

# **WHO CONFERENCE: BIOTECHNOLOGY AND GENOMICS FOR IMPROVEMENT OF HEALTH IN DEVELOPING COUNTRIES**

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## **CONCLUDING REFLECTIONS**

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### **Introduction**

I am honored to offer some personal reflections on our Conference. When I inquired about the task, Tikki Pang, WHO Director of Health Research and Cooperation, replied: "Please say something fresh, don't just repeat your Bangkok summary!" I couldn't even remember what I had said in Bangkok! Anyway, how could I repeat, since 800 people reviewing health research for development is very different from 100 people discussing the future of genomics and biotechnology? Besides, Bangkok, a wonderful city, is nothing like this tropical island of Cuba. In any case, if I make mistakes, the organizers have appointed three expert rappers to make sure that I'm accurate!

Over three lovely days in beautiful Cuba, about 120 participants (including 50 Cubans) from two dozen countries responded to ten presentations, participated in six breakout groups, and visited two biotechnology institutes on the island. We were mostly scientists, academics, and UN professionals -- sprinkled with a few representatives from industry and non-governmental organizations. The range covered was breath taking -- local genomics research, clinical services, epidemiology, bioinformatics, public perceptions, intellectual property rights, and ethical, legal, and social issues.

Our focus was the report "Genomics and World Health," soon-to-be released by the WHO Advisory Committee on Health Research. We were charged to "provide advice and guidance" about WHO follow-up. Our Conference was not about the technical sciences of genomics, but rather the link of genomics to health in developing countries. Our last two sessions on capacity building and future strategies were structured to solicit wide participation. Throughout the exchanges, we appreciated the warm hospitality of our Cuban hosts, lubricated by many rounds of mojitos!

### **Conference Themes**

We are entering a "new health world," uncertain and rapidly changing. All agreed that genomics-based biotechnology has enormous potential to accelerate the discovery of new vaccines, drugs, and diagnostics.

The genomics revolution will have an impact not only on health care, but also on agriculture (genetically modified organisms) and economics (pharmaceutical industry). Social implications will also be broad, as illustrated by Pedro Leon's description of the genetic basis of deafness as well as recent Costa Rican legislation on compulsory DNA testing so that children have the "right to know their fathers." Despite the publicity and

hype, genomics is not a panacea or magic bullet. Whatever happens, biotechnology will not solve deep-seated problems like poverty for those living under \$1-2 per day, who need drinking water, food, and livelihoods. Genomics is inherently controversial because it is central to sex, money, reproduction, race, and privacy. Warnings were issued about eugenics, cloning, discrimination, and genetic determinism. Even without genomics, we are witnessing some technological abuse, like pre-natal sex selection in some Asian societies, as discussed between Victor Penchaszadeh and Richard Cash. Public worries about “Frankenfoods” may indeed become real worries about “biological Frankensteins.”

These issues set the stage for three central Conference challenges, in my opinion. What is really bothering us about the genomics revolution? What should we do? And how can WHO play its pre-eminent role in genomics and world health?

### **What’s the Problem?**

The genomics revolution has provoked genuine disquiet, sometimes passion and even fear. Discomfort could come from insecurity about the loss of control over our lives in uncertain times. History is not entirely reassuring in this regard. Throughout human history, warfare and profits have powerfully propelled technology development. Indeed, I was surprised that the anthrax bioterrorism attack in the United States did not receive more attention. We know that powerful technologies with destructive potential, like nuclear power, can unleash unintentional consequences of far greater import than planned change. Once the genie is out of the bottle, it’s hard to put it back in. Bruce Lewenstein presented survey data of public perceptions about genomics, mostly from rich countries. Public awareness is growing, but “genetic illiteracy” and popular hype are also prevalent. As I listened, I began to interpret a new meaning to “know thyself.” That used to signal reflections about my personality, my psychology, and my behavior. With the genomics revolution, know thyself now prompts reflections about my genes and biology!

A recurring theme underlying our worries is social inequity. Inequity differs from inequality in that the latter describes objective disparity while the former introduces a normative lens on whether such inequality is perceived as fair or unfair. Inequity, therefore, is a moral judgment about the nature of inequality in society. Concern about inequity is escalating, in part, because of the globalization of private markets. Rapid transnational flows of money, goods, services, technology, culture, and people are introducing new vulnerabilities, uncertain risks, and heightened public consciousness about distant people in a shrinking world. With the exception of malaria, a greatly neglected disease, the three other infections discussed in our breakout sessions may be characterized as “diseases of globalization,” because their emergence or re-emergence is associated with rapid transnational flows. The global spread of HIV/AIDS was certainly associated with global movement. Tuberculosis, also a major neglected disease, has increased dramatically due to HIV-compromised host immunity. Resurgence of dengue fever is due, in part, to movements of people and goods that facilitate the transmission of the vector-borne virus.

Jose Maria Cantu predicted that the “fight of the 21<sup>st</sup> century” will be between the “WHO and WHM” (world health market). He suggested a fundamental tension between

WHO's mission of equitable world health and inequitable forces generated by competitive private markets. Because the poor lack purchasing power, market-driven health services will not address their health care needs. Lack of a profitable market provides little incentives for industry to pursue R&D to develop technologies against diseases of the poor. Peter Singer and Abdullah Daar urged that actions be taken to preempt a looming "genomic divide." Some have described this phenomenon as a "market failure," implying that markets serve well most purposes but leave a few social gaps. I would prefer calling the problem a "social failure," since even if markets were to function perfectly, they would not address the fundamental deficiency of the inability of the poor to command goods and services through the marketplace.

### **What Should We Do?**

How do we produce essential global public goods? How do we shape markets to generate more equitable outcomes? I address these two questions and also reflect on lessons from Cuba today and China yesterday.

Certain goods wanted and needed by everyone, like clean air and public parks, cannot be produced by private markets. Genomics R&D for technologies against neglected infectious diseases fit into this category. The term "public goods" describes these non-rival and non-excludable goods. How then can we produce global public goods? Given their non-market nature, public goods are appropriately generated by public action and public financing.

R&D, however, is expensive and time-consuming, requiring a strong infrastructure of skilled people, facilities, equipment and supplies. David Webber reported that members of the International Federation of Pharmaceutical Manufacturers Association invest \$40 billion annually in R&D. Global imbalances of investments underscore the obstacles faced by many developing countries. According to Tikki Pang, of an estimated \$5 billion invested annually in genomics research, \$3 billion is private and 75% is in the United States, which also registers about 80% of genomics patents worldwide. Some developing countries – Cuba, Thailand, India, and China – are emerging contributors to genomics research. But, what about other developing countries? Michael Wilson described a "catch-22" situation in Ghana of a vicious cycle of weak financing, little research, few facilities, no jobs, and ultimately out-migration of skilled scientists.

To remedy the R&D gap, two dozen so-called public-private partnerships (PPPs) have been created. These PPPs mostly aim to produce public goods in health. Many believe that these "push" mechanisms (production of neglected vaccine and drugs) must be balanced by "pull" forces (like subsidized vaccine purchase funds) to correct for market failure.

Can markets be shaped to generate fairer outcomes? Severe inequity is not a pre-ordained outcome of markets that involve millions of individual and collective decisions. Markets, however, are social institutions governed by humanly constructed ground rules.

Depending upon ground rules, it is possible to generate various levels of fairness. Weak initial capability upon entering competitive markets is one example of handicaps faced by many developing countries. Many also feel aggrieved because these disadvantages are historically inherited, and developing countries often lack the political and economic clout to negotiate better entry conditions.

Another ground rule is intellectual property rights (IPR). Lalji Singh described the cultural alarm of Indians as foreigners patented indigenous plants -- the neem tree, turmeric spices, and Basmati rice. The controversy over IPR will not simply go away. George Soros in his recent book, "Globalization," describes how IPR in today's knowledge-based economy should be treated differently than earlier technology eras. In the industrial revolution, either new or some commonly-owned assets became privatized -- for example, telegraph lines, railway tracks, subsurface petroleum, and manufacturing machines. Intellectual property in a knowledge-based economy poses different challenges to balance incentives for innovation, appropriate returns to an inventor, and economic progress. These historical dimensions of IPR should not distract us from practical intermediate steps that can be taken to reduce inequities in IPR management. Bibek Debroy argued that wholesale changes are neither likely nor necessary, nor must solutions be conflictual. One example of positive adjustment is ensuring royalty returns to affected genetic lineages for research participation in Costa Rica. Another potentially very significant advance is Management of Intellectual Property in Health R&D (MIHR), recently established by the Rockefeller Foundation to assist non-profit organizations negotiate IPR, licensing, and other arrangements.

As described by Luis Herrera and his colleagues, Cuba is an admirable health success story. Its 11 million people enjoy an average life expectancy of 76 years and an infant mortality rate of 6 per 1,000 livebirths -- roughly equivalent to Canada and superior to the United States. As a basic human right, health care is universal, accessible, and free.

Cuba also has adopted an "internationalist public health" policy that exported 2,600 health workers to other countries. With universal literacy, 58 universities and 115 research institutes, Cuba has one physician per 179 population and more than one teacher per 50 people. Its rich human resources are important to a state-led biotechnology sector, which has received strong political commitment and sustained investments. The state-led sector pursues vertical integration of pharmaceutical research-product-marketing, called by Dr. Herrera, a "closed cycle strategy." Drs. Moreno and Mauri described how Cuba also pursues IPR protection and marketing through "strategic alliances" with foreign firms. In the United States, we have a market-led biotechnology sector. Of course, the public sector through the NIH provides nearly \$20 billion of funding for basic research that is tapped by the private sector. Other countries, for example Thailand, have their own unique mix of state-led and market-led R&D. The lesson here is that different national patterns of R&D systems are possible, even as all nations compete in a global economy.

The history of Chinese science is also informative. China produced great scientific advances (gunpowder, printing press, and oceanic shipping) at a time when Europe was still in the Dark Ages. With such technologic prowess, why did China fall behind Europe which later experienced a vibrant renaissance? Joseph Needham, the great chemist at Cambridge University, devoted much of his life to the study of Chinese science and society. He concluded that societal culture and values are important for determining the nature of technological advance. The Chinese simply did not want to turn gunpowder into armaments nor to cross the oceans in large ships. A deeply conservative culture, the Chinese idealized the past. This interpretation of Chinese history refutes “technological determinism.” Technology is neither inevitable nor immutable. Social and cultural controls can be exercised. Whether and how the global community exercises such controls on genomics technology is a central question facing us today.

### **WHO’s Future Strategies?**

After release of “Genomics and World Health,” the WHO will launch the “Genomics for Health Initiative” (GHI). The draft terms of reference for the Initiative offers nine possible activities – annual forums, capacity building, innovation in developing countries, mobilization of financial resources, building of bioethics capacity, establishing codes of conduct, advocacy, public engagement, and global governance. The listing is intended to stimulate constructive suggestions from participants. A listing, however, must be constructed into a WHO strategy. Strategy development requires specification of a clear mission, articulation of goals and objectives, prioritization of activities, identification of audiences and constituencies, developing markers of progress, and formulation of a work plan that is feasible in terms of human, financial, and organizational resources.

Let me speculate on strategies that might be considered by the WHO. WHO’s core functions, I believe, provide the foundation of a core strategy for an Initiative. These core functions are technical cooperation, normative role, and advocacy.

**Technical Cooperation** -- WHO is a respected technical resource in world health. Expertise need not be housed within its professional staff. With its organizational legitimacy, WHO has the credibility to mobilize the best technical talent from around the world. To accelerate technical cooperation, WHO can be an effective facilitator, especially for capacity building in developing countries.

Participants agreed that in-country advanced training programs are essential for building national research capacity, a consensus view that was articulated by Jorge Allende. Long-term national commitment to doctoral research training is vital. “Brain drain” to the North can be contained by such programs, supplemented by incentives for re-entry of post-doctoral researchers who have studied abroad. Public support for and political commitment is important. One Brazilian province devotes 1% of its budget for research support.

National programs can be strengthened by South-South cooperation. Regional networking mechanisms are useful ways of formalizing these cooperative relationships. As much of the scientific resources are in rich countries, South-North cooperation also should be encouraged. Eva Harris described a North-South Central American program that combines training in basic research with public health epidemiology and proposal writing so that scientists are able to compete for funds to support their research.

These country-based and international cooperative programs must grapple with clarity about global versus local research. Enormous diversity can and should be expected in developing countries, given their variation in population, economy, technological infrastructure, and national priorities. Not every developing country can or should attempt to replicate Cuba! The Commission in Health Research for Development (Oxford University Press, 1990) described the complementarities between global research and national research. Essential national health research is more location-specific and useful for all countries to produce for solving their specific health problems. Global research is more transferable geographically. Global knowledge is contributed by all countries, in different ways according to diverse national situations, often produced in advanced centers in the North, South, and internationally. There need not be conflict between global and national research; they help us understand why national health research systems can be so diverse.

**Norms and Policies** – WHO is the only legitimate international organization that can validate best practices, including quality certification of biotechnology products. These functions are particularly important to developing countries whose less mature regulatory agencies would benefit from international validation.

Standardization and certification functions should be supplemented by specific programs in genomics. One such opportunity is information sharing. Nick Thomson of the Sanger Institute described a bioinformatics system that makes genetic advances readily accessible through the worldwide Internet. WHO should consider an alliance with the Wellcome Trust to support a public bioinformatics website that would give open access to the latest scientific information. This service would be of particular value to isolated scientists in developing countries.

WHO can also promote policies on R&D against neglected diseases. WHO need not necessarily undertake all of the direct operations, but rather it could exercise leadership. Organizational roles in R&D are shifting. Like a three-legged stool (government, industry, and civil society), partnership among multiple actors should be encouraged to pursue R&D of neglected diseases. As governments are downsized, there is corresponding fiscal pressure on inter-governmental organizations. Both for-profit and non-profit entities have proliferated. For health R&D, there are now more than two dozen public-private partnerships (PPPs), some operated within international agencies and others created as independent non-profit entities. PPPs have been established to accelerate R&D against the four infectious diseases covered in our breakout groups -- dengue, malaria, tuberculosis, and HIV/AIDS. Two disease-specific PPPs (malaria and tuberculosis) were discussed in our breakout groups. Another type of PPPs will soon

emerge. As described by Ariel Pablos-Mendez, the launch of Management of Intellectual Property for Health R&D (MIHR) that will help non-profits negotiate IPR, licensing, and other aspects of bringing affordable biotechnologies to people. This PPP is generic for all neglected diseases, not specific to any single disease.

**The Initiative** – My primary recommendation is that the Genomics and Health Initiative focus on advocacy and promotion, with some of the above technical cooperation and policies assigned to WHO departments. Global leadership through advocacy and mobilization is desperately needed in genomics and biotechnology. History has repeatedly demonstrated that social responses to new technologies are invariably delayed, with consequent negative consequences. Urgency, therefore, should be exercised in launching the Initiative to help social responses to catch up to rapid advances in science and technology.

The “Initiative” could be an agile, flexible enterprise drawing the participation of others through alliances or coalitions, not simply replicate a department of an international agency. In this type of organizational configuration, leadership is exercised not by control of budget and staff but by policy, information, and institutional steering of the many groups that together advance the Initiative’s goals. After all, the powerful actors in genomics are outside of WHO – scientists in academia, the biotech and pharmaceutical industry, NGO activists, and political leaders. The Initiative should “incentivize” these allies to fulfill the Initiative’s mission of harnessing the power of genomics and biotechnology for global health equity.

Among key constituencies is the scientific community, as scientists have demonstrated remarkable social leadership when energized, as illustrated by the role of physicians and scientists in the Nobel Prize anti-nuclear movement. Private industry, also, should be engaged for it has a stake in ensuring a fair and productive Initiative that can calm the waters for commerce. The press and media and political decision-makers are other audiences. Public opinion sets the outer boundaries for realistic options exercised by political decision-makers. Parenthetically, it would have been interesting to learn of knowledge and attitude surveys among political leaders who are responsible for making so many of the critical fiscal and legislative decisions. The proposed Annual Forums should be used as convening events to bring together key constituencies around specific themes.

For the Initiative to succeed, it will have to leverage financing and exercise normative leadership. The recent WHO Macroeconomic Commission proposed a global health research fund. Last week’s Monterrey conference on financing for development, while generating additional pledges, does not offer optimism about significantly enhanced public resources for a global NIH. More likely, the Initiative would have to obtain funding from traditional donors – the UN, development banks, bilateral donors, and foundations. After establishment, however, the Initiative should monitor and advocate for appropriate investments in genomics and biotechnology.

We should try to expand the modes of resource mobilization by shifting beyond donor charity to service fees. A “Tobin tax” on international currency transactions to support international development was an earlier idea. I had previously proposed a “health fee” for international air travelers that would support the control of infectious diseases. Such a fee would be appropriate for the health protection of international travelers, and the infrastructure created would have positive benefits beyond the traveling public. With more than 500 million international air travelers, a \$2 fee would generate revenues of \$1 billion annually (many airports charge \$10 or \$20 service fees). Another fee option, a long shot, would be modest payments from the multi-national pharmaceutical industry for global health governance. Although support for inter-governmental organizations comes from taxes paid by citizens and corporations to national governments, globalization has limited the tax collection opportunities of governments. Why shouldn’t corporations pay a direct service fee for governance that enables them to operate in global commerce?

A most important mission of the Initiative is “globalizing ethics” as suggested by Jose Maria Cantu. WHO can play a powerful role in facilitating the global dialogue. The revolution in genomics and biotechnology will generate many vexing ethical dilemmas that cannot be addressed entirely within nations. A central ethical question is: Which technology for whom, why, and how? Severe health inequities offend our moral sensibilities. Without compassion, we are not human. All of us are searching for “global democracy” in a rapidly globalizing world. Through the Genomic Health Initiative, “the WHO should act as the conscience of world health” in this time of technological and social transformation.

In conclusion, I would like to convey our gratitude to WHO for sponsoring this timely meeting, despite many obstacles not the least of which was postponement due to September 11th. The Cuban organizing committee and the PAHO national office deserve our thanks for superb hospitality and organizational arrangements. All of us look forward to supporting the Genomics and Health Initiative. In the interim, where is my next majeto? When is my next invitation to Cuba? Thank you.