# An enforceable international compact for infectious diseases: strategies to operationalize new initiatives to strengthen global health security

*Harvey Rubin and C. Kameswara Rao**

*Man has all the time lagged behind the naturally occurring pathogens in his race with them. The natural endemic, epidemic and pandemic infectious diseases have always seriously threatened global health security. In the 21st century this race has attained a new dimension with the addition of nefariously disseminated pathogens emanating from 'dual use' modern life sciences technologies, which require global responses to track, detect, prevent and treat infectious diseases, both natural or deliberately spread.*

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## Challenges to global health security

The global community has been burdened by several daunting infectious diseases such as:

(a) Malaria with 300 million new cases each year killing two million people.
(b) Hepatitis C virus, with estimated 3% of the world's population being chronically infected. About four million are newly infected each year, 80% of whom progress to a chronic infection associated with cirrhosis (about 20%) and liver cancer (about 5%).
(c) Hepatitis B virus infects about a third of the world's population. About 400 million are chronically infected and one million people die each year from the infection and/or its complications.
(d) Tuberculosis, with 10 million new cases every year accounts for two million deaths.
(e) HIV affects about 36 million people worldwide, which killed approximately 2.4 million people in 2007.
(f) Cholera still causes thousands of deaths per year[1].
(g) Large number of infants are afflicted by polio, chikungunya and botulism[2,3].

Despite the attention given to diseases like HIV/AIDS and avian influenza, some outbreaks that represent a serious burden on global health are still relatively unknown to the general public.

The reports of the US National Intelligence Council[4] and of the US Institute of Medicine[5] brought into focus the threat to global health security from microbial agents. A document of the US Central Intelligence Agency (CIA) analysed 'the darker bioweapons future' and concluded that 'the effects of engineered biological agents could be worse than any disease known to man'[6]. The US National Security Strategy cautions that 'Public health challenges like pandemics (HIV/AIDS, avian influenza)... recognize no borders'[7].

The risks to social order from infectious diseases are so great that 'traditional public health approaches may be inadequate, necessitating new strategies and responses'. The Infectious Diseases Society of America observed that, 'in a growing and frightening number of cases, the pathogenic bacteria are resistant to many approved drugs, and patients have to be treated with new, investigational compounds or older, toxic alternatives'[8]. A report of the Woodrow Wilson School of Public and International Affairs (Princeton University) warns that 'New diseases and antibiotic-resistant strains of old ones are on the rise'[9].

## Deliberate misuse of emerging technologies

The deliberate spread of infectious diseases misusing otherwise beneficial technologies (dual use) has emerged as an attractive option for bioterrorists and rogue States, and is now a major global security concern. The issue of dual use of otherwise beneficial life sciences research and technologies has been discussed in detail, by international committees and working groups as given below.

Harvey Rubin is in the Department of Medicine, Microbiology and Computer Science, and the University of Pennsylvania Institute for Strategic Threat Analysis and Response and C. Kameswara Rao is in the Foundation for Biotechnology Awareness and Education, Bangalore 560 004, India.
*For correspondence. (e-mail: chaakaaraav@yahoo.com)

(a) Committees of the US National Academies on (i) Biotechnology research in the age of terrorism (2002–03)[10], (ii) Advances in technology and the prevention of their application to next generation biowarfare threats (2004–05)[11,12] and (iii) Science and security in a post 9/11 world (2007)[13].

(b) World Health Organization's (WHO) Special Working Group on Life Science Research and Global Health Security[14], that has been meeting at different places since October 2006.

(c) The US National Institutes of Health and WHO's International Round Table on Dual Use Life Sciences Research (February 2007).

(d) The Organization for Economic Cooperation and Development's (OECD) High-level Forum on Medicines for Neglected and Emerging Infectious Diseases (June 2007).

(e) The 'Second International Forum on Biosecurity', organized by the InterAcademy Panel on International Issues (IAP), the InterAcademy Medical Panel (IAMP), the International Union of Microbiological Societies (IUMS), the International Union of Biochemistry and Molecular Biology (IUBMB), the International Union of Biological Sciences (IUBS), the Hungarian Academy of Sciences and the National Academies of the United States (March 2008).

(f) The Roundtable organized by WHO and the US Government's National Science Advisory Board for Biosecurity on 'Sustaining Progress in the Life Sciences: Strategies for Managing Dual Use Research of Concern' (November 2008).

(g) The International Workshop on Biosecurity, organized by the Chinese Academy of Sciences, IAP and the OECD (December 2008).

## Socio-economic impact of infectious diseases

The predominance of infectious diseases has an undeniable moral significance and highlights our collective failure to give this problem, with implications for the economic well-being of both the developed and developing world, the attention it deserves. It is well recognized that infectious diseases perpetuate poverty in the developing world. They destroy family structure, and limit economic and educational opportunities affecting the economic security of all nations. While the social disintegration that follows an epidemic has filtered into the public consciousness, the consequent economic disruption is less known. A few weeks after the identification of the Severe Acute Respiratory Syndrome (SARS), the disease had already cost nearly US$ 30 billion, an amount sufficient to prevent 8 million deaths from infectious disease worldwide[15]. A potential H5N1 pandemic costs much more, with economic losses approaching 600 billion dollars in the US alone, depending on the virulence of the strain[16]. The spread of pathogenic bacteria that are becoming increasingly resistant to the existing antibiotics imposes a persistent cost in terms of both health and dollars.

## New strategies to face challenges to health security

This formidable challenge calls for new strategies that integrate basic sciences, technology, and social, political, legal and economic realities. The solution should optimize trade-offs in the interplay of (a) international security, (b) global health, (c) creation and open dissemination of new knowledge and (d) maintenance and enhancement of the positive role of modern science on the economy of the developing world.

## Lessons from the past

Over the past 25 years, there have been several successful efforts at resolving complex and sometimes overlooked international issues from the perspectives of both implementation and end-stage achievements.

Six NGOs who met in October 1992 in New York founded the International Campaign to Ban Landmines (ICBL). Five years later, the International 'Convention on the Prohibition of the Use, Stockpiling, Production and Transfer or Anti-Personnel Mines and on their Destruction' entered into force and the ICBL was awarded the Nobel Peace Prize 'as a model for similar processes in the future'[17]. The essential issues surrounding infectious diseases possess similar normative force, which hopefully indicates a similar potential for progress.

The efforts of the Consultative Group on International Agricultural Research (CGIAR), under the leadership of the Nobel laureate Norman Borlaug, resulted in a massive increase in cereal yield in the second half of the 20th century, averting a global food crisis. CGIAR is an important antecedent combining North/South representation with innovative research and a truly lasting impact in some of the poorest regions in the world[18].

The magnitude of the threat of infectious diseases also necessitates a major global, investigative effort. The lasting positive impacts of international research centres are many, including fostering long-term relationships between scientists, establishing a culture of research responsibility and serving as the nucleus for safe applications of interdisciplinary sciences globally.

The key to any progress against infectious diseases is a structure that brings together diverse interests in a lasting manner. Without such a structure, the commitment to reducing the impact of infectious diseases on our national, economic and personal security will be subject to the political vagaries of the moment, leaving us unprepared for any health crisis.

## Treaties, conventions and comprehensive compacts

There is no comprehensive programme for infectious diseases and the Biological and Toxin Weapons Convention[19] is inadequate.

International treaties and conventions have some advantages like providing for an international legal basis for enforcement, creating a body of durable 'hard law' around an issue and drawing on the power of governments to regulate and license within their jurisdiction, but suffer from drawbacks such as ratification, will be slow and may limit action on urgent issues and the States may perceive enforcement clauses as an unacceptable burden, or even as a threat to their sovereignty.

While compacts have the benefits of being effective governance structures that are quick to set up and provide a framework for action, bring together a broad coalition of partners around a central issue and promote voluntary compliance of laboratories, companies, etc., the disadvantage is that enforcement relies on soft power and voluntary compliance, which may prove ineffective during a crisis.

The answer is a 'Comprehensive International Compact for Infectious Diseases', a two-pronged approach with the States as the eligible parties, and ratification as the method of participation. Treaty and compact are complementary systems that provide for parallel frameworks for different parties; the overall project will, over time, achieve the benefits of each. Domestic partners who are signatories to the compact can pressure States to comply with the treaty, as non-participation could put an organization/country at a disadvantage[20].

Several compact-like international agreements exist in such areas as human rights, environment, arms control and disarmament, and trade and finance.

Legitimacy and understanding of the overall system will be promoted through involvement of both the State and non-State actors.

## The International Compact for Infectious Diseases

Considering the general threat scenario of natural and deliberate spread of infectious diseases and the international consensus on preparing to face the threats, one of the authors (H.R.) with intellectual inputs from over a score of active microbiologists and pathologists, mostly from North America and Europe, has developed the 'International Compact for Infectious Diseases', with a four-point strategy for handling threats from infectious diseases:

*Compact core mission I:* Establish, maintain and monitor a shared international data and knowledge base for infectious diseases, including but not limited to biosurveillance information, relevant pharmaceutical data and suites of services and skills.

*Compact core mission II:* Establish, maintain and monitor a network of international basic sciences research centers that will support fundamental investigations into the pathophysiology of certain microbial threats to global health.

*Compact core mission III:* Expand capabilities for the production of vaccines and therapeutics expressly for emerging and reemerging infections.

*Compact core mission IV:* Establish, maintain and monitor international standards for best laboratory and regulatory practices.

Implementation of the four core missions of the compact will minimize the impact of infectious diseases on global health, social and economic development, and international security. The compact drives innovation and progress in four core areas: (a) information and knowledge sharing, (b) basic sciences, (c) drug and vaccine development and (d) best laboratory and regulatory practices. These missions are interconnected (Figure 1). Without a strong foundation of basic sciences, the drug and vaccine pipelines dry up. Similarly, in the absence of effective biosurveillance, it becomes difficult to project which strain of an emerging disease represents the most significant threat; which in turn hampers our ability to create countermeasures. Information technology and knowledge sharing will drive new science, which in turn can modify and inform regulatory initiatives. Standardized regulatory regimes enable new drugs and vaccines that will change global epidemiological patterns and these patterns must be reintegrated into a central database, beginning the cycle again.

### *Information technology architecture*

There already exist a large number of databases that address one or more of the issues related to global health threats, for example, WHO's revised 2005 International Health Regulations[21]. The information technology architecture proposed for the infectious disease compact (Figure 2) will seamlessly integrate most of the existing databases, make them user-friendly yet provide the necessary security and add new data as recommended by the wide user community. Though the challenges here are formidable, they are hardly insurmountable. The greatest obstacle is the need for trust between signatory nations and a willingness to share data. There are technical challenges as well. Any attempt to create a common architecture for information systems would require common ontologies. New algorithms and models of disease spread need to be developed and validated. Lastly, the language of the compact has to address the issue of member States which do not report, or significantly under-report, the incidence of communicable diseases.

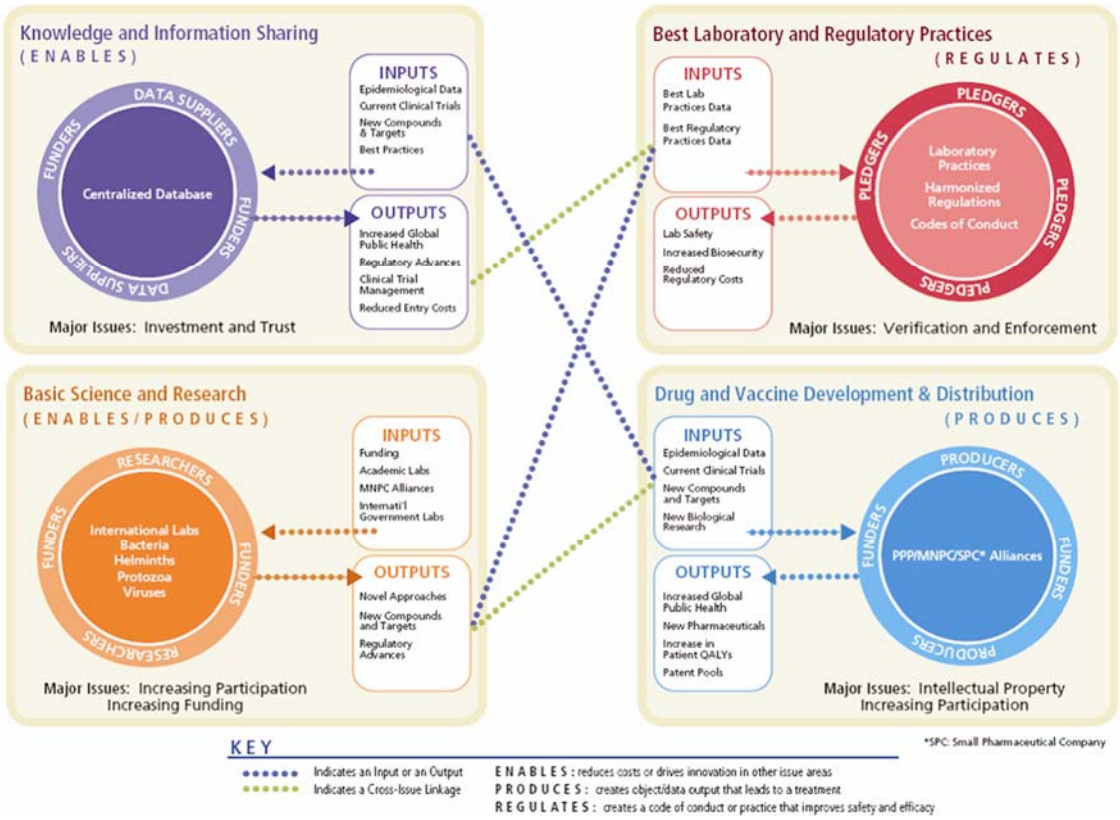


**Figure 1.** International compact for infectious disease.

## International biosurveillance and reporting

International biosurveillance and reporting faces certain challenges, particularly at the level of sophistication envisioned, which include:

(a) Integrating current initiatives into a national health IT strategy and federal architecture to reduce the risk of duplicative efforts.
(b) Developing and adopting consistent interoperability standards.
(c) Creating an open architecture that maximizes the use of off-the-shelf tools.
(d) Creating enough flexibility to bring together disparate underlying IT languages and technologies to provide a common operating picture.
(e) Generating the ability to accept multiple data formats used by agencies that provide biosurveillance information.
(f) Generating the ability to feed information back to the originating agencies providing biosurveillance information in a format each agency can accept.
(g) Identifying data flows that will evolve during the developmental process.
(h) Allowing the methods of analysis to evolve and adapt as new data become available or existing datasets are improved.
(i) Knowing and evaluating the effectiveness of the current underlying algorithms, methods and structures for biosurveillance data analysis.

### *Organization and governance*

In order to accommodate the various interested parties and work within the limits of international law, the compact will embrace a two-pronged approach, working with States in the form of a treaty and with other interested parties (NGOs, academic institutions and the private sector) as a softer, pledge-based agreement.

By providing parallel frameworks for different parties, the overall project will achieve the benefits of each. Domestic groups that pledge their membership can apply pressure to their home States, hopefully speeding ratification of the treaty framework. By bringing together both State and non-State actors, the overall aims of the compact will be debated from a variety of different viewpoints, thereby enhancing the legitimacy of the project and promoting a thorough understanding of its goals.

## Benefits anticipated from the international infectious disease compact

The compact offers diverse stakeholder and community benefits, for which it is urgent to make accelerated efforts

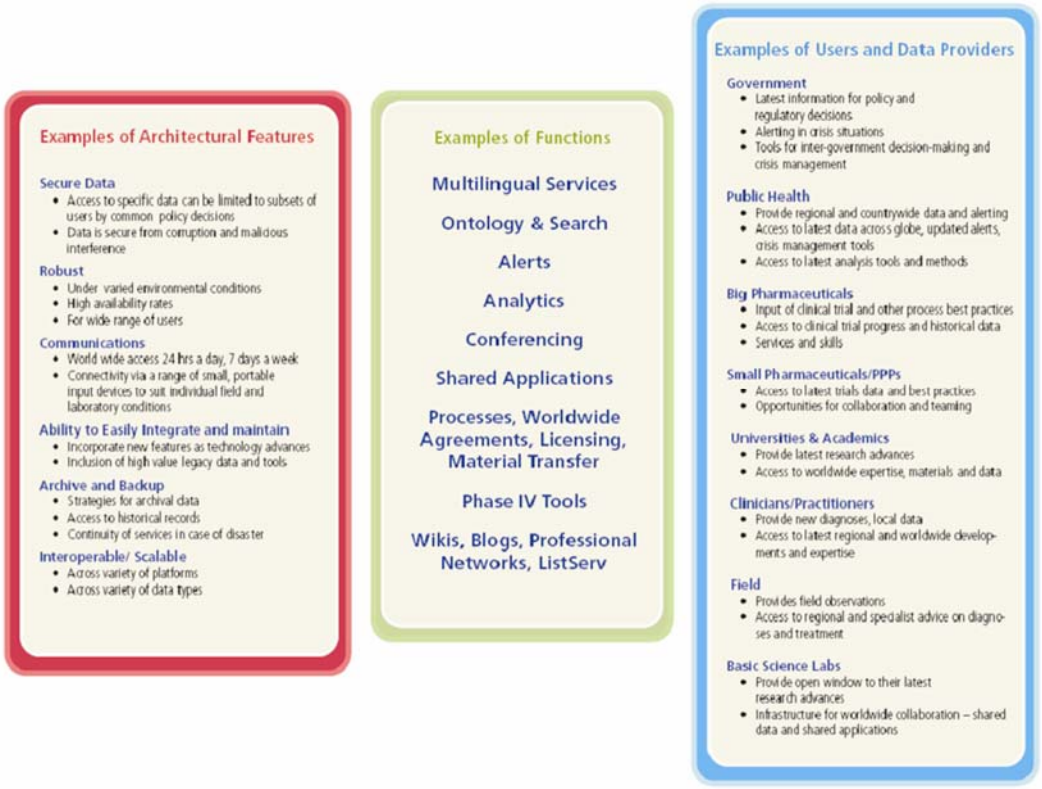


**Figure 2.** Information technology architecture.

to draft, debate, refine and implement the first ever International Compact for Infectious Diseases.

### *Stakeholder benefits*

Addressing the problem as a whole creates powerful incentives for stakeholders to participate. For example, in order to access a central database containing information on current clinical trials, epidemiological data and new compounds and targets, participants would pledge to implement best laboratory and regulatory practices. By bringing together the government, private sector and academia, the compact allows each group to institutionalize their relations with the others. Pharmaceutical companies and public–private development partnerships can find partners to help take promising leads through to development. With the inclusion of post-marketing/post-distribution clinical trial data in the database, philanthropic organizations and governments will be able to understand the effects their investments will have throughout the world. Academics will acquire additional funding streams for their research as well as input from their colleagues all over the world. Finally, all parties will work together to harmonize regulatory processes across the board, reducing barriers to market entry for the much needed therapeutics and ensuring their wider distribution.

### *Community benefits*

The compact is expected to afford the following benefits to communities from signatory nations in both the developed and developing worlds.

(a) Provide access to cheaper, more highly standardized specific therapeutics and vaccines that are relevant to the signatories.
(b) Ensure better quality control of vaccines, therapeutics and diagnostics in the developing world, leading to fewer expired or counterfeit agents.
(c) Provide access to and participation in high-level research.
(d) Provide developing and developed States with a voice in the direction of research and development.
(e) Distribute the costs and risks of research and development across a number of countries.
(f) Provide more complete datasets on emerging infections and potential pandemics.
(g) Create a more competitive market for vaccine and therapeutic development targeting diseases of relevance to signatory nations.
(h) Enhance and enable human health and well-being, economic development and basic biological research.

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