

No Excuse Left but Biotech

Will the United States start a smallpox threat creation program?

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In May, the World Health Assembly will yet again consider the question of destruction of smallpox virus. In order to politically legitimize keeping smallpox samples, the United States appears to be positioning itself to begin research that will create new threats from this eradicated virus.

By international agreement, all research with smallpox virus must take place under the World Health Assembly's (WHA) authorized research program. For many years the rationale to retain smallpox virus under that program has been dwindling, as the program's objectives that arguably required virus have been achieved.

As new and newer vaccines have been licensed, various diagnostics proven, and antiviral drugs developed, public health reasons to keep samples, held only in the US and Russia, have melted away.

Last year, experts selected by the World Health Organization (WHO) to consider the matter unambiguously reiterated their prior conclusion that there is no public health reason for the virus to continue to exist, and a separate WHO scientific committee, with more opaque procedures, has judged all but one scientific need for the virus to be exhausted. Expiry of this final, questionable, reason is imminent.

Indeed, were it not for the "saving grace" (from the US and Russian perspective) of a bare majority vote by the scientific committee on that single item (related to antiviral drugs), the WHO scientific program would be judged entirely concluded, leaving the US and Russia with no legitimacy in their fight to retain the virus.

The committee was an unusual one by United Nations standards. It was overweighted with Americans, who represented 1/4 of the voting membership - far more than their share as one among WHO's 194 Member States. In fact, US members cast more votes than those from the entire WHO African region.

By all rights, with the WHA-approved smallpox research program exhausted, the time has come for the US and Russia to finally do what they and the other WHO Member States have repeatedly agreed to do - destroy the world's remaining smallpox virus samples.

But the US is determined to keep the smallpox virus it controls, and Russia (which typically operates more quietly), wants to keep its stash as well.² The two old foes remain locked in a mistrustful long-term smallpox standoff. Disproven and unsubstantiated allegations aside, nobody else has any smallpox virus.

The American attitude was encapsulated by a former military man, once very senior in the US biodefense program and still active in policy, who I bumped into at an airport in late 2013. "*The problem with that,*" he said, referring to smallpox virus destruction, "*is that I just don't believe that the Russians would ever do it*" (i.e. destroy virus samples).

Having rejected US destruction of smallpox virus for fear of the Russians doing likewise, the Colonel jetted off to a conference in South America, to deliver a message of America's thorough dedication to peaceful and cooperative international biological research.

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² Although they aren't really "stashes". The smallpox collections that each holds are, in fact, international repositories deposited by many countries, and which WHO (at least nominally) controls.

The mistrust between Russia and US has the paradoxical effect of making this odd couple allies at the WHA. For the last several years, US diplomats have put significant effort and political capital into an arm-twisting program aimed to prevent other countries from supporting a decision to fix a date for virus destruction. Russia has too, on a smaller scale. The two have been reasonably successful, aided by medicine's failing memory of smallpox disease, which hasn't been seen in over 35 years.

"*Why get entangled?*" a diplomat at the WHA might ask, or "*what's the big deal?*" perhaps momentarily forgetting that smallpox killed two million people per year into the 1960s – when the world was bigger and the population smaller. Today, the population is bigger and much more tightly connected. Few have immunity from vaccination. Extremely few have immunity from prior exposure, before 1977, when the disease was eradicated, sort of.³

Although its escape from the lab could be catastrophic, smallpox is understandably often not the highest priority item for developing countries at the WHA. For example, African diplomats facing an Ebola epidemic or lack of HIV drugs may have little energy left to ruminate on the decades-old debate which, as in the movie *Groundhog Day*, seems to come back in more or less the same form every year.

Consistently and notably inconspicuous through it all, for most of the past decade, is a large block of countries collectively called the European Union.

Smallpox may not figure high on every agenda, but since an embarrassing fiasco in 2005 (see discussion of genetic engineering below), it has been a top WHA priority for the United States, whose diplomats have even crassly flashed scorecards of "with us" and "against us" countries in plain view of other diplomats and NGOs, and whose senior officials in Washington make loaded telephone calls to foreign capitals to avert any upstart opposition.

Convincing countries to side with the US, or at least not oppose it, was easier in the past, when earnest debate was still possible over whether there were legitimate public health reasons to keep smallpox. Under pressure, a country might remain silent, or say it preferred to retain the virus, not by openly siding with the US and Russia, but by referencing ambiguities in the reports of WHO committees.

Now these ambiguities have vanished and the official virus keepers are looking for political cover for their plans to keep it. A new rationale for retention must be invented in order for them to succeed. Generating new reasons is hard, however, because it could involve going back on previous WHA decisions, as the research program was created in order for its completion to permit consensus to destroy the virus.

Having the discussion on honest terms, however, is diplomatically unthinkable. If the US took the floor at the WHA to say, "*Madame Chairperson, we cannot destroy smallpox virus because Ivan cannot be trusted,*" which is what the American biodefensists really think, it might earn the WHA a needed dose of attention, but it would be a diplomatic disaster. A similar result would ensue if Russia took a similarly frank approach.

So the 67th WHA will face dangerous territory when it meets in Geneva beginning on 19 May. Although Russian-American mistrust and biodefense policies are the real impediment to smallpox virus destruction, many will try to pretend otherwise, in deference to diplomatic pretense.

If the virus can't be destroyed, and the reason can't be openly admitted, then some other reason to keep it will have to be invented. Apart from moral peril, the danger in doing so is that, at US and Russian prompting, WHO's members will cite "new threats", "biotechnology", and "synthetic biology" bugbears as their excuse for again postponing destruction.

³ Samples, of course, have always been maintained in the lab. Even after being eradicated from the wild, however, smallpox escaped the lab and caused deaths.

The US is actively trumping up such concerns. At January's WHO Executive Board meeting, it pushed the idea that study of "new threats" from smallpox, particularly related to synthetic biology, is needed. The "new threats" being ones we create ourselves.

Sound outlandish? US biodefense researchers genetically engineered anthrax - to make it worse (antibiotic resistant) – well over a decade ago. Russian scientists may have done so even earlier. Recently, Dutch and US researchers deliberately created new strains of potentially pandemic influenza that are arguably every bit as dangerous, and perhaps more, than smallpox.

In fact, the US first proposed to genetically engineer smallpox a decade ago. Remarkably, the WHO committee overseeing research approved. It was only through NGO campaigning and a group of countries led by Africa that the decision was overturned and WHO oversight - at least temporarily - tightened.

In the "biosecurity" world of fear-driven research on infectious disease agents, public health priorities can get turned upside down, and the fact that a disease poses a hypothetical threat if altered through biotechnology can become a reason not to prevent such terrible experiments from happening, but to go ahead and do them - out of a twisted sense of duty, suspicion of others, craving for attention (a behavior apparent in influenza research), or because that's where a government agency will put money.

"New threats" often emanate from self-serving fantasies of biodefensists. Nobody is remotely about to synthesize smallpox in a bathtub, and the world does not need, especially under WHO authorization, for US and Russian scientists to create recipes for how to cause mayhem with an eradicated disease. Or how to mutate or otherwise engineer a related virus in the direction of smallpox, towards becoming a human pathogen. (All for "defensive purposes", of course.)

Thus if governments are unwise enough to link the US's vague language about "new threats" to a delay in virus destruction, there is a dangerous possibility of opening the Pandora's Box of genetic engineering of smallpox. In the succeeding years, US and Russian scientists working for government agencies would then very likely put forward proposals for projects to manipulate the virus to unsafe ends, including experiments related to synthesizing large pieces of it, or even the whole virus, as a perverted "proof of principle".

Smallpox does not naturally cause disease in any species other than humans. Barring an accident, there are no subjects upon whom engineered viruses could be "tested". There will always be ambiguity about what evils biotechnology could create when put to destructive ends with smallpox. Is it as bad as it seems? Would this therapeutic work? The questions are largely unanswerable and the research pointless. But the ambiguities could be parlayed into dangerous experimentation in perpetuity.

Sadly, it may prove true that the US and Russia will be capable of twisting enough arms to prevent the World Health Assembly from achieving its historic opportunity to finally fix a firm date to destroy the virus. The WHA has even more to lose, however, if it allows smallpox to continue to exist purportedly out of vague concern about biotechnology and synthetic biology. Because this could lead to nightmarish smallpox experiments in the lab, such as those in the controversial research genre dubbed "gain of function" studies, setting terrible precedents, damaging WHO's reputation, and opening the door to similar experiments with more widely distributed dangerous diseases such as Ebola and SARs.

What the 67th WHA should do, of course, is to fix a date to destroy the virus. The scientific and public health prerequisites are in place to do so. Having followed the debates at the WHA for a decade now, however, I am not sanguine about the possibility of this actually happening.

The US and Russia will politicize the issue at a level beyond the briefs of the health diplomats who typically run the business of their country's delegation at the WHA. This tends to disempower and short-circuit debate at the world's highest public health meeting, which is precisely the American intent.

But if the World Health Assembly can't agree on a date to destroy smallpox virus, what it at least can do is to inject greater honesty into the discussion.

Although it could make sense for WHO to review and tighten its *existing* restrictions on creation, possession, and use of synthetic smallpox DNA, synthetic biology does not oblige any new research using smallpox virus or provide any other excuse for the virus' continued existence.

Further, there is no shortcoming in fulfillment of the WHO research program that requires retention of the virus. All of its goals that require virus have clearly been achieved and WHO public health experts have concluded there is no reason to keep it.

The WHA must not invent new pretexts for the US and Russia's failure to live up to commitments, and other Member States' lack of resolve to enforce them. There is no public health purpose to retain smallpox virus and governments shouldn't proffer a false one.

Rather, the major impediment is that the United States and Russia, who hold virus collections on the world's behalf, simply refuse to destroy them. At least let that be said clearly.