Developing Countries, Donor Leverage, and Access to Bird Flu Vaccines

CHAN Chee Khoon and Gilles de Wildt

Abstract

In early 2007, the Indonesian government decided to withhold its bird flu virus samples from WHO’s collaborating centres pending a new global mechanism for virus sharing that had better terms for developing countries. The 60th World Health Assembly subsequently resolved to establish an international stockpile of avian flu vaccines, and mandated WHO to formulate mechanisms and guidelines for equitable access to these vaccines. Are there analogous opportunities for study volunteers or donors of biological materials in clinical trials or other research settings to exercise corresponding leverage to advance health equity?

JEL Classification: I18-Government Policy; Regulation; Public Health

Keywords: avian flu vaccines, global health equity, international health security, essential medicines, public patents

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Shifting Alignments in International Health?

On February 16, 2007, the Minister of Health of Indonesia Siti Fadilah Supari informed senior World Health Organization (WHO) officials David Heyman (Assistant Director General for Communicable Diseases) and Keiji Fukuda (Director for the Global Influenza Program) that Indonesia would continue withholding its bird flu virus samples from WHO’s collaborating centres pending a new global mechanism for virus sharing that had better terms for developing countries. In breaking with the existing practice of freely sending flu virus samples to these laboratories, the health minister expressed dissatisfaction with a system which obliged WHO member states to share virus samples with WHO’s collaborating centres, but which lacked mechanisms for equitable sharing of benefits, most importantly affordable vaccines developed from these viral source materials by patent-seeking commercial entities:

Indonesia will insist on a material transfer agreement before sending the Indonesian strain of bird flu virus to foreign laboratories to prevent them from being used for commercial purposes…We agree to send the virus to the WHO with new conditions or mechanisms approved by both parties as well as by other developing countries. Until then, we won’t share the samples…The organization [WHO] sometimes forgets the good of the people in general and we want to change that…

Siti Fadilah Supari, Minister of Health, Indonesia
www.thejakartapost.com, February 17, 2007
(accessed on February 23, 2007)

A month later, the Indonesian government reiterated its stance, reported thus by The Nation (Bangkok) on March 15, 2007:

Indonesia will not share bird flu samples with the World Health Organisation without a legally binding agreement promising the virus will not be used to develop an unaffordable commercial vaccine, the health minister said yesterday. Health Minister Siti Fadilah Supari said last month’s letter of guarantee from WHO Director-General Margaret Chan was not good enough. “That’s just an agreement in principle” Supari said, [further adding that] the system, which enables influenza [virus] samples to be freely passed throughout the global community for public health purposes, needs to be revised so it is “fair for developing countries, poor countries, affected countries. We will not share our virus sample without a change in [WHO’s virus sharing] rules”. Indonesia is worried that large drug companies will use its H5N1 strain to make vaccines that will ultimately be unaffordable for developing nations.

To consolidate regional support for this initiative, a meeting of Asia Pacific developing countries was convened in late March 2007 to explore mechanisms for more equitable access to vaccines produced from virus sharing arrangements. The Indonesian decision elicited unease, but also sympathy from a cross-section of the global community, including an editorial from the Lancet:
To protect the global population, 6.2 billion doses of pandemic vaccine will be needed, but current manufacturing capacity can only produce 500 million doses. In November 2004, a WHO consultation reached the depressing conclusion that most developing countries would have no access to vaccine during the first wave of a pandemic and possibly throughout its duration…Indonesia’s move to secure an affordable vaccine supply for its population is understandable… the country has made a controversial decision not to share its H5N1 virus samples with WHO. Indonesia is instead planning to provide a US pharmaceutical company [Baxter] with the strains in exchange for technology to manufacture a pandemic vaccine. This strategy is a marked departure from the existing WHO virus-sharing system, in which influenza viruses are donated by countries and flow freely to the global community for vaccine development. Indonesia fears that vaccines produced from their viruses via the WHO system will not be affordable to them. The fairest way forward would be for WHO to seek an international agreement that would ensure that developing countries have equal access to a pandemic vaccine, at an affordable price. Such a move would demonstrate global solidarity in preparing for the next pandemic. (Lancet editorial, February 17, 2007)

On March 29, 2007, immediately following an interim agreement for Indonesia to resume sending flu virus samples to WHO, health ministers of eighteen Asia-Pacific countries issued a Jakarta Declaration which called upon WHO “to convene the necessary meetings, initiate the critical processes and obtain the essential commitment of all stakeholders to establish the mechanisms for more open virus and information sharing and accessibility to avian influenza and other potential pandemic influenza vaccines for developing countries”¹. These proposals were tabled at the 60th World Health Assembly in Geneva (May 14–23, 2007) as part of a resolution calling for new mechanisms for virus sharing and for more equitable access to vaccines developed from these viral source materials.

In the course of the deliberations, it emerged that WHO had violated the terms of the 2005 WHO guidelines² on sharing of viruses which required the consent of donor countries before WHO’s collaborating centres could pass on the viruses to third parties such as vaccine manufacturers. While discouraging the use of material transfer agreements (MTAs) at the point when donor countries transferred their virus samples to WHO, WHO’s collaborating centres nonetheless resorted to MTAs when they transferred to third parties vaccine strains containing parts of the viruses supplied by developing countries such as Indonesia, Vietnam and China. Indeed WHO’s collaborating centres themselves, as well as third parties, had sought patents covering parts of the source viruses used in developing vaccines and diagnostics³. Possibly the most contentious item on the health assembly’s agenda in 2007, the issue of virus sharing and access to avian flu vaccines remained unresolved until the final hours of the gathering when a resolution was adopted mandating WHO to establish an international stockpile of vaccines for H5N1 or other influenza viruses of pandemic potential, and to formulate mechanisms and guidelines for equitable access to affordable pandemic flu vaccines⁴. The

resolution also requested a WHO working group to draft new Terms of Reference (TORs) for WHO collaborating centres and its H5 reference laboratories for the sharing of influenza viruses, to be submitted to a special intergovernmental meeting of WHO member states.

The Indonesian standoff with WHO came on the heels of Director-General Margaret Chan’s admonishment to the Thai Ministry of Public Health in February 2007 over the issuance of compulsory licenses for HIV/AIDS and heart medications. In the course of a visit to the National Health Security Office in Bangkok, she had publicly urged the Thai health authorities to seek instead a negotiated compromise with pharmaceutical companies over high drug prices. This perceived tilt drew strong criticism from health advocates in Thailand and elsewhere who pointed out that the Thai Ministry of Public Health “has been in regular contact with the industry over high prices of its drugs in Thailand, but these negotiations have led nowhere. The best price for originator’s efavirenz is still twice the price available from Indian generic sources (US$500 per patient a year vs $224). The best offer for originator’s lopinavir/ritonavir is $2000 per patient a year, five times more than WHO’s estimate of manufacturing costs. The Thai Ministry of Health estimates that the price of clopidogrel would fall by over 90% if made generically. These are substantial price differences in a country where the average annual wage is $1400 a year.”

It is unclear whether these episodes amount to tactical shifts, let alone a more fundamental re-alignment between WHO, member states, corporate actors, and health activists on the issue of access to essential medicines. The ramifications are clear however for the interlinked concerns of global health equity and international health security.

The Indonesian government’s stance in particular was notable on three counts:

• it was explicitly a critique of WHO’s balance of pragmatism which it felt was overly accommodating of corporate priorities, to the detriment of the health and wellbeing of a key constituency that WHO was mandated to defend, the underserved communities among its member states
• it was an exercise of leverage by a source country of biological materials seeking to redress the inequities of access to what may be vitally important health inputs (avian flu vaccines) developed from these source materials


7 The Third World Network (TWN) has also criticised WHO’s “best practice” guidelines for sharing of virus samples, pointing out that a well-meaning non-profit modus operandi expected of national influenza centre laboratories, WHO collaborating centres and H5 reference laboratories, along with an expectation that candidate influenza vaccine strains be provided gratis to any vaccine producer requesting for such materials, would undercut the leverage of source countries in negotiating for fair benefit-sharing in line with the Convention on Biological Diversity’s principles of access, prior informed consent and benefit-sharing. (“Winners and losers in the sharing of avian flu viruses”. TWN Information Service on Health Issues, May 11, 2007) http://www.twnside.org.sg/title2/health.info/twninfohealth089.htm (accessed on May 12, 2007).

8 In April 2007, the US Food & Drug Administration approved the first human vaccine against H5N1 avian influenza. This pre-pandemic vaccine, approved for people aged 18 to 64 years, is administered in two doses separated by a month’s interval. The efficacy of 45 per cent (protective levels of antibody response among half the trial subjects) is quite modest but would still have an impact on population health if the protective effect extends as well to the actual pandemic viral strain. http://www.fda.gov/bbs/topics/NEWS/2007/NEW01611.html (accessed on May 24, 2007).
it was seeking equitable benefits from commercial developers not just for its nationals but for other communities as well who were likely to be sidelined by commercially-driven product development and distribution systems

Commodification and the Gift Relationship

These developments call to mind *The Gift Relationship*, a study of blood donation systems in the US and UK published by Richard Titmuss, a pre-eminent figure of UK social policy at the London School of Economics and Political Science. In this 1970 classic, Titmuss demonstrated that a blood donation system relying on unpaid donors and operated on a non-commercial basis by the public sector (UK) outperformed a system relying largely on paid donors (in cash or in kind) and on profit-driven processing and distribution (US), by the criteria of availability and affordability, quality and safety, and economic efficiency and equity.

That of course was pre-Thatcherite Britain. With the prevailing (and still tenacious) ethos of neo-liberalism, donors of biological materials which might eventually yield commercially profitable products not surprisingly come to expect a share of the financial gains made possible by their donated materials.

*John Moore v. The Regents of the University of California* (1990) for instance was a celebrated case of a leukemia patient who underwent surgery in 1976 at the University of California for removal of his cancerous spleen. The University of California was later granted a patent for a cell line called “Mo” established from his spleen, which produced valuable proteins [cytokines, including ones which mediate antibacterial and cancer-fighting activity] with a long-term commercial value estimated at over one billion dollars. Moore filed suit and demanded the return of the cells and control over his body parts, but the California Supreme Court ruled that he was not entitled to any rights to his own cells after they had been removed from his body.

This principle was re-affirmed in the New Jersey state legislature in 1996 when it enacted legal protections against genetic discrimination in employment and in health insurance. This same legislature however also rejected a draft clause which would have declared individual genomic information to be individual, private property, which prompted George Annas, professor of law and public health at Boston University to remark that it was “bizarre that other people can own your genetic information [and body parts], but you can’t”.

A neo-liberal environment thus tends to undermine altruistic (gifting) inclinations, encouraging instead pecuniary if not mercenary tendencies among donors who might otherwise be disposed towards voluntarism, communitarian practices and the common good. Bluntly put, “if researchers and their commercial sponsors are going to enrich themselves using my biological samples and personal data, why shouldn’t I get my share of it?” Publicly supported charities however such as Cancer Research UK notably continue to allow free use of its research output (such as the patented breast cancer gene BRCA2) by publicly-owned laboratories and hospitals.

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Reasserting the Public Domain: Between Commons and Commodification

Edward R. Murrow (reporter): Who owns the patent on this [polio] vaccine?
Jonas Salk: Well, the people, I would say. There is no patent. Could you patent the sun?
12 April 1955, Ann Arbor, Michigan

In the 1990s, Rural Advancement Foundation International (RAFI, now the Action Group on Erosion, Technology and Concentration, ETC) together with a network of indigenous peoples support groups proposed an international campaign aiming at a formal Declaration of a Global Genetics Commons. Sir John Sulston (2002 Nobel laureate in medicine or physiology) endorsed a very similar idea, which sought a declaration of the human genome as the common heritage of humanity and for its DNA sequences to be off limits to patents and intellectual property claims.

In the event, the idea was shelved, in part due to the realisation that even if genomic DNA sequences were not patentable, downstream technologies arising for example from transcriptomics and proteomics could still be subject to intellectual property claims.

Was the patenting of body parts and genetic information part and parcel of an unavoidable trend towards the commodification of life forms then?

A middle path which accepts intellectual property claims on these biological entities but which ensures that these are retained within the (international) public domain (vested for example in trustee institutions which are mandated to serve the public good on an equitable needs basis) is one option which may be worth exploring. Indeed the Convention on Biological Diversity (1993), in recognizing the sovereign rights of countries over their biological and genetic resources, enshrines one form of this principle.

In the US, it would be appropriate to reappraise the Bayh-Dole Act (1980) and the Stevenson-Wydler Act (1980) which markedly altered the balance between public versus private claims on intellectual property arising from publicly-funded research. Prior to 1980, patentable findings arising from federally funded research became the intellectual property of the US federal government which was vested in public agencies such as the National Institutes of Health.

13 Jane S. Smith, in her book *Patenting the Sun: Polio and the Salk Vaccine* (New York: William Morrow & Company, Inc. 1990, p. 305-312) records that Jonas Salk made these oft quoted remarks during a televised interview to announce the results of successful population trials of the killed-virus polio vaccine. Cynics, and Salk’s detractors have pointed out that lawyers for the March of Dimes foundation (his research funders) had earlier determined that no part of his vaccine procedure was new and could be patented. But that misses a point - would Salk (or the March of Dimes) have gone for a patent under the present more relaxed patent regimes, most importantly, the landmark US Supreme Court decision in *Diamond v. Chakrabarty* (1980) to allow the patenting of life forms, the Bayh-Dole (1980) and Stevenson-Wydler (1980) Acts, *John Moore v. The Regents of the University of California* (1990), all contributing towards the enabling legal environment for the rapid expansion of profit-driven biotechnology. Rather than just focus and speculate on Salk’s moral core, perhaps one should also ask what alternative enabling environments would help tilt the balance between public vs. private claims on publicly-funded intellectual property, to advance health equity and the public good? We are left pondering, for instance, what John Moore might have done if he were presented with various hypothetical scenarios for disposition of benefits arising from his cells.

14 A situation might arise for instance, akin to the following analogy which unfairly privileges those in possession of advanced means of exploiting “global commons resources”: I have a sophisticated technology which can mine this exotic mineral found within your borders. Insofar as you cannot extract it yourself, you deserve no part of the benefits from my successful exploitation of this mineral, which should be considered a “commons resource” in the “global public domain.”
The Bayh-Dole Act (1980) in essence transferred these rights to federally-funded research grantees and their institutions for commercial development. The Stevenson-Wydler Act (1980) required federal agencies to transfer technology in their possession to state and local governments and to the private sector for commercial development, albeit subject to certain march-in rights (such as compulsory licenses) which could be exercised by governmental authorities in times of urgent public need or national emergencies. These march-in rights applied to both Bayh-Dole and Stevenson-Wydler, but the Acts also provided for royalties from commercialisation to be shared with the inventor as an incentive for useful innovations.

In 2003, US Congressman Dennis Kucinich announced that he intended to introduce legislation “that would create a new network of government labs for the research, development and manufacture of pharmaceutical products and biologics… When discoveries are made, the patents would be held by the government and nonexclusive licenses would be attached to them. This would allow companies to compete to manufacture pharmaceutical products, just like generic drug companies do now. This would radically bring down the cost of drugs [and would also] increase the affordability of cures worldwide… We have watched the pharmaceutical industry fail on three counts: submitting fewer and fewer drugs to FDA for approval, creating “copycat” drugs instead of truly new cures, and raising drug prices higher every year. Our current patent system is what encourages artificial improvements and keeps prices high. It seems clear that one of the keys to public health is establishing public patents” 15.

Kucinich's initiative, an admirable but uphill struggle, would entail a rolling back of some aspects of the Bayh-Dole and Stevenson-Wydler Acts. A less ambitious strategy has been proposed by researchers at Yale and University of Pennsylvania which urges US research universities to adopt open licensing practices, what were referred to as Equitable Access Licenses16.

Five years ago, one of us (CCK) participated in European Commission (EC) grant review panels for EC-funded collaborative research between EU and Asian countries. A suggestion was made that the intellectual property arising from the projects under review could perhaps be vested in, say WHO, as an example of an international public agency, to keep the intellectual property within the international public domain. In such a scenario, WHO could for instance license these patents on a nonexclusive basis for product development so that useful and affordably-priced generics could be produced in a competitive environment. (For that to happen however, WHO would have to regain its credibility among developing countries, eroded in the aftermath of the 60th World Health Assembly in May 200717, and achieve a better balance between profit-driven production of essential medicines, and equitable access to these products. Absent this, the International Health Regulations 200518, which came into force in June 2007 and imposes mandatory disease reporting obligations on signatory member states, could reduce poorer front-line states to the role of pandemic “canaries”19 in an early warning system for emergent flu pandemics).

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19 Canaries, which were exquisitely sensitive to low levels of carbon monoxide, were early warning systems for coal miners confronted with risks of underground methane and mine explosions (or mine fires), and the resultant carbon monoxide.
The modest fees that WHO could earn from this nonexclusive licensing could perhaps further yield a small bonus by lessening the dependence of the institution on donor governments (and corporate donors), and hence expand the latitude for its independent role in international health policy advising and technical support. The recent episodes between ASEAN governments and WHO, over access to essential medicines, arguably underscore the importance of independent sources of revenue for WHO.

**Donor Leverage and Trusteeship Arrangements?**

Set in this context, the Indonesian initiative on new virus sharing arrangements is therefore noteworthy and its exercise of donor leverage may presage a consideration of trusteeships which could serve as public (international or regional) repositories of genetic resources, genomic information, and other biological materials.

The Asian financial crisis in 1997 gave impetus to a regional effort at managing financial instability caused by volatile capital flows and speculative currency attacks. Recognizing the increasing integration of East and Southeast Asian economies, a Chiang Mai Initiative emerged in May 2000, initially as a network of bilateral swap agreements among ASEAN+3 member states, which might yet evolve into a de facto Asian Monetary Fund following a May 2007 decision to multi-lateralize an $80 billion pool of foreign exchange reserves of ASEAN+3 member states. Beyond the risk of financial contagion in globalized capital markets, the SARS epidemic of 2002-2003 forcefully demonstrated the regional economic consequences of a life-threatening infectious epidemic, effects which would pale in comparison with the devastating human and economic impact of an outbreak of highly transmissible and lethal human flu on the scale of the 1918-1919 pandemic.

Notwithstanding the resolution adopted at the 60th World Health Assembly requesting WHO to establish an international stockpile of vaccines for H5N1 or other influenza viruses of pandemic potential, the limited vaccine production capacity globally, not to mention the financial needs for establishing and maintaining a stockpile of adequate size, are key issues that remain to be addressed. A persuasive case could therefore still be made that ASEAN+3 might provide a potential institutional framework for mobilizing the financial and technological resources in the region to enhance regional preparedness and response capabili-
ties in a likely epicentre of an emergent flu pandemic. This would go beyond the existing co-ordination of surveillance networks to include the development and acquisition of vaccine manufacturing capabilities, to augment regional stockpiles of avian flu vaccines which can be made available as public goods on a priority needs basis.

Beyond the immediate concerns of timely and affordable access to pandemic flu vaccines, the Indonesian initiative has also raised the intriguing possibility of other analogous instances where individuals or groups of donors of biological materials and personal data could utilize the leverage of their gift relationship in clinical trials or other research settings in furtherance of the common good (rather than succumb to mercenary tendencies encouraged by a neo-liberal ethos).

Anecdotal evidence suggests that individuals or groups volunteering in drug trials or human genome research are usually unaware of the potential commercial trajectories of downstream product development involving patenting of products or processes derived from the donated materials and personal information. These commodities could be prohibitively expensive for many end-users, as well as disruptive for follow-on research. Even health professionals involved in the recruitment of volunteers and the execution of the study may not be adequately aware of these eventualities. The rules of the US Food and Drug Administration (FDA) for instance provide for minimum standards for pharmaceutical research conducted locally or abroad, with an informed consent protocol which refers in very general terms to “benefits to the subject or to others which may reasonably be expected from the research”\(^\text{26}\). The Declaration of Helsinki on biomedical research ethics (World Medical Association general assembly, 1964; amended 2000)\(^\text{27}\), sensitive to the vulnerability of patients seeking or undergoing treatment, reiterates “the right [of patients] to abstain from participation in the [proposed] study or to withdraw consent to participate at any time without reprisal”.

We look forward to a time when research volunteers will be able to specify (elect for) prior conditionality for their participation in studies. These might range from good faith efforts to deploy the research output in a manner which serves the public good, to more explicit mechanisms aimed at equitable benefits on a needs basis.

To that end, we are planning to undertake a survey of clinical trial volunteers (and potential volunteers) to canvass their attitudes towards donation of biological materials and personal information under various hypothetical scenarios for benefit apportionment or disposition. Related to this, we are also keen to explore trusteeship arrangements\(^\text{28}\) as repositories for retaining intellectual property (IP) in the public domain, IP arising from publicly-funded biomedical and health research and involving biological materials and personal information freely donated by individual study subjects or communities.

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28 We are grateful to Cristina Blohm and Jurgen Simon of Universität Lüneburg for sharing with us their pre-publication manuscript ‘Group Consent in Population-based Research’ which included an exploration of various scenarios for trusteeship arrangements.
In summary, we intend to, and we seek potential collaborators to:

- examine the possibilities for conditional participation by volunteers in clinical trials
- conduct a survey of attitudes among clinical trial volunteers and potential volunteers, in regard to donation of biological samples and personal information, under various specified scenarios of participation in clinical trials
- explore possible mechanisms for operationalizing conditionalities in the recruitment, enrolment, consent, participation, and donation of information and samples by volunteers in clinical trials
- explore possible trusteeship arrangements to serve as repositories for retaining in the public domain intellectual property arising from publicly-funded biomedical and health research which may involve biological materials and personal information freely donated by individual study subjects or communities.