

MEETING REPORT

Expert consultation on scientific evidence linked to polio virus in Israel and Syria

Stockholm, 5 November 2013

Background

In response to the recent events of wild-type poliovirus (WPV) circulation in Israel and a cluster of poliomyelitis cases in Syria, ECDC published two risk assessments for the EU/EEA on 26 September and 24 October 2013, respectively. As a further response to these two events and the recommendations presented in the risk assessments, ECDC called an expert consultation meeting on 5 November 2013.

The focus of the meeting was to seek advice from vaccine-preventable diseases experts and polio experts in Europe on how ECDC and the EU Member States should best respond to the identified threat of wild-type poliovirus introduction and re-establishment in Europe.

On the morning of 5 November, Deputy Chief Scientist, Dr Piotr Kramarz, welcomed the group and set the scene for the discussions. Dr Kramarz highlighted the fact that as part of its mandate, ECDC delivers scientific advice to the Member States in the field of infectious disease prevention and control. When developing advice an essential step in the process is the consultation of external experts and stakeholders in the EU/EEA.

Dr Emilia Anis continued to set the scene with a presentation on the recent poliovirus event in Israel and the activities undertaken in the country in response to the detection of WPV in the environment. Dr Emma Huitric continued with a brief presentation of the two recent ECDC risk assessments, providing background information and the rationale for the current expert consultation.

In its risk assessments ECDC provided a number of recommendations to Member States in the areas of immunisation, surveillance and prevention and control measures.

To support Member States and provide scientific guidance in these areas, ECDC identified three areas of work.

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Stockholm, November 2013

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Introduction to three working groups

Acting Head of the Vaccine Preventable Diseases (VPD) programme, Dr Lucia Pastore Celentano, presented the overall aims of the meeting:

- to discuss the three areas of work;
- to identify the urgent areas where ECDC needs to provide scientific advice and support to Member States;
- to identify questions for the longer term where scientific advice and support to Member States can be developed throughout the work plan for 2014.

Dr Pastore Celentano then presented the three areas of work and the corresponding working groups that would be meeting during the remainder of the morning.

Three areas for discussion and corresponding working groups:

- Scientific evidence base for using inactivated polio vaccine (IPV) vaccination in outbreak situations in the EU/EEA;
- EU scientific model for environmental surveillance reviewing the options;
- Scientific evidence to control poliovirus transmission among refugees from areas where poliovirus is circulating.

Each working group was chaired by an ECDC VPD team member. Prior to the meeting, a background document on each area had been prepared along with open questions to guide the discussions in the working group (see Annex 3). A rapporteur was identified within each group to present the outcome of discussions at the end of the morning.

The following is a summary of the discussions held in each working group. The defined open questions are also listed. The key conclusions and suggestions from each working group are set out in the conclusions section.

Working group 1: Scientific evidence base for using IPV vaccination in outbreak situations in the EU/EEA

Chairs: Paloma Carrillo-Santisteve and Pier Luigi Lopalco (ECDC)

Rapporteur: Dr Emilia Anis

Working group participants: Mircea Ioan Popa; Alenka Kraigher; Jose Navarro-Alonso; Daniel Levy-Bruhl; Willem Van Eden; Emilia Anis; Iwona Paradowska-Stankiewicz; Paloma Carrillo-Santisteve; Pier Luigi Lopalco; Piotr Kramarz.

Defined questions for discussion

- Can inactivated polio vaccine (IPV) be considered the first choice for outbreak response in the EU/EEA? If so:
 - Would it be the first choice in any scenario among those identified in the summary (See Annex 3)
 - Would it be the first choice if cases are asymptomatic (carriers)?
 - Would it be the first choice in the event of paralytic cases?
- If oral polio vaccine (OPV) should be used, the following questions arise:
 - What would be the public acceptance of OPV, especially in those countries where IPV has been always used?
 - Since IPV is the only vaccine available in most EU/EEA Member States, what is the procedure for obtaining access to OPV and/or mOPV if needed?
 - Are there regulatory aspects governing the use of mOPV in the absence of marketing authorisation?
- In an outbreak setting should a combined (IPV/OPV) full schedule be given to an unvaccinated population? Do we have any evidence of this from past experience (in terms how effective this measure is at stopping an outbreak?)

Summary of discussions

In the event of a re-emergence of WPV circulation in the EU, an urgent response should be implemented to stop virus circulation, prevent disease cases and maintain Europe's polio-free status.

In the EU/EEA Member States, a full IPV schedule is used for childhood routine immunisation, with the exception of Poland where a sequential IPV/OPV schedule is still in use. The use of the oral polio vaccine (OPV) should be discussed where there is evidence of WPV circulation.

The occurrence of a new polio case in the EU/EEA may give rise to a number of different scenarios, with a combination of the following variables:

Polio cases	Population where cases occur	Majority (>50%) vaccinated with	Vaccination coverage
One sporadic case	General population	IPV	Very high in the general population
One small cluster (household, closed community, etc.)	Vaccine-resistant communities	OPV	Sub-optimal in the general population
Cases spread throughout the community	Groups living in poor hygiene conditions		Very high but with pockets of susceptibility

Table 1. Possible variables in th	e event of a new	polio case appearin	g in the EU/EEA

The response to one sporadic case in the general population where hygiene standards are high and vaccination coverage is good could be different to a cluster reported in a low vaccinated community living in poor hygiene conditions, or an area with large pockets of susceptible individuals. Taking this into consideration, the group pointed out that it was important to make an accurate assessment at national level in order to inform the decision on the type of vaccine to be used in response to a polio threat.

Due to the high vaccine coverage and good hygiene standards, the group agreed that IPV is considered the first choice in most of the potential scenarios within the EU/EEA. Sporadic cases or small clusters in closed communities should not justify the use of OPV.

On the other hand, the group pointed out that OPV should be taken into consideration in case of evidence of widespread WPV circulation through environmental or epidemiological surveillance.

In order to trigger an operational plan that necessitates the use of OPV, the group advised that a threshold in terms of the number of positive sewage samples, positive stool samples, or geographical spread of samples, should be defined at the national level as part of the assessment carried out in the response plan. In general, the presence of acute flaccid paralysis (AFP) cases or of WPV in stool samples spread throughout the community or across a large geographical area could be a trigger for considering OPV use.

Should a response with OPV be initiated, safety aspects would have to be considered as a priority. The risk of vaccine associated paralytic poliomyelitis (VAPP) is close to zero when OPV is administered to someone previously vaccinated with IPV. OPV should be administered if there is evidence that at least one dose of IPV has been received in the past. If only one dose has been received in the past, the simultaneous administration of IPV and OPV could be taken into consideration. In the absence of evidence of any past vaccination, and if logistics permit, a full sequential (two IPV + two OPV doses) vaccination course should be administered. This should be carried out according to national guidelines, possibly applying an accelerated schedule, however the group agreed that two vaccine doses should not be given less than four weeks apart. Shorter intervals (no less than two weeks) between doses could be considered under special circumstances after risk-benefit evaluation.

The acceptability of OPV could be challenging, especially in a Member State with no experience of OPV use in the recent past, or in the absence of a visible threat in the media. A further challenge could arise where there is a manifestation of WPV circulation in sewage without evidence of paralytic cases. For this reason, the group agreed that communication should be an essential and integral part of national response plans. A strong consensus must be reached among all healthcare professionals involved on the policies to be implemented, in order to ensure that there is clear, consistent and transparent communication with the public. Partnerships with medical organisations, non-governmental organisations, universities and other relevant organisations have to be shown to be effective in order to improve public understanding and acceptance. In the case of targeted interventions to specific communities, local leaders should primarily be involved in communication and outreach to the public.

The availability of OPV and regulatory aspects for its use may represent a challenge in many EU/EEA countries. National stockpiles are not the best option for several practical reasons and due to the risk of global stocks becoming depleted. Rules for access to international stockpiles, via WHO/UNICEF, and regulatory aspects for domestic use of OPV should be part of the national response plan (i.e. procurement of OPV should occur through the official international procurement system with WHO/UNICEF).

Working group 2: EU scientific model for environmental surveillance - reviewing options

Chairs: Assimoula Economopoulou and Daniel Palm (ECDC)

Rapporteur: Tapani Hovi

Working group participants: Mika Salminen; Tapani Hovi; Harrie Van de Avoort; Jacob Moran-Gilad; Katherina Zakikhany; Assimoula Economopoulou; Daniel Palm; Lucia Pastore Celentano; Niklas Danielsson; Emma Huitric.

Defined questions for discussion

- Given the European Regional Commission for the Certification of the Eradication of Poliomyelitis (RCC) conclusions regarding polio surveillance in Europe, should environmental surveillance of poliovirus be promoted?
- Should EU countries implement environmental surveillance for specific groups (migrants, inadequately-vaccinated populations)?
- Is environmental surveillance of poliovirus, as a supplement to AFP surveillance, feasible in the EU, taking into account laboratory costs, expertise and existing guidelines?
- How should existing WHO guidelines be elaborated to help EU Member States initiate environmental surveillance (i.e. development of standards and indicators for environmental surveillance applicable across the EU)?

Summary of discussions

The group pointed out that each Member State needs to perform its own assessment of the risk for WPV introduction and circulation, and consequently assess the need to improve their overall polio surveillance system. Environmental surveillance is feasible and could serve as an early warning system for detecting reintroduction of poliovirus. The group suggested that ECDC could play an active role in coordinating exchange of action plans between Member States. To support capacity building, ECDC invited polio surveillance experts in the working group to discuss the opportunities for strengthening Member State polio surveillance systems, with special focus on environmental surveillance for the early detection of poliovirus circulation.

Given the RCC conclusions regarding polio surveillance in Europe, should environmental surveillance of polio be promoted?

During the discussions, the group agreed that each Member State needs to perform its own assessment of the risk for WPV introduction and circulation and to assess the need to improve their overall polio surveillance system. Whilst AFP surveillance is the gold standard, environmental surveillance could provide evidence for polio reintroduction at an earlier stage (as was the case recently in Israel) and thus serve as an early warning system.

Should EU countries implement environmental surveillance for specific groups?

As described in the WHO guidelines, environmental surveillance is likely to give the most informative results if targeting a population with sub-optimal AFP surveillance, having properties putting them at increased risk of poliovirus circulation (low vaccination coverage, evidence of recent circulation of the virus within the population or close contact with another population where the virus is circulating). Experience from a variety of surveillance approaches among the meeting participants indicated that when targeting a specific population group, environmental surveillance could be easier to conduct than enterovirus surveillance.

Is environmental surveillance of poliovirus, as a supplement to AFP surveillance, feasible in the EU, taking into account laboratory costs, expertise, and existing guidelines?

Environmental surveillance has shown itself to be feasible and effective as a supplement to AFP surveillance for polio. It was suggested that the use of molecular methods for environmental surveillance could reduce the laboratory costs, as it requires less specialisation and is more readily transferable and adoptable. The reference cell culture-based method would still need to be operated in parallel to confirm results, however this could be on a smaller scale. The group highlighted the fact that the cost for maintaining a comprehensive environmental surveillance system can be relatively high, given the need to perform repeated testing and practical constraints in setting up a surveillance system that covers different geographical areas. When planning to enhance national surveillance systems, decisions need to be based on whether increased effort in AFP surveillance is more cost-efficient than setting up environmental or other types of supplementary surveillance. It was re-iterated that Member States need to make their own risk assessments on the basis of these and other facts (vaccination status, polio circulation in vicinity, contact with population where poliovirus is circulating, etc.). Based on these assessments, Member States can decide if and how their surveillance systems need strengthening and, where implementation of environmental surveillance is an option, how to achieve this. Careful planning is required on how to respond to positive signals from environmental testing, especially if environmental signals are picked up before AFP cases become evident.

How should existing WHO guidelines be elaborated to help EU Member States initiate environmental surveillance?

Environmental surveillance is technically more complex than patient testing as conducted in AFP- or enterovirus surveillance. Experts in the group highlighted the fact that some laboratory methods for environmental testing can be standardised and validated, but the range of variables valid for a particular setting or sample-type complicates the production of guidelines covering all possible aspects. At present there is a lack of standardisation and quantitative and qualitative variants of many of the laboratory methods used for environmental testing. There are existing WHO guidelines for environmental testing from 2004, and these are currently under revision in collaboration with environmental surveillance experts and WHO. The group felt that ECDC did not need to develop separate guidelines for the EU countries, but could focus on areas not covered in existing polio surveillance guidelines, including:

- Further elaboration of details on conceivable scenarios in different situations and response action options, including environmental surveillance, in cooperation with WHO and Member States;
- Comparison of national preparedness plans and sharing of best practices on how to react in the event of poliovirus (wild-type or vaccine-derived) being detected;
- Support of training activities for environmental and other types of polio surveillance;
- Facilitating twinning arrangements for sample referral;
- Direct support of polio surveillance projects or informing the European Commission of the need for funding;
- Guidance on the interpretation of testing results and what kind of public health actions should be considered in response to positive or negative results, depending on the current situation. Actions chosen will depend on multiple situational details, such as the type of surveillance signals received as well as the type of virus detected (WPV, vaccine-derived poliovirus, Sabin, etc.).

Working group 3: Scientific evidence to control poliovirus transmission among refugees from areas where poliovirus is circulating

Chairs: Tarik Derrough and Elizabeth Bancroft (ECDC)

Rapporteur: Aura Timen

Working group participants: Anders Tegnell; Tammam Aloudat; Aura Timmen; Eran Kopel; Gregory Wallace; Tarik Derrough; Elizabeth Bancroft; Verena Kessler; Denis Coulombier; Peter Kreidl.

Defined questions for discussion

- Considering the current scenario of asymptomatic refugees coming to the border of an EU country, what public health measures should be taken upon entry?
- If a clinical case of polio is diagnosed in a refugee centre, what actions should be taken?
- If a clinical case of polio is diagnosed in a migrant or member of a family hosting a migrant from Syria, what actions should be taken?

Summary of discussions

Overall summary

Working Group 3 reviewed and discussed practical measures that would need to be considered by EU/EEA Member States to ensure a) that refugees displaced in EU/EEA countries are protected from poliomyelitis at point of entry or after entry, b) that the EU/EEA population in close contact with refugees, including host families, social and healthcare workers, is protected from poliomyelitis, and c) that cases are quickly identified and contained. The populations of interest included refugees/migrants from countries with circulating WPV or countries at risk of WPV outbreaks and those in contact with these populations.

Reaching a common understanding

The initial discussion in the working group focused on reaching a common understanding of why the polio situation in Syria needed appropriate response measures in the EU. It was acknowledged that EU/EEA countries have experience of welcoming refugees/migrants from geographical areas were polio is endemic. Unlike refugees coming from other parts of the world, Syrian refugees may require specific attention. Syria has a highly mobile population that may be entering the EU directly and thus there may not be an opportunity for immunisation prior to entry (e.g. in transit refugee camps or as part of an on-going large-scale polio immunisation campaign). Moreover, Syria is geographically close to the EU with a relatively short-transfer time.

As has been reported, the vaccination programme in Syria was discontinued in 2011. Prior to that date, a mixed OPV/IPV schedule was used and vaccination coverage was reported to be high. Therefore those at highest risk of

acquiring or transmitting polio will be children <5 years (those who have not received any polio vaccination or those that have not received a full course of vaccination).

The group also recognised that polio circulation/infection may not occur among Syrian refugees in the EU but among unvaccinated or under-served EU population groups. Therefore increasing coverage among the EU population is critical as well.

The discussion focused on the situation for Syrian refugees currently entering the EU in light of the political unrest in the area.

The group discussed the scenario of refugees arriving together in the EU/EEA who had not been through a migrant camp or did not have any documentation. In this scenario, the group highlighted that a top priority was ensuring the vaccination of all children under five years of age, unless the child had proof of vaccination. An unresolved question was the use of IPV versus OPV in this population for a variety of reasons including ease of administration, supplies and the risk associated with intramuscular injections during the polio incubation period. The need to consider administration of polio vaccination through the subcutaneous route was discussed. Host countries should ensure that the refugees have all age-appropriate vaccinations, according to the host country's immunisation schedule. All missed vaccinations should be considered, not just polio. The group did not recommend testing serology pre-vaccination.

The group suggested that all EU/EEA citizens who would be working with the high-risk populations should be fully immunised against polio. The group also pointed out that in light of the planned influx of refugees, all under-vaccinated populations in the EU/EEA host countries should be vaccinated.

The group assessed that the screening of stool samples for enterovirus/polio should not be recommended, for reasons of feasibility, lab capacity, stigmatisation and limited duration of shedding. However, systematic research into stool carriage, as part of an epidemiological study, may be considered in refugee camps to better define the populations at greatest risk of incubating and transmitting poliovirus, or developing polio.

The group agreed that enhanced clinical surveillance was needed for AFP and aseptic meningitis in the populations of interest. It also suggested that a pan-EU/EEA protocol should be developed to systematically test cases of aseptic meningitis for polio. Given that clinical surveillance of poliomyelitis is not very sensitive to identifying transmission of the virus, the group supported the use of environmental surveillance in areas where there is a high risk of polio transmission (e.g. refugee camps) or clinical disease (e.g. unvaccinated groups in host countries).

The group felt that the responses to a positive environmental sample or a clinical polio case may differ, depending on the population affected, number of positive samples/cases, vaccination status of the population, or other considerations. Protocols need to be developed for these situations.

Wrap-up session

Head of Surveillance and Response Support Unit (SRS), Dr Denis Coulombier, closed the meeting, thanking all the groups for their contributions and highlighting the need for the EU/EEA to be prepared to respond to a potential polio threat. He emphasised that the situation in the Middle East was unusual and of a larger scope than expected.

Dr Coulombier highlighted that the main scope of the expert consultation meeting had been to identify the needs and priorities (e.g. to strengthen surveillance systems for polio, enhance environmental and/or enterovirus surveillance if already in place and vaccinate pockets of susceptible individuals, refugees and asylum seekers). The meeting was essential in helping ECDC to further identify areas where it could provide evidence-based scientific advice in the areas of polio prevention and control in the EU/EEA. As a next step, ECDC would consider updating its two risk assessments and combining them in a single document with the risks and recommendations presented. ECDC would also continue to work and collaborate closely with its partners at the WHO Regional Office for Europe and the European Commission to ensure to joint efforts in the provision of guidance and support.

Conclusions and next steps

There were a number of important suggestions presented by the three working groups. In addition, many technical aspects were discussed which will be useful to ECDC as it continues to consider the three areas and provide scientific advice and guidance to Member States.

The following is a summary of the key considerations and suggestions presented by the three working groups.

Scientific evidence base for using IPV vaccination in outbreak situations in the EU/EEA:

- IPV is considered the first choice in most of the potential scenarios within the EU/EEA;
- In order to trigger an operational plan that necessitates the use of OPV, a national threshold should be defined in terms of number of positive sewage/stool samples, or geographical spread;
- Should a response with OPV be implemented, safety aspects have to be considered as a priority, and even then OPV should not be administered as a first dose.

EU scientific model for environmental surveillance - reviewing options:

- AFP surveillance remains the gold standard for national poliovirus surveillance. The setting up of any supplementary surveillance system (environmental and enterovirus surveillance) should be evaluated at national level based on cost, efficiency and risk of polio reintroduction into the country (considering factors such as vaccination status of the general population, presence of unvaccinated pockets, poliovirus circulation in the vicinity, frequent contact with populations where poliovirus is circulating, etc.).
- Environmental surveillance is feasible and should be considered as a supplement to national polio surveillance plans.
- The WHO guidelines for environmental testing are currently being revised and ECDC should not duplicate or develop separate guidelines.
- ECDC could assist with capacity-building of Member State polio surveillance systems by supporting training activities for environmental and other types of polio surveillance and by facilitating twinning arrangements for sample referral.
- ECDC could play an active role in coordinating the exchange of preparedness plans and the sharing of best practices for action if circulating poliovirus is detected.

Scientific evidence to control poliovirus transmission among refugees from areas where polio virus is circulating:

- Receiving/refugee centres should assess vaccination status and vaccinate all children under five years of age from high-risk countries (e.g. Syria) on arrival in the EU/EEA against polio and other childhood-preventable diseases (unless the child has proof of vaccination).
- There is no need for systematic stool sampling of asymptomatic individuals in receiving centres unless it is in a setting where a refugee camp/epidemiological study is being conducted.
- It would be useful to enhance AFP surveillance and surveillance of aseptic meningitis in refugee centres and to consider environmental surveillance in high-risk areas (e.g. where there is a large concentration of refugees from high-risk areas or a large concentration of unvaccinated individuals).
- Appropriate booster vaccines should be provided for all EU/EEA citizens who would be working with these high-risk populations.

Annex 1. List of participants

Country	Full Name	Organisation
Belgium	ТВС	European Commission
Finland	Mika SALMINEN	National Institute for Health and Welfare
Finland	Tapani HOVI	National Institute for Health and Welfare
France	Daniel LÉVY-BRUHL	Institute for Public Health Surveillance
Israel	Jacob MORAN-GILAD	
Israel	Emilia ANIS	
Israel	Eran KOPEL	
Netherlands	Willem VAN EDEN	University of Utrecht
Netherlands	Harry VAN DER AVOORT	National Institute for Public Health and the Environment
Netherlands	Tammam ALOUDAT	Médecins Sans Frontières/Artsen zonder Grenzen
Netherlands	Aura TIMEN	National Institute for Public Health and the Environment
Poland	Iwona PARADOWSKA-STANKIEWICZ	National Institute of Public Health - National Institute of Hygiene
Romania	Mircea Ioan POPA	'Carol Davila' University of Medicine and Pharmacy
Slovenia	Alenka KRAIGHER	National Institute of Public Health
Spain	José A. NAVARRO-ALONSO	Directorate of Health Murcia
Sweden	Anders TEGNELL	Swedish Institute for Communicable Disease Control
Sweden	Katherina ZAKIKHANY	Swedish Institute for Communicable Disease Control
USA	Gregory WALLACE	Centers for Disease Control and Prevention
	Pier Luigi LOPALCO	European Centre for Disease Prevention and Control
	Niklas DANIELSSON	European Centre for Disease Prevention and Control
	Piotr KRAMARZ	European Centre for Disease Prevention and Control
	Lucia PASTORE CELENTANO	European Centre for Disease Prevention and Control
	Tarik DERROUGH	European Centre for Disease Prevention and Control
	Paloma CARRILLO-SANTISTEVE	European Centre for Disease Prevention and Control
	Elizabeth BANCROFT	European Centre for Disease Prevention and Control
	Assimoula ECONOMOPOULOU	European Centre for Disease Prevention and Control
	Denis COULOMBIER	European Centre for Disease Prevention and Control
	Daniel PALM	European Centre for Disease Prevention and Control
	Peter KREIDL	European Centre for Disease Prevention and Control
		Laropean centre for Disease Frevention and Control

Annex 2. Agenda

European Scientific Consultation Group on Vaccination (EVAG) meeting and expert consultation on scientific evidence linked to polio virus in Israel and Syria

Radisson Waterfront Congress Centre

5 November 2013, Stockholm, Sweden

Tuesday, 5 November 2013, Room C1				
08:30–09:00	European Scientific Consultation Group on Vaccination (EVAG) - Closed meeting Revised agenda, EVAG members			
08:30-09:00	Welcome and introduction to the consultation Review and adoption of the revised terms of reference for EVAG	Lucia Pastore Celentano (Acting Head of VPD Programme) Niklas Danielsson (Senior Expert in Communicable Diseases)		
09:00–12:45	Expert consultation on scientific evidence linked to polio virus in Israel and Syria EVAG members and external experts			
09:00–09:30	Welcome and setting the scene: Poliovirus event in Israel: Epidemiology, surveillance, and lab analysis (10') Wild-type poliovirus 1 transmission in Israel - What is the risk to Europe? (10') Introduction to group work (5')	Piotr Kramarz (Deputy Chief Scientist) Emilia ANIS, Jacob MORAN-GILAD & Eran KOPEL (Israel) Emma Huitric (Programme Officer VPD) Lucia Pastore Celentano (Acting Head of VPD Programme)		
09:30-11:30	Working Groups – coffe	ġ ,		
	 WG 1 – Scientific evidence base for using IPV vaccination in outbreak situations in EU WG 2 – EU scientific model for environmental surveillance - reviewing options WG 3 – Scientific evidence to control poliovirus transmission among refugees from areas where polio virus is circulating 	Paloma Carrillo-Santisteve & Pier Luigi Lopalco (ECDC) Assimoula Economopoulou & Daniel Palm (ECDC) Tarik Derrough & Elizabeth Bancroft (ECDC)		
11:30–12:45	WG presentations and conclusions	WG rapporteurs Denis Coulombier (Head of Unit Surveillance and Response Support)		
12:45-13:30	Lunch - Level 4			

Annex 3. Working group summaries – background information

Working group 1 – Scientific evidence base for using IPV vaccination in outbreak situations in the EU

Background

Polio vaccines

Two types of polio vaccines, an oral live attenuated vaccine (OPV) and an inactivated vaccine (IPV) were developed in the 1950s [1,2]. Both vaccines contain the three poliovirus serotypes 1, 2 and 3 in combination, since all are needed to provide protection against the three wild-type polio virus strains. Advantages and disadvantages of both vaccines when used in response to a polio outbreak are summarised in Table 2.

For the elimination of polio, most EU/EEA Member States have relied upon the use of OPV. However, the risk of vaccine-associated paralytic polio (VAPP) among OPV vaccinees (estimated at one case in 750 000 children receiving their first dose of OPV), and the risk of outbreaks caused by vaccine-derived poliovirus (VDPV) strains have motivated all EU/EEA countries to change their polio vaccination schedules from OPV to either IPV-only schedules, or to combination schedules with IPV in the primary series, followed by a booster dose of OPV (see Table 3) [3-5]. Only one country in the EU/EEA, Poland, maintains a combined schedule with IPV in the primary series while providing OPV as a booster. The other Member States offer IPV-only schedules for routine immunisation of children. The number of doses in the primary series and when they are recommended, as well as number of booster doses and when they are recommended vary among EU/EEA Member States [6]. Poliovirus vaccines induce good immune responses. However, waning immunity occurs and the number of booster doses required to provide life-long protective immunity is currently unknown.

Three EU countries, Finland, the Netherlands and Sweden, have relied exclusively on IPV for polio elimination. In response to outbreaks following importation into Finland in 1984 and the Netherlands in 1992, OPV was offered as a control measure [3]. In Sweden, a single case of poliomyelitis (WPV2) occurred in 1977 in a two-year-old child. Excretion of polioviruses was documented in 25 unvaccinated close contacts of the child [4]. At this time, Sweden had reached close to 100% IPV vaccination uptake among children and a majority of adults had also been vaccinated. None of the vaccinated pre-school contacts of the two-year-old case was found to excrete virus and the OPV vaccination was not deployed to control this outbreak. Sweden is one of few countries that has never offered OPV to their population.

Herd immunity can be achieved through OPV-only, combined IPV/OPV or IPV-only schedules. Evidence of herd immunity with IPV was demonstrated in the US when IPV was introduced for routine use in 1955. The reduction in the number of cases observed exceeded expectations based on the number of children vaccinated [1]. Similarly, during the outbreaks in the Netherlands in 1978 and 1992, despite widespread circulation of the virus in communities refusing vaccination throughout the country, there was only one case of polio in other Dutch communities [1,7]. However, it is important to point out that the evidence for herd immunity with IPV vaccines comes from countries where oral-oral transmission was probably the dominant mode. It is less clear if IPV is able to induce herd immunity in countries where the faecal-to-oral route is thought to be the primary means of transmission [1].

Breakthrough infections following OPV vaccination after several doses (five to seven doses) in impoverished populations has mainly been reported from India [8,9]. Waning immunity has been documented in similar settings. Clinical experience with breakthrough infections following IPV-only schedules in European populations that travel extensively shows that the IPV-only schedules provide excellent protective immunity. However, there are no formal studies confirming this clinical observation. Many travel vaccine clinics provide a booster IPV dose for Europeans travelling outside Europe.

Table 2. Advantages and disadvantages of IPV vs. OPV for outbreak response

Attribute	OPV	IPV
VAPP	Rare	None
Other serious adverse events	None known	None known
Systemic immunity	High	High
Mucosal immunity	High	Lower in the intestinal tract
Secondary transmission of vaccine virus	Yes	No
Emergence of circulating vaccine-derived poliovirus	Yes	No
Public acceptance	Possibly reduced	Potentially higher
Stockpile availability	No	Some
Current cost	Low	Usually higher

IPV: inactivated poliovirus vaccine, OPV: oral poliovirus vaccine, VAPP: vaccine-associated paralytic poliomyelitis.

Vaccination coverage in the EU/EEA

Vaccination coverage levels in the EU/EEA can be considered satisfactory as a whole (>90% for three doses of either IPV or OPV) and can largely justify the absence of disease in the region.

It is estimated that in the EU/EEA almost 70 million people in the age group 0–29 years can be considered OPVnaïve. This population represents a potentially large reservoir for the sustainment of wild poliovirus circulation in the event that polio is re-introduced into the environment.

Moreover, in the EU/EEA there are significantly large pockets of population sub-groups that are under-immunised or not immunised at all. Low immunisation levels can be identified in selected population groups (travelling communities, disadvantaged groups, those opposed to vaccine due to religious or philosophical beliefs) but also in the general population in many areas of the EU/EEA. According to a recent survey under the EVACO project (data not published)¹, low vaccination coverage areas (<90%) can also be detected in countries reporting satisfactory immunisation rates at national level (personal communication VENICE consortium, unpublished data). Lack of immunity in such population sub-groups represents a potential risk for symptomatic polio cases in the event of widespread circulation of the wild virus in the environment.

Poliovirus shedding in IPV and OPV vaccinated

Several studies discussed below have shown the effect of IPV-vaccination on poliovirus excretion following OPV-vaccination (OPV challenge studies) or natural exposure.

A recent review identified and assessed 66 OPV challenge studies, including five on IPV-only vaccinated individuals (≥3 doses) [10]. Overall, the moderate grade evidence, as assessed in the review, suggested that there is no significant effect of IPV on susceptibility to polio infection. Studies included on the duration of faecal excretion showed that the longest excretion time was among fully susceptible individuals, with a similar or slightly shorter excretion time among IPV recipients, and the shortest average duration among OPV vaccinees. The concentration of virus excreted in faeces of IPV-only recipients was lower than in fully susceptible individuals, but higher than in OPV vaccinees. In summary, IPV displayed a limited effect on susceptibility to viral exposure, and a moderate effect on the duration and concentration of excretion. Additionally, the authors reviewed the duration and concentration of oropharyngeal excretion. The weight of evidence was graded as low; however the evidence suggested a very low probability of oropharyngeal excretion for any type of immune individual, regardless of whether they had been vaccinated with IPV or OPV.

Another systematic review from 2012 assessing poliovirus shedding in stools or nasopharyngeal secretions after an OPV challenge [11] showed that, compared with unvaccinated individuals, those who were IPV-vaccinated had no protection from viral shedding, suggesting no significant protection from infection. Furthermore, when IPV was given in addition to OPV and individuals compared to those who were OPV-only vaccinated, the IPV-vaccinated individuals had no protection from viral shedding. The authors acknowledged that the impact of IPV vaccination itself on poliovirus transmission is unknown in countries where faecal-oral spread is common but this impact is likely to be limited when compared with OPV.

¹ EVACO: European Vaccine Coverage project. ECDC/VENICE

A limitation on all OPV challenge studies is that natural exposure to polioviruses may involve different amounts of ingested virus (generally lower) and different media (e.g. contaminated water, food, aerosol droplets) which could have an impact on the probability of infection or on the probability, duration and concentration of excretion, as has been indicated in published studies [10]. Another limitation is that a substantial number of the OPV challenge studies were performed using the original IPV vaccines, and results cannot be extrapolated to the new, enhanced IPV vaccines.

Until recently, OPV was the only vaccine used in Mexico. A study in the US, in an area close to the Mexican border [12], assessed the circulation of polio virus in an IPV-vaccinated population constantly challenged with an OPV immunised population. All 664 children and 22 sewage samples were found negative, showing that the risk of circulating vaccine-derived poliovirus (VDPV) is low among fully IPV-immunised populations in countries with similar structures and resources that border OPV-vaccinated populations.

Several VDPV findings have been reported so far from different EU/EEA countries and neighbouring regions [13]. A study in Switzerland revealed continuous introduction of poliovirus into the sewage system [14], however there was little evidence that these viruses had established long-term circulation in the community. High standards of hygiene possibly prevented the more efficient route of faecal-oral transmission, only permitting the less efficient route of oral-oral transmission. Research on the contribution of hygiene towards breaking the chain of poliovirus transmission to family contacts has also been published elsewhere [15].

In summary, a switch from OPV to IPV could potentially result in a situation where it might be possible to transmit OPV-derived viruses from chronically-infected persons or imported locations. However, several studies provide evidence to dispel this suspicion [16]. Additionally, many countries that have been using IPV-only for several years have not found any signs of emerging transmission of OPV-related virus in their routine AFP, environmental surveillance or via passive case notification. Therefore, all available information supports the idea that it is safe to switch from OPV to IPV in countries with high immunisation coverage [16].

There are still several areas of uncertainty with regard to poliovirus immunity and transmission. As described in a recent review by Duintjer Tebbens RJ et al. [17], key topics requiring further research that would help in the understanding of polio immunity are:

- the ability of IPV-induced immunity to prevent or reduce excretion and affect transmission;
- · the impact of waning immunity on the probability and extent of poliovirus excretion;
- the relationship between virus excretion and ability to transmit, and
- the relative role of faecal-oral versus oropharyngeal transmission.

Table 3. IPV cohorts in the EU/EEA

Country	Schedule	Birth cohorts full IPV
Austria	Full IPV 1999	1999–2013
Belgium	Full IPV from 2001	2001–2013
Bulgaria	Primary IPV from 2010	2010–2013
Cyprus	Full IPV from 1/8/2002	2002–2013
Czech Republic	Full IPV from 2007	2007–2013
Denmark	Always full IPV	All
Estonia	Full IPV from 2008	2008–2013
Finland	Always full IPV	All
France	95% of vaccinations are IPV since 1990	1990–2013
Germany	Full IPV from 1998	1998–2013
Greece	Full IPV from 2005	2005–2013
Hungary	Full IPV from 2006	2006–2013
Iceland	Always full IPV	All
Ireland	Full IPV from 2001	2001–2013
Italy	Full IPV from 2002	2002–2013
Latvia	Full IPV from 1/1/2010; previously, OPV booster at 18 months	2009–2013
Liechtenstein		
Lithuania	One booster OPV given at least until 2004	2005–2013 ?
Luxembourg	Full IPV at least from 2006	2006-2013 ?
Malta	Full IPV from 1/1/2010;	2010–2013
Netherlands	Always full IPV (OPV used in outbreak situations)	All
Norway	Always full IPV	All
Poland	OPV booster given at six years	2008–2013
Portugal	Full IPV from 2006	2006–2013
Romania	Full IPV from 2008	2008-2013
Slovakia	Full IPV from 2005	2005–2013
Slovenia	Full IPV from 2003	2003–2013
Spain	Full IPV at least from 2006	2006–2013?
Sweden	Always full IPV	All
United Kingdom	Full IPV from 2004	2004–2013

Operational plans in response to a polio outbreak in the EU/EEA

According to a report from the 27th meeting of the European Regional Certification Commission for Poliomyelitis Eradication (RCC), many, but not all EU/EEA countries have established national certification committees providing annual reports to the RCC [18]. The RCC requests the development of national preparedness plans and organised exercises to test these plans. According to the report, there are EU/EEA Member States that can improve their activities in this area. The RCC also noted that in some countries the continuity of polio vaccination programmes has been compromised by procurement problems and issues related to national immunisation schedules and has recommended improvement where needed. WHO EURO aims to work closely with affected countries in the coming years to improve vaccine availability for routine immunisation programmes.

When deciding on the vaccine to be used in response to an outbreak of wild-type polio virus circulation, there are three options: IPV, monovalent OPV (mOPV) of the outbreak type or bivalent OPV (bOPV). IPV avoids the risk of VAPP or circulation of VDPV associated with oral polio vaccines but there are questions about the effectiveness of IPV in stopping circulation. Finland and the Netherlands, two countries that have always used IPV for routine immunisation, both opted for OPV vaccination campaigns in order to stop poliovirus circulation in their populations.

Current WHO guidance on responding to a polio outbreak states that prudent preparedness to respond to a polio outbreak requires a stockpile of monovalent OPV and that UNICEF would maintain the ownership of the international stockpile to ensure universal access and rational use [19]. However, maintenance of national vaccine stockpiles may also be considered.

In order to assess the availability of and access to OPV for use in outbreak control measures, EMA (the European Medicines Agency) and ECDC conducted a joint rapid survey through their official contact points in the EU/EEA Member States (see Table 4).

With the aim of gaining a rapid overview of on-going surveillance activities and the availability of operational plans for polio virus outbreaks in EU/EEA countries, ECDC made a rapid inquiry through the EPIS-VPD platform, specifically asking about the availability of routine environmental surveillance for polioviruses; routine surveillance for human enteroviruses, availability of IPV stockpiles and updated outbreak control plans (contingency plans) for poliovirus outbreaks. Thirteen Member States reported having an updated outbreak control plan for poliovirus outbreaks and five having IPV stockpiles for outbreak control (see Table 4).

Table 4. Availability of oral and inactivated polio vaccines for use in outbreak control and outbreak control plans among EU/EEA Member States

Country	Valid marketing authorisation for OPV? ^(*)	Products and manufacturers ^(*)	Stockpiles of OPV for use in outbreak control? ^(*)	Stockpiles of IPV for use in outbreak control? ^(**)	Is there an updated outbreak control plan (contingency plan) for poliovirus outbreaks? ^(**)
Austria	No	n.a.	No		
Belgium	Yes	n.a. [#]	No		
Bulgaria	Yes	topv (GSK)	No	Yes (limited)	Yes
Croatia	No	n.a.	No	No	Yes
Cyprus	No	n.a.	No		
Czech Rep.	No	n.a.	No		
Denmark	No	n.a.	No	Yes	Yes
Estonia	No	n.a.	No	No	n.a.
Finland	No	n.a.	No	Yes (limited)	Yes
France	Yes	tOPV (Sanofi Pasteur) [#]	No	No	Yes
Germany	Yes	topv (gsk)	No	No	Yes
Greece	Yes	tOPV (Pasteur Merrieux)	No	Yes	Yes
Hungary	No	n.a.	No		
Iceland				n.a.	n.a.
Ireland	No	n.a.	No	Yes (limited)	Yes
Italy	Yes [§]	tOPV (Novartis) bOPV (Novartis) mOPV1 (Novartis) mOPV3 (Novartis)	No		
Latvia	No	n.a.	No	No	Yes
Lithuania	No	n.a.	No		
Luxembourg					
Malta	No [±]	n.a. [±]	No [±]	No	Yes
Netherlands	No	n.a.	No		
Norway	No	n.a.	No		
Poland	Yes	topv (gsk)	No		
Portugal	No	n.a.	No	No	Yes
Romania	No	n.a.	No	No	Yes
Slovenia	No	n.a.	No		
Slovakia	No	n.a.	No		
Spain	Yes	topv (gsk)	No	No	Yes
Sweden	No	n.a.	No		
UK	No	n.a.	No		

* Source: ECDC and EMA joint rapid survey of EMA official contact points ** Source: ECDC EPIS-platform urgent inquiry

§ Novartis holds marketing authorisation for four OPV products in Italy but none of the products are marketed in Italy or elsewhere in the EU.

± Reply received through the EPIS platform urgent inquiry

n.a. = not applicable, mOPV=monovalent oral polio vaccine, bOPV=bivalent oral polio vaccine (type 1 and 3), tOPV=trivalent oral polio vaccine

These countries have production of mOPV and bOPV for global use (personal communication).

In the survey carried out through the EPIS platform urgent inquiry, several countries indicated that IPV would be the vaccine used in case of an outbreak due to the fact that OPV is not licensed in the country and that there are no stockpiles available.

As an example, in the UK, if a case of poliomyelitis (suspected or confirmed) is reported, IPV-containing vaccine should be administered to household contacts immediately to prevent on-going transmission. IPV-containing vaccine may also need to be given immediately, after a case of paralytic poliomyelitis from wild virus, to other individuals in the neighbourhood, regardless of their previous history of immunisation against poliomyelitis. In the event of a larger outbreak, it may be necessary to consider the use of the appropriate monovalent-OPV (m-OPV)[20].

In Spain, if a case of poliovirus infection is reported (with or without paralysis), vaccination is recommended to all contacts with no vaccination or unknown status. The recommended vaccine is IPV, unless the characteristics of the outbreak demand the use of OPV/mOPV. If the case of poliomyelitis is confirmed, all contacts (regardless of vaccination status) should receive two doses of IPV one month apart [21].

Outside the EU/EEA, Australia faced importation of a wild poliovirus infection in Melbourne in July 2007. Australia began exclusive use of inactivated polio vaccine (IPV) in place of the Sabin oral polio vaccine on 1 November 2005. In this event, all contacts were offered a single booster dose of IPV, regardless of previous poliomyelitis vaccination history. Contacts who could not provide evidence of vaccination or a booster dose within the last 10 years, as per the Australian immunisation guidelines, were requested to provide two faecal specimens, at least 24 hours apart, for virus culture. Additionally, following confirmation of the case of poliomyelitis, contacts were grouped as follows: 1) close contacts who resided with or visited the index patient's residence, 2) fellow passengers on the airplane from Bangkok to Melbourne, 3) public contacts and staff at the general practitioner's clinic, and 4) public contacts and healthcare workers (HCWs) at the hospital [22].

Problem outline

Many different scenarios may arise in the event of a new polio case appearing in the EU/EEA, as a combination of the following variables:

Polio cases	Population where cases occur	Majority (>50%) vaccinated with
One sporadic case	General population	IPV
One small cluster (household, closed community, etc.)	Vaccine-resistant communities	OPV
Cases spread in the community	Groups living in poor hygiene conditions	

Table 5. Possible variables in the event of a new polio case appearing in the EU/EEA

Open questions and knowledge gaps

- Can IPV be considered the first choice for outbreak response in the EU/EEA? If so:
 - Would it be the first choice in any scenario among those identified above?
 - Would it be the first choice if cases are asymptomatic (carriers)?
 - Would it be the first choice in the event of paralytic cases?
- If OPV should be used, the following questions arise:
 - What would be the public acceptance of OPV, especially in those countries where IPV has been always used?
 - Since IPV is the only vaccine available in most EU/EEA Member States, what is the procedure for obtaining access to OPV and/or mOPV if needed?
 - Are there regulatory aspects governing the use of mOPV in the absence of marketing authorisation?
- In an outbreak setting, should a combined (IPV/OPV) full schedule be given to an unvaccinated population? Do we have any evidence of this from past experience (in terms of how effective this measure is at stopping an outbreak?)

References (working group 1)

- 1. Plotkin S. Poliovirus vaccine-inactivated. Vaccines. [St. Louis, Mo.]: Elsevier Saunders; 2013. p. 573-97.
- 2. Plotkin S. Poliovirus vaccine-live. Vaccines. [St. Louis, Mo.]: Elsevier Saunders; 2013. p. 598-645.
- 3. Hovi T, Huovilainen A, Kuronen T. Outbreak of paralytic poliomyelitis in Finland: Widespread circulation of antigenically altered poliovirus type 3 in a vaccinated population. Lancet. 1986;1(8495):1427-32.
- 4. Bottiger M. Experiences of vaccination with inactivated poliovirus vaccine and epidemiology round a single case of polio in 1977 in Sweden. Dev Biol Stand. 1978;41:133-6. PubMed PMID: 223905.
- Poliomyelitis prevention in the United States: Introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recommendations and Reports: Morbidity and Mortality Weekly Report. Recommendations and reports. Centers for Disease Control. 24 January 1997; 46(RR-3):1-25. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/00046568.htm.
- 6. European Centre for Disease Prevention and Control. Vaccine schedule 2013. Available at: <u>http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx</u>.
- Oostvogel PM, van Wijngaarden JK, van der Avoort HG, Mulders MN, Conyn-van Spaendonck MA, Rumke HC, et al. Poliomyelitis outbreak in an unvaccinated community in the Netherlands, 1992-93. Lancet. 1994 Sep 3;344(8923):665-70. PubMed PMID: 7915354.
- 8. Sein C. Evaluating surveillance indicators supporting the Global Polio Eradication Initiative, 2011-2012. Morbidity and Mortality Weekly Report. 2013;62(14):270-4.
- 9. Grassly NC, Jafari H, Bahl S, Sethi R, Deshpande JM, Wolff C, et al. Waning intestinal immunity after vaccination with oral poliovirus vaccines in India. Journal of Infectious Diseases. 2012;205(10):1554-61.
- Duintjer Tebbens RJ, Pallansch MA, Chumakov KM, Halsey NA, Hovi T, Minor PD, et al. Expert review on poliovirus immunity and transmission. Risk analysis: an official publication of the Society for Risk Analysis. 2013 Apr;33(4):544-605. PubMed PMID: 22804479.
- 11. Hird TR, Grassly NC. Systematic review of mucosal immunity induced by oral and inactivated poliovirus vaccines against virus shedding following oral poliovirus challenge. PLoS Pathogens. 2012;8(4).
- Gary HE, Jr., Smith B, Jenks J, Ruiz J, Sessions W, Vinje J, et al. Failure to detect infection by oral polio vaccine virus following natural exposure among inactivated polio vaccine recipients. Epidemiology and infection. 2008 Feb;136(2):180-3. PubMed PMID: 17376256.
- 13. Risk assessment from ECDC on the finding of vaccine-derived polio virus in Finland. 17 February 2009. Stockholm: ECDC; 2009. Available at: http://ecdc.europa.eu/en/healthtopics/Documents/1528_090217_risk_assessment_polio.pdf
- Zurbriggen S, Tobler K, Abril C, Diedrich S, Ackermann M, Pallansch MA, et al. Isolation of Sabin-like polioviruses from wastewater in a country using inactivated polio vaccine. Applied and Environmental Microbiology. 2008 Sep;74(18):5608-14. PubMed PMID: 18641161.
- 15. Swartz TA, Green MS, Handscher R, Sofer D, Cohen-Dar M, Shohat T, et al. Intestinal immunity following a combined enhanced inactivated polio vaccine/oral polio vaccine programme in Israel. Vaccine. 2008 Feb 20;26(8):1083-90. PubMed PMID: 18241962.
- 16. Hovi T, Shulman LM, van der Avoort H, Deshpande J, Roivainen M, De Gourville EM. Role of environmental poliovirus surveillance in global polio eradication and beyond. Epidemiol. Infect. 2012 Jan;140(1):1-13. PubMed PMID: 21849095.
- 17. Duintjer Tebbens RJ, Pallansch MA, Chumakov KM, Halsey NA, Hovi T, Minor PD, et al. Review and assessment of poliovirus immunity and transmission: Synthesis of knowledge gaps and identification of research needs. Risk analysis: an official publication of the Society for Risk Analysis. 2013 Apr;33(4):606-46. PubMed PMID: 23550968.
- 18. World Health Organization. Report of the 27th meeting of the European Regional Certification Commission for Poliomyelitis Eradication: Copenhagen, Denmark 30–31 May, 2013: WHO Regional Office for Europe; 2013. Available from: <u>http://www.euro.who.int/______data/assets/pdf__file/0016/200752/Report-of-the-27th-Meeting-of-the-European-Regional-Certification-Commission-for-Poliomyelitis-Eradication.pdf</u>.
- 19.
 Global Polio Eradication Initiative. Responding to a polio outbreak: Guidelines 2011. Available from:

 http://www.polioeradication.org/Portals/0/Document/Resources/PolioEradicators/1a.PolioOutbreakGuideline20110107.pdf.
- Public Health England. Management of susceptible cases and outbreaks. In "Green Book". Chapter 26. Poliomyelitis January 2013:326. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/148141/Green-Book-Chapter-26-Polio-
- updated-18-January-2013.pdf.
 21. Red Nacional de Vigilancia Epidemiologica. Protocolo de vigilancia y alerta de poliomielitis y PFA (article in Spanish) December 2011:13. Available at: http://www.juntadeandalucia.es/salud/export/sites/csalud/galerias/documentos/production-p
- 22. Carnie JA, Lester R, Moran R, Brown L, Meagher J, Roberts JA, et al. Public health response to imported case of poliomyelitis. Australia, 2007. Available at: <u>http://wwwnc.cdc.gov/eid/article/15/11/09-0027.htm</u>.

Working group 2. EU scientific model for environmental surveillance- reviewing options

Background

Suspected outbreak of poliomyelitis in Syria, October 2013

On 19 October 2013, WHO announced a 'hot' cluster of AFP in Deir Al Zour province in Syria, located 250 km from Damascus in the east of the country along the Iraqi border. The cluster consisted of 22 cases and the age distribution was five cases under one year old, 13 cases one-to-two years old and four cases over two years old [1]. The first cases were detected in early October. Initial tests by the national reference laboratory in Damascus indicated wild poliovirus in two cases. On 29 October, WHO confirmed isolation of wild poliovirus type 1 (WPV1) from ten of the cases under investigation. WHO also concluded that the risk of further international spread of poliovirus 1 in the region was considered to be high, given the current situation in Syria, the frequent population movements and subnational immunity gaps in the area.

Wild-type poliovirus 1 transmission in Israel, February-August 2013

WPV1 was first isolated from sewage samples collected on 9 April 2013 in Rahat, southern Israel. The isolated strain is related to strains circulating in Pakistan and to the strain detected in sewage in Cairo in December 2012. It is unrelated to the strain currently affecting the Horn of Africa. WPV1 has been detected in a total of 91 sewage samples from 27 sampling sites in southern and central Israel, collected between 3 February and 25 August 2013 [2]. In addition, WPV1 has been isolated in stool samples from 42 people (4.4% of the sampled population) tested in the area [3]. Detailed information about the carriers is missing but all the 42 cases are reported to have been vaccinated with IPV-only schedules, according to Israeli national recommendations (personal communication). No cases of paralytic poliomyelitis have been reported. This event is significant as it is the first record of widespread wild polio virus circulation with, to date, no identified cases of clinical disease.

Surveillance of polio

AFP surveillance

Acute flaccid paralysis (AFP) surveillance is the gold standard for surveillance in the polio eradication initiative [4]. The system is based on systematic, laboratory-based investigation and reporting of all AFP cases that occur at predictable rates in a population. AFP surveillance can work well in areas with limited resources and a high level of polio; for example, the current situation in Syria was detected by AFP surveillance. However, since the polio virus only causes clinical illness in approximately 1/100–1/1 000 persons infected, AFP surveillance is a blunt surveillance tool because the virus may have been transmitting quite widely in a community before clinical cases are detected. This is especially true in IPV-immunised populations; IPV recipients are protected from polio disease but not from intestinal reinfection by poliovirus.

Enterovirus surveillance

Enteroviruses cause a wide range of illnesses, including respiratory symptoms, exanthems and aseptic meningitis. Polioviruses (three serotypes) are just one minor group among of many known enteroviruses (of more than 100 types). Many clinical laboratories may only have the ability to identify enteroviruses as a 'generic' group and lack the ability to differentiate between types of enterovirus (polioviruses, echoviruses, Coxsackie viruses, etc.). Surveillance to monitor trends in circulating enteroviruses is in some countries a supplementary or significant part of the poliovirus surveillance system.

Environmental surveillance

Infected persons may shed polioviruses in their faeces for many weeks and these can be identified in sewage samples. Since poliovirus can circulate widely without causing symptoms, especially in IPV-immunised populations, environmental sampling may identify a circulating virus (wild-type, vaccine strains, or vaccine-derived polio) long before the first case of clinical disease. Environmental surveillance may be quite sensitive and able to identify low levels of viral shedding [7,8], but requires significant investment in laboratory resources and personnel. WHO states that environmental surveillance should be considered for selected populations where deficiencies in AFP surveillance are suspected and where conditions exist that render the population at risk of poliovirus circulation [6]. These include inadequate immunisation coverage, evidence of recent circulation of wild poliovirus and perceived risk of importation of wild poliovirus via cross border connection or other type of connection with populations demonstrating evidence of current poliovirus transmission.

There are guidelines for the detection of polio in sewage samples, however many parameters must be considered in environmental sampling and the guidelines are not exhaustive [6].

Current application of supplementary surveillance

Ten EU/EEA countries electing not to use AFP surveillance use supplementary surveillance for enteroviruses, environmental samples (primarily sewage), or a combination to detect polio (other AFP surveillance countries may also use some combination of supplementary surveillance). There are at least eight EU/EEA Member States using environmental surveillance and seventeen using enterovirus surveillance (see table below [9]).

Country	Environmental surveillance for polioviruses in place	Enterovirus surveillance for polioviruses in place
Bulgaria	No	Yes
Croatia	No	Yes
Denmark	No	Yes
Estonia	Yes	Yes
Finland	Yes	Yes
France	Yes	Yes
Germany	No	Yes
Greece	Yes	Yes
Iceland	n.a	Yes
Italy	Yes	n.a
Ireland	No	Yes
Lithuania	Yes	Yes
Latvia	Yes	Yes
Portugal	No	Yes
Romania	Yes	No
Slovakia	n.a	Yes
Slovenia	n.a	Yes
Spain	No	Yes
UK	n.a	Yes

Table 6. Environmental and enterovirus surveillance for poliovirus in EU/EEA countries

Assessment and recommendations for the polio surveillance system within the EU

The European Regional Certification Commission for Poliomyelitis Eradication (RCC)

The RCC uses several criteria to assess the annual performance of poliovirus surveillance. These include a health services criterion; the AFP index; timeliness of AFP reporting and the use of supplementary surveillance (enterovirus and/or environmental sampling). All RCC criteria are evaluated together to generate a summary score of the surveillance quality. According to the RCC, in 2012 two of the 30 EU/EEA Member States were assessed as having 'high' quality surveillance; 12 had 'good'; 15 had 'average'; and one had 'low' quality surveillance [5]. The RCC expressed concern over the sub-optimal state of surveillance in many countries, including the low level of AFP surveillance and the lack of detailed information on how supplementary surveillance had been conducted. The latest RCC report also concludes that for countries which consistently fail to maintain high-quality AFP surveillance and environmental surveillance. The RCC specifically highlighted the need for a standardised, comparable approach to supplementary surveillance and highlighted the on-going work at WHO and CDC to produce such guidelines [5].

ECDC risk assessments

In its risk assessment 'Wild type polio virus 1 transmission in Israel – what is the risk for the EU?' ECDC stresses the need to strengthen environmental, enterovirus and other types of supplementary surveillance for polio [9]. Member States with pockets of unvaccinated individuals should consider strengthening or establishing environmental and enterovirus surveillance in these areas, as a complement to AFP surveillance. The risk assessment also concludes that the role of environmental and enterovirus surveillance should be further discussed at the EU/EEA-level with a view to agreeing on common standards and indicators. In addition, ECDC, the Member States and EU agencies working in the area of environmental health should, in close collaboration with WHO, engage in the development of guidance for the establishment of environmental and enterovirus surveillance [9].

Existing guidelines for environmental surveillance

The AFP-based surveillance system for poliovirus is well defined and includes standards and indicators for assessment and interpretation. The WHO document 'Guidelines for environmental surveillance of poliovirus circulation' [6] includes detailed information on the collection of environmental samples, but limited information on how to incorporate environmental testing into a high-quality surveillance system. There are currently no published standards providing benchmarks for setting up or evaluating environmental testing. New guidelines on enterovirus and environmental surveillance are anticipated from WHO towards the end of 2013/early 2014 and these may include benchmarks to help Member States standardise and improve comparability of supplementary surveillance [5].

As proposed in its risk assessment following the detection of environmental polioviruses in Israel, ECDC wants to explore whether contributions can be made to developing guidance for environmental and enterovirus surveillance in the EU [9]. The decision as to whether to contribute to any such guidance is dependent on the polio situation in Israel and Syria and the scope, timeliness and EU suitability of upcoming WHO guidelines (i.e. are the guidelines suited to an area that is relatively well-resourced, has high IPV coverage and is free of endemic polio?)

In a review article, Hovi et al. outline a set of strategic and technical aspects to consider when planning to supplement polio surveillance with environmental testing [7]. These aspects include, but are not limited to:

- Feasibility in terms of cost and resources
- Selection of sampling site (sensitivity of testing influenced by method sensitivity, number of people in catchment area and frequency of testing)
- Optimisation of sample collection schedules
- Detection of virus in complex mixtures
- Standardisation and quality assurance of environmental sampling.

Questions to this working group

The list of questions relating to the setting up of environmental surveillance within EU that will be discussed during the meeting on 5 November include:

- Given the RCC conclusions regarding polio surveillance in Europe, should environmental surveillance of poliovirus be promoted?
- Should EU countries implement environmental surveillance for specific groups (migrants, inadequately-vaccinated populations)?
- Is environmental surveillance for poliovirus, as a supplement to AFP surveillance, feasible in the EU, taking into account laboratory costs, expertise, and existing guidelines?
- How should existing WHO guidelines be elaborated to help EU Member States initiate environmental surveillance (i.e. development of standards and indicators for environmental surveillance applicable across the EU)?

References (working group 2)

- 1. WHO. Global Alert and Response. Disease outbreak news: Report of suspected polio cases in the Syrian Arab Republic 2013 [cited 2013 19 October]. Available at: <u>http://www.who.int/csr/don/2013_10_19_polio/en/index.html</u>.
- 2. Global Polio Eradication Initiative. Polio this week: 28 August 2013 [cited 3 September 2013]. Available at: http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx.
- 3. State of Israel: Ministry of Health. Polio update August 18, 2013 [cited 17 September 2013]. Available at: http://www.health.gov.il/English/News and Events/Spokespersons Messages/Pages/18082013 2.aspx.
- 4. World Health Organization. Department of Immunization, Vaccines and Biologicals. Polio Laboratory Manual. Geneva: WHO; 2004. Available at: <u>http://whqlibdoc.who.int/hq/2004/WHO_IVB_04.10.pdf</u>
- WHO. Report of the 27th meeting of the European Regional Certification Commission for Poliomyelitis Eradication: Copenhagen, Denmark 30–31 May, 2013: WHO Regional Office for Europe; 2013. Available at: <u>http://www.euro.who.int/__data/assets/pdf_file/0016/200752/Report-of-the-27th-Meeting-of-the-European-Regional-Certification-Commission-for-Poliomyelitis-Eradication.pdf</u>.
- 6. World Health Organization. Department of Vaccines and Other Biologicals. Guidelines for environmental surveillance of poliovirus circulation. Geneva: WHO; 2003. Available at: http://whglibdoc.who.int/hg/2003/WHO_V&B_03.03.pdf.
- 7. Hovi T, Shulman LM, van der Avoort H, Deshpande J, Roivainen M, De Gourville EM. Role of environmental poliovirus surveillance in global polio eradication and beyond. Epidemiol. Infect. 2012 Jan;140(1):1-13.
- 8. Lodder WJ, Buisman AM, Rutjes SA, Heijne JC, Teunis PF, de Roda Husman AM. Feasibility of quantitative environmental surveillance in poliovirus eradication strategies. Appl. Environ. Microbiol. 2012 Jun;78(11):3800-5.
- European Centre for Disease Prevention and Control. Wild-type poliovirus 1 transmission in Israel what is the risk to the EU/EEA? Stockholm: ECDC; 2013. Available at: <u>http://ecdc.europa.eu/en/publications/Publications/Publications/polio-risk-assessment-transmission-in-Israel.pdf</u>
- 10. European Centre for Disease Prevention and Control. Rapid Risk Assessment on suspected polio cases in Syria and the risk to the EU/EEA Stockholm: ECDC; 2013. Available from: http://ecdc.europa.eu/en/publications/Publications/RRA%20poliomyelitis%20Syria%2021%2010%202013.pdf

Working group 3 – Scientific evidence to control poliovirus transmission in the EU/EEA among refugees from areas where polio virus is circulating

Background

The cluster of acute flaccid paralysis (AFP) due to poliovirus in Deir Al Zour, Syria represents another possible source of infection and importation of wild poliovirus to the EU/EEA (Member States). Syrian refugees and migrants are being welcomed into the EU/EEA in light of the political unrest in the area. The risk of continued transmission among refugees and re-introduction of poliovirus into Member States is not negligible. Suboptimal poliovirus surveillance and the presence of large pockets of poliovirus-susceptible EU citizens is another challenge for Member States. EU Member States receiving refugees and asylum seekers from Syria or any other area with WPV transmission should have adapted guidance to ensure that refugees have their vaccination status assessed on arrival. They should also have adequate supplies of polio vaccination for the refugees and should have developed surveillance and response systems to detect and respond to a case of polio.

Purpose of working group 3

The purpose of this working group will be to review, appraise and agree on the best scientific evidence in relation to practical measures that would need to be considered by EU Member States. These measures would ensure:

- that refugees displaced in EU countries are protected from poliomyelitis at point of entry or after entry;
- that the EU population in close contact with refugees including host families, social and healthcare workers are protected from poliomyelitis;
- that cases are quickly identified and contained in the event of:
 - the confirmation of WPV circulation in the environment
 - the identification of clinical poliomyelitis cases among refugees and/or EU citizens.

Methodology

- Review of national, international and NGO guidance documents
- Examination of vaccination schedules in EU/EEA countries
- Review of publications
- Conducting interviews of experts.

Populations of interest

- Refugees within asylum seeker centres
- Refugees in host-families
- Regular migrants from countries with circulating WPV that have arrived in the EU in recent months
- People coming into contacts with these populations.

Scenarios for discussion

Scenario 1. (Current scenario) - Asymptomatic refugees arrive at the border of an EU country. What public health measures should be taken upon entry?

When is the best time for intervention?

- At the time of entry of refugees.
- After entry.

What is the best way to assess vaccination status?

- Paperwork availability and interpretation
- Serology

If under-immunised, then what is the most appropriate vaccination schedule (number of doses, timing) for refugees and contacts?

- Each country to follow their national vaccination schedule for polio vaccination?
- Should there be EU-guidance for vaccination (in order to harmonise practices in the event that refugees move from one country to another, for example)
- Population to be prioritised.

Logistics of vaccination

- Information to the patient and/or legal caregiver?
- Informed consent prior to vaccination?
- Serology needed prior to vaccination?
- Who is vaccinating?
- Monitoring of adverse events
- Any contra-indications?
- Record of vaccination.

What should be the guidance to host families or workers at centres for asylumseekers in relation to assessment of immunity and/or vaccination?

Surveillance in a refugee setting (centre, host family)

- What is the best way to ensure adequate surveillance for clinical cases?
- Is it useful to test stool samples from asymptomatic persons to identify the rate of poliovirus carriage?
- Is it useful to test blood samples from asymptomatic persons to identify immunity status in the refugees?
- Is it useful to conduct environmental testing at the refugee centre?

Scenario 2.

- A clinical case of polio is diagnosed in a refugee centre: what actions should be taken?
- A clinical case of polio is diagnosed in a migrant or a member of a family hosting a migrant from Syria: what actions should be taken?

[This scenario will be discussed subject to time availability and may require discussions at a later stage after the meeting.]

Outbreak response guidelines (i.e. how to investigate and respond to a case of poliovirus?)

- When is an outbreak declared?
- What is the best way to carry out active case finding?
 - Increase AFP surveillance?
 - Increase enterovirus surveillance?
- Is it useful to conduct stool sampling or serology testing of asymptomatic population?
- Is it useful to carry out environmental surveillance?
- What vaccine schedule should be used for un- or incompletely-vaccinated contacts?
- What should be the trigger for vaccinating susceptible people in the population who are not contacts of the refugee or case?

Expected outputs of working group 3

- Outline of a practical guidance document adapted to EU Member States
- Algorithm (some parts may identify lack of information)
- To obtain preparedness plans from Member States (to gather best practices in EU countries and try and come up with the most-appropriate approach).