STRENGTHENING RESPONSE TO
PANDEMICS AND OTHER
PUBLIC-HEALTH EMERGENCIES

Report of the
Review Committee on the Functioning of the
International Health Regulations (2005)
and on Pandemic Influenza (H1N1) 2009

World Health Organization

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WHO Library Cataloguing-in-Publication Data

Strengthening Response to Pandemics and Other Public-Health Emergencies: Report of the Review Committee on the Functioning of the International Health Regulations (2005) and on Pandemic Influenza (H1N1) 2009.

1.Legislation, Health. 2.Communicable disease control. 3.Influenza A virus, H1N1 subtype. 4.Pandemics. 5.Disease outbreaks. 6.Disease transmission. I.World Health Organization.

ISBN 978 92 4 156433 5 (NLM classification: WA 32.1)

Book design by Sophie Guetaneh Aguettant.

Layout by Interligar.

Printed in France.

Contents

Preface

Myriad health threats have the capacity to cross borders. In anticipation and response, the World Health Organization (WHO) gives voice and leadership on behalf of the global community. WHO's principal line of defence is the International Health Regulations (2005). The emergence of the influenza A (H1N1) pandemic in April 2009 provided the first major stress test since the Regulations came into force in 2007.

This report serves two aims. First, it is an analysis of how the International Health Regulations (IHR) have so far fulfilled their purpose to provide the world adequate health security with the least-possible disruption to economies, specifically to travel, transport of goods and human rights. The Regulations were due for their first review in 2010, but the 2009 influenza pandemic intervened and led to the second focus of this report: an investigation into WHO's response to the pandemic. The two aims are separate, but intertwined.

The 2009 influenza pandemic shone a revealing light on the functioning of the Regulations. At the same time, the scope of the IHR covers a wide variety of public-health emergencies and not solely an infectious threat. Beyond testing the Regulations, the influenza pandemic exposed vulnerabilities in global, national and local public-health capacities, limitations of scientific knowledge, difficulties in decision-making under conditions of uncertainty, complexities in international cooperation and challenges in communication among experts, policy-makers and the public.

Over the past year, I have had the privilege of working with the members of the Review Committee, which comprises individuals drawn from all regions of the world, chosen for their expertise, their independence and their commitment to global health. To meet their responsibilities, they came to WHO headquarters in Geneva to listen to many hours of testimony and read hundreds of documents in a thorough process of enquiry and deliberation.

The resulting report is defined by what it is not, as well as by what it is. The report is not based on preconception, but on the evidence, as best we could ascertain it. The report is not an assessment of individual country performance or an evaluation of the cost–effectiveness of the IHR or of the response to the pandemic. Instead, the report focuses on the functioning and performance of the IHR and WHO. It is an attempt to examine the facts, arrive at conclusions and offer constructive advice aimed at improving future performance.

The Review Committee has been mindful that it was appointed on behalf of all Member States. With this mandate, we endeavoured to be consultative and inclusive. Every plenary session of the Committee was open to representatives of States Parties to the IHR, to intergovernmental and nongovernmental organizations and to the media. Everyone present heard the same testimony that the Committee heard, and the Committee benefited from written submissions and oral presentations from States Parties and others.

In advance of its final meeting in March 2011, the Committee released its draft recommendations and conclusions in the form of a Preview document. This gave States Parties to the IHR, intergovernmental organizations and nongovernmental organizations an opportunity to examine the document and evaluate its merits and defects. Their comments on the

Preview document helped strengthen the report and served to affirm its overall direction and the nature of its recommendations.

As in the Preview, this final report offers three summary conclusions accompanied by 15 recommendations. These cover a range of improvements that affect technical matters, logistics and policy. Some recommendations will require resources to implement, but none is more expensive than the cost of doing nothing.

Pandemics can be fearsome teachers. No matter what one believes about the response to the 2009 pandemic by WHO and other authorities, all must be grateful that relatively few people died. Influenza viruses are notoriously unpredictable. We were lucky this time but, as the report concludes, the world is ill-prepared for a severe pandemic or for any similarly global, sustained and threatening public-health emergency. We respectfully offer this assessment to all countries in the hope that our recommendations will assist in making the world a safer place.

Harvey V. Fineberg
Chair, Review Committee

April 2011
Geneva, Switzerland

Acknowledgements

The Review Committee wishes to thank the following members who had to resign during the course of its work: Dr Anthony Evans, Professor John Mackenzie, Dr Ziad Memish and Dr Babatunde Osotimehin.

The Review Committee received valuable contributions from States Parties, United Nations special agencies, governmental and nongovernmental organizations and individuals. In particular, the Committee wishes to thank the following individuals who were interviewed before the Committee:

Dr Masato Mugitani, Assistant Minister for Global Health and Director-General of the Special Task Force for Pandemic Influenza, Ministry of Health, Labor and Welfare, Japan; Dr Suresh Jadhav, Executive Director of Quality Assurance & Regulatory Affairs, Serum Institute of India and former President of the Developing Countries Vaccine Manufacturers' Network; Mr Tony Colgate, Scientific Coordinator of the International Federation of Pharmaceutical Manufacturers and Associations and Manager, Vaccines & Diagnostics Influenza Technical Affairs, Novartis; Dr Dirk Glaesser, Chief of Risk and Crisis Management, United Nations World Tourism Organization; Dr David Salisbury, Director of Immunisation, Department of Health, England, and Chair, WHO Strategic Advisory Group of Experts on Immunization; Dr David Reddy, Global Pandemic Task Force Leader and Ms Catherine Steele, International Head of Communications, F. Hoffman-La Roche Ltd.; Dr Andrin Oswald, Head of Vaccines and Diagnostics, Novartis; RADM Stephen Redd, Director, Influenza Coordination Unit, US Centers for Disease Control and Prevention, United States of America; Dr Hugo Lopez-Gatell Ramirez, Assistant Director General for Epidemiology, Ministry of Health and National IHR Focal Point, Mexico; Professor Didier Houssin, General-Director for Health and Interministerial Delegate on Avian Influenza for the Ministry of Health in France; Ambassador Bente Angell-Hansen of Norway and Ambassador J.J Gomez-Camacho of Mexico, co-chairs of the Open-Ended Working Group on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and Other Benefits; Dr David Butler-Jones, Chief Public Health Officer, Public Health Agency of Canada; Dr David Nabarro, Senior Coordinator for Avian & Human Influenza, United Nations System Influenza Coordination; Ms Carmen Amela Heras, Representative for IHR Issues of the Directorate General for Public Health, Ministry of Health and Social Policy and National IHR Focal Point, Spain; Dr Thomas Jefferson, Cochrane Vaccines Field; Dr Fiona Godlee, Editor-in-Chief, *British Medical Journal*; Dr Norbert Hehme, Chair of the Influenza Vaccine Supply International Task Force, International Federation of Pharmaceutical Manufacturers and Associations and Biologicals, GlaxoSmithKline; Dr Paul Benkimoun, Medical Journalist, *Le Monde*, France; Professor David Harper, Director General for Health Improvement and Protection, Department of Health, England; Mrs Else JB Andersen, Assistant Deputy Director-General, Ministry of Health and Care Service, Norway; Mr Morten Randmæl, Director, Emergency Preparedness Department, Directorate of Health, Norway; Mr Bjørn Iversen, Acting Department Director, Norwegian Institute of Public Health, Norway; Mrs Ine Måreng, Assistant Director-General, Ministry of Foreign Affairs, Norway; Dr Lars Schaade, Head of Center, Biological Safety, Robert Koch Institute,

Germany; Dr Alex Thiermann, President, Terrestrial Animal Health Code Commission and Senior Adviser to the World Organisation for Animal Health (OIE) Director General and Dr Kate Glynn, Head of Mission in the OIE Scientific and Technical Department and Focal Point for Animal-Human Health Interface Matters; Mr Paul Flynn, Parlimentarian, United Kingdom Labour Party and Representative at the Council of Europe; Dr Gérard Krause, Director, Department for Infectious Disease Epidemiology, National Public Health Institute, Germany; Professor John Mackenzie, Emergency Committee Chair, Professor of Tropical Infectious Diseases, Division of Health Sciences, Curtin University, Australia; Dr Claude Thibeault, Consultant in Aviation Medicine and Occupational Health and Medical Adviser, International Air Transport Association (IATA); Dr Aboubacry Fall, Public Health Specialist, Health Economist, Director of Prevention at the Ministry of Health, Prevention and Public Hygiene, Senegal; Dr Philip Muthoka, National IHR Focal Point Officer, Ministry of Health, Kenya; Dr Vagif Abdullayev, Alternate National IHR Focal Point, Deputy Director-General of the Republican Center of Hygiene and Epidemiology, Azerbaijan; Dr Liudmila Naroichyk, Deputy Chief Doctor on Epidemiology, Republican Centre for Hygiene, Epidemiology and Public Health, Belarus; Dr Anthony Evans, Chief, Aviation Medicine Section, International Civil Aviation Organization (ICAO), Montreal, Canada; Dr Dang Quang Tan, Chief of Border Health Quarantine Division, Department of Preventive Medicine, Ministry of Health, Viet Nam; Dr Jacques Berger, President, Sanofi Pasteur, France; Dr Atika Abelin, Director, Global Immunisation Policy, Sanofi Pasteur; Dr Patricia Leung-Tack, Director Industrial Operations Flu, Influenza Pandemic & Pneumo, Sanofi Pasteur; Dr Mike Osterholm, Director, Center for Infectious Disease Research and Policy (CIDRAP), University of Minnesota; Dr Samir Abdel Aziz El Rafie, Executive Director Surveillance Unit, Ministry of Health, Egypt; Dr Babiker Magboul, Director of Epidemiology Department, Federal Ministry of Health, Sudan; Dr Kamel Abusal, National IHR Focal Point and Community Medicine Specialist, Head, Diarrheal Disease Sector, Ministry of Health, Jordan; Ms Maritza Garcia, Registered Nurse, Epidemiologist, Chief, Epidemiological Surveillance System, Ministry of Health, Chile; Dr Karina Balbuena, Coordinator of Early Response Team, Secretariat of Prevention Programmes and Health Promotion, Ministry of Health, Argentina; Dr Geela Ali, Permanent Secretary of Health, Maldives; Dr Garib Das Thakur, Director and National IHR Focal Point, Epidemiology and Disease Control Division, Department of Health Services, Nepal; Ms Mary Murnane, Deputy Secretary, Professor Jim Bishop, Chief Medical Officer, and Ms Jennifer Bryant, First Assistant Secretary, Office of Health Protection, Department of Health and Ageing, Australia; Dr Gary Grohmann, Director, Immunobiology Section, Monitoring and Compliance Group, Therapeutic Goods Administration, Australia; Dr Jean Damascène Khouilla, Director General Public Health, Gabon; Dr Marc Sprenger, Director, and Professor Angus Nicoll, European Centre for Disease Prevention and Control (ECDC) and Dr David L Heymann, Head and Senior Research Fellow, Centre on Global Health Security, Chatham House, United Kingdom.

The Review Committee wishes to thank WHO Director-General Dr Margaret Chan, Deputy Director-General Dr Anarfi Asamoa-Baah and WHO Assistant-Director General Dr Keiji Fukuda for actively supporting the work of the Review Committee. In addition, the Committee wishes to thank the following individuals from the WHO Secretariat who provided input: Sylvain Aldighieri, Ruth Anderson, Roberta Andraghetti, Penny Andrea, Sylvie Briand, Caroline Brown, Rick Brown, Gian Luca Burci, Francis Chisaka Kasolo, Stella Chungong, Fernando Da Conceicao Silvera, Patrick Drury, Philippe Duclos, Christine Feig, Fernando Gonzalez-Martin, Max Hardiman, Hande Harmanci, Gregory Härtl, Thomas Hofmann, Helge Hollmeyer, Anne Huvos, Jean Jabbour, Takeshi Kasai,

Mika Kawano, Kristen Kelleher, Marie-Paule Kieny, Chin-Kei Lee, Ailan Li, Karen Mah, Jaouad Mahjour, Anne Hélène Mazur, Jill Meloni, Daniel Menucci, David Mercer, Anthony Mounts, Bjorg Nilsson, Isabelle Nuttall, Angela Merianos, Otavio Oliva, Satoko Otsu, Charles Penn, Zahiri Pernalete, Bruce Plotkin, Chusak Prasittisuk, Adrienne Rashford, Cecilia Rose-Oduyemi, Cathy Roth, Michael Ryan, Nahoko Shindo, Rafe Slattery, Ian Smith, Steve Solomon, Florimond Tshioko Kweteminga, Ayana Yeneabat Alemu, Maged Younes and Wenqing Zhang.

The Review Committee would like to especially thank their Secretariat. The IHR Review Secretariat was led by Nick Drager and includes Dominique Metais, Faith McLellan, Mary Chamberland, Nadia Day, Alice Ghent, Sue Horsfall, Janet Kincaid, Philipp Lambach, Linda Larsson, Fabienne Maertens, Joan Ntabadde, Les Olson, Magdalena Rabini, Sarah Ramsay, Mick Reid, Chastine Rodriguez, Alexandra Rosado-Miguel and Natasha Shapovalova.

Executive summary

Introduction

In January 2010, at its 126th session, WHO's Executive Board welcomed the Director-General's proposal to convene a Review Committee provided for in Chapter III of Part IX of the International Health Regulations 2005 (IHR). The Director-General's proposal included a request for the Committee to review the experience gained in the global response to the influenza A (H1N1) 2009 pandemic in order to inform the review of the functioning of the Regulations; to help assess and, where appropriate, to modify the ongoing response and to strengthen preparedness for future pandemics. The Committee's remit follows.

> The assessment of the global response to the pandemic H1N1 will be conducted by the International Health Regulations Review Committee, a committee of experts with a broad mix of scientific expertise and practical experience in public health. The members are some of the leading experts in the world in their respective fields.
>
> The International Health Regulations 2005 (IHR) is an international legal agreement that is binding on 194 States Parties across the globe, including all of the Member States of WHO. The basic purpose of the IHR is to help the international community prevent and respond to acute public-health risks that have the potential to cross borders and threaten people worldwide. In January 2010, the WHO Executive Board requested a proposal from the Director-General on how to assess the international response to the pandemic influenza, and then approved her suggestion to convene the IHR Review Committee to review both the pandemic response and the functioning of the IHR.
>
> The pandemic H1N1 is the first Public Health Emergency of International Concern to occur since the revised IHR came into force. The IHR played a central role in the global response to the pandemic and so review of the IHR and review of the global handling of the pandemic influenza are closely related.
>
> The IHR facilitate coordinated international action by requiring countries to report certain disease outbreaks and public-health events to WHO so that global reporting of important public-health events is timely and open.
>
> The IHR were first implemented (i.e. "entered into force") worldwide in 2007 and the Health Assembly determined that a first review of its functioning is to take place by the Sixty-third World Health Assembly in May 2010.
>
> Objectives
>
> The review has three key objectives:
>
> - Assess the functioning of the International Health Regulations (2005);
> - Assess the ongoing global response to the pandemic H1N1 (including the role of WHO); and

- Identify lessons learned important for strengthening preparedness and response for future pandemics and public-health emergencies.

Names and affiliations of Review Committee members are listed at the end of the Executive Summary. The full Terms of Reference for the Committee are listed in Appendix I. Appendix II of the report contains their biographies and declarations of interest.

Method of work

The Review Committee conducted a major portion of its work through plenary meetings at WHO's headquarters in Geneva. For transparency, these meetings were open to the media. The Committee heard testimony from individuals representing States Parties, National IHR Focal Points, intergovernmental organizations, nongovernmental organizations, United Nations agencies, industry, health professionals, experts, members of the media, chairs of relevant committees and the WHO Secretariat.

The full Committee and its working groups also met for deliberative sessions in Geneva, open only to members of the Committee and its immediate support staff. Further consultations took place among the support staff, the Chair, Professor Harvey V. Fineberg and working groups of the Committee by means of telephone conferences and e-mail exchange.

While operating independently, the Review Committee frequently sought information from WHO's Secretariat, asking for clarification of issues that arose during the information-gathering and report-writing periods. WHO staff provided written responses to many questions posed by the Committee and spoke informally with Committee members. WHO provided the Committee with unfettered access to internal documents and Committee members signed non-disclosure agreements in order to review confidential legal documents.

The WHO Secretariat developed a series of briefing notes for the Committee, providing background on issues such as: the IHR; pandemic preparedness; pandemic phases; pandemic severity; pandemic vaccine; antiviral drugs; virological monitoring; disease monitoring; laboratory response; public-health measures and the Open-ended Working Group of Member States on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and Other Benefits. The Committee had access to a series of studies that evaluated the functioning of Annex 2 of the IHR (i.e. the decision instrument for States Parties' assessment and notification of public-health events) as well as progress reports on the implementation of the IHR. At the Committee's request, the WHO Secretariat devised a matrix of the key public-health functions of the IHR and identified a broad range of non-pandemic events that had been notified to WHO since the IHR came into force. The Committee selected several events and directed the Secretariat to prepare a summary of each event to facilitate assessment of the public-health functions of the IHR.

The Committee sought to document WHO's role and management in response to the pandemic and to evaluate the effectiveness of the IHR. This required a thorough investigation of events and decisions in the course of the pandemic, an examination of criticisms of the Organization and an assessment of its achievements. The goal from the outset has been to identify the best ways to protect the world in the next public-health emergency. Throughout its deliberations, the Committee has aimed to be thorough, systematic, open and objective. This report provides a full description of the evidence presented to the Committee in interviews and documents, and the Committee's assessment and interpretation of that evidence.

Background and context

The IHR establish a regime for the routine protection of public health and provide for the management of disease threats, both in countries and at their borders. They also provide a framework for coordinated and proportionate responses to significant emerging disease threats. Such threats may range from public-health events affecting one or more countries to events of global public-health significance. The provisions of the IHR are legally binding on States Parties and WHO. The IHR introduced a number of key innovations, including the replacement of a list of notifiable diseases with a decision instrument (Annex 2), to assist countries to determine whether an event *may* constitute a Public Health Emergency of International Concern. The 2009 pandemic was the first major test of the IHR.

A review of the functioning of the IHR and of how successfully WHO performed in response to the pandemic requires an understanding of the context of the pandemic. The Review Committee identified five factors that framed the events and help explain what happened in the pandemic response. Expressed simply, they are:

- the core values of public health
- the unpredictable nature of influenza
- the threat of avian influenza A (H5N1) and how it shaped general pandemic preparedness
- WHO's dual role as a moral voice for health in the world and as a servant of its Member States
- the limitations of systems that were designed to respond to a geographically focal, short-term emergency, rather than a global, sustained, long-term event.

The core values of public health shaped the response of public-health leaders around the world to the pandemic. The main ethos of public health is one of prevention: to prevent disease and avert avoidable deaths. The response of WHO and many countries to the pandemic was a reflection of this mindset. This was affirmed in the sentiments expressed by many Member States to the Review Committee: in the face of uncertainty and potentially serious harm, it is better to err on the side of safety. Public-health officials believe and act on this conviction. It is incumbent upon political leaders and policy-makers to understand this core value of public health and how it pervades thinking in the field.

Influenza pandemics will continue to occur, if history and science are any guide. In this sense, influenza is grossly predictable. However, exactly when, where and how severe the next influenza pandemic will be, no one can predict. Because pandemics occur infrequently, there is a tendency to over-interpret the patterns of the past. For example, it may be tempting when considering the pandemics of 1918–1919, 1957, 1968 and 2009 to conclude that successive pandemics tend to decline in severity. However, four observations are too few to support this conclusion. Research, especially on genetic markers of the virus and on host factors, may eventually increase the accuracy of predictions but, at present, lack of certainty is an inescapable reality when it comes to influenza. One key implication is the importance of flexibility to accommodate unexpected and changing conditions. The ability to take action in the face of uncertainty and to adapt rapidly to new circumstances are hallmarks of sound public-health practice and emergency management.

The response to the emergence of pandemic influenza A (H1N1) 2009 was the result of a decade of pandemic planning, largely centred on the threat of an avian influenza A (H5N1) pandemic. However, H5N1 and H1N1 have markedly different characteristics. H5N1 infection in humans results in about 60% mortality among confirmed cases, yet it is only sporadically transmitted to humans and even less often between humans. When

thinking about a potential H5N1 pandemic, large numbers of fatalities could be assumed because the virus had proved itself to be highly lethal. Since H5N1 was not easily transmissible from human to human, suppression of an outbreak through the use of antiviral drugs and other measures could be thought feasible. WHO's web site has described the prospect of severe disease in a possible pandemic, which was understandable in the context of expectations about H5N1. But the reality of H1N1 was quite different. Because H1N1 caused illness that did not require hospitalization in the vast majority of cases, the question of severity of the pandemic and how to characterize it became a key challenge. As the H1N1 virus spread to several countries within days, the possibility of rapid containment, a tenet of planning in WHO's multi-stage response, was never really feasible.

Another reality that shaped the response to the pandemic is the nature of WHO itself. WHO has a dual character and mission: as a moral voice for global health, and as a servant of its Member States. As the directing and coordinating authority on international health within the United Nations system, WHO is well-positioned to be a champion for health as a human right. Its policy and technical leadership can help countries cope with an array of public-health concerns. At the same time, WHO is a servant of its 193 Member States, which meet every year at the World Health Assembly in Geneva to set policy for the Organization, approve the Organization's budget and plans and, through the Assembly's Executive Board, elect the Director-General every five years. WHO's scientific and technical aspirations for global health are constantly conditioned by the multiplicity of views, needs and preferences of its Member States.

WHO's internal response capacities to health emergencies are geared towards relatively short-term, geographically focal events, a type that WHO confronts many times each year. By contrast, the pandemic required a worldwide response lasting one to two years. Before the pandemic, Severe Acute Respiratory Syndrome (SARS) was the only global emergency in recent decades that provided WHO with a foretaste of the demands that a pandemic might entail. However, SARS lasted but a few months and affected only about two dozen countries.

Conclusions and recommendations

The Review Committee offers three overarching conclusions to underpin the recommendations that follow its investigation of the functioning of the International Health Regulations (2005) and on pandemic influenza A (H1N1) 2009.

Summary conclusion 1

The IHR helped make the world better prepared to cope with public-health emergencies. The core national and local capacities called for in the IHR are not yet fully operational and are not now on a path to timely implementation worldwide.

Summary conclusion 2

WHO performed well in many ways during the pandemic, confronted systemic difficulties and demonstrated some shortcomings. The Committee found no evidence of malfeasance.

Summary conclusion 3

The world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public-health emergency. Beyond implementation of core public-health capacities called for in the IHR, global preparedness can be advanced

through research, reliance on a multisectoral approach, strengthened health-care delivery systems, economic development in low- and middle-income countries and improved health status.

The remainder of this section summarizes the Committee's findings and reasoning and the recommendations that follow each conclusion.

Summary conclusion 1

The IHR helped make the world better prepared to cope with public-health emergencies. The core national and local capacities called for in the IHR are not yet fully operational and are not now on a path to timely implementation worldwide.

Development of the IHR required more than a decade of complex deliberations. While the IHR are not perfect, they significantly advance the protection of global health. The Committee has focused its recommendations on how ongoing implementation of the IHR can be strengthened. The IHR seek to balance the sovereignty of individual States Parties with the common good of the international community, and take account of economic and social interests as well as the protection of health. The Committee's recommendations acknowledge these inherent tensions and focus on actions that can enhance the shared goal of global public-health security.

The Committee commends the following provisions of the IHR:

- The IHR oblige WHO to obtain expert advice on the declaration and discontinuation of a Public Health Emergency of International Concern.
- The IHR strongly encourage countries to provide each other with technical cooperation and logistical support for capacity building.
- The IHR encourage establishment of systematic approaches to surveillance, early warning systems and response in Member States.
- The IHR required the establishment of National IHR Focal Points (NFPs) to create a clear two-way channel of communication between WHO and Member States.
- The IHR led a number of countries to strengthen surveillance, risk assessment, response capacity and reporting procedures for public-health risks.
- The IHR introduced a decision instrument (Annex 2) for public-health action that has proved more flexible and useful than the list of notifiable diseases it replaced.
- The IHR require countries to share information relevant to public-health risks.
- The IHR require States Parties that implement additional health measures significantly interfering with international traffic and trade to inform WHO about these measures, and to provide the public-health rationale and relevant scientific information for them.

Despite these positive features of the IHR, many States Parties lack core capacities to detect, assess and report potential health threats and are not on a path to complete their obligations for plans and infrastructure by the 2012 deadline specified in the IHR. Continuing on the current trajectory will not enable countries to develop these capacities and fully implement the IHR. Of the 194 States Parties, 128, or 66%, responded to a recent WHO questionnaire on their progress. Only 58% of the respondents reported having developed national plans to meet core capacity requirements, and as few as 10% of reporting countries indicated that they had fully established the capacities envisaged by the IHR. Further, as documented by external studies and a WHO questionnaire, in some

countries NFPs lack the authority to communicate information related to public-health emergencies to WHO in a timely manner.

The most important structural shortcoming of the IHR is the lack of enforceable sanctions. For example, if a country fails to explain why it has adopted more restrictive traffic and trade measures than those recommended by WHO, no legal consequences follow.

To remedy a number of these problems, the Committee recommends the following.

Recommendation 1

Accelerate implementation of core capacities required by the IHR. WHO and States Parties should refine and update their strategies for implementing the capacity-building requirements of the IHR, focusing first on those countries that will have difficulty meeting the 2012 deadline for core capacities. One possible way to support and accelerate implementation would be for WHO to mobilize appropriate agencies and organizations that would be willing to provide technical assistance to help interested countries assess their needs and make the business case for investment. Making the case for investment in IHR capacity building and subsequent resource mobilization would increase the likelihood that more States Parties could come into compliance with the IHR. Donor countries and organizations could take advantage of the IHR Annex 1A as a priority list for development support and also seize opportunities to share specialized resources, such as laboratories, across countries. WHO should also update the 2007 guidance on NFP functions, and include examples of good practice to reinforce the value of the IHR.

Recommendation 2

Enhance the WHO Event Information Site. WHO should enhance its Event Information Site (EIS) to make it an authoritative resource for disseminating reliable, up-to-date and readily accessible international epidemic information. States Parties should be able to rely on the EIS as a primary source for information on epidemiological status, risk assessment, response measures and their rationales. The EIS could also be used to post WHO guidance before it is made public. Additional ways to enhance the EIS include:

- Using EIS for guidance and messages to NFPs.
- States Parties allowing WHO to share more information.
- Including more events and expanding information on each event. For instance, for each event there could be maps, expanded risk assessments and recommendations, and links to relevant WHO guidance and Collaborating Centres.
- Posting all temporary and standing recommendations issued under the IHR as well as information on Member States that institute additional measures and their rationales for these, and the status of WHO's request for such a rationale.

Recommendation 3

Reinforce evidence-based decisions on international travel and trade. When States Parties implement health measures that significantly interfere with international traffic and are more stringent than those recommended by WHO, IHR Article 43 provides that the States Parties shall inform WHO of their actions. (As stated in Article 43, "significant interference generally means refusal of entry or departure of international travellers, baggage, cargo, containers, conveyances, goods and the like, or their delay, for more than

24 hours.") In such circumstances, WHO should energetically seek to obtain the public-health rationale and relevant scientific information, share it with other States Parties, and, where appropriate, request reconsideration, as stipulated under Article 43. WHO should review and assess the effectiveness and impact of border measures taken during the pandemic to support evidence-based guidance for future events.

Recommendation 4

Ensure necessary authority and resources for all National IHR Focal Points. States Parties should ensure that designated National IHR Focal Points have the authority, resources, procedures, knowledge and training to communicate with all levels of their governments and on behalf of their governments as necessary.

Summary conclusion 2

WHO performed well in many ways during the pandemic, confronted systemic difficulties and demonstrated some shortcomings. The Committee found no evidence of malfeasance.

As noted in testimony by States Parties, WHO provided welcome leadership in coordinating the global response throughout the pandemic. WHO's epidemic intelligence functions have strengthened in recent years as a result of the Event Management System, increases in Regional Office capacity, and the Global Outbreak Alert and Response Network.

The Committee commends the following actions by WHO and other partners:

- Development of influenza preparedness and response guidance to help inform national plans. Pandemic preparedness plans were in place in 74% of countries when the pandemic began.
- Effective partnering and interagency coordination (with the United Nations Children's Fund and the United Nations Office for Project Services), including close cooperation with the animal health sector (the World Organisation for Animal Health, and the Food and Agriculture Organization of the United Nations) on technical and policy issues.
- Rapid field deployment and early guidance and assistance to affected countries.
- Timely detection, identification, initial characterization and monitoring of the pandemic (H1N1) 2009 virus through the Global Influenza Surveillance Network.
- Selection of the pandemic vaccine virus and development of the first candidate reassortant vaccine viruses within 32 days of declaration of the Public Health Emergency of International Concern.
- Vaccine seed strains and control reagents made available within a few weeks.
- Early policy recommendations on target groups and dosage of vaccines by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization.
- Weekly collation, analysis and reporting of global epidemiological, virological and clinical surveillance data.
- Prompt appointment of an Emergency Committee with well-qualified individuals, which was convened within 48 hours of activation of IHR provisions.
- Efficient distribution of more than 3 million treatment courses of antiviral drugs to 72 countries.
- Establishment of a mechanism to help countries monitor their development of IHR core capacities.

The Committee also noted systemic difficulties that confronted WHO and some shortcomings on the part of WHO:

- The absence of a consistent, measurable and understandable depiction of severity of the pandemic. Even if the definition of a pandemic depends exclusively on spread, its degree of severity affects policy choices, personal decisions and the public interest. What is needed is a proper assessment of severity at national and subnational levels. These data would inform WHO's analysis of the global situation as it evolves, allowing WHO to provide timely information to Member States. The Committee does, however, recognize that characterization of severity is complex and difficult to operationalize.
- Inadequately dispelling confusion about the definition of a pandemic. One online WHO document described pandemics as causing "enormous numbers of deaths and illness", while the official definition of a pandemic was based only on the degree of spread. When, without notice or explanation, WHO altered some of its online documents to be more consistent with its intended definition of a pandemic, the Organization invited suspicion of a surreptitious shift in definition rather than an effort to make its descriptions of a pandemic more precise and consistent. Reluctance to acknowledge its part in allowing misunderstanding of the intended definition fuelled suspicion of the Organization.
- A pandemic phase structure that was needlessly complex. The multiphase structure contains more stages than differentiated responses. Defined phases leading to a pandemic are more useful for planning purposes than for operational management.
- Weekly requests for specific data were overwhelming to some countries, particularly those with limited epidemiological and laboratory capacity. Country officials were not always convinced the data they submitted were being analysed and used, particularly as the epidemic progressed. For example, some felt that continued counting of cases yielded less useful information than would have been provided by rates of hospitalization, complications and death in countries affected early on in the pandemic.
- The decision to keep confidential the identities of Emergency Committee members. Although confidentiality represented an understandable effort to protect the members from external pressures, this paradoxically fed suspicions that the Organization had something to hide. While the decision was consistent with WHO practices for other expert committees, whose identities are normally divulged only at the end of what is often a one-day consultation, this practice was not well suited to a Committee whose service would extend over many months.
- Lack of a sufficiently robust, systematic and open set of procedures for disclosing, recognizing and managing conflicts of interest among expert advisers. In particular, potential conflicts of interest among Emergency Committee members were not managed in a timely fashion by WHO. Five members of the Emergency Committee and an Adviser to the Emergency Committee declared potential conflicts of interest. None of these was determined sufficiently important to merit the members' exclusion from the Emergency Committee. The relationships in question were published, along with the names of the members of the Emergency Committee, when the pandemic was declared over on 10 August 2010. Before this information was published, however, assumptions about potential ties between Emergency Committee members and industry led some to suspect wrongdoing. The Review Committee recognizes that WHO is taking steps to improve its management of conflicts of interest, even as this review has proceeded.
- At a critical point of decision-making about the pandemic (moving from Phase 4 to 5), conferring with only a subset of the Emergency Committee rather than inviting input from the full Emergency Committee.

- The decision to diminish proactive communication with the media after declaring Phase 6 (for example, by discontinuing routine press conferences focused on the evolving pandemic) was ill-advised.
- Failure to acknowledge legitimate reasons for some criticism, in particular, inconsistent descriptions of a pandemic, or the lack of timely disclosure of relationships potentially constituting a conflict of interest among experts who advised on plans and response to the pandemic. In such instances, WHO may have inadvertently contributed to confusion and suspicion.
- Responding with insufficient vigour to criticisms that questioned the integrity of the Organization.
- Despite the ultimate deployment of 78 million doses of pandemic influenza vaccine to 77 countries, numerous systemic difficulties impeded the timely distribution of donated vaccines. Among the key difficulties was a variation in willingness to donate, concerns about liability, complex negotiations over legal agreements, lack of procedures to bypass national regulatory requirements and limited national and local capacities to transport, store and administer vaccines. Some recipient countries felt WHO did not adequately explain that liability provisions included in the recipient agreement were the same as the liability provisions accepted by purchasing countries. All these difficulties proved daunting in the midst of a pandemic; some could have been reduced by more concerted preparation and advance arrangements among all interested parties.
- Lack of timely guidance in all official languages of WHO.
- Lack of a cohesive, overarching set of procedures and priorities for publishing consistent and timely technical guidance resulted in a multiplicity of technical units within the Organization individually generating an unmanageable number of documents.

Critics assert that WHO vastly overstated the seriousness of the pandemic. However, reasonable criticism can be based only on what was known at the time and not on what was later learnt. The Committee found that evidence from early outbreaks led many experts at WHO and elsewhere to anticipate a potentially more severe pandemic than subsequently occurred. The degree of severity of the pandemic was very uncertain throughout the middle months of 2009, well past the time, for example, when countries would have needed to place orders for vaccine. An observational study of 899 patients hospitalized in Mexico between late March and 1 June 2009 showed that pandemic (H1N1) 2009 disproportionately affected young people. Fifty-eight patients (6.5% of those hospitalized) became critically ill, with complications including severe acute respiratory distress syndrome and shock. Among those who became critically ill, the mortality rate was 41% (*1*). These statistics were alarming. Even a reported mortality rate of one third that level among critically ill patients in Canada was worrisome (*2*). In August 2009, the President's Council of Advisors on Science and Technology in the United States of America released a report positing a possible scenario of 30 000–90 000 deaths from pandemic (H1N1) 2009 in the USA alone (*3*). The mid-point and upper level of this scenario turned out to be five times higher than the post-pandemic estimates of the actual number of deaths (*4*). Even so, 87% of deaths occurred in those under age 65, with the risk of death among children and working adults seven times and 12 times greater, respectively, than during typical seasonal influenza (*4*).

Some commentators accused WHO of rushing to announce Phase 6 and suggested the reason was to enrich vaccine manufacturers, some of whose advance-purchase agreements would be triggered by the declaration of Phase 6. Far from accelerating the declaration of Phase 6, WHO delayed declaration until evidence of sustained community spread in

multiple regions of the world was undeniably occurring. As far as the Review Committee can determine, no critic of WHO has produced any direct evidence of commercial influence on decision-making. In its interviews with staff and advisory committee members, including the Strategic Advisory Group of Experts (SAGE) on Immunization and the Emergency Committee, and with representatives of industry, and through its review of internal and external documents, the Review Committee found no evidence of attempted or actual influence by commercial interests on advice given to or decisions made by WHO. In the Committee's view, the inference by some critics that invisible commercial influences must account for WHO's actions ignores the power of the core public-health ethos to prevent disease and save lives.

The Review Committee offers the following recommendations.

Recommendation 5

Strengthen WHO's internal capacity for sustained response. WHO should strengthen its internal capacity to respond to a sustained Public Health Emergency of International Concern, such as a pandemic, identifying the skills, resources and internal arrangements to support a response that extends beyond a few months. Among the internal arrangements that WHO should reinforce are:

- Identify the skills, resources and adjustments needed for WHO to carry out its role in coordination and global support.
- Establish an internal, trained, multidisciplinary staff group who will be automatically released from their normal duties for an unspecified duration, with a relief rotation after a designated interval.
- Ensure a 24/7 capacity to meet the personal needs for accommodation, meals, transportation and childcare of WHO staff enlisted in a sustained emergency response.
- Establish an event management structure that could be maintained throughout a future pandemic or other sustained global public-health emergency.

Recommendation 6

Improve practices for appointment of an Emergency Committee. WHO should adopt policies, standards and procedures for the appointment and management of an Emergency Committee that assure an appropriate spectrum of expertise on the committee, inclusive consultation and transparency with respect to freedom from conflicts of interest.

- As provided in Article 48 of the IHR, WHO should appoint an Emergency Committee with the spectrum of expertise and geographical representation appropriate for each event. The Review Committee also concluded that a broader spectrum of expertise among Emergency Committee members might have been useful, including in risk communication. The Review Committee acknowledged that WHO must appoint an Emergency Committee with a set of skills and expertise that is appropriate for and particular to each event for which it is constituted. For an influenza pandemic, this expertise would include virology, laboratory assessment, epidemiology, public-health field and leadership experience, veterinary science, risk assessment and risk communication, and methodological expertise in systematic reviews of the scientific literature.
- To ensure that the full range of views is presented, WHO should invite all members of an Emergency Committee to participate in all of its major deliberations.

- WHO should clarify its standards and adopt more transparent procedures for the appointment of members of expert committees, such as an Emergency Committee, with respect to potential conflicts of interest. The identity and relevant background, experience and relationships of Emergency Committee members should be publicly disclosed at the time of their proposed appointment, with an opportunity for public comment during a period of initial, probationary service that would apply to all members. WHO should have clear standards for determining when a conflict of interest exists that warrants disqualifying an individual, and have clear procedures to determine when and on what basis exceptions may be made to obtain necessary expertise or balance. The Review Committee appreciates the need for expert consultations to be held in confidence so that the Director-General will have the benefit of candid discussion and advice. The desirability of confidential consultation heightens the burden of transparency on standards for appointment.
- As part of a more proactive and rigorous approach to managing conflicts of interest, WHO should appoint a designated ethics officer.

Recommendation 7

Revise pandemic preparedness guidance. WHO should revise its pandemic preparedness guidance in order to: simplify the phase structure (one possible paradigm would include only three phases – baseline, alert phase, pandemic); emphasize a risk-based approach to enable a more flexible response to different scenarios; rely on multisectoral participation; draw upon lessons learnt at a country, regional and global level; and include further guidance on risk assessment.

Recommendation 8

Develop and apply measures to assess severity. WHO should develop and apply measures that can be used to assess the severity of every influenza epidemic. By applying, evaluating and refining tools to measure severity every year, WHO and Member States can be better prepared to assess severity in the next pandemic. Assessing severity does not require altering the definition of a pandemic to depend on anything other than the degree of spread. Rather, while not part of the definition of a pandemic, measured and projected severity are key components of decision-making in the face of a pandemic.

The Committee recognizes that estimating severity is especially difficult in the early phase of an outbreak, that severity typically varies by place and over time, and that severity has multiple dimensions (deaths, hospitalizations and illness, with each varying by age and other attributes, such as pre-existing health conditions and access to care; burden on a health system; and social and economic factors). Descriptive terms used to characterize severity, such as mild, moderate and severe, should be quantitatively defined in future WHO guidelines so that they may be used consistently by different observers and in different settings. The Committee urges consideration of adaptive measures that would move as rapidly as possible from early counts of cases, hospitalizations and deaths to population-based rates. Severity should be assessed as early as possible during a pandemic and continually re-assessed as the pandemic evolves and new information becomes available. Severity might be assessed using a "basket of indicators" in a pre-agreed minimum data set (e.g. hospitalization rates, mortality data, identification of vulnerable populations and an assessment of the impact on health systems). Estimates of severity should be accompanied by expressions of confidence or uncertainty around the estimates.

Recommendation 9

Streamline management of guidance documents. WHO needs a strategy and document-management system to cope with the development, clearance, translation and dissemination of guidance and other technical documents in a timely and consistent way during a public-health emergency. Interim guidance should be revised as data become available. When feasible, if the guidelines have potential policy implications, WHO should make every effort to consult with Member States and provide them with advance notice of impending publications. WHO should develop the capacity to assure consistency of guidelines across the Organization, recognizing that conditions in different regions and individual countries may vary.

Recommendation 10

Develop and implement a strategic, organization-wide communications policy. WHO should develop an organization-wide communications policy and a strategic approach to improve routine and emergency communications. A strategic approach entails matching the content, form and style of communication with the media, timing and frequency that will reach the intended audience and serve the intended purpose. WHO should be prepared to sustain active, long-term communications outreach when circumstances require, to acknowledge mistakes and to respond professionally and vigorously to unwarranted criticisms. Web publishing procedures should be clarified so that changes in web pages can be historically tracked and archived. WHO should invest in a robust social media presence for rapid communication to a wider, more diverse audience.

Recommendation 11

Encourage advance agreements for vaccine distribution and delivery. In concert with efforts by Member States, and building on existing vaccine distribution systems, WHO should encourage advance agreements with and among appropriate agencies and authorities in Member States, vaccine manufacturers and other relevant parties that would facilitate approval and delivery of pandemic vaccines to low-resource countries, to increase equity in supply and support advance planning for administration of vaccines.

Summary conclusion 3

The world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public-health emergency. Beyond implementation of core public-health capacities called for in the IHR, global preparedness can be advanced through research, reliance on a multisectoral approach, strengthened health-care delivery systems, economic development in low- and middle-income countries and improved health status.

Despite the progress that the IHR represent and WHO's success in mobilizing contributions from the global community, the unavoidable reality is that tens of millions of people would be at risk of dying in a severe pandemic. The fundamental gap between global need and global capacity must be closed.

Beyond the specific measures recommended above to complete implementation of the IHR provisions and improve the functions of WHO, the world can be better prepared for the next public-health emergency through advance commitment by Member States acting individually and collectively with WHO.

The Review Committee offers the following recommendations.

Recommendation 12

Establish a more extensive global, public-health reserve workforce. Member States, in concert with WHO, should establish a more extensive global reserve workforce of experts and public-health professionals to be mobilized as part of a sustained response to a global health emergency and deployed for service in countries that request such assistance. The size, composition and governing rules for activating and deploying such an entity – the Global Health Emergency Workforce – should be developed through consultation and mutual agreement among the Member States and WHO. The number and particular skills of the experts deployed will depend on specific characteristics of the emergency to which the workforce is responding. This workforce would significantly expand the current Global Outbreak and Alert Response Network by strengthening its composition, resources and capacity, with a view towards better support for sustained responses to public-health emergencies.

At present, WHO's capacity to prepare and respond in a sustained way to any public-health emergency is severely limited by chronic funding shortfalls, compounded by restrictions on the use of funds from Member States, partners and other donors. Mindful of concerns about efficiency and accountability that motivate some of the restrictions, the Committee concludes that the establishment of a contingency fund outside of WHO, but available for deployment by WHO at the time of a public-health emergency, will be a prudent step to assure an immediate and effective global response.

Recommendation 13

Create a contingency fund for public-health emergencies. Member States should establish a public-health emergency fund of at least US$ 100 million, to be held in trust in a location and form that would be readily accessible to WHO. The fund, which would support surge capacity, not the purchase of materials, would be released in part or whole during a declared Public Health Emergency of International Concern, based on approval of a plan for expenditures and accountability submitted by WHO. The precise conditions for use of the fund should be negotiated among the Member States in consultation with WHO.

The Review Committee commends the effort by Member States to reach agreement on sharing of viruses and access to vaccines and other benefits. The Review Committee believes that success will depend on a mutual expectation of proportionate, balanced benefit and contribution by all stakeholders. An agreement that is one-sided or that expects contribution without benefit, or vice versa, will be neither acceptable nor sustainable. The Review Committee also believes that obligations and benefits not linked to a legal framework are unlikely to last.

Recommendation 14

Reach agreement on sharing of viruses and access to vaccines and other benefits. The Review Committee urges Member States and WHO to conclude negotiations under the Open-ended Working Group of Member States on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and Other Benefits. A successful conclusion to this negotiation will lead to wider availability of vaccines and other benefits and greater equity in the face of the next pandemic, as well as continued timely sharing of influenza viruses.

The Review Committee offers the following elements for consideration as part of an acceptable agreement.

Measures to expand global influenza vaccine production capacity:

- WHO should continue its practice of working with public-health laboratories to make seed vaccine virus strains widely available to all vaccine manufacturers.
- In so far as it is consistent with national priorities, risk assessments and resources, the Review Committee urges countries to immunize their high-risk populations yearly against seasonal influenza. This can reduce the burden of disease. In addition, this can increase experience with local production, distribution and delivery and encourage more global capacity for vaccine production. More generally, experience with comprehensive programmes during seasonal influenza (in such areas as surveillance, communication, professional and public education, health protection measures and pharmaceuticals) provides valuable preparation in advance of a major pandemic.
- The Committee urges countries to strengthen their capacity to receive, store, distribute and administer vaccines. Technological advances that reduce reliance on a cold chain and otherwise simplify administration will streamline these processes.
- The Committee urges Member States, international organizations and industry to aid the transfer of technologies for vaccine and adjuvant production in parts of the world currently lacking this capacity, such as Africa, through established programmes such as the Global Action Plan to Increase Supply of Pandemic Influenza Vaccines (GAP).

Measures to increase access, affordability and deployment of pandemic vaccine:

- All vaccine manufacturers should commit to a contribution of 10% of pandemic influenza vaccine from each production run to a global redistribution pool. WHO should be responsible for managing allocations from this pool based on advice from a consultative committee.
- Increased access to vaccines and antiviral drugs can be achieved through advance agreements between industry, WHO and countries. These agreements should be negotiated without regard to virus subtype, for a specified period of time (e.g. three to five years) and should be regularly reviewed and renewed.
- Other measures that may promote greater and more equitable access to vaccine include differential pricing, direct economic aid to low-resource countries and additional donations of vaccine from purchasing countries or manufacturers.
- Countries that receive donated vaccine, as any purchaser of the vaccine, should adhere to the same practices of releasing and indemnifying manufacturers from certain legal liabilities.

Measures to detect and promptly identify potential pandemic influenza viruses:

- Every Member State should commit to share promptly, according to the principles of sharing of influenza viruses and access to vaccines and other benefits, any biological specimens and viral isolates that may be related to a new or emerging influenza virus in humans with WHO collaborating laboratories. Viruses isolated from animals should be promptly sent through the appropriate animal health system. The sharing of specimens and viral isolates should be accompanied by arrangements to share benefits, including access to vaccines.

The world's capacity to prevent and limit a severe pandemic is constrained by many factors: predominant reliance on vaccine production technology that is little changed in 60 years; the need to match vaccine to particular viral strains; the inability to predict which influenza viruses will be dangerous to human health; uncertainty about the effectiveness of many pharmaceutical and public-health measures; the lack of field-based, rapid, affordable, highly sensitive and specific diagnostic tests; and limitations of infrastructure, resources and capacities in many countries. Also needed are improved knowledge of and practical strategies for implementing public-health and personal protective measures, such as handwashing, respiratory etiquette, isolation and social distancing.

Some of these limitations can be reduced over time through national and international research. Further, the results of research on personal and public-health protective measures may apply to any emerging public-health threat, especially when few or no drugs or vaccines exist. Because assessment of public-health measures typically must occur in real time in the midst of an outbreak, it is crucial to design and prepare research protocols and plans in advance. Beyond research advances, global resilience depends on host and environmental factors, so that improving health status, promoting economic development and strengthening health systems can mitigate the impact of a future pandemic virus.

Recommendation 15

Pursue a comprehensive influenza research and evaluation programme. Member States, individually and in cooperation with one another, and WHO should pursue a comprehensive influenza research and evaluation programme. This should build on a thorough review of the evidence gained in all fields from the 2009 H1N1 pandemic. Key research goals include: strengthen surveillance technology and epidemiological and laboratory capacity to improve detection, characterization and monitoring of new viruses; identify viral and host determinants of transmissibility and virulence; develop rapid, accurate, inexpensive point-of-care diagnostic tests; enhance the accuracy and timeliness of modelling projections; create broader spectrum, highly effective, safe and longer-lasting vaccines; hasten vaccine production and increase throughput; devise more effective antiviral drugs and antimicrobials to treat bacterial complications; evaluate the effectiveness of drug, vaccine, personal protective equipment, personal hygiene and social interventions; assess the effectiveness and costs of border measures and enhance risk communication. Much of this research and evaluation can and should be carried out in the absence of a pandemic. However, some studies can only be carried out during a global event such as a pandemic. For these it is essential that protocols be prepared and funding identified in advance so that research can begin without delay.

The Review Committee respectfully commends these 15 recommendations to the World Health Organization, the World Health Assembly and its Member States, and the larger global community. Table 4.1 arrays the recommendations according to the lead responsibility (WHO or Member States) and time horizon for completion (within one year, within two years, beyond two years). The Committee believes all 15 recommendations deserve to be implemented without delay.

Despite everything that was done in the pandemic, the major determinant of the consequences was the virus that caused it. In the face of a virulent influenza pandemic, or any similarly global, sustained and threatening public-health emergency, the world remains

at risk of massive disruption, suffering and loss of life. The Committee hopes that these recommendations will help WHO and its Member States be better prepared to avert, mitigate and cope with future threats to health.

Table 4.1. **Lead responsibility and timeframe to complete implementation of recommendations**

	Short Term (within 1 year)	Medium Term (within 2 years)	Long Term (beyond 2 years)
WHO Led	**Enhance the WHO Event Information Site** (Recommendation 2) **Strengthen WHO's internal capacity for sustained response** (Recommendation 5) **Improve practices for appointment of an Emergency Committee** (Recommendation 6) **Streamline management of guidance documents** (Recommendation 9) **Develop and implement a strategic, organization-wide communications policy** (Recommendation 10)	**Revise pandemic preparedness guidance** (Recommendation 7) **Develop and apply measures to assess severity** (Recommendation 8)	**Reinforce evidence-based decisions on international travel and trade** (Recommendation 3)
Country Led	**Reach agreement on the sharing of viruses and access to vaccines and other benefits** (Recommendation 14)	**Ensure necessary authority and resources for all National IHR Focal Points** (Recommendation 4)	**Accelerate implementation of core capacities required by the IHR** (Recommendation 1)
Jointly Led		**Encourage advance agreements for vaccine distribution and delivery** (Recommendation 11) **Establish a more extensive global, public-health reserve workforce** (Recommendation 12) **Create a contingency fund for public-health emergencies** (Recommendation 13)	**Pursue a comprehensive influenza research and evaluation programme** (Recommendation 15)

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I

Preparation for a global public-health emergency

I

Preparation for a global public-health emergency

Abstract

This chapter provides background for the Review Committee's assessments of the functioning of the International Health Regulations (2005) and the global response to pandemic influenza A (H1N1) 2009.

It begins with an explanation of the fundamental principles, or ethos, of public health, followed by an examination of selected seminal infectious disease threats, including previous pandemics. The ethos of public health, coupled with the experience gained and lessons identified from managing complex health emergencies, informed the International Health Regulations (IHR) and shaped the World Health Organization's global pandemic influenza preparedness and response plan. The development and subsequent revision of these two foundational documents are chronicled. The chapter reviews the influenza preparedness and response plan for events and surveillance, the systematic assessment and management of potential threats to global health and the role of multidisciplinary international response teams in assisting countries to investigate and control public health emergencies. Appendix III contains a brief description of some of the essential functions of the IHR.

A. The ethos of public health

WHO has a dual character and mission: as a moral voice for global health and as a servant of its Member States. As the directing and coordinating authority on international health within the United Nations system, WHO is well-positioned to be a champion for health as a human right. Its technical leadership can help countries cope with an array of public-health concerns. At the same time, WHO's aspirations for global health are constantly conditioned by the multiplicity of views, needs and preferences of its Member States.

Public health deals with the health of populations. Its central aim is to keep people healthy, to prevent disease and avert death. Approaches to prevention can take various forms, including medical interventions, such as vaccines, behavioural modification, engineering controls to prevent unhealthy exposures, and political, legal and policy initiatives.

Sound decisions to protect health and prevent disease depend on scientific understanding of the nature and causes of illness and on the proper accumulation and interpretation of evidence about the origins of disease and the manifold ways to prevent, mitigate and respond to its occurrence. Some concerns of public health, such as unhealthy lifestyles, may unfold over the course of decades. Others, including emergency events that abruptly threaten the health of a population, may demand rapid, complex and coordinated response in many settings simultaneously. Because of the possibility of suddenly occurring, intense

and complex threats to health, advance planning for emergencies is a fundamental part of public-health preparedness.

In practice, however, decision-making in a public-health emergency is often based on incomplete information, with uncertainty about the threat and the likely effectiveness of response measures. Plans typically must be adapted to the actual circumstances of the event. There may be competing demands within the health system and other sectors, and constraints imposed by limited resources. In a public-health emergency, decision-makers often face political scrutiny and pressure from the public and media. The ability to take informed action, despite the uncertainty dictated by the speed of events, is the essence of crisis management.

B. The continued threat of infectious diseases

The decade-long process that resulted in the 2005 revision of the IHR was prompted by a renewed appreciation of the threat of infectious diseases. Previously unknown diseases surfaced with increasing frequency; established diseases gained new footholds through global spread and by acquiring resistance to antimicrobial drugs. The terms "emerging" and "re-emerging" infections were coined to describe newly recognized, clinically distinct infectious diseases and known infectious diseases with increasing incidence in a given place or population (*1*).

The experience gained in combating outbreaks of emerging pathogens reinforced the importance of early disease detection, verification, risk assessment, prevention, mitigation and control during a global public-health emergency. One notable example was the 1995 outbreak of the highly lethal Ebola virus, a type of viral haemorrhagic fever. Cases seemed to explode out of nowhere in the Democratic Republic of the Congo (formerly Zaire). In fact, unrecognized human-to-human transmission had been occurring for weeks (*2*). The virus, presumably zoonotic in origin, was spread through direct contact with blood and other infectious bodily fluids and tissues; hospital-acquired infection was a prominent feature of the outbreak (*2*). Experts from several countries and organizations provided on-site assistance to help control the outbreak of nearly 300 cases. In its aftermath, WHO launched several initiatives to improve preparedness and response for a global emergency: a plan to scan electronic media and detect early hints or rumours of disease outbreaks was developed; an electronic communications network with WHO's 141 Country Offices was established; a virtual international rapid investigation and response network was formed; and electronically linked networks of laboratories and technical experts were developed *(3)*.

The emergence of two new human infections – avian influenza A (H5N1) and Severe Acute Respiratory Syndrome (SARS) – had profound effects on the international health community. The response to these global public-health events helped accelerate efforts to revise the IHR and to plan for a future pandemic.

The first human outbreak of avian influenza A (H5N1) was detected in 1997 in Hong Kong Special Administrative Region. Intensive investigation identified 18 cases, six of which were fatal (*4*). This was the first recognized instance in which a highly pathogenic avian influenza virus had been directly transmitted to humans and resulted in serious illness. Poultry were culled in markets in Hong Kong Special Administrative Region and on farms to contain further spread of the virus (*5*). Although seemingly quiescent for a time, by 2000 several different reassortant viruses had emerged in poultry (*5,6*). H5N1 subsequently spread among millions of wild and domestic birds from late 2003 onwards, aided in part by migratory

waterfowl (*5–7*). Although the virus proved difficult to transmit to humans, case fatality was high. As of February 2011, about 500 laboratory-confirmed human cases had been reported to WHO from 15 countries; about 60% of reported cases were fatal.

The spread of H5N1, the severity of infection in humans, the unprecedented economic and agricultural consequences of culling enormous numbers of birds and the sense that an influenza pandemic might be imminent, injected a sense of urgency into pandemic preparedness planning at local, national and global levels. It also reinforced the importance of collaboration between public-health and animal-health sectors, particularly in relation to surveillance, risk assessment, response and reporting.

The emergence of another respiratory virus, SARS-associated coronavirus, gave the global health community a preview of the demands that a pandemic or other worldwide public-health emergency would make. The first cases of SARS appeared in November 2002 in Guangdong Province, China. Over the next three months, as the number of cases and outbreaks mounted, unconfirmed reports circulated in electronic forums, such as the Global Public Health Intelligence Network and ProMED, about an unusual epidemic of respiratory disease (*8*). The situation changed abruptly when a physician who had treated ill patients travelled to Hong Kong Special Administrative Region in February 2003. Soon after arriving at a hotel, he became severely ill, was admitted to hospital and died (*9*). The doctor is believed to have infected at least 12 other hotel guests, who, in turn, transmitted the virus to others in Hong Kong Special Administrative Region and in Hanoi, Ireland, Singapore, Toronto and the United States of America, initiating chains of transmission (except in Ireland). WHO estimated that most of the world's cases of SARS originated with this one person (*10*).

WHO mobilized the Global Outbreak and Alert Response Network (GOARN) teams, issued a series of global alerts, set up a global surveillance and reporting scheme, and established epidemiological, laboratory and clinical virtual networks of experts for information sharing (*3*). The virus appeared to be transmitted person-to-person, most likely through respiratory secretions. Not surprisingly, air transportation facilitated transmission (*11*). Similar to the Ebola virus outbreak of 1995, health-care facilities often served as an unwitting locus of transmission, both among patients and health-care workers (*9*, *12–14*). Within weeks, a novel coronavirus was identified and by mid-April WHO announced that this was the definitive cause of SARS.

In the absence of medicines, control of the global epidemic fell to more traditional public-health measures, including hand and respiratory hygiene, strict adherence to infection-control measures for hospitalized patients, isolation of ill persons and quarantine of close contacts (*15*). In addition, many countries instituted exit and entry screening for international travellers. WHO declared an end to the global outbreak on 5 July 2003, but not before 8098 cases and 774 deaths were reported from 26 countries.

A review of the global response to SARS identified several lessons to be learnt, including the importance of having the capacity for early detection and for transparent reporting of unusual disease events; the difficulty of effectively communicating information to a diverse audience of policy-makers, politicians, clinicians, public-health professionals and the public about an evolving and poorly understood infection risk; the benefits of early and frequent information sharing at the global level, such as through the virtual networks of researchers established by WHO; an increased appreciation of the role that traditional measures, such as isolation and quarantine, can play in containing disease spread in ways that balance individual rights with the public good and the challenge of increasing institutional and individual capacity to sustain a response over a prolonged period of time (*10*).

The SARS outbreak and the continued spread of avian influenza (H5N1) virus reinforced the importance of zoonoses as a source of infection for humans. Human infection with zoonotic viruses can occur following contact with infected animals, animal products or contaminated environments, i.e. the "human–animal interface". Avian influenza H5N1, H7N7 and H9N2 and swine influenza H1N1 and H3N2 have resulted in sporadic human infections, including some deaths. None of these animal viruses has spread easily among humans. By contrast, the pandemic (H1N1) 2009 virus spread efficiently, resulting in sustained human-to-human transmission.

The potential pandemic risk associated with avian influenza H5N1 was the impetus behind much of the pandemic planning that occurred over the past 10 years. Public-health threats associated with H5N1 reinforced the important role of national veterinary services in planning and responding to a pandemic and spurred closer collaborations between animal-health and public-health authorities at national, regional and global levels. The international agencies responsible for animal health, the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO), together with WHO have worked to improve national capacities in surveillance of animal populations and at the human-animal interface, outbreak investigation, risk assessment and diagnostic testing. In July 2006, the Global Early Warning System for Major Animal Diseases, including Zoonoses (GLEWS) was launched by FAO, OIE and WHO. GLEWS is the first joint early-warning system for tracking animal diseases, including animal influenza. The OIE-FAO Network of Experts on Animal Influenza works in close collaboration with WHO to resolve influenza-specific issues at the human-animal interface, including contributing animal-sector information to inform the WHO vaccine strain selection process for pandemic virus candidates such as H5N1 and H9N2.

C. The International Health Regulations (2005): defending against the international spread of disease in the 21st century

> "The global community has a new legal framework to better manage its collective defenses to detect disease events and to respond to public-health risks and emergencies that can have devastating impacts on human health and economies." (*16*)

These words describe the entry into force on 15 June 2007 of the IHR (2005), a global structure aimed at preventing and responding to the international spread of disease while avoiding unnecessary interference with traffic and trade.

The IHR have their roots in 19th century international sanitary conventions aimed at controlling infectious diseases, such as cholera, smallpox and plague. The World Health Assembly first adopted the International Sanitary Regulations in 1951 to help minimize the international spread of disease. The regulations were revised and renamed the International Health Regulations in 1969.

Over time, the shortcomings of the 1969 version of the IHR became increasingly apparent. Notable problems were the limited scope of diseases covered (i.e. cholera, plague and yellow fever); the dependence on official notifications to WHO by affected countries; the scarcity of mechanisms through which WHO and affected countries could collaborate when investigating outbreaks; and an inability for WHO to make disease-control recommendations part of a legal framework (*17*). The 1969 IHR were also increasingly out of step

with human rights considerations, the growth in international travel and trade, and the threats to global health security posed by emerging and re-emerging infectious diseases and other hazards.

Development of the International Health Regulations (2005): consultation and negotiation

In May 1995 the World Health Assembly adopted a resolution requesting the Director-General begin a major review of the 1969 IHR (*18*). The complexity of devising a comprehensive legal framework that could accommodate the differing needs, capacities and political sensitivities of the Member States was daunting. Development of, and consultation on, the regulations lasted several years and raised many controversies (Box 1.1).

After the SARS epidemic, an Intergovernmental Working Group open to all Member States was established in 2004 to move the process forward. By April 2005 two rounds of intensive formal negotiations had made significant progress, but fell short of agreement on all the issues. Agreement was finally reached at a meeting only days before the annual World Health Assembly in May of that year.

The IHR encompass the traditional focus of health protection, i.e. infectious and vector-borne diseases. However, the concept of disease was broadened to include chemical and radiological hazards, risks associated with deliberate and accidental human activities and situations in which the pathogen or source of harm is new, poorly defined or unknown.

Box 1.1. **Key issues debated during the IHR (2005) negotiations**

- Should the Regulations explicitly include chemical and radiological events and events involving deliberate and accidental release?
- How could the certainty of a list-based approach be reconciled with the flexibility of a risk-based approach for the detection, assessment and reporting of events of potential public-health significance?
- Should WHO use non-official sources of information?
- What mechanism would ensure that countries were not unfairly penalized for being transparent in reporting events to WHO?
- Should countries be permitted to implement health measures over and above those in the Regulations or as otherwise recommended by WHO in response to a public-health threat, and if so, what, if anything, might WHO be able do in response?
- Should WHO be empowered to deploy field teams to assess and respond to emerging threats, irrespective of whether the affected country requested such assistance?
- With what degree of ease or difficulty should countries be permitted to opt out of certain provisions of the Regulations?
- What timeframes should be set for review, strengthening and maintenance of core capacities?
- Would constitutional arrangements, especially for federal countries, make some of the provisions unworkable (in particular, the explicit obligations related to core capacities at the subnational level)?
- Should temporary recommendations issued by the Director-General be binding on Member States?
- How could universal application of the Regulations be ensured for all populations, regardless of their status as Member States?

The principal functions of the International Health Regulations

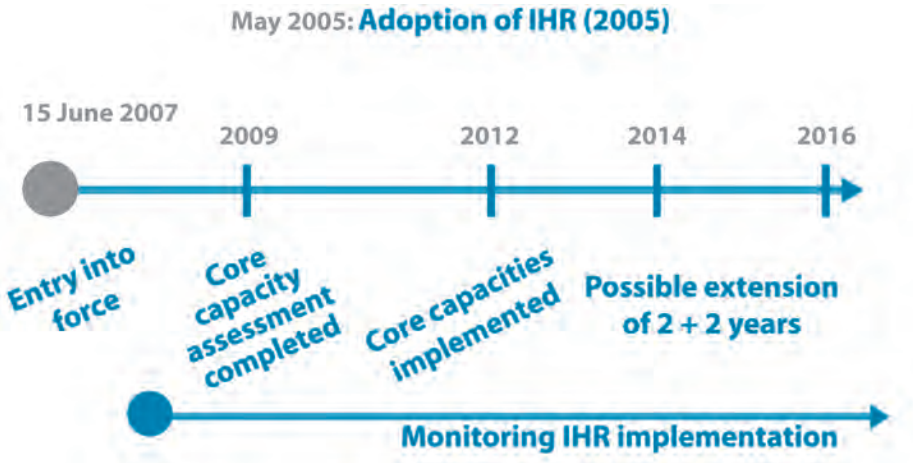
The IHR can be thought of as working at two levels. First, they establish a regime for routine public-health protection functions and provide for the ongoing management of disease threats, both in countries and at their borders. Second, they provide a framework for coordinated and proportionate responses to significant, urgent disease threats. Such threats may range from public-health events affecting one or more countries to events of global public-health significance.

After consideration of the IHR's 66 articles and nine annexes, the Review Committee identified eight principal functions upon which to base an assessment (Table 1.1). These functions represent some of the more innovative features of the IHR and are discussed briefly below and in Appendix III.

Table 1.1. **Main functions of the IHR (2005)**

IHR Articles and Annexes	Function	Description of Function
4, 5, 13, 44, Annex 1a	1. States Parties' core capacities in detection, assessment and response	Achievement of core capacities in detection, assessment and response at national and subnational levels; includes eight technical areas: – National legislation, policy and financing – Coordination and National IHR Focal Point (NFP) communications – Surveillance – Response – Preparedness – Risk communication – Human resources – Laboratory States Parties to collaborate with each other and with international organizations to ensure capacities
4–10, 44, Annex 2	2. States Parties' detection and alert operations	Detection and alert operations in place from local to national level, including NFP/WHO interactions. States Parties to collaborate in detection of events and provision of alerts about health risks
4, 5, 9–11, 14	3. WHO detection and alert operations	Procedures for surveillance, event detection, data management, risk assessment and information provision. WHO to collaborate with international organizations in event detection
13, 14, 44	4. International public-health response	Collaboration between WHO, States Parties and international organizations in event management, including: – Investigation and response (e.g. Global Outbreak and Response Network, GOARN) – Information sharing – Guidance – Logistics – Provision of technical expertise
12, 15–18, 47–49	5. Procedures for Public Health Emergencies of International Concern (PHEIC)	Provision of specific procedures for determination of a PHEIC, convening the Emergency Committee (EC), issuance of temporary recommendations and reporting of EC meetings and termination of PHEIC
14, 18–43, 46, Annexes 1b, 3–9	6. Points of entry and travel documents	WHO and States Parties' actions at points of entry to contain and reduce the spread of public-health risks, including: – Capacities and facilities at points of entry – Inspection and control regimens (e.g. ship sanitation certification, certification of vaccination, health declarations) – Establishment of capacities and facilities
42, 43	7. Avoidance of unnecessary interference with traffic and trade	Role of effective communications and follow-up with States Parties to avoid health measures that restrict traffic and trade; provision of procedures if such measures are implemented
3, 23, 31, 42, 43, 45	8. Implementation of the IHR with respect for human rights	Provision for informed consent, non-discriminatory application of health measures and confidentiality of personal data

Fig. 1.1. **Timeframes for national core capacity strengthening specified in IHR**



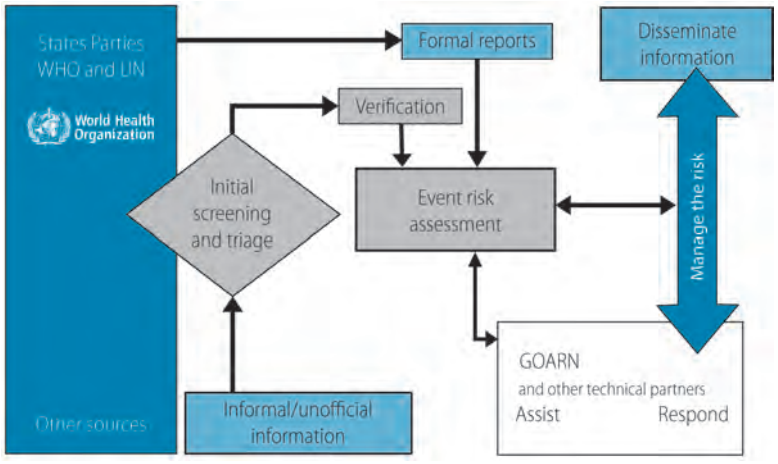
One of the foundational aspects of the IHR is the explicit obligation of States Parties to assess, strengthen and maintain "core capacities" for surveillance, risk assessment, reporting and response. These capacities need to be operational at local, intermediate and national levels, and at borders, including at designated international airports and ports. For many countries, developing such capacities will require time and resources, including technical and financial assistance from WHO. The IHR allowed for a five-year lead time before the capacities had to be operational, i.e. until June 2012, with the possibility of two, two-year extensions (Fig. 1.1) (*19*).

The notion of a single National IHR Focal Point (NFP) through which governmental–WHO IHR communications should flow is a key innovation of the IHR. An NFP is a national centre that is accessible at all times; it is an officially designated office, unit or department, rather than an individual. WHO requests verification from NFPs of events detected through its global surveillance activities. NFPs are required to respond to such requests in a timely manner, and, by applying a decision-flow diagram that is integral to the IHR (i.e. the Annex 2 Decision Instrument), to notify WHO of any event that may constitute a Public Health Emergency of International Concern (PHEIC).

The IHR set out a global leadership role for WHO that includes surveillance, risk assessment and response. WHO had implemented surveillance for a wide range of both infectious and non-infectious events in 1997. Hundreds of official and unofficial information sources are routinely monitored and cross-referenced. WHO's processes for detection, verification and rapid assessment of potential international threats to public health have evolved over time (Fig. 1.2) and accommodate the provisions of the IHR (*20*).

To support the increased volume of information that results from the IHR, WHO has developed two state-of-the-art web-based tools. The first is the Event Management Site (EMS). Information about an event is entered into the EMS and can be accessed as needed to support decision-making and risk-management activities. The EMS is used by all Regional Offices, several Country Offices and departments at WHO's headquarters; roll-out to Country Offices is continuing.

Fig 1.2. **Event management flow chart – threat detection, verification and risk assessment**

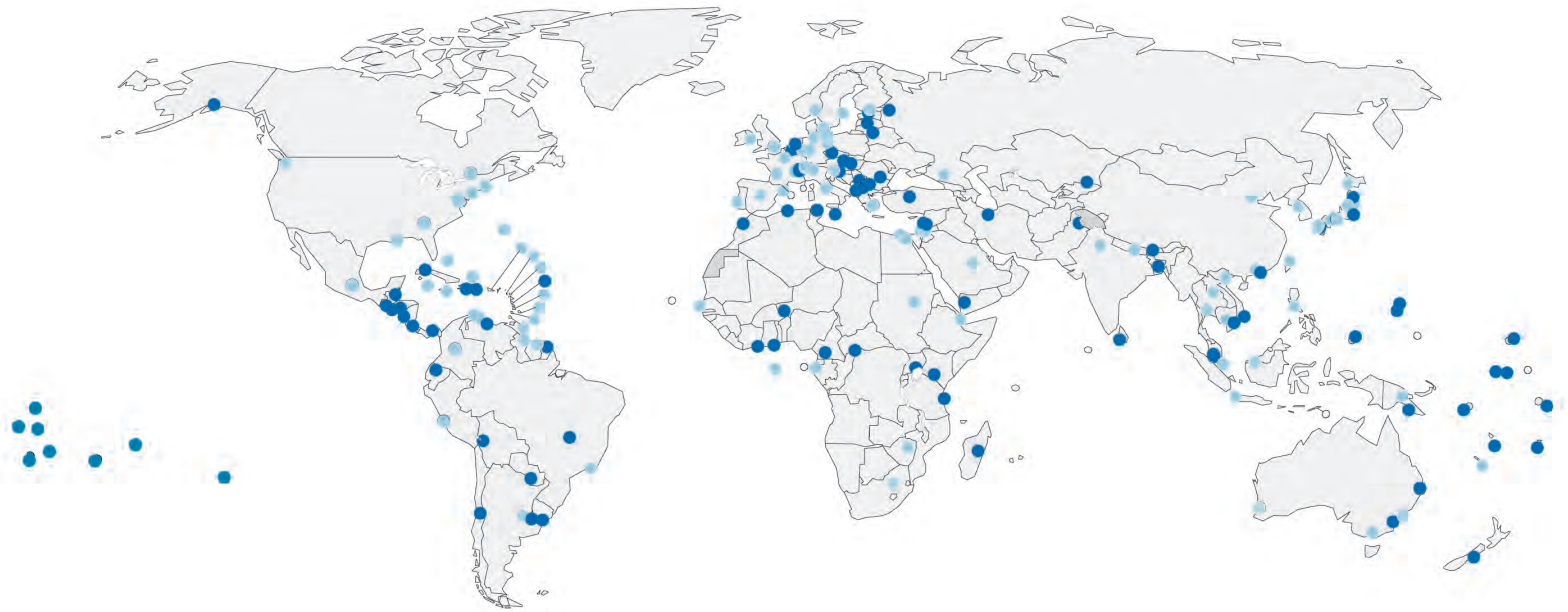


The second electronic platform is the secure, password-protected Event Information Site (EIS). EIS is accessible to NFPs, WHO heads of Country Offices and Regional Offices, WHO headquarters and certain intergovernmental organizations. EIS was developed to allow WHO to accomplish its obligations under IHR to provide relevant public-health information speedily, efficiently and confidentially. EIS contains information about verified acute public-health risks, including event-based risk assessments and Situation Reports, regional overviews of multijurisdictional events and control measures. In addition, announcements of interest are posted on the site, e.g. resource materials supporting IHR implementation and contact details.

WHO's response capacity is embodied in GOARN. In April 2000 WHO and key partners formally established GOARN to improve the coordination of international outbreak response (*21*). Through GOARN, an affected country gains rapid access to experts and resources to supplement its national capacities, and the health security of the global community is buttressed against the international spread of emerging and re-emerging pathogens. GOARN engages more than 300 technical and operational partners worldwide (Fig. 1.3).

The IHR define a PHEIC as "an extraordinary event which is determined to constitute a public-health risk to other States through the international spread of disease and to potentially require a coordinated international response". The IHR set out clear PHEIC procedures. Only WHO's Director-General has the authority to determine whether an event constitutes a PHEIC. The Director-General can make this determination only after seeking the advice of an appropriate committee of external experts (i.e. the Emergency Committee). The Director-General is required to consult the Emergency Committee before issuing temporary recommendations on appropriate health measures to prevent the international spread of disease and to avoid interference with international traffic. Countries that choose to implement more restrictive or disruptive measures must supply an adequate justification for their measures.

Fig. 1.3. **Global Outbreak Alert and Response Network (GOARN) membership, 2000–2011**



GOARN partners currently networking through GOARN Sharepoint

GOARN partners not currently networking through GOARN Sharepoint

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Although hundreds of public-health events have come to WHO's attention since June 2007, the emergence of a new influenza virus in early 2009 prompted the first (and to date the only) declaration of a PHEIC. This event became the first test of whether and how well many of the provisions of the IHR would work in practice.

As provided under the IHR, the functions, powers and duties of WHO, States Parties, ports, airports and transport operators reflect that no one actor or set of measures (e.g. border-entry controls) can provide complete protection against the international spread of disease. Rather, the IHR are premised on the interdependence of countries when faced with a public-health threat and the need for "full respect for the dignity, human rights and fundamental freedoms of persons" during responses to public-health events.

D. Overview of seasonal and pandemic influenza

Influenza is an acute viral infection that spreads easily from person to person. Seasonal influenza epidemics occur yearly during winter months in temperate regions of the world. In some tropical countries, influenza viruses circulate throughout the year, with one or two peaks during rainy seasons.

Most people who contract seasonal influenza recover without medical attention, but the infection can result in complications and death, particularly among older people, infants and people with underlying chronic medical conditions. Worldwide, seasonal influenza is responsible for an estimated 3.5 million cases of severe illness and 250 000–500 000 deaths each year (*22*).

Seasonal influenza can cause serious public-health and economic problems. In developed countries, epidemics can cause significant worker absenteeism and loss of productivity. Health facilities can become overburdened at periods of peak illness. Little is known about the effects of influenza epidemics in developing countries owing to a lack of data (*23*).

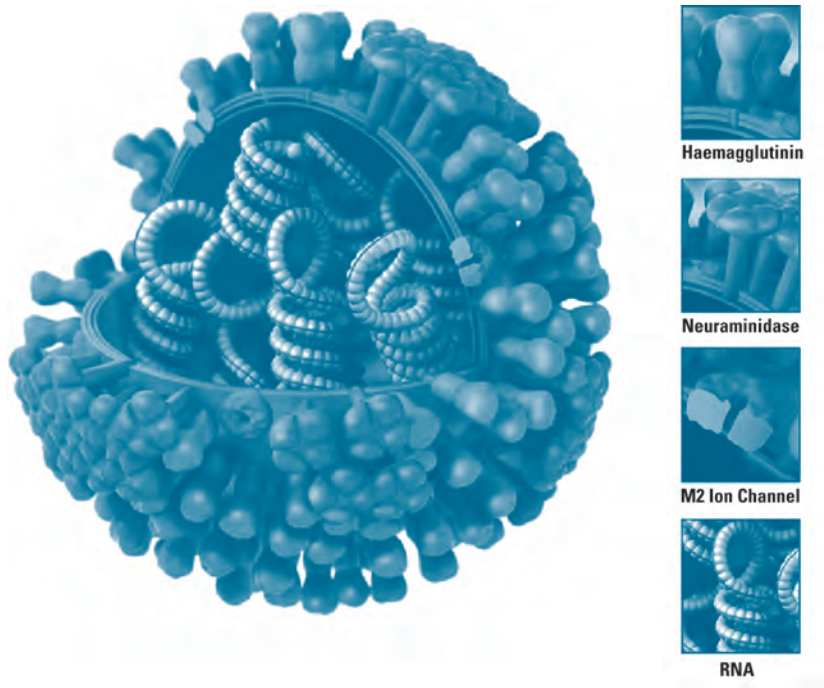
There are three types of influenza virus: A, B and C. Influenza type C usually causes either a mild respiratory illness or no symptoms at all; therefore, public-health efforts to control seasonal influenza each year are focused on types A and B. Type A viruses are divided into types based on differences in two protein–sugar complexes that stud the outer surface of the virus: haemagglutinin (H) and neuraminidase (N) (Fig. 1.4).

There are 16 known H subtypes and nine known N subtypes. Many different combinations of H and N proteins are possible but only two subtypes (i.e. H1N1 and H3N2) are currently circulating in the human population. Other subtypes are found in other animal species, most commonly in aquatic birds.

Influenza B primarily infects human beings and, in contrast with influenza A, does not have subtypes. Although it can cause substantial influenza epidemics and out-of-season outbreaks and severe disease in individuals, the magnitude of impact is usually less severe than that caused by influenza A.

The most effective way to prevent disease or severe adverse outcomes from influenza is through vaccination. Safe and effective influenza vaccines have been used for more than 60 years. Among healthy adults, influenza vaccination can prevent the majority of influenza-specific illness. Among the elderly, the vaccine reduces severe illnesses, complications and deaths (*24*). A limited number of antiviral drugs are available to forestall or treat influenza infections, and these are most effective when applied in the first few days of illness.

Fig. 1.4. **Graphical representation of the structure of a generic influenza virus**



Source: Centers for Disease Control and Prevention (adapted).

New combinations of viral surface antigens can occur when different influenza viruses simultaneously infect an animal. If the surface antigen of an influenza A undergoes a major change, then a pandemic can occur if most people do not have immunity to the new virus and the virus can be easily transmitted from human to human.

In contrast to annual epidemics of seasonal influenza, influenza pandemics are infrequent. There were three influenza pandemics recognized in the 20th century: in 1918–19, 1957 and 1968. Pandemics, by definition, affect human populations throughout the world but the characteristics of each – the countries and population segments most affected, the degree of severity of illness, the speed of geographic spread, the number of pandemic waves and the distribution across the globe – differed greatly (Table 1.2). The spectre of a potential repeat of the devastating 1918–19 pandemic profoundly influenced public-health planning for a future pandemic.

E. Planning for an influenza pandemic

Development and refinement of global pandemic preparedness plans, 1999–2009

WHO published its first global pandemic influenza preparedness plan in 1999, two years after the detection of the first human cases of avian influenza A (H5N1) in Hong Kong SAR (*25*). The plan was updated in 2005 (*26*) and again in April 2009 (*27*). The global preparedness plans were envisioned as planning tools that each country could adapt to suit its needs.

Table 1.2. **Characteristics of the three pandemics of the 20th century**

Pandemic (date and common name)	Area of emergence	Influenza a virus subtype	Estimated reproductive number	Estimated case fatality rate	Estimated attributable excess mortality worldwide	Age groups most affected (simulated attack rates)	GDP loss (percentage change)
1918–1919 "Spanish Flu"	Unclear	H1N1	1.5–1.8	2–3%	20–50 million	Young adults	-16.9 to 2.4
1957–1958 " Asian Flu"	southern China	H2N2	1.5	<0.2%	1–4 million	Children	-3.5 to 0.4
1968–1969 " Hong Kong Flu"	southern China	H3N2	1.3–1.6	<0.2%	1–4 million	All age groups	-0.4 to (-1.5)

Source: Pandemic Influenza Preparedness and Response: A WHO Guidance Document. Geneva, World Health Organization, 2009, p.13.

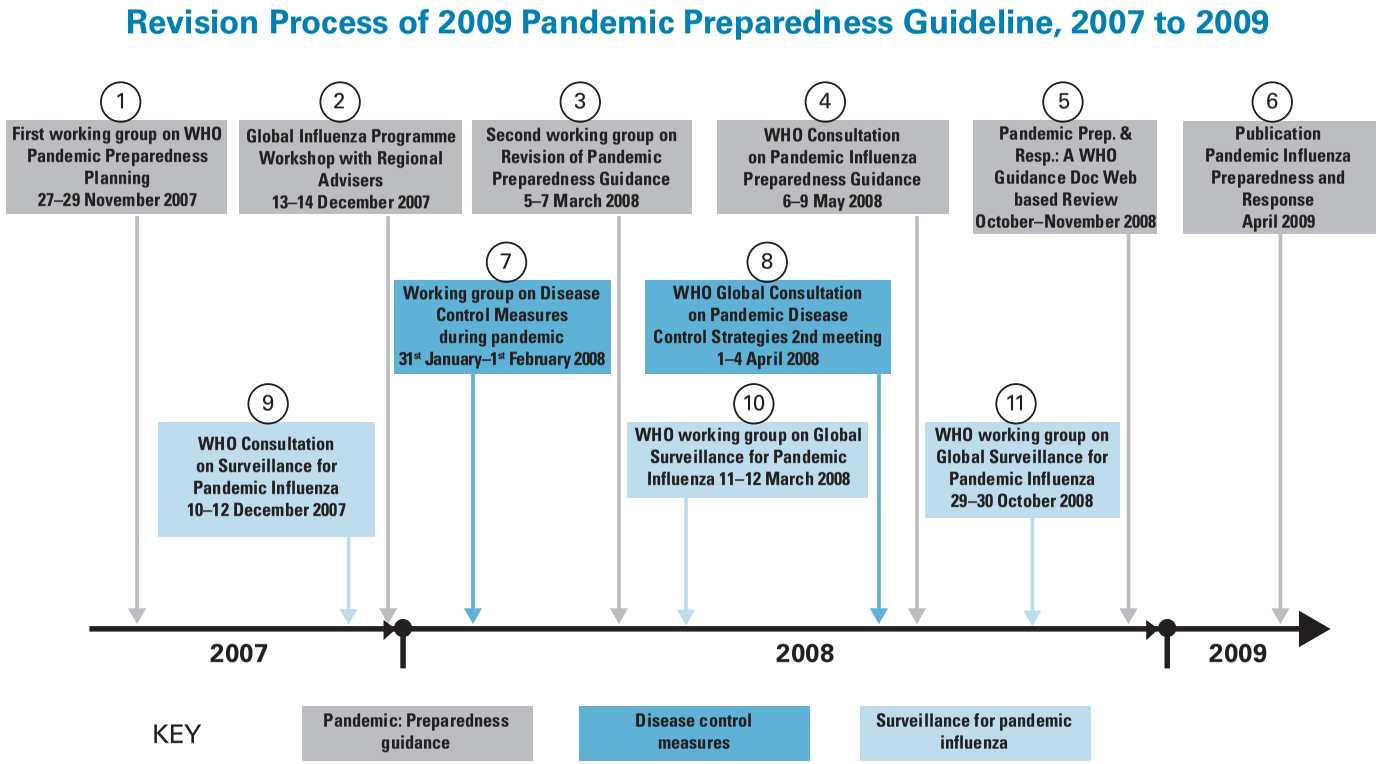
All the plans adopted a phased approach to organize actions to be taken by WHO or countries. The 2005 and 2009 plans redefined and refined the pandemic phases; emphasized actions in early phases to contain or delay the spread of a new influenza virus and recommended that many different partners, such as those in health, agriculture, education, transport, labour and defence, be included in planning activities.

Experience in several countries during the 1918–19 pandemic on mandatory case reporting, isolation of patients and quarantine of contacts contributed to the development of the 2005 WHO pandemic preparedness guidelines. Although such measures were often considered ineffective and impractical, early identification and isolation of patients in closed settings such as military barracks and college dormitories did appear to decrease attack rates, especially when combined with restrictions on movement into and out of affected communities (*28*). These findings, coupled with the general lack of availability of antiviral drugs and pandemic influenza vaccines, led to an overall emphasis on public-health interventions in the 2005 global influenza preparedness plan (*28*, *29*). By May 2007 nearly all Member States had developed an influenza preparedness plan based on the 2005 guidance.

Several events prompted WHO to call for a revision of the 2005 global plan (*27*). The ongoing geographic spread and evolution of avian influenza A (H5N1) was worrisome. New analyses of past pandemics offered insight into the evolution and spread of previous pandemics and ways to reduce transmission. One systematic review of data from cities in the United States of America during the 1918–19 pandemic reported a strong association between "early, sustained, and layered application" of public-health measures (i.e. school closures, cancellation of public gatherings, and isolation and quarantine) and reductions in measures of mortality (*30*). Two retrospective analyses suggested that quarantine (e.g. monitoring passengers and crew for illness before allowing them to disembark) may have been instrumental in delaying the arrival of the 1918–19 pandemic and reducing mortality among some island populations in the South Pacific (*31*, *32*).

Mathematical modelling studies further reinforced the potential value of public-health measures during a pandemic, provided they were implemented early and used in combination with medicines over a sustained period of time (*33*–*37*). For the first time, stockpiles of antiviral drugs were available at global, regional and country levels (although they provided coverage for only a small fraction of the world's population). Finally, modest advances had been made in vaccine research and development, and WHO had initiated the Global Action Plan to Increase Supply of Pandemic Influenza Vaccines (GAP) (*38*).

Fig. 1.5. **Revision process of the 2009 Pandemic Preparedness Guidelines, 2007–2009**



Box 1.2. Overview of major changes in the 2009 WHO Pandemic Influenza Preparedness and Response guidance

- Six-phase structure retained but revised to better reflect pandemic risk and the epidemiological situation using observable phenomena.
- Key principles for pandemic planning highlighted:
  - Inclusion of ethical principles for protecting human rights
  - Integration of pandemic preparedness and response into national emergency frameworks.
  - Incorporation of a "whole-of-society" approach.
- Harmonized with the IHR (2005) and supplemental WHO guidance for pandemic influenza surveillance, disease control measures, rapid containment and communications.
- Provision of planning assumptions and a selected evidence base.

The development of WHO's 2009 updated guidance – Pandemic Influenza Preparedness and Response – spanned a 17-month period, from November 2007 to April 2009 (Fig. 1.5).

Input into the 2009 global pandemic preparedness and response plan was sought from a broad constituency and through a variety of approaches. Several consultations were held, including topic-specific consultations that examined public-health and medical interventions, and global surveillance for pandemic influenza (*39*). A Working Group on Global Surveillance for Pandemic Influenza was formed to identify basic surveillance data needed during a pandemic – data that could be retrieved from developed and developing countries – as well as approaches to analysis and dissemination. Its deliberations led to the development of WHO surveillance guidance (*40*).

A revised draft of the plan was made available for public comment on the WHO web site from October–November 2008. More than 600 comments were received. All input was evaluated by members of the task forces and the WHO Secretariat (*27*). Publication of WHO's Pandemic Influenza Preparedness and Response coincided with the start of the 2009 pandemic.

The revised plan incorporated several new provisions (Box 1.2).

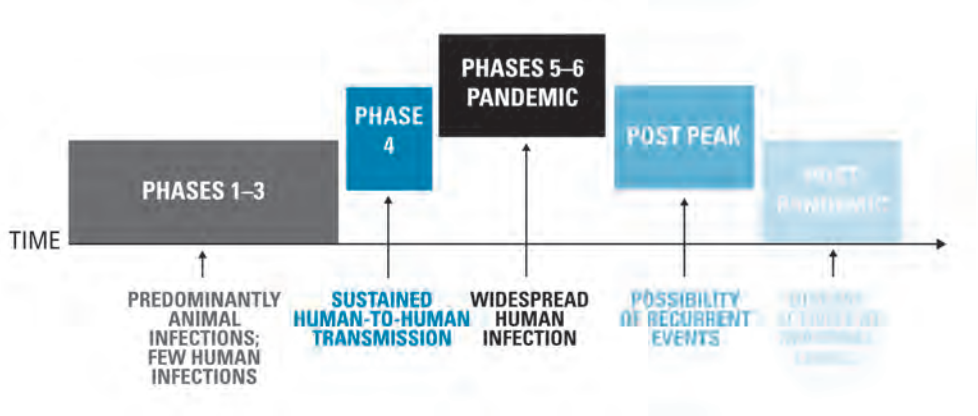
In view of the extensive work to develop national-level plans based on a phased approach, the six-phase approach was retained, although in modified form (Fig. 1.6).

Phases 1–3 and Phases 5–6 were combined. Phase 4 was characterized by sustained human-to-human transmission of an animal or human-animal influenza reassortant virus able to cause "community-level outbreaks", indicating a significant increase in the likelihood of a pandemic. At this point, WHO and the affected country could consider implementing a rapid-containment operation (*41*). The time after the first pandemic wave was divided into post-peak and post-pandemic periods. Recommended actions for WHO and national authorities were detailed for each phase (Table 1.3).

WHO Regional Offices provided direct, hands-on and in some cases financial support to countries that requested assistance in pandemic planning. Some examples of Regional activities are noted below.

The WHO Regional Office for Africa (AFRO) developed a regional pandemic influenza preparedness and response plan that was disseminated to all Member States for use in national plan development (*42*). Technical support was provided to countries to adapt their

Fig. 1.6. **Pandemic influenza phases, 2009**



Source: Pandemic Influenza Preparedness and Response: A WHO Guidance Document. Geneva, World Health Organization, 2009, p. 24.

H5N1 plans to cater to pandemic (H1N1) 2009. Thirty countries received funds from the Regional Office to implement priority pandemic activities.

The WHO Regional Office for Europe (EURO) assisted all 53 Member States through four regional meetings on pandemic preparedness, in 2005, 2006 and 2007. Several subregional workshops on pandemic preparedness were held between 2006 and 2009. Pandemic assessment missions to about 40 Member States, many jointly with the European Centre for Disease Prevention and Control, facilitated the development of preparedness plans and improvements in surveillance and laboratory capacities.

The WHO Regional Office for the Eastern Mediterranean (EMRO) supported Member States by sending technical guidelines to aid development of national preparedness plans, which were then reviewed by the regional technical units. Because Egypt was the country most affected by avian influenza A (H5N1), EMRO conducted several field missions to help the national Egyptian authorities develop a national response to H5N1 and pandemic preparedness plan. This plan was also tested through a simulation exercise.

The WHO Regional Office for the Americas (PAHO) provided technical guidance materials to individuals, communities and health professionals, which were posted on its web site. Some of these guides were created by PAHO technical experts and others were created by WHO experts and translated into Spanish. The information included the PAHO Strategic and Operational Plan to Prepare for an Influenza Pandemic 2008–2009 (*43*).

The WHO Regional Office for South-East Asia (SEARO) and the WHO Regional Office for the Western Pacific (WPRO) collaborated in the development of the Asia-Pacific Strategy for Emerging Diseases in 2005 (*44*). This strategy provided a bi-regional framework for discussing three interrelated objectives: the improved management of endemic disease, a pathway to IHR implementation and planning for pandemic preparedness. In addition, WPRO, in collaboration with the Secretariat of the Pacific Community and other partners, supported the multiyear Pacific Regional Influenza Pandemic Preparedness Project, aimed at capacity building in small Pacific Island countries and areas.

Table 1.3. **WHO pandemic phase descriptions and main actions by phase**

	Estimated probability of pandemic	Description	Main actions in affected countries	Main actions in not-affected countries
Phase 1	Uncertain	No animal influenza virus circulating among animals has been reported to cause infection in humans.	Producing, implementing, exercising, and harmonizing national pandemic influenza preparedness and response plans with national emergency preparedness and response plans.	
Phase 2		An animal influenza virus circulating in domesticated or wild animals is known to have caused infection in humans and is therefore considered a specific potential pandemic threat.		
Phase 3		An animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain community-level outbreaks.		
Phase 4	Medium to high	Human-to-human transmission of an animal or human-animal influenza reassortant virus able to sustain community-level outbreaks has been verified.	Rapid containment.	Readiness for pandemic response.
Phase 5	High to certain	The same identified virus has caused sustained community-level outbreaks in at least two countries in one WHO region.	Pandemic response: Each country to implement actions as called for in their national plans.	Readiness for imminent response.
Phase 6	Pandemic in progress	In addition to the criteria defined in Phase 5, the same virus has caused sustained community-level outbreaks in at least one other country in another WHO region.		
Post-peak period		Levels of pandemic influenza in most countries with adequate surveillance have dropped below peak levels.	Evaluation of response; recovery; preparation for possible second wave.	
Possible new wave		Levels of pandemic influenza activity in most countries with adequate surveillance are rising again.	Response.	
Post-pandemic period		Levels of influenza have returned to those seen for seasonal influenza in most countries with adequate surveillance.	Evaluation of response; revision of plans; recovery.	

Source: Pandemic Influenza Preparedness and Response: A WHO Guidance Document. Geneva, World Health Organization, 2009, p. 27.

Rapid containment: stopping an emerging pandemic

The idea for the strategy called rapid containment began in late 2005. The goal of rapid containment was to stop an influenza pandemic when the virus was initially detected and before it had spread widely (*41*). It evolved in part from the response to SARS, which demonstrated that it was possible to mobilize a complex global public-health operation and change the natural course of a disease. Further support came from two mathematical modelling studies published in 2005 (*34*, *35*). The models stipulated that detection, investigation and reporting of the first cases, followed by large-scale deployment of antiviral drugs and public-health measures to block transmission, such as isolation, quarantine and border controls, would need to be enacted rapidly in the affected area. The window of opportunity to enact these extraordinary measures was estimated to be three weeks at most. Rapid containment would likely not be attempted if the novel virus had spread

widely at the time of its initial detection or if the operations could not be put into place with sufficient speed.

To prepare for a possible rapid-containment operation, WHO received a donation of three million courses of oseltamivir to use as a stockpile. Countries were encouraged to integrate rapid-containment planning into their national pandemic influenza preparedness plans. WHO, in collaboration with Member States and technical experts, developed a rapid-containment protocol, conducted regional workshops and developed training materials. Some Member States and WHO regions had developed country and regional rapid-containment protocols and had undertaken exercises to test implementation of the rapid-containment strategy before the outbreak of pandemic influenza A (H1N1) 2009.

Rapid containment is considered an extraordinary public-health action that goes beyond routine outbreak response and disease control measures. It is intended to stop the spread of an incipient pandemic at its initial source. It is important to note, however, that pandemic preparedness and response plans used the term "containment" to connote a range of actions, e.g. prevent entry of the virus into a country or slow the geographic spread of the virus. In the same way, the term "mitigation" (sometimes used interchangeably with "containment") had different meanings depending on the context, e.g. slow the geographic spread of the virus, reduce burden of disease or reduce clinical severity of disease.

The Global Influenza Surveillance Network

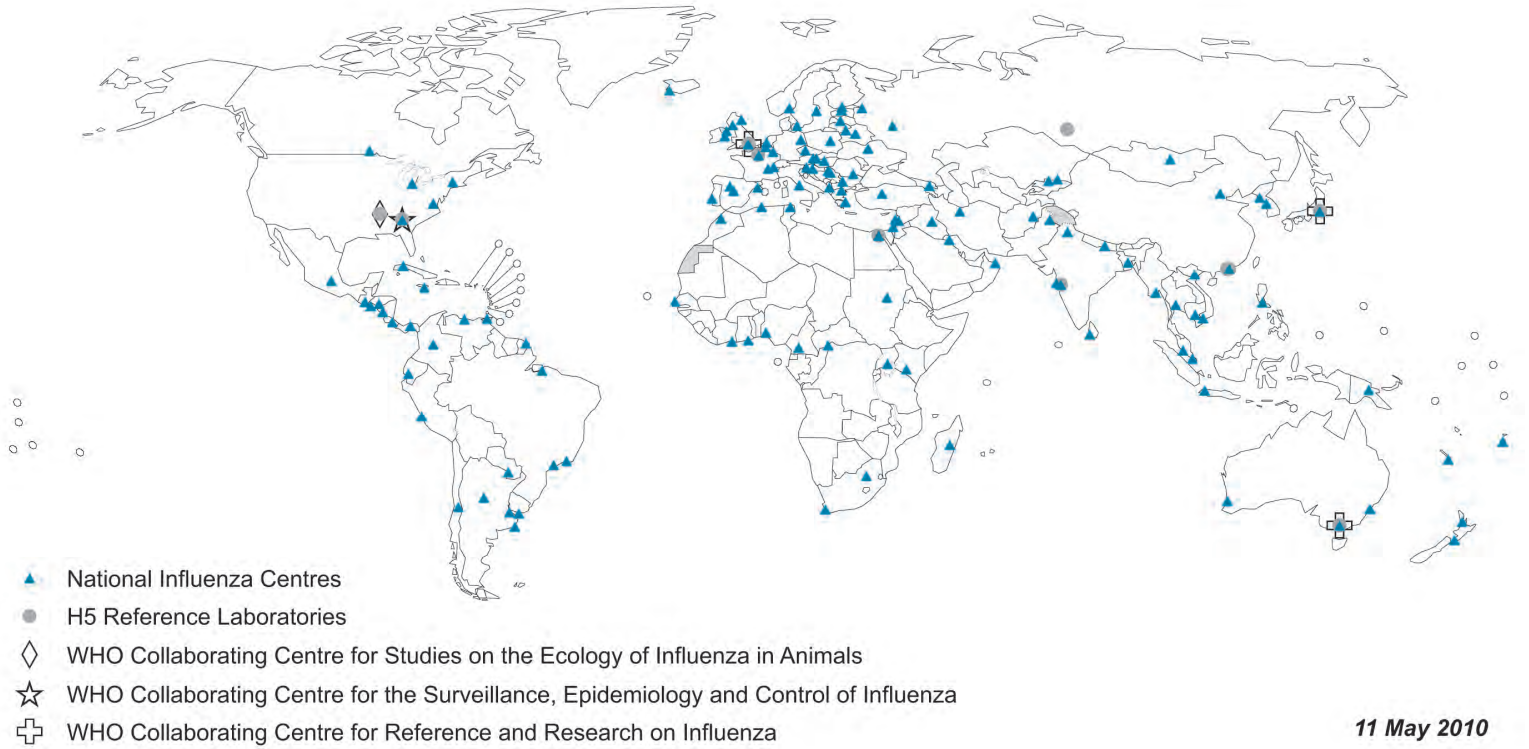
Since 1952, the WHO Global Influenza Surveillance Network (GISN) has played a pivotal role in influenza detection and monitoring. Its laboratory network tracks and analyses influenza viruses. The results determine WHO's recommendations for the northern and southern hemisphere seasonal influenza vaccines. The vaccines may be adjusted each year because influenza viruses change in minor, but immunologically meaningful ways continuously. Tracking these changes in real time, year-round, worldwide is a formidable challenge. Another important function of GISN is to detect and assess novel influenza viruses for their potential to cause a pandemic.

GISN has grown into a global partnership of 136 National Influenza Centres (NICs) in 106 countries, six highly specialized WHO Collaborating Centres (WHO CCs) and three Essential Regulatory Laboratories (ERLs) (*45*) (Fig. 1.7). Despite its reach, GISN has geographical gaps, especially in Africa.

In response to the challenges posed by influenza A (H5N1) viruses, WHO developed an ad hoc network of H5 Reference Laboratories within GISN, beginning in 2004. These actions enhanced GISN's early detection capacity for novel viruses and reinforced the importance of coordinated animal and human health surveillance (*46*).

NICs, often referred to as the "backbone" of GISN because they are the support for the entire network, are usually the principal source of expertise in influenza virus surveillance and response in their country. They collect and analyse influenza strains isolated from clinical specimens and forward representative or unusual virus isolates to a WHO CC for detailed characterization. Annually, the NICs collect more than 175 000 patient samples and submit about 2000 viruses to the WHO CCs for antigenic and genetic analyses (*45*). Although individual-level epidemiological and clinical data are not collected, NICs provide weekly reports to WHO of laboratory-based surveillance data and geographically based influenza-like activity using FluNet, a web-based electronic interactive data reporting, query and mapping system (*47*).

Fig. 1.7. **WHO Global Influenza Surveillance Network (GISN)**



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

WHO CCs specialize in advanced antigenic and genetic analyses of influenza viruses to monitor evolution and associated risks, update vaccine composition, determine susceptibility to antiviral drugs, update and produce standardized reagents used by NICs to test for seasonal influenza and provide advice and training on the most up-to-date laboratory methods to diagnose influenza.

Building public-health capacities

Preparation for a global health emergency, as championed in the IHR, relies heavily on building and maintaining core public-health capacities at local, intermediate and national levels, and at borders. While each national health system bears the burden of protecting its population in emergencies, the greatest value of the IHR capacity-building obligations may ultimately be the improvement in the way countries manage everyday public-health issues.

The IHR aim to provide a degree of certainty in national and global responses to significant public-health events:

- Countries are obligated to report significant public-health events to WHO.
- Countries are expected to exchange information and cooperate and coordinate with each other and with WHO.
- NFPs serve as a designated point of coordination and communication.
- Response measures are to be based on science, evidence of a risk to public health and to take account of WHO technical advice; countries that choose to implement more restrictive or disruptive measures must supply an adequate justification.
- Conveyance operators and the travelling public expect and deserve that any public-health measures applied at borders are as minimally disruptive as necessary to protect public health.

This report is both a review of the functioning of the IHR and an investigation of what happened during the pandemic, which was the IHR's first major stress test. The next chapter describes the events of the pandemic as they unfolded.

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II

Pandemic influenza A (H1N1) 2009

II

Pandemic influenza A (H1N1) 2009

Abstract

This chapter begins with an overview of what is known about pandemic influenza A (H1N1) 2009. There follows a descriptive timeline of selected events to illustrate how the pandemic unfolded, from emergence of the new virus subtype, through the pandemic phases and associated activities at the World Health Organization (WHO), to the start of the post-pandemic period. This account is not intended to be a comprehensive account of all activities undertaken worldwide relevant to the pandemic; rather, it describes selected key events, with emphasis on those related to WHO,[1] to illustrate the flow of events.

A. Overview of influenza A (H1N1) 2009

The emergence of a new H1N1 virus in early 2009 was the cause of the first influenza pandemic of the 21st century. Modelling estimates of the global burden of pandemic influenza A (H1N1) 2009 disease range from several tens of millions of cases to 200 million (*1*). By August 2010, when the transition from pandemic to post-pandemic period was announced, about 18 500 laboratory-confirmed deaths from pandemic influenza A (H1N1) 2009 had been recorded (*2*). The true extent of deaths attributable to the pandemic virus could, however, be significantly higher, since many people died without being tested.

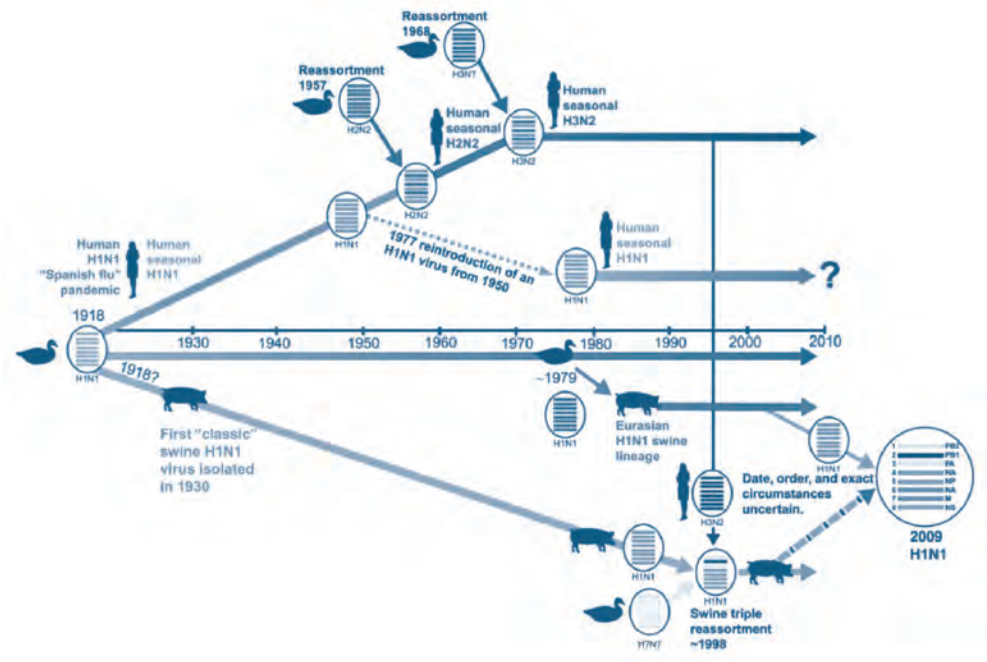
Uncomplicated pandemic (H1N1) 2009 is a self-limiting disease with symptoms similar to those of seasonal influenza: fever, cough, headache, body aches, sore throat and runny nose; nausea, vomiting and diarrhoea are more commonly reported than with seasonal influenza. Most patients with uncomplicated disease recover within a week without treatment. Spread of the virus seems to be similar to that of seasonal disease: via droplets or aerosol released when speaking, sneezing or coughing (*3*).

Beyond the preponderance of self-limiting illness, pandemic (H1N1) 2009 produced a spectrum of disease that included severe or fatal complications. The main cause of severe illness was viral pneumonia associated with severe lung damage, which resulted in respiratory failure and sometimes circulatory collapse and kidney failure (*3*).

A striking difference between pandemic (H1N1) 2009 and seasonal influenza was that most of the burden of disease in the pandemic occurred in younger age groups. One possible reason for this anomalous age distribution is the similarity between the pandemic (H1N1) 2009 virus and 1918–19-like H1N1 influenza viruses (Fig. 2.1). It is possible that older adults had greater protection against the 2009 virus because they had been exposed to 1918–19-like H1N1 influenza viruses in the first 60 years or so of the 20th century (*4*) (Fig. 2.1).

[1] While events happened in all WHO Regions, this narrative focuses on events at WHO headquarters.

Fig. 2.1. **Evolution of the pandemic influenza A (H1N1) 2009 virus**



Evolution of the 2009 H1N1 influenza A pandemic virus. The human 1918 "Spanish flu" and "classic" swine influenza A H1N1 viruses probably evolved from a single avian-adapted ancestor (left side of figure). Since 1918, genetic variation has accumulated in both human and swine influenza A lineages as a result of reassortment (explicitly shown in the figure; see bottom right for key to gene segments) and gradually, via point mutation (suggested by gradual colour transitions on the lines that represent individual lineages). The 2009 H1N1 pandemic virus appears to have been derived through the reassortment of several viruses currently known to circulate in swine.

Rates of hospitalization and death caused by pandemic (H1N1) 2009 varied greatly between countries, a reflection of such factors as the extent of virus spread and differences in health-care practices. Hospitalization rates were highest for children aged five years or younger. About 9–31% of patients admitted to hospital also needed treatment in an intensive care unit, and of these 14–46% died (*3*).

Young children, pregnant women and women who had recently given birth were shown to be at increased risk of severe pandemic (H1N1) 2009 infection. The risk of severe disease was heightened in women infected in the third trimester of pregnancy. People with chronic lung or heart conditions, neurological disorders or immune systems compromised by drugs or other diseases were also at elevated risk of more severe disease (*3*). There was some indication that morbidly obese people were also at greater risk of developing severe pandemic (H1N1) 2009 disease, but this has not been proven (*5*).

In countries of the Americas and the Pacific, indigenous populations were disproportionately affected by pandemic (H1N1) 2009 because they were more likely than the rest of the population to develop severe disease. Suggested explanations for this phenomenon

included crowded living conditions and the prevalence of underlying medical conditions, although a social component and limited access to medical care might also have been responsible (*3*).

Molecular analysis showed that pandemic (H1N1) 2009 was derived from viruses that had been circulating in pigs for many years, hence the references to "swine-origin influenza virus" and "swine flu" early in the pandemic. Pigs are susceptible to infection by both bird and human influenza viruses, as well as swine viruses, making them ideal mixing vessels for the generation of new viruses derived from different sources. In a process known as reassortment, several stages of mixing of genetic material of different virus types over the past century produced the new virus (*4*). (Fig. 2.1).

B. Emergence and detection of the virus

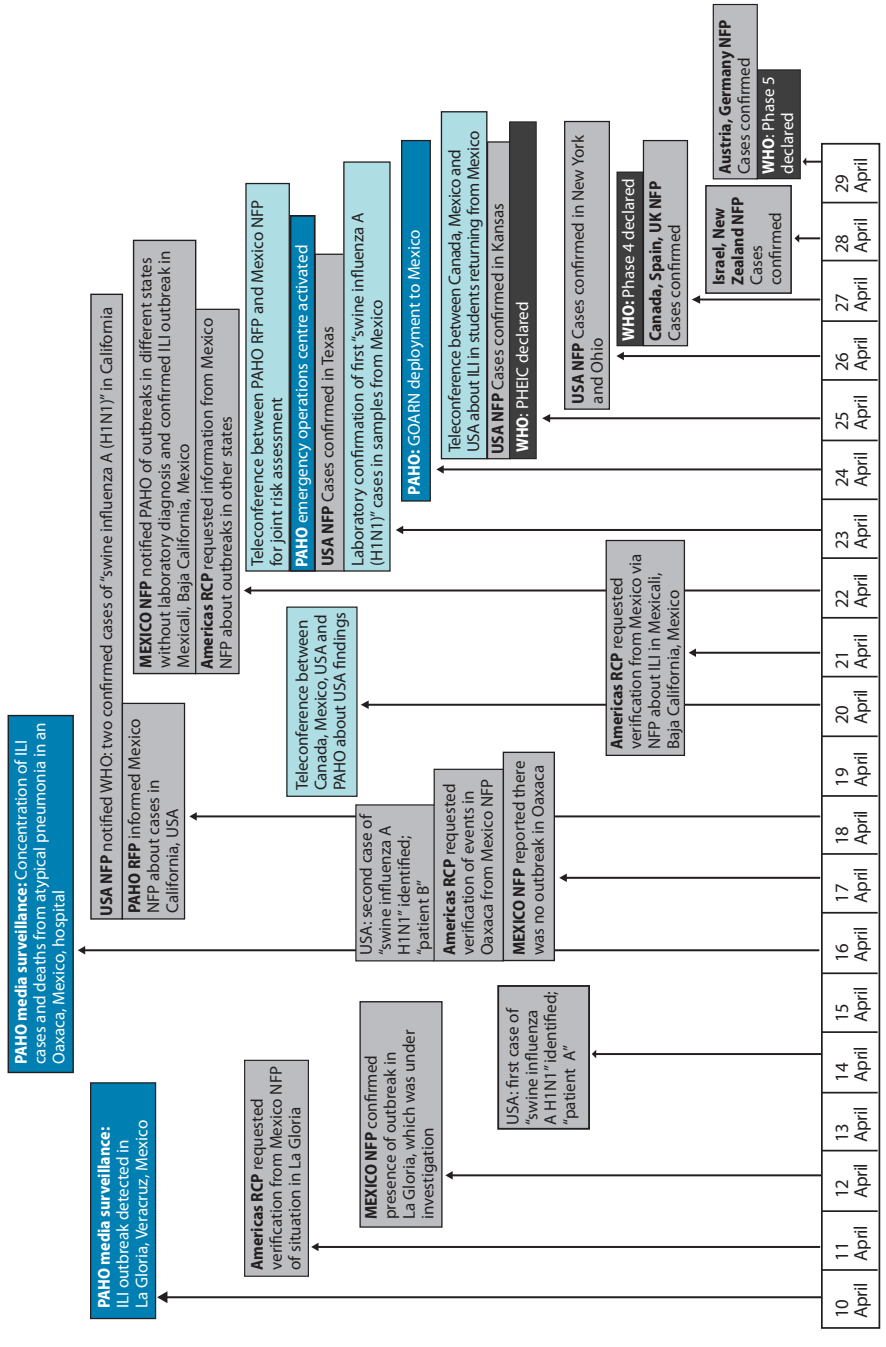
The first cases of what is now known to be pandemic (H1N1) 2009 occurred in Mexico during February and early March 2009, when national surveillance detected small outbreaks of influenza-like illness throughout the country. At the time, these outbreaks were thought to be part of the end of the usual influenza season in Mexico, albeit with a marked increase in disease activity compared with the previous year. In mid-March the Mexican Directorate General of Epidemiology issued a national epidemiological alert calling for strengthening of surveillance for acute respiratory diseases.

By 6 April 2009 active surveillance showed that one outbreak, in the rural pig-farming community of La Gloria, Veracruz, had increased to 444 cumulative cases among a population of about 2600. Speculation in the local media linked this outbreak to environmental pollution from oxidation tanks in swine farms. These reports were picked up by the Pan American Health Organization's (PAHO) media surveillance (Fig. 2.2). In response to a request from the PAHO Regional Focal Point on 12 April, the National IHR Focal Point (NFP) for Mexico confirmed the La Gloria event and reported that it might constitute a Public Health Emergency of International Concern (PHEIC), based on a risk assessment made with the International Health Regulations (2005) Annex 2 decision instrument (Appendix III, Function 2). The NFP also indicated that there was no evidence to support a link between the cases of influenza-like illness and pig farming. Mexico also shared this information with Canada and the United States of America, in accordance with tri-national public-health collaboration agreements and as encouraged under the International Health Regulations 2005 (IHR).

During the next few days, the situation evolved rapidly in Mexico. The cumulative case count in La Gloria continued to rise and other outbreaks of respiratory illness were noted in various parts of the country. A death from atypical pneumonia in Oaxaca was initially erroneously reported in the media as a case of Severe Acute Respiratory Syndrome (SARS) (Fig. 2.2). At an extraordinary meeting of the National Committee for Epidemiological Surveillance, experts concluded that the situation was of concern not only because of the increased frequency of cases, but also because severe disease was affecting young and previously healthy people. Analysis of samples revealed the presence of an influenza A virus that could not be matched to any known subtype. A second national epidemiological alert was announced on 17 April, and investigative efforts were intensified throughout Mexico (*6*).

Coincident with the outbreaks in Mexico, at the end of March two children in adjacent counties in southern California in the USA, became ill with acute respiratory illnesses.

Fig. 2.2. **Selected early events 2009**



Americas RCP = WHO IHR Regional Contact Point for the Americas. Dates reflect time zone of event.

Both children recovered uneventfully, but in neither case was it possible to identify the causal subtype of influenza A. Samples from Patient A from San Diego County and Patient B from Imperial County were sent to the US Centers for Disease Control and Prevention (CDC) for more detailed analysis. In mid-April, CDC established that both children had been infected with a new influenza A subtype with a make-up that suggested pig origin – "swine influenza A (H1N1)" – that had not previously been found in humans or animals (7). This information was reported to WHO via the NFP and shared with Mexico (Fig. 2.2).

Further outbreaks of respiratory illness continued to be identified in Mexico. Collaboration between Mexico, PAHO, Canada and the USA resulted in respiratory samples from Mexico being sent to the National Microbiology Laboratory of the Public Health Agency of Canada and to the CDC. On 23 April, separate analyses in Canada and the USA confirmed that the untypable influenza A isolated from Mexican patients and the "swine influenza A (H1N1)" from the Californian children were genetically identical (*8*).

WHO was alerted and the SHOC, WHO's Strategic Health Operations Centre at headquarters in Geneva, was activated in the early hours of 24 April, Central European Time. The SHOC is on standby to provide a single point of coordinated global response to acute public-health crises, such as infectious disease outbreaks and natural or man-made disasters, in addition to a potential PHEIC. WHO Director-General Margaret Chan, en route to New York, was briefed and went directly to PAHO Headquarters in Washington, DC. By then three further cases had been confirmed in California and two in Texas, with others in the USA under investigation. In Mexico, there were nearly 1000 mostly unconfirmed cases, including 59 deaths (*8*). The Director-General also had a teleconference with senior staff from the CDC and the Department of Health and Human Services, to discuss the cases in the USA.

At a teleconference later that day between the Director-General, Geneva headquarters staff, the Mexico Ministry of Health, PAHO and regional and country representatives, all agreed that the situation appeared to constitute a possible PHEIC. Work began at WHO to select an Emergency Committee from the IHR Roster of Experts, which consists of people nominated by Member States or directly by the Director-General under WHO Expert Advisory Panel regulations. In Mexico, measures to contain the spread of the disease started with school closures around Mexico City, later to be extended across the country. Universities, theatres and museums closed. Some countries cancelled flights to Mexico, while others halted trade. Neighbouring Latin American countries began to declare health alerts.

Twice-daily meetings of the WHO Senior Policy Group (SPG) began on 25 April. The SPG is convened by the Director-General or the Deputy Director-General when required. Its mandate is to ensure that decisions on policy issues related to an emergency can be made rapidly and through an informed process. The group consisted of the Director-General/Deputy Director-General (chair); Executive Director, Director-General's office; Assistant Director-General, Health Security and Environment; Assistant Director-General, Health Action in Crises; the Director-General's advisers; and senior staff responsible for epidemiological assessment, scientific and clinical information, operations, IHR, vaccines, communications, legal and WHO business continuity management. The objectives of each meeting were to: present highlights of the daily Situation Report; bring attention to issues that required policy decisions; and enumerate key issues that required follow-up and identify the responsible party. Official minutes of each meeting were circulated to all SPG members, Assistant Directors-General and Regional Directors.

WHO was by now the subject of great media interest, with intense focus on whether the first PHEIC would be declared. At the first Emergency Committee meeting, members would have to decide whether the situation constituted a PHEIC and whether the pandemic alert phase needed to be raised. Since 1999, WHO has issued advice on pandemic influenza preparedness. Part of this guidance defined pandemic stages or phases in order to assist Member States to respond appropriately and effectively to the perceived level of spread of a new circulating virus. The most recent guidance in place was issued in 2005, although work had been under way since then to revise and update the advice, in part to align the guidance with the IHR. The timing of the outbreaks in Mexico and the USA coincided with the finalization of this updated advice, which was posted on the WHO web site on 25 April 2009.

C. Declaration of the Public Health Emergency of International Concern

The Emergency Committee convened for the first time in the afternoon of 25 April. With the exception of one meeting in September that was done by e-mail, all Committee interactions took place via teleconference. In accordance with common WHO practice for expert advisory committees, the identities of the members of the Emergency Committee were not publicly disclosed. Having taken detailed evidence from country representatives on the evolving situations in Mexico and the USA, the consensus of the Committee was that a PHEIC was under way, but that the pandemic alert level should remain at Phase 3. The Committee underscored the need for more detailed information on the epidemiology, virology and clinical characteristics of this new virus before any further advice could be given. In line with the IHR, Committee members advised the Director-General on the announcement of the PHEIC (Appendix III, Function 5). Accordingly, when the Director-General announced the PHEIC later that day, she recommended that "all countries intensify surveillance for unusual outbreaks of influenza-like illness and severe pneumonia" (*9*).

Only two days after the Emergency Committee first met, the virus had spread both within Mexico and the USA, and new cases were now confirmed in Canada, Spain and the United Kingdom. Cases of suspected pandemic (H1N1) 2009 were under investigation in several other countries worldwide. Convening again on 27 April, the Emergency Committee debated whether the situation now warranted a phase change. Although evidence was still incomplete, there was consensus that the level should be raised to Phase 4. Other advice from the Emergency Committee to the Director-General was that containment of the outbreak, i.e. halting further spread of the virus, was not possible and the focus should be on mitigation; border closures and restrictions on international travel would be ineffective; and while the production of seasonal influenza vaccine should continue, WHO should facilitate the process of developing a vaccine effective against the new subtype.

At a press conference later that night, Keiji Fukuda, Assistant Director-General *ad interim* for Health Security and Environment, confirmed the details of the statement the Director-General had just released. In her statement, Dr Chan noted: "The change to a higher phase of pandemic alert indicates that the likelihood of a pandemic has increased, but not that a pandemic is inevitable. As further information becomes available, WHO may decide to either revert to Phase 3 or raise the level of alert to another phase." (*10*)

At the press conference, Dr Fukuda elaborated on the advice given by the Emergency Committee on temporary recommendations. As he explained to journalists, a consideration

in declaring Phase 4 was whether efforts to halt or contain the virus might be usefully employed. Rapid containment of a novel influenza virus would involve measures that included quarantine, use of antiviral drugs for the treatment and prophylaxis of affected and unaffected individuals, respectively, and exposure-reduction strategies, such as social distancing (*11*). Dr Fukuda explained that the virus had already spread too widely for containment to be feasible. Thus, the recommended focus of action was to be on mitigation, through activities such as ensuring that individuals had the information necessary to protect themselves and their communities from the more severe consequences of infection. Dr Fukuda added that, "The Director-General recommends not closing borders or restricting travel; however, it is prudent for people who are sick to delay travel and it is also prudent for returning travellers, who are coming back from any parts of the world and who have become ill to seek medical attention in line with the guidance from their national authorities." (*12*)

By 28 April, in addition to the countries where the new virus was known to be circulating, there were suspected infections in 18 further countries and laboratory-confirmed cases in Israel and New Zealand. Often the introduction of the virus to a country could be traced to an infected traveller returning home. The phase change and increase in infections worldwide resulted in even more intense media focus on WHO. Since the early hours of 24 April, a WHO communications officer was present in the SHOC day and night, and WHO had mobilized scores of internal volunteers to help staff its communications operations.

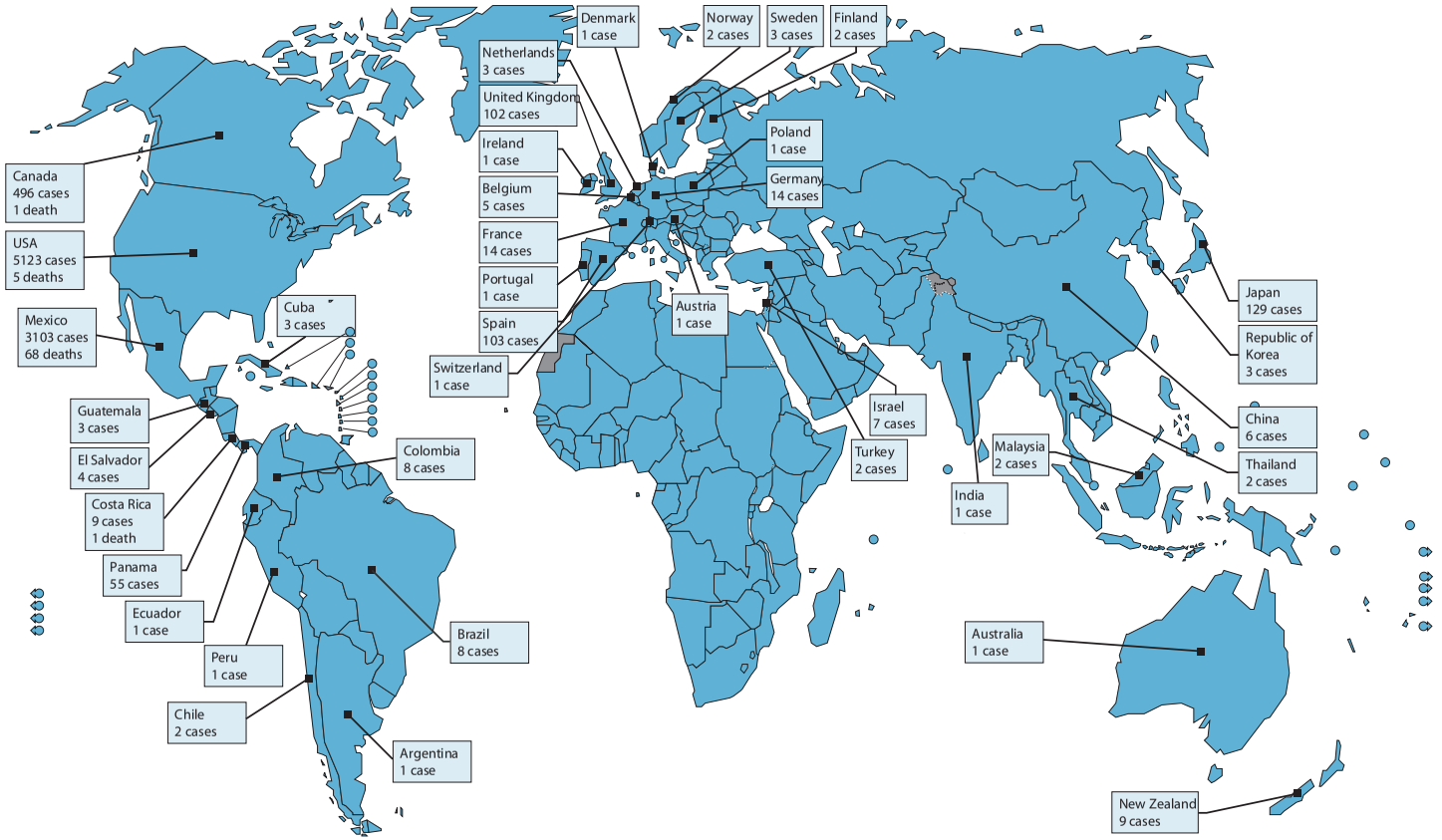
Over the next 24 hours, the situation rapidly evolved. As of 29 April, 148 cases of influenza (H1N1) 2009 were confirmed in nine countries and many more were under investigation (*13*). During the day there was news of the first death outside Mexico, that of an infant in Texas. Dr Chan held a teleconference with the chair, vice-chair, and rapporteur of the Emergency Committee. All agreed that Phase 5 had technically already been reached, since there was now human-to-human transmission in two countries within one WHO region. It was agreed that the public announcement of the phase change should be made once the entire Emergency Committee had been informed. One reason for this decision was to emphasize the need for countries not yet affected to implement their national influenza pandemic preparedness or contingency plans and to intensify surveillance measures.

At a media conference on the evening of 29 April, Dr Chan emphasized that the behaviour of a newly emergent influenza virus was by definition poorly understood and unpredictable, but she also noted that concerted work on pandemic preparedness plans meant that the world was better positioned to tackle such a threat than at any other time in history. "Above all," she said, "this is an opportunity for global solidarity as we look for responses and solutions that benefit all countries and all of humanity. After all, it really is all of humanity that is under threat during a pandemic." (*14*)

D. Mobilizing antiviral drugs and vaccines

The PHEIC affected both the agenda and format of the annual World Health Assembly of May 2009. The event was curtailed so that health officials were not kept from their national responsibilities for too long. Detailed measures were put in place in Geneva to manage any delegate reporting symptoms of influenza-like illness. "This virus may have given us a grace period, but we do not know how long this grace period will last. No one can say whether this is just the calm before the storm," Dr Chan said at the start of the Health Assembly on 18 May (*15*) (Fig. 2.3).

Fig. 2.3. **New influenza A (H1N1). Number of laboratory-confirmed cases and deaths as reported to WHO. Status as of 18 May 2009, 16:00 GMT**



Map produced:
18 May 2009 17:25 GMT

The Health Assembly provided a forum for United Nations Secretary-General Ban Ki-moon and Dr Chan to meet with about 30 pharmaceutical manufacturers and discuss the need for equity and fairness in access to vaccines for developing countries. Key parts of WHO's resource mobilization from the start of the emergency were the twin objectives of ensuring that people affected by the virus had access to medication and that unaffected individuals could access a vaccine.

Before the Health Assembly, the Director-General had noted the challenges associated with realizing these goals when she spoke to the United Nations General Assembly via videoconference. "Let me be frank. Global manufacturing capacity, though greatly increased, is still not sufficient to produce enough antiviral medication and pandemic vaccines to protect the entire world population in time. This is the reality. But we can acquire the data that guides the wise and targeted use of these interventions, conserves supplies, and, in the case of antiviral medicines, reduces the risk of drug resistance. An influenza pandemic is a global event that calls for global solidarity. As the chief technical and administrative officer of WHO, it is my job to do whatever is possible to ensure that developing countries are not left without protection. It is my duty to help ensure that people are not left unaided simply because of the place where they were born. I am working aggressively and constantly with the pharmaceutical industry to ensure access to affordable drugs and pandemic vaccine, should that be required." (*16*)

Since the earliest days of the PHEIC, North American scientists had determined that the new virus was resistant to the older antiviral drugs amantadine and rimantadine but was susceptible to the newer drugs oseltamivir and zanamivir. As pandemic (H1N1) 2009 spread, many countries worldwide were able to deploy national antiviral stockpiles. For countries unable to amass such reserves, WHO had at its disposal emergency stocks of oseltamivir. Immediately after the declaration of pandemic alert Phase 5, WHO started deploying three million doses of the drug to Mexico and to 71 pre-identified low-income countries. Within a month, this rapid-response stockpile had been delivered and WHO was to provide additional shipments as required during the course of the pandemic; some higher-income countries subsequently donated antivirals to the global response. In addition, WHO was able to exploit its medicines prequalification programme to expand the supply of generic oseltamivir and zanamivir. This programme began in 2001 to facilitate bulk purchasing of essential medicines by international procurement agencies, such as the United Nations Children's Fund, for distribution in resource-limited countries. The programme ensures that medicines supplied by procurement agencies for priority diseases meet acceptable standards of quality, safety and efficacy.

It was possible to deliver antivirals rapidly to countries since these were available as a pre-planned WHO stockpile. In contrast, it would be many months before a vaccine against H1N1 would be developed. During the first weeks of the PHEIC, it was established that immunity afforded by vaccination against seasonal influenza would not protect against infection with pandemic (H1N1) 2009. Given the speed with which the virus was being transmitted worldwide, the challenge was to create, manufacture, distribute and administer a new, effective and safe vaccine in record time.

WHO met with global pharmaceutical representatives to establish that drug companies were able to participate in the development and manufacture of a new vaccine without compromising production of seasonal influenza vaccine. By late May WHO had defined the characteristics of the emergent virus that were to form the basis of vaccine development. As a result of coordination between global parties, initial progress was rapid and

within weeks, production of vaccine seed strains had begun. National governments swiftly pre-ordered supplies and the first vaccines became available five months later.

Vaccine supplies were initially low. Manufacture of most influenza vaccine relies on growing the strain in chicken eggs. Yields were low because the strains did not grow well in this medium. Bottlenecks at subsequent steps of the production process compounded the delay in production and delivery of pandemic vaccine. WHO identified priority groups, such as health-care workers, to be vaccinated first.

By the time vaccine supplies had expanded sufficiently, public interest and concern had waned in some countries. Also, testing had determined that, in most situations, only one dose of the vaccine was required to produce an adequate antibody response rather than two, as originally envisaged. As a result, some countries were left with unused batches. In contrast to the surpluses in some parts of the world, many populations had no or limited access to vaccine throughout the period of the pandemic.

E. Declaration of the pandemic

On 11 May, less than three weeks since the declaration of the PHEIC, WHO posted information on assessing the severity of an influenza pandemic on its web site (*17*). The web posting noted: "With the exception of the outbreak in Mexico, which is still not fully understood, the H1N1 virus tends to cause very mild illness in otherwise healthy people. Outside Mexico, nearly all cases of illness, and all deaths, have been detected in people with underlying chronic conditions. In the two largest and best documented outbreaks to date, in Mexico and the United States of America, a younger age group has been [more] affected than seen during seasonal epidemics of influenza. Though cases have been confirmed in all age groups, from infants to the elderly, the youth of patients with severe or lethal infections is a striking feature of these early outbreaks."

As May 2009 drew to a close, activities at WHO began to move from an acute emergency response to a response based in the normal programmatic structures of the Organization. The Director-General and the Organization's senior representatives maintained close contact with countries to monitor events on the ground and preparedness plans. A particular concern was to ensure that Member States with more fragile health-care systems would be able to cope, should Phase 6 be declared.

At the beginning of June, the global picture was of continuing infection in the northern hemisphere and reports of activity occurring in the southern hemisphere, particularly in South America and Australia. As of 9 June, 73 countries had reported 26 563 laboratory-confirmed cases to WHO. Amid speculation that declaration of a pandemic was imminent, Dr Fukuda told the media: "And here I want to point out that by going to Phase 6, what this would mean is that spread of the virus has continued and that activity has become established in at least two regions of the world. It does not mean that the severity of the situation has increased and that people are getting seriously sick at higher numbers or higher rates than they are right now." He continued: "You would think that by going up scale would mean that the level of concern should go up, but really what the going up a scale would mean is that we are seeing greater spread of the virus. We are working with different groups to make sure these kinds of messages are understood and the difference between severity and geographical spread is understood. As I discussed last week, right at

this time, we considered the situation and the impact on countries to be relatively moderate, and this is again a critical point." (*18*)

On 11 June the Emergency Committee met once more by teleconference, having been convened a week earlier to review a WHO pan-regional dialogue on disease severity. In light of the more up-to-date evidence from countries bearing the greatest burden of disease (Fig. 2.4) and those newly experiencing influenza (H1N1) 2009, the Emergency Committee unanimously advised that the time had come to raise the alert to Phase 6 – i.e. a pandemic, according to the WHO guidance.

Speaking to the media on the evening of 11 June, the Director-General announced: "The world is now at the start of the 2009 influenza pandemic. We are in the earliest days of the pandemic. The virus is spreading under a close and careful watch. No previous pandemic has been detected so early or watched so closely, in real-time, right at the very beginning. The world can now reap the benefits of investments, over the past five years, in pandemic preparedness. We have a head start. This places us in a strong position. But it also creates a demand for advice and reassurance in the midst of limited data and considerable scientific uncertainty." (*19*) She continued by noting: "Globally, we have good reason to believe that this pandemic, at least in its early days, will be of moderate severity as we know from experience severity can vary depending on many factors from one country to another. On present evidence, the overwhelming majority of patients experience mild symptoms and make a rapid and full recovery – often in the absence of any form of medical treatment." She added that all countries, whether affected or not, should remain vigilant.

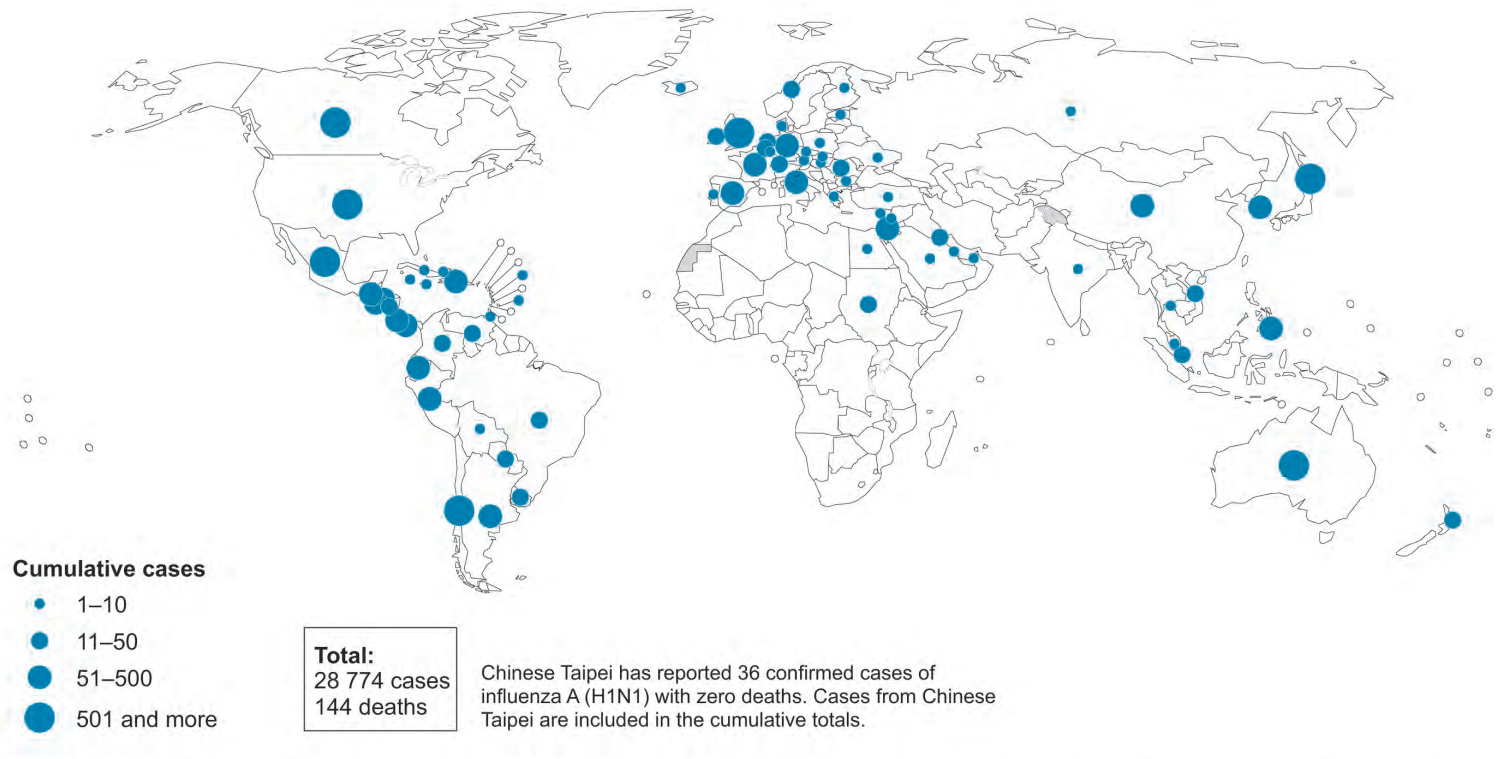
Over the next three months, pandemic (H1N1) 2009 continued to spread globally. By September, the USA was reporting influenza-like illness activity above what would be expected from seasonal influenza. In Europe and central Asia, influenza activity was generally low overall, with localized outbreaks in several countries. Japan was experiencing influenza activity above the seasonal epidemic threshold. In tropical parts of the Americas and in Asia, influenza transmission remained active; this was especially the case in southern and South-East Asia, with reports of increases in respiratory disease in Bangladesh and India. In the temperate parts of the southern hemisphere, influenza activity was decreasing to expected seasonal levels (Fig. 2.5). Continuing laboratory surveillance indicated that pandemic influenza A (H1N1) 2009 virus had become the predominant circulating influenza virus worldwide (*20*).

The Emergency Committee held its fifth meeting via e-mail, concluding on 23 September. Based on their appraisal of the situation, the Emergency Committee advised that the temporary recommendations should remain as:

- countries should not close borders or restrict international traffic and trade;
- intensify surveillance of unusual flu-like illness and severe pneumonia;
- if ill, it is prudent to delay international travel; if ill after travel, seek care.

Despite the consistency of the recommendation that traffic and trade should not be restricted throughout the PHEIC, this advice was not always followed. Mexico had suffered severe economic sanctions, especially in the early period of the emergency. Several countries had instituted bans on pork importation from Mexico, the USA and Canada, despite assurances from international organizations that pork was not a source of pandemic (H1N1) 2009 infection. Action had been taken to rename the virus, since it was felt that the use of terms such as "swine flu" created misunderstanding (Box 2.1).

Fig. 2.4. **New influenza A (H1N1). Number of laboratory-confirmed cases as reported to WHO. Status as of 11 June 2009, 14:00 GMT**

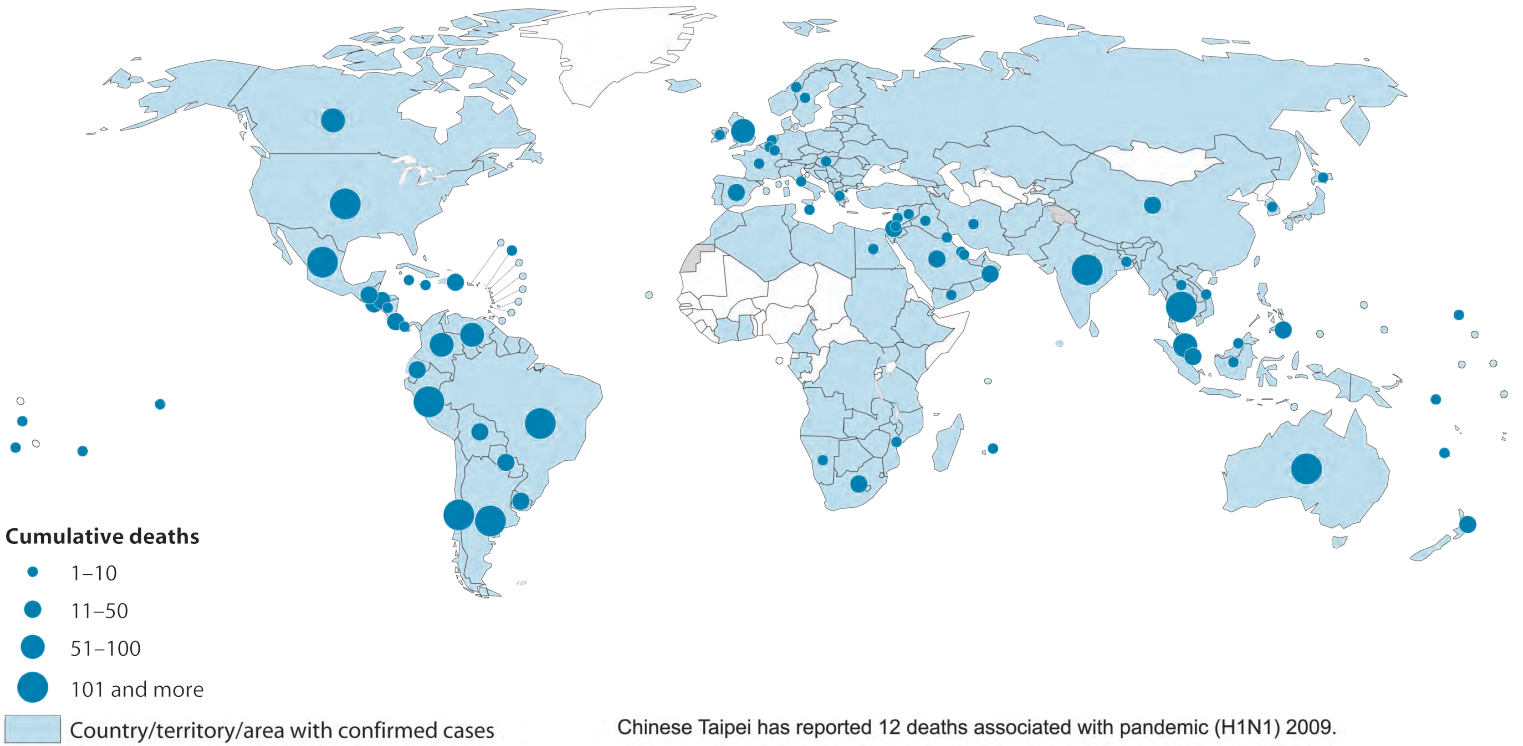


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Fig. 2.5. **Pandemic (H1N1) 2009. Countries, territories and areas with laboratory-confirmed cases and number of deaths as reported to WHO. Status as of 20 September 2009**



Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

Box 2.1. **Naming of the virus**

Initially, the media, as well as some technical experts, called the virus "swine flu", because it was shown to contain genes from swine influenza viruses. The name was soon called into question, especially by animal-health experts, because the virus did not appear to be circulating widely in animals, including swine, while it was circulating widely in humans.

Moreover, the name appeared to have contributed to some unnecessary and adverse implications for trade and animal health. Some countries were banning importation of live swine and pork and pork products from countries with human cases. One country ordered a cull of all swine in that country. However, there were no data showing increased risk of infection from exposure to swine or pork products.

At a 9 June 2009 media briefing, WHO reiterated that pork was safe and not a danger to people. Moreover, WHO pointed out the naming of a virus associated with a geographical area, as had happened with previous viruses, could result in stigmatization, and that WHO was collaborating with partners to resolve the naming issue.

On 15 June 2009, WHO organized a teleconference with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE), including many eminent animal- and public-health influenza virologists, to find a scientifically acceptable and non-stigmatizing name for the virus and the disease. The name "pandemic influenza A (H1N1) 2009 virus" was agreed to by the participants.

The Emergency Committee met again on 26 November to decide whether to renew the temporary recommendations. The Committee members unanimously agreed to renew the recommendations, with only the third recommendation modified to read: "If ill, it is prudent to delay travel." At the next Emergency Committee meeting, on 23 February 2010, it was agreed that the second temporary recommendation should be modified to advise that countries should "maintain" rather than "intensify" surveillance of unusual influenza-like illness and severe pneumonia.

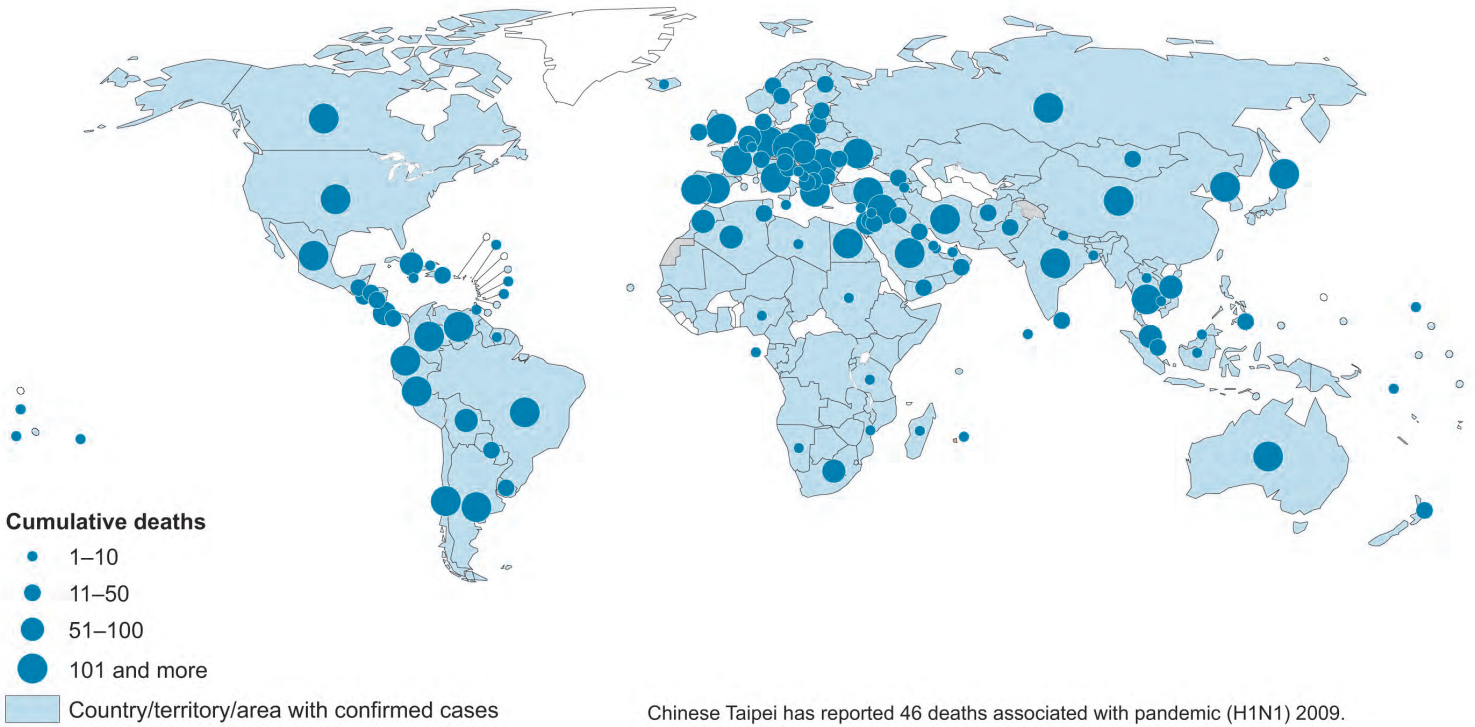
When the Emergency Committee next met at the beginning of June 2010, epidemiological analysis indicated that the period of most intense activity of pandemic (H1N1) 2009 had probably passed in many parts of the world. There was no evidence of an early start to the winter influenza season in the southern hemisphere; nevertheless, it was deemed too early for complacency, and the Emergency Committee indicated to the Director-General that further pandemic influenza was to be expected and it remained imperative for countries to be vigilant, and to maintain necessary public-health measures for disease control as well as virus and disease surveillance.

F. The post-pandemic phase

As the Emergency Committee convened for its final meeting on 10 August 2010, worldwide more than 214 countries and overseas territories or communities had reported laboratory-confirmed cases of pandemic (H1N1) (Fig. 2.6).

While noting that a small number of countries were still experiencing intense influenza epidemics largely caused by the pandemic (H1N1) 2009 virus, the Emergency Committee based its assessment on the global situation. The evidence indicated that influenza, worldwide, was transitioning towards seasonal patterns of transmission; influenza (H1N1) 2009 seemed largely to have "run its course" and would likely continue to circulate for some years to come, taking on the behaviour of a seasonal influenza virus.

Fig. 2.6. **Pandemic (H1N1) 2009. Countries, territories and areas with laboratory-confirmed cases and number of deaths as reported to WHO. Status as of 1 August 2010**



Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

The Emergency Committee therefore agreed that the global influenza situation no longer represented an extraordinary event requiring immediate emergency actions on an international scale. The Committee advised the Director-General that the world was no longer in pandemic Phase 6, that the PHEIC should be ended and that the temporary recommendations adopted in response to the PHEIC should be terminated.

At a media conference after the Emergency Committee's meeting, Dr Chan observed: "Pandemics are unpredictable and prone to deliver surprises. No two pandemics are ever alike. This pandemic has turned out to be much more fortunate than what we feared a little over a year ago. This time around we have been aided by pure good luck; the virus did not mutate during the pandemic to a more lethal form, widespread resistance to oseltamivir did not develop. The vaccine proved to be a good match with the circulating viruses and showed an excellent safety profile, thanks to expansive preparedness and support from the international community." (*21*).

Since the end of Phase 6, influenza (H1N1) 2009 has continued to circulate globally, and has so far shown signs of transmission more akin to seasonal influenza.

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III

Management of the global response

III

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Abstract

This chapter describes and assesses the functioning of the International Health Regulations (2005) and the World Health Organization's role in management of the global response to pandemic influenza A (H1N1) 2009. Eight functions of the IHR are discussed, along with the Review Committee's assessment of their efficacy since the Regulations entered into force.

The role of WHO and countries in prepandemic preparedness is described, followed by a description and analysis of the major activities of the response to the 2009 pandemic. These activities include surveillance from the initial outbreak through to the postpandemic period; the ongoing assessment of severity; interventions (both nonpharmaceutical and pharmaceutical) and technical guidance. The chapter concludes with a discussion of WHO's communications during the pandemic, from internal operations to public information.

A. International Health Regulations (2005) : implementation and evaluation

The history and development of the IHR are detailed in Chapter I. The functions of the IHR are described in Appendix III of this report. In 2010 WHO's Executive Board accepted the Director-General's proposal for a review of the IHR, under Article 54 of the IHR. The article mandates a regular review of the IHR, including a review of the studies undertaken to evaluate the functioning of the IHR Annex 2, which is the decision instrument for notification to WHO. The Review Committee's remit was to evaluate how the IHR functioned during the pandemic and other public-health events falling under the broad scope of the IHR since they entered into force in 2007. Several hundred events have been brought to WHO's attention since 2007 but the pandemic was the first designated Public Health Emergency of International Concern (PHEIC), as provided for in Article 12. The pandemic was the first event that required WHO to establish an Emergency Committee (EC) and to issue temporary recommendations.

Sources of evidence

In evaluating the functioning of the IHR, the following evidence has been particularly useful: interviews with National IHR Focal Points (NFPs) representatives and national health authorities, and their written evidence; interventions from States Parties[1] at Review Committee meetings; interviews with WHO headquarters and Regional Office staff; WHO briefing papers prepared for the Committee, including case studies of public-health events managed by WHO; other WHO documents, including guidance and training materials;

[1] States Parties are those countries that are bound by the IHR in accordance with the WHO Constitution and the IHR. There are currently 194 States Parties, which includes all 193 Member States of the WHO.

studies commissioned by WHO to evaluate the functioning of Annex 2 of the IHR and States Parties' reports on their implementation of the IHR (IHR Monitoring Framework). The Committee sought evidence from interviews with States Parties, statistics from States Parties' responses to the IHR Monitoring Framework, examples of country assessments and case studies of the use of the IHR. Other sources of evidence specific to particular functions are listed under that function.

Knowledge, training and resources to support implementation

Since the IHR entered into force on 15 June 2007 WHO has developed a range of training initiatives and guidance on the IHR, including guidance documents; regional meetings, seminars and training sessions; online training; an extensive training course and the *IHR Quarterly Bulletin*.

The WHO Contact Points in the Regional Offices support the NFPs and convene meetings to share progress, learn lessons and identify needs. Regional Offices also implement regional strategies to develop national capacities, including the provision of technical assistance and support for resource mobilization. WHO provides States Parties with feedback on progress at individual country level as well as at the regional and global level (including an annual report to the World Health Assembly).

The main mechanisms for information gathering and sharing are two electronic platforms, the Event Management System (EMS) and the Event Information Site (EIS). The EIS is the secure, password-protected information portal used by NFPs and WHO. The EMS is a project of the Alert and Response operations team within the Department of Global Alert and Response. It is an internal repository to support decision-making and risk management. It consists of data that provide a historical overview of events of potential international concern by region, country, threat, and disease or event type.

The Committee's assessment of the implementation and evaluation of the IHR is organized by IHR function.

Function 1: Surveillance and response capacities in States Parties

The Committee wanted to know: whether the IHR have stimulated national capacity building and collaboration among States Parties, especially in neighbouring countries; and to what extent States Parties have designated NFPs, have integrated the IHR into their national legislation and have made national plans for capacity building to meet the 2012 deadline.

WHO has provided a framework for States Parties to monitor development of their core capacities at the national, intermediate and community response levels, using a set of 20 global indicators. Countries are encouraged to report annually on all the indicators.

Findings

- More than half of the reporting States Parties have assessed their capacities and about one third have made national plans. Although the IHR have stimulated capacity building for surveillance and response, there is wide variation in the degree of fulfilment. States Parties are aware of the obligations and report a willingness to comply, but some note a limited availability of resources.

- As of October 2010 all but one of the States Parties have established NFPs and provided WHO with their contact details. Five States Parties indicated that their NFP is not yet available for 24-hour communications. Three NFPs have not provided e-mail contact details. About 90% of NFPs have access to the EIS. Virtually all NFPs are located within the health sector (79% in a ministry of health and 19% in a national agency). In most reporting countries, the person responsible for the position of the NFP occupies a senior political, managerial or technical position. The contact details of NFPs are available on the EIS, and WHO has established a system for regular verification and information updates. The site allows NFPs to contact directly their counterparts in other countries. There are indications of increasing use of this facility.

Implementing the IHR has implications for government functions and responsibilities across many ministries and sectors. Although integrating the IHR into national legislation is not a requirement of the IHR, an adequate legal framework to enable and support activities is needed. WHO has advised States Parties to determine whether existing legislation needs to be revised. Further, the Organization has argued that implementing national legislation may institutionalize and strengthen the IHR capacities and operations, facilitate coordination and help ensure continuity. There are several ways to incorporate the IHR into national legal systems. One is to state that the IHR constitute a legal requirement and to annex the text of the IHR or incorporate them by reference.

- About half of States Parties have changed legislation to accommodate their obligations under the IHR.
- There are several examples of how intercountry groupings have collaborated in the course of implementation of the IHR. They include: the European Union's Early Warning and Response System; the Pacific Public Health Surveillance Network; the EpiNorth and EpiSouth networks in Europe; the Global Health Security Action Group; the South East European Health Network; the Middle East Consortium of Infectious Diseases Surveillance and the Mercado Común del Sur. There are also examples of how States Parties share information, tracing information, support and supplies by direct contact between NFPs.
- States Parties are aware of their obligations to build capacity and are willing to comply. The IHR have helped build national and regional capacities for surveillance and response.

A functioning NFP and capacities for surveillance and response are the basis for the national and global systems envisaged by the IHR to safeguard against public-health events. Without these, the IHR cannot fulfil its role.

The global network of NFPs represents an early success for the IHR. Together with the WHO IHR Contact Points at the regional-office level, the NFPs make up an excellent global communication system. During the pandemic, the network of NFPs operated on a global scale for the first time and, while not perfect, proved a functional, robust means of communicating with Member States. With NFPs in virtually every country, WHO has created clear and effective channels to reach rapidly the appropriate level of government. Nevertheless, nearly half of States Parties have neither assessed surveillance and response capacities nor planned for improvements. Many have not even reported on their status. It seems clear from reports that many countries will not meet the 2012 deadline for building core capacities.

Member States have responded admirably to severe public-health events in other countries and provided technical, logistical and financial help to those affected. It is more difficult, however, to raise funds for sustained, long-term capacity building. Donor countries and organizations could take advantage of the IHR Annex 1A as a priority list for development support and also seize opportunities to share specialized resources, such as laboratories, across countries.

IHR Annex 1A does not prescribe details of the required capacities, and although the IHR Monitoring Framework provides good guidance, it is not a complete recipe for success. In 2010, WHO issued a protocol for assessing national surveillance and response capacities for the IHR *(1)*.

Function 2: Detection and alert operations in States Parties

The Committee sought to explore: to what extent IHR Annex 2 is understood and used by NFPs; whether this decision instrument leads to the identification and notification of relevant events and whether NFPs experienced any barriers to notifying WHO. In 2009 the functioning of Annex 2 of the IHR was formally evaluated for the first time *(2)*.

Findings

IHR Annex 2 is well known to NFPs (Box 3.1). Awareness can be further improved by ensuring all NFPs receive training from WHO. Half of NFPs surveyed said their country had developed legislation and operating and communication procedures to support the use of the tool. IHR Annex 2 is considered useful, but could be refined to aid interpretation of non-infectious disease events.

A study by the University of Geneva and University Hospitals Geneva (Box 3.2) found that the notification assessment process using IHR Annex 2 was highly sensitive, but only moderately specific, in keeping with the intended purpose of the decision instrument *(3)*. The reliability and validity of notification assessments might be increased by expanding guidance to provide more specific criteria for assessing common events and clearer definitions of key terms. Based on the recommendations of a technical consultation held in October 2008, WHO expanded its guidance on the use of IHR Annex 2 *(4)*. The new guidance contains 16 illustrative scenarios that are assessed against four criteria.

An internal WHO study (Box 3.3) of its event databases suggested that NFPs are not a major source of the first information WHO receives on public-health events.

In practice, there is wide variation in the way NFPs function. WHO is made aware of many events through unofficial sources, and NFPs are then asked for verification and follow-up information and usually provide this in a timely manner.

In summary, there are indications that NFPs are not yet a timely source of initial, early information on events that might constitute a potential PHEIC, but they are important for verification and follow-up information.

Box 3.1. **Studies for the review and evaluation of the functioning of Annex 2 of the International Health Regulations (2005) (University of Ottawa)**

Objective: To ascertain the level of awareness, implementation, usefulness and user-friendliness of Annex 2.

Methods: Qualitative and quantitative studies were carried out between October 2009 and February 2010, using telephone interviews with NFPs and an online survey. NFPs participated on a voluntary basis, using their language of choice for the qualitative study, and one of the six official WHO languages for the online survey.

Results: 29 NFPs (representing 15% of all States Parties) participated in telephone interviews, while 133 NFPs (representing 69% of all States Parties) completed the quantitative online survey.

Awareness and knowledge: Among all NFPs, 88% reported having excellent or good knowledge of Annex 2 and 82% had accessed WHO training on it. Access to WHO training was significantly associated with excellent or good knowledge. Case scenarios were deemed essential to improving knowledge. Some NFPs without any WHO training expressed confusion about operating and communication procedures. Awareness of Annex 2 in government was highest at national or federal level, and in agencies of health and agriculture.

Practical use and activities for implementation: 77% of NFPs reported always or usually using Annex 2 for assessing public-health events. 67% had facilitated training on Annex 2 in their country. 76% indicated their country had some legal, regulatory or administrative provisions for using Annex 2. 54% had a standard operating procedure for implementing Annex 2 and 74% had a domestic communications plan to facilitate notification to WHO.

Usefulness: 95% of NFPs found Annex 2 always or usually useful in facilitating decisions regarding notifiability of a public-health event. However, 59% of NFPs indicated that Annex 2 was never sufficiently sensitive. Concern was raised that Annex 2 was too human- and aetiology-centric, and insufficiently inclusive of events such as communicable diseases among animals, chemical spills and contaminated water or food.

User-friendliness: 89% of NFPs felt that the 24-hour timeline for notification was reasonable, but 40% of NFPs reported that they were required to obtain clearance from two to three persons or offices, which contributed to delays in notification; 67% of NFPs used the English version of Annex 2; most NFPs felt that Annex 2 criteria were clear, but could benefit from refinements in the decision instrument and checklist to prevent difficulties in interpretation; more than 90% of NFPs supported the development of an online platform to expand assessment and notification options, communicate with NFPs from neighbouring countries and share documents.

The Review Committee highlights the following observations:

- Many countries have intricate clearance processes, and notification appears to have a high threshold in some countries, which may imply a risk of political interference in the epidemiological assessment.
- NFPs need further guidance and their functions need to be strengthened. The new guidance document on IHR Annex 2 is therefore welcome. An update of the 2007 guidance on the NFP function, including examples of good practices, might be equally beneficial, as would further online training.
- Clarification is required that an NFP is a function of the State Party, and not necessarily an individual. The NFPs need to have access to information from national surveillance and early warning systems.
- The *IHR Quarterly Bulletin* is useful to NFPs.
- The EIS could be used also for guidance and messages to NFPs.
- Some WHO Regional Offices hold annual meetings for the NFPs, an excellent forum for education, discussion and creating an *esprit de corps*.

Box 3.2. **Survey on the use of Annex 2 of the IHR**

Objective: To explore the reliability and validity of the notification assessment process under the IHR.

Methods: 193 of the 194 States Parties were invited to provide a notification assessment for 10 fictitious public-health event scenarios by applying the Annex 2 decision instrument. Responses were collected through a multilingual online survey in November and December 2009. Seven experts representing all WHO regions were invited to complete the survey and their responses were treated as a gold standard. Consensus, defined as agreement among NFPs, and concordance, defined as agreement between NFPs and the expert panel, were examined. High consensus or concordance was arbitrarily defined as >70% of respondents agreeing on a given answer.

Results: Response rate and demographics: The survey was completed by 142 States Parties (response rate 74%). Half of respondents were medical doctors, and one third described themselves as epidemiologists. Twenty-six (18%) participants said they had not applied Annex 2 in the past 12 months, 72 (51%) indicated that they had applied it rarely, 20 (14%) once a month and 23 (16%) at least once weekly.

Consensus among NFPs: The median consensus for notification decisions was 78% (interquartile range 55–82%). There was higher overall agreement on which events to notify (median 80% [76–91%]), than on which not to notify (median 55% [54–60%]). In the assessment of the individual decision instrument criteria, consensus was high (>70%) on 24 of 36 occasions (67%).

Concordance between NFPs and expert panel: Concordance between NFPs and the expert panel was high for the five scenarios that were deemed notifiable by the panel (median 82% [76–91%]), but much lower (median 51% [42–60%]) for the four scenarios that were not deemed notifiable by the expert panel. NFPs' specificity was significantly lower than their sensitivity. In the assessment of the individual decision instrument criteria, there was >70% concordance on 18 of 36 occasions (50%). Of note, concordance was limited (<55%) in the assessments of the third criterion on five occasions (significant risk of international spread).

Limitations: These results tell us only what respondents think should be notified under the IHR, not what would be notified in reality. The condensation of real-life events into short fictitious scenarios necessarily involves a high degree of simplification. Finally, the gold standard proposed in this study cannot claim to provide answers that are universally correct or applicable to all settings.

Source: Haustein T, et al. Should this event be notified to the World Health Organization? Reliability of the International Health Regulations notification assessment process. *Bulletin of the World Health Organization*. 2011; 89: pp. 296-303.

Function 3: WHO detection and alert operations

The Review Committee wanted the following:

- an understanding of the flow of information on public-health events (hazard detection and risk assessment, also known as epidemic intelligence), including the extent to which the IHR have enabled WHO to receive better, more timely information;
- to know the main information sources; how the information is handled in WHO; and how WHO shares the information;
- an assessment of WHO's challenges in sharing event information with States Parties through the EIS;
- to know whether the IHR have led to increased interagency collaboration in detecting, verifying and responding to events.

The Committee examined evidence from: WHO documents; interviews with WHO staff at regional and headquarters level, and with representatives of international organizations; case studies on the use of IHR; and a demonstration of EMS.

Box 3.3. **WHO databases study for the review and evaluation of the functioning of Annex 2 of the International Health Regulations**

Objective: To evaluate WHO's experience of event surveillance since 15 June 2007, including the relationship between notified events and other events recorded by WHO.

Methods: Review of event-related databases at WHO headquarters and Regional Offices on communications, assessments and outcomes of public-health events that were reported to or identified for follow-up by WHO between 15 June 2007 and 1 January 2009.

Findings: Of 684 events recorded by WHO during the study period, 107 (16%) events were reported first by the NFP. This proportion increased over time. Among these, 23 (22%) reports provided evidence that Annex 2 was used by the notifying State Party. Of the 107 reports, six (6%) resulted in WHO providing information to all States Parties through the Event Information System and 28 (26%) States Parties received assistance from WHO in response to the event. Of 201 events requiring verification from States Parties, 11 (6%) resulted in an Event Information System posting and 52 States Parties (26%) received assistance from WHO in response to the event.

WHO receives information on events from its own surveillance, NFP notifications or consultations, and other sources. When the source is not an NFP, WHO is obliged to request the relevant States Party to validate such information. WHO might, for example, seek confirmation from the States Party that an acute public-health event is occurring. If the source is an NFP or another responsible national authority – information that appears on a government web site, for example – WHO does not seek verification but jointly assesses the risk immediately with the States Party. This process involves assembling and assessing epidemiological evidence and other relevant data to determine the likelihood of spread or extension, and the adverse health consequences that may result from the event. There are clear procedures on how WHO can share information on events with other States Parties and with the public.

Findings

Even before the IHR came into force, there had been major advances in WHO's epidemic intelligence functions, with the development of the EMS, an increase in Regional Office capacity and the Global Outbreak Alert and Response Network (GOARN). Information sources in the public domain, such as news media web sites, remain an important source of initial event information for WHO. The procedure set forth in Articles 9 and 10, which enables WHO to take into account reports from sources other than notifications or consultations, works well.

After a brief decline in information flow when the IHR came into force, information from official sources gradually increased as the NFPs were established and their roles clarified. The decline in information sharing does not necessarily signal a reluctance of States Parties to share information, but may indicate only that unverified information appears in the news sooner than NFPs are able to supply an IHR notification to WHO. The median interval between WHO's verification request and the response by States Parties was less than one day in 2007 and 2008, while the mean was days owing to a few events with long response times. States Parties should, however, strive to be the earliest source of event information through the NFPs.

In 2009 WHO's initial information on an event originated from the following sources (percentage of events): open sources (35%); NFPs (33%); other sources in the government

of affected country (7%); WHO or other United Nations (UN) agencies (22%) and WHO partner agencies (3%).

The North American collaboration in the early phases of the 2009 pandemic shows that the IHR, whose formal reporting and exchange requirements may be thought to create delays, can efficiently support global early-detection and risk-assessment functions. In the early days of the outbreak, there was effective informal contact among WHO and the Pan American Health Organization (PAHO) and NFPs, with prompt notification by the NFPs. Further, the formal notification process worked well in the United States of America, Mexico and Canada. It is important to sustain the momentum of NFP reporting that was stimulated by the pandemic.

WHO also has improved interagency cooperation with the World Organisation for Animal Health (OIE), the Food and Agriculture Organization of the United Nations (FAO) and other UN organizations in detecting and verifying events.

Although WHO has a broad mandate to share urgent information on public-health events, WHO usually obtains agreement first from the affected State Party. The process of consulting with States Parties may delay posting on the EIS.

There is an inherent tension between WHO's obligation to inform other States Parties and the affected State Party's interest in avoiding potential social and economic consequences. WHO tries to balance these priorities and sensitivities through dialogue, respecting the requirements in Article 11. For the EIS to become an even more valuable tool, States Parties should be more willing to let WHO share information.

The WHO EMS was developed to track information on public-health events. This web-based system is being extended to WHO Regional and Country Offices to share information about acute public-health events. This extension should be accompanied by an evaluation of whether the EMS at all levels has achieved the proper balance of sensitivity and specificity.

Information in EMS is fed to three other sources of information for specific audiences: the EIS, the GOARN newsletter and the Disease Outbreak News (DON) on WHO's public web site. The EMS lists many more events than those communicated through these three channels, since only some EMS events are required to be communicated under Article 11. In the first months of the pandemic, the EMS proved a useful record of WHO's first detection of rumours of acute respiratory illness, the first notified cases by country, Situation Reports and actions, and decisions taken in response to the pandemic. Because the EMS provides a global overview, WHO can link events that might initially appear unrelated or that might not be assessed as having potential international concern, were those events to be reviewed only at a national level. EMS, if used consistently and in a timely fashion by all relevant WHO staff, provides a record of the chronology of events, and becomes an information audit trail that links the actions and decisions taken with the information available at the time.

The Review Committee supports WHO's creation of an open-source version of the EMS available to States Parties, or a States Parties interface with the WHO application to support IHR communications. This expansion may be accomplished through the Information and Communication Technologies Tools for Public Health Emergency Management project, a joint undertaking between WHO's Global Alert and Response, and Information Technology and Telecommunications departments. This project aims

to create a community of practice that will make available open-source information and communication technology tools that are designed to support epidemic alert and response activities.

States Parties need to be aware of public-health risks around the globe. For this international epidemic intelligence, the EIS and other systems, such as ProMED and the Global Public Health Intelligence Network, are used. The EIS has the potential to be the global hub for all national public-health authorities on epidemic intelligence. One valuable innovation during the pandemic was the EIS being used to share regional, rather than national, Situation Reports. Developing the potential of the EIS would require the inclusion of expanded information on more events. For instance, for each event there could be maps, expanded risk assessments and recommendations and links to relevant WHO guidance and Collaborating Centres. Also, the EIS should contain all temporary and standing recommendations issued under the IHR as well as information on Member States that institute additional measures and their rationale for these or the status of WHO's request for such a rationale. These suggested enhancements of EIS content would require a significant investment of time and resources to support good public-health practice. If the EIS is not enriched in this way, other non-WHO systems of poorer quality will assume pre-eminence.

Function 4: International public-health response

The Committee wanted to know the extent to which the IHR have increased assistance and collaboration between WHO and States Parties during a public-health event, and how much they have helped to promote interagency collaboration.

Findings

WHO reports that States Parties are becoming increasingly aware of WHO's operational and response mechanisms for managing public-health emergencies. Accordingly, the ability to coordinate large-scale events has grown.

At least a decade before the IHR came into force, WHO established assistance mechanisms at headquarters and in Regional and Country Offices. Examples include distributing meningococcal and yellow-fever vaccines from the global stockpile, providing equipment and enabling access to expert networks for advice and to WHO Collaborating Centres for laboratory diagnosis.

GOARN, which serves as a primary mechanism for WHO to assist Member States during a public-health event, is described in Chapter I. The network is used to coordinate international response with technical institutions, and to deploy experts who assist national authorities in investigating and controlling outbreaks. GOARN supports the IHR by upholding the principles and procedures that were established when the network was launched in 2000.

While GOARN is acknowledged to be highly effective, what is needed to augment WHO's capacity to respond to a longer-term event is a reserve global health emergency workforce, trained in advance, and able to be seconded for up to 24 months. This team would be deployed in a PHEIC and sent where needed. WHO would organize special training, handle requests for this emergency assistance and mobilize needed elements of the workforce.

In recent years, WHO has experienced funding shortfalls that limit its capacity to respond to long-term public-health emergencies. Most funding that is provided to WHO by Member States and donors is earmarked for particular purposes and cannot be diverted. During the PHEIC, key WHO staff were obliged to devote time and energy to obtain funds urgently needed for its response. WHO expended more than US$ 75 million on the immediate response to the pandemic. This figure is apart from the costs of vaccines and drugs.

The Review Committee proposes the creation of a contingency fund, established in advance, that could be accessed without undue delay in the event of a PHEIC. The fund would be released in part or in whole, based on approval of a plan for expenditures and accountability prepared by WHO. Its purpose would be to assure WHO's ability to respond quickly, to deploy the specially trained emergency workforce where needed and to provide the level of communication, scientific and logistical support required in the regions over the longer term. It is not envisaged that this fund would be the source of monies used to purchase vaccines or antiviral drugs in the case of a pandemic. The precise conditions for use of the fund should be negotiated among Member States in consultation with WHO.

The IHR provide a framework for strengthening all aspects of international collaboration in preparedness and response, and for assistance from WHO. International organizations also report that the IHR have promoted closer relationships with WHO. These include the OIE, FAO, the International Civil Aviation Organization and the International Atomic Energy Agency. There are several examples of interagency collaboration in response to events as well as in policy and planning development.

Close relations with OIE and FAO are essential. As noted in testimony to the Review Committee, the links between WHO, OIE and FAO have been strengthened by the IHR and were important in the early days of the pandemic. The FAO/OIE Crisis Management Centre for Animal Health collaborates closely on WHO's alert and response mechanisms to coordinate field missions and enhance information exchange about field-related activities.

The IHR require States Parties to notify public-health events to WHO and, following a joint risk assessment, make it possible to share event-related information through WHO with all States Parties. However, with notification comes the concern that the country in question may find travel, tourism and trade adversely affected. To counter this risk, the IHR regulate the measures that other States Parties may implement in reaction to the event and provide for assistance and support by WHO and other States Parties to the affected country.

WHO can exert more leadership to drive this assistance, which is a cornerstone of the IHR. Although NFPs are gradually fulfilling their role at the core of the IHR activities, their role in mobilizing assistance has not been fully realized.

If all States Parties encourage their technical institutions to participate in GOARN and other international networks, this may result in significant additional international technical capacity and support. GOARN communications could be shared with all NFPs if this would help mobilize international support and experts.

Function 5: Procedures for Public Health Emergencies of International Concern

The Director-General determines whether an event constitutes a PHEIC and issues temporary recommendations after hearing the views of the States Parties directly affected and those of an Emergency Committee (EC) established to provide expert advice. Detailed provisions in the IHR lay out the terms of reference and composition of the EC.

The Review Committee wanted to know the following:

- whether the IHR procedures were followed in establishing the EC and determining the PHEIC (Article 12) on 25 April 2009;
- how members of the EC were selected;
- how the temporary recommendations were developed and communicated;
- to what extent States Parties followed these recommendations.

Background to the Emergency Committee

Constitution: As stipulated in Article 48, the Director-General selects the members of the EC from the IHR Roster of Experts, which consists of people nominated by Member States or directly by the Director-General under WHO Expert Advisory Panel regulations. Members are selected on the basis of experience and expertise relevant to the event under consideration. For this EC, relevant areas of expertise that were chosen for inclusion were acute respiratory syndromes, influenza, virology, epidemiology, laboratory practices, modelling, antiviral drugs, drug resistance, infection control, vaccines, airports, ports, aviation and maritime issues. Equitable geographical representation, as specified in Article 48, was sought, as was a balance between genders and developed and developing countries. In addition, representatives of Member States, including Mexico and the USA, the States Parties in which the outbreak began, were invited to participate, as required by Article 48. One adviser, who is also on the Roster of Experts, was invited to participate.

Roles and responsibilities: The EC's purpose is to provide views to the Director-General. Because its role is advisory only, the Director-General is responsible for final determinations. EC members were obliged to keep proceedings of meetings confidential, and not to disclose any documents or other information received. Along with their letters of invitation, members received instructions on their working methods, which specified the private nature of the meetings and the international status of members, which required them to act as international experts serving WHO exclusively, not as representatives of their governments or any other authority. The names of EC members were not made public until the Committee had finished its work, as is common practice at WHO for Expert Committees. The EC was disbanded when the PHEIC was declared over and the members' names were released.

Meetings: All meetings were conducted by teleconference, with the exception of one that was done by e-mail. The EC was convened nine times between 25 April 2009 and 10 August 2010 when the PHEIC was declared over. The Director-General held a teleconference with the chair, vice-chair and rapporteur on 29 April 2009, which replaced a previously scheduled meeting of the full Committee. The full Committee met four times before pandemic Phase 6 was declared on 11 June 2009. Between 11 June 2009 and 10 August 2010 it met four times (8 September 2009, 26 November 2009, 23 February 2010 and 1 June 2010).

An agenda and background materials, including questions for which the Director-General sought advice, were circulated by e-mail in advance of the meetings. All meetings were chaired by Professor John Mackenzie. Affected States briefed the EC with the latest information from their countries and WHO's Secretariat updated members on the current epidemiological situation. The chair then conducted discussions, generally calling upon members in alphabetical order. Decisions on the group's views to the Director-General were made by consensus.

A draft statement by the Director-General was discussed and circulated for final approval shortly after the meeting adjourned. After approval, the statement was posted on the secure WHO EIS, with alerts sent to all NFPs. It was then published on the WHO public web site.

Declaration of the PHEIC

The Director-General convened the first meeting of the EC on 25 April 2009 and asked members to advise whether the current situation constituted a PHEIC. Article 12.4, which members received via e-mail as part of a package of background documents, sets out the considerations for the Director-General in determining a PHEIC. These include information provided by the State Party where the event is occurring; the decision instrument contained in Annex 2; the advice of the EC; scientific principles, the available scientific evidence and other relevant information; and an assessment of the risk to human health, the risk of the international spread of disease, and the risk of interference with international traffic.

At the first meeting, representatives from Mexico and the USA reported that a new influenza virus, antigenically and genetically different from other influenza viruses, was being transmitted from human to human effectively enough to cause outbreaks rather than isolated, sporadic cases. It appeared to spread rapidly, demonstrating the risk of a potential pandemic virus.

The EC requested updates on the clinical, virological and epidemiological situation in Mexico and the USA, as well as on the spread to neighbouring countries. Specific areas of inquiry were: clinical severity and geographical location; virus characterization; transmissibility; details of laboratory samples sent to Canada and the USA; control measures and travel advice. The consensus of the EC was that a PHEIC was occurring but that additional information would be needed to raise the alert level from Phase 3 to Phase 4.

Temporary recommendations

The criteria provided in the IHR to determine temporary recommendations include: the views of the States Parties directly concerned; the advice of the EC; scientific principles and available scientific evidence; health measures that are not more restrictive of international traffic, and not more intrusive to persons than reasonably available alternatives that achieve an appropriate level of health protection; a risk assessment appropriate to the circumstances; and relevant international standards and instruments, and activities of other intergovernmental organizations and international bodies. Temporary recommendations, if not extended, expire automatically three months after they have been issued.

The temporary recommendations issued during the 2009 pandemic were the first under the IHR (Table 3.1). They were included in the formal Director-General statements that

Table 3.1. **Temporary recommendations issued during the pandemic**

Date	Recommendations
25 April 2009	"Concerning public-health measures, in line with the Regulations the Director-General is recommending, on the advice of the Committee, that all countries intensify surveillance for unusual outbreaks of influenza-like illness and severe pneumonia."
27 April 2009	"The Director-General recommended not to close borders and not to restrict international travel. It was considered prudent for people who are ill to delay international travel and for people developing symptoms following international travel to seek medical attention." "The Director-General stressed that all measures should conform with the purpose and scope of the International Health Regulations."
24 September 2009	"Having considered the views of the Emergency Committee, and the ongoing pandemic situation, the Director-General determined it was appropriate to continue these temporary recommendations, namely: • countries should not close borders or restrict international traffic and trade; • intensify surveillance of unusual flu-like illness and severe pneumonia; • if ill, it is prudent to delay international travel; • if ill after travel seek care."
26 November 2009	"Having considered the views of the Emergency Committee, and the ongoing pandemic situation, the Director-General determined it was appropriate to continue all three temporary recommendations, namely: • countries should not close borders or restrict international traffic and trade; • intensify surveillance of unusual flu-like illness and severe pneumonia; With an updated third recommendation, namely: • if ill, it is prudent to delay travel."
24 February 2010	"Having considered the views of the Emergency Committee, and the ongoing pandemic situation, the Director-General determined to continue the three temporary recommendations, as modified, namely: • countries should not close borders or restrict international traffic and trade; • maintain surveillance of unusual flu-like illness and severe pneumonia; • if ill, it is prudent to delay travel."

followed EC meetings. In the first two statements, however, the term "temporary recommendations" was not used, although reference was made to the IHR.

Findings

The Review Committee noted that the 2009 influenza pandemic is the only event deemed a PHEIC by WHO since the IHR entered into force. The IHR provide for a system of global epidemic intelligence. Given the definition in Article 1 of the IHR, several other events could have been declared a PHEIC, because they were extraordinary, constituted public-health risks to other States through international spread and potentially required a coordinated international response. Such events might have included such examples as Nipah virus in Bangladesh in 2009; cholera in Haiti in 2010 and poliomyelitis in central Asia in 2010.

To realize the full potential of the IHR, WHO could remind States that the IHR cover more than PHEICs, and include routine public-health functions. It appears that WHO has chosen to set a rather high threshold for the declaration of a PHEIC, probably because the process of declaring one proved to be resource-intensive. In practice, WHO's perceived need to issue temporary recommendations will be the main driver for declaring PHEICs. The risk is that this part of the IHR is seen as an instrument for only those events as rare as a global influenza pandemic.

The Review Committee found that WHO properly activated the IHR procedures for a PHEIC for the first time, convening an EC within a 48-hour time frame. The Review

Committee also found that IHR rules were followed in issuing temporary recommendations, although the temporary recommendations were not initially explicitly identified as such. Because temporary recommendations have specific legal implications, they must always be clearly identified as such, both on the public web site and on the EIS.

The Review Committee asked members of the EC by e-mail for their views on their experience of the Committee, its establishment, its way of operating and its effectiveness. Their views on the requirement for EC members to remain anonymous were particularly sought. Eight members of the 15-member Committee and one adviser responded to the e-mail.

Respondents agreed that the expertise of members was appropriate and that the meetings worked reasonably well, with processes that were open and included extensive consideration and debate. Although some members raised national issues for discussion, the general focus was on international issues. No pressure by third parties was apparent to any of the responding participants.

Respondents were critical, however, of some aspects of the EC process. The chair of the EC told the Review Committee that the EC was limited by its mandate in the provisions of the IHR and "did not exist outside meetings". This meant the EC could not independently call a meeting or act on its own initiative, and was restricted to giving its views only on request. Some respondents felt the decision to announce Phase 6 was unduly delayed. None suggested that the announcement was premature.

Professor Mackenzie, the EC chair, said in his interview with the Review Committee that at the World Health Assembly in May 2009, "Several countries made quite an impassioned plea that we didn't move to Phase 6 [until there was] good evidence of sustained transmission in some of the other countries ... going from Phase 5 to Phase 6, there are a number of ramifications, and I think that we really wanted to be absolutely certain before we jumped to that level."

Respondents observed that the EC was charged with making epidemiological conclusions that had political and financial ramifications. Some suggested that there should be separate groups of scientific and policy advisers for future ECs.

On the subject of EC members' anonymity, five respondents said names should be disclosed, in part on the grounds that greater transparency might lead to greater confidence in the recommendations. They noted that WHO's reputation has been damaged by nondisclosure, which will lead to greater pressures in the future. Some noted that if names were to be disclosed, WHO would need to support members on legal issues and in media relations.

Four respondents, including the chair, said that names should not be disclosed. In his testimony to the Review Committee, Professor Mackenzie said:

> "I think very strongly that ... the Committee should be anonymous, having served with WHO over SARS (Severe Acute Respiratory Syndrome) and knowing the kind of pressure people are under both from pharma [and] from companies wanting to do diagnostics and so on, as well as countries themselves concerned about what's happening, do they have the right diagnostics and so on? The pressure the EC could be under would be enormous, and I think the anonymity, if you like, of the Committee is absolutely essential for those conditions ... I think that although it's not actually written as part of the terms of reference of the EC, in terms of Articles 48 and 49, I think it would be useful if that, in fact, was part of the actual documentation."

The Review Committee appreciates the desire to protect members of the EC from external influence by keeping their identities confidential for the duration of their appointment. The Review Committee also appreciates the need for expert consultations to be held in confidence so that the Director-General will have the benefit of candid discussion and advice. At the same time, the lack of disclosure fosters suspicion about the interests and motivations of members of the EC. On balance, the Review Committee concluded that, in the interest of transparency, it would have been better for WHO to have disclosed from the outset the names of EC members. The Review Committee acknowledged that it would have been difficult for WHO to alter its policy of nondisclosure at a later time in part because of a reluctance to appear to give in to critics of nondisclosure. Anonymity is consistent with WHO practices for other expert committees, whose members' identities are normally divulged only at the end of what is often a one-day consultation. However, this practice was not well-suited to a Committee whose service extended over many months.

The Review Committee also concluded that a broader spectrum of expertise among EC members might have been useful, including in risk communication. The Review Committee acknowledged that WHO must appoint an EC with a set of skills and expertise that is appropriate for and particular to each event for which it is constituted. For an influenza pandemic, this expertise would include virology, laboratory assessment, epidemiology, public-health field and leadership experience, veterinary science, risk assessment/communication and methodological expertise in systematic reviews of the scientific literature.

WHO also lacked a sufficiently robust, systematic and open set of procedures for disclosing, recognizing and managing in a timely fashion conflicts of interest among EC members. Five members of the EC and an adviser declared potential conflicts of interest. None of these was deemed sufficiently important to merit the exclusion of any of the members. The relationships in question were published, along with the names of the members of the EC, when the pandemic was declared over on 10 August 2010. Before this information was published, however, assumptions about potential ties between EC members and industry led some critics to suspect wrongdoing. The Review Committee recognized that WHO is taking steps to improve its management of conflicts of interest, even as this review has proceeded.

Finally, at a critical point of decision-making on the pandemic (moving from Phase 4 to 5), the Director-General conferred with only a subset of the EC (chair, vice-chair and rapporteur) rather than inviting input from the full Committee.

Function 6: Avoidance of unnecessary interference with international traffic and trade

The IHR require States Parties to implement certain health measures without delay. In some conditions, States Parties may implement additional health measures, as long as they inform WHO and provide the public-health rationale. In such circumstances, WHO may also request the country to reconsider the application of such measures.

The Review Committee wanted to know to what extent States Parties implemented health measures in addition to the temporary recommendations during the 2009 pandemic, whether they provided a rationale for these, and how WHO dealt with them.

Findings

One of the temporary recommendations issued on 27 April 2009 that remained unchanged until the end of the PHEIC, was "not to close borders and not to restrict international travel". In the early stages of the 2009 pandemic, there was heightened concern about international transmission of the disease, resulting in public-health authorities in many countries deciding to take measures to prevent or delay introduction of the virus. WHO has surveyed States Parties, airports, airlines and shipping operators, and found that most of the responding countries provided information, in the form of posters or leaflets, to incoming travellers. During the early stages of the pandemic, 34 of 56 (61%) responding countries screened incoming passengers for disease. In most of the countries, screening was combined with isolation of suspected or confirmed cases and quarantine of their asymptomatic close contacts for 3–10 days (median eight days) *(5)*.

Two of the surveyed countries, one each from the Region of the Americas and the European Region, reported denying entry to people from affected countries. Six out of the 56 surveyed countries (11%) reported restricting the entry of animals or goods from affected countries.

According to the report, five out of the 56 surveyed countries reported having denied *free pratique* to at least one mode of transport, mostly owing to the presence of ill people on board. These responses corresponded to the experiences of a few ship operators and airlines that were refused permission to embark or disembark passengers or crew because of illness or having visited affected countries.

Half of the countries recommended that their citizens avoid travelling to affected countries during the early stages of the event; the median duration of travel advisories was five weeks. There were also some rare instances of flights to affected countries being cancelled.

In the *Weekly Epidemiological Record*, WHO commented: "The results suggest that measures introduced at borders changed during the first four months of the pandemic, showing that countries adapted to changing epidemiology and recommendations. Early in the pandemic, a few countries instituted travel and trade restrictions, and almost half recommended avoiding travel to areas affected by the pandemic; however, these restrictions and advisories were generally discontinued after a few weeks, suggesting that strategies shifted from a broad precautionary approach to more focused response measures implemented at points of entry. Control measures later shifted to communities as more information about the pandemic virus became available, perceptions of risk changed, and community transmission became more prevalent." *(5)*

During the pandemic, WHO documented the reports of trade and travel measures in its weekly Situation Reports. Although several countries, but not all, provided a rationale upon request by WHO, it appears that no country that implemented additional measures (i.e. measures that significantly disrupted international travel or trade by more than 24 hours) complied with their obligations under Article 43 to proactively inform WHO and provide the rationale for such measures. When responses were received, the explanations were made available to all States Parties on the EIS.

WHO did not receive any formal complaints from any country on additional measures. During the pandemic, some States Parties instituted measures beyond the temporary recommendations with respect to article 43 of the IHR, although none of them submitted at

their own initiative the public-health rationale for such measures and not all did so after a request by WHO.

The International Air Transport Association (IATA) submitted this statement to the Review Committee: "In many cases, Member States did not notify WHO [of additional measures and WHO] found out by third parties. The RC assumes that WHO did not energetically seek to obtain the rationale, while they certainly did, at least in one case that we are aware of … the flaw is in the IHR itself and not in WHO… if one of the objectives is to evaluate the functioning of the IHR, and meeting that objective requires a recommendation to modify the IHR, we believe that recommendation should be made."

The Review Committee notes the concern raised by IATA, but considers that, on balance, more rigorous implementation of the existing provisions in Article 43, by both States Parties and WHO, rather than amending the IHR, remains the best solution at this time. However, before considering amendments to the IHR, an intermediate step could be for WHO to ensure that countries implementing additional measures are identified on the EIS, that the public-health rationale for such measures is placed on the EIS and, if no rationale has been provided, that the EIS note on what date this information was requested. The EIS could also include clarification as to whether or not WHO has requested the country to reconsider the application of such additional measures. In the absence of sanctions for IHR non-compliance, this increased transparency would mitigate concerns about the adoption of measures that significantly interfere with international traffic.

On 27 April 2009 WHO stated: "Given the widespread presence of the virus, the Director-General considered that containment of the outbreak is not feasible. The current focus should be on mitigation measures." Still, several Member States instituted measures aimed at containing the virus, or at least delaying it from entering their territories. Clearly, some of these measures, as described above, constituted additional measures, according to Article 43.

Article 43 can be regarded as a cornerstone of the IHR. It protects affected countries against overly restrictive measures. In this respect, the IHR have the potential to improve international coordination of responses and minimize the application of restrictive measures at borders. Despite these provisions, the first country affected by the pandemic (Mexico) experienced several restrictions, such as cancelled exports of swine and cancelled flights.

Function 7: Implementation of the IHR with respect for human rights

State Parties shall implement the IHR with respect for human dignity, human rights and fundamental freedoms of persons (Article 3). This is especially relevant in the treatment of travellers at points of entry (Article 23 and 31).

The Review Committee wanted to know whether there were known instances (e.g. complaints from individuals) where human dignity, human rights and fundamental freedoms of persons have not been respected in implementing the IHR.

Findings

There is no systematic monitoring by WHO of instances where human rights are not respected in implementing the IHR. Furthermore, WHO does not have a mandate to investigate whether particular measures constitute violations of this provision in the IHR.

During the pandemic, there were media reports of travellers being quarantined and detained as a consequence.

It appears to be a weakness that WHO does not monitor whether human rights are being respected in implementing the IHR. Even if WHO does not have a mandate to investigate, it is in the spirit of the IHR for WHO to consult with States Parties when the media report practices that may be seen as violations of human rights and, in turn, the IHR. Such respect is important for public acceptance of the IHR.

Function 8: Points of entry and travel documents

The IHR have detailed provisions for health measures at borders for travellers and conveyances, for charges (Articles 40–41) and health documents (Articles 35–39).

Under Articles 19 and 20 of the IHR, States Parties must designate airports and ports expected to develop certain public-health capacities, and ports that are authorized to issue certificates to ships.

The Review Committee wanted to explore what has been learnt about the implementation and functioning of the IHR at points of entry, including the handling of documents for conveyances and health documents for passengers. The Committee also sought to learn whether States Parties understood and complied with the IHR requirements for points of entry (Articles 19 and 20 and Annex 1b). Finally, the Committee wanted to know what the IHR meant for WHO's partnerships with FAO, OIE, the World Tourism Organization and other relevant organizations (Article 14).

The Committee sought evidence on these issues from WHO documents, interviews with WHO staff at Regional Offices and headquarters, interviews with States Parties, statistics from States Parties' responses to the IHR Monitoring Framework and statistics on activity at authorized ports.

Findings

Some of the topics covered by Function 8 are relatively new and undeveloped, both for WHO and many States Parties. The greatest challenge for States Parties has been to coordinate the new requirements on emergency preparedness stemming from the many international agreements in force, such as those in the transport, maritime and aviation sectors.

Requirements to develop guidelines on ground crossings, for example, are complex undertakings for countries in the European Union, the Americas and Asia that already have subregional and regional agreements affecting such crossings.

The Review Committee found that IHR Annex 1B provides clarity on what is required to reach core response capacities, but intersectoral collaboration and coordination need to be strengthened to help countries build these capacities for the 2012 deadline. Countries had experience with public-health functions at points of entry under the old IHR (1969). The focus of the IHR (2005) is to ensure a range of capacities at all times at Points of Entry.

The IHR provide a mechanism to designate a competent authority to coordinate preparedness at each point of entry. Designating points of entry at airports, ports and ground crossings has proved difficult for some countries owing to resources. A complete picture

is not available because only a limited number of States Parties have responded to WHO's requests for this information.

Guidance and procedures are needed for the certification of ports and airports. Certification places enormous demands on resources. For example, there are about 4000 ports handling international shipping. WHO is aware of 80 countries that have 1800 ports authorized to issue ship-sanitation documents.

Japan, in testimony before the Review Committee, noted that some vessels arriving at its Points of Entry presented ship-sanitation certificates issued from ports not listed on the WHO web site. This may simply be an administrative problem, but it serves as a reminder to all States Parties with ports to ensure that they comply with the provisions of Article 20 of the IHR.

The USA recommended in its testimony that WHO continue to facilitate the development and implementation of a communication and information-sharing system to connect competent authorities at designated international points of entry. This is not intended to diminish the important oversight role of the NFP, but to improve routine communication.

Article 27 of the IHR requires that the next point-of-entry authority be informed when there is an affected conveyance. Countries have asked for the contact details of point-of-entry authorities to allow them to perform this requirement. The IHR do not stipulate that this communication go through the NFP. It is not desirable to overload the alert system with routine follow-up measures, which is why countries are asking to be able to make their own decisions. WHO is proposing to update the port list to enable a search for contact details voluntarily provided by countries.

The Maritime Declaration of Health and the Aircraft Declaration of Health can be used as communication tools under the IHR framework. Many Member States wish to use a health declaration card during public-health emergencies. IATA reported that as there was no recommended card, during the pandemic many different types were created, causing complications for airlines. IATA has proposed that documents such as health declaration cards and passenger contact tracing cards be harmonized. This is not required under the IHR but would be complementary to the Aircraft Declaration of Health.

International collaboration is critical to fulfil the requirements of this function, but it is a complex one owing to overlapping and competing mandates, and to the need for public-health to be balanced with other considerations. Most of these relationships work well but roles and responsibilities could be more clearly delineated. WHO collaborates with FAO and OIE on food-safety issues in international transportation. During the pandemic, technical cooperation between the International Civil Aviation Organization, World Tourism Organization, IATA and the Airports Council International worked well and enabled rapid production of documents.

B. Pandemic preparedness, response and evaluation: country level

From 1995–2006, public funding for health-related expenditures provided by national governments and development-assistance sources increased by almost 100% overall *(6)*. However, the global financial crisis, which began in 2007 and escalated in 2008, raised

concerns about possible effects on global health as countries tightened budgets and donors reviewed their portfolios. Low-income countries, in particular, depend on donor financing for health expenditures *(7)*. WHO examined these concerns during a high-level consultation convened in January 2009 – barely three months before the start of the H1N1 pandemic. The consultation noted the myriad ways in which health can be affected during economic difficulties; reinforced the critical importance of maintaining health investments and identified actions at country, regional and global levels to mitigate associated effects on health *(8)*. A heterogeneous picture has emerged among countries with respect to health sector resources. Some countries have decreased social spending while others have increased it or made no changes *(9)*. The financial crisis has challenged health leaders to make the health of its people, especially the most vulnerable, a priority.

After the SARS outbreak and in view of the threat posed by avian H5N1 influenza, WHO and countries began to prepare for an influenza pandemic (see Chapter I). To assess the status of this preparation, WHO did an internal review of 119 national plans, using a structured 88-item checklist. The assessment found that 68% of plans were constructed around WHO pandemic planning phases as outlined in the 2005 WHO plan. Although 72% of countries had established national committees for pandemic preparedness, only 13% and 5% had established subnational committees and plans, respectively. Only 8% of countries had tested their pandemic plans by conducting exercises before the 2009 pandemic. Only about half of countries had identified country-specific triggers for activating national response systems (Fig. 3.1).

Some countries face special challenges in influenza preparedness. Some developing countries may find plans used by developed countries not appropriate for them. Countries with limited resources need tailored, practical tools *(10)*. An analysis of six Asian countries conducted in 2008 showed that the anticipation of an avian influenza outbreak had focused attention on improved surveillance and case detection in pandemic planning. Existing protocols, however, needed greater flexibility to accommodate changing circumstances of transmission. Further, the ability to translate plans into operations appeared limited *(11)*.

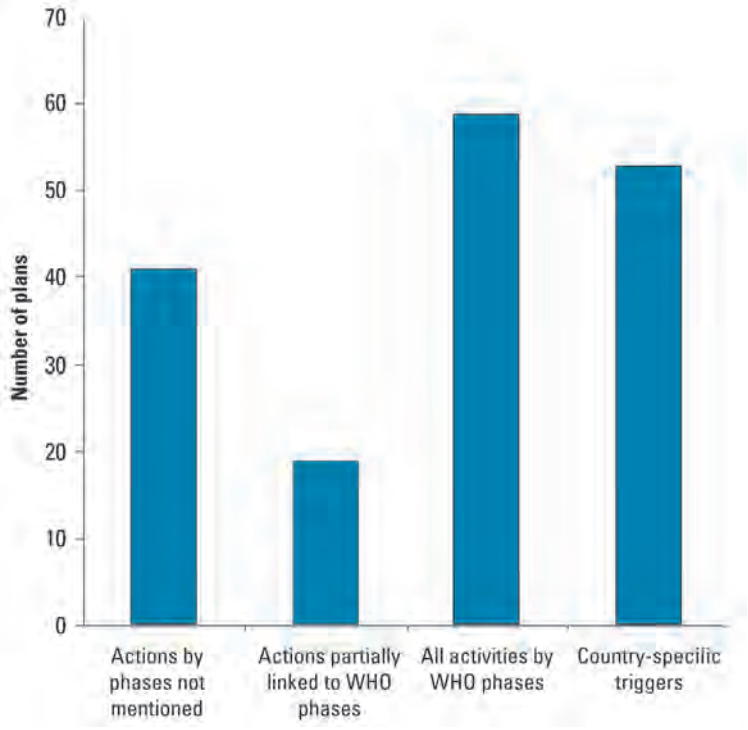
Findings: evaluation of the pandemic response

The Review Committee heard that reviews of the response were conducted by countries, WHO Regional Offices, and independent reviewers. All these acknowledged the value of planning, and the reports showed that some countries had effective and well-tested plans. Despite comprehensive guidelines from WHO, however, and the training it supported, particularly through the Regional Offices, not all countries had developed effective plans. Countries generally had sufficient resources to respond to the pandemic, but recognized that they would have had difficulty in a more serious situation. There was insufficient emphasis on multisector planning and business continuity in the health sector and beyond.

A report from the Caribbean in September 2009 concluded, like others, that:

> "Most countries were somewhat prepared to respond to a potential crisis. The preparedness efforts undertaken by the countries/territories in the Caribbean subregion since the onset of the H1N1 pandemic facilitated an effective response to the pandemic in its mild form. The lessons learned and shared experiences have alerted countries to the need to re-assess their disaster preparedness and response plans for mitigation of the potential impact of a severe H1N1 pandemic in the Region." *(12)*

Fig. 3.1. **Country-specific triggers**



A report from the WHO Regional Office for the Eastern Mediterranean (EMRO) in April 2010 stated that almost all countries in their region had developed pandemic preparedness and response plans. EMRO noted that these plans had been developed from the perspective of the health sector without full engagement of the non-health sector, and that few plans had been updated for pandemic H1N1.

A presentation made at a WHO Regional Office for South-East Asia (SEARO) conference said that while an avian influenza pandemic had been expected, overall, pandemic preparedness had made a difference in SEARO countries. Although countries generally coped with the pandemic, strains were put on the health care system, surveillance and laboratory systems, and it was clear that they might have struggled in a more severe pandemic.

In September 2009, the WHO Regional Office for the Americas (PAHO/AMRO) held a two-day meeting attended by representatives of all countries in the region to review the usefulness of their national pandemic plans *(13)*. Most countries had prepared plans, but most of these were originally aimed at responding to H5N1, with a greater severity expected. The countries found that the prevention, containment and impact-reduction measures that had been planned were not entirely applicable to the 2009 H1N1 pandemic, which caused less severe disease, but disease that was more easily transmitted. The need to be adaptable was echoed in other evaluations, such as the independent review of the United Kingdom's response, which stated that the pandemic (H1N1) 2009 virus was milder in its general impact than the H5N1 "bird flu expected and planned for". It also pointed out that in the early stages of a pandemic there is uncertainty and that: "Given the context

of uncertainty inherent in the unpredictability of the influenza virus, there is a tendency, in an emergency situation and in the absence of information, to assume the worst-case scenario and resource the response accordingly." *(14)*

Findings: health system responses: hospitals and critical-care units

Although WHO's 1999 preparedness plan did not emphasize health system response requirements, the 2005 and 2009 preparedness plans highlighted the importance of health system response and advocated interim case-finding, treatment and management protocols and algorithms; infection-control guidelines; guidance on triaging; surge capacity management and staffing strategies.

Various reviews acknowledged that the H1N1 pandemic virus resulted in relatively mild disease, and countries would have had difficulty with a more serious disease. Critical care and surge capacity were important dimensions of health system response. One of the main pressure points on health care in the 2009 pandemic was on critical-care services in hospitals *(15)*. WHO issued limited guidance on clinical care and hospital requirements before the pandemic. Respiratory intensive care was under pressure even in developed countries.

Findings: use and appropriateness of WHO pandemic preparedness guidance

Most countries had produced pandemic preparedness plans, which drew on WHO guidance. The plans were variable in their quality, scope, state of readiness and level of testing. Many were based on the anticipation of an outbreak of H5N1. Nevertheless, the value of that advance preparation was acknowledged in all the country reports, and the world was much better prepared to respond to this pandemic than it had been only a few years earlier. The process of planning, as much as the plans themselves, made a difference. Implementation of the IHR also contributed to the response. Many countries received support from WHO to prepare their plans, mainly through the Regional Offices. Much credit must go to WHO for guiding and encouraging countries to develop their own plans, as well as for the training and other support it gave to many countries to help them strengthen surveillance systems and laboratory capacity.

The major features of the guidance were highly relevant, including the need for a whole-country approach, a senior organizational structure, a link to emergency preparedness plans and the IHR and the potential range of actions for different situations. Where these features had been incorporated, the plans were highly effective. It is evident from the reviews, however, that not all countries had taken these features into account in their plans, particularly the need for a "whole-of-society" approach.

Much of the guidance and many of the plans were based on the anticipation that the next pandemic would result from an outbreak of H5N1. The potential risk of H5N1 encouraged countries to take planning seriously. The risk assessments carried out by several public-health bodies and wide media coverage that suggested a devastating outcome of such a pandemic fuelled this concern. Ministries of health quite properly responded, sometimes with comprehensive plans, and in countries with resources, by developing stockpiles of antiviral drugs. The disadvantage of this, however, was that because many plans were predicated on H5N1 and its rate of spread, countries were not as prepared for a disease that was less serious but that spread more rapidly.

Countries used WHO's phase structure for the scale of preparation required and for intensification of the response as the situation demanded; for example, when Phase 5 was declared on 29 April, WHO had already received reports of cases from nine countries. Because they recognized that the disease was spreading rapidly, countries in Europe were already on high alert and implementing their plans; it was considered inevitable that the combination of global travel and the rapid transmission of the virus would mean that disease would come quickly to Europe. In the United Kingdom, for example, the first suspected cases were identified in Scotland on 26 April and were confirmed on 27 April. By this time, the United Kingdom Health Protection Agency was issuing advice to clinicians and the public, and the United Kingdom's preparedness plan was activated.

Some countries found the global pandemic phases not appropriate for their situation. Global pandemic phase declarations were perceived as late by some early-affected countries and premature by countries that were later affected. Some countries questioned whether a pandemic declaration was necessary while others thought termination of the pandemic was too late. Some countries used global pandemic phases as an operational, rather than a planning, tool and initiated actions although no cases had been reported in their countries.

The Review Committee concluded that the phases set out in WHO guidance appeared to have been used for planning, for describing the global situation, and for some, as an operational tool to trigger action. The Review Committee recommended that for future planning it would be helpful to disentangle these features. The multiphase structure of the WHO guidance contains more stages than differentiated responses and is needlessly complex, especially for operational purposes. The Review Committee recommended that the guidance should be revised to incorporate a simplified phase structure that emphasizes a risk-based approach, while monitoring events closely and changing direction as necessary. In addition, the use of geographical spread to define global pandemic phases was less well-suited for characterizing the post-pandemic period. Pandemic viruses typically evolve into seasonal influenza and may vary in intensity from country to country. Recognizing the transition is a matter of judgement. These considerations were evident in the Emergency Committee's deliberations and in the months before their decision to recommend to the Director-General that the pandemic was over. These difficulties provide additional support for the Review Committee's recommendation to simplify the pandemic phase structure and separate operational considerations at country level from a global preparedness plan.

C. WHO: preparedness/planning and response

As the health agency of the United Nations, WHO works with the United Nations System Influenza Coordination (UNSIC) group in preparedness and response to pandemic influenza. In the 2009 pandemic, UNSIC recognized that a whole-of-society approach was necessary and provided valuable information and coordination across 13 inter-governmental agencies to support the WHO-led response during the pandemic.

WHO's role in pandemic preparedness and response is described in the 2009 guidance as covering: coordination under the IHR; designation of the global pandemic phase; making recommendations on whether and when to switch from seasonal to pandemic vaccine production; rapid containment of the initial emergence of pandemic influenza and providing an early assessment of pandemic severity on health.

After the announcement of Phase 5, in May 2009, WHO further defined its objective as: "To mitigate the impact of pandemic influenza A (H1N1) by strengthening the readiness and response capacity of countries and communities, particularly throughout the world's most vulnerable regions." Six strategic actions were specified: monitor and track disease progression; generate and transfer knowledge; guide and support countries; accelerate access to vaccines and other benefits; accelerate access to antivirals and provide global health leadership and collaboration.

In response to the early reports of disease, WHO initiated its procedures for Management of an Acute Public Health Event. The Acute Operational Period ended on 25 May 2009 and the activities of the Strategic Health Operations Centre (SHOC) were reduced as deployment of logistical and operational support to countries was reduced. With the announcement of Phase 6, pandemic operations reverted to the usual programmatic arrangements. A Pandemic Evaluation Group (PEG) was established with a remit to consolidate all the information coming in to improve the analysis and coordination of the situation. This included coordinating the delivery of scientific evidence for the Strategic Advisory Group of Experts (SAGE) on Immunization meetings. PEG had four types of information: epidemiological, clinical, vaccine-related and modelling. The group drew on the Situation Reports, which were initially produced daily, then every other day, then weekly (beginning 26 June 2009). These covered the epidemiology of the pandemic, the science that was emerging, issues around vaccines, operations and country support, communications and the IHR. Other groups were established to deal with specific issues, such as SHOCDocs, which coordinated the review and approval of technical guidance documents.

The requirements to sustain activities and support to countries put considerable strain on WHO staff. Managers were accustomed to releasing staff for short periods to manage emergencies or for specific long-term programmes. The pandemic was different. It was a prolonged global situation that required intense activity over many months. WHO does not hold substantial contingency funds; monies are deployed against priorities agreed by the World Health Assembly or donor countries. Several Member States supplied staff, but this posed difficulties for some of them over the extended period, especially when the effects of pandemic were being felt in their own countries. Short-term placements also created problems of lack of continuity and knowledge transfer. WHO senior staff acknowledged that the organization for such events needs to be reviewed, particularly if they were to cope with a more severe pandemic. WHO was not alone in recognizing considerable strain on the coordination and management of their response. Countries that had run major simulations or had experience of major outbreaks were better prepared, but the pandemic emphasized the high level of organization and resources needed to oversee such an event.

WHO Regional and Country Offices

The Regional Offices, both directly and where appropriate through their Country Offices, provided support to countries in different ways, e.g in the areas of communications, guidance and technical support. Regional Offices also mobilized teams to support local actions and strengthen systems to facilitate activities such as the distribution of antiviral drugs and vaccines.

WHO was able to help those countries affected later in the pandemic strengthen their preparedness. In August 2009, for example, the WHO Regional Office for Africa (AFRO) organized a meeting in collaboration with Member States to update participants on the

global situation, review their national preparedness and response plans, identify possible gaps and discuss strategies for resource mobilization *(16)*.

PAHO commissioned an internal independent review of its own response and shared the findings with the Review Committee. There was positive feedback from its Member States about the technical support, resource mobilization and support from WHO Representatives in countries to ministers of health. The PAHO report identified some gaps, such as the link between public-health and clinical medicine, and weakness in the management structures for overseeing and responding to the pandemic. The report concluded that, despite these weaknesses, Member States had done remarkably well, but that the response would have been unsustainable in a more protracted situation.

Overall coordination and collaboration

When Phase 6 was announced, the incident command structure detailed below was effectively transferred to the Health Security and Environment cluster, under the leadership of the Assistant Director-General (ADG) *ad interim* for the cluster.

Core functions

- Information management (GAR)
- Epidemiological, clinical, virological, and scientific and technical information (GIP)
- Planning, coordination and implementation of activities related to pandemic vaccines (IVB)
- Coordination and planning with regional and Country Offices and with GOARN (GAR and HAC)
- Requests and issues related to the IHR
- Planning and clearance of technical documents (SHOCDocs, GIP, HSE/ADGO)
- Management of media-related activities (GAR)
- Administrative support (HSE and DGO)

ADGO, Assistant Director-General's Office; DGO, Director-General's Office; GAR, Global Alert and Response; GIP, Global Influenza Programme; HAC, Health Action in Crises; HSE, Health Security and Environment; IVB, Immunization, Vaccines, and Biologicals; SHOCDocs, Strategic Health Operations Centre Documents Team.

Pandemic incident command structure

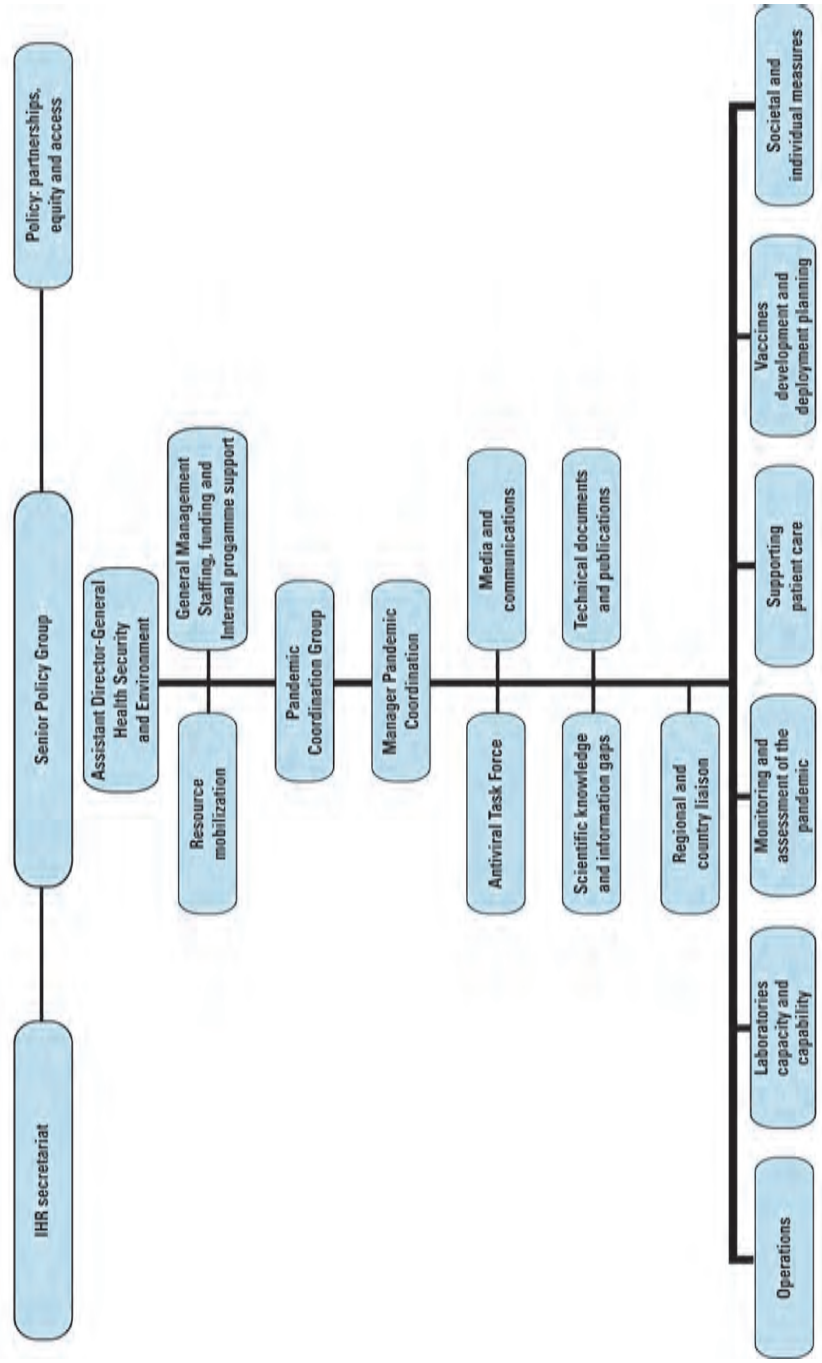
Policy was set and strategic decisions were made by the Senior Policy Group (SPG). The management structure was as follows:

- Project Executive Director (Assistant Director-General/HSE)
- Project Managing Director (temporary appointment)
- Functional Team Leads

In late July 2009 a former WHO country representative was engaged by WHO to travel to Geneva and begin organizing functional teams for the pandemic response (Fig. 3.2.).

This structure was formally announced on 7 September 2009. See Appendix IV for further details.

Fig. 3.2. **Pandemic management core functions and reporting relationships**



Source: WHO headquarters Pandemic (H1N1) 2009 Organizations and Resources. A World Health Organization brochure.

On 12 October 2009 the Assistant Director-General for Health Security and Environment was appointed Special Adviser to the Director-General on Pandemic Influenza. The Deputy Director-General temporarily assumed the post of Assistant Director-General of the HSE cluster. On 26 July 2010 the Special Adviser issued a memorandum to all department heads in the HSE cluster to prepare for post-pandemic operations and to return borrowed staff to their assigned locations.

D. Surveillance, monitoring and reporting

Monitoring an influenza pandemic requires timely and accurate information. Individual country-level data, when shared and aggregated at the global level, can help to characterize important features of the pandemic virus; guide prevention and control activities; facilitate distribution of antiviral drugs and vaccine and counter rumours and incorrect information *(17)*.

Before the H1N1 pandemic, virological monitoring of influenza viruses at global and national levels was well established through WHO's Global Influenza Surveillance Network (GISN). In addition, the IHR outline obligations and procedural mechanisms, for both countries and WHO, on early detection, surveillance, risk assessment, verification, and reporting of public-health events that might pose a global threat (see Chapter I).

To supplement these mechanisms, WHO worked with Member States and other partners to strengthen surveillance of seasonal influenza *(18, 19)* and to develop uniform guidance for disease surveillance during a pandemic.

WHO guidance for global disease surveillance during an influenza pandemic

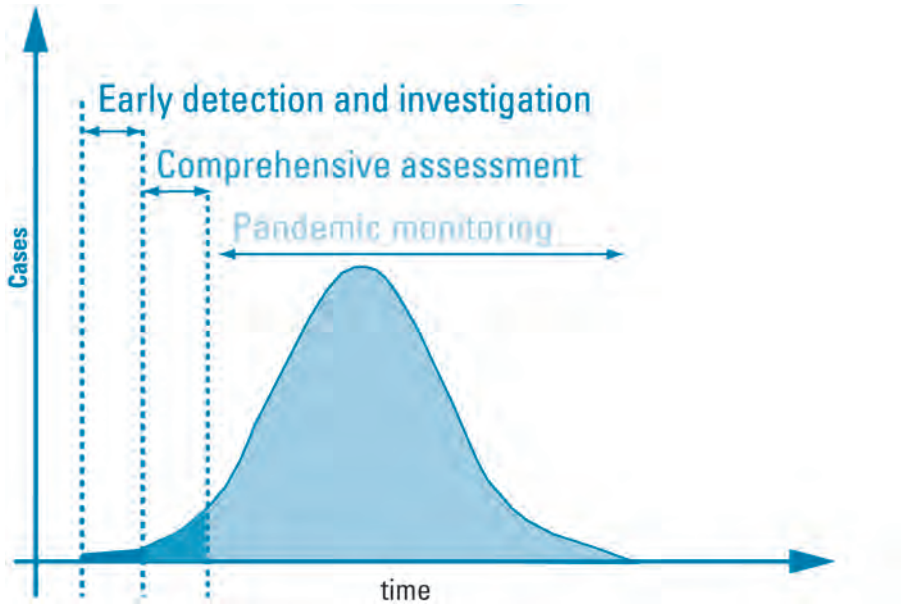
Pre-pandemic period

WHO convened a technical consultation in December 2007 to initiate the development of guidance for global surveillance during an influenza pandemic. The consultation highlighted significant challenges: surveillance systems for influenza were often not available in less-resourced countries; and surveillance schemes for influenza differed in their purpose and orientation, type and number of data sources, methodological approaches (notably the lack of a universally agreed case definition) and the level of resources to collect and process the information. Other systems, such as syndromic surveillance and the Integrated Disease Surveillance system in Africa – an early-warning system focused on rapid detection of epidemic diseases – had the potential to be used for pandemic influenza surveillance *(20)*.

WHO, in consultation with an expert working group, subsequently developed WHO's Global Surveillance during an Influenza Pandemic *(17)*. The guidance document was under review when the pandemic started and was published on WHO's web site shortly thereafter.

Countries were advised to plan for three types of surveillance activities or components to detect the emergence of new disease, characterize it and monitor its evolution (Fig. 3.3). The objective of the first surveillance component (i.e. to detect and investigate the first evidence of sustained human-to-human transmission of an influenza virus with pandemic potential) was closely aligned to the core capacities prescribed by the IHR.

Fig. 3.3. **Overview of surveillance components at national level**



Source: World Health Organization. Global surveillance during an influenza pandemic - version 1. 28 Apr 2009.

The second component (i.e. comprehensive assessment of a limited number of the earliest cases in each country) included characterization of the clinical, epidemiological and virological features of the new disease, information essential to assess the severity of the event. The third component aimed to track the country-specific geographical spread of the pandemic virus; the intensity with which disease was occurring; whether the number of cases was trending upward or downward and what impact the pandemic was having on health-care infrastructure. These qualitative indicators were intended to be feasible for every country to collect as well as useful in managing the pandemic at global and national levels.

During the pandemic

On 27 April 2009 WHO published supplemental surveillance guidance that focused on operational aspects for the detection, laboratory confirmation, monitoring and assessment of cases of pandemic (H1N1) 2009 infection *(21)*. The guidance encouraged countries to enhance their surveillance and diagnostic capacities for influenza and other acute respiratory infections, building on existing surveillance structures and resources.

As the influenza pandemic evolved, the increasing number of cases in countries with sustained community transmission made it extremely difficult, if not impossible, for countries to pursue laboratory confirmation of every case *(22)*. In some countries, this strategy was absorbing most national laboratory and response capacity, leaving little capacity for monitoring and investigating severe cases and other exceptional events. Moreover, counting individual cases was considered no longer essential in such countries for monitoring

either the level or nature of the risk posed by the pandemic virus, or to guide the implementation of the most appropriate response measures.

For these reasons, in July 2009 WHO issued updated interim guidelines for surveillance applicable to global pandemic Phase 6 *(23)*. As before, countries were asked to report: detection of their initial laboratory-confirmed cases of pandemic (H1N1) 2009 infection; weekly aggregated case numbers (if feasible); descriptive information about early cases; unusual events that could represent a change in the epidemiological and clinical characteristics of the pandemic virus and virological surveillance data. Laboratory testing of a sample of suspected cases of pandemic (H1N1) 2009 was recommended, especially to confirm infection in new areas and to test severe cases. For countries experiencing community-wide transmission, the guidance signalled a shift in focus from individual case counts to reporting the national status of the pandemic using the four qualitative indicators. Member States that had influenza surveillance systems were asked to provide, on a weekly basis, quantitative information on influenza-like illness and severe acute respiratory illness.

Coincident with the Director-General's announcement on 10 August 2010 of the move to the post-pandemic period, WHO published surveillance guidance for this period. These guidelines focused on: early detection of unusual events that might indicate a shift in the severity or pattern of disease associated with influenza, or the emergence of a new virus; the establishment and monitoring of baseline rates of severe respiratory disease, including the severity, disease burden and impact of influenza; the description and monitoring of vulnerable groups at highest risk of severe disease; and the detection of antigenic or genetic changes in circulating viruses, or the appearance of antiviral resistance *(24)*.

Virus sharing and virological surveillance

The GISN facilitated rapid sharing and analysis of virological specimens throughout the pandemic; as of 5 June 2010, 155 countries had shared 26 066 samples (of viral isolates and clinical specimens) with WHO Collaborating Centres. The WHO Shipment Fund Project, launched in 2005, aided the sharing of specimens and viruses. During the H1N1 pandemic, the fund supported 316 shipments from 81 countries at a cost of more than US$ 400 000. WHO also provided specimen collection materials (swabs and viral transport medium) to resource-poor countries.

Within days of the announcement that a new H1N1 influenza A virus had been detected, the WHO Collaborating Centre at the United States Centers for Disease Control and Prevention developed a real-time reverse transcriptase polymerase chain reaction (RT-PCR) detection method and prepared testing kits. Between 1 May 2009 and 10 August 2010, 2168 PCR kits (approximately 1000 tests per kit, or more than 2 million tests) for detection of pandemic (H1N1) 2009 were made available upon request free of charge to laboratories worldwide (this included 709 kits distributed in the United States of America).

Diagnostic testing and monitoring the evolution of the H1N1 virus formed the core of the laboratory response to the pandemic. The National Influenza Centres (NICs) tested more than two million clinical specimens during 2009 and reported weekly virological surveillance data to FluNet. From 19 April 2009–19 May 2010, WHO Collaborating Centres identified more than 11 000 positive specimens. Initially, the main objective was to test specimens from all suspected cases as rapidly as possible to assess the level of spread of the pandemic virus. This information was communicated to the NFP and enabled WHO to monitor and report laboratory-confirmed cases of infection. Laboratories were also encouraged to send any influenza A-positive specimens that could not be subtyped to the

WHO Collaborating Centres for subtyping. As the pandemic evolved, laboratory testing was done on a more selective basis to support epidemiological monitoring. In addition, priority was given to testing viruses from more severely ill patients to determine whether changes in the virus were contributing to more severe disease.

Throughout the pandemic, WHO asked country laboratories to send representative positive clinical specimens and pandemic viruses to WHO Collaborating Centres for characterization. The Collaborating Centres performed antigenic and genetic analyses of more than 6000 virus isolates from 19 April 2009–19 May 2010. The GISN's Collaborating Centres, Essential Regulatory Laboratories and other partner institutions worked to develop pandemic vaccine virus candidates and reagents *(25)*; within 32 days of the declaration of the Public Health Emergency of International Concern, the A/California/7/2009-like virus was selected as the pandemic vaccine virus and the first candidate vaccine reassortant virus was available for vaccine development. The first of several potency testing reagents for the pandemic (H1N1) 2009 virus vaccine was available a few weeks later, on 13 July 2009. Molecular sequencing to monitor possible viral drift found that all viruses were antigenically similar to the A/California/7/2009 vaccine virus, with only minor genetic variation *(25)*. GISN also actively monitored the resistance of the H1N1 pandemic virus to antiviral drugs and developed antiviral susceptibility testing protocols. Susceptibility testing underpinned national and global antiviral recommendations. Serological studies conducted by WHO Collaborating Centres found evidence of cross-reacting neutralizing antibodies to the pandemic virus among older adults, which helped explain observed disease patterns.

From the start of the pandemic, WHO coordinated regular teleconferences with GISN laboratories and other partners, such as the International Federation of Pharmaceutical Manufacturers and Associations, the Developing Countries Vaccine Manufacturers network and other global manufacturers. Beginning in June 2009, WHO organized additional weekly technical teleconferences focused on pandemic (H1N1) 2009 influenza reassortant viruses that appeared the most optimal for use in vaccine production. This collaborative approach facilitated the development of candidate reassortant vaccine viruses directly after the recommendation of the vaccine virus strain.

As evidenced by these achievements, the Review Committee members believed that in this instance GISN had worked well and facilitated the timely detection, identification, initial characterization and monitoring of the pandemic (H1N1) 2009 virus and the first time that a worldwide laboratory initiative was well-coordinated for an extended period of time. Earlier experience in the H5N1 outbreaks had raised questions about the willingness of some countries to share readily viral isolates.

The pandemic resulted in an increase in some countries' diagnostic capabilities through decentralization of testing and improved microbiological techniques at the national level (*13*). The level of laboratory response required to meet the needs of the pandemic exceeded capacity in some countries, however. There were geographical gaps in virological surveillance, particularly in Africa. At the start of the pandemic there were eight NICs in Africa, of which five were active. As reported by the WHO Secretariat, many countries in the African, South-East Asian and Eastern Mediterranean Regions have limited laboratory capacity. Capacity is limited at both national and subnational levels in many countries.

The WHO Secretariat reported that nearly a year after the pandemic, some countries were still not able to detect and report a case of pandemic (H1N1) 2009. During the pandemic, even well-resourced laboratories ran into problems when they did not have appropriate

testing algorithms in place. In the beginning of the pandemic in some instances, testing of all suspected cases of pandemic influenza exhausted supplies of reagents and the ability to test severely ill and hospitalized patients. The Collaborating Centres provided a limited supply of reagents to NICs; although they were also available commercially, lower-resourced countries were unable to afford them. This points to the need for more equitable access to laboratory reagents.

The increased volume of specimens submitted to laboratories for testing presented difficulties for countries. In resource-poor countries with limited capacity, laboratories were overwhelmed with trying to meet clinical needs within their own countries and to supply specimens for global surveillance. The Secretariat reported that results from many laboratories were not included in global analyses because the information was not entered into FluNet. Some countries modified their laboratory-testing strategies; patients with severe disease or risk factors, for example, were more likely to have specimens collected and tested. This may have introduced some bias in assessing what proportion of circulating influenza viruses were seasonal influenza as opposed to pandemic viruses, and points to the need for laboratory and clinical surveillance to work closely together.

These surveillance needs reinforce the importance of strengthening both regional and local capacities. The WHO Secretariat has reported that efforts to enhance laboratory capacities at NICs and to enrol more NICs and Collaborating Centres in GISN are ongoing. Since the pandemic began, an additional 10 NICs and one Collaborating Centre (in China) have been enrolled. In addition, efforts are continuing to automate data collection and reporting, improve training in laboratories and to use measures such as quality assurance testing. This will facilitate linking epidemiological and laboratory information, improving regional and global communicable disease response and enabling collaboration between NICs. The Secretariat noted that such efforts must continue but will require continued support by Member States and other donors.

Global disease monitoring and reporting

WHO began to post global surveillance data on its web site on 24 April 2009. These "situational updates" were posted on a near-daily basis until 6 July 2009. Each report provided data on the cumulative number of laboratory-confirmed cases and deaths as well as newly confirmed cases. Cases were also mapped geographically.

After the publication of updated surveillance guidance in July 2009, global disease reporting underwent several changes. First, countries were no longer required to test and report individual cases of pandemic (H1N1) 2009 infection. As a result, tabular data on the cumulative number of cases and deaths were reported by WHO region with the explicit proviso that these numbers were "underestimates of the real numbers". Regional-level reports of deaths continued until 1 August 2010, although two regions had not provided updated information for several months. National reporting was initiated for: qualitative indicators for the global geographical spread of influenza; trends in acute respiratory diseases; the intensity of respiratory disease activity and the impact of the pandemic on health-care services. As the pandemic progressed, 60–80 countries typically reported weekly qualitative indicator data. According to the WHO Secretariat, this qualitative information was valuable and often more timely than quantitative data. In addition to situational updates, WHO provided more detailed summaries of the epidemiological situation in the *Weekly Epidemiological Record*.

The 2009 influenza pandemic was the first large global event monitored under the IHR. WHO's weekly collation, analysis and reporting of global epidemiological, virological and clinical surveillance data meant that the world was kept informed in real time about what was happening. WHO and countries confronted formidable challenges, however, in their monitoring of pandemic disease. Information provided to the Review Committee from countries' experience and from the WHO Secretariat highlighted several issues.

- The lack of a mechanism for systematic reporting of standardized country-level data was particularly problematic. Instead, WHO actively collected and analysed data from a variety of sources, including NFPs, media reports, published reports and information posted on the official web sites of national health authorities, publications in peer-reviewed journals, informal WHO-coordinated technical networks and FluNet virological surveillance data *(26)*. Although these efforts yielded useful information, they were inefficient and resource-intensive.
- Counts of cases and deaths were the data most consistently reported by Member States and were useful for tracking the early spread of the pandemic. Case counts and fatalities were incomplete, however, and represented only a portion of the total spectrum of disease.
- More useful information early in the pandemic came through teleconferences with affected countries and partners, GISN and informal clinical and epidemiological networks.
- Detailed information to monitor the epidemiological and clinical characteristics of the pandemic virus and to conduct critical risk assessments was a critical need. Comprehensive surveillance data on influenza-like illness and severe acute respiratory infection were unavailable from many countries, however, especially those that lacked seasonal influenza surveillance systems. The qualitative indicator data provided some insights but were necessarily limited. Interestingly, virological monitoring data (i.e. the percentage of specimens that tested positive) was used as a proxy to indicate where the most intense transmission was occurring.
- Countries with pre-existing surveillance systems did not collect data in a uniform format, which made it difficult or impossible to compare data between countries. For example, understanding risk factors for clinical disease severity was a high priority, but countries often grouped their data using different combinations of risk factors, which was difficult to disaggregate. Similarly, countries also used different age groupings.
- At times there were delays in reporting routine pandemic surveillance data from the country level to the WHO regional level and from the regional level to WHO global level.
- Although the IHR define countries' responsibilities for minimum surveillance, the requirement for routine monitoring of events once they have been reported is less clear.

Disease surveillance capacity and approaches varied greatly among countries. Active surveillance (e.g. investigating clusters of acute respiratory infection in the community or monitoring hospitalized cases) and passive surveillance approaches were used, including rumour surveillance in some countries. A review of surveillance in EMRO noted that "monitoring the event through media channels was very important for countries at the beginning to determine the trend of the disease globally."

Ideally countries should have programmes for investigating new events and for monitoring progress over time; which of these are most active at any given time will depend on the stage of the pandemic in a given country.

Surveillance and reporting are resource-intensive activities. The Review Committee noted that information requirements should be limited to the minimum necessary; weekly requests for specific data were overwhelming for some countries, particularly those with limited epidemiological and laboratory capacity. Country officials were not always convinced the data they submitted were being analysed and used, particularly as the pandemic progressed. If adjustments are required, such changes should be promptly relayed to countries and other partners.

Despite the many challenges, it was possible to monitor the evolution of the pandemic and identify important trends. Improving international approaches for surveillance, including the identification of a minimum data set, that can lead to better and more timely data remains an important goal. Continued counting of cases yielded less useful information than would have been provided by rates of hospitalization, complications and death in countries affected early on in the pandemic.

E. Assessment of pandemic severity

A pandemic's severity is an important component of pre-pandemic planning and for response activities. Minimizing pandemic-associated morbidity and mortality is inextricably bound to an understanding of severity. Although there is agreement on the importance of estimating a pandemic's severity, how to measure severity is less clear.

Assessing severity: pre-pandemic considerations

Pandemic severity was discussed during the development of WHO's 2009 guidance on pandemic influenza preparedness and response. A WHO global consultation on pandemic disease control strategies in April 2008 cited several challenges in assessing severity. First, severity would likely differ from country to country because of differences in health services, the health status of the population and social and behavioural factors. Second, the paucity of reliable and complete information in the early stages of a pandemic would limit the robustness of any severity assessment. Assessments in the first-affected countries might not have adequate specificity to be useful to countries not yet affected. Third, severity would likely change over time as the pandemic evolved. Consequently, pandemic severity would need to be continually assessed.

The consultation considered the differences between global and national assessments of severity. There was support for an overall global-level assessment of severity based on the pandemic's direct consequences on health. Indirect consequences, determined by a range of economic, cultural and behavioural factors, would likely be country-specific. Still, countries would be encouraged to undertake national-level assessments using any combination of health and non-health indicators that suited their needs. Potential health-related indicators of global pandemic severity, such as the case fatality rate, were considered. It was agreed that many of the proposed indicators would be difficult to measure, in part because of the unavailability of timely data and potential bias resulting from under-recognition, under-reporting and misclassification of cases.

The feasibility of developing a global severity index was raised during the consultation. It was noted that the USA had developed such a tool—a five-point scale called the Pandemic Severity Index. It was based on epidemiological characteristics such as case fatality rate

(< 0.1 to > 2%) as indicator variables *(27)*. WHO decided that a pre-determined index would be impossible to use, owing to global variability.

The consultation did not finalize a set of indicators but noted that interpretation of early data would be based on a range of health-sector indicators and expert advice. These indicators would be selected to reflect the complexity of severity, yet allow WHO to provide a qualitative assessment of global severity using a simple three-level scale (mild, moderate and severe).

The assessment of pandemic severity was reviewed again in a May 2008 WHO-led global consultation on further development of the pandemic preparedness guidance. Retrospective assessments of past pandemics had used terms ranging from "mild" (in the order of seasonal influenza) to "severe" (greatly elevated levels of death and disease, as occurred during the 1918–19 pandemic). An assessment based on direct health impacts would likely result in varying outcomes between and within countries, regardless of how severity was defined. Consultants expressed concern that a numerical scale (e.g. 1–10*)* might imply a degree of precision that was not achievable and result in complex formulations. Pre-pandemic consultations had advocated for simplicity and for indications of what is not known. The May 2008 consultation linked severity assessments with national capacity for pandemic surveillance *(17)*.

The consultation report concluded that earliest assessments of severity should use more than one indicator and offer qualitative and quantitative information for expert interpretation. The experience of Egypt in developing a severity index was also discussed in a WHO conference held in Cancun in 2009 and at the EMRO Ministerial Meeting held in Cairo.

The outcome of these consultations, WHO's guidance on pandemic influenza preparedness and response *(28)*, was released at the start of the pandemic. The guidance stated that one of WHO's key responsibilities during the pandemic would be to provide early assessments of pandemic severity based on observable effects on health. Quantitative and qualitative data on health impacts would be used to estimate severity using a three-point scale of mild/intermediate/severe. The guidance listed case fatality rate, unusually severe morbidity, unexpected mortality patterns and unusual complications as potential health indicators of severity.

WHO's approach to assessing severity during the pandemic

Rapid global assessment of severity

At the beginning of the 2009 pandemic, WHO attempted to make a rapid global assessment of severity based on health-related information. The WHO Secretariat provided the Review Committee with a detailed outline of key activities and outcomes relevant to its assessment of severity (Appendix VII). WHO sought information from early-affected countries during a series of teleconferences (29 April 2009, 5 May 2009 and 1 June 2009) as well as through bilateral discussions.

The WHO Secretariat reported to the Review Committee that although it had received preliminary data on health impacts from Mexico, the USA and Canada, an internal assessment on 28 April 2009 concluded that data were insufficient to assess severity at the global level.

The 29 April 2009 and 5 May 2009 teleconferences were noteworthy for a wide spectrum of reported clinical disease, ranging from Mexico's experience of a severe, rapidly spreading disease, to sporadic, mild disease reported by Canada and the USA *(29, 30)*. Participants cautioned that it would take time for a fuller picture of the virus to emerge. Within three weeks of the announcement of the PHEIC, on 11 May 2009 WHO described the factors that influence overall pandemic severity *(31)*. It noted that with the exception of the outbreak in Mexico, the H1N1 virus tended to cause "very mild illness in otherwise healthy people" but "more severe and lethal infections in people with underlying conditions".

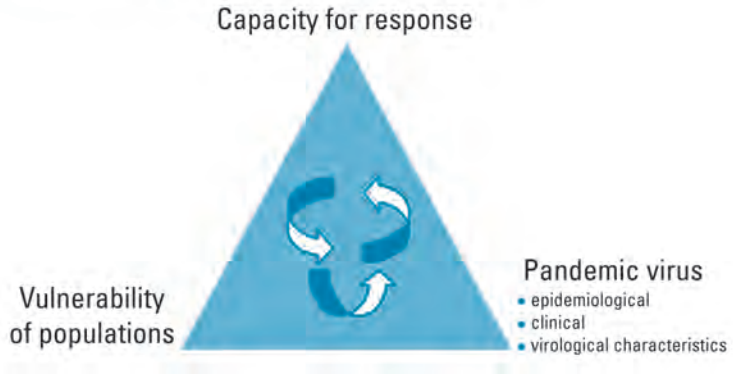
WHO began to develop data collection tables to organize information on the epidemiological, clinical and virological characteristics of early cases from affected countries. These were sent to NFPs for verification and consistent patterns of information about the characteristics of the pandemic virus were noted across countries. On 29 May 2009 WHO published a three-part framework for assessing severity (Fig. 3.4): (i) the pandemic virus and its virological characteristics and epidemiological and clinical manifestations; (ii) the vulnerability of the population, related, in part, to the level of pre-existing immunity to the virus in the population and the proportion of persons with risk factors for serious illness or death and (iii) the capacity for response (access to health care, communication and social mobilization) and advance preparedness and response *(32)*. Epidemiological, clinical and virological data available to WHO were also summarized.

On 5 June 2009 the Emergency Committee (EC) reviewed reports from regional teleconferences that had been held on 1 June, at which participants discussed a severity scale and indicators, including comparisons with seasonal influenza activity, and whether a severity scale should be set at a global or country level. Participants expressed concern about the use of the term "mild" in a severity classification; an alternative terminology such as moderate/aggravated/severe was discussed.

During the 11 June 2009 meeting of the EC, severity and the factors that influence it were raised. Members agreed that the pandemic's severity should be described as "moderate". Their recommendations on severity were:

- At this early stage, the illness associated with the pandemic is characterized as having moderate severity, meaning that the vast majority of cases recover spontaneously without specific treatment, but as with seasonal influenza, a small proportion of cases suffer serious illnesses that infrequently can result in death.

Fig. 3.4. **Severity Assessment Framework**



- The severity of the illness will be closely monitored using a "basket" of features, including the clinical course, the genetic make-up of the virus, the impact on health services and the impact on the wider socioeconomic situation. WHO should inform the world of changes in the severity pattern shown by the pandemic.

Coincident with the move to pandemic Phase 6 on 11 June 2009, the Director-General pronounced the overall severity of the pandemic to be "moderate" *(33)*, reflecting that:

1. Most people recovered from infection without the need for hospitalization or medical care.
2. Overall, national levels of severe illness appeared similar to levels seen during local seasonal influenza periods.
3. Overall, hospitals and health-care systems in most countries had been able to cope, although some localities had been stressed.

Ongoing assessments throughout the pandemic

WHO reassessed pandemic severity continually as an integral part of surveillance and monitoring. The Pandemic Evaluation Group, comprised of WHO staff from the Director-General's Office, Global Influenza Programme, Global Alert and Response, Communications and WHO coordinators for the virtual clinical, epidemiological and virological networks, reviewed new data. Several indicators were used to assess five dimensions of severity (i.e. how many people are getting sick; how many people are dying; what is the proportion of severe cases; is there a shift in risk groups and how is the health system coping?). Information was sought from ministry of health web sites, country reports, literature reviews and teleconferences with country-level health professionals, including regular teleconferences with virological, epidemiological and clinical networks. WHO also investigated any unusual events reported during the course of the pandemic, including the first case of antiviral resistance (July 2009) *(34)* and the viral mutation (D222) in three fatal cases *(35)*.

Authorities in countries and regions (e.g. European Centre for Disease Prevention and Control) undertook epidemiological characterizations of the pandemic including risk assessments of its severity and usually came to similar conclusions as WHO.

Severity assessment among subpopulations at higher risk

Subpopulations at higher risk have either an increased chance of becoming infected or ill, or increased disease severity once infected. Although risk groups for seasonal influenza have been well defined, during the pandemic other higher-risk groups emerged. Pregnancy, certain ethnicities and possibly obesity were identified as conferring an increased risk (although the role of confounding factors has not yet been completely determined). WHO reported to the Review Committee that data on these variables were not always available for cases early in the pandemic, which in turn decreased the ability to identify associated risks.

Challenges to the assessment of severity

WHO assessments of severity were complicated by the evolution of the disease situation, the inconsistent availability of new data (e.g. reporting delays owing toZ backlogs in

laboratory testing) and the association of many variables with specific settings, locations or points in time.

Severity was difficult to calculate in real time. First, data for some variables were not available early in the pandemic, even from countries with well-developed health infrastructures. Second, baseline data for indicator variables are important but were not known for many countries. The variability in reported severity (e.g. focal areas of severe disease) throughout the pandemic may have reflected changes in baselines owing to changes in surveillance and testing methods. When retrospective quantitative comparisons were made using adjusted baselines, some of these differences were not as significant as they first appeared. Third, factors not related to the disease can affect the calculation of indicator variables. For example, hospitalization rates were strongly influenced by national protocols. Mexico and other countries early in the pandemic hospitalized all cases to control disease spread. Other national protocols called for hospitalization of all pregnant women, which artificially increased rates of hospitalization. Conversely, countries with limited hospital capacity reported lower rates. A similar situation existed when calculating intensive care unit (ICU) admissions or ventilator use, which are heavily influenced by ICU capacity and the availability of ventilators. For all variables, the impact of population- or subpopulation-based health parameters and health infrastructure (including access to care) were difficult to disentangle.

The Committee does recognize that characterization of severity is complex and difficult to operationalize. The Review Committee noted, however, that the absence of a consistent, measurable and understandable depiction of severity was problematic. Even if the definition of a pandemic depends exclusively on spread, its degree of severity affects policy choices, personal decisions and the public interest. What is needed is a proper assessment of severity at national and subnational levels. These data would inform WHO's analysis of the global situation as it evolves, allowing WHO to provide timely information to Member States. WHO's use of semiquantitative terms such as "mild" and "moderate" compounded the confusion: they were not defined but they were used to describe both clinical illness in individuals and the severity of the pandemic.

The WHO Secretariat acknowledged that assessing a pandemic's severity in a way that is rapid, scientifically acceptable and generally relevant for the many countries and subpopulations in the world remains a significant challenge. WHO reported that it plans to revisit this issue, in collaboration with experts and Member States.

The Review Committee took note of assertions by critics that WHO overstated the seriousness of the pandemic. However, reasonable criticism should be based only on what was known at the time and not on what was later learnt. The Committee found that evidence from early outbreaks led many experts at WHO and elsewhere to anticipate a potentially more severe pandemic than subsequently occurred. The degree of severity of the pandemic was uncertain throughout the middle months of 2009, well past the time, for example, when countries would have needed to place orders for vaccine. An observational study of 899 patients hospitalized in Mexico between late March and 1 June 2009, showed that pandemic (H1N1) 2009 disproportionately affected young people. Fifty-eight patients (6.5% of those hospitalized) became critically ill, with complications including severe acute respiratory distress syndrome and shock. Among those who became critically ill, the mortality rate was 41% *(36)*. These statistics were alarming. Even a reported mortality rate of one third that level among critically ill patients in Canada was worrisome (*37)*. In the USA in August 2009 the President's Council of Advisors on Science and Technology released a report positing a possible scenario of 30 000–90 000 deaths from pandemic (H1N1) 2009

in the USA alone *(38)*. The midpoint and upper level of this scenario turned out to be five times higher than the post-pandemic estimates of the actual number of deaths *(39)*. Even so, 87% of deaths occurred in those under age 65, with the risk of death among children and working adults seven times and 12 times greater, respectively, than during typical seasonal influenza *(39)*.

The Review Committee also explored a related criticism that WHO had eliminated severity from its definition of a pandemic. The Review Committee examined the WHO pandemic preparedness guidelines published in 1999, 2005 and 2009. While none of the three preparedness guidelines provides an explicit definition of the word *pandemic* (i.e. a phrase labelled "definition"), each document does contain language that *describes* when a pandemic state has arisen. In describing the conditions of a pandemic, the 1999 document refers to "consistent disease patterns indicating that serious morbidity and mortality is likely in at least one segment of the population". In the 2005 and 2009 documents, the characteristics of a pandemic are described in the context of explanations of the pandemic phases (Box 3.4).

Among the factors that may be considered in moving from one phase to another, the 2005 guidelines include "severity of illness". The 2009 guidelines stress the importance of providing information on severity, but more clearly separate this discussion from criteria for moving from one phase to another. Despite the mentions of severity, in none of these guidance documents is severity explicitly put forward as a requisite defining element of a "pandemic". However, a clear separation between the occurrence of a pandemic and its severity appeared only in the most recent of the three guidance documents. WHO could reasonably assert that it had not changed the definition of a pandemic. At the same time, severity had been mentioned in earlier descriptions of what to expect in a pandemic and as an element that may be considered in moving from one phase to another. The changes with respect to severity that were incorporated in the 2009 guidelines, rather than a last-minute alteration, were the result of longstanding efforts to make the guidelines more crisp and operational.

The potentially confusing distinction between defining a pandemic and describing what to expect in a pandemic was evident in WHO's web narrative. On 4 May 2009, WHO's web narrative stated, "An influenza pandemic occurs when a new influenza virus appears against which the human population has no immunity, resulting in epidemics worldwide with enormous numbers of deaths and illness. With the increase in global transport, as well as urbanization and overcrowded conditions, epidemics due to the new influenza virus are likely to quickly take hold around the world." Later the same day, WHO altered its web-based description of what to expect in a pandemic, eliminating references to the expected severity of a pandemic, and left no indication on the web site that the change had been made. Further modifications were made on 5 May, when the following statements were inserted:

- "A disease epidemic occurs when there are more cases of that disease than normal. A pandemic is a worldwide epidemic of a disease."
- "Pandemics can be either mild or severe in the illness and death they cause, and the severity of a pandemic can change over the course of the pandemic …"
- "If the pandemic evolved to become severe and widespread over time, we could also expect…"
- "Effective pandemic preparedness around the world is essential to mitigate the effects of a pandemic, particularly if it becomes severe."

This issue is also discussed in the section on communications.

Box 3.4. Language used in 1999, 2005 and 2009 WHO pandemic preparedness plans with respect to the terms *pandemic* and *severity*

1999:

"The Pandemic will be declared when the new virus sub-type has been shown to cause several outbreaks in at least one country, and to have spread to other countries, with consistent disease patterns indicating that serious morbidity and mortality is likely in at least one segment of the population."[1]

2005:

"The distinction between phase 3, phase 4 and phase 5 is based on an assessment of the risk of a pandemic. Various factors and their relative importance according to current scientific knowledge may be considered. Factors may include rate of transmission, geographical location and spread, severity of illness, presence of genes from human strains (if derived from an animal strain), and/or other scientific parameters."

"Pandemic period. **Phase 6.** Increased and sustained transmission in the general population.

Rationale. Major change in global surveillance and response strategy, since pandemic risk is imminent for all countries. The national response is determined primarily by the disease impact within the country."[2]

2009:

"An influenza pandemic occurs when an animal virus to which most humans have no immunity acquires the ability to cause sustained chains of human-to-human transmission leading to community-wide outbreaks. Such a virus has the potential to spread worldwide, causing a pandemic."

"**PHASE 6.** Pandemic in progress. In addition to the criteria defined in Phase 5, the same virus has caused sustained community level outbreaks in at least one other country in another WHO region."

"Providing an early assessment of pandemic severity on health.

As soon as possible, WHO will provide an assessment of pandemic severity to help governments determine the level of interventions required as part of their response. As outlined in section 1.1., past influenza pandemics have been associated with varying levels of illness and death …

It is likely that information will be limited early in the pandemic while the demand for information simultaneously escalates. If pandemic surveillance is to provide sufficient information and data to assess severity, countries need to review their existing surveillance capacity to address the weaknesses to be prepared for pandemic surveillance. Essential components of an effective pandemic influenza surveillance system will include:

- Early detection and investigation;
- Comprehensive assessment; and
- Monitoring.

Potential health indicators of severity:

- Case fatality rate
- Unusually severe morbidity
- Unexpected mortality patterns
- Unusual complications."[3]

[1] Influenza pandemic preparedness plan. The role of WHO and guidelines for national and regional planning. Geneva: World Health Organization; April 1999.

[2] WHO global influenza preparedness plan. The role of WHO and recommendations for national measures before and during pandemics. Geneva: World Health Organization; 2005. http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5.pdf

[3] Pandemic influenza preparedness and response: a WHO guidance document. Geneva: World Health Organization; 25 April 2009. http://www.who.int/csr/disease/influenza/pipguidance2009/en/index.html

F. Public-health measures

Measures to limit transmission of pandemic influenza are broadly divided into those that are pharmaceutical (e.g. antivirals and vaccines) and non-pharmaceutical, which are often referred to as public-health measures (e.g. isolation of patients and quarantine of contacts). Non-pharmaceutical measures were used during the pandemics of the 20th century, although their effectiveness had not been systematically evaluated. Measures such as isolation, quarantine, infection control and social distancing were widely used during the outbreak of SARS in 2003. Although SARS highlighted the role such measures can play, their impact during a pandemic was less certain because of influenza's different clinical, epidemiological and virological characteristics.

Development of WHO guidance on public-health measures before the pandemic

The development of both the 2005 and 2009 global pandemic preparedness guidelines included a global consultation to review disease control measures that could be used during a pandemic and the available evidence base. The first was convened in March 2004 against the backdrop of growing concern about the accelerated geographical spread of highly pathogenic avian influenza H5N1. Several themes emerged, including:

1. The effectiveness of public-health measures is linked to the characteristics of a pandemic virus (e.g. principal mode of transmission, attack rate in different age groups and duration of virus shedding);
2. cost, available resources, ease of implementation within existing infrastructures and acceptability by the public are key considerations in decision-making related to the use of public-health measures;
3. no single intervention would be sufficient. Multiple interventions implemented in tandem would be necessary;
4. ongoing review would be required during a pandemic to accommodate possible changes in the evolution of the virus;
5. improvements in public-health capacity building and modernization of public-health law would be necessary to underpin and support the measures,
6. protection of human rights must be maintained during the application of public-health measures;
7. effective implementation was critically dependent on good communication and social mobilization.

The 2005 WHO global influenza preparedness plan included an annex that detailed in tabular form specific recommendations for non-pharmaceutical public-health interventions *(40)*. The supporting evidence base was detailed in two peer-reviewed publications *(41, 42)*. Importantly, it was noted that the development of evidence-based guidance was inextricably linked to what is known about how influenza is spread and specific risk factors that can affect transmissibility (e.g. host factors, pathogen factors, environmental factors). Available data were limited, however, often observational or anecdotal in nature and based on studies of seasonal influenza.

A second global consultation on pandemic disease control strategies was convened in April 2008. The consultation's objectives included discussions on the measures and supporting evidence for their effectiveness, and on the practicalities of implementing such interventions in various settings. Background papers on various disease-control strategies

were prepared by working groups. Findings from this consultation contributed to the Global Consultation on Pandemic Preparedness in May 2008, during which time public-health measures were again reviewed. The discussions and documents from these consultations helped inform WHO's 2009 guidelines for pandemic influenza preparedness and response *(28)*, which described public-health measures that could be applied at individual/household, societal/community and international travel/trade levels. A brief overview that summarizes selected evidence for these measures is found in Annex 1 of the guidelines *(28)*. In general, the evidence base for many public-health measures is limited.

Guidance and public-health measures during the pandemic

On 27 April, after the second meeting of the Emergency Committee the Director-General stated that "given the widespread presence of the virus … containment of the outbreak is not feasible. The current focus should be on mitigation measures." The temporary recommendation issued on 28 April, after WHO declared Phase 4, stated that border closures and restricting international travel were not recommended. It advised that it was considered prudent for people who were ill to delay international travel and for people developing symptoms following international travel to seek medical attention. That advice did not change and was included in many of the Director-General's statements.

Countries implemented a range of measures, both public-health and pharmaceutical, with the intention of slowing down the spread of the virus or to mitigate its effects. To support these measures, WHO issued a series of guidance documents during the pandemic. This guidance reflected the evolving situation as more information became known, especially the experience of countries that were affected early in the pandemic. Some of the key guidance documents included:

- Advice on the use of masks in the community setting in Influenza A (H1N1) outbreaks (*43*).

The interim guidance, published in May 2009, acknowledged that there was a lack of firm evidence on the use of masks in the community, but advised that people could use masks at their discretion. It reinforced that masks should be worn and disposed of carefully, as incorrect use could increase transmission. This advice was similar to the guidance of many countries.

- Behavioural interventions for reducing the transmission and impact of influenza A(H1N1) virus: a framework for communication strategies *(44)*.

This document, published in June 2009, was developed after requests from countries for technical guidance to prepare communication strategies, messages and materials. It focused on the individual and family level, and included a checklist for strategic communications.

- WHO consultation on suspension of classes and restriction of mass gatherings to mitigate the impact of epidemics caused by the new influenza A (H1N1) *(45)*.

This document summarized a teleconference that WHO had convened on 27 May 2009, bringing together public-health officials from six countries and other experts. It highlighted the experiences and early lessons from the outbreaks of pandemic influenza A

(H1N1) 2009 virus in communities or closed settings. Recommendations on the application of public-health measures were included.

- Reducing transmission of pandemic influenza (H1N1) 2009 in school settings *(46)*.

In this second school-related guidance document, published in September 2009, WHO set out a more comprehensive framework for reducing transmission in schools. Experience with pandemic (H1N1) 2009 in many countries had shown that schools could be important amplifiers of transmission, within and across the wider community *(47)*. The document outlined a framework for national and local health and school authorities to consider when developing pandemic planning and decision-making guidance to reduce school-associated pandemic (H1N1) 2009 infections. Information received on the effectiveness of school closures in reducing transmission of pandemic (H1N1) influenza was summarized.

- Interim planning considerations for mass gatherings in the context of pandemic (H1N1) 2009 influenza *(48)*.

During the pandemic some countries needed to prepare for mass gatherings with international visitors, such as the 2009 Hajj, the Winter Olympics in Canada and the football World Cup in South Africa. WHO issued interim guidance in November 2009 after review by the WHO Virtual Interdisciplinary Advisory Group on Mass Gatherings. The report drew on previous guidance and reports from countries that had already been affected by the pandemic. It set out a risk-assessment approach with factors to be taken into account. Countries also developed specially tailored guidance on social measures for their specific needs; for example, the Saudi Arabian authorities developed detailed planning arrangements for the Hajj *(49)*.

Country experiences with public-health measures

Countries implemented a range of public-health measures. None of these was taken in isolation, but rather as a "package" of measures aimed at reducing transmission and potentially to slow the progress of the virus. Health authorities generally encouraged personal (e.g. hand washing) and respiratory hygiene, although advice varied based on individual and cultural norms. In Mexico, which was affected in the early stages of the pandemic, there were nationwide school closures, whereas in most countries the decision to close schools was a local one, sometimes using national guidance. The Committee heard anecdotal evidence that some countries considered that school closures had slowed the spread of the virus in the community. In addition, analyses conducted early in the pandemic in some countries suggested that closing kindergartens and primary schools may have had a "considerable effect" in reducing transmission albeit with substantial economic and community costs *(47)*. However, the usefulness of school closures should be further evaluated in detail. Guidance on the cancellation of mass gatherings varied from country to country; the Committee emphasized that planning needs to be firmly based on risk assessment, rather than "generic" guidelines.

Countries took different approaches to public-health measures at borders. These ranged from giving information through posters and leaflets, passive screening by asking travellers to report symptoms and temperature screening to identify potential influenza cases. Some countries concluded that border screening would be ineffective in slowing a highly transmissible strain of influenza and that it would consume considerable resources that

could be better employed in other areas of disease control. Other countries, particularly some island countries, considered that screening at the borders, in conjunction with other awareness-raising and post-travel measures, could be worthwhile in delaying the spread of the virus.

IATA, whose members comprise all major passenger and cargo airlines, indicated that countries' varying approaches to border control were confusing for airlines. Not all countries advertised their measures and pilots did not know what to expect on landing. This had a cascade effect, delaying aircraft turnaround times. The Secretariat indicated that although WHO requested information from countries on many occasions, it was not always forthcoming. The Committee noted that border controls are the prerogative of sovereign states, but can have an impact on other countries and world travel and trade. In the Committee's view, such measures should be based on evidence.

During the pandemic several countries evaluated the implementation and effectiveness of public-health measures. However, as such measures are not taken in isolation, it is difficult to ascribe benefit to individual ones, and there remains uncertainty about the evidence base. The Committee encourages WHO to coordinate the review of all these studies and evaluations, with a view towards amending future guidance and underpinning future research.

G. Pharmaceutical interventions

Antiviral drugs

WHO guidance

WHO first reviewed the role of antiviral drugs in pandemic response in 2002, which led to the publication in 2004 of WHO Guidelines on the Use of Vaccines and Antivirals during Influenza Pandemics *(50)*. These guidelines provided a framework for further publications: in 2006 on clinical guidance for using antiviral drugs to treat avian H5 infections in humans *(51)* and in 2007, the WHO Interim Protocol: rapid operations to contain the initial emergence of pandemic influenza *(52)*.

Because the influenza A (H1N1) 2009 viruses are resistant to the adamantanes (M2 ion-channel inhibitors), the neuraminidase inhibitors were the main antiviral drugs used during the pandemic. Oseltamivir (an oral agent) and zanamivir (an inhalational agent) were the most widely used clinically.

WHO global and regional antiviral drugs stockpile

Since 2005, planning for an influenza pandemic has included the possibility of launching a rapid-containment operation to halt the outbreak in its earliest stage and avert its spread. Central to this strategy was the establishment of a stockpile of antiviral drugs, pre-positioned, with logistics in place to release and rapidly deploy the stockpile to the location of the outbreak.

In 2006 Roche, the manufacturer of the antiviral drug Tamiflu (oseltamivir), agreed to donate five million doses to be held as a stockpile that could be deployed as part of a rapid-containment operation. Three million doses were held in storage by Roche at two locations: in Basel, Switzerland, and in Joppa, Maryland, USA. An additional two million were given to WHO to be pre-positioned at WHO headquarters, Regional Offices and at the United

Nations Humanitarian Regional Depot (UNHRD) in Dubai, United Arab Emirates. WHO worked with Roche to develop conditions to govern the release of the stockpile, along with the procedures that would allow for its effective deployment. Channels of communication were established at all levels, from operational logistics to senior decision-making, and a plan of action was put in place.

WHO embarked on a series of consultations and training exercises with operational partners, such as the United Nations World Food Programme (the UN agency responsible for managing the depot in Dubai), to test the procedures that would drive a rapid-containment exercise. Deployment of the stockpiles was integral to these exercises. The exercises also took into consideration the complex shipping and transport needs down to the field level to ensure that the procedures were understood by all and could be activated in an emergency without delay. Where problems were identified, adjustments were made.

In 2008 these plans were activated when a media report noted suspected human-to-human transmission of avian influenza (H5N1) in Indonesia. While WHO was verifying the information, the pre-deployment activities necessary before a possible release of the stockpile were launched. WHO quickly determined that the report was an unsubstantiated rumour so deployment of the stockpile was not necessary. The experience offered a valuable opportunity, however, to validate the plans.

In April 2009, after the first reports of novel H1N1 infections were reported to WHO from Mexico and the USA, a rapid-containment operation was considered. On 29 April 2009, an Antiviral Task Force was established at WHO headquarters to oversee deployment of the stockpile. As containment was not considered feasible, on 2 May 2009 WHO decided to distribute the antiviral treatment courses held in the global stockpile to 71 lower-income countries and to Mexico. The stockpile had been created for a containment operation. Roche agreed, however, to new terms for the release of the stockpile, enabling it to be distributed to multiple locations around the world. On 3 May, a list of beneficiary countries was agreed. A distribution plan was developed in coordination with the targeted countries to respond to legal issues, accelerate shipping processes, facilitate customs clearance processes and coordinate delivery schedules with WHO Country Offices and forwarding agents. Dates of significant events include:

- 3 May 2009: Documentation processing for the shipment of antiviral stocks begins
- 7 May 2009: First shipments arrive (in Gambia, Ethiopia and Angola)
- 15 May 2009: 80% of stockpile delivered
- 25 May 2009: Final shipment arrives (in Ukraine)

In addition to the deployment of the global stockpile held in storage by Roche, the WHO Regional Office for Africa released the regional stockpile, which was pre-positioned at the UNHRD in Dubai. Each of the 46 Member States of the African region received 1000 treatment courses and an additional 10 000 treatment courses were made available to each of the Intercountry Support Teams in the African region. The WHO Regional Office for Africa and headquarters coordinated this response. Operations in UNHRD Dubai began on 5 May and were completed by 20 May 2009. In addition to supplies of antiviral drugs, respiratory syndrome investigation kits were pre-positioned in all Member States, via WHO Country Offices, between May and October 2009.

Since the release of the stockpile, Roche has replenished both the global stockpile (three million doses) and the regional stockpile (two million doses) held in Dubai, under the original terms of the agreement.

WHO medicines prequalification programme

To facilitate the purchase of oseltamivir by WHO and other UN organizations, and to facilitate access to generic oseltamivir, a call for "Expressions of Interest" was issued under the WHO medicines prequalification programme in 2007. The one product prequalified as a result was manufactured by the Indian company Cipla (oseltamivir capsules). A second call for Expressions of Interest for prequalification was issued in June 2009 to encourage additional manufacturers to apply and to include zanamivir as eligible for inclusion. As a result of this and the first call, eight influenza antiviral products from four manufacturers (Cipla, GlaxoSmithKline, Roche and Strides Arcolab) have now been prequalified.

Development of new WHO guidelines

Immediately after the isolation of the pandemic influenza A (H1N1) 2009 virus, it was reported that this new virus was sensitive to the neuraminidase inhibitors (oseltamivir and zanamivir). Global market authorizations and national and global stockpiles led to an expectation that these medicines would have an important role in pandemic response and mitigation. However, the development of evidence-based treatment guidelines was challenging, and at the time controversial, owing to several factors:

1. The lack of information on clinical features and treatment of pandemic influenza A (H1N1) 2009 disease at the start of the pandemic.
2. Much of the published data on the use of antivirals were from prospective studies of acute self-limiting illness in the general population and may not have been applicable to other cases, such as severe or complicated illness or those in low-resource settings.
3. Other antiviral medicines, investigational or regional products, and adjunctive treatments were available, but little evidence exists on their effectiveness.
4. New information continued to emerge throughout the course of the pandemic.

A two-stage process was followed to develop the guidelines. First, an independent review of evidence was undertaken. Evidence, comprising both systematic reviews and observational data, was assessed according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology *(53)*. Second, an expert panel was convened to develop recommendations based on the assessed evidence. Guidelines were published on the WHO web site, including a description of the process used, details of the evidence considered and its GRADE assessment, and details of expert panel members, their affiliations and declarations of interests. Guidelines were published in preliminary form in April and May 2009 and formally in August 2009. Treatment recommendations were based on evidence drawn from seasonal influenza, and from observational data on the treatment of the more serious influenza H5N1 virus infections. Revised guidelines were published in February 2010 *(54)*, by which time observational data on the treatment of serious illness resulting from pandemic (H1N1) 2009 virus infection were available. These new data demonstrated that prompt treatment with the approved neuraminidase inhibitors was associated with improved clinical outcomes.

Monitoring effectiveness of antiviral drugs

WHO monitored two aspects of the effectiveness of antiviral drugs in treating pandemic (H1N1) 2009 influenza illness. First, information on the clinical efficacy and safety of the medicines was collected through close interaction with clinicians and public-health agencies. This was achieved through regular teleconferences of the clinical networks,

face-to-face meetings at which data were presented, and review of data published in medical journals. In addition, a dialogue was maintained with the principal pharmaceutical manufacturers to obtain efficacy and safety data from ongoing clinical studies and routine safety monitoring. All of this information provided the basis for guidelines development and for other publications, such as web briefings. It also provided a sound evidence base from which to support and advise Member States.

Second, WHO actively monitored for the emergence of viruses resistant to the antiviral medicines. Information was received from participants in WHO's GISN, including NICs and WHO Collaborating Centres, and from Member States reporting under the IHR. This mechanism worked well. Additional information was retrieved from national government web sites, public-health agency reports and journal publications. Three global teleconferences were held with key laboratories, agencies and experts after significant case reports were published. As a result of this activity, WHO collated information on 285 cases of antiviral resistance reported by 21 countries during the period June 2009 to May 2010. All but one of these cases involved viruses carrying the H275Y substitution in the neuraminidase, which has been shown to confer resistance to oseltamivir, but not zanamivir. There were no reports of reassortment between the pandemic (H1N1) 2009 virus and the circulating seasonal H1N1 virus.

The 285 reported cases were the only documented cases from more than 20 000 clinical specimens evaluated from at least 92 countries, indicating that antiviral-resistant pandemic (H1N1) 2009 viruses were not generally circulating. Nevertheless, there were three case clusters in which limited local transmission occurred (accounting for 19 of the 285 cases), and a small number of other cases where person-to-person transmission may have occurred. Clinical impact was most evident in severely immunocompromised individuals. Results were reported in the weekly pandemic situation updates, in the *Weekly Epidemiological Record* and through occasional web briefing notes.

Findings

The deployment of the antiviral stockpile with minimal notice, in an uncertain and rapidly evolving situation, demonstrated the importance of having a substantial number of doses, packed and ready to be shipped, but also of having tested systems, procedures and channels of communication to mobilize an effective operation. A successful operation depends on a multidisciplinary team working in synergy across several organizations, in multiple locations, with the ability to scale up to higher decision-making levels and with the flexibility to adapt to changing demands.

There was good feedback from countries about the speed and usefulness of this deployment, which demonstrated the value of advance preparation. While there was monitoring of efficacy and safety of the antiviral drugs during the pandemic, a review is needed of their effectiveness, drawing on all the studies that were initiated in several countries.

Vaccines

Advice and recommendations

Advice on vaccines and vaccination was provided by the Strategic Advisory Group of Experts (SAGE) on Immunization. SAGE reports to the WHO Director-General on issues

ranging from vaccine research and development to immunization delivery. The mandate of SAGE is to provide strategic advice rather than technical input *(55)*.

SAGE is organized through working groups, which serve on a time-limited basis to review and provide evidence-based information and options for the recommendations SAGE will make. The SAGE Ad hoc Policy Advisory Working Group on Influenza A (H1N1) vaccines *(56)* was convened for the first time on 29 April 2009. Unlike other SAGE working groups, and in view of the perceived urgency of the situation, no public call for nominations had been made. Instead, the group brought together representatives of SAGE, the WHO Global Advisory Committee on Vaccine Safety and the Expert Committee on Biological Standardization, so that expert advice could be efficiently coordinated. The work of this ad hoc group informed SAGE recommendations on vaccination issued on 19 May 2009 *(57)*, 7 July 2009 *(58)* and 29 October 2009 *(59)*.

Candidate vaccine strains

In addition to monitoring circulating influenza virus strains and recommending annual seasonal vaccine composition, GISN detects and assesses novel influenza viruses for pandemic potential. GISN recommends which novel influenza virus strains can be used to develop prototype pandemic vaccines, and develops candidate vaccine strains, which are provided free of charge to any manufacturer on request.

The emergence of avian influenza A (H5N1) underscored that global production capacity for influenza vaccines is insufficient to protect the world's population against a pandemic of highly fatal influenza. In addition, although many influenza virus strains with pandemic potential are contributed to GISN by low- and middle-income countries, access to pandemic vaccine developed from these strains tends to be limited to high-income countries and those with domestic influenza vaccine production capacities.

The Sixtieth World Health Assembly in May 2007 requested the WHO Director-General convene an Intergovernmental Meeting to develop a framework to ensure pandemic influenza vaccine viruses were widely shared and that there was equitable access to the vaccines that result *(60)*.

These principles of public availability of key information and free distribution of vaccine strains were respected during the influenza A (H1N1) 2009 pandemic. The gene sequence of wild-type pandemic H1N1 was made publicly available on 27 April 2009. By 8 May 2009 samples of wild-type virus had been sent from reference laboratories to vaccine manufacturers, all of which were in Europe or the USA because they had the necessary high-level biological containment facilities.

The first candidate vaccine viruses produced by classical reassortment were released for distribution on 27 May 2009, and the first strains produced by reverse genetics on 22 July 2009. The candidate reassortant vaccine viruses were promptly distributed on request to all vaccine manufacturers with Biosafety Level 2+ facilities.

The gene sequences of all vaccine strains were promptly made available in publicly available databases.

Vaccine development

When a new influenza strain emerges, several steps are required before an effective vaccine can be developed and administered. The first step is to rule out the possibility that

existing seasonal vaccines will produce adequate immunity to the new strain. Sera from people vaccinated with existing seasonal vaccines are tested against the new strain. This process is organized through WHO's network of Collaborating Centres and Essential Regulatory Laboratories. By 7 May 2009 it was clear that existing seasonal H1N1 vaccines did not protect against pandemic influenza A (H1N1) 2009 and that a new vaccine would be required.

The second necessary step is to modify the wild strain to grow efficiently in eggs so that it can be used for vaccine production. This modification also ensures that the vaccine virus is sufficiently attenuated to be manipulated under Biosafety Level 2+ conditions. Two methods are used: classical reassortment with high-growth strains, and a proprietary technology based on reverse genetics. The third step is to develop reference viral antigen and standardized antiserum to allow vaccine potency to be measured. This process requires coordination between manufacturers, reference laboratories and regulatory agencies. This step is not necessary for live attenuated influenza vaccines.

The final step involves clinical trials in human volunteers to assess safety and immunogenicity. Regulatory approval for marketing and widespread use is provided by regulatory agencies on the basis of the results of laboratory testing and clinical trials.

WHO held a first teleconference with Collaborating Centres and Essential Regulatory Laboratories on 27 April 2009. At twice-weekly, then weekly and later fortnightly teleconferences, information was shared on virus characterization, risk assessment and vaccine-strain development and selection. The first candidate reassortant vaccine virus was available on 27 May 2009, and the first reagents for vaccine potency assessment were available on 13 July.

The first vaccines were available for deployment by late September 2009, 20 weeks after virus isolation, from manufacturers in China, Hungary and Australia. In these three countries, vaccination campaigns started on 21 September, 29 September and 30 September, respectively. By 31 December 2009 vaccines against pandemic influenza A (H1N1) 2009 had been licensed from 22 companies worldwide. By comparison, developed-country seasonal influenza vaccination programmes anticipate a delay of about six months from strain selection to large-scale production.

Registration pathways used in various countries differed. For example, some regulatory agencies registered pandemic influenza A (H1N1) 2009 vaccines as a variation of seasonal influenza vaccines. The European Medicines Agency used a pre-agreed procedure based on a "mock-up registration" obtained previously by Baxter, GlaxoSmithKline and Novartis for their candidate H5N1 vaccines.

Almost all pandemic influenza A (H1N1) 2009 vaccines were licensed for use in all populations older than one year of age, including in pregnant women.

Vaccine production and donation

To ensure that developing countries would have access to vaccine in the event of an influenza H5N1 pandemic, the World Health Assembly had requested that WHO establish a vaccine stockpile. As of April 2009 two vaccine manufacturers, GlaxoSmithKline and Sanofi Pasteur, had pledged 50 million and 60 million doses of H5N1 vaccine, respectively, although no legal agreements for donations were in place.

On 19 May 2009 the WHO Director-General and the UN Secretary-General held a high-level meeting with chief executive officers of all known influenza vaccine manufacturers to advocate equitable access to pandemic influenza A (H1N1) 2009 vaccine by developing countries. GlaxoSmithKline and Sanofi Pasteur agreed to convert their H5N1 vaccine donation pledge to pandemic influenza A (H1N1) 2009 vaccine and to increase the number of doses to 150 million.

During May and June 2009 WHO surveyed influenza vaccine manufacturers' planned seasonal and pandemic production. Results of this assessment were made publicly available *(61)*. Manufacturers were asked whether they would be willing to reserve 10% of real-time production for acquisition by – but not necessarily donation to – UN agencies. Many producers were constrained by advance purchase agreements with high-income countries, so it was estimated that only limited amounts of pandemic influenza A (H1N1) vaccine would be available in 2009 for purchase by UN agencies.

Negotiations with manufacturers and governments for vaccine donations were initiated in late July 2009 but progressed slowly. It was envisaged that legal agreements would have to be concluded with at least four manufacturers and a dozen donor governments, on the donor side, and with almost 100 governments on the recipient side. It was decided that a single legal framework acceptable to all parties should be put in place. WHO negotiations proceeded first with GlaxoSmithKline, under the premise that the agreement reached would form a template for other manufacturers. An agreement for vaccine donation by GlaxoSmithKline was signed on 9 November 2009, with delivery of donated vaccine originally scheduled to begin in late 2009. CSL Australia, MedImmune and Sanofi Pasteur signed agreements on the same legal terms in December 2009. In January 2010, a legal agreement was reached for Novartis to facilitate donations made by donor governments of Novartis products, since this manufacturer declined to become a donor to the WHO pandemic vaccine deployment initiative.

Legal agreements with donor governments for pandemic influenza A (H1N1) 2009 vaccine donations were reached after the first agreements with manufacturers. The USA agreed on 16 December to donate vaccine from its own stocks, followed by Australia (22 December), France (15 January 2010), Belgium (29 January 2010), Switzerland (16 March 2010), Norway (19 March 2010), Italy (16 April 2010), the United Kingdom (28 May 2010) and Singapore (21 June 2010).

Production capacity, equitable access and technology transfer

The first discussion between the WHO Director-General and vaccine manufacturers to evaluate pandemic vaccine production capacity and timelines, and to advocate equity in vaccine availability for developing countries, was held on 29 April 2009. This teleconference was attended by manufacturers from high-income countries, most of which were members of the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) and by vaccine manufacturers from low- and middle-income countries, many of which belong to the Developing Country Vaccine Manufacturers Network (DCVMN). This teleconference was followed by a high-level meeting on 19 May 2009 between the WHO Director-General and the UN Secretary-General with chief executive officers of all known influenza vaccine manufacturers to advocate equitable access. Weekly teleconferences between WHO and all interested manufacturers followed. These were organized, on the manufacturers' side, by the IFPMA and the DCVMN. No vaccine donation agreements

were reached with manufacturers outside the IFPMA, mainly because the first pandemic vaccines registered by DCVMN manufacturers became available only in mid-2010.

Global capacity for influenza vaccine production is insufficient to protect more than a fraction of the world's population. In 2006 WHO developed a Global Action Plan (GAP) to increase supply of pandemic influenza vaccines following extensive consultation with all stakeholders on candidate reassortment vaccine virus *(62)*. The GAP prioritized three strategies to increase pandemic vaccine production capacity. The first proposed to increase coverage of seasonal vaccine worldwide in order to increase demand and to encourage manufacturers to invest in capacity to meet the new demand. The second was to promote the establishment of new production sites, including in developing countries. The third was to enhance research and development for novel influenza vaccines, since innovative vaccines have the potential to solve or at least substantially alleviate the shortfall in production capacity.

As part of the second strategy, WHO has since 2007 provided technical and financial support to manufacturers in 11 low- and middle-income countries to acquire the technology to produce influenza vaccine. WHO negotiated a licence for an egg-based live attenuated influenza vaccine from an influenza vaccine manufacturer in the Netherlands to WHO, and a material transfer agreement with a Russian Federation institute to secure access to the virus strains needed to manufacture the vaccine. These agreements allowed WHO to grant sublicences to two developing country manufacturers (SII in India and GPO in Thailand). The manufacturers were thus provided with access to the materials needed for the manufacture of live attenuated influenza vaccine, for the benefit not only of local markets but also for other developing countries without the capacity required for influenza vaccine production.

WHO also entered into collaboration with the Netherlands Vaccine Institute (NVI) as an additional support in capacity strengthening. NVI acts as the hub to support technology transfer and provides technical expertise in vaccine production to manufacturers in developing countries. As part of this agreement, NVI developed a platform for producing candidate vaccines, as well as standard operating procedures for production, quality assurance, and other activities needed to support final production of the vaccines. During the influenza A (H1N1) 2009 pandemic, three manufacturers in low- and middle-income countries were able to license pandemic vaccines used in their countries.

Seasonal versus pandemic vaccine production

The decision to suspend seasonal influenza vaccine production so that all production capacity can be used for pandemic vaccine is entirely in the hands of manufacturers and major purchasers. The decision that production of pandemic vaccine can safely be scaled down or suspended in favour of seasonal vaccine is also in the hands of manufacturers.

Neither SAGE nor an Emergency Committee convened under the IHR are charged by their terms of reference with advising on whether a vaccine against an emergent virus should be produced or when production of seasonal influenza vaccine should be suspended in favour of pandemic vaccine.

Vaccine deployment and in-country distribution

By the end of the H1N1 Deployment Initiative in September 2010, 200 million doses of pandemic influenza A (H1N1) 2009 vaccine had been pledged for donation, and 122.5

million doses had been contractually committed. Seventy million syringes and 500 000 sharps-disposal boxes had been pledged and committed (Becton-Dickinson donated 25 million syringes through AmeriCares to WHO; USAID donated 10.5 million syringes and 95 775 safety boxes to WHO. The remaining items were intended to be donated directly to countries). A fund of around US$ 57 million was available to cover shipment costs and to help countries distribute and deliver donated vaccines.

Plans were originally made to distribute 200 million doses of vaccine to nearly 100 countries. In view of the population size of potential recipient countries and of the volume of vaccines likely to become available, the WHO Director-General decided to offer each eligible country enough vaccine to immunize up to 10% of their population, which was considered sufficient to vaccinate health-care workers and higher-risk groups, including pregnant women. Vaccine was to be distributed in two tranches: sufficient to vaccinate 2% of the population (e.g. health-care workers) in a first shipment and the remainder in a second shipment. Small countries would receive their whole allocation (if less than 100 000 doses) in the first tranche in order to reduce transaction costs; large countries would receive less than their 2% allocation in the first tranche in order to allow all eligible countries to receive some vaccine as soon as possible.

Before receiving donated vaccine, countries were required to sign a letter of agreement with WHO and to provide a deployment plan showing they had a strategy in place to reach the target groups as well as sufficient financial resources, inclusive of WHO financial support. By May 2010, 84 agreements had been signed but only 65 countries had completed their plans. Between late February 2010, when donated vaccine became available, and the end of May 2010, 38.8 million doses of vaccine were distributed to 60 countries. All vaccine doses were sent with sufficient numbers of syringes and sharps disposal boxes. By the end of May 2010 nearly all eligible countries in the Americas, South-East Asia and the Western Pacific had received vaccine. Only 19 of 44 eligible African countries had received vaccine, the shortfall resulting mostly from the absence of finalized deployment plans. In six instances, delivery of donated vaccine was hindered because of delays in recipient countries providing regulatory approval for vaccine import.

In total, 78 million doses of pandemic influenza A (H1N1) 2009 vaccine were deployed to 77 countries. The Review Committee heard concerns about the delay in deploying vaccines, and recognized that the reasons were complex and multifactorial. These systemic difficulties will need to be tackled on a number of fronts to improve a future response.

H. WHO guidance documents

Some guidance documents were in place at the beginning of the pandemic, including: WHO Global Influenza Preparedness Plan (2005); WHO interim protocol: rapid operations to contain the initial emergency of pandemic influenza (October 2007); Infection Prevention and Control of Epidemic- and Pandemic-Prone Acute Respiratory Diseases in Health Care (June 2007); Pandemic Influenza Preparedness and Mitigation in Refugee and Displaced Populations: WHO Guidelines for Humanitarian Agencies (May 2008); Reducing Excess Mortality from Common Illnesses during an Influenza Pandemic (October 2008) and WHO Rapid Advice Guidelines on Pharmacological Management of Humans Infected with Avian Influenza A (H5N1) Virus (June 2006).

During the pandemic, about 60 documents were published, most before August 2009. The early documents, such as the advice on the use of masks, were not based on new data; these

could perhaps have been written and posted on the web site in advance as part of general pandemic preparedness. Alternatively, co-publishing or cross-posting arrangements could have been made with agencies, such as the United Kingdom Health Protection Agency or the US Centers for Disease Control and Prevention.

In the early stages of the pandemic, there was no organization-wide strategic assessment or prioritization of the guidance that would be needed; rather, decisions were made by individual technical units or in response to requests from countries. A large number of documents were prepared, but the Director-General had decided that, to ensure accuracy and consistency, all documents for release would have to be cleared by a single individual, the Assistant Director-General, Health Security and Environment. Not surprisingly, this created a backlog of unpublished documents.

As a result, the number of guidance documents published was limited and not systematic in coverage, with gaps in important areas, such as the evaluation of border measures. Few documents were translated, owing to a lack of available funds. This difficulty points to the wider issue of WHO not having contingency funds for such a global emergency. Support came from borrowed staff from other areas, but such a situation is sustainable only over a short period, and cannot cover increased communication and translation needs, for example. As a result of the pressure on document production, a group and processes were established for generating emergency guidelines (SHOCDocs). The purpose of SHOCDocs was to ensure quality through a peer-review process and to eliminate redundant or low-priority documents. However, there were still delays in many publications.

WHO did issue some clinical guidance, but this was subject to the same problems of delay. WHO also held teleconferences with clinicians to share their experiences, which were reported as valuable by the participants. For a future fast-moving situation, WHO should consider the most effective ways of sharing and transmitting clinical information, working in partnership with clinical experts, organizations and institutes.

The Review Committee found that both headquarters and Regional Offices issued guidelines. The Regions operate independently and may adapt guidance from headquarters to their own particular situation. However, there is no clear mechanism to ensure that guidelines are reconciled. WHO should develop the capacity to assure consistency of guidelines across the Organization, recognizing that conditions in different regions and individual countries may vary.

I. Communications

The capacity to relay information quickly and clearly on different media platforms (television, radio, print, web), across cultures and in many languages is essential to the effective management of a public-health emergency. This section examines the performance of WHO's internal and external communications during the pandemic. It examines how the Organization managed surge capacity and adapted its normal communications operations to risk communications and dealt with external criticism. The Review Committee interviewed key communications staff at headquarters and in the regions and noted in testimony and documents the contribution of communications to the management of the pandemic.

Daily operations

Communications activities at headquarters are decentralized. The Director-General's office has dedicated communications staff who report to a Director of Communications. Clusters have their own communications officers, based either in the Assistant Director-General's Office or within individual departments.

The Web Team has a structure that parallels communications staffing. The corporate communications pages of the web site that appear at the site's entry level include the media centre, general organizational information and subjects of general interest. They are edited by the Web Team, which is in the Communications Department of the Director-General's Office. Pages covering technical guidance, details on scientific meetings and events, and reports are edited by staff in individual departments. All web content is the responsibility of the Assistant Director-Generals at headquarters or of the Regional Director in Regional Offices.

Media reports are monitored daily. Communications officers evaluate how WHO's work is being communicated to the public and whether messages need refining. Communications staff alert technical and senior staff in their departments to important issues. When necessary, they are passed to senior management staff.

Risk communications

During a public-health emergency, a risk communications strategy helps stakeholders to define those risks, identify hazards, assess weaknesses and promote community resilience, thereby increasing the capacity to cope with the difficulties. Such is the importance of risk communications that it has been identified as one of the elements of the capacities that States Parties must develop by the IHR 2012 deadline.

WHO's strategy for risk communications is based on five principles: planning, transparency, announcing early, trust and listening. As a result of experience gained in previous outbreaks, WHO developed the WHO Outbreak Communication Guidelines (2005), and the WHO Outbreak Communication Planning Guide (2008). These guidelines have been applied to all WHO communications training, not just in emergencies.

WHO also refined its internal communications procedures for a public-health emergency through a series of training workshops, by developing a training package in 2006 and conducting a major public-health security exercise in June 2008.

Beginning of the pandemic

The Director-General's announcement on 25 April 2009 of a PHEIC was major news for all media outlets. As the primary voice for global public health, WHO was under extreme pressure to provide information and advice. The Organization quickly scaled up its communications structure. Staff from across headquarters formed a centralized "surge capacity team", led by the Communications Team Leader for the Global Alert and Response Department, within the Health Security and Environment Cluster. The position of Director of Communications in the Director-General's Office was vacant at the time.

At the peak of worldwide media interest in May, more than 45 communications officers answered enquiries at headquarters in a 24-hour operation that was coordinated with Regional Offices. Up to 15 other people handled calls, managed logistics, and coordinated

virtual press conferences, studio broadcasts and the on-site management of information technology services provided to journalists. At the start of the pandemic, headquarters staff worked around the clock. Later, several factors reduced the number of people available late at night. These included the longer-term nature of the effort, as well as fatigue and family commitments. The Organization took advantage of differences in time zones and switched calls to PAHO at midnight Central European Time, and from there to WHO Regional Office for the Western Pacific, before headquarters resumed responsibility the following morning. The surge structure was disbanded after six weeks, in mid-June 2009, and most staff returned to their departments or clusters. Although media and public interest was still constant, a team of three (later increased to six) full-time communications officers remained.

Policy decisions were made by the Organization's Senior Policy Group (SPG), which met daily and sometimes twice daily from the beginning of the pandemic. Communications staff were integrated into the SPG from the outset. After the meetings, key decisions were relayed to the rest of the communications team. From there, standard operating procedures allowed communication to flow from headquarters to the Regional Offices, through the SHOC structure, and to regional communications staff and Member States. The communications team held daily teleconferences with regional counterparts. Talking points, a list of key messages for the media, were distributed twice daily to Regional and Country Offices at the peak of the pandemic to ensure consistent information was being distributed throughout the Organization. Talking points were also distributed to other UN agencies, such as the United Nations Pandemic and Avian Influenza Communications Group, as well as to the EU Member States and Institutions Communications Network, the Global Health Security Action Group, the Network Communications Group, and ministry of health communications staff in countries where media interest was most intense.

The two primary channels of external communication during the acute phase of the pandemic were the media and WHO's web site. Press briefings began on 26 April 2009. At the beginning they were held daily, and then every other day and weekly as events demanded. The briefings gave journalists direct access to WHO's technical experts and were usually led by the Director-General; the Special Adviser to the Director-General on Pandemic Influenza; the Director, Initiative for Vaccine Research; the Director, Global Alert and Response and the WHO spokesperson.

Within the hour, audio files of the press conferences were posted on the web site and transcripts followed within three hours. A tent was erected in the grounds at headquarters to accommodate the media; 50–100 journalists used this facility during the first weeks of the pandemic. More than 40 virtual briefings were conducted by global teleconference, enabling journalists around the world to participate. Thousands of interviews for radio, television and by telephone were handled by communications staff at headquarters alone. In one week, more than 250 000 media stories on the pandemic were generated in English.

WHO's web site was critical to communicating its messages and technical information. Briefing Notes and Frequently Asked Questions were published on a regular basis. Eighty-six postings of WHO's Disease Outbreak News (DON) were devoted to the pandemic from April 2009 to August 2010. The DON provides detailed information, such as confirmed cases and deaths, for health professionals, journalists and the general public, and is published as required.

The public was an increasingly important audience for WHO. At one point, the web site received almost two million visits in three hours. A dedicated pandemic influenza web site

was created on 26 April, the day the PHEIC was declared. The site was a repository for technical guidance and general information for the public. WHO's Twitter feed and an RSS feed were was used to disseminate newly updated information.

External criticisms

Criticisms about WHO's response to the pandemic began to appear in the media in July 2009. One of the charges against WHO was that it changed the definition of a pandemic without notice. In the regular content review of web pages related to influenza pandemics as part of established emergency procedures, WHO's web manager identified two pages that required modification. The first, related to pandemic preparedness *(63)*, was changed on 4 May 2009 after the review showed that the terms "pandemic" and "H5N1 pandemic" were being used interchangeably. These terms created the impression that a pandemic would be caused only by H5N1.

The wording "enormous numbers of deaths and illness" referred to a lethal H5N1 pandemic scenario. The text was edited to be more reflective of the current H1N1 outbreak. The second page was a posting concerning H5N1, with a title that implied that it described an influenza pandemic in general terms. For clarity, "avian influenza" was added to the title. WHO followed standard industry practice by not deleting web pages. However, modifications to page content and versioning were not evident to readers. These changes, which were made without special notice or explanation, invited suspicion of a surreptitious shift in definition rather than an effort to make the descriptions of a pandemic more precise and consistent. From May 2009, all web-page changes were tracked and each revision was dated.

A second criticism was that WHO was moving faster than necessary to declare Phase 6 for the benefit of the pharmaceutical industry *(64)*. The first response from WHO to these allegations appeared only on 3 December 2009 and took the form of a Briefing Note on its web site, which detailed WHO's efforts to guard against conflicts of interest *(65)*. This was almost five months after the issue had initially been raised. This delay did not help dispel the allegations.

Further, in December the Council of Europe asked for immediate investigations into the "handling of the H1N1 pandemic" *(66)*. At a hearing on 26 January 2010, Dr Fukuda stated that "the influenza pandemic policies and responses recommended and taken by WHO were not improperly influenced by the pharmaceutical industry". Dr Fukuda had made similar statements at a WHO virtual press conference on 14 January 2010 *(67)*.

From October to December 2009, the media continued to make allegations about conflicts of interest among EC members, and asked WHO to publish its Declaration of Interest for WHO experts form. WHO published a statement on 22 January 2010, responding to allegations of conflicts of interest and what was, by then, being labelled by critics as a "fake" pandemic *(68)*. The conflict of interest policy was further explained by the WHO Executive Secretary of the Strategic Advisory Group of Experts (SAGE), who met with the UN Palais media corps in Geneva on 10 February 2010 to explain how SAGE deals with these issues *(69)*.

On 3 June 2010 further criticisms were levelled at WHO in an editorial in the *British Medical Journal (BMJ)* about conflicts of interest and conduct during the pandemic. WHO issued a statement on 8 June 2010 from the Director-General to *BMJ* editors, denying any conflict of interest and announcing the review of WHO's performance through this

Committee *(70)*. On 10 June WHO published a Briefing Note on its web site explaining its actions during the pandemic *(71)*.

Findings: external criticisms

The Review Committee found that WHO needs to improve its response to criticism by acknowledging when it may have erred or contributed to misunderstanding and by responding professionally and vigorously to unwarranted criticisms.

WHO's response to unfounded allegations appeared passive and slow. Some of these accusations emanated from social media sites (blogs, Facebook and Twitter), were unaccompanied by scientific evidence and were clearly unfounded. Other allegations, however, came from standard information sources and should have been dealt with proactively and transparently. The Committee understands that WHO regards itself a technical organization and, as such, technical work is its top priority. It may not have been publicly criticized in this way before and did not know how to respond appropriately. It was clear from interviews with senior communications staff that spending a great deal of time responding to every criticism and accusation directed at the Organization would not have been a wise use of limited resources. The Committee considers that the Organization needs a clear policy and mechanism for responding to criticism.

WHO's reluctance to acknowledge any mistakes and face up to its part in fostering concerns, for example, through its withholding the identities of members of the Emergency Committee, handling of conflict of interest, and undocumented alteration of web language describing pandemics, in turn, diminished its ability to respond to unfounded allegations, such as rushing ahead with declaring Phase 6 or collusion with pharmaceutical companies. WHO did not go far enough either in recognizing and acknowledging criticism that was legitimate or in refuting unfounded allegations. Distinguishing between the two is difficult, especially in real time, yet that discrimination and a more vigorous response in both directions are the essence of a communication strategy that sustains credibility.

WHO highlights trust as one of its principles of risk communication. This principle was fostered in the early stages as WHO tried to make its decisions and rationale for moving from phase to phase transparent. Some of that trust was diminished through its lack of transparency on conflicts of interest and its relative silence on disclosing the names of the EC members. This created a vacuum that allowed further criticism. The Organization has since recognized that it requires greater transparency to maintain the trust of the public.

Findings: strengths

WHO's communications response to the PHEIC displayed many strengths by applying its principles of risk communication during the acute phase:

- Communications staff mobilized early and actively engaged with the media.
- Phase changes were announced as soon as they were determined.
- Briefing Notes and Frequently Asked Questions were distributed.
- Key information for countries and health-care professionals was published on the web site. Many Member States said they received accurate information in a timely manner and were able to take the appropriate action in their countries as a result.
- The Organization quickly called upon its internal resources to establish a strong surge capacity team, which proved an effective strategy.

- Regional Offices indicated that the flow of information from headquarters was timely, effective and allowed the Organization to produce consistent messaging across the world.
- The Review Committee found that WHO dealt with technical issues quickly in the early stages of the pandemic. For example, questions about the safety of pork were discussed in an Information Note (No. 2/2009), Human-animal interface aspects of Influenza A/H1N1, on 30 April.
- The day before the announcement of Phase 6, WHO provided its Country Offices with communication packets containing three guidance tools regarding severity, public-health actions to be instituted and risk communication. These packets were the first attempt to collate material to assist the response at country level. While this action was commendable, the Committee felt the packets would have been more useful had they been distributed earlier.

Findings: improvements needed

The Review Committee found that WHO's communications response could be improved by learning from experience during the pandemic.

A major barrier to communication was the lack of surge capacity for translation services during the pandemic. The volume of information generated by the Organization exceeded resources. The result was an information gap in some countries, which affected the effectiveness of time-sensitive messages.

Disbanding the communications surge team at Phase 6, a crucial point in the pandemic, proved an unfortunate decision. The Director-General and her communications staff testified that continued long-term surge capacity, not only in communications but also elsewhere in the Organization, was untenable. Competing needs for resources in its daily business and ensuring continuity of WHO's regular activities took priority. Limited funding and inadequate numbers of staff are obstacles to sustained surge capacity.

Social media (i.e. Facebook, Twitter, YouTube etc.) have given global communication new dimensions. Because WHO had no policy on and few resources dedicated to social media, the Organization's dialogue with the outside world was compromised.

The use of new information technologies, including social networks, should be an essential part of WHO's strategic communications planning. Research, training and guidelines for Member States in this area would also be beneficial for response at a regional and national level.

In headquarters, links between departments and corporate-level communications within WHO are not as structured as they could be. WHO has no written plan for strategic communications during an emergency. The development of an Organization-wide plan that will improve normal and risk communications, incorporating longer-term outreach, is essential. Reputation management should be included in the plan as should improved transparency regarding changes to web content.

Since the review process began, communications staff have evaluated their work during the pandemic and work to improve policies has begun. Engagement with new media tools is increasing, with the use of Twitter, Facebook, YouTube and other forums. A Director of Communications is now in place in the Director-General's office.

Member States have identified communication needs during their own country reviews. The most frequently cited is strengthening risk communications at local, national and regional level by increasing human and institutional capacity, most notably through training to develop skills and raise awareness.

Member States should consider developing strategies for engaging with the media and public through planned communication on complex public-health issues. The pandemic highlighted the difficulty in communicating complex scientific principles, conveying severity, uncertainty and risk. New approaches that go beyond pure information dissemination need to be considered. Improving the content and reach of information products (referred to by some countries as Information, Education and Communication materials), especially in local languages, has been noted by many Member States as a critical element to increasing awareness. Materials need to be audience-specific, disseminated in the most appropriate method for the target group, be it written (guidelines, leaflets), audio (television and/or radio spots) or interactive workshops. Developing methods to evaluate the usefulness of these materials – how they are received, perceived and used by target groups – could be considered.

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IV

Conclusions and recommendations

IV

Conclusions and recommendations

The Review Committee offers three overarching conclusions to underpin the recommendations that follow its investigation of the functioning of the International Health Regulations 2005 (IHR) and on pandemic influenza A (H1N1) 2009.

Summary conclusion 1

The IHR helped make the world better prepared to cope with public-health emergencies. The core national and local capacities called for in the IHR are not yet fully operational and are not now on a path to timely implementation worldwide.

Summary conclusion 2

WHO performed well in many ways during the pandemic, confronted systemic difficulties and demonstrated some shortcomings. The Committee found no evidence of malfeasance.

Summary conclusion 3

The world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public-health emergency. Beyond implementation of core public-health capacities called for in the IHR, global preparedness can be advanced through research, reliance on a multisectoral approach, strengthened health-care delivery systems, economic development in low- and middle-income countries and improved health status.

The remainder of this document summarizes the Committee's findings and reasoning and the recommendations that follow each conclusion.

Summary conclusion 1

The IHR helped make the world better prepared to cope with public-health emergencies. The core national and local capacities called for in the IHR are not yet fully operational and are not now on a path to timely implementation worldwide.

Development of the IHR required more than a decade of complex deliberations. While the IHR are not perfect, they significantly advance the protection of global health. The Committee has focused its recommendations on how ongoing implementation of the IHR can be strengthened. The IHR seek to balance the sovereignty of individual States Parties with the common good of the international community, and take account of economic and social interests as well as the protection of health. The Committee's recommendations acknowledge these inherent tensions and focus on actions that can enhance the shared goal of global public-health security.

The Committee commends the following provisions of the IHR:

- The IHR oblige WHO to obtain expert advice on the declaration and discontinuation of a Public Health Emergency of International Concern.

- The IHR strongly encourage countries to provide each other with technical cooperation and logistical support for capacity building.
- The IHR encourage establishment of systematic approaches to surveillance, early warning systems and response in Member States.
- The IHR required the establishment of National IHR Focal Points (NFPs) to create a clear two-way channel of communication between WHO and Member States.
- The IHR led a number of countries to strengthen surveillance, risk assessment, response capacity and reporting procedures for public-health risks.
- The IHR introduced a decision instrument (Annex 2) for public-health action that has proved more flexible and useful than the list of notifiable diseases it replaced.
- The IHR require countries to share information relevant to public-health risks.
- The IHR require States Parties that implement additional health measures significantly interfering with international traffic and trade to inform WHO about these measures, and to provide the public-health rationale and relevant scientific information for them.

Despite these positive features of the IHR, many States Parties lack core capacities to detect, assess and report potential health threats and are not on a path to complete their obligations for plans and infrastructure by the 2012 deadline specified in the IHR. Continuing on the current trajectory will not enable countries to develop these capacities and fully implement the IHR. Of the 194 States Parties, 128, or 66%, responded to a recent WHO questionnaire on their progress. Only 58% of the respondents reported having developed national plans to meet core capacity requirements, and as few as 10% of reporting countries indicated that they had fully established the capacities envisaged by the IHR. Further, as documented by external studies and a WHO questionnaire, in some countries, NFPs lack the authority to communicate information related to public-health emergencies to WHO in a timely manner.

The most important structural shortcoming of the IHR is the lack of enforceable sanctions. For example, if a country fails to explain why it has adopted more restrictive traffic and trade measures than those recommended by WHO, no legal consequences follow.

To remedy a number of these problems, the Committee recommends the following.

Recommendation 1

Accelerate implementation of core capacities required by the IHR. WHO and States Parties should refine and update their strategies for implementing the capacity-building requirements of the IHR, focusing first on those countries that will have difficulty meeting the 2012 deadline for core capacities. One possible way to support and accelerate implementation would be for WHO to mobilize appropriate agencies and organizations that would be willing to provide technical assistance to help interested countries assess their needs and make the business case for investment. Making the case for investment in IHR capacity building and subsequent resource mobilization would increase the likelihood that more States Parties could come into compliance with the IHR. Donor countries and organizations could take advantage of the IHR Annex 1A as a priority list for development support and also seize opportunities to share specialized resources, such as laboratories, across countries. WHO should also update the 2007 guidance on NFP functions, and include examples of good practice to reinforce the value of the IHR.

Recommendation 2

Enhance the WHO Event Information Site. WHO should enhance its Event Information Site (EIS) to make it an authoritative resource for disseminating reliable, up-to-date and readily accessible international epidemic information. States Parties should be able to rely on the EIS as a primary source for information on epidemiological status, risk assessment, response measures and their rationales. The EIS could also be used to post WHO guidance before it is made public. Additional ways to enhance the EIS include:

- Using EIS for guidance and messages to NFPs.
- States Parties allowing WHO to share more information.
- Including more events and expanding information on each event. For instance, for each event there could be maps, expanded risk assessments and recommendations, and links to relevant WHO guidance and Collaborating Centres.
- Posting all temporary and standing recommendations issued under the IHR as well as information on Member States that institute additional measures and their rationales for these, and the status of WHO's request for such a rationale.

Recommendation 3

Reinforce evidence-based decisions on international travel and trade. When States Parties implement health measures that significantly interfere with international traffic and are more stringent than those recommended by WHO, IHR Article 43 provides that the States Parties shall inform WHO of their actions. (As stated in Article 43, "significant interference generally means refusal of entry or departure of international travellers, baggage, cargo, containers, conveyances, goods and the like, or their delay, for more than 24 hours.") In such circumstances, WHO should energetically seek to obtain the public-health rationale and relevant scientific information, share it with other States Parties, and, where appropriate, request reconsideration, as stipulated under Article 43. WHO should review and assess the effectiveness and impact of border measures taken during the pandemic to support evidence-based guidance for future events.

Recommendation 4

Ensure necessary authority and resources for all National IHR Focal Points. States Parties should ensure that designated National IHR Focal Points have the authority, resources, procedures, knowledge and training to communicate with all levels of their governments and on behalf of their governments as necessary.

Summary conclusion 2

WHO performed well in many ways during the pandemic, confronted systemic difficulties and demonstrated some shortcomings. The Committee found no evidence of malfeasance.

As noted in testimony by States Parties, WHO provided welcome leadership in coordinating the global response throughout the pandemic. WHO's epidemic intelligence functions have strengthened in recent years as a result of the Event Management System, increases in Regional Office capacity and the Global Outbreak Alert and Response Network.

The Committee commends the following actions by WHO and other partners:

- Development of influenza preparedness and response guidance to help inform national plans. Pandemic preparedness plans were in place in 74% of countries when the pandemic began.
- Effective partnering and interagency coordination (with the United Nations Children's Fund and the United Nations Office for Project Services), including close cooperation with the animal health sector (the World Organisation for Animal Health and the Food and Agriculture Organization of the United Nations) on technical and policy issues.
- Rapid field deployment and early guidance and assistance to affected countries.
- Timely detection, identification, initial characterization and monitoring of the pandemic (H1N1) 2009 virus through the Global Influenza Surveillance Network.
- Selection of the pandemic vaccine virus and development of the first candidate reassortant vaccine viruses within 32 days of declaration of the Public Health Emergency of International Concern.
- Vaccine seed strains and control reagents made available within a few weeks.
- Early policy recommendations on target groups and dosage of vaccines by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization.
- Weekly collation, analysis and reporting of global epidemiological, virological and clinical surveillance data.
- Prompt appointment of an Emergency Committee with well-qualified individuals, which was convened within 48 hours of activation of IHR provisions.
- Efficient distribution of more than 3 million treatment courses of antiviral drugs to 72 countries.
- Establishment of a mechanism to help countries monitor their development of IHR core capacities.

The Committee also noted systemic difficulties that confronted WHO and some shortcomings on the part of WHO:

- The absence of a consistent, measurable and understandable depiction of severity of the pandemic. Even if the definition of a pandemic depends exclusively on spread, its degree of severity affects policy choices, personal decisions and the public interest. What is needed is a proper assessment of severity at national and subnational levels. These data would inform WHO's analysis of the global situation as it evolves, allowing WHO to provide timely information to Member States. The Committee does, however, recognize that characterization of severity is complex and difficult to operationalize.
- Inadequately dispelling confusion about the definition of a pandemic. One online WHO document described pandemics as causing "enormous numbers of deaths and illness", while the official definition of a pandemic was based only on the degree of spread. When, without notice or explanation, WHO altered some of its online documents to be more consistent with its intended definition of a pandemic, the Organization invited suspicion of a surreptitious shift in definition rather than an effort to make its descriptions of a pandemic more precise and consistent. Reluctance to acknowledge its part in allowing misunderstanding of the intended definition fuelled suspicion of the Organization.
- A pandemic phase structure that was needlessly complex. The multiphase structure contains more stages than differentiated responses. Defined phases leading to a pandemic are more useful for planning purposes than for operational management.

- Weekly requests for specific data were overwhelming to some countries, particularly those with limited epidemiological and laboratory capacity. Country officials were not always convinced the data they submitted were being analysed and used, particularly as the epidemic progressed. For example, some felt that continued counting of cases yielded less useful information than would have been provided by rates of hospitalization, complications and death in countries affected early on in the pandemic.
- The decision to keep confidential the identities of Emergency Committee members. Although confidentiality represented an understandable effort to protect the members from external pressures, this paradoxically fed suspicions that the Organization had something to hide. While the decision was consistent with WHO practices for other expert committees, whose identities are normally divulged only at the end of what is often a one-day consultation, this practice was not well suited to a Committee whose service would extend over many months.
- Lack of a sufficiently robust, systematic and open set of procedures for disclosing, recognizing and managing conflicts of interest among expert advisers. In particular, potential conflicts of interest among Emergency Committee members were not managed in a timely fashion by WHO. Five members of the Emergency Committee and an Adviser to the Emergency Committee declared potential conflicts of interest. None of these was determined sufficiently important to merit the members' exclusion from the Emergency Committee. The relationships in question were published, along with the names of the members of the Emergency Committee, when the pandemic was declared over on 10 August 2010. Before this information was published, however, assumptions about potential ties between Emergency Committee members and industry led some to suspect wrongdoing. The Review Committee recognizes that WHO is taking steps to improve its management of conflicts of interest, even as this review has proceeded.
- At a critical point of decision-making about the pandemic (moving from Phase 4 to 5), conferring with only a subset of the Emergency Committee rather than inviting input from the full Emergency Committee.
- The decision to diminish proactive communication with the media after declaring Phase 6 (for example, by discontinuing routine press conferences focused on the evolving pandemic) was ill-advised.
- Failure to acknowledge legitimate reasons for some criticism, in particular, inconsistent descriptions of a pandemic, or the lack of timely disclosure of relationships potentially constituting a conflict of interest among experts who advised on plans and response to the pandemic. In such instances, WHO may have inadvertently contributed to confusion and suspicion.
- Responding with insufficient vigour to criticisms that questioned the integrity of the Organization.
- Despite the ultimate deployment of 78 million doses of pandemic influenza vaccine to 77 countries, numerous systemic difficulties impeded the timely distribution of donated vaccines. Among the key difficulties was a variation in willingness to donate, concerns about liability, complex negotiations over legal agreements, lack of procedures to bypass national regulatory requirements and limited national and local capacities to transport, store and administer vaccines. Some recipient countries felt WHO did not adequately explain that liability provisions included in the recipient agreement were the same as the liability provisions accepted by purchasing countries. All these difficulties proved daunting in the midst of a pandemic; some could have been reduced by more concerted preparation and advance arrangements among all interested parties.
- Lack of timely guidance in all official languages of WHO.

- Lack of a cohesive, overarching set of procedures and priorities for publishing consistent and timely technical guidance resulted in a multiplicity of technical units within the Organization individually generating an unmanageable number of documents.

Critics assert that WHO vastly overstated the seriousness of the pandemic. However, reasonable criticism can be based only on what was known at the time and not on what was later learnt. The Committee found that evidence from early outbreaks led many experts at WHO and elsewhere to anticipate a potentially more severe pandemic than subsequently occurred. The degree of severity of the pandemic was very uncertain throughout the middle months of 2009, well past the time, for example, when countries would have needed to place orders for vaccine. An observational study of 899 patients hospitalized in Mexico between late March and 1 June 2009 showed that pandemic (H1N1) 2009 disproportionately affected young people. Fifty-eight patients (6.5% of those hospitalized) became critically ill, with complications including severe acute respiratory distress syndrome and shock. Among those who became critically ill, the mortality rate was 41% (*1*). These statistics were alarming. Even a reported mortality rate of one third that level among critically ill patients in Canada was worrisome (*2*). In August 2009, the President's Council of Advisors on Science and Technology in the United States of America released a report positing a possible scenario of 30 000–90 000 deaths from pandemic (H1N1) 2009 in the USA alone (*3*). The mid-point and upper level of this scenario turned out to be five times higher than the post-pandemic estimates of the actual number of deaths (*4*). Even so, 87% of deaths occurred in those under age 65, with the risk of death among children and working adults seven times and 12 times greater, respectively, than during typical seasonal influenza (*4*).

Some commentators accused WHO of rushing to announce Phase 6 and suggested the reason was to enrich vaccine manufacturers, some of whose advance-purchase agreements would be triggered by the declaration of Phase 6. Far from accelerating the declaration of Phase 6, WHO delayed declaration until evidence of sustained community spread in multiple regions of the world was undeniably occurring. As far as the Review Committee can determine, no critic of WHO has produced any direct evidence of commercial influence on decision-making. In its interviews with staff and advisory committee members, including the Strategic Advisory Group of Experts (SAGE) on Immunization and the Emergency Committee, and with representatives of industry, and through its review of internal and external documents, the Review Committee found no evidence of attempted or actual influence by commercial interests on advice given to or decisions made by WHO. In the Committee's view, the inference by some critics that invisible commercial influences must account for WHO's actions ignores the power of the core public-health ethos to prevent disease and save lives.

The Review Committee offers the following recommendations:

Recommendation 5

Strengthen WHO's internal capacity for sustained response. WHO should strengthen its internal capacity to respond to a sustained Public Health Emergency of International Concern, such as a pandemic, identifying the skills, resources and internal arrangements to support a response that extends beyond a few months. Among the internal arrangements that WHO should reinforce are:

- Identify the skills, resources and adjustments needed for WHO to carry out its role in coordination and global support.

- Establish an internal, trained, multidisciplinary staff group who will be automatically released from their normal duties for an unspecified duration, with a relief rotation after a designated interval.
- Ensure a 24/7 capacity to meet the personal needs for accommodation, meals, transportation and childcare of WHO staff enlisted in a sustained emergency response.
- Establish an event management structure that could be maintained throughout a future pandemic or other sustained global public-health emergency.

Recommendation 6

Improve practices for appointment of an Emergency Committee. WHO should adopt policies, standards and procedures for the appointment and management of an Emergency Committee that assure an appropriate spectrum of expertise on the committee, inclusive consultation and transparency with respect to freedom from conflicts of interest.

- As provided in Article 48 of the IHR, WHO should appoint an Emergency Committee with the spectrum of expertise and geographical representation appropriate for each event. The Review Committee also concluded that a broader spectrum of expertise among Emergency Committee members might have been useful, including in risk communication. The Review Committee acknowledged that WHO must appoint an Emergency Committee with a set of skills and expertise that is appropriate for and particular to each event for which it is constituted. For an influenza pandemic, this expertise would include virology, laboratory assessment, epidemiology, public-health field and leadership experience, veterinary science, risk assessment and risk communication and methodological expertise in systematic reviews of the scientific literature.
- To ensure that the full range of views is presented, WHO should invite all members of an Emergency Committee to participate in all of its major deliberations.
- WHO should clarify its standards and adopt more transparent procedures for the appointment of members of expert committees, such as an Emergency Committee, with respect to potential conflicts of interest. The identity and relevant background, experience and relationships of Emergency Committee members should be publicly disclosed at the time of their proposed appointment, with an opportunity for public comment during a period of initial, probationary service that would apply to all members. WHO should have clear standards for determining when a conflict of interest exists that warrants disqualifying an individual, and have clear procedures to determine when and on what basis exceptions may be made to obtain necessary expertise or balance. The Review Committee appreciates the need for expert consultations to be held in confidence so that the Director-General will have the benefit of candid discussion and advice. The desirability of confidential consultation heightens the burden of transparency on standards for appointment.
- As part of a more proactive and rigorous approach to managing conflicts of interest, WHO should appoint a designated ethics officer.

Recommendation 7

Revise pandemic preparedness guidance. WHO should revise its pandemic preparedness guidance in order to: simplify the phase structure (one possible paradigm would include only three phases – baseline, alert phase, pandemic); emphasize a risk-based approach to enable a more flexible response to different scenarios; rely on multisectoral participation;

draw upon lessons learnt at a country, regional and global level; and include further guidance on risk assessment.

Recommendation 8

Develop and apply measures to assess severity. WHO should develop and apply measures that can be used to assess the severity of every influenza epidemic. By applying, evaluating and refining tools to measure severity every year, WHO and Member States can be better prepared to assess severity in the next pandemic. Assessing severity does not require altering the definition of a pandemic to depend on anything other than the degree of spread. Rather, while not part of the definition of a pandemic, measured and projected severity are key components of decision-making in the face of a pandemic.

The Committee recognizes that estimating severity is especially difficult in the early phase of an outbreak, that severity typically varies by place and over time, and that severity has multiple dimensions (deaths, hospitalizations and illness, with each varying by age and other attributes, such as pre-existing health conditions and access to care; burden on a health system and social and economic factors). Descriptive terms used to characterize severity, such as mild, moderate and severe, should be quantitatively defined in future WHO guidelines so that they may be used consistently by different observers and in different settings. The Committee urges consideration of adaptive measures that would move as rapidly as possible from early counts of cases, hospitalizations and deaths to population-based rates. Severity should be assessed as early as possible during a pandemic and continually re-assessed as the pandemic evolves and new information becomes available. Severity might be assessed using a "basket of indicators" in a pre-agreed minimum data set (e.g. hospitalization rates, mortality data, identification of vulnerable populations and an assessment of the impact on health systems). Estimates of severity should be accompanied by expressions of confidence or uncertainty around the estimates.

Recommendation 9

Streamline management of guidance documents. WHO needs a strategy and document management system to cope with the development, clearance, translation and dissemination of guidance and other technical documents in a timely and consistent way during a public-health emergency. Interim guidance should be revised as data become available. When feasible, if the guidelines have potential policy implications, WHO should make every effort to consult with Member States and provide them with advance notice of impending publications. WHO should develop the capacity to assure consistency of guidelines across the Organization, recognizing that conditions in different regions and individual countries may vary.

Recommendation 10

Develop and implement a strategic, organization-wide communications policy. WHO should develop an organization-wide communications policy and a strategic approach to improve routine and emergency communications. A strategic approach entails matching the content, form and style of communication with the media, timing and frequency that will reach the intended audience and serve the intended purpose. WHO should be prepared to sustain active, long-term communications outreach when circumstances require, to acknowledge mistakes and to respond professionally and vigorously to unwarranted

criticisms. Web publishing procedures should be clarified so that changes in web pages can be historically tracked and archived. WHO should invest in a robust social media presence for rapid communication to a wider, more diverse audience.

Recommendation 11

Encourage advance agreements for vaccine distribution and delivery. In concert with efforts by Member States, and building on existing vaccine distribution systems, WHO should encourage advance agreements with and among appropriate agencies and authorities in Member States, vaccine manufacturers and other relevant parties that would facilitate approval and delivery of pandemic vaccines to low-resource countries, to increase equity in supply and support advance planning for administration of vaccines.

Summary conclusion 3

The world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public-health emergency. Beyond implementation of core public-health capacities called for in the IHR, global preparedness can be advanced through research, reliance on a multisectoral approach, strengthened health-care delivery systems, economic development in low and middle-income countries and improved health status.

Despite the progress that the IHR represent and WHO's success in mobilizing contributions from the global community, the unavoidable reality is that tens of millions of people would be at risk of dying in a severe pandemic. The fundamental gap between global need and global capacity must be closed.

Beyond the specific measures recommended above to complete implementation of the IHR provisions and improve the functions of WHO, the world can be better prepared for the next public-health emergency through advance commitment by Member States acting individually and collectively with WHO.

The Review Committee offers the following recommendations.

Recommendation 12

Establish a more extensive global, public-health reserve workforce. Member States, in concert with WHO, should establish a more extensive global reserve workforce of experts and public-health professionals to be mobilized as part of a sustained response to a global health emergency and deployed for service in countries that request such assistance. The size, composition and governing rules for activating and deploying such an entity—the Global Health Emergency Workforce—should be developed through consultation and mutual agreement among the Member States and WHO. The number and particular skills of the experts deployed will depend on specific characteristics of the emergency to which the workforce is responding. This workforce would significantly expand the current Global Outbreak and Alert Response Network by strengthening its composition, resources and capacity, with a view towards better support for sustained responses to public-health emergencies.

At present, WHO's capacity to prepare and respond in a sustained way to any public-health emergency is severely limited by chronic funding shortfalls, compounded by restrictions on the use of funds from Member States, partners and other donors. Mindful of concerns

about efficiency and accountability that motivate some of the restrictions, the Committee concludes that the establishment of a contingency fund outside of WHO, but available for deployment by WHO at the time of a public-health emergency, will be a prudent step to assure an immediate and effective global response.

Recommendation 13

Create a contingency fund for public-health emergencies. Member States should establish a public-health emergency fund of at least US$ 100 million, to be held in trust in a location and form that would be readily accessible to WHO. The fund, which would support surge capacity, not the purchase of materials, would be released in part or whole during a declared Public Health Emergency of International Concern, based on approval of a plan for expenditures and accountability submitted by WHO. The precise conditions for use of the fund should be negotiated among the Member States in consultation with WHO.

The Review Committee commends the effort by Member States to reach agreement on sharing of viruses and access to vaccines and other benefits. The Review Committee believes that success will depend on a mutual expectation of proportionate, balanced benefit and contribution by all stakeholders. An agreement that is one-sided or that expects contribution without benefit, or vice versa, will be neither acceptable nor sustainable. The Review Committee also believes that obligations and benefits not linked to a legal framework are unlikely to last.

Recommendation 14

Reach agreement on sharing of viruses and access to vaccines and other benefits. The Review Committee urges Member States and WHO to conclude negotiations under the Open-ended Working Group of Member States on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and Other Benefits. A successful conclusion to this negotiation will lead to wider availability of vaccines and other benefits and greater equity in the face of the next pandemic, as well as continued timely sharing of influenza viruses.

The Review Committee offers the following elements for consideration as part of an acceptable agreement.

Measures to expand global influenza vaccine production capacity:

- WHO should continue its practice of working with public-health laboratories to make seed vaccine virus strains widely available to all vaccine manufacturers.
- In so far as it is consistent with national priorities, risk assessments and resources, the Review Committee urges countries to immunize their high-risk populations yearly against seasonal influenza. This can reduce the burden of disease. In addition, this can increase experience with local production, distribution and delivery and encourage more global capacity for vaccine production. More generally, experience with comprehensive programmes during seasonal influenza (in such areas as surveillance, communication, professional and public education, health-protection measures and pharmaceuticals) provides valuable preparation in advance of a major pandemic.
- The Committee urges countries to strengthen their capacity to receive, store, distribute and administer vaccines. Technological advances that reduce reliance on a cold chain and otherwise simplify administration will streamline these processes.

- The Committee urges Member States, international organizations and industry to aid the transfer of technologies for vaccine and adjuvant production in parts of the world currently lacking this capacity, such as Africa, through established programmes such as the Global Action Plan to Increase Supply of Pandemic Influenza Vaccines (GAP).

Measures to increase access, affordability and deployment of pandemic vaccine:

- All vaccine manufacturers should commit to a contribution of 10% of pandemic influenza vaccine from each production run to a global redistribution pool. WHO should be responsible for managing allocations from this pool based on advice from a consultative committee.
- Increased access to vaccines and antiviral drugs can be achieved through advance agreements between industry, WHO and countries. These agreements should be negotiated without regard to virus subtype, for a specified period of time (e.g. three to five years) and should be regularly reviewed and renewed.
- Other measures that may promote greater and more equitable access to vaccine include differential pricing, direct economic aid to low-resource countries and additional donations of vaccine from purchasing countries or manufacturers.
- Countries that receive donated vaccine, as any purchaser of the vaccine, should adhere to the same practices of releasing and indemnifying manufacturers from certain legal liabilities.

Measures to detect and promptly identify potential pandemic influenza viruses:

- Every Member State should commit to share promptly, according to the principles of sharing of influenza viruses and access to vaccines and other benefits, any biological specimens and viral isolates that may be related to a new or emerging influenza virus in humans with WHO collaborating laboratories. Viruses isolated from animals should be promptly sent through the appropriate animal health system. The sharing of specimens and viral isolates should be accompanied by arrangements to share benefits, including access to vaccines.

The world's capacity to prevent and limit a severe pandemic is constrained by many factors: predominant reliance on vaccine production technology that is little changed in 60 years; the need to match vaccine to particular viral strains; the inability to predict which influenza viruses will be dangerous to human health; uncertainty about the effectiveness of many pharmaceutical and public-health measures; the lack of field-based, rapid, affordable, highly sensitive and specific diagnostic tests; and limitations of infrastructure, resources and capacities in many countries. Also needed are improved knowledge of and practical strategies for implementing public-health and personal-protective measures, such as handwashing, respiratory etiquette, isolation and social distancing.

Some of these limitations can be reduced over time through national and international research. Further, the results of research on personal and public-health protective measures may apply to any emerging public-health threat, especially when few or no drugs or vaccines exist. Because assessment of public-health measures typically must occur in real time in the midst of an outbreak, it is crucial to design and prepare research protocols and plans in advance. Beyond research advances, global resilience depends on host and environmental factors, so that improving health status, promoting economic development and strengthening health systems can mitigate the impact of a future pandemic virus.

Recommendation 15

Pursue a comprehensive influenza research and evaluation programme. Member States, individually and in cooperation with one another, and WHO should pursue a comprehensive influenza research and evaluation programme. This should build on a thorough review of the evidence gained in all fields from the 2009 H1N1 pandemic. Key research goals include: strengthen surveillance technology and epidemiological and laboratory capacity to improve detection, characterization and monitoring of new viruses; identify viral and host determinants of transmissibility and virulence; develop rapid, accurate, inexpensive point-of-care diagnostic tests; enhance the accuracy and timeliness of modelling projections; create broader spectrum, highly effective, safe and longer-lasting vaccines; hasten vaccine production and increase throughput; devise more effective antiviral drugs and antimicrobials to treat bacterial complications; evaluate the effectiveness of drug, vaccine, personal protective equipment, personal hygiene and social interventions; assess the effectiveness and costs of border measures and enhance risk communication. Much of this research and evaluation can and should be carried out in the absence of a pandemic. However some studies can only be carried out during a global event such as a pandemic. For these it is essential that protocols be prepared and funding identified in advance so that research can begin without delay.

The Review Committee respectfully commends these 15 recommendations to the World Health Organization, the World Health Assembly and its Member States, and the larger global community. (Table 4.1) arrays the recommendations according to the lead responsibility (WHO or Member States) and time horizon for completion (within one year, within two years, beyond two years). The Committee believes all 15 recommendations deserve to be implemented without delay.

Despite everything that was done in the pandemic, the major determinant of the consequences was the virus that caused it. In the face of a virulent influenza pandemic, or any similarly global, sustained and threatening public-health emergency, the world remains at risk of massive disruption, suffering and loss of life. The Committee hopes that these recommendations will help WHO and its Member States be better prepared to avert, mitigate and cope with future threats to health.

Table 4.1. **Lead responsibility and timeframe to complete implementation of recommendations**

	Short Term (within 1 year)	Medium Term (within 2 years)	Long Term (beyond 2 years)
WHO Led	**Enhance the WHO Event Information Site** (Recommendation 2)	**Revise pandemic preparedness guidance** (Recommendation 7)	**Reinforce evidence-based decisions on international travel and trade** (Recommendation 3)
	Strengthen WHO's internal capacity for sustained response (Recommendation 5)	**Develop and apply measures to assess severity** (Recommendation 8)	
	Improve practices for appointment of an Emergency Committee (Recommendation 6)		
	Streamline management of guidance documents (Recommendation 9)		
	Develop and implement a strategic, organization-wide communications policy (Recommendation 10)		
Country Led	**Reach agreement on the sharing of viruses and access to vaccines and other benefits** (Recommendation 14)	**Ensure necessary authority and resources for all National IHR Focal Points** (Recommendation 4)	**Accelerate implementation of core capacities required by the IHR** (Recommendation 1)
Jointly Led		**Encourage advance agreements for vaccine distribution and delivery** (Recommendation 11)	**Pursue a comprehensive influenza research and evaluation programme** (Recommendation 15)
		Establish a more extensive global, public-health reserve workforce (Recommendation 12)	
		Create a contingency fund for public-health emergencies (Recommendation 13)	

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Appendices

Appendix I

Terms of reference for the IHR Review Committee and method of work

The assessment of the global response to the pandemic H1N1 will be conducted by the International Health Regulations Review Committee, a committee of experts with a broad mix of scientific expertise and practical experience in public health. The members are some of the leading experts in the world in their respective fields.

The International Health Regulations 2005 (IHR) is an international legal agreement that is binding on 194 States Parties across the globe, including all of the Member States of WHO. The basic purpose of the IHR is to help the international community prevent and respond to acute public-health risks that have the potential to cross borders and threaten people worldwide.

In January 2010, the WHO Executive Board requested a proposal from the Director-General on how to assess the international response to the pandemic influenza, and then approved her suggestion to convene the IHR Review Committee to review both the pandemic response and the functioning of the IHR.

The pandemic H1N1 is the first public-health emergency of international concern to occur since the revised IHR came into force. The IHR played a central role in the global response to the pandemic and so review of the IHR and review of the global handling of the pandemic influenza are closely related.

The IHR facilitate coordinated international action by requiring countries to report certain disease outbreaks and public-health events to WHO so that global reporting of important public-health events is timely and open.

The IHR were first implemented (i.e. "entered into force") worldwide in 2007 and the Health Assembly determined that a first review of its functioning is to take place by the 63rd World Health Assembly in May 2010.

Objectives

The review has three key objectives

- Assess the functioning of the International Health Regulations (2005);
- Assess the ongoing global response to the pandemic H1N1 (including the role of WHO); and
- Identify lessons learned important for strengthening preparedness and response for future pandemics and public-health emergencies.

The Committee

The IHR Review Committee is made up of approximately 27 members who have been selected from the roster of experts under the IHR structure or other WHO expert committees. The committee members represent a broad mix of expertise, practical experience and backgrounds, and include experts from developed and developing countries.

The members are some of the leading experts in the world in their respective fields. They are not WHO staff, nor do they receive funding from WHO for their contributions to the review process. Names of the committee members were made public prior to the first meeting.

At the first meeting, Professor Harvey V. Fineberg was elected as chair; Professor Babatunde Osotimehin was elected as vice-chair; and Dr Silvia Bino was elected as rapporteur.

The IHR Review Committee is considered a WHO expert committee and so its operations and structure follow regulations for WHO expert advisory panels and committees, and provisions of the IHR.

Proceedings

The committee will determine its methods and schedule of work.

The first meeting was held 12–14 April 2010 at WHO headquarters in Geneva.

Observers invited to the first meeting included representatives of all States Parties to the IHR (194 countries), United Nations organizations and relevant intergovernmental organizations, and nongovernmental organizations in official relations with WHO.

The committee will advise the Director-General of its views and findings. Based on the committee's advice, the Director-General will provide an interim report to the World Health Assembly in May 2010, and an expected second, final report to the World Health Assembly in May 2011.

Participation by countries (IHR States Parties)

Countries will have the opportunity to make brief statements to the committee at the first meeting, and may also submit comments to the Review Committee on key issues, concerns and lessons learned related to the pandemic response and functioning of the IHR.

Method of work

The Review Committee conducted a major portion of its work through plenary meetings at WHO's headquarters in Geneva. For transparency, these meetings were open to the media. The Committee heard testimony from individuals representing States Parties, National IHR Focal Points, intergovernmental organizations, nongovernmental organizations, United Nations agencies, industry, health professionals, experts, members of the media, chairs of relevant committees and the WHO Secretariat.

The full Committee and its working groups also met for deliberative sessions in Geneva, open only to members of the Committee and its immediate support staff. Further consultations took place among the support staff, the Chair and working groups of the Committee by means of telephone conferences and e-mail exchange.

While operating independently, the Review Committee frequently sought information from WHO's Secretariat, asking for clarification of issues that arose during the information-gathering and report-writing periods. WHO staff provided written responses to many questions posed by the Committee and spoke informally with Committee members. WHO provided the Committee with unfettered access to internal documents and Committee members signed non-disclosure agreements in order to review confidential legal documents.

The WHO Secretariat developed a series of briefing notes for the Committee, providing background on issues such as: the IHR; pandemic preparedness; pandemic phases; pandemic severity; pandemic vaccine; antiviral drugs; virological monitoring; disease monitoring; laboratory response; public-health measures; and the Open-ended Working Group of Member States on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and Other Benefits. The Committee had access to a series of studies that evaluated the functioning of Annex 2 of the IHR (i.e. the decision instrument for States Parties' assessment and notification of public-health events) as well as progress reports on the implementation of the IHR. At the Committee's request, the WHO Secretariat devised a matrix of the key public-health functions of the IHR and identified a broad range of non-pandemic events that had been notified to WHO since the IHR came into force. The Committee selected 18 events and directed the Secretariat to prepare a summary of each event to facilitate its assessment of the public-health functions of the IHR.

The Committee sought to document WHO's role and management in response to the pandemic and to evaluate the effectiveness of the IHR. This required a thorough investigation of events and decisions in the course of the pandemic, an examination of criticisms of the Organization and an assessment of its achievements. The goal from the outset has been to identify the best ways to protect the world in the next public-health emergency. Throughout its deliberations, the Committee has aimed to be thorough, systematic, open and objective. This report provides a full description of the evidence presented to the Committee in interviews and documents, and the Committee's assessment and interpretation of that evidence.

Appendix II

Affiliations and biographies of Review Committee members*

Dr Preben Aavitsland, Deputy Director/State Epidemiologist, Division of Infectious Disease Control, Norwegian Institute of Public Health, Oslo, Norway

Preben Aavitsland, MD, is State Epidemiologist of Norway and Deputy Director of the Division of Infectious Disease Control at the Norwegian Institute of Public Health, which is the National IHR Focal Point of Norway. He also serves on the Advisory Forum of the European Centre for Disease Prevention and Control, and leads the EpiNorth network of communicable disease control in northern Europe. He is a consultant at the Oslo Contraception Clinic, a not-for-profit clinic run by a nongovernmental organization.

Dr Aavitsland was part of the Norwegian delegation to the Intergovernmental Working Group, which negotiated the revision of the International Health Regulations in 2004–2005. He has been a key adviser to national health authorities on pandemic response and pandemic preparedness and served at different times as Chair or Secretary of the Institute's Pandemic Incident Group. In 2008, he chaired a WHO technical consultation on guidance and evaluation of Annex 2 of the IHR.

From 1997–2009, he was medical editor of the *Journal of the Norwegian Medical Association*. He has authored 70 original articles in peer-reviewed journals, mainly on the epidemiology of HIV infection, hospital-acquired infections, and on outbreaks of infectious diseases. He supervises several Ph.D. students affiliated with the University of Oslo, where he also received his own medical certificate.

Professor Tjandra Y. Aditama, Director General of Disease Control and Environmental Health, Ministry of Health, Jakarta, Indonesia

Tjandra Yoga Aditama, MD, is Director General of Disease Control and Environmental Health, Ministry of Health, Indonesia.

Dr Aditama is the Responsible Person for the National IHR Focal Point in Indonesia, and was involved in Indonesia's response to H5N1 events and the 2009 influenza H1N1 pandemic. Dr Aditama was also a temporary adviser to WHO's South-East Asia Regional Office on noncommunicable diseases in February 2011.

Dr Aditama has been Professor of Pulmonology and Respiratory Medicine, Faculty of Medicine, University of Indonesia, and Adjunct Professor in the Centre for Environment and Population Health, Griffith University, Australia. He has authored more than 100 publications.

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* The Director-General wishes to thank the following Members who have resigned during the pendency of the Committee: Dr Anthony Evans, Professor John Mackenzie, Dr Ziad Memish, Dr Babatunde Osotimehin.

Professor Aditama has been involved in the health sector in government management positions and as an academic researcher. After finishing his medical studies, he worked as the head of health centres in several municipalities. He did his specialist training in pulmonology and respiratory health (consultant in infection) at the University of Indonesia. He was vice-director and then a director at Persahabatan Hospital, Jakarta, in the early 1990s.

Dr Silvia Bino, Associate Professor of Infectious Diseases, Head, Control of Infectious Diseases Department, Institute of Public Health, Tirana, Albania

Silva Bino, MD, Ph.D, is the Head of the Control of Infectious Diseases Department of the Institute of Public Health and an Associate Professor of Infectious Diseases at the Faculty of Medicine, Tirana University, Albania. She was the Director of National Public Health Institute from 2000–2006, and has devoted her career to novel strategies to control infectious diseases and strengthen surveillance systems in resource poor countries.

Dr Bino coordinated surveillance, diagnostic, and response activities for pandemic influenza A (H1N1) 2009 in Albania. She is also in the national group for IHR implementation, and has been involved in IHR implementation in Southeastern Europe.

Dr Bino has been the Regional Coordinator of the network to strengthen surveillance and control of communicable diseases in South-eastern Europe, which has fostered strengthening of early warning systems, policy development, preparedness and response, applied epidemiology training and expert and institutional collaboration in IHR implementation.

Since 2000 she has been coordinating the Immunization program and helped to establish a syndromic Early Warning System in Albania.

She has authored different articles on infectious diseases published in professional and scientific journals and has participated in the writing of different guidelines, books and reports related to infectious diseases, influenza and public-health surveillance.

She has served as consultant to WHO and other UN agencies and until April 2009 was a member of Strategic Advisory Group of Experts on Immunization.

She earned her medical and doctoral degrees from Tirana University and followed with postgraduate training on infectious diseases, microbiology, epidemiology and public health in Switzerland, Belgium, the United Kingdom and the USA.

Dr Eduardo Hage Carmo, Epidemiologist, South American Government Institute of Health (ISAGS) Project of the Union of South American Nations (UNASUR), Institute of Collective Health of the Universidade Federal da Bahia and consultant to the Secretariat of Health Surveillance of the Ministry of Health, Brazil

Eduardo Hage Carmo, MD, PhD, is an Epidemiologist with the South American Government Institute of Health (ISAGS) of the Union of South American Nations (UNASUR), Rio de Janeiro, and with the Institute of Collective Health of the Universidade Federal da Bahia, Bahia, Brazil. He is also a consultant to the Secretariat of Health Surveillance of the Ministry of Health, Brasilia, Brazil and the Former Director of Epidemiologic Surveillance from March 2007 to February 2011, Ministry of Health, Brasilia, Brazil.

As Director of Epidemiologic Surveillance at the Brazilian Ministry of Health, he was responsible for managing the preparation for and response to pandemic influenza A

(H1N1) 2009, including in related governmental decision making. All of his scientific production has been supported by public institutions. His work as Director also focused on epidemiologic surveillance, communicable diseases, preparedness and response to public-health emergencies, public-health evaluation, health technology, prevention and control measures, international health, and IHR implementation at regional and national levels. Since 2002 he has collaborated with PAHO and WHO on IHR revision processes, and implementation and monitoring, including the development of tools, procedures, and training methodology. Since 2003 he has participated in WHO consultative meetings on influenza preparedness and response, contributing to the development of regional and national plans.

Since 1986 his academic career has been focused on public health, epidemiology, epidemiologic surveillance, communicable diseases, and the International Health Regulations. Dr Carmo has authored and coauthored book chapters on epidemiological transition and communicable disease surveillance, as well as 27 articles, and received the J. Snow and Fred L. Soper awards.

He has received his medical degree, and his masters and doctoral degrees in public health, from Universidade Federal da Bahia, Brazil. Dr Eduardo Hage Carmo, Epidemiologist, South American Institute of Governance in Health (ISAGS) Project of the Union of South American Nations (UNASUR), Institute of Collective Health of the Universidade Federal da Bahia, and consultant to the Secretariat of Health Surveillance of the Ministry of Health, Brazil.

Dr Martin Cetron, Director, Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Martin Cetron, MD, is Director, Division of Global Migration and Quarantine (DGMQ) at the US Centers for Disease Control and Prevention (CDC). He also holds faculty appointments at the Emory School of Medicine and the Rollins School of Public Health. He served in CDC's Division of Parasitic Diseases and Bacterial Respiratory Diseases before joining DGMQ in 1997.

Dr Cetron has been a leader in public-health emergency preparedness and response activities at CDC. He played a leadership role in CDC responses to the 2001 anthrax bioterrorism incident, the 2003 global SARS epidemic, the 2003 US monkeypox outbreak, the 2005 Hurricane Katrina/Rita response, and pandemic influenza A (H1N1). He is part of the CDC pandemic influenza preparedness and response leadership team. During the 2009 H1N1 pandemic, he led CDC's activities for international border responses and community mitigation strategies.

He was part of the US delegation to the negotiations on the revision of the International Health Regulations. Dr Cetron has served as an expert consultant to WHO on IHR and pandemic influenza preparedness and response.

His primary research interests are international health and global migration, with a focus on emerging infections, tropical diseases, and vaccine-preventable diseases in mobile populations. He has coauthored more than 100 publications.

He is a graduate of Dartmouth College and Tufts Medical School. He trained in Internal Medicine at the University of Virginia, in Infectious Diseases at the University of Washington, and the Epidemic Intelligence Service at CDC.

Dr Omar El Menzhi, Director, Directorate of Epidemiology and Disease Control, Ministry of Health, Rabat, Morocco

Omar El Menzhi, MD, is Director of Epidemiology and Disease Control at the Ministry of Health in Morocco. For 25 years he was head of health services in various regions of Morocco, and then regional health director for the Greater Casablanca area from 2007 to 2009. He has spent most of his professional career in health policy and health services management, focusing on the implementation and evaluation of health programmes.

Dr El Menzhi is the Responsible Person for the National IHR Focal Point in Morocco, and was significantly involved in his country's response to the 2009 H1N1 pandemic. He has helped develop strategy documents on various topics ranging from the national strategy for continuing education to communicable and noncommunicable disease control.

He received his MD degree from the Université Mohammed V de Rabat; a Master's degree in Public Health from the Free University of Brussels; a health leadership development certificate; and an advanced degree in malaria studies from the University of Bordeaux, France.

Dr Yuri Fedorov, Deputy Director, Federal Centre on Plague Control, Federal Service for Surveillance of Consumer Rights Protection and Human Well-being, Moscow, Russian Federation

Yuri M. Fedorov, DSc, PhD, is Deputy Director, Federal Centre on Plague Control, Department of Epidemiological Surveillance and Sanitary Protection of the Territory of Russian Federation, Federal Service for Surveillance on Consumer Rights Protection and Human Well-Being. He is Professor of Epidemiology at Moscow Medical University (post-graduate training).

He has 30 years of experience in planning, supervision, and implementation of national programmes on prevention and control of communicable diseases at the national level, as well as training of personnel at regional level.

He participated in development and implementation of the IHR (2005).

Professor Harvey V. Fineberg, President, The Institute of Medicine, Washington DC, USA

Harvey V. Fineberg, MD, PhD, is President of the US Institute of Medicine. He served as Provost of Harvard University from 1997 to 2001, after 13 years as Dean of the Harvard School of Public Health. He has devoted most of his academic career to the fields of health policy and medical decision-making. His past research has focused on the process of policy development and implementation, assessment of medical technology, evaluation and use of vaccines, and dissemination of medical innovations.

Dr Fineberg helped found and served as president of the Society for Medical Decision Making and also served as consultant to the World Health Organization. At the Institute of Medicine, he has chaired and served on a number of panels dealing with health policy issues, ranging from AIDS to new medical technology.

He was an informal adviser to the US Government (including the US CDC and the Department of Health and Human Services) on H1N1 during the outbreak.

Dr Fineberg is co-author of *Clinical Decision Analysis, Innovators in Physician Education,* and *The Epidemic that Never Was*, an analysis of the controversial federal immunization

program against swine flu in 1976. He has co-edited several books on such diverse topics as AIDS prevention, vaccine safety, and understanding risk in society. He has also authored many articles published in professional journals. Dr Fineberg is the recipient of several honourary degrees and the Joseph W. Mountin Prize from the US CDC. He earned his bachelor's, medical, and doctoral degrees from Harvard University.

Mr Andrew Forsyth, Team Leader, Public Health Legislation and Policy, Office of the Director of Public Health, Ministry of Health, Wellington, New Zealand

Andrew Forsyth, BA (Hons), Diploma Public Health, is Team Leader, Public Health Legislation and Policy, New Zealand Ministry of Health. As part of this role, he contributes to the operation of the New Zealand National IHR Focal Point. During 2009, Mr Forsyth was involved in the national planning and intelligence functions of New Zealand's response to pandemic influenza.

He has more than 20 years of experience in the areas of health workforce and environmental health policy. More recently, he has led the development of legislation for drinking-water, the national cervical screening programme, and a major review of New Zealand's core public-health statute, the Health Act 1956. He participated in preliminary consultation rounds and the subsequent inter-governmental negotiations in 2004 and 2005 that produced the revised International Health Regulations. He has served as a consultant to WHO and provided training on the implementation of the IHR (2005) in the Pacific.

He earned his BA (Hons) from Victoria University, Wellington, and his Diploma in Public Health from the University of Otago, Wellington School of Medicine.

Dr Claudia Gonzalez, Partner-Director, EPI-Sur Consultores, and Professor, Center of Epidemiology and Public Health Policy, Universidad del Desarrollo, Santiago, Chile

Claudia Gonzalez, MPH, is a consultant with EPI-Sur Consultores, an international consulting firm that provides advice and consulting services in the area of health to international organizations, governments and nongovernmental organizations. It has consulted for PAHO on infectious diseases (including on influenza), for Chilean universities and for the government. Starting in January 2011, Dr Gonzalez also holds a teaching position with the Center of Epidemiology and Public Health Policy, Universidad del Desarrollo, Santiago, Chile.

From 2005 until July 2010, she was Epidemiology Coordinator for the Chilean Ministry of Health, focusing on epidemiological surveillance and the development of studies for decision-making in public policy. Before that, she worked in the Epidemiology Department research unit, where she was involved in developing the national epidemiological surveillance model, the Chilean national health objectives for the decade 2000–2010, and population surveys to measure quality of life and the prevalence of disease and risk factors in various populations.

Beginning in 2002 she was extensively involved in drawing up the National Plan for Pandemic Control; in 2009 she was in charge of the executive secretariat of the Committee for the Control of Outbreaks and Health Emergencies, the body responsible for handling the 2009 H1N1 pandemic in Chile. She was also head of the IHR (2005) National Focal Point and responsible for implementing the IHR in Chile.

She is the author of a number of articles in national and international scientific journals and has also been involved in drafting a range of guidelines and books on epidemiological

studies on cancer, HIV/AIDS, and communicable diseases, including pandemic influenza A (H1N1) 2009 virus.

She has attended a number of international meetings and forums organized by WHO/PAHO on influenza and IHR (2005).

Dr Mohammad Mehdi Gouya, Director-General, Centre for Disease Control, Ministry of Health and Medical Education, Tehran, Islamic Republic of Iran

Mohammad Mehdi Gouya, MD, is the Director General of the Centre for Disease Control (CDC), Ministry of Health and Medical Education, Islamic Republic of Iran and Chief Adviser to the Deputy of Health of the Ministry of Health and Medical Education. Since 1990 he has been Assistant Professor in the School of Medicine of Iran University of Medical Sciences, where his research has focused on public-health issues. Dr Gouya serves as the head of the National Focal Point of the International Health Regulations, and was responsible for developing the pandemic preparedness plan in his country. He is also Chair of the National Influenza Technical Committee, as well as a member of the Supreme Council of Health in the Cabinet.

He is a regional WHO adviser of WHO for AIDS (AIDS/HIV/STD Regional Advisory Group, ARAG), and also a member of a Programme Coordinating Board of UNAIDS. He has also been a temporary WHO adviser in the areas of the EMRO Regional Framework on Health Promotion, injury prevention, and tuberculosis.

He also served as a National Project Director in the following projects: the Global Fund Against AIDS, Tuberculosis, and Malaria, an HIV/AIDS Project with CDC; and Secretariat of national committees on HIV/AIDS, TB, malaria, and zoonotic diseases, immunization and noncommunicable diseases. He has served as a member of the Permanent Commission of the Secretariat of the National High Council for Food Health and Safety.

He earned his medical degree from Jondishapour University, Ahvaz, Islamic Republic of Iran, and specialized in infectious and tropical diseases at Tehran University of Medical Sciences, Islamic Republic of Iran. He also earned a MPH from Tehran University of Medical Sciences.

Dr Amr Mohamed Kandeel, Chief of Preventative and Endemic Diseases Sector, First Undersecretary, Ministry of Health and Population, Egypt

Amr Mohamed Kandeel, MD, PhD, is First Undersecretary for Preventative and Endemic Diseases Sector, Ministry of Health and Population, Egypt. He is a graduate of the faculty of medicine, Ain Shams University, Egypt 1990. He has a diploma in public health, a master's degree in epidemiology, a diploma in infection control and a PhD in public health. After 17 years as Epidemiologist, Director of the Infection Control Department, and Director of General Directorate of Communicable Disease Department, Ministry of Health and Population, he served as the Ministry's Undersecretary for Preventive Affairs, Preventive Sector, from 2008 until June 2010 and as Chief of Cabinet, Minister's Office, from June 2010 until March 2011.

Dr Kandeel is the head of the National IHR Focal Point for Egypt, and has participated in planning, preparedness and response to H1N1. He has attended many WHO consultations on H1N1, H5N1 and IHR.

Dr Kandeel's career has focused on public health and epidemiology in the preventive sector in the Ministry of Health and Population. He also participated in the planning, evaluation, and monitoring of infection control programs in health facilities, as well as in the development of the Egyptian National Infection Control guidelines and in the planning, evaluation and monitoring of national campaigns for Polio eradication, neonatal tetanus and measles.

He is a supervisor of vaccine deployment in Egypt. Also, Dr Kandeel has supervised the program of EPI, surveillance unit and participated in all outbreak investigations from 2004 until June 2010 in Egypt.

In the field of communicable diseases, Dr Kandeel participated in production of an annual bulletin for communicable diseases for Egypt, planning and upgrading of the national strategies for communicable diseases control, formation of a system for evaluation and monitoring of communicable diseases control for primary health care facilities and a research project in this area. Dr Kandeel has published 14 articles on various topics in the field of public health in international journals.

Dr Arlene King, Chief Medical Officer of Health, Ontario Ministry of Health and Long-Term Care, Toronto, Ontario, Canada

Arlene King, MD, MHSc, FRCPC, is Chief Medical Officer of Health, Ontario Ministry of Health and Long-Term Care, Canada. She is an internationally recognized expert in immunization, infectious diseases and pandemic preparedness. She is also an adjunct professor at the Dalla Lana School of Public Health, University of Toronto. Before joining the Ministry, Dr King was Director General of the Centre for Immunization and Respiratory Infectious Diseases (including influenza and pandemic influenza) at the Public Health Agency of Canada (PHAC). She held several other positions with Health Canada/PHAC, including the position of Director General, Pandemic Preparedness.

From 2006 to 2009, Dr King was responsible for the oversight of health sector pandemic planning for Canada. When pandemic influenza A (H1N1) 2009 occurred, she served as the technical response lead for the Public Health Agency of Canada. From June 2009 to August 2010, she led the pandemic response in Ontario as the Chief Medical Officer of Health for the province.

She also held various key positions at the British Columbia (BC) Centre for Disease Control, and served as a Medical Officer of Health in Vancouver and Burnaby, BC, as well as a family physician in northern Alberta, Canada.

Dr King has been an adviser to the World Bank and CIDA on emerging infectious diseases. She served on the Board of the Global Alliance on Vaccines and Immunization (2004–2006). She has been a consultant to WHO on polio, SARS, and influenza, and is a member of the PAHO technical advisory group on immunization and the WHO AFRO Polio Eradication Certification Commission. Until 2009, she was the lead for Canada in the intergovernmental discussions concerning virus sample and benefits sharing.

Dr King received her medical degree from McMaster University and certification in Family Medicine from the University of Calgary. She received a Master's degree in Health Sciences from the University of British Columbia and is a Fellow of the Royal College of Physicians and Surgeons of Canada in Community Medicine.

Professor Abdulsalami Nasidi, Former Director, Public Health, Federal Ministry of Health, Abuja, Nigeria

Abdulsalami Nasidi, MD, PhD, is a medical officer with more than 32 years of experience in clinical medicine, public health, virology and the development of vaccines and biological products. Formerly Director of Public Health and Director, Special Duties, in the Federal Ministry of Health of Nigeria, he is now retired from Government. He currently serves as Chair of the EchiTAb Study group, Nigeria/UK, and Chair/Executive Officer of the Reach Care Foundation, Nigeria. He is also Special Technical Adviser to the Minister of Health.

He headed the Federal Vaccine Production Laboratory in Yaba for 7 years; while there he introduced a new method for the production of yellow fever vaccine, which was used successfully for the control of the 1986/1987 yellow fever outbreak in Benue State. In 2008, he was appointed Chairman of the Presidential Task Force on Polio Eradication and Route Immunization, whose measures led to the reduction of the circulating wild polioviruses in Nigeria by early 2009 and recent gains in polio eradication and routine immunization.

Appointed as Nigeria's Chief Epidemiologist in 1991, he helped develop a disease surveillance and notification system and a monthly epidemiological bulletin. In that position, he was also responsible for the IHR activities in the country. Dr Nasidi was also the Responsible Person for the National IHR Focal Point.

He was among 16 people who established the Global Fund to fight AIDS, TB, and Malaria, in Brussels, Belgium. He established Nigeria's Country Coordinating Mechanism and served as its Chair for six years. He also initiated a National Centre for Disease Control (NCDC) for Nigeria.

He headed the Nigerian health sector taskforce response to the H1N1 pandemic, and participated in designing the national response to the pandemic. With the outbreak of H1N1, he played an active role in establishing a Nigerian laboratory in Abuja capable of diagnosing the influenza viruses, which then became the WHO reference laboratory for the country.

Dr Nasidi is Vice Chair/Chief Executive Officer of the recently established nongovernmental organization "Reach Care Foundation", which currently is collaborating with the Institute of Virology, Baltimore, United States of America, and with the Nigerian Federal Ministry of Health.

He has served on several WHO committees, most recently as Nigerian delegate and as Vice-Chair in the Intergovernmental Meeting on Pandemic Influenza Preparedness: Sharing of Influenza viruses and access to vaccines and other benefits. He also participated in the related technical working group for three years and served as Chair of the Technical Working Group.

He has authored more than 50 scientific publications and has been recognized by his country with a national honour, Officer of the Order of the Niger (OON).

Dr Nasidi earned his medical degree from Kalinin State Medical School, Tver, Russian Federation, and his doctoral degree from the Ivanovsky Institute of Virology, Academy of Medical Sciences, Moscow, Russian Federation.

Professor Paul Odehouri-Koudou, Director, National Institute of Public Hygiene, Abidjan, Côte d'Ivoire

Professor Paul Odehouri-Koudou, MD, is Director of the Côte d'Ivoire National Institute of Public Hygiene and Professor of Infectious and Tropical Diseases at Abidjan-Cocody University. He was Director of Community Health and Executive Director of the Modern and Traditional Medicine Collaboration Project from 2000 to 2001.

He has been involved in his country's implementation of the IHR (2005), and, in 2007, organized a workshop on IHR implementation in Côte d'Ivoire. He is the Responsible Person for the National IHR Focal Point in his country, and had a significant role in the country's response to the H1N1 pandemic. He is also a member of the Côte d'Ivoire National Committee of Independent Experts on Vaccination and Vaccines.

Professor Odehouri-Koudou served as an expert member of the WHO-AFRO African Advisory Committee for Research and Development, 2001–2002 and 2004.

He is the author of many articles on communicable diseases, including specifically AIDS, published in important international journals. He has been honoured by his country as Officer, and Commander, of the Order of Merit of National Education of Côte d'Ivoire, and Chevalier of the National Order of Côte d'Ivoire.

Professor Paul Odehouri-Koudou earned his doctoral degree in medicine (docteur d'Etat en Médecine) from the Faculty of Medicine of the Abidjan-Cocody University.

Dr Nobuhiko Okabe, Director of Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Tokyo, Japan

Nobuhiko Okabe, MD, PhD, is Director of Infectious Disease Surveillance Center of the National Institute of Infectious Diseases, Japan. His fields of expertise are infectious disease control, paediatric infectious diseases, and immunization.

Dr Okabe currently works with Japan's National IHR Focal Point, and was a consultant or temporary adviser during the early stages of the IHR revision process. He is currently the Chairman of the Ministry of Health, Labour and Welfare Committee advising on the revision of the National Pandemic Preparedness Plan. Prior to the H1N1 2009 pandemic he was a chairman of the Pandemic Preparedness Plan Advisory Committee in Japan and was involved in establishing related guidelines. During the H1N1 2009 pandemic, he participated in the response, and was a member of the Advisory Committee concerning the H1N1 pandemic in the Cabinet Office of the Ministry of Health, Labour and Welfare. In the early 1990s, he served as Regional Adviser for Communicable Disease Control and Prevention, World Health Organization Western Pacific Regional Office in Manila, Philippines.

Dr Okabe earned his medical and doctoral degrees from Jikei University, Tokyo, Japan.

Professor Dr Mahmudur Rahman, Director of the Institute of Epidemiology, Disease Control and Research (IEDCR) & National Influenza Centre (NIC), Ministry of Health and Family Welfare, Dhaka, Bangladesh

Mahmudur Rahman, MD, MPH, PhD, is Director of the Institute of Epidemiology, Disease Control and Research and National Influenza Center, Ministry of Health and Family Welfare, Bangladesh.

Professor Rahman was the key facilitator in establishing the National Influenza Center, Biosafety Level 3 and Nipah laboratories, and web-based disease surveillance in Bangladesh. He led the H1N1 2009 pandemic response in Bangladesh. Since 2005 he has been involved in pandemic preparedness planning, exercises, and functions relating to the IHR.

He was Associate Professor and then Professor and Head of the Department of Epidemiology, National Institute of Preventive and Social Medicine. He has devoted most of his academic career to the fields of epidemiology and public health. His past research has focused on disease surveillance, communicable and noncommunicable disease epidemiology and public-health policy issues.

He is serving as a member of the Expert Review Committee for Polio Eradication and of the Scientific Advisory Committee on Visceral Leishmaniasis for WHO's Special Programme for Research and Training in Tropical Diseases.

Professor Rahman was Managing Editor of the *Journal of Preventive and Social Medicine,* and editor of the "Text Book of Community Medicine and Public Health". He has authored 72 research publications and studies published in international and national journals.

He earned his medical degree from Chittagong Medical College, Bangladesh, and his graduate degrees in primary health care management from Mahidol University, Thailand, and his doctorate in epidemiology from the University of Cambridge, UK.

Dr Palliri Ravindran, Director, Emergency Medical Relief, Directorate General of Health Services, Ministry of Health, New Delhi, India

Palliri Ravindran, MD, MBA, is Director, Emergency Medical Relief, Directorate General of Health Services, Ministry of Health, Government of India; he was previously Assistant Director-General.

His areas of expertise have been in planning, prevention, mitigation, preparedness, and response strategies for disaster health, including public-health emergencies at national level. Dr Ravindran coordinated his country's efforts in managing SARS, avian influenza, and pandemic influenza 2009. He joined the Government Health Service and practiced clinical medicine for 15 years before joining the Administration in 1997.

Dr Ravindran has attended meetings at SEARO, WHO as an expert or a temporary adviser, and was employed at WHO, SEARO for a short term in 2007. He was a WHO fellow in Risk Assessment and Health Promotion at Mahidol University, Thailand.

He received an Australian Leadership Award fellowship conferred by the Nossal Institute for Global Health, University of Melbourne, Australia.

He obtained his medical degree and pursued his postgraduate education in public health at Delhi University; he also has an MBA in disaster management from the Guru Gobind Singh Indraprastha University in Delhi.

Professor José Ignacio Santos, Professor and Head of the Infectious Diseases Unit, Department of Experimental Medicine, Faculty of Medicine, National Autonomous University of Mexico, Mexico City, Mexico

José Ignacio Santos, MD, is Professor and Head, Infectious Disease Unit, Department of Experimental Medicine, National Autonomous University of Mexico, Mexico City, Mexico.

Prior to accepting this position, he was General Director of Hospital Infantil de México Federico Gómez, one of Mexico's National Institutes of Health. In 1997–2004, Dr Santos was director of Mexico's National Infant and Adolescent Health Program and Immunization Program; he was earlier also Mexico's liaison member of the Advisory Committee on Immunization Practices with the US Centers for Disease Control and Prevention.

Dr Santos also serves other international health agencies, including on the board of trustees of the International Center for Diarrheal Research in Dhaka, Bangladesh; the Measles Working Group of WHO's Strategic Advisory Group of Experts; the board of counsellors of the Pediatric Dengue Vaccine Initiative; the Pan American Health Organization's Technical Advisory Group on Vaccines and Immunizations; and the Data and Safety Monitoring Board for the WHO Measles Aerosol Project.

Dr Santos is past president of the Mexican and Pan-American Infectious Diseases Societies and is a fellow of the Infectious Disease Society of America. He is a member of the advisory group of the Pediatric Global Research Priorities of the American Academy of Pediatrics.

Dr Santos received his medical and paediatric training at Stanford University and clinical immunology and infectious diseases training at the University of Utah.

Ms Palanitina Tupuimatagi-Toelupe, Director General of Health and Chief Executive Officer of the Ministry of Health, Samoa

Ms Palanitina Tupuimatagi-Toelupe, NZRN, MHPEd, BEd, GradDipHEd, AdvDip Business Management, is the Director General of Health and Chief Executive Officer of the Ministry of Health, Samoa.

Ms Toelupe pioneered a number of public health protection and health promotion programmes in Samoa and, more recently, the health reforms in her country that culminated in the establishment in 2006 of the National Health Service as the Government's biggest health service provider, separating it from the Ministry of Health, now the monitoring and regulatory authority in health. She was also instrumental in the promotion and domestic implementation of health-related WHO and UN Conventions such as the WHO Framework Convention on Tobacco Control, the Convention on the Elimination of All Forms of Discrimination Against Women, and the Convention on the Rights of the Child.

As Director General of Health, she leads the national drive on health system strengthening based on health promotion and primary health care. She also led her country's preparedness and response to the H1N1 pandemic and is Chair of the National Health Task Force for Disaster Preparedness and Response. She is extensively involved in IHR implementation and promotion, as her office is the National IHR Focal Point. As Director General, she is also currently an Alternate Member of the WHO Executive Board, having led Samoa's delegations to the Board's 124th, 126th and 128th sessions.

She served as Head for the Advancement of Women in the Ministry of Women, Community and Social Development, from 1998–2005, after 18 years as the Public Health Chief Health Educator and Health Promotion Specialist in the Ministry of Health. For the past decade, she has concentrated on institutional governance, technical and professional leadership, policy development, and health regulatory reforms.

She received all of her tertiary education and degrees from universities in New Zealand, Australia and the National University of Samoa in affiliation with the United States International University.

Professor Patricia Ann Troop, Independent, Former Chief Executive, Health Protection Agency, London, United Kingdom

Patricia Ann Troop, CBE, DSc, FRCP, FFPH, was formerly founding Chief Executive of the UK Health Protection Agency (HPA), a new body combining national agencies and local teams to provide an integrated service across infections, chemical, radiation and other environmental hazards and emergency preparedness. Since her retirement from the HPA in 2008, Professor Troop has chaired or been a member of national committees, supported work of the European Centre for Disease Prevention and Control and WHO, and is a non-Executive Director of Cambridge University Hospitals Foundation Trust. She is a visiting professor at two universities and continues to write and teach.

The HPA was the National IHR Focal Point for the UK, and carried out most of the work concerning the IHR with WHO. With regard to the H1N1 2009 pandemic, the HPA carried out surveillance, laboratory activities, epidemiology assessment, modelling and most operational planning.

After beginning her career as a clinician, she spent 30 years in public health and health service management. She has worked at the local, regional and national levels, across the breadth of public health. Her work included the initiation of the "5 a day" programme on nutrition and review of a number of major services, such as paediatric intensive care across England. She was appointed Deputy Chief Medical Officer for England in 1999, where her responsibilities included health protection, disaster response, international health, oversight of many national bodies, and chairing national committees. In both her national roles, Professor Troop led the response to national emergencies.

She has written or contributed to many published reports and papers. She was honoured as Commander of the Order of the British Empire (CBE) for contributions to Public Health, and awarded Doctorates of Science by two universities (University of East Anglia and Cranfield University) and Outstanding Alumnus by Manchester University.

Dr Kumnuan Ungchusak, Senior Expert in Preventive Medicine, Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Bangkok, Thailand

Kumnuan Ungchusak, MD, MPH, is the senior expert in preventive medicine, Department of Disease Control, Thai Ministry of Public Health, and adviser to the Department on the International Health Regulations. He is a member of the National Committee on Avian Influenza and Pandemic Influenza, and he oversees surveillance, investigation, risk assessment, and related communications activities of the Ministry.

Since his initial training, he has acted as a field epidemiologist, supervising communicable disease surveillance and outbreak investigation in the country. He was Director of Thailand FETP and then Director of the Bureau of Epidemiology from 2001–2008, overseeing the country's surveillance and investigation network.

From 2007–2008 he was in the National IHR Focal Point. He also played an important role in the establishment of the Surveillance Rapid Response Teams, which are now functioning in every district and province of Thailand.

His recent work is related to avian influenza, pandemic influenza, and any Public Health Emergency of International Concern, especially in the Mekong region. He has been a temporary adviser for WHO on disease surveillance, field epidemiology training, and disease modelling. Dr Ungchusak has also been a short-term consultant to WHO's South East-Asia and Western Pacific Regional Offices on the Asia Pacific Strategy for Emerging Diseases.

He received his MD from Siriraj Medical School, Thailand, and his Master's Degree in Public Health from Mahidol University. He completed a two-year Field Epidemiology Training Program (FETP) under the Thai Ministry of Health, and received certification by the board of Preventive Medicine of the Thai Medical Council.

Professor Kuku Voyi, Professor and Department Head, School of Health Systems and Public Health, University of Pretoria, Pretoria, South Africa

Kuku Voyi, PhD, is professor and department head of Environmental and Occupational Health in the School of Health Systems and Public Health at the University of Pretoria, South Africa. Her areas of expertise include exposure assessment, surveillance and human health risks, and environmental and occupational epidemiology. Her research interests are in the etiology of disease, environment and health, environmental epidemiology, and health systems.

Dr Voyi is coordinator of the Health Emergencies in Large Populations course (HELP South Africa). She is subject matter expert for her University's contribution to the WHO International Health Regulations Implementation course with regard to surveillance and risk assessment and a member of the WHO AFRO African Advisory Committee for Health Research and Development. She has been an expert adviser for various national entities. She is also a Member of the International Commission on Occupational Health, and a reviewer of the journal *Health South Africa*.

She has also been a technical adviser for WHO, including as to Institutional Analysis for the Algiers Ministerial Declaration (WHO AFRO) 2008 and a member of the Consultative Group on Emergencies training for the African Region 2009. Dr Voyi has recently provided advice to WHO's Regional Office for Africa in the areas of health research and development, on neglected tropical diseases, and on training for health emergencies in Africa.

Professor Voyi served as Chair of the School of Health Systems and Public Health from 2004–2010, and is the immediate past Chair of the South African Medical Research Council Board.

She received her postgraduate education at the University of Cape Town.

Professor Yu Wang, Director-General of Chinese Center for Disease Control and Prevention, Beijing, China

Yu Wang, MD, PhD, is Director General of the Chinese Center for Disease Control and Prevention (China CDC), Ministry of Health of China.

As Director-General of China CDC, Professor Wang established the laboratory bio-safety management system and improved infectious disease surveillance and reporting systems in China. He directed the emergency preparedness and responses to H5N1 avian influenza in humans, hand-foot-mouth disease, influenza A H1N1 2009 pandemic and other emerging health threats.

Prior to his current position, Professor Wang was Director for the Institute of Hepatology, People's Hospital of Beijing Medical University and later Vice-President of Beijing Medical University, responsible for research activities and applied sciences development. In 2000 he was appointed Deputy Director-General of China National Center for Biotechnology Development, Ministry of Science and Technology (MOST), and then Deputy Director-General of the Department of Agriculture and Social Development, MOST. In his positions at MOST, he was responsible for the funding and administration for biotechnology research and development. He helped development of national ethics guidance on human embryonic stem cell research.

He is vice-chairman of the Chinese Association of Prevention Medicine, and executive board member of International Association of National Public Health Institutes.

He earned his medical degree from Beijing Medical University and his doctoral degree from Jichi Medical School of Japan. His research field was molecular virology and the immunology of hepatitis virus.

Dr Sam Zaramba, Senior Consultant Surgeon, Former Director General of Health Services, Ministry of Health, Kampala, Uganda

Sam Zaramba, MD, is Senior Consultant Surgeon, and the former Director General of Health Services in Uganda. Prior to that position, he was the Director responsible for Clinical and Community Health in the Ministry of Health of Uganda.

Dr Zaramba has extensive experience in Health Service Delivery in developing countries and globally. Dr Zaramba practiced clinical medicine for over 10 years at Mulago National Referral Hospital as a specialist surgeon in otorhinolaryngology. He then chose to work in Health Services Management with its challenges in a resource-poor country. He has a special interest in tropical infectious diseases, including particularly the neglected tropical diseases impacting Uganda and the region.

He has advocated for integrated disease control and vector control nationally and globally, as well as the successful strategy of the "Child Health Days Plus" campaign in Uganda. He also initiated several other public-health related projects in Uganda, such as routine immunization, improved nutrition, health education and hygiene, distribution and treatment of insecticide impregnated nets. He was instrumental in development of the ten year health policy and the strategic plans guiding health service delivery in Uganda.

He chaired the WHO AFRO Regional Program Committee 2007/2008 and was the Chairperson of the WHO Executive Board in Geneva for its 125th and 126th meetings. He is a member of the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases (STAG-NTD). Dr Zaramba was recently requested to be part of the (WHO board of patient safety) and a temporary adviser in relation to the Global Health Workforce Alliance, in February 2011. Finally, he was recently requested to be the Executive Director of a nongovernmental organization working on issues of neglected tropical diseases and community health and development.

Dr Zaramba has co-authored articles on neglected tropical diseases with colleagues at the Vector Control Division of the Ministry of Health. He is a graduate of Makerere Medical School for both graduate and undergraduate studies. He received Health Services Management training at Birmingham University, UK, Boston University, USA, and Harvard University, USA.

Declaration of interests

Professor José Ignacio Santos

In 2009–2010 Dr Santos gave 4 lectures or presentations at meetings in Viet Nam, the Philippines, Australia and China funded by the pharmaceutical industry (mainly GlaxoSmithKline) for which he received total honoraria of less than $10 000 USD, and his expenses were covered. Three lectures concerned the introduction of vaccines in Latin America; one involved the Mexican experience in the influenza H1N1 pandemic.

Professor Kuku Voyi

Professor Voyi, a professor at the University of Pretoria, supervised the university's contribution to the Surveillance, Early Warning and Response component of the WHO International Health Regulations Implementation Course being offered in 2010–2011. The university and WHO concluded an agreement for the performance of work (APW) in 2009 for an amount less than $15 000 related to this contribution to the IHR course; part of this amount covered less than 20% of Dr Voyi's salary for 6 months.

The interests summarized above do not give rise to a conflict of interest such that the experts concerned should be partially or totally excluded from participation in the Emergency Committee. However, following WHO's policy, they were disclosed within the Committee so that other members were aware of them.

Many of the Review Committee Members have extensive governmental experience and expertise – and consulting with WHO – in the areas that are the subject of the Review Committee proceedings, which were considered very relevant and important for the challenging tasks faced by the Committee.

Appendix III

Summary of the International Health Regulations 2005 (*1*)

Function 1: Surveillance and response capacities

Core capacities for surveillance, assessment and response need to operate at the local level, at the intermediate level (e.g. provincial or state level, depending on a country's constitutional arrangements) and at the national level. Certain capacities, including surveillance, response and reporting, must also be operational at points of entry, such as designated ports, airports and ground crossings. The core capacities are described below (*2*).

Core capacity 1: National legislation, policy and financing

The International Health Regulations 2005 (IHR) provide obligations and rights for States Parties. States Parties have been required to comply with and implement the IHR starting with their entry into force in 2007. To do so, States Parties need to have an adequate legal framework to support and enable implementation of all of their obligations and rights. In some States Parties, implementation of the IHR may require that they adopt implementing or enabling legislation for some or all of these obligations and rights. New or modified legislation may also be needed by States to support the new technical capacities being developed in accordance with IHR Annex 1. Even where new or revised legislation may not be specifically required under the State Party's legal system for implementation of provisions in the IHR, States may still choose to revise some legislation, regulations or other instruments in order to facilitate implementation in a more efficient, effective or beneficial manner. Implementing legislation could serve to institutionalize and strengthen the role of IHR and operations within the State Party. It can also facilitate coordination among the different entities involved in implementation. Detailed guidance on IHR implementation in national legislation is available. In addition, policies that identify national structures and responsibilities (and otherwise support implementation) as well as the allocation of adequate financial resources) are also important.

Core capacity 2: Coordination and National IHR Focal Point communications

The effective implementation of the IHR requires multisectoral/multidisciplinary approaches through national partnerships for effective alert and response systems. Coordination of nation-wide resources, including the designation of a National IHR Focal Point (NFP), which is a national centre for IHR communications, is a key requisite for IHR implementation. The NFP should be accessible at all times to communicate with the WHO IHR Contact Points and with all relevant sectors and other stakeholders in the country. The States Parties must provide WHO with annually updated contact details for the NFP.

Core capacity 3: Surveillance

The IHR require the rapid detection of public-health risks, as well as the prompt risk assessment, notification and response to these risks. To this end, a sensitive and flexible

surveillance system is needed with an early warning function. The structure of the system and the roles and responsibilities of those involved in implementing the system need to be clear and preferably should be defined through public-health policy and legislation. Chains of responsibility need to be clearly identified to ensure effective communications within the country, with WHO and with other countries as needed.

Core capacity 4: Response

Command, communications and control operations mechanisms are required to facilitate the coordination and management of outbreak operations and other public-health events. Multidisciplinary/multisectoral Rapid Response Teams should be established and be available 24 hours a day, seven days a week. They should be able to rapidly respond to events that may constitute a public-health emergency of national or international concern. Appropriate case management, infection control and decontamination are all critical components of this capacity that need to be considered.

Core capacity 5: Preparedness

Preparedness includes the development of national, intermediate and community/primary response level public-health emergency response plans for relevant biological, chemical, radiological and nuclear hazards. Other components of preparedness include mapping of potential hazards and hazard sites, the identification of available resources, the development of appropriate national stockpiles of resources and the capacity to support operations at the intermediate and community/primary response levels during a public-health emergency.

Core capacity 6: Risk communication

Risk communications should be a multilevel and multifaceted process that aims to help stakeholders define risks, identify hazards, assess vulnerabilities and promote community resilience, thereby promoting the capacity to cope with an unfolding public-health emergency. An essential part of risk communication is the dissemination of information to the public about health risks and events, such as outbreaks of disease.

For any communication about risk caused by a specific event to be effective, it needs to take into account the social, religious, cultural, political and economic aspects associated with the event, as well as the views of the affected population. Communications of this kind promote the establishment of appropriate prevention and control action through community-based interventions at individual, family and community levels. Disseminating the information through the appropriate channels is also important.

Communication partners and stakeholders in the country need to be identified, and functional coordination and communication mechanisms established. In addition, it is important to establish communication policies and procedures on the timely release of information. Transparency in decision-making is essential for building trust between authorities, populations and partners. Emergency communications plans need to be developed, tested and updated as needed.

Core capacity 7: Human resources

Strengthening the skills and competencies of public-health personnel is critical to the sustainment of public-health surveillance and response at all levels of the health system and the effective implementation of the IHR.

Core capacity 8: Laboratory

Laboratory services are part of every phase of alert and response, including detection, investigation and response, with laboratory analysis of samples performed either domestically or through Collaborating Centres. States Parties need to establish mechanisms that assure the reliable and timely laboratory identification of infectious agents and other hazards likely to cause public-health emergencies of national and international concern, including shipment of specimens to the appropriate laboratories if necessary.

Function 2: Detection and alert operations

The IHR require States Parties, via their NFP, to communicate with WHO in relation to all potentially serious public-health events. Domestic events detected by national surveillance systems must be assessed by States Parties using pre-defined criteria as set out in Annex 2 of the IHR. The Annex 2 decision instrument provides a risk-based approach for national authorities to determine whether an event should be notified to WHO on the grounds that it *may* constitute a potential Public Health Emergency of International Concern (PHEIC). Notification must be given when events fulfil at least two of the following four criteria: (1) serious public-health impact; (2) unusualness or unexpectedness; (3) significant risk of international spread; (4) significant risk of international travel or trade restrictions. All cases of smallpox, wild-type polio, novel subtype human influenza and Severe Acute Respiratory Syndrome (SARS) are notifiable events. NFPs are responsible for notification.

With a view to encouraging timely reporting, the IHR specify the timeframes within which the risk assessment and any subsequent notification must occur as 48 and 24 hours, respectively.

In addition to notifying WHO of events that have the potential to become PHEICs, States Parties must inform WHO of unexpected or unusual public events outside their own territories. Further, events that are "near misses" for notification (i.e. events that do not meet the criteria for notification or for which there is insufficient information to apply the decision instrument), may also be the subject of consultations with WHO (Article 8). The NFP notifies, consults with and conveys information about unusual public-health events to the WHO IHR Contact Point located in each of WHO's six Regional Offices (*3,4*). States Parties should also collaborate with each other in the detection and assessment of events, and in their response to them. Collaboration includes the provision of technical, logistical and financial assistance for a specific event or capacity building (Article 44).

Function 3: WHO detection and alert operations

The IHR oblige WHO to rapidly identify, verify and assess public-health risks that are of potential international concern. These activities are conducted at headquarters in Geneva as well as in Regional and Country Offices.

Function 4: International public-health response

Mounting an international public-health response requires sustained coordination and cooperation between WHO, States Parties, intergovernmental organizations and other international bodies in the areas of information sharing, guidance, logistics and expertise. The IHR provide a framework of standardized measures that States Parties should implement routinely at their borders for the protection of public health. The IHR also define the measures that can be taken at borders in response to a specific public-health risk. At the request of a State Party, WHO can provide technical guidance and assistance in event management and help countries assess the effectiveness of control measures.

Function 5: Procedures for Public Health Emergencies of International Concern (PHEIC)

The IHR set out procedures for determining whether a serious event constitutes a PHEIC. The IHR define a PHEIC as "an extraordinary event determined to constitute a public-health risk to other States through the international spread of disease and to potentially require a coordinated international response". A PHEIC is determined by the Director-General of WHO, but only after consultation with an Emergency Committee.

The Emergency Committee also provides advice to the Director-General on issuing, modifying, extending and terminating "temporary recommendations", which are defined as "non-binding advice issued by WHO for application on a time-limited, risk-specific basis, in response to a public-health emergency of international concern, so as to prevent or reduce the international spread of disease and minimize interference with international traffic". Temporary recommendations are, in effect, emergency recommendations for the management of major public-health events. They establish global benchmarks for response measures and are intended to minimize the likelihood that countries will implement inconsistent, uncoordinated and unjustifiable measures when faced with an emerging threat to public health.

Function 6: Avoidance of unnecessary interference with international traffic and trade

The IHR enjoin States Parties not to implement health measures beyond those provided for in the IHR or those described in WHO recommendations. In particular, they discourage measures that are overly restrictive of international traffic when reasonable alternatives exist to achieve the appropriate level of health protection. The IHR highlight the importance of effective communication between States Parties and WHO to avoid unnecessary interference with traffic and trade. The IHR define significant interference as "refusal of entry or departure of international travellers, baggage, cargo, containers, conveyances, goods, and the like, or their delay, for more than 24 hours". Under Article 43, however, the IHR 2005 do authorize States Parties to implement additional measures in response to a specific public-health risk or to a PHEIC. Such measures can even override certain other provisions in the IHR. When a State Party adopts such additional measures and they cause significant interference to international travellers, craft, and goods, then the State Party must inform WHO and provide the public-health rationale for the measures. WHO must then share this information with other States Parties, and may request the State Party implementing the additional measures to reconsider them.

Function 7: Implementation of the IHR with respect for human rights

Implementation of the IHR 2005 with "full respect for the dignity, human rights and fundamental freedoms of persons" is one of the underlying principles set out in Article 3. This principle is exemplified in language throughout the IHR. For example, Article 23 prescribes that informed consent is needed (except in instances of imminent public-health risk to others) for medical examinations, vaccination, prophylaxis or other health measures. Article 43 further stipulates that health measures undertaken in accordance with the IHR "shall be applied in a transparent and non-discriminatory manner". Article 45 details how personal data are to be treated and protected so as to maintain confidentiality.

Function 8: Points of entry and travel documents

Actions taken by States Parties at points of entry are intended to prevent and reduce the spread of public-health risks caused by international traffic, including travellers, craft and goods (*5*). The IHR define a point of entry as "a passage for international entry or exit of travellers, baggage, cargo, containers, conveyances, goods and postal parcels, as well as agencies and areas providing services to them on entry or exit". The IHR oblige States Parties to designate their international airports and ports and, if deemed necessary for public-health reasons, specified ground crossings as points of entry. As with the other core capacities, deadlines are given for States to have assessed (June 2009) and subsequently met (15 June 2012) certain core capacities at these designated points of entry. These requirements include capacities that must be operable at all times and others that must be able to be activated as part of an emergency response (*6*). The IHR also include detailed actions and provisions to reduce the international spread of disease through routine measures, such as inspection procedures and issuing health documents (e.g. ship sanitation certificates, certificates of vaccination or other prophylaxis and health declarations).

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Appendix IV

H1N1 functional teams and terms of reference*

1. Monitoring and assessment of the pandemic (GIP, GAR, IHR)

Track and assess regional and global progression, transmission and impact of human infection to provide countries, the public and partners with the best information upon which to act

- Regular, timely and authoritative information on disease spread and impact
  - Provide reporting standards and mechanisms for data aggregation
  - Reinforce and use existing surveillance networks
  - Generate composite and descriptive epidemiology
  - Compile, analyse and synthesize national and regional reporting of H1N1 cases into global information products
- Rapid identification, verification and characterization of events in newly affected countries
  - Use WHO's alert and response system, including IHR National Focal Points, WHO Country and Regional Offices
- Ongoing pandemic assessment
  - Generate clinical, epidemiological and virology trend data, including resistance to antivirals
  - Support forecasting and modelling to inform the ongoing risk assessment
  - Monitor national control measures, under the provisions of the International Health Regulations (2005)

2. Support to patient care (GIP, GAR)

Support national, regional and international assessment, response and mitigation efforts by generating scientific, evidence-based knowledge that is rapidly shared to achieve optimal effectiveness of interventions

- Evidence-based tools and guidelines for effective patient care, including hospital, community and home-based care
  - Develop and convene expert networks to gather and assess current knowledge of the disease and effectiveness of interventions

* Functional teams and key departments with a detailed list of responsibilities and activities. GIP, Global Influenza Programme; GAR, Global Alert and Response; IHR, International Health Regulations; IVB/IVR, Immunization, Vaccines and Biologicals, and Initiative for Vaccine Research; HPR, Health Promotion Unit; HAC, Health Action in Crises; DGO, Director-General's Office; ADGO, Assistant Director-General's Office; RPC, Research Policy and Cooperation.

  - Ensure that available tools and standards reflect the best available knowledge, including in the following areas:
- Laboratory and virology
- Diagnostics and biosafety
- Clinical management
- Infection control
  - Ensure that lessons learnt and best practices from affected countries are rapidly documented and shared
- Tools and standards disseminated and adapted for country and community use
- Technical guidance for use of antivirals and other pharmaceutical interventions
  - Generate and issue recommendations on safe, timely and effective use
  - Generate guidelines for monitoring resistance and occurrence of serious adverse events
  - Provide policy guidance to developing countries to monitor adverse effects and drug resistance
  - Provide technical support and policy guidance to countries on regulatory issues, supply chain management and preparation of additional formulations as needed

3. Laboratory response and capacity (GIP, IHR, GAR)

Coordination of national, regional and global influenza laboratory diagnosis, surveillance and response, provision of virological evidence and support to pharmaceutical and non-pharmaceutical interventions:

- Efficient GISN laboratory response and virus surveillance
- Valid laboratory diagnostic protocols and reagents
- Updated viruses for pandemic vaccine development and production
- Real-time monitoring of susceptibility of emerging viruses to antiviral drugs
- Support laboratory capacity building for short-term pandemic response and long-term capacity building

4. Societal and individual measures (GIP, GAR, HPR)

Support national, regional and international assessment, response and mitigation efforts by generating scientific, evidence-based knowledge that is rapidly shared to achieve optimal effectiveness of interventions;

- Evidence-based tools and guidelines for effective societal and individual measures for prevention of infection
  - Develop and convene expert networks to gather and assess current knowledge of the disease and effectiveness of interventions
  - Ensure that available tools and standards reflect the best available knowledge, including in the following areas:
    - Societal/home-based/non-pharmaceutical interventions, and
    - Occupational health
  - Ensure that lessons learnt and best practices from affected countries are rapidly documented and shared
  - Tools and standards disseminated and adapted for country and community use

5. Vaccine development and deployment planning (IVB/IVR, GIP, GAR)

Facilitate and accelerate the availability and access of countries to quality vaccines;

- Accelerated quality vaccine production and access
  - Establish baseline of global production capacity
  - Accelerate production through actions of collaborating centres
  - Facilitate technology acquisition and transfer
  - Ensure quality of vaccines procured by UN agencies
  - Facilitate harmonized regulatory standards among national authorities and with supra-national bodies
- Technical guidance for vaccine introduction and use
  - Produce policy recommendations on optimal vaccination strategies
  - Generate guidelines and associated tools to facilitate rapid and timely deployment of vaccines
  - Provide technical support and policy guidance to countries on regulatory issues for fast-track approval of vaccines by national authorities
  - Generate guidelines for post-marketing surveillance and vaccine safety and effectiveness
  - Provide technical support to countries for vaccine deployment

6. Operations (GAR, GIP, HAC, IVB/IVR)

Provide accessible guidance and direct technical assistance (in support to and in close collaboration with Regional Offices) for capacity strengthening, and field support to countries and communities for health readiness and mitigation, especially in the world's most vulnerable regions;

- Provide adapted strategic and technical guidance for national and community application
  - Support development or refinement of national, regional and local plans and strategies to prevent, cope with and mitigate pandemic, including guidance for control measures at borders and points of entry
  - Support for national response planning, prioritization and coordination
  - Develop training material and adapt technical documentation according to context, including rapid detection and alert and investigation mechanisms, access to diagnostics, infection control, case management, and community interventions
  - Develop material and adapt technical documentation for specific regional, subregional and national context as appropriate
  - Develop frameworks and tools for triage, surge-capacity planning, clinical guidelines etc. for pandemic response
- Provide direct technical assistance and field support to targeted countries
  - Develop mission-specific materials, including training and post-mission feedback mechanisms
  - Use the integrated operational platform to mount and support deployments of multidisciplinary expert teams
  - Access technical and scientific resources through global and regional networks, including the Global Alert and Response Network (GOARN)

  - Support health education campaigns to improve community preparedness and resilience to pandemic
  - Enhance country capacity for effective risk communication
  - Operate and fund the influenza sample shipment system to support rapid and reliable diagnostics
- Support urgent training and workshops for readiness, mitigation and community intervention
  - Conduct training and workshops at regional and subregional level, emphasizing the means to maximize reach
  - Develop institutional arrangements for continuous strengthening of health services readiness, including training, simulations and testing of emergency response plans
  - Develop capacities for risk communication across the entire health system, including the community

Develop/enhance country capacity for assessment of points of entry, and border and ground crossings;

- Coordinate the distribution of available international antiviral stockpiles
  - Distribute current stocks to targeted countries
- Facilitate access to critical supplies and equipment in targeted countries
  - Provide technical support and policy guidance to countries to improve delivery and access to vaccines, antivirals and other essential medicines
- Coordinate activities with WHO Member States, using the framework of the International Health Regulations, through Regional and Country Offices and IHR National Focal Points

7. Technical documents and publications (GIP, GAR)

- Tracking of all technical documentation relating to pandemic H1N1 influenza, from concept to clearance for web publication, ensuring implementation of standard WHO corporate procedures related to publications
  - Facilitate senior management approval for all documents at initial planning stage
  - Facilitate contribution and review across disciplines and departments through development stage
  - Provide editorial and layout oversight and provide recommendations to pandemic management group and ADG
  - Facilitate senior management clearance of finalized documents
  - Maintain database of all documents that are planned, in development and published
  - Coordinate technical publications with media and communications activities

8. Media and communications (GAR, GIP, DGO)

- Lead external communications on response through media and web, and support Member States in their pandemic communications
- Proactively plan WHO's public communications
- Ensure generation of briefing notes, Frequently Asked Questions, Talking Points and other materials to support effective communications by designated technical and communications staff
- Manage press briefings

- Manage response to media enquiries, with designated technical staff and H1N1 Communications Team using agreed Talking Points to respond to media enquiries in a coordinated fashion
- Monitor H1N1 media coverage and discussion of H1N1 in other communications forums
- Maintain, develop and update the public information sections of the H1N1 web site; use appropriate new technologies for increased electronic outreach
- Coordinate with technical publications
- Coordinate, guide and support, in conjunction with Regional and Country Offices, to Member State pandemic communications capacity building (as part of operations)

9. Scientific knowledge and information gaps (GIP, GAR, IVR, RPC)

- Monitor effectiveness of response, identify knowledge gaps and lessons learnt, and their application to the public-health research agenda
- Facilitate adoption and coordination of public-health research agenda in five streams:
  - reducing the risk of reassortment of pandemic virus with animal viruses;
  - limiting the spread of epidemic and pandemic influenza;
  - minimizing the impact of seasonal and pandemic influenza;
  - optimizing the treatment of patients with seasonal and pandemic influenza; and
  - promoting the application of modern public health-tools

10. Resource mobilization (ADGO/DGO)

- Guide the H1N1 technical teams on approaches, strategies and opportunities for resource mobilization
- Ensure advocacy with potential donors
- Elaborate requests for donors
- Follow up on reporting to donors

11. General management: staffing, funding, internal programme support (ADGO)

- Facilitate and guide budget allocation
- Track funding implementation
- Coordinate with other H1N1 workplan responsible areas (DGO, General Management Group, HAC)
- Coordinate deployment of human resources globally
- Manage awards and expenditures
- Provide for infrastructural support
- Develop administrative procedures for headquarters and regional implementation as needed
- Coordinate administration with Global Service Centre and Regional Offices
- Provide operational support for WHO's response to H1N1

12. Pandemic coordination management (ADGO/Pandemic/ Coordination Group/Pandemic Coordination Manager)

- Direct and coordinate the work of the functional teams within headquarters
- Ensure adequate coordination across WHO
- Communicate with Regional Offices, Country Offices and partners
- Support resource mobilization and allocation
- Support the functioning of the common platform
- Support the Assistant Director-General in his capacity as member of the Pandemic Senior Policy Group
- Ensure that WHO response is aligned with the Senior Policy Group decisions and guidance

13. Policy issues: global leadership, partnerships, equity and access (ADGO/DGO)

Provide global health leadership and stimulate/support effective regional and global collaboration across sectors

- Ensure the coordination of the global response, including partnerships and alliances
- Provide guidance to other UN agencies, programmes and funds (including linkage with UN System Influenza Coordination) and to specialized intergovernmental organizations (e.g. International Organization for Migration) to ensure that the pandemic health consequences will be effectively managed by the UN system
- Ensure that all sectors have appropriate information to minimize societal and economic disruptions
- Support Member States in collaboration with funding partners, including the World Bank, regional development banks, International Monetary Fund, private foundations, other international financial institutions, and the private sector in their efforts to mitigate the pandemic impact and build sustainable public-health capacity
- Coordinate and collaborate with the Inter-Agency Standing Committee

Facilitate and accelerate the availability and access of countries to effective antivirals, vaccines, other commodities and funding

- Advocate for appropriate antiviral production and fair distribution
  - Establish baseline of antiviral production capacity
  - Advocate for negotiated price and procurement contracts for developing countries

Appendix V

Pandemic management core functions

Policy issues: global leadership, partnerships, equity and access
Provide global health leadership to support regional and global collaboration and facilitate and accelerate access of countries to resources.

Pandemic coordination management
Direct and coordinate the functional teams within WHO headquarters and communicate with Regional Offices and partners.

Resource mobilization
Advocacy and resource mobilization with potential donors.

Scientific knowledge and information gaps
Identify, monitor and close scientific knowledge gaps.

Media and communications
Provide communications support on media, web and training to Member States.

Technical documents and publications
Plan, track and edit all technical documentation.

General management
Staffing, funding, internal programme support for H1N1 pandemic activities.

Vaccine development planning
Facilitate and monitor vaccine development, regulations and policy.

Vaccine deployment planning
Facilitate and accelerate access of countries to quality vaccine.

Antiviral task force
Facilitate and accelerate access of countries to quality antivirals.

Operations
Provide guidance and technical assistance to Regional and Country Offices for capacity strengthening and field support.

Laboratory response and capacity
Coordination of national, regional and global influenza laboratories for diagnosis, surveillance, response and vaccines.

Monitoring and assessment
Track and assess regional and global disease progression, transmission and impact.

Support to patient care
Support national, regional and global activities on patient care.

Societal and individual measures
Support national, regional and global assessment, response and mitigation efforts on societal and individual measures.

Source: WHO headquarters Pandemic (H1N1) 2009 Organizations and Resources. A World Health Organization brochure.

Appendix VI

Internal WHO documents consulted by Review Committee

The WHO Secretariat developed a series of briefing notes for the Review Committee, providing background on issues such as: the IHR; pandemic preparedness; pandemic phases; pandemic severity; pandemic vaccine; antiviral drugs; virological monitoring; disease monitoring; laboratory response; public-health measures; and the Open-ended Working Group of Member States on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and Other Benefits. The Committee had access to a series of studies that evaluated the functioning of Annex 2 of the IHR (i.e. the decision instrument for States Parties' assessment and notification of public-health events) as well as progress reports on the implementation of the IHR. At the Committee's request, the WHO Secretariat devised a matrix of the key public-health functions of the IHR and identified a broad range of non-pandemic events that had been notified to WHO since the IHR came into force. The Committee selected several events and directed the Secretariat to prepare a summary of each event to facilitate its assessment of the public-health functions of the IHR.

WHO provided the Committee with unfettered access to internal documents. These records included meeting minutes of: the Emergency Committee, the Senior Policy Group, the Pandemic Evaluation Group, and the Ad hoc Policy Advisory Working Group on Influenza A (H1N1) Vaccines. Other documentation included minutes of teleconferences involving WHO Regional Offices, WHO Collaborating Centres and Essential Regulatory Laboratories, the International Federation of Pharmaceutical Manufacturers and Associations and other vaccine manufacturers, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and OFFLU (the OIE-FAO global network of expertise on animal influenzas).

Committee members signed non-disclosure agreements in order to review confidential legal documents, such as vaccine agreements.

Written submissions from Member States and full transcripts of oral evidence taken by the Committee were also made available.

Appendix VII

WHO's assessment of pandemic severity: key events during 2009

28 April: Based on preliminary quantitative and qualitative data on health impacts of influenza A (H1N1) 2009 from Mexico, the United States of America and Canada, a WHO internal assessment concluded that clinical, epidemiological and surveillance data were insufficient to assess the severity of the event globally. WHO continued to seek data from affected countries.

29 April: Affected countries provided data at a WHO ad hoc scientific teleconference (*1*). No standardized reporting tools were used; thus, data were not directly comparable between countries. Mexico reported 26 confirmed cases (seven deaths), 1551 suspected cases (84 deaths) and many severe cases. The USA reported 64 confirmed cases (one death) from 14 states; initial cases were mild influenza-like illness (ILI), but some of the more recently reported cases at that time were severe. All 13 confirmed cases in Canada had mild ILI.

29 April: The Medical Research Council Centre for Outbreak Analysis and Modelling at Imperial College, London, United Kingdom, prepared a confidential report for WHO describing early findings: "Case mortality lying in the range seen in 20th-century pandemics, with the best guess (from Mexican data) being something comparable (or perhaps a little worse) than 1957." The report concluded that: "Seasonality and other factors currently make it impossible to predict the time course of the pandemic in the next few weeks. Ongoing and expanding community transmission can however be expected."

30 April: Work began on a series of data collection tables for severity assessment and country profiles.

1 May: WHO prepared draft tables for severity assessment based on information received, which were sent to National IHR Focal Points for verification.

5 May: Countries provided updated clinical and epidemiological data as well as simple qualitative severity data using a matrix that WHO had developed at a WHO technical consultation on disease severity (*2*). The objective was to gain an overall qualitative indication of severity. Participants assessed the severity in their countries to be intermediate or moderate. It was concluded that many questions still could not be answered, that the situation would likely evolve over time, and that although illness to date had been mainly mild, further spread of the virus would likely increase the number of severe cases and deaths.

11 May: A WHO web briefing on assessing the severity of an influenza pandemic is posted to provide observations based on preliminary data and information on severity implications (*3*).

11 May: A paper published early online by *Science* included a discussion of severity implications (*4*).

29 May: Considerations for assessing the severity of an influenza pandemic are published (*5*), outlining WHO's framework for assessing severity and summarizing relevant data.

1 June: At a WHO consultation involving six regional teleconferences, participants agreed that the disease did not have the features of seasonal influenza but was not as severe as the 1918 pandemic. The number of cases of ILI was significant but the impact on health-care systems was moderate.

11 June: WHO's Director-General publicly stated: "Although the pandemic appears to have moderate severity in comparatively well-off countries, it is prudent to anticipate a bleaker picture as the virus spreads to areas with limited resources, poor health care, and a high prevalence of underlying medical problems." (*6*)

11 June: A Question and Answer on Phase 6 posted on the WHO web site included a discussion of severity (*7*).

20 November: Estimates of the reproductive rate of the virus were published (*8*).

22 December: A briefing note on comparing deaths from pandemic and seasonal influenza was published (*9*).

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Appendix VIII

Glossary of terms and abbreviations

ACI	Airports Council International
ADG	Assistant Director-General
ADGO	Assistant Director-General's Office
AFRO	Regional Office for Africa
AMRO	Regional Office for the Americas
APA	Advance Purchase Agreement
BSL	Biosafety Level
CDC	US Centers for Disease Control and Prevention
COE	Council of Europe
DCVMN	Developing Countries Vaccine Manufacturing Network
DDG	Deputy Director-General
DG	Director-General
DGO	Director-General's Office
DON	Disease Outbreak News
EC	Emergency Committee
ECDC	European Centres for Disease Prevention and Control
EIS	Event Information Site
EMA	European Medicines Agency
EMRO	Regional Office for the Eastern Mediterranean
EMS	Event Management System
ERL	Essential Regulatory Laboratories
EURO	Regional Office for Europe
FAO	Food and Agriculture Organization of the United Nations
GAP	Global Action Plan to Increase Supply of Pandemic Influenza Vaccines
GAR	Global Alert and Response
GIP	Global Influenza Programme
GISN	Global Influenza Surveillance Network
GHSAG	Global Health Security Action Group
GLEWS	Global Early Warning System for Major Animal Diseases including Zoonoses
GOARN	Global Outbreak Alert and Response Network

GPHIN	Global Public Health Intelligence Network
GRADE	Grading of Recommendations Assessment Development and Evaluation
HAC	Health Action in Crises
HSE	Health Security and Environment
IAEA	International Atomic Energy Agency
IATA	International Air Transport Association
ICAO	International Civil Aviation Organization
ICT4PHEM	Information and Communication Technologies Tools for Public Health Emergency Management
ICU	Intensive care unit
IFPMA	International Federation of Pharmaceutical Manufacturers and Associations
ILI	Influenza-like illness
IHR	International Health Regulations (2005)
IVB	Immunization, Vaccines and Biologicals
NFP	National IHR Focal Point
NIC	National Influenza Centre
OIE	World Organisation for Animal Health
PACE	Parliamentary Assembly of the Council of Europe
PAHO	Pan American Health Organization
PEG	Pandemic Evaluation Group
PHEIC	Public Health Emergency of International Concern
PPR	Pandemic Preparedness and Response
ProMED	Program for Monitoring Emerging Diseases
RD	Regional Director
RT-PCR	Real-time reverse transcriptase polymerase chain reaction
SAGE	Strategic Advisory Group of Experts on Immunization
SARS	Severe Acute Respiratory Syndrome
SEARO	Regional Office for South-East Asia
SHOC	Strategic Health Operations Centre
SPG	Senior Policy Group
UN	United Nations
UNHRD	United Nations Humanitarian Response Depot
UNICEF	United Nations Children's Fund
UNIP	Urgent Needs Identification and Prioritization
UNSIC	United Nations System Influenza Coordination
WHA	World Health Assembly
WHO	World Health Organization
WHO CC	WHO Collaborating Centre
WPR	Western Pacific Region
WPRO	Regional Office for the Western Pacific