

30 September – 1 October 2015 // Copenhagen, Denmark

15th meeting of the European Technical Advisory Group of Experts on Immunization (ETAGE)



**World Health
Organization**

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ABSTRACT

The 15th full meeting of the European Technical Advisory Group of Experts on Immunization (ETAGE) took place on 30 September to 1 October 2015 to review and discuss immunization activities and developments in the WHO European Region and provide advice to the WHO Regional Office on appropriate activities. Main topics for discussion included the feasibility and value of serosurveys in support of measles and rubella elimination; progress made and upcoming activities and challenges in switching from trivalent oral polio virus vaccine (tOPV) to bivalent oral polio vaccine (bOPV) and the increased requirements for laboratory containment of poliovirus stocks; continuing medical education, communications and immunization advocacy; the implementation of the monitoring and evaluation framework of the European Vaccine Action Plan 2015-2020 and reporting on EVAP implementation to the Regional Committee in 2017 and 2021; Polio Outbreak Simulation Exercises (POSE); impact and future directions of the New and Underutilized Vaccines Initiative (NUVI) Surveillance Networks for rotavirus and invasive bacterial disease; the 2015 measles and rubella elimination goal and the protocol for reporting back to the Regional Committee; vaccine supply issues and the recent vaccine pricing study publication.

KEYWORDS

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CONTENTS

Abbreviations	4
Executive summary	4
Introduction	8
Opening remarks.....	9
Update on Strategic Advisory Group of Experts on Immunization (SAGE) discussions, recommendations, and agenda items for October 2015 meeting	10
Review of 2014 ETAGE recommendations and implementation status.....	11
Regional VPI Progress Report, October 2014 to– October 2015	12
Measles and Rubella Elimination: feasibility and need for serosurveys.....	15
The OPV switch in the European Region	19
Wild polio virus containment: progress made, upcoming activities and challenges.....	21
Communications, continuing education and immunization advocacy.....	24
Advocacy and resource mobilization for immunization	27
EVAP Monitoring and Evaluation Framework	28
Polio Outbreak Simulation Exercise (POSE)	31
Rotavirus and Invasive Bacterial Disease Surveillance Networks	31
Update on NITAGs.....	35
Measles and rubella elimination, the 2015 goal and reaching consensus on the ETAGE role in announcements and formal processes to report back to the Regional Committee in 2016	36
Update on measles and rubella elimination action plan and updated policies and strategies for the European Region.....	36
Vaccine pricing publication and vaccine supply issues	39
Vaccine supply issues.....	40
Conclusions and recommendations.....	42

Abbreviations

AEFI	adverse event following immunization
aP	acellular pertussis vaccine component
BCG	Bacillus Calmette-Guérin vaccine (tuberculosis vaccine)
bOPV	bivalent oral polio vaccine
CME	continuous medical education
cVDVP	circulating vaccine-derived polio virus
cVDPV2	circulating vaccine-derived poliovirus type 2
DTP	diphtheria, tetanus and pertussis combination vaccine
ECDC	European Centres for Disease Control
ELISA	enzyme-linked immunosorbent assay
ESPID	European Society for Paediatric Infectious Diseases
ETAGE	European Technical Advisory Group of Experts on Immunization
EVAP	European Vaccine Action Plan 2015-2020
GAPIII	WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of OPV use
GAVI	global Vaccine Alliance
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GVAP	Global Vaccine Action Plan
HCWs	health care workers
IgG	immunoglobulin G
IPV	inactivated poliovirus vaccine
IBD	invasive bacterial diseases
JRF	WHO/UNICEF Joint Reporting Form
MCV	measles containing vaccine
MIC	middle income country
MMR	measles, mumps, rubella combination vaccine
MR	measles, rubella combination vaccine
NUVI	New and Underutilized Vaccines Initiative
NITAG	National Immunization Technical Advisory Group
NRAc	National Regulatory Authorities for Containment
NVC	National measles and rubella Verification Committee
OPV	oral polio vaccine
OPV2	oral polio vaccine type 2
PCV	pneumococcal conjugate vaccine
POSE	Polio Outbreak Simulation Exercises
Regional Office	WHO Regional Office for Europe
RC	Regional Committee for the WHO European Region
RCC	Regional Commission for the Certification of poliomyelitis eradication
RV	Rotavirus
RVC	Regional measles and rubella Verification Commission
SAGE	Strategic Advisory Group of Experts on Immunization
SIA	supplementary immunization activity
TIP	Tailoring Immunization Programmes
tOPV	trivalent oral polio vaccine
UNICEF	United Nations Children's Fund
VDPV	Vaccine-derived poliovirus
VPD	Vaccine-preventable diseases

VPI	Vaccine-preventable Diseases and Immunization Programme of the WHO Regional Office for Europe
WER	Weekly Epidemiological Record
WHA	World Health Assembly
wP	whole-cell pertussis vaccine component
WPV	wild poliovirus
WPV2	wild poliovirus type 2

Executive summary

The 15th meeting of the European Technical Advisory Group of Experts on Immunization (ETAGE) was held on 30 September to 1 October 2015 in Copenhagen, Denmark to review and discuss immunization activities and developments in the WHO European Region and provide advice to the WHO Regional Office on appropriate activities.

Main topics for discussion included:

- the feasibility and value of serosurveys in support of measles and rubella elimination;
- progress made and upcoming activities and challenges in switching from trivalent oral polio virus vaccine (tOPV) to bivalent oral polio vaccine (bOPV) and the increased requirements for laboratory containment of poliovirus stocks;
- continuing medical education, communications and immunization advocacy;
- the implementation of the monitoring and evaluation framework of the European Vaccine Action Plan 2015-2020 and reporting on EVAP implementation to the Regional Committee in 2017 and 2021;
- an introduction to Polio Outbreak Simulation Exercises (POSE); impact and future directions of the New and Underutilized Vaccines Initiative (NUVI) Surveillance Networks for rotavirus and invasive bacterial disease;
- the 2015 measles and rubella elimination goal and the protocol for reporting back to the Regional Committee;
- vaccine supply issues and the recent vaccine pricing study publication.

Serosurveys clearly have a role to play in support of measles and rubella elimination, but the technical and resource implications of serosurveillance can be substantial. Any decision to undertake these studies should be taken with clear and focussed public health objectives and not where other data or indicators provide sufficient information to recommend an intervention and how best to implement it. To be of the greatest use serosurveys should be focused and targeted on particular population groups or geographic areas considered to be at risk.

Current inactivated polio vaccine (IPV) supply problems and the challenges to identification and disposal of trivalent oral polio vaccine (tOPV) stocks are of concern. The legislative and licensure issues regarding bivalent oral polio vaccine (bOPV) that some countries face, together with the possibility of logistical difficulties in effecting the change-over from tOPV to bOPV, threaten successful completion in accordance with the proposed timeline. In this regard, there are particular concerns over lack of timely progress towards bOPV licensure in the Russian Federation and Ukraine.

There has been significant progress in immunization communications and considerable achievements have been made over the last year on a number of projects conducted by the WHO Regional Office. The WHO European Region is currently taking a global lead in the development of approaches and materials in some critically important areas and the work conducted is receiving considerable global interest.

The establishment of an ETAGE Working Group on the European Vaccine Action Plan (EVAP) to support and develop preparation of annual and interim reports over the next five years, will be an important development. Further discussions are required to determine the expected roles and responsibilities of ETAGE members in the functioning of this Working Group.

The recent detection of circulating vaccine-derived polio virus (cVDVP) in Ukraine, against a background of low immunization rates, and the lack of an immunization outbreak response to date, is of great concern. This scenario represents a major threat to the polio-free status of the Region. Also of concern is the existence of populations in Romania apparently vulnerable to polio importation and reestablishment of transmission. Every effort should urgently be made to increase population immunity and surveillance sensitivity in these populations.

Development of the polio outbreak simulation exercises (POSE) has been a great success and significant progress is being made in implementing this important preparedness activity. It is also apparent to ETAGE that the Secretariat's application of scenario-based simulation exercises on this and other areas of work (i.e. vaccine safety and resource mobilization) has drawn significant attention and demand from partners and other WHO Regional Offices to adopt and adapt the European Regional Office work beyond the Region's borders.

The rotavirus (RV) surveillance and invasive bacterial diseases (IBD) surveillance networks established in the Region by the New and Under-utilized Vaccines Implementation (NUVI) team have provided some valuable information on burden of disease and the effects of introduction of new vaccines. The networks now need to focus on the practicalities of establishing sustainability and it would be beneficial to incorporate these networks into other surveillance networks that exist within the Region.

There has been steady progress in establishing and strengthening National Immunization Technical Advisory Groups (NITAGs) but there remains a continuing need for support and funding from governments, international funders and partners to ensure the sustainability of these bodies in the most vulnerable countries. Together with the international partners, ETAGE will remain actively involved in supporting training for NITAG members.

There is now a low likelihood of achieving measles elimination in the Region in line with the 2015 elimination target, but Regional rubella elimination may be attainable in the near future, in advance of measles elimination. Efforts to achieve control of both diseases must be redoubled in the Region to attain these important elimination goals.

The Regional report on vaccine pricing is an important new development and work should be continued to update the report over time. There are significant concerns over the recent vaccine supply shortages, particularly those affecting BCG and acellular pertussis-containing vaccines. Some Member States appear to have very limited or inadequate mechanisms in place to respond to fluctuations in vaccine supply, and little or no resilience in the face of vaccine supply interruptions. Further efforts are urged to support these countries in developing appropriate mechanisms to ensure sustainability of vaccine supplies and avoid vaccine stock-outs.

Introduction

The European Technical Advisory Group of Experts on Immunization (ETAGE) meets annually to review the progress of the Vaccine-preventable Diseases and Immunization Programme (VPI) towards the European Regional disease prevention goals. The 15th meeting of ETAGE was conducted from 30 September to 1 October 2015 at the WHO Regional Office for Europe (Regional Office), Copenhagen, Denmark.

Professor Pierre Van Damme (outgoing chairman) opened the meeting and handed over the chair to the incoming chairman, Professor Adam Finn. Professor Christian Perronne was vice-chair, and Dr Ray Sanders was rapporteur.

Objectives of the meeting were to:

- discuss the rationale of serosurveys in the context of verifying measles and rubella elimination in the European Region, and present feedback from the European Measles-Rubella Laboratory Network to ETAGE's request regarding serosurveys (January 2015);
- update ETAGE on the status of progress in preparing for the bOPV switch in the Region and poliovirus containment requirements in line with the Global Action Plan (GAPIII);
- to present and discuss activities in the field of advocacy and communications in Member States;
- brief ETAGE members on the monitoring and evaluation framework of the European Vaccine Action Plan 2015-2020 (EVAP) and discussion of the engagement of ETAGE members in the annual reporting process on implementation of EVAP;

- provide an update on progress in development of scenario-based polio outbreak simulation exercises (POSE);
- update ETAGE on progress and current status of New and Underutilized Vaccines Initiative surveillance networks established to monitor rotavirus diarrhea and invasive bacterial disease and to identify and discuss future roles and direction for these networks;
- establish a shared understanding on the role of ETAGE and the process that will be undertaken, in reporting to the Regional Committee on the 2015 measles and rubella elimination goal;
- update ETAGE on planned activities to address Global and Regional developments targeting measles and rubella elimination;
- update ETAGE on vaccine supply issues, WHO advice and potential areas of action, and on activities undertaken to provide vaccine price transparency.

Opening remarks

Dr Guenaël Rodier, Director, Division of Communicable Diseases, Health Security, and Environment, opened the meeting on behalf of the WHO Regional Director and welcomed ETAGE members, representatives of partner agencies and regional immunization initiatives, and staff from WHO headquarters. As outgoing chairman of ETAGE, Professor Van Damme was thanked on behalf of the Regional Director and the Secretariat for his 10-year chairmanship guiding ETAGE and providing invaluable technical advice and advocacy in support of the WHO Vaccine-preventable Diseases and Immunization Programme (VPI). A warm welcome was extended to the incoming chairman of ETAGE, Professor Adam Finn. Sincere thanks and acknowledgement was also given to Dr John Edmunds, who on completion of the maximum permitted time serving as an ETAGE member retires from the Group after this meeting.

In his last address as ETAGE chairman, Professor Van Damme, expressed his appreciation to WHO for the support, generosity and trust given to ETAGE during his tenure. The role of ETAGE has continued to evolve as the technical demands placed on VPI have increased and the level of professional and scientific scrutiny risen. This has resulted in the work of ETAGE becoming far more visible than previously, placing increased demands for participation on ETAGE, and underscoring the importance of ETAGE in implementing the VPI programme of work.

Mr Robb Butler, acting Programme Manager, VPI, welcomed participants on behalf of the VPI team and presented the proposed agenda and programme for the meeting.

Update on Strategic Advisory Group of Experts on Immunization (SAGE) discussions, recommendations, and agenda items for October 2015 meeting

At its meeting in April 2015 SAGE concluded that progress towards elimination of circulating vaccine-derived poliovirus type 2 (cVDPV2) was on track as the last detected virus-associated case was in December 2014 and the last positive environmental sample was collected in March 2015. Reviewing the plans, preparedness and timeline for withdrawal of oral polio vaccine type 2 (OPV2) SAGE recommended that all countries should plan for April 2016 as the designated date for global OPV2 withdrawal – the switch from trivalent oral polio vaccine (tOPV) use to bivalent oral polio vaccine (bOPV) use. SAGE will review a report from the polio working group at its meeting in October 2015 to confirm the date for the global tOPV to bOPV switch.

Recognizing that the provision of multiple vaccine injections during the same visit has raised safety concerns in some middle-income countries (MICs), and following a systematic review of evidence, SAGE recommended that countries provide training to health care workers on co-administration practices, techniques to mitigate pain, safety and effectiveness of vaccines and training on improved communication strategies with parents. To enhance sustainable access to vaccines and enable introduction of new vaccines for populations in MICs, SAGE endorsed the MIC Strategy 2015-2020.

Reviewing evidence on progress towards building a platform to provide influenza vaccine during pregnancy, SAGE concluded that while the vaccine was effective in preventing laboratory-confirmed influenza illness maternal vaccination is not a universal recommendation but should be considered by countries with existing or new influenza vaccination programmes. SAGE encouraged WHO to promote more research to generate generalizable data for maternal immunization into routine antenatal care in low resource settings and encouraged documentation of experience gained in delivering maternal influenza vaccine.

With regard to pertussis vaccination schedules, SAGE concluded there was no compelling evidence to change from the currently recommended 3-dose primary series, with the first dose administered at age 6 weeks; with subsequent doses given 4–8 weeks apart, at age 10–14 weeks and 14–18 weeks. However, countries successfully using alternate primary series with adequate surveillance should continue with these schedules.

In addition to receiving the regular status reports and updates from advisory and working groups, at its meeting in October 2015 SAGE will discuss polio eradication and the date for the tOPV to bOPV switch, progress made on implementing the Global Vaccine Action Plan (GVAP), malaria and Ebola vaccines, the status of measles and rubella elimination and the requirement for a supplemental dose

of measles-containing vaccine (MCV) in infants aged less than 9 months. In addition to holding formal meetings, SAGE is responsible for the publication of position papers, including recent papers on hepatitis E vaccine, pertussis vaccines and reducing pain at the time of vaccination. To provide evidence for the decision-making process SAGE has established a range of Working Groups, and enhanced operating processes for these Groups are now being developed, including introduction of membership rotation for longstanding Groups and systematic use of Grading of Recommendations Assessment, Development and Evaluation (GRADE) to assess the quality of evidence. Discussion groups on methodology have also been established to discuss evidence to decision tables, good practice statements and guidelines adaptation. A Wikipedia project on gaining better exposure of SAGE-related materials and decisions is making good progress but continues to be challenged by the requirement to obtain a Creative Commons Open Access license for WHO materials and publications featured in the Weekly Epidemiological Record (WER).

Discussion

The current SAGE recommendation on maternal vaccination with influenza vaccine is to continue with vaccination where it is now in use, but this recommendation is under review. Available evidence is in favour of maternal vaccination, but the evidence is not as strong as previously anticipated. More information from developing countries, and more specific analysis of data, is required before a revision to the recommendation can be considered. There appears to be little enthusiasm for maternal vaccination in MICs in Europe, but the WHO Regional Office will continue to offer technical support to Member States conducting assessments and developing action plans.

Review of 2014 ETAGE recommendations and implementation status

Implementation of 2014 recommendation on pertussis:

- The Regional Office maintains the position on vaccination against pertussis as recommended by SAGE and recognized by ETAGE;
- The Regional Office continues advocating for high-quality laboratory-based surveillance for pertussis.

Implementation of 2014 recommendation on establishing a Regional hepatitis B control goal:

- Regional hepatitis B control targets, priority activities, and indicators are developed, and have been discussed and agreed with Member States at the Regional Meeting for National Immunization Programme Managers (September 2015).
- A collaboration agreement has been established with the United States Centers for Disease Control and Prevention (US CDC), including financing of relevant activities.
- The next steps include gaining internal approval of the final document, establishing a Regional Verification Committee and defining the verification process.

Implementation of 2014 recommendation on measles and rubella elimination:

- An extraordinary meeting of ETAGE was held on 30 January 2015 to review and discuss measles and rubella elimination in the WHO European Region, to be briefed and provide input on the advocacy plan for the European Vaccine Action Plan (EVAP);
- As requested by ETAGE, a detailed strategy and operational plan, including specific actions and timelines for achieving measles and rubella elimination goals, has been prepared and the review and discussion of the plan is included in the current meeting programme;
- An investigation of the feasibility and value of conducting serosurveys in support of measles and rubella elimination has been conducted, and the review and discussion of the results is included in the current meeting programme.

Implementation of recommendation on the development of training materials on immunization for continuous medical education (CME) schemes:

- Training materials for CME on vaccination for health professionals have been produced in collaboration with the European Society for Paediatric Infectious Diseases (ESPID) using a platform developed for training materials on antimicrobial resistance. A funding source for implementation has been identified, materials are currently under review and pilot testing is ready to begin.

Regional VPI Progress Report, October 2014 to– October 2015

A large part of the VPI programme of work has been built upon responding to the recommendations of ETAGE and on developing and implementing the European Vaccine Action Plan 2015-2020 (EVAP). The Regional Immunization Programme Managers Meeting, held in Antwerp at the start of September 2015, was structured around the EVAP and its strategic objectives. Positive feedback has been

received from participants of this meeting following introduction of a more participatory, discussion-based format for the meeting.

The Regional measles and rubella Verification Commission (RVC) will meet at the end of October 2015 to review the third year of annual reports from Member States. It is anticipated that several countries will provide evidence of continued interruption of measles and/or rubella elimination for a period of at least 36 months, documenting achievement of elimination. Although this will provide some positive messaging, it is clear that the 2015 elimination target for the European Region will not be met, as over 15,000 cases of measles are estimated to have occurred in the Region in the first 6 months of 2015. Large outbreaks of measles have been detected in a number of countries (Kyrgyzstan, Bosnia and Herzegovina, Kazakhstan, and Germany, among others), reflecting the epidemiological situation seen in 2013 and 2014. According to the case-based data received in the first half of 2015, eighty-three percent of reported measles cases were not immunized or had no record of vaccination, and 43% were aged 20 years or above. Issues around the new migrant and mobile populations are of increasing concern in the region and there is a need to discuss the development of clear and effective joint messages from all partner agencies on how to respond to the current situation. Although rubella surveillance remains sub-optimal, a decreasing incidence of rubella has been reported since 2014, with fewer than 600 cases reported in the first half of 2015.

The Regional Commission for the Certification of poliomyelitis eradication (RCC) met in Sarajevo in June 2015 and determined that three Member States, Bosnia and Herzegovina, Romania and Ukraine remain at high risk of polio transmission following possible importation. One of the high risk countries, Ukraine, reported circulating vaccine-derived poliovirus (cVDPV) in August 2015. Despite efforts from the international partner agencies to monitor and mount a suitable response to the detection, little has yet been implemented by the national authorities to meet the challenge.

A new data manager will be joining the VPI team, and a new data assistant has been in post since July 2015. An external review of the VPI surveillance databases and procedures is planned for November and December 2015.

The Polio Laboratory Network has maintained its high quality performance in 2015 and the accreditation review of all laboratories for 2016 is completed. The Regional enterovirus surveillance guidelines have been completed and published. The Network continues to provide assistance with the testing of samples from Syria and the Palestinian territories but there are concerns that this is placing additional strain on key Network laboratories in Turkey and the Netherlands. Transition to the new polio laboratory testing algorithm is the Network focus for the remainder of 2015, together

with preparing the Region for the more stringent laboratory containment requirements associated with the tOPV/bOPV switch, described in the WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of OPV use (GAPIII).

Significant progress has been made towards vaccine self-sufficiency in the Region as overall government funding for vaccines has continued to increase. All countries in receipt of GAVI support fulfilled their co-financing requirements in 2014, and all five GAVI-graduating countries (Armenia, Azerbaijan, Georgia, Republic of Moldova and Uzbekistan) have a costed graduation action plan in place to address identified challenges. Implementation of the plans is supported and monitored by VPI. The Regional Office continues to provide a wide range of technical support to Member States to improve financial stability through development of multi-year planning for immunization, capacity building and strengthening evidence-based decision making in-country. An immunization financing workshop was held in Istanbul in November 2014, a multi-year planning workshop in Copenhagen in April 2015, and a resource mobilization workshop in June/July 2015, with a second planned for November 2015. An advocacy toolkit for resource mobilization has been developed providing guidance on the process and sample templates for advocacy messages.

The WHO Sentinel Surveillance system for diseases preventable by New and Under-utilized Vaccines (NUVI) for rotavirus diarrhoea and invasive bacterial disease has been established in 7 countries in the Region, starting in 2006. Under this GAVI-supported programme, rotavirus vaccine has been introduced in Armenia, Republic of Moldova, Georgia, Uzbekistan and Tajikistan, and pneumococcal conjugate vaccines introduced in the Republic of Moldova, Armenia, Georgia, Azerbaijan and Uzbekistan.

Although the new vaccines have been well accepted by the public and by health care workers, the lower coverage rates achieved reflect a general decline in vaccine coverage rates seen for many routine immunization programmes. Assessing this decline, the main challenges appear to be concerns of health care workers over the safety of vaccines, together with a general scepticism over the value of vaccination, and increasing incidence of parents refusing to have children vaccinated. In response WHO has developed training materials for health care workers on vaccine safety and contraindications and is planning sub-regional training for front-line health workers in key countries.

There are currently National Technical Advisory Groups on immunization (NITAGs) established in 43 Member States in the Region, and NITAG members have participated in several meetings and workshops throughout the year, including the recent Programme Managers Meeting in Antwerp. An

on-going evaluation of the NITAGs of Armenia, Belarus, Georgia and the Republic of Moldova is being conducted in collaboration with the SIVAC Initiative.

There has been increased WHO involvement in developing surveillance for adverse events following immunization (AEFI) and vaccine safety, including responding to a vaccine safety scare during the recent measles mass immunization activity in Kazakhstan. VPI has also been active in developing materials and guidance on vaccine price transparency and access to affordable vaccines. WHO has conducted joint appraisals in the GAVI-supported countries to review implementation performance and identify remaining challenges, and the technical assistance required to address remaining challenges in 2015-2016 has been determined for each of the seven countries appraised.

Measles and Rubella Elimination: feasibility and need for serosurveys

At its extraordinary meeting in January 2015, ETAGE proposed that consideration be given to implementation of a standardized serosurvey process in the context of verifying measles and rubella elimination. Further discussion was recommended to weigh the benefits and resources needed to implement such an initiative. In this respect, the rationale for serosurveys, taking into account the immunity gaps predicted to exist in many countries, laboratory needs, capacity to support such an initiative by WHO and by the countries, and the possible programmatic impact, were discussed. Details of a Regional review of serosurveillance capabilities and feed-back from the Measles-Rubella Laboratory Network were also provided. Discussion points included the expected or anticipated results of conducting measles and rubella serosurveys in the European Region; potential value added by conducting serosurveys rather than other programmatic interventions, such as broad-based supplementary immunization activities based on analysis of existing immunization coverage, diseases surveillance and outbreak data. The potential implications for WHO and Member States in terms of human, financial and technical resources required and the expected risks and challenges were also discussed.

Serosurveys can be a direct measure that can be of use to a vaccine programme, theoretically indicating the proportion of a population immune to a particular pathogen. Seropositivity, however, is not necessarily the same as protection against a pathogen, as serosurveys usually measure the level of specific immunoglobulin G (IgG) detectable in serum or plasma and this does not correlate well with the level of functional, protective antibodies. Results are often reported relative to WHO standards, measured in International Units per millilitre (IU/ml), but many of the commonly available assays are not validated against the WHO standards and have a wide range of sensitivities and specificities.

The two main methods of sampling populations include use of residual sera from routine laboratory testing and serum banks, and population-based sampling where specimens are collected specifically for survey. Use of residual samples can be relatively inexpensive and convenient, but may not be representative of the population of interest. Individuals who have serum samples taken for diagnostic testing are not necessarily representative of the entire population and it is difficult to identify and control potential biases that may arise for this approach, as detailed risk-factor information is not available. Population-based sampling is complex and expensive to organise, but can be planned to minimise sampling bias and collect additional information, such as vaccination histories. A cost-benefits analysis is critical in guiding the decision whether or not to conduct a seroprevalence study. Before starting any serosurvey activity it is essential to clearly define the public health question being asked, and determine that the activity will address that question in a clear and unambiguous way.

Serum is the preferred specimen for laboratory testing, but use has been made of dried blood spots and oral fluids. Plaque reduction neutralization (PRNT) is the gold-standard assay that has been validated against the WHO standard reference sera, but is time-consuming and technically demanding. A variety of enzyme-linked immunosorbent assays (ELISA) are commercially available, relatively inexpensive, technically straightforward to perform, and by far the most popular assays in use. Newer assay formats, such as the Luminex bead-based multiplex assay, are also becoming available but experience in their use is limited. The different commercial assays available differ in sensitivity and specificity, and have been developed for use as tools for laboratory confirmation of infection, not for sero-epidemiological studies. As a result, positive/negative cut off values recommended by manufacturers are almost invariably too high, resulting in an underestimation of population seroprevalence levels. Mixture modelling or similar complex statistical treatments are often needed for interpreting seroprevalence data.

Seroprevalence studies are not feasible for all countries or all circumstances, and it may be more appropriate to make use of existing data, for example, by the reanalysis of databases on measles and rubella serological status gained through IgG screening of women of child-bearing age, in order to estimate population immunity. Existing serum collections, for example from blood donors, HIV screening of women during prenatal care, nutritional surveys, etc., can effectively be used and tested for measles and rubella antibodies to estimate population seroprevalence profiles without the need to conduct new surveys.

In the European Region there is a long history of collecting immunization coverage information, dates of vaccine introduction and target groups, and disease surveillance data. Member States are

aware of the history of their own immunization programmes, of any history of programmatic problems with vaccine delivery and the quality and sensitivity of national disease surveillance data, and are aware of subnational populations or specific age groups that are highly likely to represent immunity gaps. In many countries broad serological profiles of particular population groups can be anticipated without the need for serosurveys. In some countries, however, the persistent low incidence of disease has led to an inability to provide quantitative data or credible estimates of population susceptibility levels, providing the potential for serosurveys to generate information not available from other sources. Guidance on conducting serosurveys in support of measles and rubella elimination in the WHO European Region was published in 2013¹ to support decision-making in countries on the use of serosurveys and for developing protocols adequate for specific countries, populations and epidemiological situations. In general, serosurveys can be useful for determining population immunity profiles, and provide a supporting line of evidence for documenting the elimination of measles and rubella, particularly in adolescents and adults, but should be targeted and focussed on particular groups considered at risk.

In 2008 and 2009 concerns were raised over the existence of gaps in population immunity and low quality disease surveillance in Tajikistan, leaving the country at high risk of transmission of wild poliovirus (WPV) following the importation. In 2010, due to an outbreak of poliomyelitis and the need to define immunity to all three types of wild polio virus, a nationwide serosurvey for vaccine preventable diseases (VPD) was conducted, targeting persons aged 1–24 years, assigned to five age groups. A sample size of 540 subjects within each age group were recruited, participants selected through stratified multi-stage cluster sampling (25 of 69 districts and cities were selected in the first stage). Although the serosurvey results confirmed immunity gaps for different antigens in minority populations and specific regions, the survey provided no new information, as the high risk populations could already been identified from existing immunization coverage information.

Following the recommendations of ETAGE the European Measles and Rubella Laboratory Network have been consulted on their views on serosurveillance at the WHO European Regional Reference Laboratory meeting in London in February 2015 and at the WHO Global Laboratory Network

¹ *Guidance on conducting serosurveys in support of measles and rubella elimination in the WHO European Region*. WHO Regional Office for Europe. 2013. Available online at: http://www.euro.who.int/__data/assets/pdf_file/0011/236648/Guidance-on-conducting-serosurveys-in-support-of-measles-and-rubella-elimination-in-the-WHO-European-Region.pdf?ua=1

Meeting in Geneva in June 2015. Four main concerns and potential challenges were raised. Concerns were raised over appropriate sampling of a given population and providing resources for implementation of sampling designs. Laboratory results are often not simple to interpret, as immunity or protection does not always equate with IgG seropositivity, and cell-mediated immunity is known to be a strong factor in protection against measles. The high cost and resource burden of serosurveys may drain resources and pose a potential threat to other programmatic interventions. Although immunity gaps are already known to exist in several European countries, through the high quality epidemiologic data available, very often no programmatic action is taken to address these gaps. The Laboratory Network members advised that any proposed serosurvey should answer a clear public health question tailored to a specific country context, and the study design and protocol, laboratory tools and results interpretation must be selected and adapted in order to answer the public health question. When evidence is lacking and cannot be provided from other sources, serosurveys can be an important option to obtain seroprevalence information, particularly on hard-to-reach groups, but generally, large serosurveys are not recommended.

Discussion

Europe continues to experience outbreaks of measles and rubella, so obviously there continue to be populations that are not immune to infection. Serological testing focuses on providing individual correlates of protection or susceptibility, rather than population protection or susceptibility. There appears to be a need to establish 'serological signatures' of populations at different stages of measles and rubella elimination. It would be of use to establish such a serological signatures immediately after an outbreak, for example, or in populations with good evidence that measles and rubella have been eliminated for many years, or in populations that have not experienced an outbreak for some years but for which concerns exist over the level of vaccine coverage. If these signatures can be established the information would be helpful to national authorities considering whether or not they have a public health problem, and will help define the details of that problem. Without some clear indication of the serological profile of a protected population, or an at-risk population, it is difficult to interpret the results of any serosurvey in terms of population immunity or susceptibility.

Most countries in the Region have both historical and current data and other information that can be used to predict and identify immunity gaps and at-risk populations. This data may not be perfect, and may require complex reanalysis to extract the relevant information. Data is also analysed and modelled at the Regional level, and Regional concerns over potential susceptible and at-risk

populations are discussed with countries. A major cause of failure to establish a suitable intervention in an at-risk population before an outbreak occurs is not lack of suitable data, but lack of political commitment to provide resources to prevent a potential outbreak.

There is a broad consensus that serosurveys have a role to play, but they need to be designed properly, and conducted within a broader context of strategic and resource-based thinking. They may have a broader role than that historically played, particularly if the science can be improved to make it easier to interpret the results at a population level. Serosurveys may be helpful to provide data on population immunity in selected places to predict the at-risk populations where there is an information gap, and provide evidence to encourage political commitment for an appropriate intervention. The discussion now needs to move forward to establish the specifics of serosurvey use, by defining the circumstances under which they would be most useful and how they should be conducted and resourced within the broader framework of immunization.

The OPV switch in the European Region

The global absence of all persisting circulating vaccine-derived type 2 polioviruses (cVDPV2) for at least 6 months will trigger the withdrawal of type 2 OPV, and as of April 2016 it is expected that global trivalent oral poliovirus (tOPV) use will be replaced by bivalent oral polio vaccine (bOPV) use. Confirmation of the date for the OPV switch is expected at the upcoming meeting of SAGE in October 2015. As of early 2016, countries still using OPV will be required either to change to the use of inactivated polio vaccine (IPV) or replace current tOPV use with bOPV use.

In the European Region there are currently eight Member States (Armenia, Azerbaijan, Georgia, Kyrgyzstan, Republic of Moldova, Tajikistan, Turkmenistan, Uzbekistan) using OPV alone and a further 12 are using OPV together with IPV in a sequential schedule. Of these 20 Member States, 10 use the vaccine in their primary series and a further 10 use it as a booster dose. Although all OPV-using countries had planned to introduce IPV before the end of 2015, problems with vaccine procurement have delayed introduction in seven countries, introduction now expected at some time during 2016. There continues to be a problem with global supply of IPV, with demand exceeding supply, and it is becoming increasingly likely that at least four of the countries intending to switch to IPV will not receive vaccine supplies until the end of the first quarter 2016 at the earliest. The greatest challenge is currently in supply of standalone IPV, particularly in the single-dose presentation, which comes from a single manufacturer. All countries considered to be a high risk for polio are being supplied with IPV in the 10-dose format. Most of the challenges faced relate to procurement of appropriate vaccines in sufficient quantity. Eight Member States (Albania, Armenia,

Azerbaijan, Georgia, Kyrgyzstan, Tajikistan, Turkmenistan, and Uzbekistan) and one territory (Kosovo) procure through the UNICEF tender process. A significant advantage of this is that supply of vaccine is guaranteed by UNICEF, even if there may be delays in supply. A further 11 countries are self-procuring and one, the Russian Federation, is self-producing. Because of national tendering requirements and the relatively low volumes of vaccine required, many of these countries are experiencing challenges in securing vaccine supplies from producers.

In response to the challenge posed by the tOPV to bOPV switch, WHO called a meeting of representatives of the immunization programmes and national regulatory authorities of OPV-using countries in December 2014 to review and discuss expedited licencing of polio vaccines in their countries. A formal alert regarding the switch was issued to OPV-using countries in May 2015, and numerous country visits and presentation to NITAGs have been made. Guidelines on the switch were distributed in May 2015 and global training of consultants to support the switch was conducted.

Field-testing of the switch guidelines was undertaken in Kazakhstan in May from 25 May to 6 June 2015. During field testing a WHO consultant met with all principal stakeholders, including representatives from the Ministry of Health, Ministry of the Economy, the national regulatory authority, and the vaccine supply agency and others. It became apparent that there was very little diversity in the vaccines licenced for use in the country, in the case of bOPV only one product was licenced, and legal requirements prohibit the use of expedited licencing of other products. It is also illegal to dispose of unused vaccine procured with state funding, so any remaining stocks of tOPV must be fully utilized before the April deadline. To date, the country has not placed its procurement order for bOPV, but has developed a draft plan for managing the switch.

A sub-regional workshop on the switch was conducted in June-July 2015, following which country planning was initiated. Participating countries agreed they could complete the planning process by the end of September 2015, in anticipation of the formal announcement from SAGE in October 2015. Participants agreed that monitoring of the switch was possible, but that full independence of the monitoring process, as stipulated in the Global Guidelines, was not feasible. Training for the switch, and monitoring the switch process, will be the most costly components but will be dependent on state funding, as the process will not be supported from international funds.

A session on the switch was also conducted at the Regional Programme Managers meeting in Antwerp in September 2015. A Regional meeting on switch readiness will take place during the first quarter of 2016.

One of the significant challenges faced by the Region is the lack of availability of bOPV; expedited registration of the vaccine is not legally acceptable in several countries; there are a limited number of suppliers; several countries are late in launching their vaccine tenders; and at a time of huge global demand very few suppliers are interested in responding to relatively low volume tenders. Another challenge is the situation in the Russian Federation, where bOPV can be manufactured but the national regulatory authorities are demanding a full clinical trial of bOPV as a new product before it can be licenced. Ukraine also poses a significant challenge where there is no access to militant-controlled areas and no official information available on immunization activities there. There have been long-standing problems with vaccine procurement in Ukraine, and these problems continue. No bOPV has been licenced for use and there is no certainty over the amount of tOPV currently present in the country. Almost 4 million doses of tOPV were imported into the country for outbreak response activities, but it currently appears unlikely that these doses will be used before April 2016.

In addition to the major challenges two additional problems faced include the monitoring of a number of small, self-proclaimed quasi-states that are not officially recognised by the international community and do not report to WHO. In addition, several countries are currently holding excess stock of tOPV that will be difficult to fully utilize before April 2016 but national laws prevent destruction or disposal of these stocks.

Discussion

It was generally concluded that the tOPV-bOPV switch is feasible, but that some tOPV will probably remain in the Region after the global switch date, and not all countries will have access to the bOPV they need to fully maintain their immunization programmes through the switch period. UNICEF has guaranteed that bOPV will be available to all countries using UNICEF tender, but concerns exist for several smaller countries that are self-procuring.

Wild polio virus containment: progress made, upcoming activities and challenges

At the request of the Global Commission for the Certification of Poliomyelitis Eradication, as of September 2015, 51 Member States of the Region provided an official statement confirming the eradication of wild poliovirus type 2 (WPV2) in their countries. No response to the request was received from Italy and San Marino, but based on other evidence provided it was concluded that WPV2 had been eradicated worldwide on 20 September 2015.

As part of the Regional Certification process in 2002 all Member States were required either to dispose of all wild poliovirus infectious and potential infectious materials, or to subject them to laboratory containment. All countries were required to establish an inventory of all facilities holding wild poliovirus materials, and to document the materials held. Each subsequent year Member States have been required to provide an updated inventory of all facilities holding polio-infectious materials and documentation on facilities holding wild poliovirus materials. In 2013, a total of 65 facilities in 22 countries reported holding wild poliovirus materials. Reports received from 50 Member States in 2014 show 69 facilities holding wild poliovirus materials in 21 countries. When the original inventories were created there was no requirement to document the type of wild poliovirus being held, but with the global eradication of WPV2 it becomes necessary to document where remaining laboratory stocks of WPV2 and WPV2-infectious materials are being held.

The WHO global action plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of OPV use (GAPIII) were published in 2014. This action plan aligns the safe handling and containment of poliovirus infectious and potentially infectious materials with the WHO Endgame Strategy, and describes timelines and requirements to be completed in preparation for poliovirus type 2 containment. It also addresses type-specific containment of WPV together with OPV/Sabin polioviruses, consistent with the goal of sequential cessation of OPV use after type-specific WPV eradication.

The Global Action Plan recognises three categories of facilities that may have poliovirus laboratory materials: essential facilities holding WPV; essential facilities holding OPV/Sabin materials but no WPV; and non-essential facilities. The Plan calls for all Member States to conduct national laboratory surveys and establish wild poliovirus type 2 (WPV2) inventories, destroy unnecessary WPV2 materials, designate essential poliovirus facilities and transfer necessary WPV2 materials to these essential poliovirus facilities by the end of 2015. All OPV2/Sabin2 materials should be destroyed, transferred or contained by July 2016. Essential poliovirus facilities are expected to implement GAPIII (Annex 2 or 3; safeguards) and demonstrate that appropriate and validated risk reduction procedures have been established and implemented. As of September 2015, 11 facilities in 8 Member States in the Region have informally communicated their interest in becoming essential poliovirus facilities.

It has been proposed that National Regulatory Authorities for Containment (NRAC) should certify all remaining polio facilities according to the requirements of GAPIII, and that the certification reports be submitted to the Regional Certification Commission (RCC) for evaluation. It is essential, therefore, that all Member States have established and functional NRACs. A containment certification scheme,

currently in draft form, describes the roles and responsibilities of the various stakeholders, including the facilities themselves, the NRACs, WHO and the international oversight bodies.

The Region faces a number of challenges in meeting the requirements and proposed timeline of GAPIII. The containment requirements outlined are based on a risk-management approach, rather than on attempting to ascribe a set level of risk presented by poliovirus, but the current laboratory method for detecting poliovirus in diagnostic specimens relies on cell culture, an inherently high-risk procedure. As yet, direct detection of polioviruses in diagnostic specimens without culturing the virus is not possible. In addition, manufacturers of IPV currently depend on growing very high titres of defined wild poliovirus strains to produce vaccine, and it is not yet clear how IPV can be produced economically under high containment conditions. The European Region currently has large IPV manufacturing facilities in four of its Member States.

The Regional Office has sent letters to the Ministers of Health and National Polio Containment Coordinators informing them of the GAPIII requirements and proposed timeline for implantation. Meetings have been held with European IPV manufacturers and with the Regional Polio Reference Laboratories. A biorisk management GAPIII training course has been provided to representatives of all members of the Regional Polio Laboratory Network. A high-level meeting with the Health Attachés from each of the countries with IPV manufacturers is being planned. The processes of verifying the Regional containment laboratory inventory, identifying potential essential facilities, establishing a Regional inventory of retained Sabin strain and Sabin-related materials, and providing ethical bioresearch awareness training are all on-going.

Discussion

It is essential that the poliovirus diagnostic capabilities in the Region be maintained, but not all diagnostic laboratories will belong to essential polio facilities. The ability of diagnostic laboratories to receive and test specimens, to conduct required quality control and quality assurance activities, and to be proficiency tested, must be maintained. It is clear that as the increasing laboratory containment requirements are applied, some level of compromise will be required to ensure that essential functions are maintained but that laboratories carrying out these functions pose the lowest possible risk.

Communications, continuing education and immunization advocacy***Developing an online vaccination course for health care workers in the WHO European Region***

Recognizing that health care workers (HCWs) have significant influence over immunization behaviour but that HCW commitment to immunization has sometimes been low, and availability and variety of suitable training opportunities were limited, in 2013 ETAGE recommended that WHO support the development of training materials on immunization for continuous medical education (CME) schemes. A partnership between WHO, the European Society for Paediatric Infectious Diseases (ESPID) and the University of Oxford Technology-Assisted Lifelong Learning (TALL) was established to develop an online vaccination course for HCWs. The online build of that course has now been completed and the training course is set to be launched before the end of 2015.

The course has been called “Wiser Immunisers” and is directed towards all HCWs involved in immunization. An interactive, clinical approach has been adopted, focussing on a range of vaccine preventable diseases, vaccines, contraindications and communications, and includes discussion of the common misconceptions around immunization and vaccines. The course consists of six modules, each expected to take two hours to complete. The course will be European Union accredited and there will be a small joining fee, currently proposed at €50 with lower concessional rates. A moderated participant forum has been established, together with the opportunity to access and question course facilitators. A pilot version will be launched during November 2015 with 170 participants, and a formal evaluation process will then take place. Plans are in hand to expand access to all parts of the Region, and to translate the materials into other languages and contexts. Gaining accreditation status outside of the European Union will be a challenge that needs to be addressed, together with expanding the modes of delivery so that the material can be incorporated into formal training modules in different parts of the Region. Securing ongoing financial and time commitments will also be a challenge to establishing sustainability.

Discussion

It may be possible to involve students from the annual vaccinology course, held in Antwerp, to be involved in pilot testing and providing feedback. It may also be possible to engage the pool of ESPID fellows in translating the materials into additional languages. Payment of the full joining fee will not be possible for potential students in several parts of the Region and some form of subsidy system will be required if the course is to become sustainable. ESPID is attempting to bring all of its educational activities together into a single coordinated programme. Options are being explored for developing a partnership, probably with a commercial company on a profit-sharing basis, to

generate income that can be used to support course participants who cannot afford to pay the full joining cost.

Responding to vaccine deniers

WHO is currently developing a document providing spokespersons of health authorities with guidance on how to respond to vaccine deniers in public debate or interview. The evidence base for the guidance is a review of peer-reviewed journal articles in the areas of public health, psychology, communication science and argumentation. Vaccine refusers represent an extreme end of a vaccine hesitancy continuum; vaccine deniers are a subset within the vaccine refusers group, are not open to a change of mind and usually refute scientific evidence that does not support their position. The document provides a 3-step approach to developing a response: identify the topic the vaccine refuser is addressing; identify the technique the vaccine refuser is using; and use the document to choose the correct response in each case, combine the responses and design the message. The document provides a range of typical arguments and techniques used, and arranges them into a diagnostic tool the spokesperson can use. It also provides a set of key arguments a spokesperson can use in responding to vaccine deniers.

This document is intended as a starting point for a much larger project on responding to vaccine deniers and, when finalized, will serve as a guide for workshops that will include scenario setting and simulation exercises.

Resilient programmes: Managing vaccine safety-related events communications

Communication of vaccine safety-related events needs to include public perceptions about vaccines and a wide range of other factors that may affect public trust in vaccines and the authorities delivering them. Programmes need to be able to monitor, detect, and recognize events, and respond to them appropriately so that situations do not develop into crises. There is also a need to ensure resilient populations, by encouraging the public to understand both the risks and benefits of vaccination and for them to demand immunization services from local and national authorities.

Many Member States in the Region have a low capacity for preparedness and response to vaccine safety-related events, often linked to lack of available funding and human resources. It can also be linked to the lack of a coordinated structure in place to deal with events, with many different government bodies and agencies having some level of responsibility for responding to an event, but doing so in an uncoordinated manner. In response to this challenge WHO in 2012 developed a guide for countries on preparing for, and responding to, these events. This guide is now being revised and

developed into a reference document, a web-based library of tools and supporting documents and a training workshop package.

It needs to be recognised that there is a significant difference between the evaluation of risk that an epidemiologist would make and the level of risk perceived by a member of the public. One way to bridge this gap is through effective communications, which can readily be called upon when needed. The training materials go through a situation analysis involving events of low, medium and high impact level and provide guidance on how to respond appropriately. An important aspect of developing this material has been to review what has already happened, how events have been responded to in the past, and strengthen the best-practices approach. The training workshop ends with a one-day simulation exercise that tests both the training materials and the participants.

Following the workshops participants are requested to prepare specific action points for changing or improving systems and capacity in their countries. The intention is to review the level of implementation after approximately 6 months to determine if the workshop has been effective. Feedback from participants suggest that they gain confidence in being able to respond to events, learn key messages from past events and do have tools available for responding to any future events.

Discussion

There are many reasons why there is discussion about vaccine side-effects, in part because in some Member States there is a lack of trust in the capacity of the State to protect individuals, often associated with the current right to refuse and past social history. In some of the Newly Independent States the concept of AEFI is not well understood and the idea that there is a need to communicate with the public is not readily grasped.

This is one of the areas where WHO Europe is working in advance of work at WHO Geneva, and there are proposals to further develop this project for global use. There has, however been no formal evaluation of the guide and this is now needed, together with establishment of an evidence-base on the positive impact of the workshops. This project has been conducted in a very open, transparent and evidence-based manner but when the tool is evaluated, great care must be taken to ensure that grounds are not provided for vaccine refusers to contort the process and claim that by encouraging communication of the benefits of vaccination, attempts are being made to hide the risks, that do exist at very low levels, associated with vaccination.

Advocacy and resource mobilization for immunization

An objective of EVAP is to ensure long-term domestic funding of immunization programmes, sustainable financial investment and political commitment to immunization. To support Member States in achieving this objective, WHO has embarked on the development of advocacy tools and materials to enhance the profile of immunization programmes and increase public knowledge about vaccines. In many Member States immunization is not always the highest public health priority, and external funding is often not available. There are often competing demands for funding for health, with other higher profile demands, and the value of immunization and the risks associated with underfunding are not always fully appreciated or understood. Although countries may allocate very large budgets to the purchase of new or additional vaccines, other components of the immunization systems may be grossly underfunded and under resourced.

In response to this challenge WHO produced a workbook on advocacy and resource mobilization for immunization. In order to ensure the workbook addressed the key issues and challenges, and that the material supplemented already available tools and guidelines, the workbook was developed based on extensive desk research and active engagement of national immunization managers and partners. It was found that of the existing materials on advocacy and resource mobilization, none was focussed on decision makers or addressed the issue of creating awareness within the health system. Key messages include the necessity of knowing, in detail, the budget requirements in order to justify the investment; identifying and understanding the national decision makers, influencers and partners; building relations with the stakeholders and actively engaging them in immunization; and actively setting the agenda for immunization.

The workbook provides a step-by-step approach to resource mobilization. The aim, however, is not to have countries simply follow this process on every occasion but to motivate immunization programme managers and staff to be aware of their own role and the role of decision-makers. In addition to the workbook, a web-based immunization advocacy library has been developed. This includes information on areas requested by Member States, including specific guidance and infographics countries can use and modify, and information on cost-effectiveness studies conducted by countries in the Region.

A training workshop for countries of the western Balkans has been conducted. The next workshop will take place in November and include the GAVI-supported countries. There will be in-country missions to provide technical support to develop national action plans in 2016, with follow-up

workshops or meetings. This will make it possible to monitor the implementation process at country level.

Discussion

Providing statistical comparisons between countries can be a motivation generating high political-level interest, but it is necessary to understand the motivation of national decision makers. In some countries decision makers are not motivated by comparisons with other countries, so other approaches are required and messages need to be shaped accordingly. Many countries in the Region are interested in using the tools and approaches developed, particularly those that are aware of imminent threats to immunization funding. Although the main issues and barriers within the European Region are still being explored, use of this approach could be extended to other Regions. Negotiations have started on the use of the workbook and materials in other Regions, particularly for use in GAVI-eligible countries, but this requires extensive training and material development in the other Regional Offices.

It would be helpful to the process if a member of ETAGE could be assigned to participate in this important area of work. Recognizing that all the communications projects remain works in progress, ETAGE nevertheless applauds the work that has been done, encourages further development and will attempt to provide support and guidance as necessary.

EVAP Monitoring and Evaluation Framework

Annex 2 of the European Vaccine Action Plan (EVAP)² provides an outline of the monitoring and evaluation framework, which is aligned with the framework described in the Global Vaccine Action Plan (GVAP). The framework makes use of the existing mechanism of data collection, the WHO-UNICEF Joint Reporting Form (JRF), so that countries do not have to collect and report additional data. The framework includes six indicators for the six EVAP goals, and 13 indicators for the five EVAP objectives. 2015 is the first year of EVAP implementation, so the first reporting will take place

² *European Vaccine Action Plan 2015–2020*. WHO Regional Office for Europe 2014. Available online at: http://www.euro.who.int/__data/assets/pdf_file/0007/255679/WHO_EVAP_UK_v30_WEB-new-sticker.pdf?ua=1

in 2016, and annual progress reports will be prepared by the Secretariat following receipt of the JRF data for 2015.

Annual Regional reports will be forwarded to the monitoring and evaluation team of GVAP, who will compile the Regional reports into a Global report. This will be forwarded to the SAGE working group established for GVAP, who will draft the implementation report for a given year, and that report will be reviewed by SAGE. After review by SAGE the report will be forwarded to the World Health Assembly (WHA) through the Executive Committee and then shared on the broader platform of the independent Expert Review Group (iERG) for the UN Secretary General's Global Strategy for Women's and Children's Health.

It is proposed that the VPI Secretariat collects the required data from countries and conducts a preliminary analysis from April to mid-June each year. A working group, chaired by a designated ETAGE member, would then draft the annual progress report from mid-June to mid-July. ETAGE would review and endorse the EVAP annual progress report for submission to the GVAP Secretariat before the end of July. In addition to the annual reports, a mid-term report to the Regional Committee would be made in 2017 and a final report in 2021. This proposal would require dedicated full-time staff in the Regional Office and the establishment of a standing ETAGE working group, chaired by a designated ETAGE member.

Discussion

The proposed Regional monitoring and evaluation process has a number of component parts and may require the input from more than a single ETAGE member, and it is also possible that two or more ETAGE members could share the considerable workload. While the working group should be chaired by an ETAGE member, it will include members of the VPI secretariat and consultant. In addition to drafting the annual reports, one of the tasks of the working group will be to review the indicators and determine if they require modification or revision over the six years of implementation. ETAGE is committed to support this process and further discussions are required to determine exactly how that will be achieved.

Update on the cVDPV detection in Ukraine

On 28 August 2015, two acute flaccid paralysis cases with highly-diverged VDPV type 1 were reported by the Polio Regional Reference Laboratory in Moscow. Both cases came from Zakarpatskaya oblast, in the far west of Ukraine, sharing international borders with Romania, Hungary, Slovakia, and Poland. This is a multi-ethnic oblast with significant minority and mobile populations, including approximately 14,000 registered Roma. The cases came from villages

approximately 70km apart. Sequence analysis of the virus isolates revealed a total of 18 identical shared mutations, and one had an additional nine mutations, suggesting virus circulation involving more than just these two individuals, with the possibility of up to two years of silent transmission. They were classified on 29 August 2015 as circulating VDPVs and their detection was classified as an outbreak.

The WHO Regional Office responded immediately by placing staff on the ground to advise on the necessary response. On 1 September 2015, the Ukraine Ministry of Health announced the outbreak and committed to a nationwide vaccination response of three rounds of vaccination targeting all children up to six years of age, with one round extended to children up to 10 years of age. It also planned to begin an accelerated routine vaccination effort in September. The tOPV vaccine donated by Canada earlier this year was planned to be used in support of this activity, and the first batch of 1.5 million doses was available in the country from May 2015. Unfortunately that vaccine was thawed and refrozen, which does not impair the quality or safety of the vaccine, but according to existing local legislation invalidates it for use. An additional 2.2 million doses of tOPV arrived in the country on 22 September 2015, but no immunization response has been initiated to date. Multiple objections and concerns have been raised in-country to justify the lack of outbreak response. WHO has assisted in developing the outbreak response plan, vaccine plan, advocacy and communications, resource mobilization, and has conducted a full case investigation and review of AFP surveillance. Despite everything being in place to mount an outbreak response, and very high-level calls for action from WHO and the international community, there has, to date, been no effective response from Ukraine.

Discussion

The outbreak area in Ukraine shares a border with Romania, a country already considered to be at high risk of poliovirus transmission following importation. National authorities in Romania have been advised to intensify poliovirus surveillance and to conduct supplementary immunization activities. This message is being amplified at high level within WHO and the international partner agencies. Romania has already switched to the routine use of IPV and the current recommendation is not to initiate an outbreak response as there is no indication, as yet, that the virus has entered Romania, but increased vigilance is required.

Polio Outbreak Simulation Exercise (POSE)

The Polio Outbreak Simulation Exercise (POSE) project was initiated in 2011 in collaboration with Public Health England as a way for countries to critically review and update their national plans on responding to the detection of WPV and VDPV, with the aim of increasing the level of preparedness to a possible WPV or VDPV event, improving capacity to respond, and improving risk communication and use of the IHR mechanism. POSE is designed to form the basis for a facilitated discussion on polio importation preparedness and is scenario driven, but linked to real life situations and experience. The target audience includes the Ministry of Health, public health authorities, clinicians, laboratories, communications professionals and multiagency partners.

The project has been conducted in three phases; the first (POSE I) involved Bosnia and Herzegovina, Montenegro and Serbia, the second (POSE UK) was conducted in the United Kingdom when an additional communications components were added, and the third (POSE II) has conducted for Armenia, Azerbaijan, Georgia and Ukraine. After POSE I Bosnia and Herzegovina succeeded in establishing a composite national preparedness plan, something that had appeared impossible before that. POSE II demonstrated that Ukraine was unable to respond effectively to polio importation, particularly with regard to engaging an immunization response. Ukraine has still not provided a national preparedness plan.

In 2014, the RCC urged all Member States to test their national preparedness plans using the POSE model. Following this recommendation three models for the use of POSE have been developed. All Member States are encouraged to use POSE to conduct a national outbreak simulation exercise using an *off-the-shelf exercise* model that is now available for downloading and implementation. POSE III will be an inter-country exercise involving five Member States in Central Europe to be conducted in Bucharest, Romania in October 2015. POSE IV will be an inter-regional exercise with 5 countries from the WHO European and Western Pacific Regions to be conducted in November 2015.

Rotavirus and Invasive Bacterial Disease Surveillance Networks

In the European Region there are two sentinel surveillance networks for diseases preventable by new and underutilized vaccines, one for rotavirus diarrhoea surveillance and one for meningitis surveillance. Surveillance for rotavirus diarrhoea is established in seven Member States (Armenia, Azerbaijan, Georgia, Republic of Moldova, Tajikistan, Ukraine and Uzbekistan) and surveillance for meningitis is established in 5 Member States (Armenia, Azerbaijan, Georgia, Ukraine and Uzbekistan). The Regional Networks are part of Global Networks that were established in 2007

through the unification of pre-existing networks under WHO Coordination. Approximately 80% of participating Member States are, or were, GAVI eligible.

The objectives of the surveillance networks are to establish baseline disease burden estimates before vaccine introduction, to provide data to justify vaccine introduction, and identify circulating pathogen strains. Additional objectives after vaccine introduction include monitoring vaccination programme impact in conjunction with epidemiological studies, and monitor changes in circulating pathogen strains. The networks are based on sentinel surveillance for hospitalized cases of children less than five years of age, targeted at the syndromes of diarrhoea and meningitis, and are supported by laboratory networks. Implementation is supported by WHO with GAVI funding in GAVI eligible countries, although the approach is encouraged elsewhere.

The primary goal in establishing surveillance sites within the networks is to ensure there is high quality data that is comparable over time and between sites. To that end standardized protocols, case reporting forms and laboratory methods have been established. For each network there is a common results database with standardized variables. Development of quality control and quality assurance has been paramount, with monitoring visits made to participating hospitals and laboratories, use of surveillance performance indicators, quality control retesting of a proportion of specimens by Regional Reference laboratories and participation of all sites in WHO external quality control programmes.

Of the seven Member States conducting surveillance for rotavirus, five (Armenia, Georgia, Republic of Moldova, Tajikistan and Uzbekistan) have now introduced rotavirus vaccine. Data collected over the past 6 years suggests a clear burden of rotavirus diarrhoea during the winter months, with approximately 60% of diarrhoea cases admitted to sentinel sites being rotavirus-positive during these months. As countries have introduced rotavirus vaccine there is evidence of declining rotavirus positivity rates, in comparison with the rates in countries that have not introduced the vaccine. Evidence from the Republic of Moldova demonstrates a significant decline in rotavirus-associated hospitalization after vaccine introduction, with the greatest declines seen in the vaccinated age groups, but declines also observed in older age groups.

Each year participating laboratories submit a selection of positive specimens for genotype analysis, and from this the programme obtains an indication of the range of rotavirus genotypes by geographical distribution and over time. This data can be compared with available global data on rotavirus genotype distribution, and also with data provided through the European Union's EuroRotaNet.

The rotavirus surveillance network is now well-established and producing reliable, useful data. It requires relatively few resources, is cost-effective and can be extended to address multiple public health-related questions. Challenges remain over how the network will be sustained when funding support from GAVI is withdrawn.

Of the six Member States participating in meningitis surveillance, all except Azerbaijan and Belarus had introduced *haemophilus influenzae* type B (Hib) vaccine prior to joining the network, and four (Armenia, Azerbaijan, Georgia and Uzbekistan) have now introduced pneumococcal conjugate (PCV) vaccine. All suspected meningitis cases, regardless of anticipated aetiology, are enrolled for study. Based on clinical and biochemical analysis of blood and cerebro-spinal fluid (CSF) testing the probable bacterial meningitis cases are identified, and of those cases, a specific bacterial aetiology is sought through further laboratory testing.

Of the almost 2,500 suspect cases with lumbar puncture specimens investigated between January 2010 and June 2015, 46% were considered to be probable bacterial meningitis cases, and of these *Streptococcus pneumoniae* was identified in 11%; Hib in 5%; and *Neisseria meningitides* in 20%. Isolation rates can be biased by the choice of hospital selected for the sentinel site, as some are general paediatric hospitals while others tend to specialise in treating suspected meningococcal cases and a larger proportion of those cases are referred there.

One of the key contributions this network has made in recent years is the introduction and evaluation of non-culture methods for confirming the diagnosis of bacterial meningitis. Culture alone was shown to identify a bacterial aetiology in approximately 15% of probable cases, this could be increased through the use of latex agglutination or the binax assay to approximately 35%; and further increased to approximately 50% through use of PCR.

The bacterial meningitis surveillance network has provided information on the relative frequency of different aetiologies among hospitalized cases of invasive disease, driving the development of laboratory capacity. Among well characterized cases of probable bacterial meningitis, a vaccine preventable aetiology has been identified for approximately 40-50%, and some information on the circulating serotypes and serogroups has been provided. However, the network faces some significant challenges. Many different factors influence the ability of the network to detect meningitis cases and accurately determine the aetiology, and the surveillance system does not monitor total burden of disease (e.g. non-hospitalized, non-invasive infections). In addition, meningitis accounts for only a small proportion of disease due to *Streptococcus pneumoniae*, and

the small numbers of bacterial meningitis cases identified limits ability of the network to detect changes over time (e.g. to monitor vaccine impact).

A 2013 external strategic review of the networks recommended the future focus should be on developing and strengthening better-performing sites, with no further expansion of the networks and withdrawal of support from poorly performing sites. A need for improve data quality and consistency of output was noted, this being most relevant for the bacterial meningitis network. The justification for continuing the rotavirus surveillance network in a post-GAVI environment appears to be relatively straightforward as the network is providing information that is useful to countries that introduce rotavirus vaccine and to those that do not. Justification for continuing support for the bacterial meningitis surveillance network is more difficult, as the usefulness of the surveillance data for monitoring the impact of vaccine introduction has been limited because of the timing of vaccine introduction and the small number of meningitis cases identified. If the surveillance could be expanded to include pneumonia and sepsis, then usefulness of information collected may be increased. The existence of this network of trained and assessed bacteriology laboratories also improves capacity of countries to address other objectives (e.g. AMR, outbreak response). Nevertheless, the technical, logistic and funding challenges presented are significant.

Discussion

ETAGE is appreciative of, and supports, the work that has been conducted in the face of some significant challenges, but the networks now need to focus on the practicalities of establishing sustainability. It would be beneficial to incorporate these networks into other surveillance networks that exist within the Region. It is questionable if four detection methods are necessary for bacterial meningitis surveillance when PCR is becoming the standard methodology and its use should be promoted above other methods. Serotyping is conducted on all positive specimens in an effort to investigate pneumococcal serogroup replacement following introduction of PCV. However, the small number of specimens identified through the existing surveillance, which is limited to meningitis together with the need for pre-vaccine baseline data, makes monitoring serotype replacement challenging. It is known that introduction of PCV has an impact on pneumococcal carriage, and this requires a system for non-invasive sampling, such as sampling nasopharyngeal aspirates.

ECDC have established a pneumococcal surveillance network with 15 sentinel sites investigating invasive pneumococcal disease. It would be beneficial to share the protocols and experience with this network with the WHO network.

Update on NITAGs

There are now 43 Member States with National Immunization Technical Advisory Groups (NITAGs). Nine Member States remain without official NITAGs, and there is no information on one Member State. 2015 has seen an increase in the amount of networking between NITAGs to exchange experience and strengthen collaboration. There was a session for NITAGs at the Programme Managers Meeting in Antwerp in September, and a recent collaborative study visit from the NITAGs of Belarus and Georgia to the Netherlands. It is intended that this exchange of information and experience between NITAGs will be continued and extended through a twinning process facilitated by WHO.

This year has also seen the start of NITAG evaluation activities, with the establishment of WHO performance and outcome indicators. The NITAGs GAVI-eligible countries are being evaluated this year, and it is intended that the evaluation process will be extended in 2016 to include NITAGs from other middle-income countries. The intention is to involve members of well-functioning NITAGs into this area of work as they understand the practical aspects of establishing and running NITAGs.

Broader-based training of NITAGs has now been conducted for several years, and this will be supplemented with more targeted training addressing specific issues. In collaboration with SIVAC, the twinning process and study tours will be continued and extended to encourage further collaboration between the well-functioning NITAGs and NITAGs from middle income countries. Participation of ETAGE members in meetings with NITAGs has been greatly appreciated and highly productive, and it is hoped that this can continue. Advocacy for establishment of NITAGs in the remaining nine Member States is urgently needed and best use is made of high level advocacy when the opportunity arises.

The greatest challenges include the lack of sufficient funds to maintain the NITAGs in middle income countries. Funding from GAVI can be used to fund meetings and training workshops in GAVI-eligible countries, but not for providing direct support or for technical visits to the countries. Of great concern is the potential lack of sustainability of NITAGs in the GAVI-graduating countries. Although some funding is provided through established graduating plans, this is unlikely to be provided long-term and the NITAGs may not be sustainable. It is necessary to develop a strong message to the international partners that many of these countries will require support for their NITAGs for several years.

Discussion

It is essential Member States understand that NITAGs need to be established as independent standing committees. The NITAG should include individuals with specific expertise in vaccines and immunization, including the budgetary and legislative aspects of immunization programmes.

Measles and rubella elimination, the 2015 goal and reaching consensus on the ETAGE role in announcements and formal processes to report back to the Regional Committee in 2016

It is now accepted that the Regional goal for measles and rubella elimination in 2015 will not be met, and a formal report to the WHO Regional Committee (RC) on the missed goal will be required in September 2016. The Regional Verification Commission for Measles and Rubella Elimination (RVC) will hold its 4th meeting in October 2015 to analyse the 2014 annual update reports from Member States and declare the status of transmission and elimination of measles and rubella in Member States and in the Region as a whole. Although data for 2015 will not be available from countries until October 2016, it is now accepted that the formal report to the RC will acknowledge the missed 2015 elimination goal – based on the report developed by the RVC and ongoing transmission of both viruses in the Region in 2015.

This year the RVC is required to endorse the data and provide an assessment of the elimination status of the Region by country, based on the first three years of reporting by Member States. A mechanism needs to be developed to bring together members of the RVC and ETAGE, probably through an extraordinary meeting March 2016, to review the RVC report and endorse the decision not to set a revised measles and rubella elimination target date. This will form the basis of a proposed RC resolution at its meeting in September 2016.

It would be most helpful to have a focal point on measles and rubella elimination in ETAGE to participate in the RVC meeting and to work with the RVC in preparing for the RC meeting in 2016. It is also essential to review current action plans for elimination and seek guidance from ETAGE on the additional approaches and activities that will be required post-2015 in order to maintain momentum in Regional measles and rubella elimination.

Update on measles and rubella elimination action plan and updated policies and strategies for the European Region

A significant amount of work has been conducted since 1997 by WHO, international partners and Member States towards achieving measles and rubella elimination in the Region. Many new and

inventive approaches and new techniques have been introduced over the past five years, one of which has been introduction of the verification process. Recent approaches from the social sciences have been introduced in an attempt to understand and counter vaccine hesitancy. These new approaches represent a large investment in time and resources, but many have yet to be evaluated. Development and application of new approaches is not unique to the European Region, but has been conducted within the context of the Global framework for measles and rubella elimination. The Regional strategic plan for elimination of measles and rubella was introduced in 1997, followed by the *Strategic Plan for Measles and Congenital Rubella Infection in the European Region of WHO* in 2003, *Eliminating measles and rubella and preventing congenital rubella infection WHO European Region strategic plan 2005–2010* in 2005 and the *Package for Accelerated Action: 2013-2015* in 2013. In 2015 the *Mobilization Plan* was issued, describing actions to be conducted during 2015, including country support, provision of technical advice, country missions, providing support to the verification process and communications and messaging.

The Global framework for verifying the elimination of measles and rubella was established in 2013, but remains under review by WHO and SAGE with the view to modifying the framework when necessary. The European verification framework was updated in 2014, with the next update due in 2016, to include the latest modifications in verification processes and procedures, which group countries by the level of achievement and verifies elimination at the country level.

During the Global meeting of RVCs in June 2015, it was concluded that a WHA resolution on global measles eradication would be useful and consideration should be given to creation of the Global Verification Committee or similar body. The roadmap for elimination needs to be finalized with input from the RVCs and the SAGE Special Working Group, and clear indicators for monitoring progress and indicators for quality of congenital rubella syndrome surveillance were urgently needed. Standardization across WHO Regions is important but it is not critical that all definitions and indicators used are exactly the same.

Developing Regional activities for post-2015 is ongoing and subject to review and open to comment and advice from the technical bodies and partners. The Region now needs to consider additional operational approaches to convincing Member States to implement the Regional elimination strategies. Member States are being requested to provide opinions on what they see as possible operational approaches and strategy modifications that could advance the elimination programme.

One main challenge remains the lack of commitment to the elimination goals on the part of some Member States, often related to competing priorities within their health care systems and

associated with a lack of capacity and resources. It must be recognised that the capacity of WHO to directly influence major change in Member States in the European Region is limited, and multiple approaches to persuading countries to adopt and implement recommendations are necessary. A plan of action or similar document addressing elimination activities after 2015 will be based on the review of activities conducted to 2015 and a review of the lessons learned. The new plan is being developed to maintain the momentum achieved so far, with updated technical information, and should be available in draft format by the end of 2015 or beginning of 2016. The final document should be available for publication in early 2016.

Discussion

ETAGE is aware that this is an area of enormous difficulty and appreciates the quality and volume of work that has already been directed at achieving the Regional elimination goals.

The benchmark for monitoring the case investigation rate is two discarded suspected measles/rubella cases per 100,000 population, but there are problems with in-country interpretation of the definition of a suspected measles/rubella case and it is probably that rash and fever cases that may meet the suspected case definition are not always being reported. There also appears to be a lack of active scrutiny of measles/rubella data in some countries that, if present, would highlight anomalies and deficiencies in the surveillance data. The role of the National Verification Committees is to endorse information provided by the national authorities, who should be conducting appropriate active scrutiny of the information being provided. However, differing approaches are being adopted by different countries, based on existing national structures and legal requirements.

The importance of providing additional opportunities for vaccination is a critical component of the strategy. Additional opportunities include supplementary immunization campaigns, which can be highly targeted, catch-up campaigns, and other activities targeted on specific age-groups or populations through modification of the routine immunization programme or *ad-hoc* intervention. Experience has shown that achieving a 95% 2-dose coverage through routine vaccination is not the only requirement, but that total population immunity levels must be high, and population immunity gaps must be closed, if elimination is to be achieved. This message should be made very clear to all Member States.

A very large number of documents, including reports, strategic plans and technical guidance, have been issued, and opportunity should be taken to consider which have been most successfully implemented, and which have not, and how they can be made more effective using a best practices approach. Asking individual representatives of NVCs on how best to communicate key messages in

their countries may facilitate tailoring of the message to specific countries and circumstances and be helpful to the process. Ranking of countries according to elimination achievement will permit the RVC to approach individual Member States and investigate the specific strategies in use and the success of implementation.

The need for ETAGE technical input into the post-2015 planning is well-recognized, as is the complexity and heterogeneity of the Region, and that although successful implementation or provided technical requirement in one country does not necessarily match a success or requirement in another.

Vaccine pricing publication and vaccine supply issues

Following a recommendation of SAGE in 2014 and a 2015 WHO resolution, there is now a process in place to monitor vaccine pricing through some Member States making information publically available. Several initiatives exist, including the WHO Vaccine Product, Price and Procurement (V3P) Project, all components of a multi-part solution to increase affordability and access to vaccines in middle income countries coordinated through the international partners. In the WHO European Region, following ETAGE recommendations in 2011 and 2014, and discussions held at the 2014 Programme Managers Meeting, a Vaccine Price Review has now been conducted and the results published³. The review is based on pricing information provided through the WHO/UNICEF Joint Reporting Form and harmonized within the V3P database. The data includes general information on pricing, availability, publication and legal restrictions, and product specific data (14 variables) including product, presentation, manufacturer, procuring agency, total number of doses/units, price per dose and terms of delivery, and contract details. In all, 28 Member States in the Region have shared their information.

Analysis of the database shows that for 22 products routinely used in the Region, only one or two manufacturers exist. These products tend to be the newer vaccines or combinations, as the traditional EPI vaccines usually have multiple manufacturers. Large price variations exist for most products, in particular new vaccines. Lack of obvious trends in the price paid related to income level of the Member State as well as to vaccine presentation or formulation raises questions whether a

³ World Health Organization Regional Office for Europe. 2015 Review of vaccine price data.

Available at: www.euro.who.int/en/publications/abstracts/review-of-vaccine-price-data-submitted-by-who-european-region-member-states-through-the-whounicef-joint-reporting-form-for-2013-2015

chosen vaccine formulation is a rationale choice, whether the paid vaccine prices are equitable and affordable and whether vaccine procurement systems are efficient and the vaccine market is healthy.

A main challenge to this work is that relevant data is owned by different bodies within the countries, for example by the National Immunization Programme, health insurance bodies or Ministry of Health procurement departments, and information is often not available in countries with decentralized vaccine procurement systems. There are also issues over data confidentiality and how this relates to commercial practice, data completeness and quality, and how shared costs, incurred for initial shipping, storage and delivery, are reported.

The next steps include expanding country commitment towards vaccine price transparency, seeking ETAGE support for advocacy, and promoting online access to the V3P platform and database. Additional activities are also required for increasing capacity in Member States on accessing, analysing, interpreting and using vaccine price data. A 3-day training workshop is planned to be held in December 2015.

Discussion

ETAGE recognises the importance of this work and encourages continuation of Regional activities to update the report over time. Member States may decide on the vaccine price data they provide to the V3P database and have full control on their own data. There is open access to the shared vaccine price data through the V3P portal that offers various types of data analysis. Country names are not displayed in the database because the country name should not be used as a price-driver. The database contains information on the origin of product, but WHO has attempted to focus attention on quality, and quality assurance, rather than country of origin of vaccines. The database was originally designed as a very comprehensive tool collecting a wide range of information, but it proved to be too broad and information was not being made available by countries, so the scope of the database was reduced to better match the capacity to easily collect data.

Vaccine supply issues

WHO/UNICEF JRF data is used to conduct annual monitoring of vaccine stock-outs. The observed trend over the past several years has been for a decline in the number of stock-outs reported at national level. The EVAP goal is to have no more than three reported vaccine stock-outs per year. Historically there were no major differences in the number of stock-outs reported by middle income countries and high income countries.

2015 has seen a significant rise in the attention of the media to vaccine supply issues, as Member States have reported facing vaccine supply shortages. Some Member States, including Kazakhstan, Lithuania and Bosnia and Herzegovina made requests to WHO for support in addressing vaccine supply shortages. Decreased supply of WHO pre-qualified BCG vaccines by global manufacturers and an increase in vaccine demand led to globally reduced BCG vaccine supplies starting in 2014. A guidance document on how to prioritize supply and the use of BCG vaccine was prepared and published by WHO⁴. A shortage of global supply of acellular pertussis (aP)-containing vaccines, was also apparent with the increasing number of Member States facing vaccine supply shortages. These vaccines are used mainly by upper level middle income and high income countries and are not supplied through UNICEF SD. Accordingly, WHO has no formal mechanism to obtain information on potential supplies and timelines of production, or country demand and forecasting for procurement. In April 2015 the subject on vaccine supply shortages in European

Union countries was brought to the agenda of the European Commission's Health Security Committee. In response, WHO prepared a questionnaire on vaccine supply shortages for specific products, to which 25 Member States responded. Of the 25 member States, 20 have reported supply-related shortages, and additional information suggests that at least another seven Member States in the Region are also facing vaccine supply shortages.

A total of 16 products have been reported to be in short supply, the most frequently reported being BCG, aP-containing vaccines and whole-cell pertussis (wP)-containing vaccines. The BCG shortage is due to suspension of production of SSI vaccine and delays in changing licensing requirements to allow procurement of alternatives. Solutions have included suspending immunization of infants for a period of one to four months, identification of new suppliers, and procurement of unregistered products. Problems with supply of aP-containing vaccines have been recognised since 2014 when smaller countries failed to receive tender offers and many countries started experiencing long delays in contracts being fulfilled. Solutions have included switching to new products, modifying vaccination schedules, delaying primary vaccinations, postponing school vaccination or seeking assistance from neighbouring countries.

⁴ World Health Organization. Guidance on how to prioritize globally constrained BCG vaccine supply to countries. 2015. Available at: www.who.int/immunization/diseases/tuberculosis/BCG-country-prioritization.pdf

Key messages to countries resulting from this experience include prioritizing primary immunization activities, reviewing vaccine procurement and vaccine stock monitoring systems, adopting multi-year forecasting and longer-term contracting and actively developing supply risk mitigation strategies.

The main challenges include the limited information available on global vaccine supply markets and global demand. Information is available only for products and for countries procuring through UNICEF Supply Division. There is no Regional mechanism to monitor vaccine stock levels. The current mechanism to monitor stock-outs using JRF reports is designed for progress monitoring and is not adequate to identify gaps and assess the needs throughout the year. Expanding the scope of work will require considerable commitment and investment from WHO, the Member States, international partner agencies and vaccine manufacturers.

Discussion

The potential links between vaccine prices and supply problems have not yet been investigated but the data should be available in the database, and will be assessed. The supply situation is getting worse with time. In some cases manufacturers appear to be driving some of the problems by encouraging Member States to adopt the newer vaccines, pushing up demand. This is a very complex area that needs to be monitored. The Region is looking to SAGE to provide some action points on tackling this problem, but in the interim the Region will need to develop some response strategies in support of Member States.

Conclusions and recommendations

Conclusions

The continued personal attention and support for immunization given by the WHO Regional Director is greatly appreciated by ETAGE, as is the high level of technical competence in support of immunization services demonstrated by the secretariat in undertaking an increasing workload.

ETAGE greatly appreciates receiving updates on progress made in the implementation of recommendations made in previous meetings, and sees this as an important component of the meeting and of the ongoing work of ETAGE.

The opportunity for further technical discussions on the rationale for, and practical implications of, serosurveys in the context of verifying measles and rubella elimination in the Region are appreciated. ETAGE acknowledges that the technical and resource implications of serosurvey studies can be substantial and that any decision to undertake these studies should be taken with clear and

focused public health objectives and not done where other data or indicators provide sufficient information to recommend an intervention and how best to implement it.

ETAGE notes the current inactivated polio vaccine (IPV) supply problems and the challenges to identification and disposal of trivalent oral polio vaccine (tOPV) stocks. ETAGE has significant concerns over the legislative and licensure issues regarding bivalent oral polio vaccine (bOPV) that some countries face and the possibility of logistical difficulties in effecting the change-over in accordance with the proposed timeline. In this regard, ETAGE has particular concerns over lack of timely progress towards bOPV licensure in the Russian Federation and in Ukraine.

ETAGE applauds the significant progress and achievements made over the last year on several projects in immunization communications. ETAGE recognises that the WHO European Region is currently leading the world in this critically important area and acknowledges and appreciates the high quality ground-breaking work being conducted.

ETAGE acknowledges the importance of establishment of a European Vaccine Action Plan (EVAP) working group to support and develop preparation of annual and interim reports over the next five years and agrees to participate in this activity.

ETAGE notes with concern the recent detection of circulating vaccine-derived polio virus (cVDVP) in Ukraine, against a background of low immunization rates, and the lack of an immunization outbreak response to date. This scenario represents a major threat to the polio-free status of the Region. ETAGE are also greatly concerned over the apparent vulnerability of populations in Romania and encourage efforts to increase population immunity and surveillance sensitivity there.

ETAGE commends the Secretariat for the polio outbreak simulation exercises (POSE) programme and appreciates and applauds the significant progress being made in implementing this important preparedness activity. It is also apparent to ETAGE that the Secretariat's application of scenario-based simulation exercises on other areas of work (i.e. Vaccine safety and resource mobilization) has drawn significant attention and demand from partners and other WHO Regional Offices to adopt and adapt the European Regional Office Secretariats work beyond the Region's borders.

ETAGE commends the new and under-utilized vaccines implementation (NUVI) programme for the work conducted by the rotavirus (RV) surveillance network and acknowledges the value of the invasive bacterial diseases (IBD) surveillance network over recent years. The networks now need to focus on the practicalities of establishing sustainability and it would be beneficial to explore greater linkage of these networks with other surveillance networks that exist within the Region.

ETAGE recognises the need for continued support and funding from governments, international funders and partners throughout the Region for development of sustainable NITAGs. Together with their partners, ETAGE will remain actively involved in supporting training for NITAG members.

ETAGE recognises with regret that there is now a low likelihood of achieving measles elimination in the Region in the near future, but that Regional rubella elimination may be attainable in the shorter term. Efforts to achieve elimination of both diseases must be redoubled in the Region, concomitant with increased political commitment on the part of Member States attain the goals.

ETAGE greatly values the Regional report on vaccine pricing and encourages continuation of work to update the report over time. ETAGE notes the wide variation in central vaccine purchasing price reported by those countries in the Region from which data are available. ETAGE notes with concern the recent vaccine supply shortages, particularly those affecting BCG and acellular pertussis-containing vaccines. ETAGE notes that some Member States appear to have very limited or inadequate mechanisms in place to respond to fluctuations in vaccine supply and little or no resilience in the face of vaccine supply interruptions.

Recommendations

1. Recognizing that significant population immunity gaps to measles and rubella exist in many countries in the Region, and that these gaps will not be closed through routine childhood immunization, ETAGE recommends:
 - Member States apply additional efforts to identify immunity gaps using existing serological data pertaining to populations with known coverage history or, if necessary, through new studies, to characterise the serological profiles/features of populations at risk of outbreaks.
 - The WHO Secretariat assemble the evidence base for populations considered at risk of measles and rubella outbreaks and identify specific circumstances in which serosurveys could materially contribute to policy making, or galvanization into action, to avoid vulnerability and prevent outbreaks.
2. With regard to the proposed global switch from tOPV to bOPV use, recognizing the possibility of insufficient supplies of IPV and legislative issues on bOPV introduction in some setting in the next few months, ETAGE recommends that a contingency plan be formulated by WHO by 15 November 2015 to address potential problems.
3. ETAGE recommends the Secretariat give careful consideration to the various communications projects focussing on minimizing any vulnerability to external distortive commentary and to

develop plans to evaluate and demonstrate the impact of these educational, training and communication schemes, with which ETAGE may assist.

4. Recognizing the important role ETAGE will play in the process of monitoring and evaluating implementation of EVAP, the Secretariat is recommended, as a matter of urgency, to facilitate further discussions with ETAGE on the establishment of an ETAGE Working Group on EVAP monitoring and evaluation and to determine the expected roles and responsibilities of ETAGE members in the functioning of this Working Group.
5. ETAGE urges every effort be made to promote progress in establishing effective outbreak response immunization campaigns in Ukraine.
 - Romania is at risk of importation of cVDPV from Ukraine and efforts are required to increase population immunity, particularly in those populations living in areas close to the border with Ukraine.
 - Efforts should also be made to improve the quality of environmental surveillance in Ukraine and neighbouring countries, particularly Romania.
6. ETAGE recommends that RV and IBD surveillance networks focus on engagement and collaboration with all sites, networks and agencies already functioning in this area within the Region.
 - With regard to IBD surveillance, consideration should be given to streamlining and standardizing methodology (particularly with regard to well-standardised and automated qPCR approaches) and, with regard to bacterial epidemiology, considering non-invasive carriage studies using molecular detection methods in healthy children and adolescents.
7. Recognizing that the 2015 Regional measles and rubella elimination target will not be met, and given the apparent disparity in likelihood of achieving the measles and rubella elimination goals at the same time, consideration should be given to separation of the two Regional targets.
 - ETAGE recommends that efforts to achieve higher primary schedule vaccination coverage are complemented by identifying and providing immunization coverage of susceptibles in older age groups. These groups represent significant challenges to elimination that are increasing in importance with the passage of time.
8. ETAGE recommends that the Regional report on vaccine pricing be made widely available, particularly to national purchasing authorities, in order to encourage greater equity and improved function of the vaccine market.

- Continuing efforts should be made to strengthen capacity for vaccine supply planning and procurement in the Region, and all countries should be encouraged to review their vaccine supply interruption contingency plans.

The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

Member States

Albania	Cyprus	Ireland	Netherlands	Spain
Andorra	Czech Republic	Israel	Norway	Sweden
Armenia	Denmark	Italy	Poland	Switzerland
Austria	Estonia	Kazakhstan	Portugal	Tajikistan
Azerbaijan	Finland	Kyrgyzstan	Republic of Moldova	The former Yugoslav
Belarus	France	Latvia	Romania	Republic of Macedonia
Belgium	Georgia	Lithuania	Russian Federation	Turkey
Bosnia and Herzegovina	Germany	Luxembourg	San Marino	Turkmenistan
Bulgaria	Greece	Malta	Serbia	Ukraine
Croatia	Hungary	Monaco	Slovakia	United Kingdom
	Iceland	Montenegro	Slovenia	Uzbekistan

World Health Organization

Regional Office for Europe
UN City, Marmorvej 51, DK-2100 Copenhagen Ø, Denmark
Tel.: +45 45 33 70 00 // Fax: +45 45 33 70 01
Email: contact@euro.who.int // Website: www.euro.who.int