ECDC Advisory Forum

AF13/Minutes

Minutes of the 13th meeting of the Advisory Forum
Stockholm, 19–20 February 2008

Table of Contents

Page

Opening and welcome

1. The Chair, Director of ECDC, opened the meeting and welcomed the Advisory Forum (AF) members and alternates to the AF's thirteenth meeting.

2. The Director welcomed the members from Greece (Evaggelia Kouskouni and Konstantina Gerolimatou) attending the Advisory Forum for the first time; she also welcomed Srdan Matic from the WHO Regional Office for Europe.

Adoption of the draft agenda and noting the declarations of interest

(document AF13/2 Rev.1)

3. The Director informed the AF that item 8 on the draft agenda ('surveillance objectives'), had to be postponed until the next meeting since several aspects of this proposal had not been finalised. The agenda was adopted with the addition of two items under other matters: the HPV guidance document and the draft guidance document on childhood immunization

4. With regards to the items to be discussed by the working groups, several members asked that in the future, the selection of items should take place at the adoption of the agenda. AF members will be asked in advance to inform the Secretariat – preferably within 14 working days before the start of the meting – of the items they would like to suggest for inclusion on the AF agenda and those for discussion by the working groups.

5. The Director reminded all participants to complete the declaration of interest form and return it to the Secretariat.

Director's and Heads of Units' briefing on ECDC's work progress since the last meeting of the AF

6. The Director briefed the AF on recent developments. Most importantly, the Annual Work Programme and budget for 2008 (EUR 40.1 million, 40 new posts) had been approved, and a list of CB had been approved and published. 2008 would be a crucial year for collaboration, but the Director expressed confidence that relationships would develop well and synergetic effects would occur.

7. The Director also reported that the long-term surveillance strategy had been endorsed by the Management Board. The laboratory strategy, however, was still under discussion. One reason for this is a parallel effort on the part of the Commission. ECDC wants to ensure that its laboratory strategy will be in line with the Commission's paper on laboratory policy and therefore has decided to wait until the Commission has finalised its paper.

8. The Early Warning and Response System (EWRS) has transferred operations to ECDC. The Director was happy to announce cooperation with three additional countries, namely Turkey, Cyprus and the Former Yugoslav Republic of Macedonia. She also referred to the upcoming MB /AF joint working group scheduled for 26 February and asked for the participation of two additional AF members. Topics scheduled for discussion are IHR, scientific advice, Strategic Multiannual Programme (SMP) indicators, vaccination policy, CB's, and external groups of experts. (In addition to the representative of France, the representative of Slovenia later confirmed her willingness to join the working group).

9. Johan Giesecke, Head of the Scientific Advice Unit, reported on the guidance that his unit has given on HPV vaccines in EU countries. Johan Giesecke thanked the AF members for the valuable input his unit had received from the AF's members. Other activities included a research symposium on TB; a joint ECDC-WHO workshop on immunization in Sofia, Bulgaria; and expert meetings on HIV testing and multidrug-resistant bacteria. Especially well received was his unit's work on a childhood immunization schedule that has been actively supported by the AF. Risk assessment of emerging influenza antiviral drug resistance is continuing, as is the implementation of KISatECDC (Knowledge and Information service), while a status report on pandemic influenza preparedness in the EU/EEA was finalised in December 2007.

10. Andrew Amato, Deputy Head of the Surveillance Unit, reported on a successful TESSy (The European Surveillance System) training course. TESSy is now in a two-month pilot phase and will be officially rolled out on 1 April. Other activities included the finalisation of the European Action Plan on TB control, ongoing work on data collection for the upcoming Annual Epidemiological Report, and a successful meeting with EISS (European Influenza Surveillance Scheme) to agree on the transition plan. Andrew Amato also mentioned the HIV and TB networks' coordination agreements with WHO, and informed that EuroCJD coordination contract has been awarded, and three laboratory surveillance tenders were about to be published, two regarding food-borne diseases and the other one on invasive bacteria.

11. Denis Coulombier, Head of the Preparedness and Response Unit pointed out that EWRS had started operating from ECDC on 17 November 2007. Currently, a mirror site is being set up to assure continuous service. Further activities included November 15 and December 5 meetings with CB's on threat detection and response. Travel activities included a trip to Austria in preparation for UEFA EURO 2008™, visits to Portugal and Hungary in order to assess training needs, and the emission of two expert teams to Moldova concerning mumps. In Stockholm, PRU was happy to receive a delegation from the Chinese Center for Disease Control and Prevention that was gathering information in order to better prepare for the Beijing Olympics in August 2008. PRU is also revamping its plan for emergency operations.

12. Karl Ekdahl, Head of the Health Communication Unit, updated the AF on the Web portal project, which will include a full set of communication tools, and on the *Eurosurveillance* website which will receive a complete makeover. *Eurosurveillance* already merged its weekly and monthly releases into one single electronic publication published every Thursday. It now boasts 12 600 subscriptions. In the meantime, ECDC website remains fully functional.

13. Finally, Alain Lefebvre, Country Relations and Coordination, informed the AF on the online availability of the CB list. Also, he and his team designated general and specific contact points for surveillance (December 2007), the latter in conjunction with TESSy training activities. In order to verify names and functions, questionnaires were sent to all CB's; a copy was also sent to AF members.

14. A representative asked for a more detailed update on the role of CDC China. In response to the question, John O'Toole (ECDC) answered that the SARS outbreak in 2003 showed the importance of direct communication links with Asia and China. Being able to simply talk to colleagues in China should prove to be a real advantage.

15. The Director added that all MoUs outside the EU/EFTA (including the one with CDC China) were mainly for information exchange. There is no mandate for activities outside EU/EFTA, although exceptions are possible under certain conditions.

16. A representative expressed concerns that ECDC could be negatively affected by too close a relationship between CDC Atlanta and CDC China. He also pointed out that the IHR already provided clear procedures and structures, and a focus on bilateral contacts could be counterproductive.

17. In response, John O'Toole said that ECDC's excellent relations with CDC Atlanta were not affected by having established contacts with CDC China. The MoU between ECDC and CDC China facilitated communication and did not replace or even bypass the IHR.

18. The Commission's representative (DG SANCO) used the opportunity to report on the latest restructuring effort in Luxembourg. Unit C3 is now composed of three unit's teams. Also, a new 2008–10 work plan was released, including specific unit management plans. Looking back at 2007, he mentioned some of the major achievements of his unit, including the 'Green Paper on Bio-Preparedness'. Specifics (mission, team, working areas) are available online.

19. One member referred to DG SANCO's efforts aimed at the tracking of passengers exposed to infectious diseases. A representative cautioned that there were at least two other such projects under way, and that DG SANCO would be well advised to wait for their conclusions. The Commission's representative replied that DG SANCO's efforts were predominantly aimed at a procedural paper describing incidents that would trigger standard operational procedures. Such a paper would not interfere with other projects.

Adoption of the draft minutes of the Advisory Forum held in Stockholm, 13-14 November 2007

(document AF12/4)

20. The minutes were adopted with a few editorial amendments and corrections were proposed to paragraphs which will be included in the final version.

Meetings of the AF Working Groups on priorities for scientific advice in 2008

21. Johan Giesecke gave a short presentation on prioritizing scientific advice that raised several questions: Who should be consulted and in which order, what defines a priority setting, what is the ideal time frame in respect to inclusion in the annual work plan, and is it sufficient to consult CB's indirectly through their respective AF members? A representative suggested that at least two working groups should be established, one discussing the methodology behind the prioritization process, one the actual prioritization issues. His move was seconded by another representative.

22. Given the importance and complexity of the subject, the AF agreed to have one working group to discuss methodology while the other two groups would focus on identifying actual priorities for scientific work.

23. To conclude, the Director, in addressing several of the issues raised during the discussion, agreed that all these issues were important and required further discussion during the next AF meeting. She stressed the important role of the AF in all ECDC activities. The childhood immunisation schedule for example, although still in a draft stage, was made available to the AF at a very early stage because ECDC wanted early input from the AF on this politically sensitive matter.

24. The AF forum then split up in three working groups that discussed scientific advice.

Feedback from the AF's ad hoc Working Group on Competent Bodies: outcome of meeting 18 February 2008

25. Angel Kunchev (Bulgaria) gave feedback on the discussions of the Working Group that was established to examine the way the CB interact with ECDC. The Working Group – comprised of AF representatives from eight countries and the Commission– had its first meeting on 18 February. Issues discussed included the need to clarify roles and responsibilities of the CB and the AF, the importance of keeping the number of contact points/focal points limited, and the need for flexible collaboration mechanisms that can be adapted to the structure of each country. The next steps in the work of this group are as follows: feedback of the discussion will be provided to the MB/AF Working Group meeting on 26 February, work will continue thru electronic exchange, and the group will meet again in April if necessary.

26. Another member of the Working Group made a clarification regarding one point in the first slide of the presentation which indicated that 'ECDC needs to have direct and unrestricted access to scientific expertise in the EU'. In this regards, he wished to remind that the CB represent the national perspective; therefore, when ECDC needs to have access to the national scientific position of a country, the CB are to be consulted.

27. One representative highlighted that several clarifications are needed on the terminology used in order to reach a common understanding; furthermore, a common procedure to be followed by all countries is needed. Therefore, a formal discussion on the way of interacting with the CB is needed. The Director acknowledged that the Working Group should agree on common terminology and define the meanings of the different terms used, and present this at a later stage. A representative then added that for the issues of data collection the procedure is clear, but clarifications are needed for other areas, like for example urgent inquires.

28. A question was raised from the floor on how work with the CB is progressing. The Director gave an update, informing that the list of CB was adopted in the MB11 meeting and is published on the website. A formal collaboration will start and sub-regional meetings were held to prepare for this. By spring 2009 the close collaboration will be institutionalized. She stressed that ECDC needs to take into account the differences between countries in terms of size, capacity, and agreement is required on common rules. Because in the surveillance area ECDC needs to move forward fast, the collaboration in this field will have to be institutionalized sooner.

29. At the closing of the discussion, the Director clarified the role of different bodies. She informed that clarification of roles will be added to the report and that work on the issue will continue.

Priorities for the work on scientific advice in 2008: discussion and feedback from the AF Working Groups

30. The Chairs (representatives of Italy, Germany and Slovenia) of three working groups established during the AF meeting to discuss the priorities for the work on scientific advice presented the outcomes of their meetings.

Working group I

31. Gérard Krause (Germany) presented the conclusions from Working Group I, which dealt with the prioritization process. The group agreed on four steps in order to provide a methodology for prioritization: selection of items/subjects/tasks, definition of criteria, definition of scales for each criterion and definition of weights for each criterion. The different internal and external bodies or organisations that should participate in the process were mentioned, and the sequence for the procedure was described, including first an AF brainstorm session to come up with a list of issues and then a prioritization scheme. A list with possible examples of criteria was also presented, the most important of which is the European added value.

32. After this presentation, the Director as well as Johan Giesecke acknowledged the usefulness of this approach.

Working group II

33. Stefania Salmaso (Italy) presented the responses of the Working Group to a number of questions forwarded to the AF related to the prioritization process. The group concluded that the process should start with input from the CB on what Member States consider to be the most relevant issues. This information should be forwarded to the AF in order to assess priorities, and a list should then be consolidated in correspondence between this body and ECDC. The consolidated list should be presented to the AF in its May meeting, and it can then be used as a basis for the ECDC Work Plan.

34. The criteria for priority setting should take into account topics that need coordination at EU level, issues common to several countries, as well as emerging issues. On the optimal timing for the process, the group recommended having the consolidated list ready to be presented to the AF in its May meeting, in time for inclusion in next year's ECDC Work Plan. The group agreed on the need for a separate consultation of AF and CB. For the exchange of ideas between AF meetings, the group suggested developing an electronic forum. It also suggested that output of independent scientific panels should be reviewed by ECDC and commented upon if necessary.

35. Additionally, the group suggested a classification of each piece of scientific advice to be developed, according to the desired output, in order to clarify to AF members what type of document they are requested to review:

- Scientific review of literature: performed by an independent group.
- Guidance: implying choice by ECDC.
- Opinion: implying advice by ECDC.
- Guidelines: implying consensus.

Working group III

36. Irena Klavs (Slovenia) presented the outcome of the discussion on the list of five priority activities for scientific advice provided to this Working Group. Some general remarks were made before presenting the results. The group appreciated that the list included topics from the ECDC Work Plan and items for future work, but some issues will arise due to unanticipated events or due to requests from the European Commission. Clearer definitions are needed, as there are varying uses for terms like recommendations, guidelines, analysis and review. More agreement on what ECDC should be doing was also requested. It is not clear if

ECDC should be moving further from making reviews and providing scientific advice into the area of providing evidence-based options to countries to choose from. Additionally, some rationale on the European added value is needed.

37. The assessment on the level of priority of the different activities for specific health topics included in the list was then explained:

- Antimicrobial Resistance/Healthcare-associated infections: The two most relevant issues are guidance on strategies for control of MRSA in hospitals and other health care facilities, and guidance on strategies for the control of MRSA in the community.
- Food- and water-borne diseases (FWD): Priority should be given to the work on Listeria, the review of existing national guidelines in EU Member States for prevention and control of Norovirus outbreaks in closed community settings, and the review of published work on comparability of incidence data for FWD and definition of important factors affecting comparability of FWD incidence data.
- HIV/AIDS, STI, Hepatitis B & C: Priority was given to the question on what are policies, practices and barriers to HIV testing in the EU and how to overcome these barriers.
- Influenza: Two priority issues were identified; these are the transmission of influenza viruses and their reduction, and influenza antiviral resistance.

38. The Chair of this group explained that due to the lack of time, the prioritization of the remaining topics in the list provided could not be performed.

39. After these presentations, the Director opened the floor for discussion on the methodology issues.

40. One member of the AF called attention to the fact that prioritization can't be done merely through a scientific approach; axiological input is also needed, because judgement is involved. Therefore, the approach proposed by Working Group I on taking into account weighting of criteria was considered vital.

41. One representative requested that a paper summarizing the various information presented during this item be prepared and presented at the next AF meeting.

42. Another member reminded of the need to further clarify the role of the scientific panels.

43. Johan Giesecke expressed his agreement to the presentation of a proposal by the Working Groups I and II in the next AF meeting. Regarding the role of the scientific panels, he explained that it is evolving and that a paper is being prepared for the MB meeting in March in order to clarify this issue.

44. The Director acknowledged that a methodology is needed; therefore ECDC will develop the proposal and present it at a next AF meeting. For this, Johan Giesecke will work with the Chairs of the Working Groups in order to prepare a document. For the future, the timing of this discussion should be moved to an earlier stage, so that it can feed into the Work Plan development process. She also informed of the upcoming meeting of the MB/AF Working Group, where a paper on ECDC's scientific advice will be discussed, and the topic will then be presented at the next MB meeting in March. The issues raised as priorities in the presentations will feed into these discussion. Johan Giesecke added that Standard Operating

Procedures are being developed for the work with external groups of experts, including scientific panels.

45. Johan Giesecke reminded of the fact that in ECDC's Founding Regulation, in articles 6 and 7, some confusion exists on terminology, as the words scientific opinion and expert advice are used. Therefore, further definitions are needed. Regarding this, the representative of the Commission added that a revision of the ECDC regulation will be prepared, and a working document will be made available for input.

46. It was requested that the presentations made by the three Working Groups be made available to all participants.

47. The meeting proceeded with the discussion of the presentation of Working Group III. Johan Giesecke thanked this group for highlighting those areas considered as priorities for the scientific advice, but mentioned that it will not be possible to cover all of them. The Director recommended having an electronic consultation, so that the views of this group can be addressed in view of preparing a list of priorities. If the list of priorities is more extensive, some activities could be transferred to the 2009 Work Plan.

48. One AF member suggested that when the methodology is ready, it should be applied to the list presented by Working Group III.

EU-wide coordinated approach to risk assessment: principles and tools for rapid risk assessment (document AF13/6)

49. Johan Giesecke presented the recent history and current status of the process of development of a common approach to risk assessment in the EU. He briefed on the outcome of the 3rd Meeting of Chairs of Commission and Agency Scientific Committees/Panels in November 2007 at ECDC. One decision at this meeting was to organize a workshop on 'Risk Assessment Terminology and Approaches to Evaluating Scientific Evidence on Environmental and Health Issues', on 28-29 May 2008 in Copenhagen, with the aim of increasing the general understanding of the use of risk assessment terminology, and the assessment and interpretation of evidence as input to precautionary interventions to reduce risk. A diagram with an interim ECDC terminology was then presented.

50. Members raised concerns regarding some definitions and possible different meanings for words like 'risk', 'hazard', 'threat', depending on the contexts, and also regarding the separation between risk and probability of occurrence.

51. Preben Aavitsland (Norway) then presented the EpiNorth Risk Assessment of Events Tool (EpiRisk Tool), which has been tested as a pilot and has shown its effectiveness. It helps to decide how much resources are needed in a risk assessment and provides for a rapid but systematic approach. He explained the steps included in the process: description of event, rapid disease overview, assessment of impact of event, assessment of potential for spread, preventability. It includes a chart to summarize the current and future risk, classifying it from low to high depending on the factors of likelihood of future spreads and impact. It includes also a guide on actions to take.

52. Denis Coulombier mentioned that the use of such tools provides a framework and a checklist that make it possible to assess the background of decisions taken.

53. In answer to some comments raised from the floor, Preben Aavitsland acknowledged a suggestion put forward for improvement of the tool, on documenting at what point the user of the tool is on the assessment of a threat. He also clarified that the tool considers 'likelihood' rather than proper numbers.

Implementation of the case definitions for reporting of communicable diseases to ECDC *(document AF13/7)*

54. Andrew Amato, Deputy Head of Unit, Surveillance, updated the AF on the implementation of the case definitions. As the legal text will not indicate what category should be reported for each disease, an agreement is necessary on the case definition categories that need to be reported for each disease at EU level as well as the frequency of reporting (minimum expected). On 30 January 2008 epidemiologists participating in the TESSy training workshop agreed that as a minimum all confirmed cases should be reported. For the other categories disease-specific objectives are under development and will be finalised in the coming months and these should determine what should be reported. Reporting according to the new case definitions will officially start from 1 January 2009 onwards.

55. The Commission's representative pointed out that the implementation of the case definitions shall not suffer excessive delay but must respect legal aspects. The time-consuming – but compulsory – translation of the long technical document may also delay the process. The Commission's translation services already contacted certain Member States for support to properly translate the technical terms. Some of the AF's members might be approached. Member States' opinions vary whether the draft should be put into an EC's decision and submitted to the Network Committee. Decision will be put to qualify majority of the Network Committee's members at its June meeting.

56. The Director underlined the case definitions' approval by the Network Committee in December 2007 as a major first step towards improving data comparability at EU level. Questioned on the on-going review of the internal document, the Commission's representative clarifies that if a country submits data to ECDC, it should comply with these case definitions' rules. The Commission's role is to supervise the Member States' adoption and compliance with the case definition.

57. Several members expressed their doubts about a coercive approach in the reporting implementation and asked for a more pragmatic one as well as some flexibility from the Commission. Each country should be authorised to send some data that is not necessarily strictly compliant due to their specific surveillance system limitations, especially for the confirmed cases. Insisting on laboratory confirmation for all diseases may be detrimental and harm the gradual process of adoption if countries feel threatened by the Commission's potential sanctions. Also there are a lot of sentinel (sample based) systems in use that provide CD data that do not cover the whole country population denominator. This approach is very efficient for diseases of high incidence provided that the reporting "sentinels" are sufficiently representative of the population. The TESSy concept, based on case reporting, can integrate sentinel data.

58. The Director pledged that ECDC will strive for a smooth collaboration with the Member States and reassured them of ECDC's full support. However data comparability is important and necessary to ensure the quality of the next Epidemiological report due in two years time.

59. A representative mentioned that whenever new case definitions were published the MS had a major effort in explaining these to their reporting clinicians. Andrew Amato agreed that it was important to publicise these definitions to all those who may need to use them, but there must be a clear distinction made that these definitions were solely for surveillance purpose and were not intended to be used for clinical diagnosis purposes.

60. The WHO's representative recalled its active role and close collaboration during the revision of the case definitions. He informed the AF that the case definitions will be extended to the 53 European countries, contributing to a major improvement towards standardization at EU level, and proposed further exchanges with ECDC on the to-be-reported diseases. The issue of data comparability is however much larger than this and underreporting will also need to be dealt with soon.

61. The Commission's representative stated that data reported by Member States should comply with the case definitions. How Member States comply with legal requirements is up to them. There are two different issues: one is the legal obligation and the other one is how to improve the data quality.

62. The Director concluded that Commission and ECDC will need to discuss further the strategy and instruments to be used to encourage and support the MS to adopt these case definitions to the maximum extent.

Proposal for the procedure to revise and prioritise the list of diseases for EU surveillance *(document AF13/8)*

63. Andrew Amato reminded the AF that, at the request of the EC, ECDC will work on preparing a revision of the diseases listed in Decision 2000/96/EC and identify the priority diseases for enhanced surveillance jointly with Member States and the EC. The revision has been made necessary by the occurrence of new diseases in the EU (e.g. Avian Influenza, Chikungunya) and the development of new vaccines (e.g. rotavirus, HPV, etc). The AF was informed of the proposal to nominate a group from the CBs in Surveillance and so several members with dual roles may be approached in the near future to appoint some experts to work on the criteria to be used. Once the criteria would be agreed then these would be applied to the present list and also other potential CDs to come up with a proposal. The proposal for the criteria to be used may be ready to be discussed at the next AF in May. The whole exercise of the revision of the list could be prepared in the second half of 2008 with a view to be presented for approval at the Network Committee meeting in December 2008. The discussion on the prioritisation exercise would probably continue in 2009.

64. A representative who welcomed the initiative invited ECDC to consider the methodology used by Canada and suggested that this assessment should include criteria for identifying which diseases shall be taken off the list, another way of prioritising.

65. Another representative also welcomed this approach and mentioned that this exercise needs to be studied carefully –those diseases that will be reported to EWRS, like polio or smallpox need not be included in this list.

66. A representative said that this was indeed necessary and asked that the criteria should also include how often this exercise to revise the list should be repeated, as this has consequences at the MS level. She asked that this revision should not be done too often, and certainly not every year or two.

67. The Director concluded that this will be discussed again at the AF and the June meeting of the Network Committee should also help clarify how to move forward on this issue.

Update on the EWRS and the EPIS communication platform

(document AF13/9)

68. Denis Coulombier recalled that the AF asked to be briefed on the state of play of EWRS and the Epidemic Intelligence System (EPIS). A couple of incidents have happened since ECDC operates EWRS on 17 November 2007 that drives ECDC to plan a full geographical replication. The prototype for IHR notification developed by ECDC was presented to the AF. Denis Coulombier also presented the threat tracking tool, a database of the threats followed up in ECDC. The tool is almost completed and the security issue is currently being tested with some levels of confidentiality. It allows mapping threats. EPIS is a platform for communication to complement EWRS, TESSy and TTT.

69. To a member who stressed the importance of an easy connection to the tools for on-duty officers (i.e. from mobile phones), Denis Coulombier reassured that this option was considered.

Epidemic intelligence: update on recent threats in the EU

70. Denis Coulombier informed the AF that the serious event that had happened since the last AF was from the emergence of viable oseltamivir resistant influenza viruses in Norway and elsewhere and gave the floor to Preben Aavitsland (Norway).

71. Preben Aavitsland explained that the surveillance system for influenza of Norway and the Norwegian Institute of Public Health (NIPH) was similar to those in others European countries, with primary care (clinical) and virological surveillance. Viruses are forwarded to WHO Collaborating Centre in the UK, and the associated VIRGIL network hub laboratory at the Health Protection Agency (HPA – UK). As of 24 January, 16 A/H1N1 strains from Norway have been analysed by HPA, and 12 (75%) of these were found to be highly resistant to oseltamivir. The analysis continued in house in Norway. By 13 February, cumulatively 66 % were resistant. On 25 January, this resistance was notified to WHO (through the IHR mechanism), to the Member States, the European Commission and ECDC (through EWRS) An informative public message was posted on web sites in Norwegian, English and Russian and an early warning sent to all hospitals. NIPH started a continuous dialogue with ECDC and WHO, increased the surveillance. The findings were published by the VIRGIL group in *Eurosurveillance*. The resistance raised two key questions: 'Did oseltamivir use cause the emergence and persistence of these strains?' and 'Do the resistant strains cause a different clinical picture of influenza?' So far NIPH answered negatively to both.

72. Preben Aavitsland clarified that the A/H1/N1 virus was dominant in Europe. When that was allowed for the percentage redropped from 75 to 66 %. The strains were from a number of parts of Norway from a number of age-groups. I.e. the viruses were widely distributed and transmitting readily. This was not a small outbreak.

73. The AF had then a telephone conference with Maria Zambon, Head of influenza virology, and coordinator of the influenza component of Virgil network. She described the VIRGIL project which is a 2004-8 time limited EU funded project under FP6 with a goal of building a network. It concerned Hepatitis B & C but she was only concerned with the influenza component. It only looked at viral isolates but undertook testing almost in real time at the HPA laboratories. For this 2007-8 season samples were received from the WHO

Collaborating Centre in London on 18 January, testing started on 21 January. Initially she did not believe the results findings significant numbers of the predominant influenza A viruses this season (A/H1N1 viruses) highly resistant to the neuraminidase inhibitor (NI) oseltamivir but repeat testing confirmed that.

74. The central laboratory procedure is that specimens are tested using phenotypic methods in vitro and then backed up with genetic sequencing to confirm the findings. What was found was typical of a previously observed H274Y mutation with a 500 to 1000 fold loss of susceptibility to standard dose of oseltamivir. But the key difference was that by their wide distribution these had to be 'fit' influenza A viruses that could transmit readily. It would confidently be expected that oseltamivir would be ineffective for these viruses. This was the first time this had been observed anywhere in the world. However the same viruses were found to be sensitive to the other NI zanamivir and. 99% of the non-H1N1 viruses tested were susceptible to NIs. Of the initial 1200 A/H1N1 specimens tested about 230 had the resistant phenotype–genotype. It was noted that this was only for A/H1N1 and that the proportion of all viruses that were A/H1N1 varied considerably by country. There was some trend analysis, e.g. in France the proportion of A/H1N1s resistant had actually increased through the season. Because of training given by the HPA lab and its quality assurance work funded by VIRGIL a number of countries were now able to do genotypic testing but at least 6 EU countries could not and the HPA lab is doing that work for them. Also the HPA lab is unique in doing the confirmatory phenotypic testing routinely.

75. The representative from France informed the AF on the situation at national level. The 40% resistance average masks geographical heterogeneity. Paris and the north-east region are characterised by a +50% resistance average while it is only 20% in the south-east region. No data are available yet for the south-west. The provisional analysis suggest an increase in the proportion of resistance through the season. Since samples remain to be processed they will need to wait for the final analysis to conclude definitively.

76. Answering a question on how the resistance works, Maria Zambon explained that it had been considered that oseltamivir was an especially useful drug because it worked across all 9 different described neuraminidases (N1-9) since the fine character of the neuraminidase enzyme site did not vary. The N1 site is such that the H274Y residue and its resistance is distinct. What is not yet clear precisely is what is the compensatory mutation involved that allows the virus to get round the N and what advantage it gives the virus.

77. Answering other questions, Maria Zambon clarified that the same effect be seen for the N1 in H5N1 (the 'bird flu' virus) would not necessarily be observed as the N1 differs genetically between that in H1N1 and H5N1 by about 20%. She also repeated that this was a new phenomenon this season and explained that in previous seasons around 250 A/H1N1 isolates had been tested and only one was resistant though it was one with the H274Y mutation.

78. About the resistance in other influenza viruses, Maria Zambon explained that the other A viruses circulating this year were H3N2, though these were few in number in most countries and less than 1% are outliers with higher than usual resistance. Concerning the observed risk factors, Maria Zambon stated that this is unclear and needed an analytic study. It is also unclear how this happened. However she observed that the viruses were not all identical, some were being seen outside Europe and that this looked more like a 'star burst' event happening elsewhere i.e. perhaps outside Europe.

79. Piotr Kramarz, Deputy Head of the Scientific Advice Unit and leading the ECDC response with Angus Nicoll the influenza coordinator, presented the ECDC response and plan of action with regards the influenza antiviral resistance. After the initial response following the alert on 25 January 2008, ECDC worked on a sustained response. ECDC immediately created an internal response team (ART) drawing on all four technical units. This has being convening weekly teleconferences with the Commission, the most affected Member States, WHO-Europe, WHO HQ, EISS-Centre, VIRGIL and EMEA. ECDC had published an interim risk assessment on Jan 28th which will be reviewed and updated following critical comment and as more information becomes available. ECDC had been trying to organise an analytic study and had made proposals for this. Piotr Kramarz thanked and acknowledged the contributions from the EISS, VIRGIL & ESAC networks as well as WHO. A number of inputs were requested from the AF and Competent Bodies, notably gathering data through the EISS-ECDC database.

80. A member welcomed ECDC's pragmatic approach and suggested to take the occasion for modelling at the end of the season. Several members supported the proposal to conduct an analytical study. Piotr Kramarz clarified that ECDC was currently working on a protocol with the affected and did not yet entered into the practicality.

81. Two members underlined that it was important to have supranational activity and asked for more details on the rationale, hypothesis, the protocol designs and the collection of standard information. They emphasised the importance of developing the epidemiological side and suggested that ECDC should investigate which information was needed and coordinate this allowing all countries to participate.

82. One member expressed his disappointment that there was already a European analytic study and criticized ECDC's response for not doing enough on the epidemiological side. The Norwegian representative agreed it was unfortunate that no rapid analytical study was yet underway but explained that it was ECDC's fault as it had been trying to lead the process but that not every affected country had yet agreed a study was needed or what form it would take and that there were problems of coordination and data-sharing between the virologists and public health experts at the national level in some countries. He agreed that a European analytical study is needed. However, other members stressed that an analytical study engaging a high degree of data collection at member state level without a clear hypothesis identified to test for and the lack of public health and clinical impact of resistance should be taken into consideration. In addition, the protocol proposed by ECDC was based, for sample size estimation, on unrealistic hypothesis.

83. Piotr Kramarz explained that there was already a protocol for an analytic study investigating some hypotheses about gender, age, previous use of oseltamivir, location and other potential risk factors and welcomed members to contribute to this work. Angus Nicoll pointed out that the basic data had to come from data being uploaded by virologists into the EISS-VIRGIL database which had been augmented by EISS and that it was important that virologists be supported in getting the additional data and encouraged to upload. He explained that it had been agreed that ECDC and WHO would have equal access to that data in real time.

84. The Chair concluded that there is an agreement for an analytical study and invited all Member States to contribute to the protocol on which some work still needed to be done.

85. A representative acknowledged that the guidance on HPV vaccine is a good and comprehensible document but informed the AF the advocacy group questioned the sentence

'*No conflicts of interest were declared by any of the Panel members*.' It appeared however from the conflict of interest forms that one expert did mention one. The quality of the document is not questioned but transparency shall prevail to ensure credibility.

86. Johan Giesecke clarified the statement *'no conflict of interest'*, the sentence was not phrased properly. The chair of the panel was linked with both producers and acknowledged it. In her case, there was no conflict of interest. The document is not biased to one or the other producer. However Johan Giesecke agreed to rephrase the sentence.

87. The Chair suggested amending the sentence on ECDC's website and insisted that conflict of interest statements from the experts are carefully checked in house. She also proposed to post all declaration of interest from panels' experts on ECDC website identically to AF and MB members. A representative proposed to clearly mention on ECDC website that ECDC decided to rephrase the sentence and to amend the document.

88. A member proposed the creation of an internal committee to decide on the 'grey cases' of conflict of interest. If an expert points out a conflict of interest, the internal committee shall decide. Some members insisted in taking the conflict of interest seriously to protect the scientific community and the credibility of its work.

Update on listeriosis prevalence in the EU countries

89. In response to a specific request by France, Johanna Takkinen, from the Surveillance Unit, presented an overview of Listeriosis. She first reminded the AF of the microbiological and some epidemiological characteristics of the *Listeria monocytogenes.* Listeriosis is a rare but severe invasive human disease and a steady increase in reported number of listeriosis cases in EU is noticed. A short descriptive analysis of human data based on zoonoses report and food data based on RASFF notifications was presented. The current EU legislation (Commission Regulation 2073/2005) for ready-to-eat (RTE) food products was also presented as well as the proposed ECDC 2008 action plan against listeriosis.

90. Several representatives congratulated ECDC on taking up this issue. A number of representatives informed the AF about the alarming increase of notified cases of listeriosis at national level, especially affecting elderly people. Even if not an immediate threat, InVs notified the growing level of contamination and infections over the last three years to the French Ministry of Health as well as to the national Food Agency in order to initiate further risk assessment, identify hypothesis and plan further research and surveillance activities. Because this increase was not clustered to France, this is why they raised the question with ECDC and proposed the issue for the Agenda of the AF meeting. The UK also mentioned the sustained rise in cases in their country. He mentioned that this was a particularly difficult disease to study especially due to the age groups most affected. He suggested that ECDC needs to look at the current legislation on acceptable levels in the 'risk' foods and in particular they need to look at hospital and care homes meals especially. Regarding the proposed work plan, an analytical (case-control) study may have to be considered.

91. The representative from Ireland welcomed this initiative and reported that in their country this is mainly a problem in infants especially in those immigrants coming from Eastern European countries (similar for trichinella and botulism).

92. A number of representatives agreed that the fight against listeriosis should be addressed at the EU level and can benefit from the interactions between ECDC and the CB as well as even closer collaboration with EFSA. A member suggested contacting another international

specialised disease network from the US CDC. Another one proposed a combined approach that might include reconsidering the current food legislation.

93. A representative mentioned the worrying raise in listerioris meningitis, that has now become the third most common cause of meningitis in Denmark. On contacts with food people should be encouraged to change behaviour (i.e. how elderly people store food).

94. The Commission mentioned that this was important work and they will communicate with those in the EC responsible for Food Safety so that they can contribute to this initiative.

95. Johanna Takkinen agreed on the suggestion of a member to conduct a dedicated analytical study of data, combined with an analysis of the food and veterinary data. The increase in infection in elderly people in many EU countries is notable and further analyses of available data should be performed. Liaising with the CB is of course of great added value for ECDC as well as closer collaboration with the US CDC and EFSA. The Director informed the members that this proposed work plan will be updated with their comments.

96. Regarding the plans for preparing a detailed report on the epidemiological situation state of art on listeriosis, Andrew Amato asked whether the AF would like to see ECDC make recommendations based on the data that will be analysed on this subject. A representative suggested including the most likely hypothesis explaining an increase (i.e. introduction of new treatment that may have facilitated the infections, changes in food habits, change in the way widely distributed foods are processed…). The recommendations on the needs for future research should also be presented, together with the review of the state of art of this infection and its prevention. ECDC should also work closely with EFSA on this issue since some of the determinants of this increase may be related to change in ways of how foods are processed.

Update on the development of the strategy for ECDC cooperation with microbiology laboratories and research institutes in the EU

97. Johan Giesecke recalled the members that the paper shall be considered as a ‘living document’ and recapitulated the consultation process since the project started in 2006. Following the MB 10 request that ECDC works with Member States’ nominated experts in the field of public health microbiology, a number of National Microbiology Focal Points (NMFPs) have been appointed. Four areas of Framework of actions (2007-2013) have been identified: 1.) Situational analysis and coordination; 2.) Strengthening surveillance systems and methods towards improving quality and comparability; 3.) Emergency response laboratory assistance and capacity building and 4.) Scientific support and training.

98. The Director suggested postponing the discussion to the May AF meeting and slowing down the process for the time being. When an agreement with the Commission is reached, ECDC will be more able to carry on the work and ensure data comparability.

99. Johan Giesecke informed the AF that the NMFPs are not used to represent their country and asked the AF members to support them in their new tasks. One member pointed out that support from the Member States should be also considered. The capacity to answer cannot be left on the shoulders of laboratory people but shall be seeked at a higher level. The Director recalled Member States have appointed the NMFPs and the MB had asked ECDC to work with them on laboratory issues.

Need for accurate contact information in the system used in crisis situations

100. This item was included on the agenda at the request of Petri Ruutu, representative from Finland who introduced some proposals to strengthen the communication at European level in crisis or understaffed institutions contexts (i.e. over summer holidays, Christmas Day). Contacting ECDC on-duty officer or the IHR WHO/EURO contact person in Copenhagen is usually quite easy. Things get more complicated in case of a crisis starting at 5 o'clock Friday afternoon. EWRS allows permanent access and provides telephone numbers but that might not be enough. Outdated contact information at national level appears on IHR (i.e. incorrect data for Finland). Contact information on EWRS also is not always updated. Fields where phone numbers of 24-hours duty officers are posted vary from country to country. This diversity may reduce efficiency. Two questions to improve the current situation: How does the updating data process work? How to be sure that data is updated? Also the Health security working group overlaps. A backup should exist when normal access fails. On a technical level, too many systems exist accessible with different user names and passwords. It creates confusion and weakens the system. In a crisis situation, the complexity of the system and the accuracy of the information are under question.

101. The Commission's representative pointed out the difficulty to have three different systems (EWRS, IHR and RAS-Bichat). The key question is keeping the three lists of contact details updated. Concerning IHR, Member States notify their contact points to WHO and shall copy ECDC and the Commission. WHO has no obligation to transmit information. Contact information for EWRS and RAS-Bichat are updated through the Member States' Permanent Representations. Member States often inform the Commission informally but contact information is updated only upon official communication; which explains delays. If the legislation is amended in the future, a solution should be found to avoid the transmission of information through permanent representation and shorten the long procedure at national level. A competent authority in the health sector at national level could nominate the contact point but an official authorisation is necessary.

102. Denis Coulombier ensured the members that technical solutions to synchronise everything can be found at EU level. The Director insisted that ECDC shall work in this direction and recalled that ECDC is building a web portal with an active directory centralising all systems operated by ECDC It is already implemented for EWRS and TESSy.

103. The Commission's representative underlined that both ECDC and the Commission have a 24 hours duty. On the very long run, the Commission's representative proposed to have one list if EWRS and IHR treat the same issue but it requires legal changes. He also suggested having functional mail boxes without names to reduce the need to update information.

104. Alain Lefebvre informed the AF that ECDC will send regular requests by e-mail (i.e. every six months) to the CB to check the validity of the information gathered in the country database. Member States are invited to limit the number of contacts in the system.

105. A member insisted that the field mentioning the 24 hours duty phone number should be completely separated to avoid misunderstanding. Another member suggested circulating private home phone numbers at the condition they won't fall into public domain.

106. The Director agreed on a member's proposal to have a chart describing the relations between ECDC, the CB and other affiliated groups and concluded inviting the AF to carry on working on this issue that will be brought back to the next AF meeting.

Other matters and closure

107. Johan Giesecke recalled the first round of consultation of the 'green paper' of the childhood immunization schedule. As this document was considered as sensitive, members' inputs were seeked from the very beginning. Comments received from the AF were transmitted to the panel and a reviewed version will be circulated.

108. One member said that the process can be modulated as ECDC is growing and questioned which issues should be treated internally and which externally. If treated externally expectations, desire outputs and mandate shall be clearly formulated. Johan Giesecke agreed that these problems find their roots in ECDC's current rapid growth: it is learning by doing experience. He acknowledged the importance of formulating thoughtfully the scientific questions and ensured that ECDC will pay even more attention in the future.

109. A member insisted on the importance of a more balanced approach with a mix of scientific and public health experts. With ECDC growing, its inputs should increase. Johan Giesecke supported the idea to invite the panel member for a hearing at an AF meeting.

110. The WHO representative briefed the AF on WHO's long experience of dealing with questions such as panels' independence and ethics issues and kindly offered support. WHO recently developed guidelines for developing guidelines and has an important human experience. He also advocated having behavioural aspects taken into account. Pure science only cannot explain why people don't systematically take a HIV test. He insisted on the importance of understanding ECDC's mission and argued that it is not to be a research institute but to deliver more practical commendation for policy makers in the Member States and at the Commission.

111. Members expressed different opinions on who shall chair the panels, an independent scientific expert or ECDC / a member of the AF. The Director concluded that this issue will continue to evolve and will be brought back to the MB.

112. One member pledged for a more active cooperation with EU-neighbouring countries and for an increased cooperation at expert level rather than at ministerial one. The Director underlined that ECDC closer cooperation could also operate in the future through the EPI South and North networks as well as though WHO for non EU-European countries.

113. Finally, the Director thanked the members for their participation and invited them to submit any item for the agenda of the next AF meeting and also to propose items for discussion by the working groups, within a 14 working days notice before the start of the next AF meeting.