual disease occurrences.

- More research into what kind of signals we can detect in our normal data flow, and identify which ones are important and could signal that there is something going on.

2.1.3.2 Influenza

- Research on search patterns on specific web pages and telephone calls to medical helplines. For example the system that runs in Sweden now could be further developed.

2.1.3.3 Smallpox

- Research on exercises or stress tests in hospitals and healthcare systems on very unusual disease occurrences, in order to find indicators of the resilience of the systems to detect the disease in that kind of situation. This is not an easy task as hospitals and healthcare systems are already regularly under stress.

2.2 Outbreak investigation

Question 2. On a national level, what would be the procedure to undertake an outbreak investigation? What examples of good practice, improvements and innovations on outbreak investigation are you aware of?

2.2.1 Current good practice

2.2.1.1 Unknown disease

- The procedure to undertake an outbreak investigation of an unknown disease would be the same as for a known disease. The internal protocols, questionnaires and other tools available would be used and adapted for the investigation.
- There is a procedure for putting together special outbreak investigation teams with staff from the Public Health Agency. In case of a need for extra resources there are procedures to shift resources within the Agency.
- As Sweden is a relatively small country in terms of population, therefore it would be easy to locate the necessary skilled people for the outbreak investigation team, on the other hand the absolute number of skilled people would be limited.
- There are good professional networks between the Agency and the zoonotic sector and among laboratories that may help to deal with an unknown disease threat.
- A priori there are skilled personnel in Sweden to face an unknown disease threat, but in case it would not be possible to find skilled personnel on a specific subject, there are already communication lines with the European Centre for Disease Prevention and Control (ECDC) and the Commission that could be used to find it.

- There are set procedures for sharing information on a national, European and international level. These systems would work well in the event that there is need to notify there is an unusual occurrence.
- On the national level there is good communication between different authorities identified as International Health Regulations (IHR) connected authorities. For instance, communication between the Public Health Agency of Sweden and authorities in the zoonotic area and the antibiotic resistance area functions well.

2.2.1.2 Influenza

- An influenza pandemic has never started in Sweden, but the outbreak investigation procedure has been tested for small outbreaks quite often and works reasonably well.

2.2.1.3 Smallpox

- The outbreak investigation would also involve the security services, police and other stakeholders not involved in regular investigations. The Public Health Agency of Sweden has been involved in exercises together with these stakeholders, and there are networks connecting them that would allow communication and identification of skilled personnel for the outbreak investigation team.

2.2.2 Improvement needs or challenges

2.2.2.1 Unknown disease

- In case of needing extra staff resources to the ones available at the Agency, there are no set procedures for recruiting more staff.
- Discussions about procedures may help, on the other hand it is not easy to set up procedures for such an unusual event.
- On an international level the communication lines to notify an outbreak are working reasonably well, but when the situation becomes more complicated and there is a need to keep on sharing big amounts of data and with many stakeholders, then the systems are not performing that well, as they are not really designed for it.

2.2.2.2 Influenza

- No specific improvement needs were mentioned.

2.2.2.3 Smallpox

- The interaction with the security services and the police needs to be further elaborated because it is only sketched at this time.

- A smallpox exercise has never been run. In this case there is the added factor of being a disease with the potential for high mortality, therefore difficult to know how the stakeholders would react in a real situation.

2.2.3 Innovation and research needs

2.2.3.1 Unknown disease

- Develop procedures on how to exchange resources between different European countries. ECDC is already playing a role in this sense, but there is for instance a question on how much skilled personnel ECDC could provide to work in different countries.
- Adapting the systems to be more resilient and sturdy when sharing big amounts of data and with many stakeholders.
- Develop a discussion forum on an international level.
- On a national level, setting up a specific team and training people for these rare occurrences that may not happen in years, has not been a good experience in the past.

2.2.3.2 Influenza

- No specific innovation or research needs were mentioned.

2.2.3.3 Smallpox

- Running live exercises, to get stakeholders acquainted with the problems that would be encountered.

2.3 Risk assessment

Question 3. On a national level, what would be the procedure to undertake a risk assessment? What examples of good practice, improvements and innovations on risk assessment are you aware of?

2.3.1 Current good practice

2.3.1.1 Unknown disease

- There is a set procedure for risk assessment in the Public Health Agency of Sweden. In this procedure risk assessments done by ECDC and World Health Organization (WHO) are taken into account for the national risk assessment and a risk assessment team is selected on an *ad hoc* basis depending on the availability and the kind of personnel required.

2.3.1.2 *Influenza*

- Unless the pandemic started in Sweden, a formal risk assessment would most likely not be performed, and the risk handling would be based on the risk assessments from ECDC and WHO.

2.3.1.3 *Smallpox*

- The possibility of a deliberate release of smallpox has been discussed with the security authorities and it is considered unlikely that Sweden would be the primary target of this kind of attack. However, Sweden may be a secondary target because of cases travelling to and from the intended target. In this scenario, most of the risk assessment would most likely be done by different international agencies, and Sweden would follow these assessments.

2.3.2 Improvement needs or challenges

2.3.2.1 *Unknown disease*

- Sharing background data faster and more extensively among countries. Sometimes this process is not done very quickly.

2.3.2.2 *Influenza*

- No specific improvement needs or challenges were mentioned.

2.3.2.3 *Smallpox*

- In case Sweden would be a primary target, the risk assessment would be complex as it would also include other stakeholders such as security authorities and other agencies. There is no specific procedure for this kind of situation, there is a kind of Chemical, Biological, Radiological, Nuclear (CBRN) action plan from the Contingency Agency that is not operational on that kind of level. The risk assessment procedure would need to be developed *ad hoc*, which would be challenging.

2.3.3 Innovation and research needs

2.3.3.1 *Unknown disease*

- Develop systems for sharing background data among countries in an easier and faster way.

2.3.3.2 *Influenza*

- No specific innovation or research needs were mentioned.

2.3.3.3 *Smallpox*

- Once again, running live exercises, to learn how to handle this situation more in detail.

- Making risk assessments beforehand or getting more understanding and knowledge about the risk before it happens, the resources needed to put into preparedness depending on the probability of bioterrorist scenarios to happen.

2.4 Surveillance

In this section questions explored the capacity of the national surveillance system to obtain key information for the risk assessment using four examples.

Question 4. How would the Swedish surveillance systems get information to calculate the clinical attack rate, case fatality rate, proportion of severe cases and hospital admission rate? What examples of good practice, improvements and innovations on surveillance are you aware of?

2.4.1 Current good practice

2.4.1.1 Unknown disease

- In Sweden there is the possibility to add a new disease to the surveillance system within 24 hours. It can be done quickly as soon as there is enough information on the disease to develop a case definition. With this surveillance system it would be possible to collect clinical information on cases and if they are or have been hospitalized or not at the moment they are notified.

- In order to know the severity of cases there is already an influenza surveillance system, a network with the intensive care units that could notify the severe cases of the new disease, if needed. This information could be used as an indication of the more severe cases.

- The Public Health Agency of Sweden does not have direct access to the death registry on an individual level, but there is a procedure to get that information if needed and it is carried out regularly. Once a year the surveillance systems of almost all notifiable diseases are run against the death registry in order to find how many cases died during a given interval of time after being notified. The death register is updated continuously so the information is very current. Running the analysis with an unknown disease would be possible by asking the death registry for the information using the personal identifiers.

2.4.1.2 Influenza

- With the surveillance systems in place it is possible to calculate the attack rate for influenza that is laboratory confirmed or diagnosed in a given population.

- From the network of intensive care units, the Public Health Agency of Sweden gets continuous data on the number of influenza patients that are treated in intensive care, data that can be used as an indicator of the severity of cases.

- Once a year the influenza surveillance system is run against the death registry, so it would be possible to run that kind of analysis.

2.4.1.3 Smallpox

- Smallpox is already a notifiable disease, so as long as the number of cases is reasonable and the health system is not overwhelmed the regular surveillance system would be used to get the information to calculate the clinical attack rate.

2.4.2 Improvement needs or challenges

2.4.2.1 Unknown disease

- Adding a new disease to the surveillance system would work as long as the number of cases is limited. If there would be a big amount of cases increasing in a quick way the system would get overwhelmed as it is designed to get data on all of the cases or none of them.

- Even if a new disease can be added to the surveillance system within 24 hours, the surveillance system is not really geared to collect data on severity because it only collects data on the patient's first contact with the healthcare system and severity may develop later.

- It would be difficult to get the rate of hospitalizations among the reported cases as hospitalizations may occur after cases are notified. At the moment there is no system to follow hospital occupancy or to assess the stress the hospital system is under. Using the surveillance system and the network of the intensive care units, it would be possible to know how many cases of the new disease are occupying beds in the intensive care units, but that would only show the most severe cases and not the complete picture of the number of hospitalized cases.

- It is important to realize that surveillance systems would not provide all the data needed on an unknown disease as they are not geared for it. Therefore it would be necessary to add other systems to get the information needed.

- As in other regular surveillance systems it would not be possible to know about the number of cases in society that do not seek healthcare.

2.4.2.2 Influenza

- With the current surveillance systems it is not possible to know if the patient is in hospital or not. It would be necessary to add hospitalization information to the surveillance system, which is possible to do, but not in place at the present time.

2.4.2.3 Smallpox

- No specific improvement needs or challenges were mentioned.

2.4.3 Innovation and research needs

2.4.3.1 Unknown disease, Influenza and Smallpox

- As the surveillance systems in place would have limitations to get key information in the early stages of the pandemic, setting up a focused surveillance system using the first cases (first few 100 cases) would be very useful.

2.4.3.2 Smallpox

- Develop better procedures for this scenario.

3 Case study from Ireland

3.1 Outbreak detection

Question 1. On a national level, how would the surveillance system in Ireland detect an outbreak? What examples of good practice, improvements and innovations on outbreak detection are you aware of?

3.1.1 Current good practice

3.1.1.1 Unknown disease

- In Ireland any pathogen causing public health concern is notifiable according to the legislation, and if it is urgent, it can be telephoned in immediately.

- Cases would most likely present either at their General Practitioner (GP) or be admitted to a hospital. Clinicians are very familiar with what they are required to report to the medical officer of the Irish Public Health departments throughout the country if they see a cluster of unusual pathogens, even if the cause is unknown. The Health Protection Surveillance Centre (HPSC) has regular contact with the microbiological, infectious disease, intensive care and emergency physicians, and if there was a severe event, the physicians would probably get directly onto HPSC as well.

- There is also regular communication with clinicians in relation to IHR alerts that the HPSC receives.

- HPSC educates the medical students in one of the colleges at Trinity College about IHR and the need to notify public health. We use some of the methodology developed in a previous European project, REACT [5], working with case based scenarios to discuss when it is appropriate to discuss concerns with public health.

- The HPSC gets regular feedback on all the crude deaths from the central registries offices before they are coded. Hereby unusual or unexplained deaths could be picked up.

- The system for early alerting of national authorities, other member states and WHO works well.

- In Ireland there is a close collaboration between HPSC, the veterinary institutions and the department of agriculture. There is a national zoonotic committee that is formed by veterinarian members and human health members. There is mutual communication of alerts or events, on influenza and other diseases or issues.

Moreover protocols have been developed together, for example on response to avian influenza outbreaks.

3.1.1.2 Influenza

- A new influenza A virus would most likely be detected in the laboratory as an influenza that the laboratory would not be able to subtype. This would have to be sent to one of the WHO Collaborating Centres for Reference and Research on Influenza to determine if it was a novel influenza. This system would work well.

3.1.1.3 Smallpox

- If a smallpox case was diagnosed the clinician notifies the case to the local department of public health, and they would notify HPSC and enter the data into the Computerized Infectious Disease Reporting (CIDR) system. If the case was in the Dublin area, the clinician would likely contact HPSC directly as well. HPSC would then inform the health department at government level, ECDC and WHO.

- One advantage of being a relative small country is that something observed locally would very quickly come to national attention.

3.1.2 Improvement needs or challenges

3.1.2.1 Unknown disease

- The HPSC education of medical students on the need to notify public health does not cover all medical students in the country.

- In 2000, Ireland faced an event of an unknown pathogen. There was an outbreak of severe sepsis in intravenous drug abusers detected in Scotland. Ireland alerted their emergency departments and discovered cases. CDC requested to become involved (at that time ECDC was not established), a process that involved a lot of politics at the time. One of the problems with the outbreak was the diagnosis of the pathogen that eventually was identified as a new form of clostridium, which was named *Clostridium Novyi*. At that time it was not a notifiable disease. Another difficulty was to get the heroin to be tested, and later to send the heroin to CDC for testing. After this event, the legislation was changed and outbreaks of an unknown pathogen causing public health concern became notifiable. This is considered a good practice; clinicians can notify authorities knowing that they are following the statutory law without fears of being accused of breaking patient confidentiality, particularly when criminal charges might arise as a result.

3.1.2.2 Influenza

- No specific improvement needs or challenges were mentioned.

3.1.2.3 Smallpox

- The key point in detection of smallpox is that the clinical teams suspect and recognize it, because otherwise the diagnosis may be delayed.

- It is also very important that clinicians know and are assured by the knowledge of the basic infectious control procedures to put in place if they suspect a case. Anxiety can slow down the management of the situation, because health workers get concerned about infection control, personal protective equipment, risk to themselves, risk to their families etc.

3.1.3 Innovation and research needs

3.1.3.1 Unknown disease

- Getting in on the undergraduate programs for all medical students to ensure that they are all familiar with the need to notify public health, the responsibilities under the IHR and detection of abnormal clusters.

- Communication is one of the best things to invest in. Health professionals can get overloaded or tired with information, so it is important to find a balance. A good practice would be presenting at their conferences, trying to improve their knowledge of who they should contact if they are concerned about something, and making sure that they are aware that those lines of communication are open.

- During the *C.Novyi* outbreak the need for a European Reference Laboratory that could investigate an unknown pathogen became apparent. Obviously the type of reference laboratory required would be dependent on the mode of transmission and clinical signs e.g. anaerobic pathogen as in that outbreak spread through unsafe injection practices versus an airborne pathogen. While recognising the subsidiarity principle, we need to improve mechanisms to fund and support transfer of specimens within Europe when urgent outbreaks arise.

3.1.3.2 Influenza

- No innovation or research needs were mentioned.

3.1.3.3 Smallpox

- Surveys among the hospital doctors asking if they would be able to diagnose smallpox or other unusual infections, how they keep updated, if they would welcome any sort of educational procedure to keep the knowledge up-to-date.

That could enable e.g. adjusted online educational material for clinicians who would receive credits for continued professional development, required for their medical registration.

- Increase the level of awareness of the health workers on unusual infections on a six-month or yearly basis. For example in a newsletter, bringing to attention for instance the different presentations of a disease, asking to please discuss with an infectious disease expert and the local public health department if they have any concern. A good idea would be to combine it with other briefings, for instance briefings on Ebola last year or Zika virus this year.

3.2 Outbreak investigation

Question 2. On a national level, what would be the procedure to undertake an outbreak investigation? What examples of good practice, improvements and innovations on outbreak investigation are you aware of?

3.2.1 Current good practice

3.2.1.1 Unknown disease

- Ireland has a National Public Health Outbreak Response (NPHOR) and that comes into play in major events, depending on the extent and severity of the disease.

- Local areas investigate outbreaks frequently, and they do not involve HPSC unless it affects more than one area or if the disease is particularly severe.

- Depending on the seriousness of the outbreak, a national public health outbreak response team called NPHORT could be convened immediately. NPHORT would be formed by members of the HPSC and the regional public health departments. In the ministry of health there would be another more senior national public health emergency team (NPHET). The NPHORT would invoke the emergency procedures; have regular, if necessary daily, meetings; conduct the first few hundred cases surveillance; and produce regular situation reports. The situation reports would be sent to the regions, members of the national public health response teams, and NPHET.

- There are outbreak documents that specify who should be considered to be involved during an outbreak, the teams worked well previously with the Ebola and H1N1 pandemic.

- If there was evidence that it was a serious event, HPSC would send notifications through Early Warning Response System (EWRS) and the WHO IHR.

- Ireland is a relatively small country, but has well trained public health professionals in HPSC and the public health departments around the country, so would have no difficulty with the epidemiological response; describing the outbreak; and trying to identify the transmission routes. But in case of a very severe unknown disease, they probably may need assistance in relation to reference laboratories, and would not hesitate to seek assistance from ECDC, Public Health England (PHE), or, if necessary, CDC.

- Ireland has well-trained epidemiologists, microbiologists and infectious disease clinicians, but if the situation was overwhelming extra resources might be needed. The more recent developments to mobilize outbreak response teams at a European level that have just recently come into fruition would help.

- Ireland has not much experience in relation to chemical hazards but there are contracts in place with the UK authorities, and assistance would be sought from them.

- If a rapidly spreading very severe illness required extra funding for the outbreak investigation, the government would make the funding available, so funding would not be an issue.

- In Ireland it would be possible to immediately add the new pathogen to the CIDR system and set up an enhanced module in which microbiologists in laboratories, public health doctors and surveillance scientists could enter data.

- Information would be provided to the public, and to health professionals on a national and international level. There would be regular national media events, weekly if not more frequently, informing on the developments, number of cases and deaths etc. All the information would be made available publically and uploaded to the HPSC website.

3.2.1.2 Influenza

- All the systems that are working for seasonal influenza would be used for pandemic influenza. Using the systems regularly in non-pandemic times, enables to do it during a pandemic.

- The seasonal influenza reports are considered good and would be produced for pandemic influenza as well.

- The team for the outbreak investigation and risk assessment would be easier to form because it is a known disease. The relevant experts are already identified. These professionals are considered to have the necessary knowledge and skills for the task.

3.2.1.3 Smallpox

- Each local department has its own outbreak plan. Also, in addition to a local response there would be a national response. There are relevant experts with enough knowledge on smallpox to perform the outbreak investigation.

- The infectious disease advice for managing the smallpox cases would be developed at the national level and then communicated to the local hospitals.

- On a national level the communication with stakeholders is well established via email. Email is well used among hospital clinicians, labs and public health but it is not well used to communicate to primary care practitioners. There would also be local and national teleconferences communicating the issues, making sure that information was cascaded down to the relevant personnel.

3.2.2 Improvement needs or challenges

3.2.2.1 Unknown disease

- There is a current strategy for e.g. foodborne pathogens taking specimens and sending them to the virus reference laboratory and the bacterial microbiology department to enable both virological and bacteriological testing. For an unknown disease there are newer molecular diagnostic techniques that would be applied and the protocols could be better developed for what kind of laboratory specimen would be needed. The UK and Scotland have some procedures and if needed, HPSC would contact them to gain access to the most updated version of their procedure.

3.2.2.2 Influenza

- There is an Intensive Care Unit (ICU) surveillance system mainly used for seasonal influenza. The information is currently faxed to the HPSC, but it would be useful to develop a computerized system.

3.2.2.3 Smallpox

- One very important issue that would arise during the contact tracing of smallpox, or other similar infections, would be managing and quarantining the contacts until

they are either cleared or identified as cases. It would be very difficult to find holding locations at short notice and security issues could prove very problematic. In addition, the population would not be prepared and may not want to listen, so it would be necessary to find good ways to communicate the logic and a rationale behind what the authorities are doing to the general public.

- There is no contingency funding within the health service in Ireland for emergencies. If a severe event arose the government would be requested to provide emergency funds for the necessary management issues. Resources would not be guaranteed, and therefore resources could be an issue. The difficulty is ring-fencing funding, as other issues may arise.

- When setting up the outbreak teams, one issue might be reaching people outside office hours. While at the moment public health specialists are available on a 24/7 basis, the system is fragile and does not have access to other healthcare professionals.

- It is necessary to improve the communication with the primary care doctors, particularly electronic communication. Some primary care doctors do not have email and this could be an issue, because it would be necessary to send hard copies of the information, which is both time and resource consuming. A simple option could be to send media messages for clinicians inviting them to check their email or look to the website for information. A national cascade system needs to be developed.

- Not all localities have infectious disease consultants, so it would be necessary to get input from other areas.

- If the outbreak was developing on an international level the national outbreak team would have to make the correct links with the international stakeholders for mutual aid.

- In this kind of situation, ECDC would get queries from countries with and without cases and it would be important to get the same information out to both, so that the same structured preparation would be in place.

- There might be other practicalities that apply to any sort of emergency. The first meeting might be by teleconference and sometimes technologies do not work well.

In case of having a physical meeting, choosing the appropriate location, getting access to the relevant building, etc.

3.2.3 Innovation and research needs

3.2.3.1 Unknown disease

- The point of care testing, for contacts or people coming to the GPs could improve and would enable a much more effective response.

- The UK has developed some protocols for investigation of an unknown pathogen. Those protocols could be strengthened and made available on a European wide basis. Depending on the different modes of transmission (droplet, airborne, blood borne, etc.), it would be possible to agree on the appropriate investigations for each of these scenarios, microbiological initial specimens needed, etc.

- It would be helpful if ECDC, CDC, or another institution had ready-to-use protocols for the methodology of an unknown pathogen, so that in case of an event these could immediately be put into action. These protocols could be the result of a research project answering questions like: what are the best specimens to take and where would be the most appropriate laboratories to send these to, in the event of an unknown pathogen? It would be useful to have protocols developed to also cover other possibilities such as chemicals or environmental hazards.

- In Europe, if there is a major event, EWRS is overwhelmed when every country responds with its status and situation reports. It makes it difficult and time consuming for the member states to get the relevant information. A more efficient communication platform is needed, to enable the member states to more effectively and coherently monitor the situation throughout Europe, the response, and the plans; and to allow the sharing of ideas and discussing of the collective response.

- On a European level, it is important to ensure that there is rapid sharing of the laboratory advances, particularly molecular techniques, as they become available.

- Also on a European level, it might be important to have some arrangements that could enable earlier assistance rather than having to depend on the US.

- WHO and ECDC are jointly holding courses on foodborne outbreaks; it would be good to encourage courses like those. Encouraging multidisciplinary training and making it available is important to improve outbreak investigations.

3.2.3.2 Influenza

- Develop a computerized automated system for communication between ICUs and national public health authorities, in order to get as near to real-time data as possible. It would also be useful to extend this system to all hospitalized cases.

3.2.3.3 Smallpox

- Make it compulsory for the health service at local and national level to perform exercises once a year at the very least. Not just table top exercises but live exercises if possible, and then look at the evaluation of those for possible improvements.
- Exercising and practicing the national and local procedure, particularly outside office hours, could be helpful.
- Setting up a communication system for urgent information to the primary care doctors and/or improving the electronic communication with them, based on a survey.
- A simple and worthwhile research task would be asking governments and health service administration if they have contingency funds in place, if they are willing to access those funds and how they are being fenced.
- Another question would be asking countries and the relevant health authorities to share how they have addressed issues in managing serious infection in terms of identifying contacts, isolating them, providing support in terms of food and medicines, the security issues around isolation, and communicating those issues with the general public.
- Identifying holding locations and procedures for contacts, not just for smallpox, but for other diseases too. The communication with the population can be improved before a situation arises, by holding briefings for key media personnel, so that they understand the rationale behind the actions of the authorities. When the situation arises, at least some media personnel might then be able to help communicate what is happening to the general population.
- Within the health services, at senior management level, the department of health should identify contingency funds for this type of situations.
- It would be very useful if ECDC specified that they have relevant experts available to deal with specific diseases like smallpox, botulism, ricin, etc. A process that could be worthwhile developing at ECDC, is to assess their capacity for identifying the individuals who could provide expertise, to demonstrate that they have been

briefed and that when the situation arose they could contact them, and also have backups in case someone was uncontactable. It would be reassuring for the member states if ECDC demonstrated that they had considered these issues and had plans in place to acquire the relevant expert advice to support the member states.

3.3 Risk assessment

Question 3. On a national level, what would be the procedure to undertake a risk assessment? What examples of good practice, improvements and innovations on risk assessment are you aware of?

3.3.1 Current good practice

3.3.1.1 Unknown disease

- The risk assessment would normally be part of the practice of NPHORT, and they would bring the risk assessment to the NPHET, the ministry level.
- In an emergency HPSC would activate the emergency response measures and go to a level 2 emergency. This level involves most of the teams in the HPSC dropping what they are doing. One team would then look after normal business. The rest would form into the appropriate surveillance teams; response teams; teams checking the literature, the web, and what else is happening in the world if it was a worldwide phenomenon. HPSC has people identified to slot into those roles and teams.
- The normal practice in the outbreak response team would be to develop situation reports describing: the epidemiological features of the disease, the epidemic curves, number of people affected, hospitalized and in the ICUs, the number of deaths and how rapidly the disease is spreading. There are templates for that, which would be put into operation. The risk assessment would be based on this information obtained from the field investigation of the first few 100 cases.
- Ireland uses ECDC risk assessments on a regular basis, these are very valued. If an unknown disease emerged in another country and there were risk assessments performed elsewhere, they would be utilized.

3.3.1.2 Influenza

- In Ireland there is an extensive surveillance system in operation throughout the year for influenza, reporting less frequently but still in operation out of the influenza season. It encompasses a sentinel GP influenza-like illness surveillance

system coupled with a sentinel GP laboratory testing. This system is also used to test influenza vaccine efficacy as part of a European Influenza - Monitoring Vaccine Effectiveness (I-MOVE) project. We also monitor Out of Hours Calls for flu like illness from Out of Hours primary care centres, respiratory admissions to sentinel hospitals, and absence monitoring from sentinel schools. The best innovation recently has been the ICU surveillance system which operates from all ICUs in the country. This was initiated during the 2009 pandemic but has been maintained since. An admission and discharge surveillance form are sent to HPSC on all laboratory confirmed influenza cases in ICU. We also get some minimal information on all hospitalised cases with laboratory confirmed influenza from the laboratories as laboratory confirmed influenza is a notifiable disease. We also monitor the number of influenza outbreaks in schools, nursing homes and other institutions. We also are informed on a weekly basis of all deaths from the Central Statistics Office prior to coding.

- Because of the extensive improvements in influenza surveillance in recent years we are in a good position to comment on the severity of the influenza season as it emerges. It would be good to replicate this throughout Europe and have good ICU surveillance throughout Europe.

3.3.1.3 Smallpox

- If it was thought to be a deliberate release, it would become a security and police issue and they would take charge of the problem with input and support from the health service.
- There is a procedure for these kind of risk assessments, the department of health has a standing interdepartmental emergency committee for dealing with serious issues. This committee would coordinate the risk assessment. In case of a deliberate release, the committee would be chaired by the department of justice and the police.
- There is not a permanent team in place for risk assessments, but members are preselected, so the team would be set up quickly. This team has good skills and has worked well in previous emergency situations.

3.3.2 Improvement needs or challenges

3.3.2.1 Unknown disease

- As observed in previous pandemics or emergencies, professionals are usually very quickly off the mark if it is necessary to activate the public health. However, during a prolonged emergency, organizing shift work, stopping burnout, fatigue,

and exhaustion is a challenge. The tendency is to have people working very long days and that is often not sustainable.

3.3.2.2 Influenza

- There is a delay in Ireland in the statutory requirement to record deaths and this does cause problems in detecting acute increases in deaths from any cause.

3.3.2.3 Smallpox

- No specific improvement needs or challenges were mentioned.

3.3.3 Innovation and research needs

3.3.3.1 Unknown disease

- Training and modules on rapid risk assessments would be really helpful. ECDC is going to improve their rapid risk assessment methodologies. If afterwards this methodology and further training was spread throughout Europe, that would be very helpful, especially for an unknown pathogen where it is not possible to review literature.
- Sharing templates on risk assessment among countries, and agreeing on the most important things to include, would enable usable model templates. Ready to use templates and excel sheets to collect the needed information could also be useful.
- It would be important to learn how to avoid burnout and enable shift work. This is particularly more difficult in small countries, where there are relatively less professionals. In this field some research questions could be: What procedures from other areas of civic society, such as defence forces, could be applied? How to maintain an emergency response over a prolonged period? How do we prevent fatigue and burnout from affecting the required response?

3.3.3.2 Influenza

- On a European level, it would be a good idea to compare the templates that countries have for the first few hundred cases, and to make sure that all collect the same parameters to enable the modellers to share and compare the data. Having agreed templates would be a good idea.
- It would also be important to assess if a specific number of sites could conduct the first few hundred intensive monitoring. Countries could be better prepared by having such an agreement on a European basis.

3.3.3.3 Smallpox

- No specific innovations or research needs were mentioned.

3.4 Surveillance

In this section the questions explored the capacity of the national surveillance system to obtain key information for the risk assessment using four examples.

Question 4. How would the surveillance systems in Ireland get information to calculate the clinical attack rate, case fatality rate, proportion of severe cases and hospital admission rate? What examples of good practice, improvements and innovations on surveillance are you aware of?

3.4.1 Current good practice

3.4.1.1 Unknown disease

- The clinical attack rate would be obtained from the field investigation of the first few hundred cases, looking at attack rates in families and in cohorts, for instance in schools. If the unknown pathogen could be identified by serology, then it could be possible to estimate the proportion of infections that are symptomatic. The main idea would be to try to identify denominator data (people at risk), then it is a question of checking how many of them that have symptoms.

- The new pathogen would be added to CIDR. Through an enhanced surveillance form, public health professionals would enter all the necessary information on each case: the clinical symptoms, severity, hospitalization and on occasion death.

- HPSC regularly gets data on the number of deaths from the registry offices. In the death registration there is usually a time lag, because there is not an official requirement to urgently register deaths. In a severe situation, it would be possible to enhance that surveillance by asking GPs to inform of any deaths that fit the syndrome, but that would have to be set up at the time. The enhanced surveillance of hospitalized and ICU cases, could also provide information on deaths occurring.

- One way to obtain information on severity would be to get information from the hospitals on all the hospitalized cases, and how many were in the ICUs to get the proportion of very severe cases. There is also a sentinel GP system that at the moment provides data on number of flu, measles, rubella, and food poisoning cases, etc. that visited the GP.

- If there was no laboratory test and no serology, it would be very difficult to know the number of people who are affected and have not seen a GP. Maybe it could be possible to use an internet surveillance system like the ones used for flu, asking: Have you been ill with X syndrome, but did not attend a GP?

- The hospitalization rate could be obtained if there was a laboratory test available for the new disease. Then it would be possible to know how many confirmed cases were hospitalized, because laboratories can indicate if a specimen comes from a patient from the hospital or from the community. The enhanced data on the ICUs can also give information on hospitalizations.

3.4.1.2 Influenza

- Ireland has several systems in operation for seasonal influenza: sentinel GP influenza-like illness (ILI), the GP Out of Hours surveillance system (proportion of influenza-related calls to GP afterhours or during the weekends), the ICU critical care surveillance system (confirmed influenza cases admitted to critical care units), the National Virus Reference Laboratory (NVRL) surveillance (showing the influenza positivity reported from the NVRL for all respiratory specimens), mortality surveillance (Influenza-associated deaths reported as the primary/main cause of death by the physician or if influenza is listed anywhere as the cause of death on the death certificate), event-based influenza surveillance system on outbreaks notified to HPSC.

- In case of a new influenza pandemic, the clinical attack rate would be obtained from the field investigation of the first few hundred cases, looking at proportions with symptoms in families, school cohorts etc. For influenza it is possible to do serology, so it is feasible to assess the proportion of symptomatic infections.

- The case fatality rate estimate for influenza may be affected by the fact that not all deaths occur in laboratory-confirmed cases, there might also be deaths that are put down to heart attacks, strokes, etc. but that may have been precipitated by influenza. A lot of acute respiratory deaths would occur in hospital, and could be retrieved. But it would also be necessary to look at the excess all-cause mortality rate, in systems like European Monitoring of excess Mortality for public health action (EuroMOMO), even though it might be hampered by the delay in the death registration.

- Influenza is notifiable by the laboratories in Ireland so it would be possible to know if the specimens are coming from a hospital ward or from an outpatient. The ICU surveillance system would provide the number of severe cases hospitalized in the ICUs. There are also sentinel hospitals that weekly record the number of total respiratory admissions over all admissions and this allows the yearly assessment of the severity of influenza.

3.4.1.3 Smallpox

- Enhanced information collection would be developed very quickly using email initially and then transferring to the CIDR-system, once a questionnaire was uploaded, reducing the workload. On a regular basis, there is a system whereby, if not urgent, routine laboratory confirmed results are sent electronically to the local departments, then entered in the CIDR system; this method could be used in long term surveillance.

- In Ireland there is a good network of infection control teams in the hospitals and the community and HPSC has good relations with them, so in an acute situation it would be possible to get the relevant data required for surveillance and decision making.

3.4.2 Improvement needs or challenges

3.4.2.1 Unknown disease

- Performing a field investigation with the first few 100 cases to look at the epidemiological parameters in relation to a new pathogen is considered a good practice. This is an intensive piece of work. Is it necessary to conduct it in every country?

- If the event lasted a long period of time, the first 100 cases investigations should not be periodically repeated unless changes were suspected that would make a difference in the decision making, for example in vaccine or antivirals development. If the investigation needs to be repeated, the question would again be if this could be done in a few areas or centres so that the resources elsewhere could be focused on the response.

- If there was not a laboratory test available for the new disease (so that the laboratories could not provide information on whether the cases were hospitalized or not) and the situation was serious, the solution would be to try to get information on hospitalization directly from the hospitals, but currently this is not easy to retrieve. One solution would be to send public health professionals to all the hospitals to retrieve the data. This work would probably have to be a paper-based system and they would bring the data back out and then put it on the CIDR system for HPSC. If the situation was serious enough the disease would be made notifiable to facilitate for the public health professionals to get the data from hospitals in a quicker way.

- Depending on the speed required, the information could be sent by email (which would be the quickest), but with obvious issues concerning data encryption.

- The registration of deaths should be improved, to get more immediate recordings.

3.4.2.2 Influenza

- It would be important to be able to record all deaths, not just laboratory-confirmed deaths and ensure timely registration of death data.

3.4.2.3 Smallpox

- The number of deaths would be followed up on a daily basis with the local hospitals. Waiting for deaths to be registered in the death registry would be a too slow process.

3.4.3 Innovation and research needs

3.4.3.1 Unknown disease

- Develop a better automated system for ICU surveillance or even for hospitalized patients not admitted to ICUs, to get better data on hospitalized cases.

- Develop information technology that would enable a template on a tablet or something similar, so that, if necessary, the public health professionals could go into hospitals, get the data on all hospitalized cases and the subset of ICU patients, and immediately send it to HPSC.

- To shorten the delay in death registration, one solution could be legislation similar to the emergency powers act in the United States, the model act that they have for emergency situations. On a European wide basis, it would be helpful enabling legislation to get data quicker.

3.4.3.2 Influenza

- If possible, developing a better system for serology. Innovative solutions to detect antibodies without having to take blood, in saliva for example.

- Developing a method that would enable quick point of care testing, would be very helpful, not only for influenza.

3.4.3.3 Smallpox

- It may be worthwhile considering doing an exercise in having to obtain detailed new surveillance information very quickly, and assessing how long it takes and what the practical issues are.

4 Case study from England

4.1 Outbreak detection

Question 1. On a national level, how would surveillance system in England detect an outbreak? What examples of good practice, improvements and innovations on outbreak detection are you aware of?

4.1.1 Current good practice

4.1.1.1 Unknown disease

- A new unknown disease could be detected through numerous routes. The most likely mechanism whereby PHE would hear about an unusual cluster of cases would be through the clinical notification system, from an astute clinician reporting through the local health protection teams to PHE. The other way would be through more indirect routes: media reports of an unusual illness in-country; and if the disease emerged in another country, through official mechanisms like WHO or EWRS reporting, from bilateral arrangements with other countries, or media reports via horizon scanning.

- Most diseases fall under particular syndromes. In England there are syndromic surveillance systems, so if someone is presenting with for example acute diarrhoea or meningitis, the case is potentially notified for further investigation as a suspect case. The syndromic surveillance systems in primary care, and more recently also in secondary care, including Emergency Departments, look at a range of different syndromes reported through routine data extracts from routine electronic health information systems. Detecting an unusual signal could be one way to detect a new disease.

- A good example is the detection of MERS-CoV, which was picked up by the combination of the astuteness of a clinician together with a virologist in PHE and the information that the Netherlands shared internationally through the media. The clinician and virologist had intensively investigated a patient with severe respiratory illness who had returned from travel to the Middle East in September 2012. The fact that no cause for the illness had been found, together with the ProMed posting of public media reports of the discovery of a novel coronavirus by the Erasmus Medical Centre (EMC), led the PHE virologist to flag this, get the appropriate samples, and look for pan-coronavirus. They discovered that it was pan-coronavirus positive but seasonal coronavirus negative, and the specific sequence data revealed that it was the same virus as that detected by EMC in

September 2012 in a case from Saudi Arabia. That was the first alert of this new emerging infection, it led to an IHR and EWRS posting by the UK and it led many countries to put in place surveillance systems for severe pneumonia in individuals returning from the Middle East.

- There is close collaboration between PHE and the veterinary agencies. Mainly through the Human Animal Infection Risk Surveillance (HAIRS) group, a multi-agency cross-government group, which has professionals from the human and veterinary side coming together monthly to talk about incidents and also do risk assessments for any novel pathogens. Above that, there is the UK Zoonosis Animal Disease and Infections (ZADI) group, a more strategic group which oversees the cross-collaboration and meets every quarter. There is also a looser network of professionals who are interested in zoonosis, people from the public health side and from the veterinary side, who do some training sessions or workshops together.

- The collaboration between PHE and the veterinarian institutions is not regulated by law, but there is a constant sharing of information and collaboration between them. This collaboration has been shown to be resilient in pandemic times, e.g. the H1N1 influenza pandemic, and in the case of avian influenza.

- PHE will each year contribute to the UK zoonosis report which has data from the animal side and from the human side for various zoonotic infections. So there is some sharing of data there, and when there is a specific incident there would be collaboration for management and control and sharing of data as well.

4.1.1.2 Influenza

- The most likely scenario is that the new influenza pandemic would emerge in another part of the world and be picked up through international intelligence.

- If the pandemic arose in the UK, England has strong clinical and virological public health systems that would rapidly pick up a new emerging influenza pandemic, most likely detecting it at an early stage through the seasonal influenza surveillance systems.

- There is a system for notifying all ICU admissions with influenza and there is a sentinel hospital-based system for confirmed influenza as well, therefore if the laboratories picked up (imported) cases due to an unsubtypable influenza it would rapidly come to the notice of PHE.

4.1.1.3 Smallpox

- The national IHR focal point is in PHE, and right from the beginning, even on suspicion, an early warning would be sent to WHO and ECDC, even if it is just a selective exchange on EWRS or alert by phone. This might also be important in order to check whether there have been other notifications abroad.

- Smallpox does not exists in nature, therefore if a case was detected it would be assumed it was a deliberate release, and the specific guidelines around deliberate release for smallpox would be followed.

4.1.2 Improvement needs or challenges

4.1.2.1 Unknown disease

- If the unknown disease results in a very severe outcome with an unusual clinical presentation it would most likely be detected by the surveillance systems, but if the disease was very mild causing little health impact then it might be quite difficult to detect.

- A surveillance system focused on ICU surveillance was developed specifically for the London Olympics in 2012, the undiagnosed serious infectious illness (USII) surveillance was intended to pick up USII resulting in ICU admission, but it was very resource intensive, and was not sustainable in long term. The problem with these types of systems is the balance between the public health need versus the demands on clinicians.

- A useful resource could be the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) – a global initiative [6].

4.1.2.2 Influenza

- No specific improvement needs were mentioned.

4.1.2.3 Smallpox

- The detection would mainly depend on an acute clinician suspecting the disease and notifying PHE urgently. If alerted by another country about cases then awareness raising etc. If a case presented at an emergency department the notification might come through emergency department surveillance systems, although PHE should have already been alerted urgently.

- For other diseases PHE epidemiologists tend to know their counterpart at ECDC or WHO, but for smallpox it is not that clear from the beginning who would be the appropriate person to talk to, who the expert in smallpox is.

- England has access to good technological systems, but there are other countries where this is not the case, and that might lead to a delay in the early recognition of smallpox. It is a concern that it is not an equal playing field.

4.1.3 Innovation and research needs

4.1.3.1 Unknown disease

- No specific innovations or research needs were mentioned.

- The UK is aware of the development of systems to improve detection, for example the development of international platforms such as GHSAG/ GHSI/ WHO.

4.1.3.2 Influenza

- No specific innovations or research needs were mentioned.

4.1.3.3 Smallpox

- On an international level, it would be useful to develop an electronic system that made it easier to identify the contact persons and experts from different institutions and, made it possible to automatically update when people change jobs or move. Through that kind of system contact persons could be directly reached, for instance with a web-based tele-and video-conference system. Another way would be for each institution to have an emergency number that would be the conduit to the specific contacts, so that people would only need to know one number and could be easily redirected.

- It is necessary to find solutions with technology that is available anywhere in the world to enable early contact. More and more people have access to mobile phones, so perhaps developing an app would be a solution.

4.2 Outbreak investigation

Question 2. On a national level, what would be the procedure to undertake an outbreak investigation? What examples of good practice, improvements and innovations on outbreak investigation are you aware of?

4.2.1 Current good practice

4.2.1.1 Unknown disease

- Often local public health protection teams deal with clinical diagnoses; for instance, meningitis, gastroenteritis, etc. where there is no laboratory diagnosis and the underlying etiological agent is unknown. There is a standard approach for gathering further clinical, epidemiological and biological information to try to pin

down the diagnosis: A local clinician sees a patient with a serious infectious disease, and would notify the local health protection team. The local health protection team would work with them to gather further information on the patient demographics, the epidemiological data, recent travel history, recent unusual exposures in terms of contacts with animals etc., trying to understand the cause and whether there are any other individuals with a similar illness. They would check what samples had been taken and whether any of those resulted in a definitive diagnosis. However, if there are some unusual features in terms of the clinical presentation, and the routine diagnostics come up negative, and they identify a further case, that might be the point at which the clinical judgement would be used to notify upwards towards the regional and national level. At that point PHE would get involved to provide further expert advice from the national specialist team to assist the investigation.

- At PHE there is a wide range of specialists with different skills on public health, epidemiology, and microbiology, and we advocate a multiagency approach with close links to the National Health Service, NHS, the Department for Environment and Rural Affairs, the Animal and Plant Health Agency and the Environment Agency so it would be possible to find skilled professionals for the outbreak investigation team in a timely manner.
- In case of a national emergency, a national emergency committee would be brought together, gathering key players across government so that the emergency can be managed in a joined up way. PHE would feed into that committee and contribute to the Scientific Advisory Group for Emergencies (SAGE).
- In a national health emergency there would be redeployment within the PHE organization so that people move into working in that particular area, so that they can support the work 24/7. There are emergency funds that can help support that activity so that it can run continuously, and there are special systems in place for emergencies at different emergency levels.
- Probably there would be enough expertise within the country for the outbreak investigation, although because of the international implications there would be international elements as well. It might be necessary to work closely with WHO and with ECDC, to notify the infection, explain the steps that were going on in the country and share findings, as in 2012 with MERS-CoV.
- On the international level PHE shares information with WHO through the IHR mechanisms, and with ECDC through the EWRS mechanisms. It is important to have

systems and mechanisms to be able to easily and rapidly share information. The recent experiences have built those systems pretty well, both ECDC and WHO have been very good at developing systems to rapidly and promptly share information across international boundaries, for example in the 2009 influenza pandemic.

- Another element is sharing microbiological findings. During the early detection of MERS-CoV the ability to access sequence data that were held by the Netherlands was valuable and allowed the understanding that there was a clear link between the case diagnosed in the Netherlands and the case diagnosed in England.
- PHE has protocols, which can be adapted to new emerging infections, for the rapid investigation of the first few hundred (FF100) cases and their close contacts to try to understand the clinical presentation, transmissibility, case severity and estimate the predicted impact on the population.
- The basic methodological approach would be the same for any new and emerging disease, and PHE is continually refining PHE Incident and Emergency Response Plan and Concept of Operations so that when something happens they are able to move as fast as possible. There is quite a lot of ongoing work on the modelling side trying to maximize the utility of data that arises from acute outbreak investigations and to predict what the population impact might be of a new emerging infection.
- On a national level there are various information sharing partners. The information would be shared within the organization ensuring that everyone at the appropriate level is aware of the situation, and the information would also be shared with other national partners, particularly with the ministry and department of health and other agencies as appropriate, keeping them aware.
- The information would be used for developing guidance for clinicians, lab and public health and also be shared with the health and scientific community and with the public, to keep them abreast of what is going on. So there are elements of keeping the public aware, but also public health messaging linked to that.

4.2.1.2 Influenza

- An influenza outbreak investigation would be conducted at the local level initially. PHE might give expert input into how it would be conducted, and if it then turned out to be a new emerging subtype of influenza then PHE would be aware of that, and be very actively involved in the management of the outbreak.
- The outbreak investigation procedure would be similar to the one mentioned for an unknown disease. The outbreak investigation team would be based on people with

expertise, ensuring that they had the relevant skill mix that would enable the management and investigation of such an outbreak.

- There are special committees that would be convened in the event of a pandemic who would then be responsible for the national management of the outbreak across the health services and across the population. They would provide scientific advice to government. This is called the Scientific Advisory Group for Emergencies (SAGE).

4.2.1.3 Smallpox

- The most important thing is to have already developed guidelines and the smallpox plan agreed with the Department of Health, so that there is an outbreak plan for PHE that would be followed. PHE would establish an outbreak control team that would be the incident lead as well. With this team the whole investigation could be managed while having an oversight of exactly what was happening. Tasks would be assigned and entered in a database, and a task manager would follow this up, so that the outbreak control team could make sure that those actions had been carried out. Everything should be documented so that it can be audited and followed up as needed. It is very important to have a pre-prepared strategy to know what needs to be done in such an incident, for instance describing the primary control measures like ring vaccination.

- The investigation team would be multi-agency. Within the outbreak plan the suggested membership of the outbreak control team is defined, including members from government, the department of health, NHS and from PHE. PHE would define the main stakeholders and ensure that they all were invited to the outbreak control team, to be all involved and take responsibility in the investigation and response. The Incident Director would lead the Incident Management Team and produce daily (or less frequent depending on incident) SITREPS and contribute to government reports and Common Recognised Information Picture (CRIP) [7]. The selection process is flexible and can be reviewed if other experts are required. In the case of smallpox there would also be connections with international teams, in particular with ECDC and WHO.

- The outbreak investigation would follow the regular procedure in descriptive epidemiology (time, place, person), with special focus on establishing where the cases had been exposed and defining those areas for the epidemiological investigations. There would be contact tracing and monitoring of contacts of cases.

- PHE has a team in charge of developing exercises and training programs, these programs make teams better because when people have already worked together it

becomes easier to do it in a real situation. These exercises are carried out yearly and may not be specific for smallpox, for instance recently there was an exercise on a deliberate release of anthrax.

- The exercises and training are part of PHE, but other stakeholders are usually invited as well. The exercises might be table-top exercises on a scenario, but at least people invited would be brought together face-to-face. In case of a smaller exercise there might be a teleconference instead. There is also experience acquired during real situations like the H1N1 pandemic, Ebola and Zika virus in which the procedures have worked well.
- Each of the organizations that might be pulled in, for example to the outbreak control team, are expected to have contingency plans in place and surge capacity that they would be able to activate if the need arose. In case the whole system became overwhelmed and more resources were needed, that would then have to go up through to government, and they would have to allocate further resources.
- On a national level, the channels of communication are good. PHE would be expected to do daily situation reports for the experts working on a higher level, using a standard format and updating them as the situation evolves. There is a constant flow of information that can go both ways. There are shared comms with communications across the agencies and government for consistent messaging.
- For the healthcare professionals guidance and information would be given in a clear way explaining what data are being collected and why they are collecting it, as it is very important to explain the purpose and that they are collecting data for a purpose. PHE would use rapid communication to health protection units and NHS through the Department of Health CAS (Central Alerting System) alert.

4.2.2 Improvement needs or challenges

4.2.2.1 Unknown disease

- Developing guidance when there is little information or evidence available and the need to use a precautionary approach particularly in the early stages of an incident can constitute a challenge.

4.2.2.2 Influenza

- No specific improvement needs were mentioned.

4.2.2.3 Smallpox

- The difficulty with smallpox is that it does not exist in nature so the clinical awareness is not there. It is important to ensure that the training and exercises are

done and that the preparedness is there, making sure that all the processes and the framework are in place to deal with an incident.

- Smallpox cases do not generally become infectious until they are quite severely ill, which means that there is a certain limit as to who would become exposed. Of course it is not exactly the same as Ebola, but there is a certain similarity, so the templates, the databases, web-based collection of cases and contacts, and the way to follow up and monitor cases that were set up for Ebola, could be adapted and used in case of smallpox.

- It is important to make sure that communications are fully open on an international level as well as nationally.

- On a national level, it is important to have a good communication strategy, and that the information to the public, to health professionals, or higher up to government, is consistent. The main thing would be that messages go through one point of contact and are signed off so that nothing slips through that might lead to misinformation somewhere along the line.

4.2.3 Innovation and research needs

4.2.3.1 Unknown disease

- No specific innovations or research needs were mentioned.

4.2.3.2 Influenza

- No specific innovations or research needs were mentioned.

4.2.3.3 Smallpox

- Developing a web-based call-up, maybe having lists of people that could be called upon, already listing their skills, would help in faster deploying the necessary people.

- Developing new technologies, making things easier, having more web-based systems, so that it is easier to track and follow. Maybe questionnaires that could be filled in online, where everything would go straight into the database making the information available much more rapidly and easily for the team who are investigating the incident.

- To facilitate communication, team members should know and see each other. Teleconferences, maybe using a web-based tele-and video-conference system would probably make information flow better than if only using email or phone.

- One thing England is working on is having a cohort of people who are trained in doing certain tasks. For instance being a task manager, or an incident director, so there are specific cohorts of people who are trained in specific roles and can be called upon.

4.3 Risk assessment

Question 3. On a national level, what would be the procedure to undertake a risk assessment? What examples of good practice, improvements and innovations on risk assessment are you aware of?

4.3.1 Current good practice

4.3.1.1 Unknown disease

- PHE has a mechanism where they look at the different aspects of a new infection to try and ascertain different elements of it, and to use that to try to determine: a) the transmissibility and vectors, b) the severity of the infection, c) the interventions available, and d) the predicted impact on the population, using those different elements to then formulate an assessment on what the risk is to the English population. The Human Animal Infections and Risk Surveillance (HAIRS) group are important as more than 70% of emerging infections are zoonotic; HAIRS have two risk assessment processes for (1) zoonotic and (2) risk to UK population. These risk assessments also document gaps in information and evidence.
- PHE also follows the risk assessments from organizations like ECDC and WHO.
- PHE would also consult external experts as appropriate.
- PHE has a risk assessment process that is used for emerging respiratory infections arising globally. That could also be used for an unknown disease.
- In the event of an emerging infection needing a certain level of response, there would be a team convened, and one of its responsibilities would be on risk assessment. This team would be selected to provide specialist advice. Within PHE there is a wide range of expertise so the relevant professionals would be selected to join the team and provide a holistic perspective.

4.3.1.2 Influenza

- PHE has a risk assessment process that is used for emerging respiratory infections arising globally. PHE would be assessing against a range of criteria looking at the transmissibility and severity of this new emerging influenza virus, trying to understand what the predicted impact might be. At the beginning the information on each of those indicators will be quite limited, therefore PHE would try to

rapidly gain knowledge from investigations that PHE would undertake, but also from investigations abroad.

- The risk assessment team would work well. It would be based on the scientific input from the PHE specialist team on the epidemiology and microbiology, virology side combined with the emergency response expertise to manage the incident. The emergency itself would be staffed with people from different parts of the organization to ensure that PHE could respond 24/7.

4.3.1.3 Smallpox

- The risk assessment procedure has been developed by PHE and is fairly well established. The emerging infections and zoonosis team is in charge of the risk assessments for any emerging or novel infections, including smallpox. The team has expertise and would adapt to the situation, establishing collaboration with other PHE experts or internationally if necessary.
- Parameters that would be considered are severity, uncertainty, context of the incident, and the likelihood of spread. There is a level assigned for the different levels of risk, from very low to very high. A smallpox scenario would clearly have a very high impact for public health.
- It is important to restate that the risk assessment evolves across the incident. For example the ECDC risk assessments are very useful and valuable, and they are reviewed and revised as information emerges. The key thing about the risk assessment is that it is not set. PHE has a horizon scanning function looking at all the international information available and drawing anything relevant into the risk assessment. If an incident was happening in a particular country or a particular region PHE would look there, but also to WHO, CDC, etc., to harvest information.

4.3.2 Improvement needs or challenges

4.3.2.1 Unknown disease

- No specific improvement needs or challenges were mentioned.

4.3.2.2 Influenza

- No specific improvement needs or challenges were mentioned.

4.3.2.3 Smallpox

- Continue with regular training.
- Every incident and outbreak is unique, so the important thing is that there is a protocol, something to follow, but adapted specifically for the incident you are dealing with. The case definition, the initial risk assessment, etc. should evolve as the incident evolves. Remaining adaptable is the most important thing.

4.3.3 Innovation and research needs

4.3.3.1 Unknown disease

- No specific innovations or research needs were mentioned.

4.3.3.2 Influenza

- In order to improve the risk assessment methodology PHE is trying to develop a more formal scoring mechanism, based a bit on the WHO integrated risk assessment (IRA) tool.

4.3.3.3 Smallpox

- For the horizon scanning, PHE keeps an eye on Twitter and different social media, however perhaps there are more innovative ways to collect data.

4.4 Surveillance

In this section the questions explored the capacity of the national surveillance system to obtain key information for the risk assessment using four examples.

Question 4. How would the surveillance systems in England get information to calculate the clinical attack rate, case fatality rate, proportion of severe cases and hospital admission rate? What examples of good practice, improvements and innovations on surveillance are you aware of?

4.4.1 Current good practice

4.4.1.1 Unknown disease

- Getting key information to calculate the clinical attack rate of a new emerging infection could potentially be challenging and would depend on the clinical presentation, how widespread the disease was, etc. PHE could come up with clinical attack rates relatively quickly using the existing systems or adaptions of the existing systems, by using for instance the existing clinical notification system, and the routine syndromic surveillance system and potentially tweaking them. The syndromic surveillance system covers a range of syndromes, not just respiratory and you can extract data on a daily basis. The use of the FF100 system and possibly ISARIC.

- Biological sampling. Depending on the infection, PHE might utilize the existing sentinel primary care system, the GP sentinel network, or NHS 111 and adapt it and potentially get samples through that mechanism, which could then be analysed, once there was a test available. This could be used to calculate the rates of laboratory confirmed infections in individuals consulting primary care.

- To calculate the case fatality rate the procedure would depend on the infection severity. If the case severity was very high, then the FF100 cases approach, following up the first identified cases, ascertaining their outcome, following up their close contacts and identifying cases at an early stage, would be used to get a handle on case severity and look at outcome. This would give a better perspective on the disease spectrum; by following them up it would be possible to determine the proportion that is hospitalized, in ICU and who died.
- There is an issue with the cases that have asymptomatic infection or very mildly symptomatic infection. The approach to get the actual infection severity rate would be biological sampling and testing of blood samples, looking for evidence of a serological response to the new infection. But that is dependent upon having a serological assay which may take a while to develop.
- England has also developed approaches whereby, if it is a less severe infection and once the infection is generalized, PHE would adapt and use information from different levels of the current surveillance systems; the GP surveillance, hospital surveillance, and mortality surveillance. With this information PHE would then estimate the case severity in terms of the likelihood of going on to be hospitalized, admitted to ICU, and dying. The FF100 cases approach is part of the initial detection and assessment, and the other systems (GP, hospital and mortality surveillance) would be used to monitor the spread of the infection and the population impact. These systems are working well for seasonal influenza so there is also a level of readiness for a future pandemic.

4.4.1.2 Influenza

- For influenza there are good systems to develop an understanding of what the clinical attack rate is. Seasonal influenza surveillance systems would be adapted in the event of a pandemic. The routine surveillance systems, both in primary care and community surveillance systems, would be used together with integrated swabbing to get an overall, and by age, attack rate. These systems were tested during the H1N1 pandemic and there have been various adaptions of the systems to improve them.
- The approach to get the case fatality rate of the new influenza would be a similar to the one mentioned for the unknown disease. On the one hand, if it was a very high case fatality rate, using the FF100 cases approach would give an early indication of what the case severity was; on the other hand, if it was a lower case fatality ratio, using the routine systems would provide an indication of the case

severity, because quite a large number of cases would have to be accumulated. That would take a little bit longer, but using analysis of the GP, hospital, and mortality data it would be possible to come up with some estimates with the uncertainties around those.

- In England there is a hospital-based surveillance system for influenza which would be the system used to get data on the hospital admission rate.

4.4.1.3 Smallpox

- Smallpox is a notifiable disease in England, the 'proper officer' i.e. the Registered Medical Practitioners, as well within the local authorities, would notify clinical cases and the laboratories would also have to notify the positive samples into the Second Generation Surveillance System (SGSS) to PHE. There would be an enhanced surveillance with contact tracing and case finding. In an early situation when all cases could be tested, a possible way to calculate the attack rate would be using the confirmed cases notified from the reference laboratory, and make assumptions as to the population exposed.

- The automated reporting systems are reasonably good. From the laboratory side, there is an automated system that pulls data out of the laboratory into the national surveillance system. However, the system is not automated from the clinician side.

- PHE would most likely get the number of severe cases and deaths from the enhanced surveillance system, as cases would be followed up. It would also be possible to get information from the hospital episodes data.

4.4.2 Improvement needs or challenges

4.4.2.1 Unknown disease

- No specific improvement needs or challenges were mentioned.

4.4.2.2 Influenza

- No specific improvement needs or challenges were mentioned.

4.4.2.3 Smallpox

- Perhaps there could be technological improvements in the data capture systems, and the way data are pulled into one system. Behind that, it would be necessary to work out exactly what should be pulled into the databases as well. For instance, sometimes things are reported because they are miscoded. However it is not possible to get rid of human error altogether, but making sure that the systems are slick and pull in the correct data would help.

- Ensure that there are service agreements right from the outset so that PHE have access to the necessary data, for instance if data from the death registry is needed.

- Previously, setting up a system to collect data on severity from ICUs has taken some time. If it would be necessary to set up such a system, it would be ideal if the required processes were set up well in advance and the agreements to access data in case of an event, were already in place ready to go.

- In case of an overwhelming scenario, although the methodology might establish itself and become easier to deal with, it might actually be more difficult to capture good data given the sheer numbers and the overwhelming nature of the scenario. Having good surveillance systems and making sure that there would be enough human resources in this situation would also be important.

- Smallpox is a very difficult scenario because it is not naturally occurring and there is no current system to build on.

4.4.3 Innovation and research needs

4.4.3.1 Unknown disease

- No specific innovations or research needs were mentioned.

4.4.3.2 Influenza

- No specific innovations or research needs were mentioned.

4.4.3.3 Smallpox

- Making the surveillance systems as automated as possible would be helpful. Develop a web-based reporting system for ICUs for example, to make it as easy as possible for healthcare workers to provide the data and for PHE to access the data. Social media and telephone applications could also be used for this purpose.

- Having some prior understanding of what national policies were, and harmonizing them across Europe and the world.

5 Case study from the United States (US)

5.1 Outbreak detection

Question 1. On a national level, how would the surveillance system in the US detect an outbreak? What examples of good practice, improvements and innovations on outbreak detection are you aware of?

5.1.1 Current good practice

5.1.1.1 Unknown disease

- A likely scenario would be that an unknown disease was identified by clinicians, reported to the state health department or directly to CDC. If reported to the state health department and laboratory testing was inconclusive, then the state health department would contact CDC. CDC would then form a lead group to respond the initial inquiry.

- There is no specific threshold or protocol to decide when an event should be investigated or not, each event is assessed individually. The regular practice is to investigate all outbreaks of diseases whether the cause is known or not.

- The time to recognize an unknown pathogen in the laboratory has shortened over the last decades. Now laboratory testing with genome sequencing allows rapid identification of an unknown pathogen, for instance, the SARS coronavirus, or the subtyping of a known one, like influenza.

- There is no perfect way to measure the success of outbreak detection of an unknown disease, because either the disease has been identified, and that is sort of a measure of success, or it has not, and then it would be impossible to know. But a way to measure this could be thinking about diseases that have been going on for a long period of time before being recognized. In that case it is difficult to come up with instances in the US when diseases have been spreading for a prolonged period without detection.

- There is a working group at CDC called Unknown Respiratory Disease Outbreak Group (URDO), which meets periodically to review reports on respiratory diseases. Responsibility for respiratory diseases is spread between different groups at CDC and the URDO group is a way to coordinate these groups and assign responsibilities, both in the laboratory and on the epidemiology side. If the responsibility for a discovered unknown disease was spread between groups at CDC, a group similar to URDO could be formed. It is important that each group has the ability to quickly

determine if they are the right group to handle the disease and, if not, transfer it to the group/s that might be responsible.

- There is good collaboration and communication between the veterinarian institutions and CDC, there is an agreement between the U.S. Department of Agriculture (USDA)_and the CDC. There are periodic consultations concerning human laboratory findings and animal laboratory findings between CDC and the veterinarian authorities, recently particularly with regards to poultry and swine since it seems that the influenza viruses are circulating among these animals and as such present a risk for people. For instance, in 2015 there were 85 viruses circulating in turkeys and poultry in the US and there was a study done to make sure that people, both in contact and not in contact with the animals, were not infected with the viruses.

5.1.1.2 Influenza

- The H1N1 is quite a good example of detection. In the US there are systems of testing individuals that have influenza or influenza-like illness. Occasionally a virus is identified that is not one of the seasonal viruses, in that case there is further work on antigenic and genotypic characterization and an epidemiological investigation starts.

5.1.1.3 Smallpox

- The likelihood of smallpox being recognized by a clinician would depend on where the case occurred and where the person who had the disease first appeared in the medical setting. But once smallpox was suspected, the notification to the state and CDC would be very quick as it is a notifiable disease and people would immediately recognize the severity of the event.

- The detection of smallpox would also have a law enforcement element.

5.1.2 Improvement needs or challenges

5.1.2.1 Unknown disease

- If the unknown disease was an infectious disease, the laboratories would be able to identify it quickly. But if it for instance was environmental, or from unknown causes, then an epidemiological investigation would be undertaken and the process would take longer.

5.1.2.2 Influenza

- No specific improvement needs or challenges were mentioned.

5.1.2.3 Smallpox

- No specific improvement needs or challenges were mentioned.

5.1.3 Innovation and research needs

5.1.3.1 Unknown disease

- The laboratory diagnosis for infectious diseases is critical, and learning how to use the new tools more effectively is important. For example, the first year that CDC sequenced all reported listeria isolates, an outbreak was detected that would otherwise have been undetected. If this becomes standard practice, things that would not have been linked in the past will be.

- On genome sequencing there are two things; one is getting the right kind of specimens to a laboratory that has wide capability, and the other is getting the technologies for the laboratories in the field.

- Trying to understand the laboratory findings is also important, with new technology many times multiple pathogens are identified. Understanding what that means and identifying the causative pathogen, requires experience.

- It would be interesting, but challenging, to look into the history of infectious disease detection to identify instances of diseases that have been circulating for a long time before they were detected.

5.1.3.2 Influenza

- No specific innovation or research needs were mentioned.

5.1.3.3 Smallpox

- Improving the detection of smallpox would probably be a question of training the clinicians to diagnose the disease.

5.2 Outbreak investigation

Question 2. On a national level, what would be the procedure to undertake an outbreak investigation? What examples of good practice, improvements and innovations on outbreak investigation are you aware of?

5.2.1 Current good practice

5.2.1.1 Unknown disease

- In the US there is a procedure to undertake outbreak investigations. When an event is identified by a state, they are responsible for making a preliminary assessment on whether they have the capability within the state to respond or whether they require assistance from CDC. Essentially CDC is invited by the state departments to

assist in the investigations. If more than one state is involved in the event, CDC would lead the consortium of states. The event can also be identified by CDC and then communicated to the state.

- When the information comes to CDC, there is a rapid triage to make sure that the experts get the information and are brought into the discussion on the right investigation approach.

- For the selection of the outbreak investigation team, there is a negotiation with the state and CDC, and within CDC, to decide on the right group and what level of support is needed. The team selection is done *ad hoc*, looking for the experts in the areas relevant to the problem, and adapting the size and composition to determinants like the urgency, severity of disease, number of cases, etc.

- Other institutions may also be involved in the outbreak investigation. For instance, there is a standardized procedure in the case of a foodborne disease; CDC, the FDA (Food and Drug Administration) and the US Department of Agriculture would work together to identify the vehicle.

- At CDC there is considerable experience in doing field investigations, so forming a team in 24-48hrs for domestic events is feasible for CDC.

- In a specific situation like Ebola, there were pre-configured teams of up to 10 people that would be sent if there was a case. People on these teams were available to travel very quickly. Having pre-configured teams may not be valuable for every situation since the kind of expertise needed depends very much on the problem.

- On the global level, the US has developed a structure called the Global Rapid Response Team, with the idea to be able to get people to a place within 24 hrs to make an initial assessment, and responders are posted around the world. There is also a larger team, around 25 people, in the US that would be ready to go, as well as a larger staff of volunteers from CDC that would be available to augment that initial team. The idea is to have one group ready to be deployed immediately, another group within 24-72 hours and then a larger group that would be deployed after a longer lead time.

- The methodology used for the outbreak investigation depends on the problem. For an unknown disease, the protocol that most closely would fit the disease would be

adapted and used. There are relatively standardized approaches, for instance there is a standard questionnaire for a diarrheal disease outbreak to identify the food vehicle. Similarly for an influenza pandemic, there are standardized investigations to look at transmission and severity, similar to "the first 100 cases" but not quite that prescriptive. Cluster investigations or investigations in specific geographical locations would be undertaken to assess severity along the lines of the 100 cases. In the case of an unknown disease the start would probably be laboratory findings and then backtracking to the cases and use that information to find the source.

- Communication between the States and CDC works very well, because of the common understanding of the shared responsibility to work quickly and thoroughly. Particularly initially when the state has the responsibility of the initial notification.

- CDC works with WHO and their regional offices and the country offices depending on the event. Like other countries, the US has a responsibility to work as part of the global and international system IHR, to be transparent, thorough, and cooperate when requested by a country or WHO, trying to respond with the capabilities available.

5.2.1.2 Influenza

- When a new influenza virus is identified there is a field investigation, looking for the exposure: if it was an animal exposure, whether there is human to human transmission, and key questions on severity and transmissibility.

- In this scenario it is helpful that the systems that would be used to respond in a pandemic are used for seasonal influenza.

- In terms of communication within the country the procedure would be the same as for other diseases. In this case, after the initial period, the same systems that are used to present the characteristics of seasonal influenza (for instance weekly email reports and web posting), would be used to disseminate the information.

5.2.1.3 Smallpox

- As there is already knowledge on smallpox, there would be fewer questions concerning the disease itself (transmissibility and severity), so the investigation could focus on other aspects like the exposure, and whether there were other, undetected, cases.

- The main differences between this and the other scenarios is the law enforcement element and that the main workload for CDC would be identifying and

implementing control measures, the quick provision and use of the vaccine and implementing plans to take care of the severe cases.

- There is a collaboration and communication procedure with the law enforcement to prepare this kind of events. The law enforcement would investigate the group that is responsible, questions like whether it is an isolated or simultaneous event or if more events are expected, to help the health side understand what more might be happening.
- The communication with the public would not be that different from other events. The important thing from a communication standpoint would be information about what is being done, the plan for countermeasures, what is uncertain (which might not concern the disease but how it is going to unfold in the country, particularly whether there would be a single or multiple events).

5.2.2 Improvement needs or challenges

5.2.2.1 Unknown disease

- The Global Rapid Response Team is not problem specific, so one challenge is linking the expertise at CDC with the people who are ready to go for the specific problem.
- One of the big challenges of international communication is recognizing problems correctly, because at times countries do not want to be forthright, other times there is a request for help that CDC cannot meet, and sometimes there are disagreements on what has to be done. Setting expectations and meeting those expectations is a communication issue. These are inherent challenges that will probably always exist, to some extent. The only solution would be more experience and lessons learnt that show that being transparent is in the long term helpful. There is no real technology or innovation that can improve that, other than working as partners.
- The experts' world is small; experts working in a field can easily know other experts working in the same field and there might be direct communication among experts on an international level before CDC, WHO or Pan American Health Organization (PAHO) get involved. The challenge in that case is the sharing of that information through the organizations, so it becomes known when there are big decisions that have to be made, and so that the information reaches the right level of authority to take decisions.
- For the overseas part of an outbreak investigation, challenges in coordination arise frequently. When different groups work within a country, ideally the different

groups form a single team under a unified command structure. When there is a good understanding of the responsibilities and sharing of the work, things work better.

- For domestic outbreaks CDC has not really come across a problem when they need people from outside to augment capacity. If necessary, US government can reassign people within government or hire people. In the hypothetical situation that there was a technical or laboratory capability only in one place elsewhere in the world, the solution would be organizing a collaboration.
- Domestically, sometimes it can be challenging when there are disagreements on the responsibilities of CDC in the outbreak investigation. For instance, there might be one part of the federal government that thinks that CDC should be doing more, another part that thinks that CDC should be doing less. Sorting out those expectations can take time.
- There might be some communication challenges when there are several states involved. But there is still a rule that pretty much applies that the states have the responsibility on things that are happening in their jurisdictions.

5.2.2.2 Influenza

- No specific improvement needs or challenges were mentioned.

5.2.2.3 Smallpox

- The main challenge would be that there has not been an outbreak of smallpox in quite a long time, there is not a lot of experience nowadays.

5.2.3 Innovation and research needs

5.2.3.1 Unknown disease

- On the global level, understanding of the local culture is a recurring issue, as recently with Ebola. Societies are quite complicated, and bringing the anthropologists' capability to understand that complexity and integrate that knowledge into an emergency response, and learning how to communicate is challenging. The urgency and time frame may be an issue as anthropology studies may take time and there should be a way to distil that critical information so that the interventions are appropriately tailored for the population. It is important to understand what the population needs, rather than just imposing a solution that may be perceived as not a solution at all. This is an issue that is not so much in the domestic area, but there are some domestic aspects too.

- The need of personnel resources usually comes later on, when some of the resources have been used. Language skills can be a scarce resource. For example with Ebola in Guinea, the number of French speakers that worked at CDC that speak French well to operate in that environment is fairly limited. CDC worked with a number of groups in an attempt to solve that. The Field Epidemiology Training Program in the DRC provided teams that worked in Guinea, also teams from Canada travelled to Guinea to work. It was enormously helpful that those countries and individuals volunteered. There were also concerns that Guinea Bissau was at risk for Ebola, because even fewer people speak Portuguese than French. When there is need, people with language skills are looked for internally, within CDC.
- In case extra resources and funding were needed in the US, accessing such resources more quickly would require a legislative solution. The Federal Emergency Management Agency (FEMA) has a system for emergency declaration and there is a source of funding that is very well organized with a lot of capability to respond to emergencies. There is not anything like that on the public health side and the FEMA system could be a model for a Public Health Emergency funding system.

5.2.3.2 Influenza

- No specific innovation or research needs were mentioned.

5.2.3.3 Smallpox

- As there has not been an outbreak of smallpox in quite a long time, there is less experience to fall back on than e.g. in the 1970s, the only way to improve that would be training.

5.3 Risk assessment

Question 3. On a national level, what would be the procedure to undertake a risk assessment? What examples of good practice, improvements and innovations on risk assessment are you aware of?

5.3.1 Current good practice

5.3.1.1 Unknown disease

- For influenza there is a quite well developed system for risk assessment; that approach would also be taken for any infectious disease, including a new unknown disease.
- The team that investigates the outbreak is also the one responsible for the risk assessment. This works well because the team is responsible for collecting the information so they have a good understanding of the information.

- The outbreak investigation teams have also skills and knowledge on risk assessment as it is part of the training of doing field investigation and they are aware of the things that are important to be collected for a good risk assessment.
- Knowing about other risk assessments, especially if there is disagreement, is important information that CDC takes into account, particularly early on when the characteristics of the disease are not well known. However, the comparison would not be done in a formal, consensus building, process. The Emergency Committee that WHO convenes under the IHR is the formal structure that would attempt to resolve differences in what countries have identified, it is a system that in general works well and is constantly being improved.
- There is a need to try to understand the differences in findings, but sometimes it is not possible to resolve them. Every country has the responsibility to take the action that they believe is appropriate for their country and that often means using their own risk assessment. For instance with H1N1, some countries appeared to have a more severe pandemic than other countries and some of the reasons for this are unknown.

5.3.1.2 Influenza

- There is quite a body of experience with influenza viruses, so at first the characteristics of the disease caused by the new virus would be explored: clinical characteristics, epidemiological characteristics of transmissibility and severity, and placing it in context with other influenza viruses. That process would lead the decision making for the response.
- There is a kind of a hierarchy for the progression of the response depending on the results of the risk assessment process. In the case of influenza the last thing that would be done would be to create a specific diagnostic test, it might not even be distributed if it is not necessary, but it would be just developed to hold. That can be done just with the sequence information, so that would be done very early, and would not be terribly expensive. The ultimate version would be to produce, at commercial scale, a specific vaccine against that virus for humans. Between these two extremes, there are a number of increments, for example, the creation of vaccine candidates, to testing of the virus against antivirals, etc.

5.3.1.3 Smallpox

- In the case of the smallpox scenario, the security and law enforcement would participate in the investigation, which they would not in a natural event.

- The risk assessment procedure would be the same, but there would be other information needed like the likelihood of other events occurring at the same time in other locations, so there would probably be some other sources of information. Moreover, much would be known about the disease itself.

5.3.2 Improvement needs or challenges

5.3.2.1 Unknown disease

- Adapting the influenza risk assessment procedure for an unknown disease would not apply so well if the disease did not transmit from person to person. In that case it would be necessary to understand the source of the disease and maybe the inoculum that would be required to cause an infection. Probably there is not a lot of work that can be done in advance other than having that kind of mind-set, taking into account the kinds of very urgent research that would be needed.
- It is not the case in the US, but there is a risk of having two different teams, one for outbreak investigation and a different one for risk assessment. In that case, having those teams working as closely as possible, even if they are distinct units, is very important because the risk assessors need to understand what is happening in the field.

5.3.2.2 Influenza

- No specific improvement needs or challenges were mentioned.

5.3.2.3 Smallpox

- No specific improvement needs or challenges were mentioned.

5.3.3 Innovation and research needs

5.3.3.1 Unknown disease

- Moving the laboratory technology to the field would help, as earlier detection would allow more time for the risk assessment and provide more complete information.
- There is no separate training for risk assessment in the epidemiological training that professionals get, and it is normally something that is conducted as part of outbreak investigations, but there might be some value of having the risk assessment training more formalized.

5.3.3.2 Influenza

- No specific innovations or research needs were mentioned.

5.3.3.3 Smallpox

- No specific innovations or research needs were mentioned.

5.4 Surveillance

In this section the questions explored the capacity of the national surveillance system to obtain key information for the risk assessment using four examples.

Question 4. How would the surveillance systems in the US get information to calculate the clinical attack rate, case fatality rate, proportion of severe cases and hospital admission rate? What examples of good practice, improvements and innovations on surveillance are you aware of?

5.4.1 Current good practice

5.4.1.1 Unknown disease

- The key information to calculate the clinical attack rate, the proportion of severe cases, the case fatality rate, and the hospital admission rate, would not come from the running surveillance systems but from a field investigation triggered by the problem.
- In the case of the clinical attack rate, a household investigation could be used. The route of transmission would determine the kind of investigation that would be done. If the route of transmission was not known, the investigation would be more difficult, but essentially there would have to be an epidemiological investigation. There would be geographically localized investigations in different settings and locations, to have some chance or likelihood that it is representative.
- For a notification system of an unknown disease it would be necessary to set up or adapt an existing system. For instance for Zika virus the system that was adapted was the one to report cases of West Nile Virus.
- In order to get information on the case fatality rate, at the time of the field investigation, there would be cases that already died and there can be a follow up of the severe cases in the course of the investigation.
- For seasonal influenza, there are also existing systems for identifying the number of deaths in children. There is a system for flu for 122 cities that follows the number of deaths each week due to pneumonia and influenza.
- The flu systems would work pretty well for diseases that have very widespread transmission. If there were a laboratory test for the new disease, and the new disease mimicked influenza; respiratory transmission, respiratory symptoms or increased susceptibility for pneumonia, it would be possible to directly adapt that system. This is not a good system for detection without a laboratory test because it

would be difficult to know which fraction of cases with a particular clinical syndrome is caused by the new disease.

- There is also a network of sentinel hospitals around the US, the emerging infections programme, which is a population-based surveillance system for severe diseases and covers a population of about 20 million people. If there were a new disease for which there were a diagnostic laboratory test or that had a characteristic clinical syndrome, those hospitals could be charged with identifying those severe cases. These data could be used to calculate the fatality rate and the hospitalization rate.
- If for some reason the characteristics of the disease changed during the pandemic, for instance affecting a different age group, becoming more severe or there are laboratory changes of the pathogen, it might be necessary to repeat the field investigations to get information on the new situation.

5.4.1.2 Influenza

- In order to get key information to calculate the clinical attack rate for influenza a field investigation would be conducted. In general there would be a standardized approach, so not just one investigation but several investigations would take place, searching for well-defined populations, so that it could be possible to be sure that the transmission occurred within that unit. Probably the first step would be a request for information about the cases' families. Other examples would be looking for information about school or university outbreaks.
- For H1N1 the surveillance system worked extremely well, the system was flexible so that it was possible to change it in time. Planning for flexibility in the surveillance systems is at least as important as having a thorough plan. So having people that can foresee the kind of system that is going to be needed and having enough time to develop the system is important.
- For the first cases of H1N1 for example, there was an extensive questionnaire; when the number of cases increased, there was an adaptation to line listing reporting. Then, as the number of cases continued to grow, that line list collapsed to just summary reporting. And as the number of cases grew even more, the system that was used to measure the number of cases was the sentinel system where the hospitalized cases, with laboratory confirmation, were identified and there were correction factors used to calculate, from the proportion of people that were hospitalized, how many cases occurred in the community and there was also an estimation of the number of deaths from the non-hospitalized cases. So the system had to evolve as the number of cases increased. The estimation system depends on

the field investigations for some of the assumptions about the total number of cases.

- For influenza there is a system to report deaths in children, it is not complete reporting, because not all deaths are identified, but it is an indicator of the severity among the cases and transmissibility in children.

5.4.1.3 Smallpox

- There would be a field investigation, but the advantage is that there would be much already known on the disease, so it would be easier to refine the specific questions.
- In the US there are practices, in order to be prepared for this kind of scenario.
- If there were a widespread event the emerging infections programme would be used to get information on severity and case fatality.

5.4.2 Improvement needs or challenges

5.4.2.1 Unknown disease

- No specific improvement needs or challenges were mentioned.

5.4.2.2 Influenza

- During the H1N1 pandemic there was lot of work on how to define the severity of an influenza pandemic and the initial plans was based on measuring case fatality rate. This has limitations particularly for less severe pandemics, since many cases would need to be identified before it would be possible to calculate a case fatality rate. Moreover, less severe cases would be less likely to be identified.

5.4.2.3 Smallpox

- Smallpox is a disease included in the national reporting system. In case of an event it may be necessary to make adaptations so that the system could serve the countermeasure distribution and operate quickly enough to direct the intervention.

5.4.3 Innovation or research needs

5.4.3.1 Unknown disease

- One of the most important things would be to make the period when a disease is really unknown as short as possible, so that is an issue of laboratory testing for infectious diseases. Without a laboratory test the challenge is having to rely on clinical and epidemiologic factors that are inherently less precise.
- Planning and training to be flexible. It is very important to have the right balance of collecting information, enough manpower and analyses so that the surveillance system can be used to make decisions.

5.4.3.2 Influenza

- No specific innovations or research needs were mentioned.

5.4.3.3 Smallpox

- Continue performing practices would help.

6 Conclusions

6.1 Current good practice

Current good practice in a number of areas were outlined in the case studies and workshop.

The key issues were:

In terms of outbreak detection and the traditional notifiable disease surveillance, two aspects were highlighted: (a) having cases of unknown severe disease be notifiable, and (b) having notifiable syndromes, i.e. not only specific diseases based on the etiologic agent. Two other types of surveillance systems were also highlighted; ICU surveillance, and non-clinical or syndromic surveillance (e.g. surveillance of calls to medical advice hotlines).

Another key aspect was the established collaboration between experts in different networks, in particular having a well-developed infectious disease clinic system, a well-functioning collaboration between the veterinarian and public health side, and cross-sectional networks on antibiotics and laboratory issues. Collaboration between public health experts and the medical education system was also mentioned e.g. teaching medical students disease notification.

For the actual outbreak investigation strong local capacity and resources was considered essential, as was having predefined teams and standardized processes on a national and senior level. The US capacity for global rapid response team deployment was also noted.

With regard to actual investigation, the First Few 100 cases (FF100) procedure developed by the UK was mentioned repeatedly as advantageous.

All the interviewed countries would share information with WHO, ECDC, and neighbouring countries, as applicable. Specifically, the information sharing through WHO and ECDC was seen as efficient by the larger countries, although it was noted that there was a need to establish better communication platforms for intersectional stakeholders; healthcare workers; and for national, EU and global level stakeholders.

Another current good practice was conducting regular exercises. The exercises had the beneficial effect of training, but also connecting experts who would need to collaborate in future outbreak investigations.

For risk assessments having procedures and teams in place was considered essential. Moreover, it was noted as favourable if the outbreak investigation and risk assessment were carried out by the same team. Overall, countries also stated that they took risk assessments by ECDC and WHO into account when conducting their national risk assessments.

For the surveillance of an unknown disease, pandemic influenza or smallpox, it was noted that having the surveillance or outbreak investigation procedure already in place was of value, e.g. GP sentinel, hospital sentinel, mortality surveillance, and the FF100. It was envisaged that these systems can be adapted for example for a novel emerging infectious disease. Similarly, current good practice for notifiable disease surveillance systems included not only a computerized infectious disease reporting system, but also the capacity to add to the system (a) an infectious disease within 24 hours and (b) enhanced surveillance forms.

6.2 Innovations needed

In the case studies and the workshop the informants mentioned several possible areas for innovation and research. The key issues were:

In the area of outbreak detection, new tools are being developed both in regard to big data and on the laboratory side. For the latter the application of the new technologies, including the interpretation of the results, was specifically highlighted as a challenge. The calibration and interpretation of the quickly developing detailed data from microbiology and how it can be used to improve preparedness will take a lot of resources. Similar challenges were envisaged for the detection and interpretation of signals from big data.

The need for improved environmental assessment and sampling techniques to identify threats was also noted.

In the countries investigated, experts would be available for the scenarios included in the case studies, nonetheless having a network of experts in specific fields and keeping rosters of these experts with up-to-date contact information requires innovative methods to be sustainable.

Surveillance for certain aspects of disease detection would, in many countries, rely on astute clinicians. How to keep the clinicians informed and knowledgeable of a wide range of rare diseases requires new methods since continual education of clinicians is a

challenge. A possible avenue noted could be development of online educational material for clinicians who would receive credits for continued professional development.

For national outbreak investigations, communication with healthcare workers would prove challenging since in at least one country some GPs do not have access to email. For the global outbreak teams improved understanding of local culture is key and requires the development of anthropological methods that would allow the team to rapidly gain this knowledge.

Overall, training in outbreak investigation internationally and nationally is needed, especially concerning smallpox for which there is less experience available.

A need for agreements between countries was noted for outbreak investigations. Agreements are suggested to include enabling (a) better information sharing, e.g. with shared investigation protocols; (b) sharing and managing case data; and (c) predetermined sites for FF100, when possible. These arrangements could also include the establishment of fora for discussion internationally.

Similarly, there is a need to determine risk assessment parameters, especially for severity, and their weighted importance. In addition it was suggested that the development of a system for sharing these parameters between countries could increase the validity of risk assessments and could be examined.

Another aspect is bringing laboratory technologies closer to the field, thus enabling more time for risk assessments and more complete information.

Sharing of risk assessment templates, for example for different transmission routes, could also be beneficial for the risk assessment process in the countries, as could more formal training in risk assessments. Additionally, conducting risk assessments in advance, for example for smallpox, was mentioned as a possible avenue worth exploring.

A need for training of governmental stakeholders in terminology, procedures and other key information in case of a pandemic was identified.

For the surveillance of an unknown disease, smallpox or pandemic influenza, several possible surveillance system improvements were noted: flexible electronic data reporting that allows quick adaptation when necessary; better data capturing systems;

and automatized surveillance collecting data from patient files, for all hospital levels including ICU. But, not all surveillance would be improved by automatization, mortality surveillance could be improved by quicker reporting of deaths, and by having a regularly applied procedure in place to update case data with data from the death registry. Other improvements concern the taking of samples, e.g. detection of antibodies without drawing blood or a methodology that would enable quick development of point of care testing. In addition, in some countries a surveillance system may need to be developed to capture symptomatic persons not seeking care, and another system for surveillance of hospital bed occupancy.

The development of pandemic research studies in advance of a pandemic was highlighted, as was the need to assess baseline community-level data to allow adequate risk assessment in case of a new threat.

The level of capacity for surveillance and risk assessment varied significantly between countries and there is a need for greater standardisation of resources available within member states for surveillance.

Finally, despite redeployment as part of emergency procedures, personnel management to avoid burnout can be a challenge. It was suggested that approaches currently being used in the defence sector may be useful to adapt for solutions in pandemic management.

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Annex 1 Overview of surveillance systems in four countries

	England	Ireland	Sweden	US
Notifiable diseases **a) unknown,** **b) influenza,** **c) pandemic influenza,** **d) smallpox**	a) Partly covered by syndromes being notifiable, and partly covered by the fact that other diseases that may present significant risk to human health are notifiable b) Influenza virus is notifiable – but not the disease c) Influenza virus is notifiable – but not the disease d) Smallpox is notifiable	a) A serious outbreak of infectious disease is notifiable b) Influenza is notifiable c) Influenza of a new or re-emergent sub-type is notifiable d) Smallpox is notifiable	a) A disease that is or is suspected of being contagious, is notifiable if the disease has spread remarkably within an area or is deemed a serious disease b) Influenza virus is only notifiable by doctors at microbiological laboratories or the person responsible for such a laboratory c) Influenza virus is only notifiable by doctors at microbiological laboratories or the person responsible for such a laboratory d) Smallpox is notifiable	a) Not notifiable b) Influenza-associated paediatric mortality is notifiable c) Novel influenza A virus infections are notifiable d) Smallpox /Variola is notifiable Note: Some nationally notifiable diseases are not reportable in some states.
Surveillance system for notifiable diseases – type of system	Notifiable diseases are reportable by phone, letter, encrypted email, or secure fax machine using a specific form.	Computerised Infectious Disease Reporting (CIDR) system. An electronic reporting system.	SmiNet. An electronic reporting system.	National Notifiable Diseases Surveillance System (NNDSS) (NEDSS/NBS). An electronic reporting system.
Type of surveillance of unknown disease	If notifiable it is reported via a specific form by phone, letter, encrypted email, secure fax machine.	If notifiable it is reported via the Computerised Infectious Disease Reporting (CIDR) system.	If notifiable it is reported via an electronic infectious disease reporting system (SmiNet).	Via (1) sentinel surveillance with eleven major emergency medicine departments nationwide (EMERGEncy ID NET (EIDN)) and (2) a web-based

				platform for local, state, and territorial health departments to report all waterborne and foodborne disease outbreaks and enteric disease outbreaks transmitted by contact with environmental sources, infected persons or animals, or unknown modes of transmission to CDC (National Outbreak Reporting System (NORS)).
Intensive care unit (ICU) surveillance - and of what	Confirmed influenza cases admitted to ICUs and confirmed influenza deaths in ICU.	ICU admissions of influenza (LAGR v3 database).	Laboratory confirmed influenza cases admitted to ICU (SIR-I).	
Hospital surveillance - and of what	Hospital sentinel scheme - the weekly number of laboratory confirmed influenza cases hospitalised.	Sentinel Hospital admissions surveillance – respiratory admissions.		Hospitalization Surveillance — Laboratory confirmed influenza-associated hospitalizations in children and adults.
Non-clinician-based surveillance	Monitors the calls for health advice to NHS 111. (Remote Health Advice)		Analyses the web searches on a national healthcare run website 1177.se. (Webbsök) Monitors the calls to the national medical hotline 1177 Vårdguiden. (Hälsoläge)	
Surveillance systems currently	**Microbiological surveillance** (GP sentinel and laboratory-based non-sentinel).	**Microbiological surveillance** (GP sentinel and laboratory-based non-sentinel).	**Microbiological surveillance** (GP sentinel and laboratory-based non-sentinel).	**Microbiological Surveillance** (laboratory-based non-sentinel).

applicable to influenza				
	Outpatient illness surveillance influenza-like illness (ILI) – a) Sentinel GPs and b) Medical Officers of Schools; acute respiratory infection (ARI) - outbreaks in institutional setting as they occur.	**Outpatient illness surveillance** influenza-like illness (ILI) – a) sentinel GPs and b) GP Out-of-Hours services.		**Outpatient illness surveillance** influenza-like illness (ILI) – sentinel.
	Disease severity and mortality surveillance a) Sentinel hospital admissions surveillance - laboratory confirmed influenza cases b) ICU surveillance – admissions of confirmed influenza cases and confirmed influenza deaths. c) Mortality surveillance: death registrations – analysed for excess mortality using European Monitoring of excess Mortality for public health action (EuroMOMO).	**Disease severity and mortality surveillance** a) Sentinel hospital admissions surveillance – respiratory admissions, b) ICU surveillance - admissions of laboratory confirmed influenza cases. c) Mortality surveillance: all death registrations – analysed for excess mortality using the EuroMOMO algorithm and used for enhanced surveillance of influenza deaths.	**Disease severity and mortality surveillance** a) – b) ICU surveillance – laboratory confirmed influenza cases. c) Mortality surveillance: all death registrations – analysed for excess all-cause mortality using EuroMOMO and used for enhanced surveillance of influenza-associated deaths.	**Disease severity and mortality surveillance** a) Hospitalization surveillance - laboratory confirmed influenza-associated hospitalizations in 70 counties. b) - c) Mortality surveillance: (1) death certificate data on pneumonia and influenza deaths – all US deaths. (2) Death certificate data with pneumonia or influenza listed as the underlying or contributing cause of death - 122 US cities. (3) laboratory-confirmed influenza-associated death in a child (notifiable).
	Influenza notifications – the virus is notifiable.	**Influenza notifications**	**Influenza notifications** – the virus is only notifiable by microbiological laboratories.	**Influenza notifications -** laboratory-confirmed influenza-associated death is

				notifiable.
	Non-clinician-based surveillance Monitors the cold/flu calls for health advice to NHS 111.		**Non-clinician-based surveillance** 1) Monitors the calls for fever in children to the national medical hotline. 2) Analyses the web searches for influenza and influenza symptoms on a national healthcare run website.	

For more detailed information:

https://www.gov.uk

http://www.hpsc.ie

https://www.folkhalsomyndigheten.se

http://www.cdc.gov

http://www.euromomo.eu

Annex 2 Case study questionnaire

Welcome Dr NN and thank you for accepting to participate in the project.

Everything all right?

As we said on the invitation this interview will be recorded. Is that ok for you?

Here sitting with me is NN also working at the PANDEM Project. S/he will only be an observer and I will conduct the interview.

The interview is divided into three parts. Each one will correspond to questions on one of the three scenarios: an unknown disease, a deliberate release of smallpox and a new pandemic influenza.

The estimated duration of the interview is 2 hours.

The time assigned for the first scenario will be 1hour, and half an hour for each of the other two.

Just as a reminder:

The aim of the interviews is to find examples of:

- Good practice
- Improvements needed
- Research questions or innovations needed

in current systems, practices and technologies for risk assessment and surveillance.

We are going to ask repeatedly about examples of good practice, improvements and innovations. Once the manuscript draft of the case study is available we can forward it to you so that you can give feedback and add missing examples. This is completely optional. Would you like to do it?

You can interrupt the interview at any moment if you have any doubt or if you would like to take a pause. Are you ready to start?

UNKNOWN DISEASE

We will start the interview with the scenario of an UNKNOWN DISEASE emerging in your country.

The first questions will be on OUTBREAK DETECTION:

On a national level, how would your surveillance system detect an outbreak of a symptomatic unknown disease?

Is there any plan or procedure?

What would be the surveillance system used: notifiable system, event-based system, syndromic surveillance system, other?

What are the tools, skills and systems/structures that would work well for the outbreak detection of an unknown disease?

Which improvements would be needed to detect an unknown disease?

Which innovations or research could improve the detection of an unknown disease?

To finalize the OUTBREAK DETECTION section: Which examples of good practice, improvements and innovations on outbreak detection would you like to add?

Once the first cases of an unknown disease are detected it would be necessary to conduct an OUTBREAK INVESTIGATION to get relevant information for a risk assessment.

What would be the procedure on a national level to undertake an outbreak investigation for an unknown disease?

How would you select the investigation team?

Would the selection procedure work well? In time?

Which improvements would be needed to select the team?

Which innovations could improve the team set-up?

Do you think that it would be possible to build a team with all necessary skills/or enough knowledge?

Would the selection procedure work well? In time?

Which improvements would be needed to get a skilled team? Is there any lacking skill or need for training?

Which innovations or research could improve the outbreak investigation?

In case you could not locate the necessary personnel resources for the team in your country, how would you proceed? Is there a system?

Would the selection procedure work well? In time?

Which improvements are needed to acquire personnel? (Get foreign personnel)

Which innovations or research could improve the acquisition of personnel if needed? (*What could improve the mobility or personnel for outbreak investigations?)

In case of needing other kinds of resources (funding, technologies…), is there any procedure?

Could the resource need be well covered with the procedure in place?

Which improvements could help to face the resource need?

Which innovations could improve the acquisition of resources?

What would be the methodology used for the outbreak investigation? (Is there a set procedure? For instance, first 100 cases study?)

Would the outbreak methodology work well?

Which methodology improvements could help in the outbreak investigation?

Which innovations or research in outbreak investigation methodology are needed?

The next question is on information dissemination: Once you have the first results of your outbreak investigation what is the procedure to share that information on a national level?

Would the communication of information work well? In time?

Which improvements are needed in communication for this scenario?

Which innovations would help to improve communication?

What is the procedure to share information on an international level? (Example: EU and WHO.)

Would the communication work well? In time?

Which improvements are needed in communication for this scenario?

Which innovations would help to improve communication?

To finalize the OUTBREAK INVESTIGATION section: Which examples of good practice, improvements and innovations on outbreak investigation of an unknown disease would you like to add?

Once you have confirmed that an unknown disease is emerging in your country and need to decide on which control measures should be taken it is time for a RISK ASSESSMENT.

On a national level, what would be the procedure to perform a risk assessment?

Is it a set procedure? Structured, non-structured…? Is it based on a particular method? Which one?

Would that procedure work well?

Which improvements are needed in risk assessment of an unknown disease?

Which innovations could improve the risk assessment of an unknown disease?

For the risk assessment is there a dedicated team? Or is there a procedure to select it?

Would the selected team work well for the risk assessment of an unknown disease? / Would the selection procedure work well? In time?

Which improvements are needed in the team? / Which improvements are needed to select the team?

Which innovations could improve the team / team selection?

Does the dedicated team have all necessary skills / Do you think that it would be possible to build a team with all necessary skills/or enough knowledge?

Would the selected team work well for the risk assessment of an unknown disease? / Would the selection procedure work well for the risk assessment of an unknown disease? In time?

Which improvements are needed in the team? Is there any lacking skill or need for training? / Which improvements are needed to get a skilled team? Is there any lacking skill or need for training?

Which innovations could improve the team skills or knowledge / the selection of a skilled team?

If the institute does not perform its own risk assessment, who would provide the risk assessment that would be used to manage a pandemic? *(examples, ECDC, WHO, department of defence)

To finalize the RISK ASSESSMENT section: Which examples of good practice, improvements and innovations on risk assessment of an unknown disease would you like to add?

Now we will continue with some questions on how the SURVEILLANCE systems would be used during the pandemic to get key information on the unknown disease. For that, we will focus on four examples.

How would your surveillance systems get information to calculate the CLINICAL ATTACK RATE for the unknown disease?

Would the system work well to get clinical information on cases? In time?

Would the system work well to get the number of people at risk? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would you get information to calculate the CASE FATALITY RATE for the unknown disease?

Would the system work well to get the number of deaths among cases? In time? *Do you have direct access?

Would the system work well to get the number of cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would you get information to calculate the PROPORTION OF SEVERE CASES for the unknown disease?

Would the system work well to get the number of severe cases among cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would your surveillance systems get information to calculate the HOSPITAL ADMISSION RATE for the unknown disease?

Would the system work well to get the number of hospitalized cases among cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

If they answer that they would do it punctually with a research study/first 100 cases:

If the pandemic lasts months, how would you monitor these measurements over time?

Would that system work well?

What would be the improvements needed for long term monitoring?

Which innovations could help in long term monitoring?

To finalize the SURVEILLANCE SYSTEM section: Which examples of good practice, improvements and innovations on outbreak investigation of an unknown disease would you like to add?

Would you like to take a short pause or do you want to continue?

SMALLPOX PANDEMIC

Now we will continue with the scenario of a DELIBERATE RELEASE OF SMALLPOX.

The first questions will be on OUTBREAK DETECTION:

On a national level, how would your surveillance system detect an outbreak of SMALLPOX?

Is there any plan or procedure?

What would be the surveillance system used: notifiable system, event-based system, syndromic surveillance system, other?

What are the tools, skills and systems/structures that would work well for the outbreak detection of a smallpox outbreak?

Which improvements would be needed to detect a smallpox outbreak?

Which innovations or research could improve the detection a smallpox outbreak?

To finalize the OUTBREAK DETECTION section: Which examples of good practice, improvements and innovations on SMALLPOX outbreak detection would you like to add?

Now we will continue with the questions on the OUTBREAK INVESTIGATION.

What would be the procedure on a national level to undertake an outbreak investigation for a deliberate release of SMALLPOX?

What would be the differences with the previous scenarios? In team selection, skills or knowledge needs, cover other resource needs and outbreak investigation methodology?

How would you select the investigation team?

Would the selection procedure work well? In time?

Which improvements would be needed to select the team?

Which innovations could improve the team set up?

Do you think that it would be possible to build a team with all necessary skills/or enough knowledge?

Would the selection procedure work well? In time?

Which improvements would be needed to get a skilled team? Is there any lacking skill or need for training?

Which innovations or research could improve the outbreak investigation?

In case you could not locate the necessary personnel resources for the team in your country, how would you proceed? Is there any system?

Would the selection procedure work well? In time?

Which improvements are needed to acquire personnel? (Get foreign personnel)

Which innovations or research could improve the acquisition of personnel if needed? (*What could improve the mobility or personnel for outbreak investigations?)

In case of needing other kinds of resources (funding, technologies…), is there any procedure?

Could the resource need be well covered with the procedure in place?

Which improvements could help to face the resource need?

Which innovations could improve the acquisition of resources?

What would be the methodology used for the outbreak investigation? (Is there a set procedure? For instance, first 100 cases study.)

Would the outbreak methodology work well?

Which methodology improvements could help in the outbreak investigation?

Which innovations or research in outbreak investigation methodology are needed?

The next question is on information dissemination: What is the procedure to share information on a national level?

What would be the differences with the previous scenario?

Would the communication of information work well? In time?

Which improvements are needed in communication for this scenario?

Which innovations would help to improve communication?

What is the procedure to share information on an international level? (Example: EU and WHO.)

Would the communication work well? In time?

Which improvements are needed in communication for this scenario?

Which innovations would help to improve communication?

To finalize the OUTBREAK INVESTIGATION section: Which examples of good practice, improvements and innovations on outbreak investigation of a smallpox outbreak would you like to add?

Now we will continue with the questions on RISK ASSESSMENT. On a national level, what would be the procedure to perform a risk assessment?

What would be the differences with the previous scenario?

Is it a set procedure? Structured, non-structured…? Is it based on a particular method? Which one?

Would that procedure work well?

Which improvements are needed in the risk assessment of a smallpox outbreak?

Which innovations could improve the risk assessment of a smallpox outbreak?

For the risk assessment is there a dedicated team? Or is there a procedure to select it?

Would the selected team work well for the risk assessment of a smallpox outbreak? / Would the selection procedure work well? In time?

Which improvements are needed in the team? / Which improvements are needed to select the team?

Which innovations could improve the team skills/knowledge / team selection?

Does the team have all necessary skills / would it be possible to build a team with all necessary skills/or enough knowledge?

Would the team work well for risk assessment of a smallpox outbreak? / Would the selection procedure work well for the risk assessment a smallpox outbreak? In time?

Which improvements are needed in the team? Is there any lacking skill or need for training? / Which improvements are needed to get a skilled team? Is there any lacking skill or need for training?

Which innovations could improve the team skills or knowledge? / the selection of a skilled team?

If the institute does not perform its own risk assessment:

Who would provide the risk assessment that would be used to manage the pandemic? *(Examples, ECDC, WHO, department of defence)

To finalize the RISK ASSESSMENT section: Which examples of good practice, improvements and innovations on risk assessment of a smallpox outbreak would you like to add?

Now we will continue with some questions on how the SURVEILLANCE systems would be used during the pandemic to get key information in the SMALLPOX outbreak:

How would you get information to calculate the CLINICAL ATTACK RATE for a smallpox outbreak?

What would be the differences with the previous scenario? *As applicable:* Smallpox is a notifiable disease, are there already systems in place that can already provide this information?

Would the system work well to get clinical information on cases? In time?

Would the system work well to get the number of people at risk? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would you get information to calculate the CASE FATALITY RATE for a smallpox outbreak?

What would be the differences with the previous scenario? *As applicable:* Smallpox is a notifiable disease, are there already systems in place that can already provide this information?

Would the system work well to get the number of deaths among cases? In time? *Do you have direct access?

Would the system work well to get the number of cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would you get information to calculate the PROPORTION OF SEVERE CASES for a smallpox outbreak?

What would be the differences with the previous scenario? *As applicable:* Smallpox is a notifiable disease, are there already systems in place that can already provide this information?

Would the system work well to get the number of severe cases among cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would your surveillance systems get information to calculate the HOSPITAL ADMISSION RATE for a smallpox outbreak?

What would be the differences with the previous scenario? *As applicable:* Smallpox is a notifiable disease, are there already systems in place that can already provide this information?

Would the system work well to get the number of hospitalized cases among cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

If they answer that they would do it punctually with a research study/first 100 cases:

If the pandemic lasts months, how would you monitor these measurements over time?

Would that system work well?

What would be the improvements needed for a long term monitoring?

Which innovations could help in long term monitoring?

To finalize the SURVEILLANCE SYSTEM section: Which examples of good practice, improvements and innovations on smallpox surveillance would you like to add?

Would you like to take a short pause or do you want to continue?

INFLUENZA PANDEMIC

We will start the interview with the scenario of a NEW INFLUENZA PANDEMIC emerging in your country.

The first questions will be on OUTBREAK DETECTION:

On a national level, how would your surveillance system detect an outbreak of a new influenza pandemic?

Is there any plan or procedure?

What would be the surveillance system used: notifiable system, event-based system, syndromic surveillance system, other?

What are the tools, skills and systems/structures that would work well for the outbreak detection of the new influenza?

Which improvements would be needed to detect the new influenza?

Which innovations or research could improve the detection of the new influenza?

To finalize the OUTBREAK DETECTION section: Which examples of good practice, improvements and innovations on outbreak detection would you like to add?

Now we will continue with the questions on the OUTBREAK INVESTIGATION to get relevant information for a risk assessment. What would be the procedure on a national level to undertake an outbreak investigation for influenza?

What would be the differences with the previous scenarios? In team selection, skills or knowledge needs, cover other resource needs and outbreak investigation methodology?

How would you select the investigation team?

Would the selection procedure work well? In time?

Which improvements would be needed to select the team?

Which innovations could improve the team set up?

Do you think that it would be possible to build a team with all necessary skills/or enough knowledge?

Would the selection procedure work well? In time?

Which improvements would be needed to get a skilled team? Is there any lacking skill or need for training?

Which innovations or research could improve the outbreak investigation?

In case you could not locate the necessary personnel resources for the team in your country, how would you proceed? Is there any system?

Would the selection procedure work well? In time?

Which improvements are needed to acquire personnel? (Get foreign personnel)

Which innovations or research could improve the acquisition of personnel if needed? (*What could improve the mobility or personnel for outbreak investigations?)

In case of needing other kinds of resources (funding, technologies…), is there any procedure?

Could the resource need be well covered with the procedure in place?

Which improvements could help to face the resource need?

Which innovations could improve the acquisition of resources?

What would be the methodology used for the outbreak investigation? (Is there a set procedure? For instance, first 100 cases study.)

Would the outbreak methodology work well?

Which methodology improvements could help in the outbreak investigation?

Which innovations or research in outbreak investigation methodology are needed?

The next question is on information dissemination: What is the procedure to share information on a national level?

What would be the differences with the previous scenario?

Would the communication of information work well? In time?

Which improvements are needed in communication for this scenario?

Which innovations would help to improve communication?

What is the procedure to share information on an international level? (Example: EU and WHO.)

Would the communication work well? In time?

Which improvements are needed in communication for this scenario?

Which innovations would help to improve communication?

To finalize the OUTBREAK INVESTIGATION section: Which examples of good practice, improvements and innovations on outbreak investigation of a new influenza pandemic would you like to add?

Now we will continue with the questions on RISK ASSESSMENT.

On a national level, what would be the procedure to perform a risk assessment?

What would be the differences with the previous scenario?

Is it a set procedure? Structured, non-structured…? Is it based on a particular method? Which one?

Would that procedure work well?

Which improvements are needed in risk assessment of a new influenza pandemic?

Which innovations could improve the risk assessment of the new influenza pandemic?

For the risk assessment is there a dedicated team? Or is there a procedure to select it?

Would the selected team work well for the risk assessment of the new influenza? / Would the selection procedure work well? In time?

Which improvements are needed in the team? / Which improvements are needed to select the team?

Which innovations could improve the team skills/knowledge / team selection?

Does the team have all necessary skills / would it be possible to build a team with all necessary skills/or enough knowledge?

Would the team work well for risk assessment of a new influenza pandemic? / Would the selection procedure work well for the risk assessment of the new influenza pandemic? In time?

Which improvements are needed in the team? Is there any lacking skill or need for training? / Which improvements are needed to get a skilled team? Is there any lacking skill or need for training?

Which innovations could improve the team skills or knowledge? / the selection of a skilled team?

If the institute does not perform its own risk assessment:

Who would provide the risk assessment that would be used to manage a pandemic? *(examples, ECDC, WHO, department of defence)

To finalize the RISK ASSESSMENT section: Which examples of good practice, improvements and innovations on risk assessment of a new influenza pandemic would you like to add?

Now we will continue with some questions on how the SURVEILLANCE systems would be used during the pandemic to get key information on the new influenza. For that, we will focus on four examples.

How would you get information to calculate the CLINICAL ATTACK RATE for the new influenza?

What would be the differences with the previous scenarios? *As applicable:* Influenza is a notifiable disease, are there already systems in place that can already provide this information?

Would the system work well to get clinical information on cases? In time?

Would the system work well to get the number of people at risk? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would you get information to calculate the CASE FATALITY RATE for the new influenza?

What would be the differences with the previous scenarios? *As applicable:* Influenza is a notifiable disease, are there already systems in place that can already provide this information?

Would the system work well to get the number of deaths among cases? In time? *Do you have direct access?

Would the system work well to get the number of cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would you get information to calculate the PROPORTION OF SEVERE CASES for the new influenza?

What would be the differences with the previous scenarios? *As applicable:* Influenza is a notifiable disease, are there already systems in place that can already provide this information?

Would the system work well to get the number of severe cases among cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

How would your surveillance systems get information to calculate the HOSPITAL ADMISSION RATE for the new influenza?

What would be the differences with the previous scenarios? *As applicable:* Influenza is a notifiable disease, are there already systems in place that can already provide this information?

Would the system work well to get the number of hospitalized cases among cases? In time?

Which improvements are needed in the surveillance system to get these data?

Which innovations could help to get these data?

If they answer that they would do it punctually with a research study/first 100 cases:

If the pandemic lasts months, how would you monitor these measurements over time?

Would that system work well?

What would be the improvements needed for long term monitoring?

Which innovations could help in long term monitoring?

To finalize the SURVEILLANCE SYSTEM section: Which examples of good practice, improvements and innovations on influenza surveillance would you like to add?

Now we have finished with the questions of the case study and will continue with some short questions on the collaboration with the veterinarian institutions.

- Is there a collaboration between the veterinarian institutions and the Public Health Institute?
- How is the collaboration structured?
- Is it voluntary or is it regulated by law?
- How resilient is this collaboration in pandemic times?
- Is there a regular exchange of data? On demand?

Thank you very much for participating in this interview, your input is valued very much.

I will come back to you by email once we have the draft of the case study so that you can add or change something if you want.

END OF INTERVIEW