Smallpox InfoBrief #5

Written by Edward Hammond for the Third World Network and smallpoxbiosafety.org, May 2011
Fifth in a series of short informational briefings on the issue of destruction of smallpox virus stocks

Maintaining Clarity about Smallpox Research and an Essential Public Health Purpose

It can be anticipated that the primary method that Russia and the United States will use to advance their argument that remaining smallpox virus stocks should be retained will be to sow confusion about what smallpox research is essential for public health and what has been proposed for other reasons. Whereas the World Health Assembly (WHA) has only authorized specific research that is essential for public health in the interim before virus destruction, some virologists specializing in smallpox (and other orthopoxviruses) have expressed interest in a variety of other kinds of research with the virus. The United States in particular has promoted some of these suggestions as they offer pretext for refusing to fix a new destruction date. These hypothetical studies, however, are not essential and any putative benefit of them is outweighed by the public health benefit of virus destruction.

It is understandable that some poxvirologists are interested in continuing to work with smallpox. After all, smallpox is the most costly infectious disease scourge to ever attack humanity, killing hundreds of millions in the 20th Century alone. Smallpox is also the most exotic and unusual virus on the planet – held for decades in the two WHO repositories. Publications on it have a unique cache and even a mystique of danger that basic research or papers on the average stomach bug will never have.

The WHA, however, has never authorized research using smallpox virus for the sake of intellectual curiosity, or to answer questions unrelated to smallpox disease.[1] Instead, it has authorized research that is both essential for public health and which falls into the specific categories of sequencing, diagnostics, vaccines, and anti-viral drugs (as well as an animal model to support the latter two types of studies). Thus, suggestions that smallpox virus be used in studies that fall outside the scope of those areas approved by WHA can and should be roundly rejected, as the WHA has repeatedly concluded that public health is best served by virus destruction.

Where is it easier to sow confusion, and where it must be expected that proponents of virus retention will try hardest to create uncertainty, will be about what is essential within the areas for which WHA has authorized research. Here, the field of debate will likely be the language of WHO's *Scientific review of variola virus research, 1999–2010* (WHO/HSE/GAR/BDP/2010.3). Although this review, and the report of the Advisory Group of Independent Experts to review the smallpox research program (AGIES) (WHO/HSE/GAR/BDP/2010.4) which should be read with it, conclude that there is no

[1] For example, it has been suggested that smallpox virus could be used to help study the human immune system or in long-term research related to other diseases.

essential public health purpose in retaining smallpox virus stocks, it is easy to parse, or misconstrue, the language of those reports to create a contrary impression.

The task has been made easier by conflict of interest in the report authorship. Each chapter in the *Scientific review of variola virus research document* has been authored or co-authored by a scientist affiliated with the ministries that operate one of the two Repositories – i.e. the United States or Russian governments, whose perspective scientists in their employ likely felt an obligation to try to reflect.

Thus, the scientific review is littered with short passages that could be taken out of context to support virus retention. In this respect, a key phrase that was frequently used that can be manipulated in WHA discussions is the notion of "increased confidence". The scientific review document, *while not concluding in any case that any new research is essential*, repeatedly notes that more research involving smallpox virus could "increase confidence".

For example, on vaccines, the scientific review notes that if more new vaccines are developed, there would be "increased confidence" in these vaccines if they are tested against live smallpox. This statement would be easy to manipulate to say, for example, "*we support the review's conclusion that increased confidence in vaccines would be achieved by virus retention*", but it is invalid to suggest that this constitutes a conclusion by the scientific review that such research is essential for public health.

That's because first, second, and third generation vaccines against smallpox are proven effective, have obtained regulatory approval, are stockpiled, and more can be produced. The essential public health goals for vaccine research have thus been met. New vaccines are not essential for public health and, by obvious implication, neither is "increasing confidence" in them. Yet it is possible that proponents of retaining smallpox virus will take the "increased confidence" argument out of context and present it as if the scientific review concluded that such research is essential for public health, an argument that is not scientifically supportable.

Another example of an area apt for the promotion of misunderstanding is the animal model. Here, repeated experiments have failed to produce sufficiently positive results.[2] Now, after years of suggestions at meetings of the Advisory Committee on Variola Virus Research (and by NGOs) that animal model research with smallpox be abandoned in favor of alternatives (e.g. monkeypox in monkeys), the AGIES has made this recommendation in the major review.

Some virus retention proponents are nevertheless attempting to manufacture an argument for more smallpox research by saying that a better animal model is required for approval of smallpox antiviral drugs. Here, the phrase "*more time is required*" can be found in the scientific review paper. This argument for more time, however, is based not upon public health analysis, rather, it refers to a domestic regulation of the United States that has never

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[2] Despite many attempts, animals exposed to smallpox virus simply have not exhibited smallpox disease that parallels the course of human infection, meaning that studies using such models do not yield much data of use in studying the human disease.

been used in practice, the US Food and Drug Administration's so-called "animal rule". In reality, however, not only does the animal rule not require an animal model using smallpox virus, but the AGIES specifically analyzed this argument and concluded that US regulators and scientists should agree on a route to approval for smallpox drugs that does not use an animal model utilizing smallpox virus.

Nevertheless, it would be easy for a proponent of retention to concoct a phrase such as "*the major review concludes that more time is required to develop an animal model*", without also mentioning that the "requirement" was not supported by the AGIES or public health analysis and instead stems from a debated interpretation of a domestic regulation of one Member State.

Although many ways exist to misconstrue the major review's conclusions to make it appear to support additional smallpox virus research, in reality the major review identified no new research that is essential for public health. In this aspect, the report of the AGIES – the public health review that Member States requested in WHA Resolution 60.1 (2007) is especially clear. Nevertheless, Member States supporting virus destruction need to be especially attuned to statements that do not properly reflect the review itself, such as claims that the review concludes that "more time is needed" to complete WHA authorized research goals or that "increased confidence" in satisfied goals constitutes a reason for continued virus retention.