World Health Organization

INTERGOVERNMENTAL MEETING ON PANDEMIC INFLUENZA PREPAREDNESS: SHARING OF INFLUENZA VIRUSES AND ACCESS TO VACCINES AND OTHER BENEFITS
Provisional agenda item 3

A/PIP/IGM/4
9 October 2007

Sharing of influenza viruses and access to vaccines and other benefits: Interdisciplinary Working Group on Pandemic Influenza Preparedness

Report by the Director-General

1. The Director-General has the honour to transmit herewith to the Intergovernmental Meeting the Chairman's summary of the debate at the interdisciplinary working group on pandemic influenza preparedness convened in accordance with resolution WHA60.28.

2. The meeting took place in Singapore, from 31 July to 4 August 2007, under the chairmanship of Dr Viroj Tangcharoensathien (Thailand).

3. Following circulation of the summary and its attachments after the meeting, comments received from participating Member States have been incorporated. In the appendices to the annexed Chairman's summary they are reproduced, as submitted, and appear in bold type, with attribution.

ANNEX

Sharing of influenza viruses and access to vaccines and other benefits: Interdisciplinary Working Group on Pandemic Influenza Preparedness (resolution WHA60.28 (paragraph 2(5))

(Singapore, 31 July – 4 August 2007)

Chairman's summary

1. In resolution WHA60.28, the World Health Assembly requested the Director-General, inter alia, to convene an interdisciplinary working group to revise the terms of reference of WHO Collaborating Centres, H5 Reference Laboratories, and national influenza centres, devise oversight mechanisms, formulate draft standard terms and conditions for sharing viruses between originating countries and WHO Collaborating Centres, between the latter and Third Parties, and to review all relevant documents for sharing viruses and sequencing data, based on mutual trust, transparency, and overriding principles exemplified in the text of paragraph 2(5).

2. Accordingly, such a group was convened and a meeting held in Singapore, from 31 July to 4 August 2007, with membership consisting of 22 Member States from all six WHO regions; the host country, Singapore, also participated.[1] Participants adopted the provisional agenda (Appendix 2).

3. This report summarizes the discussions of the Working Group; it does not represent a collective or consensus view of members. In order to foster free and frank exchanges of views, it was proposed to hold the meeting under the Chatham House Rule, which protects the identity and affiliation of the source of comments made at a meeting, but in comments submitted after the meeting some members of the Working Group stated that they had understood that this condition had only applied to the discussion of the standard terms and conditions for the transfer and use of influenza-virus-related biological materials.

Areas of discussion

4. After consultations, the discussions were organized around three main areas: sharing of viruses and information, and subsequent benefits; development of standard terms and conditions and terms of reference for the transfer of influenza viruses among, and use by, national influenza centres, WHO H5 Reference Laboratories and WHO Collaborating Centres and Third Parties, and terms of reference for such centres and laboratories; and oversight mechanisms. It was agreed that the focus of discussion should be on a potential pandemic rather than seasonal influenza. Some participants cautioned that the limited scope would have to be reflected in the standard terms and conditions and the terms of reference.

5. This report summarizes the discussions in each area. The appendices on standard terms and conditions, terms of reference, and oversight mechanisms are presented as working documents rather

[1] Paragraph 2(5) of resolution WHA60.28 envisaged a membership of 24. However, two members of the Working Group, Egypt and Tunisia, did not attend; see Appendix 1 for the list of participants.

than agreed texts, because consensus was not reached on all aspects; indeed some members of the Working Group considered that consensus was not reached on any aspect. Participants also discussed whether the term "Global Influenza Surveillance Network" should be used in conjunction with the standard terms and conditions.

SHARING OF VIRUSES AND INFORMATION, AND SUBSEQUENT BENEFITS

6. Although the Working Group did not have an explicit mandate to discuss the sharing of benefits, some participants stressed the need to assert their major concerns in this area. A separate document, which was discussed during the meeting would be submitted to the Director-General for her consideration when preparing the reports requested under paragraph 2 of resolution WHA60.28.

Principles for sharing the benefits

7. Most participants agreed in principle that better access to human influenza vaccines, in particular those against H5N1 and pandemic disease, is one of the most important benefits. Equally important were: sharing of information on influenza virus strain evolution and of representative viral strains for both surveillance and production of reagents for reference and diagnostic purposes; support for capacity building in resource-limited countries in order to establish and strengthen influenza surveillance, including laboratory diagnostic capacity; and the establishment of influenza vaccine production capacity. Technology transfer and access to technologies were also discussed.

8. Participants also agreed in principle that the sharing of benefits should be based on health needs, that pandemic preparedness should be strengthened, and that the pooled benefits should be managed by WHO. Further, the distribution of any stockpiled vaccines or access to pandemic vaccines should be based on public health criteria. Participants further agreed that, for continuing pandemic risk assessment and immediate risk response, influenza viruses must be made available rapidly; some participants indicated that the viruses should be made available immediately. Some members of the Working Group in a position to do so expressed a commitment to provide benefits, as yet undefined, to countries in need.

9. Many issues remained to be clarified. It was recalled that resolution WHA60.28 requested the Director-General to report to the intergovernmental meeting on fair and equitable sharing of benefits.

Intellectual property rights issues related to pandemic influenza vaccines

10. The meeting was informed that the expert report on the patent issues related to influenza viruses and their genes, commissioned by the Director-General in accordance with resolution WHA60.28, was almost completed.

11. The overriding concern expressed by most members of the Working Group was that neither intellectual property rights nor prior informed-consent requirements, if any, should stand in the way of developing and producing a pandemic influenza vaccine, whose availability would be a top priority in the event of a pandemic.

DEVELOPMENT OF STANDARD TERMS AND CONDITIONS FOR THE TRANSFER AND USE OF INFLUENZA VIRUSES BETWEEN NATIONAL INFLUENZA CENTRES, WHO H5 REFERENCE LABORATORIES, WHO COLLABORATING CENTRES AND THIRD PARTIES, AND TERMS OF REFERENCE FOR SUCH CENTRES AND LABORATORIES

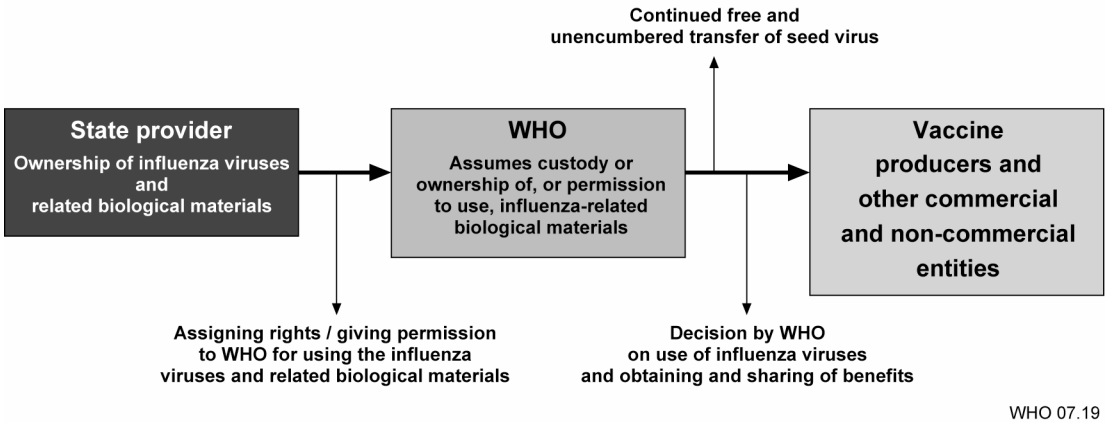
"Ownership" of influenza virus-related biological materials

12. Participants discussed a proposal by one member of the Working Group that WHO should be granted ownership (or custodianship, trusteeship, permission to use, or right to use) of influenza virus-related biological specimens as a means to preserve and facilitate a multilateral approach to virus sharing for risk assessment, rapid vaccine manufacturing, and more equitable sharing of benefits. Although no conclusion was reached, this proposal was well received, being seen as offering a new perspective on ways to transfer and use influenza viruses. Many members of the Working Group indicated that their governments would need to give further consideration to this proposal in order fully to understand its implications.

The main Parties engaged in the transfer and use of biological materials

13. Participants discussed the relationships between the three main Parties engaged in the transfer and use of influenza viruses for vaccine development: the Member State that provides specimens/samples (the State provider), as the First Party; Collaborating Centres, H5 Reference Laboratories and essential non-commercial national and other laboratories as Second Parties; and Third Parties. Some participants proposed that Third Parties should include only commercial vaccine research institutes and vaccine manufacturers whereas others proposed that diagnostic and medicine manufacturers should be included. A possible approach to multilateral sharing of influenza viruses and related biological material as well as of the equitable sharing of benefits (see Figure) was circulated during the meeting but not discussed.

Figure. Proposed potential approach as alternative for international handling of influenza viruses



Standard terms and conditions

14. Participants discussed standard terms and conditions that should govern the relationships and transactions between the three Parties. Major concerns voiced by some members of the Working Group about sharing of influenza viruses related to: intellectual property rights pertaining to products developed from shared viruses; and the need for more complete, timely and transparent information for tracking the flow of biological materials and information through the Global Influenza Surveillance Network and to Third Parties, and guidelines for whether virus genetic sequence data should be routinely posted on a public database.

15. In particular, concerns were expressed about intellectual property rights over biological specimens submitted to the network. The participating directors of WHO Collaborating Centres confirmed that their centres do not and will not seek to obtain intellectual property rights on any viruses received from Member States. There was support for WHO's overseeing of influenza surveillance and tracking the flow and distribution of biological specimens, through the Network to Third Parties, including those in the public and private sectors, and academic institutions. Some members of the Working Group were concerned that a sample-tracking mechanism should not place an overwhelming administrative burden on WHO or the laboratories participating in the Network.

16. Time constraints meant that consideration of the document on standard terms and conditions ended with discussion of paragraph 24.

Terms of reference for WHO Collaborating Centres

17. During discussion of the terms of reference for the WHO Collaborating Centres, comments were made on the technical performance of the Centres, in particular their assistance in securing national influenza laboratory preparedness and response, capacity building, and the need to strengthen this assistance. The issue of distribution of non-vaccine viruses and viruses not selected as reference influenza viruses remains unresolved in relation to the standard terms and conditions.

18. Some members of the Working Group raised concerns about the difficulty of assessing whether a WHO Collaborating Centre had observed its terms of reference, as some of those required subjective assessment. Concern was also expressed about the danger of overburdening the Centres.

19. Participants were invited to submit comments for revision of the existing terms of reference for the H5 Reference Laboratories and national influenza centres. Owing to time constraints and the complexity of the issues, the discussion on the laboratories in the Global Influenza Surveillance Network (WHO Collaborating Centres, H5 Reference Laboratories and national influenza centres) was not completed, although draft terms of reference for all three types of laboratories were distributed at the meeting. After the meeting, participants submitted additional comments on the terms of reference for the H5 Reference Laboratories and national influenza centres. The consolidated texts are attached as Appendices 3–7. There were conflicting views as to whether the WHO Secretariat should also draft terms of reference for the essential non-commercial vaccine-development laboratories.

Next steps

20. Although further work is needed, the current document on standard terms and conditions (Appendix 3) helps to clarify the relationships between Member States, WHO's Secretariat and WHO's partner institutions and laboratories, and between all the foregoing parties and Third Parties. Uncertainty remained about the rights and responsibilities of each Party. Participants expected that

further discussions at the Intergovernmental Meeting would clarify the details of definitions, which were not discussed by the Working Group, and the financial, legal and operational implications of a new framework (see Appendices 3–6).

OVERSIGHT MECHANISMS

21. A proposed draft of the key elements of an oversight mechanism was discussed and amended. The Working Group completed its consideration of the review and elaboration of the scope, goals and objectives, and the modes of operation for this mechanism, although there was no formal agreement on the contents of this document.

22. Two options were proposed for the oversight mechanism: one was to use WHO's Internal Auditor, with independent experts (although consultation with WHO's Legal Counsel indicated that this option was not legally feasible), and the other was to call on an independent body of experts. The chief consideration was to elaborate a mechanism that is independent, impartial, practical and accountable to Member States. The advantages and disadvantages of each option were highlighted. The goals and objectives of the oversight mechanism are mainly to monitor and, when necessary, recommend remedial actions concerning the sharing of viruses and benefits, and compliance with the standard terms and conditions and terms of reference by all Parties concerned (see Appendix 7).

CONCLUSIONS AND NEXT STEPS

23. Consensus was not reached on all issues, and thus the texts in Appendices 3–7 should not be considered as agreed texts. The Secretariat will revise the working documents produced during the meeting on: development of standard terms and conditions and terms of reference for the transfer of influenza viruses among, and use by, national influenza centres, WHO H5 Reference Laboratories and WHO Collaborating Centres and Third Parties, and terms of reference for such centres and laboratories; and oversight mechanisms. The revised texts will be submitted to the Intergovernmental Meeting, although some participants, in comments submitted after the meeting, did not recall agreement on this decision. For sharing of viruses and information, and subsequent benefits, the participants recommended that a document should be sent to the Director-General for the sole purpose of assisting in the preparation of her report to the Intergovernmental Meeting.

24. Subject to resolution of the conflicting views (see paragraph 19 above), the Secretariat would draft terms of reference for the essential non-commercial vaccine strain development laboratories, for consideration at the Intergovernmental Meeting. Some participants, in comments submitted after the meeting, did not recall this request to the Secretariat.

25. Harmonization of technical terms across the appendices remains to be done.

APPENDIX 1

LIST OF PARTICIPANTS

MEMBERS

WHO AFRICAN REGION

CAMEROON

Professor L.F. BELLA ASSUMPTA HIAG, Directeur de la Lutte contre la Maladie, Ministère de la Santé Publique,Yaoundé

GHANA

Dr L. AHADZIE, Deputy Director of Public Health Department, Head of National Surveillance Unit, Ghana Health Service, Accra

NIGERIA

Dr A. NASIDI, Director, Special Projects, Federal Ministry of Health, Abuja

SOUTH AFRICA

Mrs C. KOTZENBERG, Cluster Manager, Non-Communicable Diseases, Department of Health, Pretoria
Dr M.R.R. MALOBA, Director, Communicable Diseases, Department of Health, Pretoria

WHO REGION OF THE AMERICAS

BRAZIL

Sr. S. ALCAZAR, Assessor Especial para Asuntos Internacionais, Ministério da Saúde, Brasília
Dr J.R. PIO MARINS, Chief of Infectious Diseases, Ministry of Health, Brasília

CANADA

Ms G. WISEMAN, International Health Division, International Affairs Directorate, Health Policy Branch, Health Canada, Ottawa, Ontario
Mr T. BOOTH, Director, Viral Diseases Division, National Microbiology Laboratory, Winnipeg, Manitoba
Ms S. LE BRIS, Senior Policy Advisor, Pandemic Preparedness Secretariat, Public Health Agency of Canada, Ottawa, Ontario

CHILE

Sra. X. AGUILERA, División de Planificación Sanitaria, Ministerio de Salud de Chile

UNITED STATES OF AMERICA

Mr D.E. HOHMAN, Health Attaché, Permanent Mission of the United States of America, Geneva
Mr M. ABDOO, Director, Office of Multilateral Affairs, Office of the Secretary, Health and Human Services, Washington, D.C.
Mr D. SINGER, Acting Deputy Coordinator and Senior Medical Policy Adviser for the State Department, Avian Influenza Action Group, State Department, Washington D.C.

WHO SOUTH-EAST ASIA REGION

BANGLADESH

Professor M. RAHMAN, Director, Institute of Epidemiology Disease Control and Research, Ministry of Health and Family Welfare

INDIA

Dr A.C. MISHRA, Director, National Institute of Virology, Pune

INDONESIA

Dr W. LUKITO, Adviser to the Minister of Health for Health Policy, Ministry of Health, Jakarta
Dr T.K. ADIMIDJAJA, Secretary General, National Institute for Health Research and Development, Jakarta
Dr P.M.D. SASONO, Head of Biomedical and Pharmaceutical Research Centre, National Institute for Health Research and Development, Jakarta
Dr D.H. MUJLONO, Senior Research Fellow and Specialist Physician, Eijkman Institute for Molecular Biology, Jakarta
Mr H. PARSOMAL, Adviser to the Minister of Health, Ministry of Health, Jakarta
Mr I.Y. PRAPTI, Head of Traditional Medicine and Medicinal Plant Research, National Institute for Health Research and Development, Tawangmangu-Solo
Dr O.D. SAMPURNO, Head of Programme and Budget, National Institute for Health and Research Development, Jakarta

Dr E.R. SEDYANINGSIH, Director, Biomedical and Pharmaceutical Research Centre, National Institute for Health Research and Development, Jakarta
Dr T. SOENDORO, Director General, National Institute for Health Research and Development, Jakarta
Dr I. TANTORO, Adviser to the Minister of Health for Health Protection, Ministry of Health, Jakarta

THAILAND

Dr VIROJ TANGCHAROENSATHIEN **(Chairman)**, Director, International Health Policy Programme, Ministry of Public Health, Nonthaburi
Dr TANAPOJ EKKAYOKKAYA, Department of Intellectual Property, Nonthaburi
Mr PATHOM SAWANPANYALERT, Director, National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Nonthaburi
Mr VITHET SRINETR, Environmental Officer, Biological Diversity Division, Office of Natural Resources and Environmental Policy and Planning, Ministry of Natural Resources and Environment, Bangkok
Dr SRIPEN TANTIVESS, Pharmacist, International Health Policy Program, Bureau of Policy and Strategy, Ministry of Public Health, Nonthaburi

WHO EUROPEAN REGION

FRANCE

Dr J.-C. MANUGUERRA, Head, Laboratory for Urgent Response to Biological Threats, Institut Pasteur, Paris

GERMANY

Professor G. PAULI, Robert Koch-Institut, Berlin
Mr F.-J. BINDERT, Deputy Director-General for Infectious Disease Control and Health Protection, Federal Ministry of Health, Bonn

TURKEY

Dr A. COŞKUN, Deputy General Director, General Directorate of Primary Health Care Services, Ministry of Health, Sihhiye-Ankara

UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND

Ms J. NEWSTEAD, Head of International Cross-Government and Secretariat – Pandemic Flu, Department of Health, London
Dr S. INGLIS National Institute for Biological Standards and Control, South Mimms, Hertfordshire

WHO EASTERN MEDITERRANEAN REGION

IRAN (ISLAMIC REPUBLIC OF)

Dr B. SADRIZADEH, Special Advisor to the Minister of Health and Medical Education, Ministry of Health and Medical Education, Tehran

MOROCCO

Dr R. EL AOUAD, Director National Institute of Hygiene, Ministry of Health, Rabat

WHO WESTERN PACIFIC REGION

AUSTRALIA

Ms M. MURNANE, Deputy Secretary, Department of Health and Ageing, Canberra
Mr S. COTTERELL, Assistant Secretary, Health Protection Policy Branch, Department of Health and Ageing, Canberra
Dr J. HALL, Principal Medical Adviser, Office of Health Protection, Department of Health and Ageing, Canberra
Professor J. HORVATH, Department of Health and Ageing, Canberra

CHINA

Dr JUN Xing, Division Director, Department of International Cooperation, Ministry of Health of China, Beijing
Dr SHU Yuelong, Director, Chinese National Influenza Centre, Beijing

JAPAN

Dr E. SEKI, Director, Blood and Blood Products Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, Tokyo
Dr H. INOUE, Director, International Cooperation Office, International Affairs Division, Minister's Secretariat, Ministry of Health, Labour and Welfare, Tokyo
Ms C. NAKAJIMA, Officer, Specialized Agencies Division, International Cooperation Bureau, Ministry of Foreign Affairs, Tokyo
Dr T. SHOBAYASHI, Director, Planning and Coordination of Infectious Diseases Control, Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, Ministry of Health, Labour and Welfare, Tokyo

VIET NAM

Dr NGUYEN TRAN HIEN, Director, National Institute of Hygiene and Epidemiology, Hanoi

HOST COUNTRY

SINGAPORE

Dr CHEW SUOK KAI, Deputy Director of Medical Services (Epidemiology and Disease Control), Ministry of Health, Singapore
Dr R. LIN, Head, National Public Health Laboratory, Ministry of Health, Singapore
Dr B. KOH Assistant Director, Communicable Disease Surveillance, Ministry of Health, Singapore

OTHER PARTICIPANTS

World Intellectual Property Organization

Mr A. TAUBMAN, Acting Director and Head PCT and Patents Arbitration and Mediation Center, and Global I.P. Issues, Global Issues Division, Geneva, Switzerland

Scientific Advisory Group of Experts

Dr L. MENDIS, Emeritus Professor of Microbiology, University of Colombo, Consultant in Medical Education, Faculty of Medicine, Colombo, Sri Lanka

Influenza Pandemic Task Force

Dr A.J. MOHAMMAD, Director-General of Health Affairs, Ministry of Health, Muscat, Oman

WHO Collaborating Centres for Reference and Research on Influenza

Dr N. COX, Director, WHO Collaborating Centre for Reference and Research on Influenza, Chief, Influenza Branch, Viral Disease Division, National Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America
Dr A. HAY, Director, WHO Collaborating Centre for Reference and Research on Influenza, National Institute for Medical Research, London, United Kingdom of Great Britain and Northern Ireland
Professor A. KELSO, Director, WHO Collaborating Centre for Reference and Research on Influenza, Parkville, Victoria, Australia
Dr M. TASHIRO, Director, WHO Collaborating Centre for Reference and Research on Influenza, Department of Viral Disease and Vaccine Control, National Institute of Infectious Diseases, Tokyo, Japan

WHO SECRETARIAT

Dr P. CARRASCO, Policy Adviser, Vaccine Security Immunization, Vaccines and Biologicals
Dr C. DOLEA, Medical Officer, Human Resources for Health
Mr N. DRAGER, Acting Director, Ethics, Trade, Human Rights, and Health Law

Dr K. FUKUDA, Coordinator, Global Influenza Programme
Dr P. GULLY, Director, Office of the Assistant Director-General, Communicable Diseases
Dr D. HEYMANN, Assistant Director-General for Communicable Diseases and Representative of the Director-General for Eradication of Polio
Dr A. ONG, Executive Officer, Office of the Director-General
Dr A. HUVOS, Technical Officer (Legal), Global Influenza Programme
Mr B. PLOTKIN, Technical Officer (Legal) International Health Regulations Secretariat
Dr ZHANG Wenqing, Medical Officer, Global Influenza Programme
Dr W. ALEMU, Medical Officer, Infectious Diseases, Regional Office for Africa
Dr J. BARBOSA DA SILVA, Acting Unit Chief, Communicable Diseases Prevention and Control, Pan American Sanitary Bureau
Dr H. CAUSSY, Virologist/Scientist, Department of Communicable Diseases, Communicable Disease and Surveillance Unit, Regional Office for South-East Asia
Ms K. TIMMERMANS, Technical Officer, Regional Office for South-East Asia
Dr C. BROWN, Technical Officer, Communicable Disease and Surveillance Unit, Department of Communicable Diseases, Regional Office for Europe
Dr H. EL BUSHRA, Regional Adviser, Emerging Diseases, Regional Office for the Eastern Mediterranean
Dr T. KASAI, Regional Adviser, Communicable Disease Surveillance and Response, Regional Office for the Western Pacific

APPENDIX 2

Interdisciplinary Working Group on Pandemic Influenza Preparedness

(Singapore, 31 July – 4 August 2007)

Provisional agenda

1. **Opening of the meeting**
2. **Sharing of viruses and information, and subsequent benefits**
3. **Development of standard terms and conditions and terms of reference**
4. **Oversight mechanisms**
5. **Closure of meeting**

APPENDIX 3

Standard terms and conditions for the transfer and use of Influenza Biological Materials

This document has not been agreed by all IDWG participants.

A. Scope

1. These Terms and Conditions (STCs) recognize the importance of timely [**USA:**[*] **The definition of timely in this context was never discussed, and the definition proposed by the WHO Secretariat is deficient. The U.S. proposal was that in all contexts, timely requires a quantitative definition**] international sharing of Specimens as a contribution to risk assessment and risk response, and the need for effective and transparent international mechanisms aimed at ensuring fairer and more equitable sharing of benefits, including improved access to, and distribution of treatments, and vaccines, to those in need, especially in developing countries and in a sustainable manner.

2. The STCs govern the transfer and use of biological materials between or among GISN Entities and are a core part of the Terms of Reference of the NICS, WHO CCs and H5Reference Laboratories. They apply to all Second Party partners and Third Parties for services performed for GISN. Acceptance of GISN Biological Materials (as defined below) constitutes acceptance of the following STCs. These are the only Terms and Conditions applicable to the transfer and use of Biological Materials.

B. Identification of Parties

3. The parties include:
   a. First party: **[USA: The United States proposed that we should only refer to this entity as the "First Party" to avoid confusion.]**, is the State or national entity (NIC or non-NIC) that provides the Specimens.
      i. "National Influenza Centres" (NICs): National influenza reference laboratories that have been designated by a Ministry of Health and recognized by WHO under defined TORs.
      ii. "Non-NICs": laboratories designated by a government, that comply with the same TOR as NICs.
   b. Second party: "Second Party" is WHO, of which GISN is a programme activity implemented with the following partners:

[*] Note from the WHO Secretariat: the USA, in its revisions, has requested deletion of capital letters in terms. This has been done only once for each term.

i. WHO Collaborating Centres for Reference and Research on Influenza (WHO CC): influenza centres of excellence that have satisfied WHO criteria for designation and have accept defined Terms of Reference (TORs). [**Thailand: It should be made clear that St Jude's Hospital is one of the Third Parties, not one of the Second Parties, in this STCs.]**

ii. WHO H5 Reference Laboratory (H5RL): an influenza laboratory that has been designated by WHO to fulfil the defined TORs that bridge the gap in H5 diagnostic capacity worldwide.

iii. Essential national regulatory laboratories: specialized government laboratories involved in WHO influenza vaccine selection and development process;

iv. Laboratories involved in specific WHO influenza projects (e.g. WHO Polymerase chain reaction (PCR) working group, WHO External Quality Assurance Project (EQAP)).] **[UK: The following sentence seems redundant. Second party is WHO, or entities recognized as designated by WHO, as represented by WHO GIP; WHO CCs, essential national regulatory lab]**

c. Third party includes but is not limited to influenza vaccine manufacturers, commercial research laboratories and [diagnostic companies], that request and receive GISN Biological Materials or parts thereof. **[UK: We understood that GISN Biological Materials would be changed throughout to Biological Materials]**

C. <u>Definitions [USA: The definitions were not discussed by the IDWG.]</u>

4. "Specimens" are the original biological material provided by the First Party. They include: original clinical specimens, wild influenza virus isolates, including genes, sequences (and parts thereof) and polynucleotides as well as the polypeptides they encode. **[UK: This is a potentially confusing extension of the definition of specimen. We believe it is unnecessary and should be deleted. Specimen should clearly refer to the actual material supplied by the first party. This wording could be taken to imply that any material that happens to include identical polynucleotides or polypeptides, even if not supplied by the First Party, is defined as a specimen. This would be incompatible with subsequent definitions.]** Specimens also includes related epidemiological and clinical information.

5. "Candidate Influenza Vaccine Viruses" are viruses selected by WHO CCs and processed by WHO CCs and Essential national regulatory laboratories for purposes of influenza vaccine development. [**UK: Not all labs doing this at present have a formal regulatory function (e.g. NYMC). System for seasonal flu vaccine production has evolved informally over 40 years, operates under huge time pressure and is finely balanced. Removing key labs from the system would put whole system at risk]**

6. "Influenza Reference Viruses and Diagnostic Reagents" are viruses selected, updated and maintained by WHO to assist GISN and global research on influenza, and relevant diagnostic reagents such as standard antigens, antisera. Influenza Reference Viruses and Diagnostic Reagents are available free of charge, on request, to all First Parties, research institutes and non-commercial entities. **[UK: this last sentence is out of place in the definitions section here and is covered in D: Conditions and F: Rights and responsibilities of Second Party] [Germany: This part should be moved to Conditions.][UK: This definition is now inconsistent with the outcome of discussion at the meeting, summarised by Julie Hall's paper on the last day. A strong view was expressed by UK, supported by Australia, China and others, that the additional text added by China last thing on Thursday night (leaving no opportunity for discussion) created a definition that was too broad and ill-defined.**]

7. Biological Materials" is used to refer collectively to Specimens, Candidate Influenza Vaccine Viruses, and Influenza Reference Viruses. **[UK: This term should be consistent with the definition in 6]**

8. "Progeny": are descendants from any wild, vaccine or reference virus in GISN. **[Thailand: Progeny should also include cells from cells as well, not only viruses from viruses.] [UK: This now seems redundant - we could not find any reference to 'progeny' in the document as it now stands.]**

9. "Biological Materials Request Form" refers to the attached form that shall be used to request transfer of Biological Materials.
10. "Timely" describes the shortest possible time for shipment of Specimens from the First Party to the Second Party

11. "Risk Assessment" is the comparison of wild influenza virus sequence information to identify any significant viral drift, shift, or mutation that might suggest resistance to antiviral medicines.

12. "Risk Response" is preparedness for a seasonal influenza epidemic or pandemic influenza by development of diagnostic test kits, antivirals and vaccines and ensuring the broadest possible access.

D. <u>Conditions</u>

13. Specimens are provided free of charge by a First Party (NIC or non-NIC) to the Second Party partners in fulfilment of their public health responsibilities, including those contained in the International Health Regulations (2005). In return, the Second Party partners will provide, free of charge, to the First Party, ~~C~~candidate ~~I~~influenza ~~V~~vaccine ~~V~~viruses,~~ I~~influenza ~~R~~reference ~~V~~viruses and ~~D~~diagnostic ~~R~~reagents **[UK: This is acceptable but only if Definition 6 is narrowed as suggested above and in accord with Julie Hall's summary.]** , sequence information, outcome of the Risk Assessment, and access to benefits **[USA: These benefits are as yet undefined.]**

14. Biological ~~M~~materials are provided to any recipients without any warranty whatsoever, either express or implied, as to their quality, viability, purity, merchantability, suitability or fitness for a particular purpose. The recipient shall ensure that the ~~B~~biological Materials will at all times be used and/or handled in compliance with all relevant and applicable national and international laws, rules and regulations governing the use of biological materials. The recipient agrees to assume full and sole responsibility for any and all claims and liabilities resulting from or otherwise related to the possession and use of the Biological Materials.

15. Recipients of Biological Materials shall assume all responsibility for any claims, costs, damages or expenses resulting from or otherwise related to the possession and use of the Biological Materials. Recipients undertake to handle Biological Materials in a safe and proper manner, complying with all relevant national and international laws and regulations applicable to the handling of infectious substances.

E. Rights and Responsibilities of the First party [Germany: In the following, only responsibilities are listed, but no rights – change title?]

16. The First Party shall ensure that the ~~S~~specimens are handled, packed and shipped to a WHO CC of its choice in a timely [**USA: See note above regarding the definition of timely**] manner in accordance with applicable national and international regulations on the shipment of Infectious Substances. Documentation accompanying Specimens shall properly identify the "Specimens", and include a traceability**[Canada]**/tracking[**USA]** number, as well as a copy of these STCs, and a Specimen submission form signed by the First Party. [**UK: We believe that it should be a responsibility of the First Party to ensure as far as possible the integrity of the sample (i.e. that it contains useful infectious material). There should be an SOP to cover this.]**

17. (new para) First Party shall enter information/identification of the Specimen into a common database (minimal dataset), that the WHO Secretariat will develop, along with a system to track viruses through the GISN system.

F. Rights and Responsibilities of Second Party [Germany: same comment as above]

18. Second Party partners receiving, handling or using Biological Materials in their GISN capacity shall use the materials solely in accordance with their GISN TORs, and shall neither seek Intellectual property rights **[UK: We disagree on this point. We do not believe it will always be in the interests of the network and Member States as a community to prevent development of IPR rights. There are circumstances in which this could be helpful. In any case, for tidiness, would seem that this point should be dealt with under Ownership and IPR Section.]** nor

seek to derive financial gain from their use. More specifically, Second Party partners shall not sell, offer for sale or otherwise use for purposes other than those specified in their TORs. [**USA: We pointed out the redundancy here**.]

19. Second Party partner shall provide the First Party with all necessary information for Risk Assessment derived from their analysis of the Specimen~~s~~, as soon as possible, as more specifically detailed in the GISN TORs.

20. Second Party partners may transfer Biological Materials [**USA: Specifically we need to clarify the definition of biological materials.**] to other entities within the Second Party partner and from Second Party partner to First Party for use in accordance with these STCs, and applicable GISN TORs.

21. (new para) WHO shall develop a database for the GISN to track movement of all viruses throughout the GISN system. **[USA: Redundant – see para 17.]** The Second Party partner shall be responsible for entering data on virus movements into the database.

22. The Second Party partner shall consider ways to promote the involvement, participation and recognition of scientists from the First Party in research related to influenza, and shall properly attribute scientists from the First party in scientific publications through citation of the submitting scientist's name and source country on any medical or scientific journal publication, consistent with rules for authorship outlined by the International Committee of Medical Journal Editors.

23. Use or transfer of Biological Materials by a Second Party partner for a purpose, or in a manner, outside the scope of the Second Party partner TORs shall require prior agreement of the First Party. **[UK: The impact of this clause depends entirely on what the TORs specify. At present there are no TORs for the non-essential labs, which represent the main interface with vaccine manufacturers. Any requirement for prior agreement from First Parties for transfer of individual vaccine candidate strains to manufacturers would be very damaging to the ability to respond rapidly.][USA: Strike this entire paragraph].**

24. Use or transfer of Biological Materials by the Second Party partner for a purpose, or a manner, inconsistent with these STCs or applicable TORs, may subject the Second Party partner to investigation under the GISN Oversight Mechanism if a Member State so requests or if routine monitoring reviews so warrant.

Discussion finished here

G. Transfer to & Use by Third Parties

Old 23. Second party partners may not transfer Specimens to any entities not listed in Article 19 above without receipt of a duly completed and signed Biological Materials Request Form from the party requesting the Specimens and authorization from the First Party.

Old 24. WHO CC's may transfer free of charge Candidate Influenza Vaccine Viruses to Third Parties or other GISN Entities upon receipt of a duly completed signed GISN Biological Materials Request Form. The WHO CC shall regularly inform the State Provider of such transfers, including the name of the Third Party Recipient and the Candidate Influenza Vaccine Viruses provided.

Old 25. WHO CC's may transfer free of charge Seasonal influenza reference viruses to Third Parties or other GISN Entities for non commercial purposes upon receipt of a duly completed signed GISN Biological Materials Request Form. The WHO CC shall regularly inform the State Provider of such transfers, including the name of the Third Party Recipient and the Candidate Influenza Vaccine Viruses provided.

25. Third Parties may only request GISN Biological Materials from WHO CCs. Only WHO CCs are authorized to provide GISN Biological Materials to Third Parties.

26. Requests from a Third Party for GISN Biological Materials will be considered only upon receipt by a WHO CC of a duly completed and signed GISN Biological Materials Request Form from the Third Party. The Request Form includes these STCs and requires the Third Party to identify the specific GISN Biological Materials requested and state the purpose for which it intends to use each specific Material.

27. Any and all transfers of GISN Biological Materials from WHO CCs to Third Parties shall be subject to these STCs. Any transfer of GISN Biological Materials in response to receipt of a duly completed GISN Biological Materials Request Form shall be clearly labelled as "GISN Specimens" or "GISN Candidate Influenza Vaccine Viruses" or "GISN Seasonal influenza reference viruses" and a copy of these STCs shall be included in the shipping documents.

28. Third Party Recipients of GISN Biological Materials shall not transfer, sell, offer for sale or otherwise use the Materials for purposes other than those specified on the approved GISN Biological Materials Request Form. Any use of the GISN Biological Materials that differs from or is inconsistent with the purpose stated in the GISN Biological Materials Request Form and/or these STCs will require the agreement of [the State Provider][WHO].

29. Where use of GISN Biological Materials results in publication of an article by a Third Party in a scientific publication, the Third Party shall ensure that proper attribution is given to the State Provider/originating laboratory and include originating country scientists in the conception, execution of the research and the drafting of the article. Proper attribution of State Provider scientists in any medical or scientific journal publication should be done in a manner that is consistent with the guidelines for authorship and acknowledgement stipulated by the International committee of Medical Journal Editors in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals.

Ownership & Intellectual Property Rights

30. No party (including GISN Entities and Third Parties) receiving, handling and using GISN Biological Materials shall claim ownership rights over GISN Biological Materials.

31. Any Party (including GISN Entities and Third Parties) receiving, handling and using GISN Biological Materials seeking patent protection or other intellectual property rights in respect of such Materials, shall disclose in the patent application, the country from where the Biological Materials were collected and the GISN strain designation provided by the GISN CC.

32. Any Party that uses GISN Biological Materials in a manner that results in, or may result in, financial gain,shall consult with WHO to identify how such Party will contribute to WHO's Coordinated International Sharing of Influenza Viruses & Benefits and shall sign a Contribution Agreement to that effect.

G. <u>WHO Determination of a Public Health Emergency of International Concern</u>

33. In the event that the WHO Director General determines the existence of a Public Health Emergency of International Concern (PHEIC) as defined in the International Health Regulations (2005), or under circumstances where the detemination of a PHEIC is imminent, these STCs may be abrogated in whole or in part.

World Health Organization (WHO)
Global Influenza Surveillance Network (GISN)

GISN BIOLOGICAL MATERIALS REQUEST FORM

This Form must be completed, signed and sent by fax or email to a WHO Collaborating Centre for Reference and Research on Influenza

* * *

Institution/Company Requesting GISN Biological Materials
Name & Address **Phone/Email Contact Information**

_____ _____

_____ _____

GISN Specimens **Seasonal Influenza Reference Viruses** ☐ **Candidate Influenza Vaccine Virus** ☐

GISN Strain Designation of Materials Requested:

_____

_____

_____

Purpose for use of GISN Specimens:

_____

_____

_____

Financial Gain anticipated from Use of Specimens? ☐ **YES** ☐ **NO**

If **YES** I undertake to consult with WHO as specified in Paragraph 37 of the World Health Organization Global Influenza Surveillance Network Standard Terms and Conditions for Transfer and Use of GISN Specimens (STCs).

By signing and submitting this Request Form I confirm that I have read and accept the STCs.

_____ _____

Name & Title **Date**

APPROVED: ☐ **YES** ☐ **NO**

Name & Title **Date**

cc: State Provider, WHO/GIP

COPY OF THIS FORM MUST BE INCLUDED WITH THE SHIPPING DOCUMENTS

Contribution Agreement to
WHO's Coordinated International Sharing of Influenza Viruses & Benefits
By and between WHO and [COMPANY NAME]

In consideration for the use of GISN Biological Specimens, as defined herein, [COMPANY NAME] agrees to contribute to the following components of the WHO's Coordinated International Sharing of Influenza Viruses & Benefits.

Examples of possible contributions by Manufacturers

1. Cash : as a % of sales or other defined formula contributed to a WHO managed trust fund.

AND/OR

2. Access to technology:

a. Royalty Free Licences
The Company agrees to grant on request, a non-exclusive, royalty-free license to any domestic influenza vaccine manufacturer from developing and least developed countries to use its intellectual property and other protected substances, products (including technology), know-how, information used in the process of influenza vaccine development and production. A copy of the request should also be sent to WHO.

AND/OR

b. **Transfer of Technology & Know-How**
The Company agrees on request to allow access to and transfer of, its technology and related know-how particularly to domestic influenza vaccine manufacturers from developing and least developed countries especially to the Providing Country and other countries in need. A copy of the request should also be sent to WHO.

AND/OR

c. Pandemic & Pre-pandemic Vaccines
The Company agrees to set aside X% of vaccines for developing and least developed countries especially to those in need and particularly during the pandemic period. These vaccines will be made available at an affordable price for developing countries and least developed countries. The Company, in pricing its products should consider "Affordable price" for developing countries as a price no higher than cost per unit + X% (e.g. 5%), while for least developed countries as "no profit no loss", particularly during the pandemic period

AND/OR

3. Access to diagnostics, antivirals and vaccines
   a. Contribute to stockpile of H5N1 vaccines and ancillary supplies, support downstream management of this stockpile, equitable distribution,
   b. Provide antivirals
   c. Provide funds for advance procurement arrangements for pandemic vaccines
   d. Donate funds to constitute a supply of safe and effective H5N1 and pandemic vaccines

e. Donate or earmark part of the Advanced Market Purchasing (AMP) by some Member States and manufacturers of pandemic vaccines, for access by affected countries during pandemic.
f. In the event of a pandemic, the Company agrees to transfer at least 60% of every production batch of vaccines developed to an international stockpile prior to commercialization.
g. In pre-pandemic period the Company agrees to transfer at least 40% of every production batch of vaccines developed to an international stockpile prior to commercialisation.

AND/OR

4. Vaccine development [for some MS having potential vaccine production capacity but spill-over to all MS]
    a. Provide access to technologies
        i. Royalty free license to intellectual property protected technologies
        ii. Access to and use of regulatory approval data [clinical trial data for registration]
    b. Transfer technology [clarify which specific technologies, e.g. platform technologies or vaccine production]
    c. Contribute to fund national investments to increase vaccine production capacity in developing countries

APPENDIX 4

Core Terms of Reference for WHO Collaborating Centres for Reference and Research on Influenza (including WHO Collaborating Centre on Surveillance, Epidemiology, and Control of Influenza)

This document has not been agreed by all IDWG participants.

The title, WHO Collaborating Centre for Reference and Research on Influenza, designates, through a defined WHO application process, centres of excellence on influenza which:

- Meet all core Terms of Reference (TOR) for WHO Collaborating Centres for Reference and Research on Influenza (WHO CCRRI) listed below. This includes the maintenance of Biosafety Level 2 and Biosafety Level 3 laboratory facilities;
- Work under the coordination of the WHO Global Influenza Programme (GIP)[i]; and
- Receive adequate long-term governmental and/or other non-commercial financial support to fulfil the core TOR for WHO CCRRI.

The core TOR constitute minimum requirements; an individual WHO Collaborating Centre for Reference and Research on Influenza may have additional functions in its TOR in discussion with and agreed upon with WHO GIP.

Core Terms of Reference

All influenza clinical specimens, candidate influenza vaccine viruses and other influenza viruses will be distributed subject to Standard Terms and Conditions for Transfer and Use of Specimens (STC).

A. Advisory role

1. Provide data and advice to WHO concerning suitable influenza viruses for use in vaccines against seasonal, A(H5N1) and other influenza virus with a potential to cause a pandemic; participate in the development and timely availability of the candidate influenza vaccine viruses;
2. Advise the WHO Global Influenza Surveillance Network (GISN)[ii] on laboratory methods for diagnosis of influenza, including the adoption of new diagnostic approaches, the improvement of laboratory practices and other operational needs;
3. Serve as ready technical resources globally to WHO on routine influenza surveillance and influenza emergencies, especially on influenza outbreaks with pandemic potential.

B. Technical performance

1. Strengthening the WHO Global Influenza Surveillance Network

a. Maintain and strengthen active communication and collaboration with National Influenza Centres (NICs)[iii] and other national influenza laboratories to ensure that high quality clinical specimens and/or viruses are received and up-to-date information is exchanged;
b. Conduct training and provide support to NICs and other national influenza laboratories, especially those in developing countries, on laboratory techniques and skills, including diagnosis, data analyses, risk assessment and other critical capacities;

c. Develop, update and produce laboratory diagnostic reagents for circulating influenza viruses and distribute to NICs and other national influenza laboratories;

2. Laboratory analyses and other related activities

a. Isolate in both cell culture and embryonated eggs influenza viruses causing or with the potential to cause human infections;
b. Develop and produce antisera in ferrets against representative influenza viruses causing or with the potential to cause human infections;
c. Conduct complete antigenic and genetic analyses of influenza viruses causing or with the potential to cause human infections;
d. Develop data for recommending appropriate vaccine viruses for use globally, including semi-annual data for seasonal influenza vaccine viruses and, for pandemic preparedness, ongoing data for influenza vaccine viruses with a potential to cause a pandemic;
e. Participate in the development of candidate influenza vaccine viruses for seasonal influenza semi-annually and for influenza pandemic preparedness;
f. Conduct antiviral susceptibility testing of circulating influenza strains, as part of routine surveillance, and provide findings to WHO at least twice every year;
g. Select, maintain and update a group of influenza reference viruses, including seasonal, A(H5N1) and other influenza viruses with pandemic potential, and corresponding antisera if available; update the availability of reference viruses and corresponding antisera, if any, to WHO, which will maintain a web page on the WHO web site;
h. Actively initiate research on influenza viruses, engaging laboratories providing clinical specimens and/or viruses; rapidly share findings of public health significance with WHO.

3. Global influenza response and preparedness

a. Provide expertise and laboratory support, in coordination with WHO, to Member States to assist in influenza outbreak response, especially those associated with influenza viruses having pandemic potential;
b. Assist WHO in the development of standards, recommendations and policies concerning the broad areas of influenza surveillance, response and preparedness.

C. <u>Communication and distribution of viruses and/or clinical specimens</u>

1. Laboratory analyses and results

a. Provide data and/or results timely to originating laboratories/countries providing clinical specimens and/or viruses and to WHO;
b. Alert WHO and the country from which the specimens were provided on unusual findings, especially those related to seasonal or pandemic influenza risks obtained from the analysis of the specimens.

2. Gene sequences

a. Seasonal influenza
   - Upload available sequences of HA and NA genes, and other genes, to a publicly accessible database after each WHO semi-annual vaccine composition consultations, unless otherwise instructed by the laboratory or country providing the specimens.

b. A(H5N1) and other influenza viruses with pandemic potential
   - Upload available sequences of HA and NA genes, and other genes, to a publicly accessible database within 3 months after sequencing done, unless otherwise instructed by the laboratory or country providing the specimens. [**Germany: What is the rationale for 3 months?]**
   -

c. Post a list of virus isolates/specimens analysed but not approved for public use.

d. (old c) Appropriately acknowledge originating laboratories/countries providing clinical specimens and/or viruses.

3. Scientific presentations and publications

a. Actively engage scientists from originating laboratories/countries in scientific projects associated with research on specimens from these countries and engage them actively in preparation of manuscripts for presentations and publications;
b. Appropriately acknowledge in the presentations and publications the contributions of various collaborators, including laboratories/countries providing clinical specimens, viruses or reagents.

4. Influenza clinical specimens and influenza viruses

Share i**nfluenza clinical specimens and influenza viruses, in a timely and unrestricted manner,** with laboratories working in coordination and in collaboration with GIP, including

i. Other WHO CCs for laboratory analyses as defined above;
ii. Other laboratories involved in WHO coordinated specialized activities, (e.g. the WHO External Quality Assessment Project for the detection of subtype influenza A viruses using PCR; the WHO influenza PCR primer updating), and other activities whose purpose is to strengthen global influenza surveillance and other risk assessment and risk response; as well as capacity building.
iii. Key national regulatory laboratories, including FDA, NIBSC and TGA, which are involved in the WHO process of candidate influenza vaccine virus selection and development, as well as vaccine potency reagent development.

5. **Candidate influenza vaccine viruses** are selected and developed under the coordination of WHO, for development and production of vaccines against seasonal, A(H5N1) and other influenza viruses with a potential to cause a pandemic. The candidate influenza vaccine viruses include wild type viruses and high-growth reassortant viruses, including those prepared by reverse genetics.

   a. Distribute to appropriate recipients on request, including influenza vaccine manufacturers, diagnostic companies, research institutes and others interested in receiving influenza vaccine viruses;
   b. Report the distribution status to WHO, which will maintain a list of recipients on the WHO web site.

6. **Influenza reference viruses** are a group of viruses selected, maintained and updated by WHO CCs as antigenically and genetically representative of important groups of viruses,

including seasonal, A(H5N1) and other influenza viruses with pandemic potential. These viruses are often used to generate corresponding antisera. Both reference viruses and corresponding antisera will be:

a. Distribute, on request, to NICs and research institutes for non-commercial activities including surveillance, reference and research; the laboratories/countries providing the original clinical specimens and/or viruses will be notified of the distribution;

7. Distribution of influenza clinical specimens and influenza viruses, for purposes beyond those described above, will require approval from the laboratories/countries providing the original clinical specimens and/or viruses.

[i] WHO Global Influenza Programme http://www.who.int/csr/disease/influenza/en/
[ii] The WHO Global Influenza Surveillance Network http://www.who.int/csr/disease/influenza/surveillance/en/index.html
[iii] WHO designated National Influenza Centers http://www.who.int/csr/disease/influenza/centres/en/index.html

APPENDIX 5

Terms of Reference for National Influenza Centers

This document has not been agreed by all IDWG participants.

The title, National Influenza Center(NIC), recognizes, through a defined WHO process, national influenza laboratories which:

- Function as members of the WHO Global Influenza Surveillance Network (GISN)[i] in coordination with the WHO Global Influenza Programme (GIP)[ii];
- Are formally designated by the country Ministry of Health and officially recognized by WHO; and
- Fulfill the Terms of Reference (TOR) for NICs.

The TOR constitutes minimum requirements for a NIC being a member of the WHO GISN; an individual NIC may have additional obligations under the authority of its Ministry of Health.

Terms of Reference for National Influenza Centres as members of the WHO Global Influenza Surveillance Network

A. Core functions

1. Serve as the key reference point between WHO and the country of origin on all issues related to influenza virological surveillance, laboratory diagnosis of influenza infection in humans and sharing of influenza clinical specimens and/or viruses with WHO;

2. Participate actively in WHO global influenza surveillance activities and maintain active communication and collaboration with other members of the WHO GISN, including WHO Collaborating Centers and other National Influenza Centers.

B. Technical performance

1. Collect appropriate clinical specimens from patients year-round and especially during influenza seasons and outbreaks;
2. Act as a collection point for influenza viruses where available from laboratories within the country;
3. Review, expand and maintain sufficient coverage of influenza virological surveillance in the country;
4. Isolate in cell culture and/or embryonated eggs seasonal/ influenza viruses under appropriate laboratory containment;
5. Conduct preliminary characterization of influenza virus type and subtype;
6. Store original influenza positive clinical specimens for at least 18 months at -70 ^{o}C;
7. Provide technical advice and support to other influenza laboratories in the country, on specimen collection and shipment logistics, laboratory diagnosis, laboratory biosafety and other operational procedures related to influenza virological surveillance;

8. Select seasonal/ influenza viruses, especially those of geographical and possibly antigenic and genetic representativeness, for further characterization in WHO Collaborating Centers for Reference and Research on Influenza (CC RRI).

C. Communication and exchange

1. Alert WHO GIP immediately on the emergence of unusual outbreaks of influenza or influenza-like illness, the detection/isolation from humans of A(H5) or other influenza viruses with a potential to cause a pandemic, or of influenza viruses that cannot be readily identified with WHO diagnostic reagents provided through the WHO GISN;

2. Report regularly to WHO FluNet[iii], weekly during influenza seasons, the extent of influenza activity in the country, virological surveillance data and other relevant information of public health importance;

3. Provide to national authorities and the general public, information on influenza viruses circulating in the country;

4. At least twice every year make shipments to WHO CCRRI of a selection of representative seasonal influenza virus isolates and all influenza virus isolates which gave low titres in HI tests using WHO diagnostic reagents provided through the WHO GISN:

    a. For northern hemisphere countries, once in November and once in early January;
    b. For southern hemisphere countries, once in June and once in mid-August;
    c. For tropical countries, depending on influenza activity, make shipments of recent virus isolates timely to be included in the next WHO vaccine composition recommendation, either for northern hemisphere or southern hemisphere; and
    d. For all countries, make shipments of any unusual viruses within one week after detection.

5. Initiate shipments to WHO CCRRI of clinical specimens and/or viruses from all suspected/confirmed infections of A(H5) and other influenza in humans, within two weeks after detection or isolation of the virus with potential to cause a pandemic; include in the shipment information of time, geographical, epidemiological and clinical factors associated with the suspected/confirmed human infections, for the purpose of ongoing and rapid WHO global pandemic risk assessment and response, as well as and pandemic preparedness.

[i] http://www.who.int/csr/disease/influenza/surveillance/en/index.html
[ii] http://www.who.int/csr/disease/influenza/en/
[iii] http://gamapserver.who.int/GlobalAtlas/home.asp

APPENDIX 6

Terms of Reference for WHO H5 Reference Laboratories

This document has not been agreed by all IDWG participants.
The title, <u>WHO H5 Reference Laboratory,</u> designates, through a defined WHO process, on an *ad-hoc* basis[1], a national influenza laboratory which:

- Meets the WHO Criteria for accepting positive results of H5 infection in humans[2], which ensures that the laboratory conducts reliable diagnosis of influenza A(H5) infection in humans, and that the positive results of A(H5) detection are accepted by WHO as confirmatory without external verification in a WHO Collaborating Center (CC) for Reference and Research on Influenza (RRI); and
- Fulfills the Terms of Reference (TOR) for WHO H5 Reference Laboratories.

Terms of Reference for WHO H5 Reference Laboratories

A. <u>Core functions</u>

1. Provide accurate laboratory diagnosis of influenza infection in humans to assist in rapid outbreak response, especially those suspected of being associated with avian influenza A(H5) viruses; and
2. Provide A(H5) laboratory diagnostic services to its own country and beyond when needed.

B. <u>Technical performance</u>

1. Provide advice to clinics, hospitals and other specimen collection sites on safe and appropriate clinical specimen collection, storage, packaging and shipping;
2. Conduct accurate laboratory diagnosis of specimens received, typing and subtyping influenza viruses, especially the confirmation of A(H5) human infections; and
3. Provide expertise and laboratory support in response to A(H5) avian influenza outbreaks.

C. <u>Communication and exchange</u>

1. Report immediately to WHO and the originating laboratory the results of laboratory diagnostic tests, especially the detection of A(H5) viruses and any other important findings;
2. Actively seek approval from the Ministry of Health of the originating laboratory for sharing the A(H5) clinical specimens and/or viruses with WHO for further characterization in the WHO CCRRI; and
3. Provide feedback to WHO on the use of WHO recommended diagnostic protocols and primers to assist WHO in the update of laboratory diagnostic recommendations.

[1] WHO maintains an up-to-date list of WHO H5 Reference Laboratories
[2] Web-link to Criteria

APPENDIX 7

Oversight Mechanism of sharing of virus and equitable benefit

This document has not been agreed by all IDWG participants.

Scope

The scope of the Oversight Mechanism covers the functions of the following parties:

- The First Parties - The State Providers (the National Influenza Centres and other laboratories designated by a government),
- The Second Parties which include WHO CCs, essential public regulatory laboratories, and relevant WHO projects/programs.
- The Third Parties

Goals

To monitor, evaluate and ensure the effectiveness of, and maintain the trust in, the WHO GISN

Objectives

- To monitor and evaluate the conduct and effectiveness of GISN First and Second Parties with Third Parties
- To monitor and evaluate compliance with the Standard Terms and Conditions and the TORs by GISN entities and Third Parties
- To monitor and evaluate proper benefit sharing within the GISN and provision of benefits by Third Parties
- To recommend remedial action to be taken

Principles

- Participation/ involvement of Member States
- Transparency
- Fairness
- Objective assessment
- Independence
- Free from conflict of interest

Options for an Oversight Mechanism

Option	Pro	Cons
1. WHO Internal Audit + independent experts	Existing mechanism, less costly, can be implemented immediately relying on experienced Internal Audit staff	Skill mix focuses more on budget, financial and management audits, not programmatic nature of influenza work. However, this deficiency ~~could~~ ~~can~~ should be minimized by the contribution of additional technical experts There is potential conflict of interest, whereby it is a WHO Network that is subject to "oversight"
2. Independent oversight committee of experts	Independent group, Free from conflict of interest and confirmation through signing of Conflict of Interest (COI) undertaking, Skill mix can be selected appropriately Better accountability Easy to change and flexible	Can be costly but depends on size of the panel, difficult to assemble meeting in urgent situation, No permanent core to prepare needs assessment, organize visits, prepare reports and co-ordinate work.

Modes of operation

- Routine annual reports based on minimum dataset required from First, Second and Third Parties, to serve as basis for routine monitoring by the Oversight Mechanism
- Enquiries into significantly abnormal situations identified by routine monitoring or by any other party
- Assessment process shall be conducted by the oversight panel
- Reporting of monitoring and assessment to go to WHO DG, and decision on remedial action is vested in WHO DG
- The Oversight panel shall provide an annual report to the EB and WHA

Sanction clauses

- To be determined

Term of reference for the Oversight Panel

- Appointment by the DG through WHA resolution
- Membership: six technical experts, each from the six WHO regions.
- Termination/ review of the Expert Panel – to be defined

= = =