10.3 Smallpox eradication: destruction of variola virus stocks

Secretariat note: “In line with the request by the Sixty-fourth World Health Assembly (Decision 64(11)) the Secretariat provides the full report of the WHO Advisory Committee on Variola Virus Research, which held its fifteenth meeting in September 2013 (Document EB134/34). The report combines the annual review of the virus stocks held in the repositories, the research undertaken and proposals submitted with a consideration of the research conducted over the past three years and the need of variola virus for further research on public health measures. In addition, the report will be provided of the Advisory Group of Independent Experts to review the smallpox research programme (AGIES), which was reconvened in order to consider the recommendations and decisions of the Committee.”

Background

This document reports the work undertaken by the Secretariat in preparation for the 67th World Health Assembly. It summarizes the conclusions of both the Fifteenth meeting of the WHO Advisory Committee on Variola Virus Research (Geneva, 24 and 25 September 2013) and the second Advisory Group of Independent Experts 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 (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).

PHM / TWN Comment

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 most recently 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 onevery 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.