16.3 Smallpox eradication: destruction of variola virus stocks

Contents

In focus at WHA67

The WHA67 will consider the Secretariat report, A67/37, a revision of EB134/34 following the debate within the Board. The focus of discussion will again be whether to set a timetable for the destruction of variola stocks. However, there was some concern expressed at the Board regarding modern biosynthetic technologies and the DG proposes to convene an expert group to advise. This will attract some comment as well perhaps.

Background

Immediate

The document considered by the EB in Jan 2014 (EB134/34) reported on work undertaken by the Secretariat in preparation for the 67th World Health Assembly. It summarized the conclusions of both the Fifteenth meeting of the WHO Advisory Committee on Variola Virus Research (ACVVR) in Geneva, 24 and 25 September 2013, and the second Advisory Group of Independent Experts (AGIES) to review the smallpox research programme (Geneva, 5 and 6 November 2013), and the recommendations of a meeting of the Strategic Advisory Group of Experts on immunization (SAGE) in Geneva, 5–7 November 2013. The latter Group based its conclusions and recommendations on the outcome of an expert consultation on smallpox vaccines and the WHO smallpox vaccine stockpile (Geneva, 18 and 19 September 2013).

History

Destruction of variola (smallpox) virus stocks is one of the oldest standing issues on the World Health Assembly's agenda. Even before smallpox was declared eradicated in 1980, debate began among WHO Member States about how to eventually destroy all remaining laboratory samples of the virus. In the late 1970s and 80s, worldwide collections of these samples were

either destroyed or sent to two WHO Repositories for safekeeping. In the midst of the Cold War, these repositories were unsurprisingly located in Russia and the United States.

After the samples were condensed to two locations and Member States confirmed they held no more viruses on their own, in 1990 the United States pledged to destroy the stocks located at the WHO Repository in Atlanta once a virus sample was genetically sequenced. This sequencing project was done and, in 1996, the World Health Assembly resolved to destroy all remaining stocks by 1999.

Destruction of the virus is possible because smallpox vaccines are manufactured from a related virus called vaccinia. And in the unlikely event that smallpox ever reappeared in the wild, it is vaccinia virus and not variola virus that is needed to make new vaccines.

When 1999 came, as the WHA's date to destroy the remaining virus stocks approached, the United States and Russia both balked, refusing to implement the WHA resolution. Part of their hesitancy related to mutual distrust – each feared the other might use the virus as a weapon (even though it is not especially well suited for such use).

Instead of destroying the viruses deposited by many Member States in the WHO Repositories, Russia and the US kept them, and insisted on performing further research with them, research that is especially risky given transmissibility of the virus between humans, its high fatality rate and often debilitating effects on survivors. Moreover, globally, immunity against infection was on the decline, with the termination of routine vaccination programs in developing countries in the late 1970s and 80s. (Many developed countries stopped vaccinating earlier.)

After the 1999 failure to destroy the viruses, the WHA agreed to allow a time-limited and specific research program with the remaining stocks. This research program was wholly restricted to enumerated purposes deemed essential for public health. These were additional sequencing, new diagnostics, a new generation of vaccines, development of antiviral drugs, and development of an animal model of smallpox infection, using variola virus, in order to support vaccine and antiviral studies.

Some experts, including participants in the successful eradication program, never warmed to the research program, feeling that the risks outweighed the benefits or, as the American who led the WHO Eradication Program quipped, the less that was done with variola virus, the better. Fewer risks, fewer suspicions.

Nevertheless, for more than a decade the US and Russia – but especially the US – have conducted smallpox studies under the theoretical supervision of a WHO committee called the Advisory Committee on Variola Virus Research (ACVVR). This committee has suffered from opaque procedures and geographic imbalance and, by 2005, had caved in to US pressures to the point of approving genetic engineering experiments with smallpox.

This latter research approval prompted a reaction from civil society, including members of the Peoples' Health Movement, and from WHO Member States. There was great concern

expressed that initiating genetic engineering experiments with WHO endorsement with the virus was a dangerous idea and precedent.

The WHO Director-General, under pressure, reversed the ACVVR's decision, setting into motion a series of WHA debates on destruction of the virus samples that could culminate in another decision to destroy the virus stocks at the upcoming 67th WHA in 2014. A notable development in this process was a Major Review of the research program, released in 2011 and discussed by the WHA in 2012. Although the Major Review concluded that the research program was largely complete, the 64th WHA could not agree on a new date for destruction of the virus stocks, postponing the discussion until the upcoming 67th WHA.

(A series of NGO publications track the process of the WHA's debate since 2005, including the major review, in great detail. These papers can be downloaded at www.smallpoxbiosafety.org.)

One important organizational outcome of the Major Review was the establishment of a second WHO committee to assess the variola virus research program. This committee is the Advisory Group of Independent Experts (AGIES) to review the smallpox research program. Whereas the ACVVR has opaque procedures and outsized representation from some countries and institutions with vested interest in continuing variola virus research, the AGIES is composed of public health experts, has a clear structure, and is not beholden to the interests of specific governments and research agencies.

The AGIES met in late 2013 and unequivocally concluded that no essential public health purpose remains for retaining the variola virus stocks, meaning that the WHA should now move to again fix a date for their destruction. Many viruses have been sequenced, many new, rapid, and accurate diagnostics have been developed, several new generation vaccines have been developed, licensed, and in some cases stockpiled, and two new antiviral drugs are in late stages of regulatory review, with the US Food and Drug Administration having stated that no further studies utilizing variola virus will be necessary for their licensure.

Remarkably, the ACVVR, which at its last meeting in 2013 had more voting representatives from the United States than some entire WHO regions, largely agrees with the AGIES public health experts. The ACVVR's only area of disagreement with the AGIES relates to the desirability to keeping variola virus for further antiviral drug studies. But there, the Committee favored retaining the virus by only a bare majority. Thus, if it were not for the outsized representation of the USA (which wielded 4 votes out of 15 attendees), the committee would have voted to recommend destroying the virus samples on every count.

Although the United States and Russia are likely to resist, the 67th WHA could – and should - take a historic decision to fix a new destruction date for the virus. With the WHA authorized research program satisfied in the view of a majority of experts, no technical obstacles to destruction remain. It is simply a matter of WHO Member States' political will.

Notes of EB134 debate here.

TWN comment. Smallpox - WHO Executive Board passes the buck to the World Health Assembly

TWN IP Info, 28 January 2014 (http://www.twnside.org.sg/title2/health.info/2014/hi140104.htm)

Dear Friends and Colleagues

Smallpox: WHO Executive Board passes the buck to the World Health Assembly

For the first time since 2011, the World Health Assembly (WHA) will undertake a substantive consideration of destruction of smallpox virus stocks when it meets in May 2014. At the meeting of the World Health Organization's Executive Board on 20-25 January 2014, a preliminary exchange of views revealed significant disagreement among Member States.

This despite a WHO public health expert committee concluding that no public health purpose remains to retain the virus stocks, held at WHO Repositories in the US and Russia. The committee says that sufficient sequences, diagnostics, and vaccines exist, and that anti-viral drug research is sufficiently advanced, so that the stocks can now be destroyed.

Some countries favored fixing a date of destruction of the virus, while others said doing so was premature. Some, particularly the US, appear to favor expansion of the research programme to address "new threats", a move that could indefinitely delay destruction of the stocks if taken on board by the WHA.

There is concern among experts that the US is attempting to raise fears about the "threat" of synthetic biology as a means to try to gain WHA approval to expand the research programme (and thus provide justification for virus retention), and that such an expansion could possibly include genetic engineering experiments, the subject of prior controversy at the WHA.

Please find below a report on the Executive Board's discussion on the issue.

With best wishes

Third World Network

Smallpox: WHO Executive Board passes the buck to the World Health Assembly

Austin, Texas, 28 Jan (Edward Hammond) – For the first time since 2011, the World Health Assembly will undertake a substantive consideration of destruction of smallpox virus stocks when it meets in May 2014.

At the meeting of the World Health Organization's Executive Board on 20-25 January 2014, a preliminary exchange of views revealed significant disagreement among Member States on the issue.

The research program on virus stocks of the eradicated disease, which since the 1980s have been held only at WHO repositories in Russia and the United States, is reaching its conclusion. The research was only authorized for public health purposes, and all Member States of the World Health Assembly have agreed to destroy the stocks once this is completed. According to a WHO's public health expert committee (the Advisory Group of Independent Experts (AGIES)

to review the smallpox research program), no public health purpose remains to retain them. The AGIES says that sufficient sequences, diagnostics, and vaccines exist, and that anti-viral drug research is sufficiently advanced, so that the stocks can now be destroyed.

Another WHO oversight committee (the Advisory Committee on Variola Virus Research, ACVVR), which has less transparent operations and heavy representation from smallpox labs, somewhat disagrees. The ACVVR concludes that for most purposes, no need for smallpox virus remains, however, voting by a small majority late last year, it concluded that a narrow scientific rationale exists to retain stocks in order to finalize studies on anti-viral drugs. But in its bare majority ballot on anti-viral drugs, members from the United States cast over 25% of the vote, more than some entire WHO regions, such as Africa.

On the evening of 23 January, the WHO Executive Board took up the issue, and the exchange of views that took place suggests that discussions at the World Health Assembly will be difficult. Some countries favored fixing a date of destruction of the virus, while others said doing so was premature. Some, particularly the United States, appear to favor expansion of the research program to address what it terms "new threats", a move that could indefinitely delay destruction of the stocks if taken on board by the WHA.

China and Iran were clearest in calling for the WHA to set a destruction date for the virus. Iran recalled its statement from the 64th WHA calling for a destruction date and called for a mechanism to oversee destruction to be set up. China said that the research program had come a long way and that is was now time for use of live variola virus to stop and for strict and effective restrictions to be placed on artificial variola. China called for the process of destruction to begin, and for Member States to have equal footing in access to the results of the research program.

Most stridently opposed to destruction were, unsurprisingly, Russia and the United States. Russia noted the results of research conducted at the WHO Repository located within Russia and said these were of use to the international community. Russia said that it was working on antiviral drugs and that virus retention was justified and necessary. Russia did not specifically address the conclusion of the AGIES that the research program no longer has a compelling public health purpose.

The United States said fixing a destruction date is premature, and drew particular attention to what it termed as "new threats" stemming from synthetic biology. The US considered that release of synthetic DNA could have "catastrophic" consequences, and supported the suggestion by Mexico (see below) that the WHO Director General form an expert group to report on variola virus and synthetic biology.

The United States has long held the position that it would agree to destroy the viruses in the WHO Repository in Atlanta once the WHA-authorized research program is completed. The US, observers noted, was now facing greater pressure to do so because of the conclusions of the AGIES that retaining the virus no longer has a public health purpose. Pressure is building on the US also because its outsized representation on the ACVVR appears to be the only reason why that Committee too did not vote to destroy the virus on every count.

Thus, there is concern among experts that the United States is attempting to raise fears about the "threat" of synthetic biology as a means to try to gain WHA approval to expand the research

program (and thus provide justification for virus retention), and that such an expansion could possibly include genetic engineering experiments, the subject of prior controversy at the WHA. (This aspect of the Executive Board discussion will be addressed in greater detail in a future TWN article.)

Several other countries said that they could agree to continued retention of stocks, with varying degrees of enthusiasm. Brazil, Panama, Argentina, Australia, Japan, Lithuania, Albania, Saudi Arabia and Malaysia were among these. Most of these countries offered short statements with few details other than to note progress in the research program and the opinion that it is premature to destroy the stocks.

A few of these countries offered perplexing rationales for retention, such as an alleged need for more vaccines, despite the conclusion of both the AGIES and the ACVVR that sufficient vaccines exist. These include less "reactogenic" vaccines suitable for immunologically vulnerable populations and, of course, it was effective vaccines that have existed since the 1960s that led smallpox to be eradicated from the wild in the first place. Smallpox vaccines are not made from variola virus (which causes smallpox), but from Vaccinia, a related virus; hence live variola virus is not needed for vaccine production.

Canada's intervention was a mixed bag. On the one hand, Canada notably stated that no public health purpose remained for retention of the virus stocks. On the other, it said the stocks should be destroyed when "necessary measures" were in place. Among these, Canada mentioned that Member States should certify that they are free of variola virus, a suggestion that first came up at the 64th WHA, where it was proposed by the United States.

Specifics on this proposal are thin. Neither the United States nor Canada have addressed the fact that the WHO has already conducted a certification process. This took place in the 1970s and early 80s when, under WHO supervision, existing variola virus samples (at dozens of labs across the world) were either destroyed or deposited by Member States in WHO Repositories. (Originally five, now reduced to two.) The certification proposed by the US and now Canada thus duplicates work already done by WHO, and no specific rationale for re-certification has been proffered.

South Africa affirmed its commitment to prior WHA decisions that the virus stocks should be destroyed, and noted that variola DNA fragments found a few years ago in a South African lab would shortly be destroyed, in coordination with WHO.

Mexico and several othercountries proposed that the WHO Director-General establish an expert group to report on variola virus and synthetic biology. The schedule and parameters of this group are unclear. The Director-General noted that she would try to obtain the resources for such an expert group which, presumably, would make a report to the WHA in May. It is unclear why this task could not be assigned to the existing AGIES committee, if necessary, supplemented by advisors.

Destruction of smallpox virus stocks will next be formally considered as a substantive agenda item at the 67th World Health Assembly, beginning on May 19, 2014 in Geneva.

PHM advocacy priorities

PHM urges the MSs to commit to the final destruction of the remaining stocks of variola virus.

Notes from WHA67 debate

Document

- A67/37

Azerbaijan: The question has not been raised in a correct manner. The issue is clear before us is to eradicate the stocks. We believe that the conclusion of the working groups and experts did not allow us to take decision now.

Canada : we will submit the comments in writing, we accept the conclusions, that we believe that the virus vials should be destroyed if no need for them, but we are not ready to submit a time.

Zimbabwe: will submit statement. no need to retain virus. no support to have further discussions. ban experiments with smallpox

Russian federation : I would like to draw the attention in particular to one issue, we support the recommendation, on the variola virus, we need to keep alive to generate antiviral medicines. as stated by secretariat that there should be new dates for destruction, we need to wait for the scientific results which would be crucial for PH, WHO should provide us with accessibility in case it shall be needed for vaccination or research, considering future research we believe the consultative committee of WHO have for many years supervised the issue we want to attach to the principle of justice and access, and as russia has access the stocks, we would work on making the medicines/vaccines (generated) available.

US: still conduct virus research. The virus will be kept till the research is finished. The day for destruction did not arrive. Gene synthesis technology. We still research if the virus can be created synthetically. We are afraid of the creation of un-authorized synthesis of variola virus. That is why, we should, be able to keep developing antidote.

Lithuania: work of advisory group welcomed. work done under virus research supervision A big % of population has not been vaccinated against smallpox. not the right time to destroy bank

Libya:

Liberia: on behalf of Afro. This issue has been on the agenda for years. We cannot delay the decision any more. There is no need to keep alive variola virus for any public health reason. We need a decision and prevent this item to be on the agenda from time to time.

Georgia: thank you. enormous job; last years, is one of the biggest achievements of science; problems remains; so needs to be careful on decisions; support new expert groups analysing

evidence; Should maintain virus strains monitored under WHO supervision, before making final decisions.

Pakistan: Aligns itself with EMRO statement. There is no public health needs to retain the virus. We support fixed destruction date of the virus.

China: thanks. agree of the use of smallpox alive virus research. ...

India: All elements of the WHO research agenda on the virus are completed. No need for the virus for public health needs. No technical problems against fixing date for destruction of the virus.

South Africa: thanks the secretariat. Pleased to confirm that South Africa has destroyed stocks. We strongly support the view to work towards clear timelines.

Korea: appreciate the secretariat. Korea recognize bio terrorism as a threat. We support then to keep the virus to keep on the research to respond to any bioterrorism attacks. Expert committee to advise about the need and date of destruction.

Philippines: applauds outcomes. recommends reasonable timeline for destruction of stocks. reiterate not authorizing research not essential to health

Argentina:

Indonesia: it was earlier agreed that the stocks will be destroyed. Final destruction.

Japan: the ultimate goal is to respond to bioterrorism. destruction should not be at this moment. Appropriately, a time frame should be established

Nigeria: destruction does not mean that countries and others will do it. terrorism issue. should still keep stocks, in case of having to respond to outbreak

Iraq (for EMRO): we want to review the smallpox research; WHA 64 decision that confirmed previous decisions, that the stocks need to be destroyed; WHA52, DEMANDED DESTRUCTION of the stocks as well. Although timelines for research have been extended and exhausted the research have been prolonged; but all necessary research requiring the live virus has been completed; the destruction of the virus would ensure that it wouldn't be released deliberately or by accident. We demand the destruction of the remaining stocks.

Monaco: in favor of experts working group, then decide the definitive date to destroy stocks

Brazil : it would be premature to fix a date. We support the position of postponing the date for destruction to give time for research and vaccine. We support establishing an expert group to advise about the biosynthesis.

Lesotho: Aligns with Nigeria on behalf of AFRO, we support the report of making an expert committee, to ensure future threats of the reemergence of the virus are avoided.

UK: supports US to not destroy. not enough evidence. support establish expert group

Mexico: terms on which we agree should consider retaining the stocks for research purpose for favor of public health and also for security reason.

NGO

- 16.3 Medicus Mundi International (MMI)

DG: MS are divided. some says we need more work to find counter-measures; others say we need to find a date! nobody said a date… scientific community are divided on this subject. needs experts from all over. ask permission to set a research group.

No objections.

agenda item closed.