

Polio eradiction and laboratory containment programme of wild polioviruses in Belgium. Laboratory survey and inventory phase

by

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Abstract

The world will be declared free of wild poliovirus transmission when the World Health Organization (WHO) Global Commission for the Certification of the Eradication of Poliomyelitis is satisfied that all WHO Regions have documented the absence of wild poliovirus circulation for at least three consecutive years and all wild poliovirus materials in laboratories are adequately contained. Indeed, the risk of reintroduction of wild polioviruses from the laboratory to the community must be minimized. The Global Commission has established the requirements for laboratory containment of wild polioviruses. These requirements are described in two phases: the Laboratory Survey and Inventory Phase and the Global Certification Phase. The Laboratory Survey and Inventory Phase has been achieved in Belgium. A total of 411 institutions/laboratories have been surveyed in 2002 in order to identify those retaining wild poliovirus or potentially infectious materials. Taking into account the risk assessment performed on the 11 non-respondents and their exclusion from the survey, it has finally been considered that a 100% response rate

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has been reached. The laboratory survey has initially identified 8 laboratories holding wild poliovirus materials. In June 2004, this number was reduced to 5. All of these laboratories comply with the Belgian regional biosafety regulations on 'contained use' of pathogens and with WHO BSL-2/polio requirements. Belgium is now ready to initiate the Global Certification Phase. However, this phase will only begin when one year has elapsed without isolation of wild poliovirus anywhere in the world.

Keywords: containment, eradication, inventory, laboratory survey, poliovirus

Introduction

In 1988, the World Health Assembly adopted a resolution calling for global eradication of poliomyelitis by the end of 2005. A global goal of disease eradication has previously only been accomplished for smallpox. In June 2002, the World Health Organization (WHO) European Region was certified as free of indigenous wild poliovirus transmission, joining the WHO Regions of the Americas and the Western Pacific. The world will be declared poliomyelitis-free when the WHO Global Commission for Certification of the Eradication of Poliomyelitis is satisfied that all WHO Regions have documented the absence of wild poliovirus circulation in human populations, the only natural reservoir, for at least three consecutive years and all wild poliovirus materials in laboratories are adequately contained.

The Global Commission has established the requirements for laboratory containment of wild polioviruses, and the 2nd edition of the global action plan for laboratory containment of wild polioviruses describes those requirements in detail (1). Guidelines on how to implement the requirements have been issued and adapted by the WHO Regions (for European Region: 2). The WHO global action plan for laboratory containment of wild polioviruses aims to identify laboratories worldwide that store wild poliovirus and potentially infectious materials, and ensure that those materials are handled under appropriate biosafety conditions after eradication of the disease. Once polio has been eradicated, the only sources of wild poliovirus will be in biomedical laboratories. The probability of a laboratory-associated poliovirus infection is small, but the consequences increase with time. An accidental or intentional transmission of wild poliovirus from a laboratory or vaccine production site into a growing non-immune community, after eradication of the disease and stopping of vaccination, could represent a public health threat of global proportions.

The Global Certification Commission requirements for containment of wild polioviruses are described in two phases: the Laboratory Survey and Inventory Phase and the Global Certification Phase.

The first phase covers the period when the number of polio-free countries and regions are increasing, but wild polioviruses continue to circulate somewhere in the world. During this phase, all countries are required to survey all biomedical laboratories to identify those with wild poliovirus or potentially infectious materials and encourage destruction of all unneeded materials. It is also necessary to develop a National Inventory of laboratories that retain such materials and submit it to the Regional Certification Commission and to instruct these laboratories to implement biosafety measures for safe handling, appropriate for the materials stored and the procedures being carried out. Laboratories to be surveyed include not only those associated with 'classical' poliovirus laboratory functions but also laboratories in other sectors that could potentially have materials in storage collected during a time when wild poliovirus was circulating.

The second phase will only begin when one year will have elapsed without isolation of wild poliovirus anywhere in the world.

The present paper aims to describe how the Laboratory Survey and Inventory Phases was conducted in Belgium and the results thereof.

Methods

Responsibilities

Containment activities undertaken in the frame of the polio eradication programme in Belgium have been placed under the responsibility of the Scientific Institute of Public Health (IPH), Federal Public Service Health, Food Chain Safety and Environment. A biosafety expert of the Division of Biosafety and Biotechnology (SBB) of IPH has been appointed as a focal point (National Coordinator) for the national containment process.

The National Containment Coordinator has been working in coordination with the National Certification Committee (NCC) on Eradication of Poliomyelitis. The National Coordinator had also to cooperate with the Belgian Regional authorities.

In Belgium, all activities involving the contained use of genetically modified organisms (GMOs) and/or pathogens (for human, animals or plants) must be authorized or notified in accordance with the regional regulations on this matter (3). These regulations include provisions for an assessment of the contained uses as regards the risks to human health and the environment that these contained uses may incur.

Any installation or laboratory where operations in which wild polioviruses, pathogens for human of biological class of risk 2, are cultured, stored, used, destroyed or disposed is thus regulated in this context and must be previously authorized by the regional competent authority.

The Cooperation Agreement of 25 April 1997 between the federal state and the regions on the administrative and scientific coordination concerning biosafety (4) has instituted the SBB, with the Biosafety Council, as the single biosafety scientific advisory system common to the federal and regional authorities. The SBB holds information on all laboratories that have notified activities in which GMOs and/or pathogens are involved.

National Laboratory List

The following registers or lists of institutions/laboratories have been used to establish the National Laboratory List used for the survey:

- the databases of institutions/laboratories that have notified contained uses of GMOs and/or pathogens according to the regional regulations, hosted by the SBB at IPH;
- the official list of registered medical diagnostic laboratories, managed by the Unit of Clinical Biology of the IPH;
- the database of companies and laboratory departments available on the internet site of the Belgian Bioindustries Association (5).

For the process of establishing the National Laboratory List, the different above-mentioned lists have been merged and redundant information has been eliminated. No attempt was made to identify all the laboratories within each institution that could be relevant and could be included in the list. Focus was on the inclusion of all the institutions where wild poliovirus infectious or potentially infectious materials could be retained. Indeed, from the legal point of view, the exploitant of the institution is legally responsible for the contained uses of pathogens in all the laboratories of his/her institution. The survey letters and forms have thus been addressed to the organization/institution head to lead the survey inside his/her own institution.

Survey questionnaires

Survey questionnaires have been sent to all institutions/laboratories included in the National Laboratory List. These questionnaires have been built up following the recommendations laid down in the 'Guidelines for Implementation of Laboratory Containment of Wild Poliovirus' (2) and adapted to the Belgian linguistic and regulatory situation.

The survey mailing included an introduction letter, an inventory form for the person in charge of the institution, and an inventory form with its accompanying letter for the person in charge of the laboratory.

National Plan of Action

A national Plan of Action has been elaborated in order to help surveyed institutions/laboratories and to promote the implementation of the WHO programme on containment in Belgium.

Results

National Laboratory List and Survey

In accordance with the regional regulations on contained use of pathogens and GMOs, nearly 400 institutions/laboratories reported more than 1100 'contained use' activities at the moment of the survey. The corresponding databases give an overview of institutions and laboratories handling pathogenic organisms and GMOs in Belgium. Different types of installations are involved: federal, regional or provincial scientific institutes, universities and associated institutes or centres, high schools, diagnostic clinical laboratories including hospitals, private laboratories, small companies and large industries. Representative institutions of all these sectors have been included in the survey. Two other registers have also been used to complete or to control the completeness of these 'contained use' databases. The final National Laboratory List contained a total of 411 institutions that have been surveyed.

The National Laboratory Containment survey has been conducted in Belgium in 2002. After sending 2 reminders to non-responding institutions, a 95.9% response rate was reached.

The list of institutions/laboratories that had been contacted but had not answered the survey was sent to the Belgian regional environment ministers to let the inspection bodies of the regional authorities check these institutions/laboratories. The SBB obtained a feedback from the regions for 6 out of 17 non-responding institutions. None of them retained wild polioviruses. Taking into account this information, a 97.3% response rate has been achieved.

The 11 non-responding institutions were subsequently submitted to a thorough risk assessment. On the basis of knowledge of the activities performed in these institutions and of the results of the survey obtained for similar institutions, it has been concluded that these non-respondents

can be considered to have a very low probability of retaining wild poliovirus infectious materials. They have thus been excluded from the survey afterwards. Taking into account the risk assessment performed on the non-respondents and their exclusion from the survey, a 100% response rate has been achieved.

Three types of responses were obtained: institutions and laboratories that did not retain wild poliovirus infectious materials, institutions and laboratories that clearly retained wild poliovirus infectious materials and doubtful responses. These last cases have been resolved by direct phone contact with the person responsible for the laboratory (<1%).

National Laboratory Inventory

The laboratory survey has identified 8 laboratories holding wild poliovirus materials. They were all included in the inventory. The type of activities (control, diagnostic, research, production, teaching) of laboratories retaining wild poliovirus infectious materials has been encoded in this inventory as well as the nature of retained materials (wild poliovirus strains, infectious, potentially infectious materials only). All the institutions/ laboratories known to work with poliovirus on the basis of local previous knowledge have responded to the survey and gave expected results.

The list of institutions/laboratories retaining wild poliovirus and/or (potentially) infectious materials was sent to the Belgian regional authorities for control and inspection. In June 2004, the number of laboratories retaining wild poliovirus materials was reduced to 5, following the encouragement to destroy or to ship wild poliovirus materials to a reference laboratory. All of these reference laboratories have notified the Belgian regional competent authorities of their activities under the regional biosafety regulation on 'contained use' of pathogens. All of them have been inspected by the regional inspection services: they all comply at least with the BSL-2/polio requirements (1). Production facilities of inactivated polio vaccine comply at least with BSL-3 requirements (1) specific for large-scale production units.

Discussion

The number of surveyed institutions as well as the number of laboratories in the inventory are comparable with those obtained in other countries of the WHO European Region (6).

The response rate that has been reached for the survey is high, even though there was no strict legal support to demand compliance on

responding to the survey. The mailing reminded the addressees of the regional regulations on contained use of pathogens, and it was also mentioned that this survey was performed at the request of WHO. These two elements were persuasive enough to lead to a response.

When the containment activities in the frame of the polio eradication programme begun, Belgium already had all legal instruments in place in order to develop adequate laboratory containment procedures. Indeed, with regard to the process of laboratory containment of wild poliovirus, this regulatory context provided:

- advanced databases for contained use data from which it was possible to extract a provisional national laboratory list for the polio survey;
- as mentioned above, the persuasion strength to lead institutions and laboratories to comply with the survey;
- a compulsory authorization for any installation or laboratory culturing, storing, using, destroying or disposing of wild polioviruses. The legally binding requirements concerning the containment measures are clearly listed in the authorization and adapted to the contained use. Specific requirements for poliovirus laboratories can be included in such an authorization, directly referring to the WHO requirements.

Phase I of the polio containment activities in Belgium was reported to WHO/EURO Regional Certification Commission (7).

As the Laboratory Survey and Inventory Phase has been achieved, Belgium is now ready to initiate the Global Certification Phase. However, this phase will only begin when one year has elapsed without isolation of wild poliovirus anywhere in the world. During this phase, nations are required to:

- notify biomedical laboratories that poliovirus transmission has been interrupted.
- instruct laboratories on the National Inventory to select one of the following three options:
 - render materials non-infectious for poliovirus or destroy them under appropriate conditions;
 - transfer wild poliovirus infectious and potential infectious materials to laboratories capable of meeting the required biosafety standards;
 - implement biosafety requirements appropriate for the laboratory procedures being carried out (BSL-2/polio or BSL-3/polio).
- document completion of all containment requirements for Global Certification.

Conclusion

The Laboratory Survey and Inventory Phase has been achieved in Belgium. A 100% response rate has been obtained for the survey. In June 2004, the number of laboratories retaining wild poliovirus materials was reduced to 5. They all comply at least with the biosafety requirements.

Belgium is now ready to initiate the Global Certification Phase after one year has elapsed without isolation of wild poliovirus anywhere in the world.

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Samenvatting

De wereld zal vrij van overdracht van wild poliovirus verklaard worden wanneer de "Global Commission for the Certification of the Eradication of Poliomyelitis" van de Wereld Gezondheidsorganisatie (WGO) ervan overtuigd is dat alle WGO-regio's de afwezigheid van het circuleren van wild poliovirus voor ten minste 3 jaar goed gedocumenteerd hebben, en dat elk wild poliovirus materiaal op de juiste wijze is ingeperkt. Het risico dat wild poliovirus vanuit het laboratorium opnieuw in de populatie zou verspreid worden, moet inderdaad tot een minimum beperkt worden. De "Global Commission" heeft de vereisten voor de inperking van wild poliovirus in laboratoria vastgelegd. Deze vereisten worden verdeeld over 2 fasen: de "Laboratory Survey and Inventory Phase" en de "Global Certification Phase". De "Laboratory Survey and Inventory Phase" is voor België reeds beëindigd. In 2002 werd bij 411 inrichtingen/laboratoria een enquête uitgevoerd om de laboratoria te identificeren die wild poliovirus of potentieel infectieus materiaal in hun bezit hebben. Rekening houdend met een risico-evaluatie van 11 inrichtingen die niet op de enquête reageerden en hun uitsluiting uit de enquête, werd finaal besloten dat de enquête voor 100% beantwoord werd. De enquête had oorspronkelijk 8 laboratoria geïdentificeerd die wild poliovirus in hun bezit hadden. In juni 2004 werd dit aantal herleid tot 5. Elk van deze laboratoria voldoet aan de regionale bioveiligheidswetgeving inzake ingeperkt gebruik van pathogenen en aan de WGO BSL2-poliovereisten. België is nu klaar om met de "Global Certification Phase" te beginnen. Niettemin zal deze fase enkel van start gaan wanneer er één jaar voorbijgegaan is zonder dat er ergens in de wereld wild poliovirus geïsoleerd werd.

Résumé

Le monde sera déclaré libre de transmission du poliovirus sauvage quand la Commission Globale pour la certification de l'éradication de la Poliomyélite de l'Organisation Mondiale de la Santé (OMS) aura vérifié que toutes les régions de l'OMS ont documenté l'absence de circulation de poliovirus depuis au moins trois années

consécutives et que le matériel poliovirus sauvage en laboratoire est correctement confiné. En effet, le risque de réintroduction du poliovirus sauvage du laboratoire à la communauté doit être minimisé. La Commission Globale a établi des exigences pour le confinement des poliovirus sauvages en laboratoire. Ces exigences sont décrites en deux phases: une enquête des laboratoires et une phase d'inventaire et la phase de certification globale. La phase "Laboratory Survey and Inventory" a été réalisée en Belgique. Un total de 411 institutions/laboratoires ont fait l'objet de l'enquête en 2002 de manière à identifier ceux qui détenaient du poliovirus sauvage ou du matériel potentiellement infectieux. Prenant en compte l'évaluation du risque réalisée pour les 11 non-répondants et leur exclusion de l'enquête, il a été finalement considéré qu'un taux de 100% de réponse a été atteint. L'enquête des laboratoires a initialement identifié 8 laboratoires possédant du poliovirus sauvage. En juin 2004, ce nombre a été réduit à 5. Tous ces laboratoires se conforment aux législations régionales belges relatives à l'utilisation confinée de pathogènes et avec les exigences du niveau de confinement BSL-2/polio de l'OMS. La Belgique est maintenant prête à initier la Phase Globale de Certification. Cependant cette phase ne commencera en Belgique que quand une année se sera écoulée sans isolement de poliovirus sauvage quelque part dans le monde.

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