Pandemic Influenza Preparedness Framework Partnership Contribution 2013-2016

Gap Analyses

Laboratory & Surveillance

Burden of Disease

Regulatory Capacity Building

Risk Communications

World Health Organization

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ACRONYMS

AFR	African Region
AMR	Region of the Americas
CDC	Centers for Disease Control and Prevention
EMR	Eastern Mediterranean Region
EUR	European Region
GISRS	Global Influenza Surveillance and Response System
IHR	International Health Regulations (2005)
ILI	Influenza-Like Illness
NIC	National Influenza Centre
PC	Partnership Contribution
PCR	Polymerase Chain Reaction
PIP	Pandemic Influenza Preparedness
SARI	Severe Acute Respiratory Infection
SEAR	South-East Asia Region
WHO	World Health Organization
WPR	Western Pacific Region

INTRODUCTION

'The world is ill-prepared for a severe pandemic or for any similarly global, sustained and threatening public health emergency.'[1]

The influenza A(H1N1) pandemic of 2009 was the first pandemic of the 21st century, and similarly to the earlier SARS outbreak, it highlighted the importance of preparedness, and called attention to the urgency for countries to take action to increase their capacities.

Two systemic reviews were undertaken following the 2009 pandemic: a review of the functioning of the International Health Regulations (2005)[2] ("IHR") and a review of the deployment of A(H1N1) vaccine[3]. Both reviews generated lessons learned and identified areas where global action was needed to strengthen the world's capacity to effectively and efficiently respond to a pandemic event. These two reviews have been relied on extensively as bases for assessing global gaps and needs in pandemic preparedness.

The 2009 pandemic highlighted significant weaknesses at many levels: global, regional and country. One lesson learned from the 2009 pandemic was that the capacities and needs of countries vary greatly. For example, most countries had prepared for a pandemic of high severity and some had difficulty adapting their national and subnational responses to a more moderate event. Accurate risk assessments arising from effective laboratory and surveillance activities proved critical. Communication was also found to be of immense importance: the need to provide clear risk assessments to decision-makers placed significant strain on ministries of health; and effective communication with the public was challenging particularly within an online and social media context.

Another lesson learned was that the principles of pandemic influenza management can be applied to other public health emergencies. Some of the overarching objectives of emergency risk management for health are to: strengthen country capacities to manage health risks from all hazards; establish comprehensive emergency risk management practices and procedures in the health sector; and enable and promote multisectoral linkages and integration across the whole-of-government and the whole-of-society.

These and other lessons learned have provided significant information on the specific areas that are targeted for capacity strengthening in the first three years of implementation of pandemic preparedness activities using Partnership Contribution funds.

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[1] Chair, IHR review Committee, http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf.
[2] http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf.
[3] http://www.who.int/influenza_vaccines_plan/resources/h1n1_vaccine_deployment_initiaitve_moll.pdf.

Background: the PIP Framework

The Member State-led process that culminated in the adoption of the Pandemic Influenza Preparedness (PIP) Framework started in 2007, spurred in large part by the threat of a possible A(H5N1) pandemic. The process lasted four years and resulted in a unique international arrangement that both promotes global action to prepare for pandemics and establishes the bases for a more structured, efficient and equitable response.

Among its many tools, the PIP Framework establishes a benefit-sharing system that aims to, *inter alia*, increase global capacities to prepare for pandemic influenza. To do so, the benefit-sharing system includes an annual contribution (the 'Partnership Contribution' or 'PC') to WHO by influenza vaccine, diagnostic and pharmaceutical manufacturers that use the WHO Global Influenza Surveillance and Response System (GISRS).[4] The Framework specifies that the PC resources are to be used to improve pandemic preparedness and response, by *inter alia*, conducting disease burden studies, strengthening laboratory and surveillance capacity, and access and effective deployment of pandemic vaccines and antiviral medicines[5].

In 2012, the Director-General's PIP Advisory Group made several recommendations regarding the allocation of PC resources and their use. More specifically, they proposed to allocate 70% of the PC to pandemic preparedness and 30% to a reserve for pandemic response activities. The Director-General accepted these recommendations and, as required, submitted this proposal to the 131st Executive Board that approved this division of funds through 2016. The Advisory Group further recommended that the majority (70%) of preparedness resources be used to support surveillance and laboratory capacity building and that 10% each be allocated for disease burden studies, strengthening regulatory capacity to improve access and effective deployment of pandemic vaccines and antiviral medicines, and strengthening risk communications. The Director-General accepted these recommendations.

The Advisory Group articulated several principles and factors that should considered in allocating PC resources. Specifically, allocations should:

- Take into account PIP Framework principles including fairness, equity, the public health risk and need of all countries and the particular vulnerability of H5N1;
- Be evidence-based and consider indicators, adapted to the Framework, such as core capacities under the IHR, income, health and epidemiology;
- Consider the critical foundation of epidemiological and laboratory surveillance;
- Take into account the modest amount of PC resources;
- Consider the need to ensure the involvement of at least one country from each WHO region while retaining a primary focus on countries with the highest need.

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[4] GISRS is an international laboratory network that has been in existence since 1952. It currently comprises 141 national laboratories recognized as National Influenza Centres (NICs), 6 WHO Collaborating Centres (CCs), 5 Essential Laboratories (ERLs), and 12 H5 Reference Laboratories.
[5] See Framework section 6.14.4.

Determining global gaps and needs

To ensure that the highest impact is achieved with limited PC resources, it is important to properly assess the global capacity of influenza pandemic preparedness and response in order to guide the use of available resources in areas selected for strengthening so that targeted and country-specific interventions may be tailored. This document describes the methodology used to assess global capacities, with as much regional granularity as possible, and presents findings. The gap analysis for laboratory and surveillance capacity was based on findings contained in the *Technical Studies under Resolution WHA63.1[6],* completed in early 2011, and information from on-going global surveillance and response activities by WHO and countries. For other areas of gap analyses, the Secretariat used the findings and recommendations from recent global consultations, studies and/or review processes, such as:

- Report of the Review Committee on the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009[7];
- Main operational lessons learnt from the WHO Pandemic Influenza A(H1N1) Vaccine Deployment Initiative[8];
- Workshop on international regulatory capacity enhancement for influenza vaccines[9];
- Inter-agency meeting following the workshop on Enhancing Communication around Influenza Vaccination - Atlanta, CDC, 13 June 2013.

The information and, in some cases, recommendations, contained in these reports and studies provided the initial bases to prioritize the areas to be addressed to improve pandemic preparedness. Further analyses using different factors and criteria were then applied to develop more refined regional gaps and needs; WHO regional offices played a pivotal role in prioritizing potential recipient countries for each of the focus areas.

Gap analyses: what they do and don't provide

The gap analyses provide a global and regional snapshot of gaps and needs in the four focus areas for PC investment and served as the bases for regional offices to prioritize countries within regions so as to ensure achievable and measurable impact with the PC resources.

The global and regional analyses were derived from aggregating individual country-level data. Country-specific analyses of gaps and needs, however, are not presented in this report. Using a limited number of indicators to carry out complex country analyses has inherent risks but more detailed analyses require far more time, involvement with, and investment by country partners to be properly developed. For this reason, the first activity in each of the countries selected to receive PC funds, will be to develop a focused, country-specific gap analysis to establish baseline indicators and targets against which to measure results.

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[6] http://www.who.int/influenza/resources/technical_studies_under_resolution_wha63_1_en.pdf.
[7] http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf.
[8] http://www.who.int/influenza_vaccines_plan/resources/h1n1_vaccine_deployment_initiaitve_moll.pdf.
[9] http://www.who.int/immunization_standards/national_regulatory_authorities/wirceiv_report_18jan2012.pdf.

Implementation and achievement of the targets will be routinely monitored. Reporting on achievement of outcomes will be based on indicators developed from the country specific gap analyses.

CHAPTER 1

Laboratory and Surveillance

1. BACKGROUND AND OBJECTIVE

Directing the largest portion of PC resources to surveillance and laboratory capacity building reflects both the foundational importance of influenza surveillance to pandemic preparedness and response, as well as critical gaps in this capacity at global and national levels. Surveillance is essential to detect the emergence of new influenza viruses and the start and end of epidemics; advance the understanding of the epidemiology and seasonality of influenza; estimate the burden of disease; and guide public health interventions.

This Chapter reviews and assesses global influenza laboratory and surveillance capacities with a view to assisting in the overall process of prioritizing countries for selection by the Director-General for capacity strengthening using the PC. The findings supported the development and refinement of the outcome, outputs and activities for the PC Implementation Plan for Laboratory and Surveillance Capacity Building.

A well-functioning influenza laboratory and surveillance system requires 3 capacities:

- The capacity to **detect** emerging influenza viruses, in particular those with human pandemic potential;
- The capacity to **monitor** the evolution of influenza viruses, their epidemiology and impact;
- The capacity to **share viruses and information** in a timely manner with other laboratories for global initial risk assessment, and relevant response measures, as appropriate.

Detection and monitoring

A timely and effective response to an influenza pandemic relies on the capacity of countries to **detect** the emergence of a novel influenza virus at an early stage in order to perform an initial assessment of risks associated with the virus, an initial assessment of the virulence of the virus, develop diagnostics and candidate vaccine viruses, and implement early response measures. On-going **monitoring** of the situation, through routine influenza surveillance will guide the public health response strategy. The two are inter-related and complementary but require different strategies.

Effective detection functions require several key elements, including:

- mechanisms to recognize and report unusual events;
- laboratories and staff trained to correctly identify novel viruses; and
- capacity to fully characterize a novel virus.

While it is not necessary or feasible for every country to acquire the capacity to fully characterize a novel virus, it is essential that characterization services be accessible to every country through the shipping of samples to reference laboratories.

Routine **monitoring** of influenza provides baseline historical data to assess the importance of a newly emerged virus and its potential impact as reflected in the magnitude of mild and severe disease. In addition, the data gathered through routine monitoring provide the means to define high-risk groups; identify important epidemiologic patterns such as geographic and seasonal variations; and monitor for changes in the behaviour of a novel virus.

Effective monitoring requires:

- laboratory capacity for routine diagnostic testing to monitor circulating viruses;
- surveillance of cases of influenza-like illness (ILI); and
- surveillance of severe respiratory acute infections (SARI).
- Mechanisms for collecting, analysing, and reporting data.

Country-level capacities for virological and disease surveillance are not always developed in parallel and may differ in their level of function.

Sharing viruses and information

Sharing of information and viruses is necessary to understand the global pattern of influenza virus drift (or changes) and the selection of appropriate viruses for vaccine production. Timely sharing of such information is even more critical during a pandemic; it underpins global risk assessment and defining national and global response strategies. During the 2009 influenza H1N1 pandemic, the virus spread to all continents in less than 9 weeks. The ability to track the virus and its impact as it moved around the world was critical to providing advance information to unaffected countries. The management of this kind of global public health emergency requires the strengthening of international collaboration in addition to the strengthening of national capacities.

All capacities cannot be developed at the same time. Therefore countries with the weakest influenza surveillance capacities should begin by developing an adequate detection capacity. This requires training in real time polymerase chain reaction (PCR) which is currently the standard technology for virus detection. PCR capacity should be available in every country. Surveillance of ILI enables a country to develop basic information on the seasonality of influenza within its borders; this is a capacity that should also be strengthened. Finally, surveillance for SARI at representative sentinel sites is needed to provide data on the usual levels of severe respiratory disease and the factors that place individuals at increased risk.
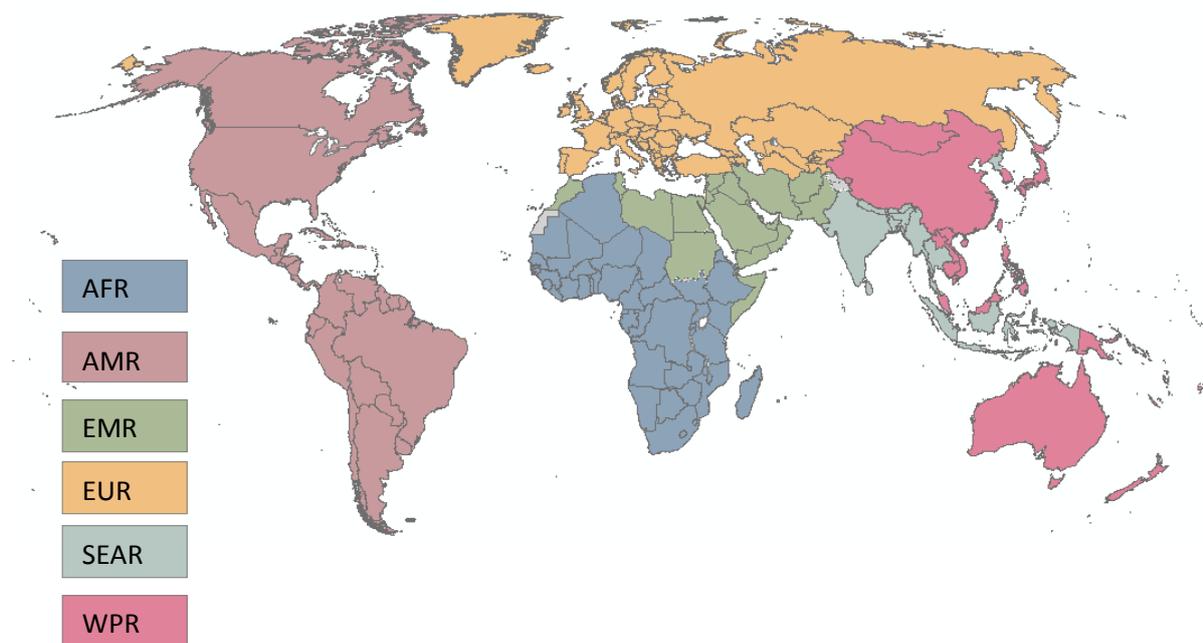
2. METHODOLOGY

Factors to assess countries' laboratory and surveillance capacities were selected based on recommendations from the PIP Advisory Group that they should include International Health Regulations (IHR) core capacities as reported to WHO, income, health and epidemiology, and the particular vulnerability of some countries to A(H5N1). The PIP AG recommendations were further refined by influenza experts to include influenza-related factors such as PCR capacity, influenza virus shipping capacity and the status of ILI or SARI surveillance. Annex 1 provides a full description of each factor including the data source from which it was derived.

The analyses were performed using existing data; new data were not collected to support the gap analyses because of time and financial constraints. Although reliance on existing data posed some limitations on the analyses (e.g. in some instances data were not available or not up-to-date), it was possible to develop an overview of global gaps in laboratory and surveillance capacities.

Findings are presented by WHO Region (see map).

WHO Regions, 2013[10]

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[10] African Region (AFR); Region of the Americas (AMR); Eastern Mediterranean Region (EMR); European Region (EUR); South-East Asia Region (SEAR); Western Pacific Region (WPR)

2.1. Methodology to develop the gap analysis for "detection"

To assess global and regional detection capacities, a scoring system was developed to group countries by level of need. This provided a basis for defining detection capacity baselines and targets.

The scoring system was based on the following factors:

- IHR indicator 3.2.1: implementation status of event-based surveillance. The information for this factor was based on 15 questions in the IHR survey which is required to be completed by IHR States Parties on an annual basis. Data were from the 2013 survey; for countries that did not report in 2013, surveys were searched in reverse chronological order until data were available for as many countries as possible [factor short name: IHR indicator 3.2.1];
- Presence of a WHO-recognized National Influenza Centre (NIC) [factor short name: NIC]
- Adequate polymerase chain reaction (PCR)-capacity defined as scoring 80% accuracy in the WHO External Quality Assessment Project (EQAP) which uses panels of coded samples of influenza viruses to assess the performance of participating laboratories [factor short name: PCR];
- Demonstrated capacity to ship influenza viruses specimens in accordance with international standards and regulations [factor short name: Shipment].

Figure 1. Algorithm for scoring the detection capacity for each country
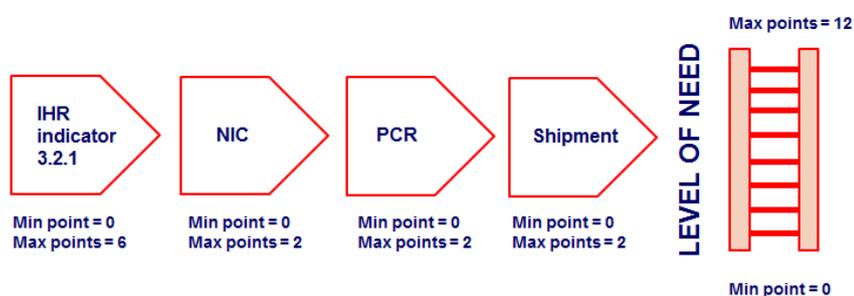
Points were assigned to each of the factors and then summed across factors (Figure 1) to provide a "detection capacity score" for each country (Score range: 0-12); countries most in need had the lowest scores.[11] Countries were stratified into four levels of influenza surveillance capacity, as illustrated below.

Capacity levels	Score
Low (level 1)	Score <= 4
Weak (level 2)	Score > 4 and <=8
Moderate (level 3)	Score > 8 and <= 10
High (level 4)	Score > 10

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[11] Data were compiled using Microsoft Excel and transferred into Stata 11 for analysis.

Table 1: Summary of DETECTION CAPACITY factors, source of data and limitations

FUNCTION	CAPACITY	Factor	Source	Limitations
DETECT	Capacity to detect an unusual cluster of respiratory cases and to report it in a timely manner	IHR detection capacity	IHR core capacities assessment	Self-assessment by countries
	Influenza laboratory capacity	Existence of a NIC	GISRS data	Only countries participating in the GISRS network
	Capacity to identify correctly influenza virus by subtype	Adequate PCR	GISRS data	Only countries participating in the EQAP
	Capacity to ship samples to reference laboratories in countries where full virus characterization capacity is not available	Shipping capacity	Shipping fund project data	Only countries using the shipping fund project

DETECTION data limitations by factor

Table 1 provides a summary of capacities, factors, and data sources and limitations for assessing detection capacities, as more fully developed below.

IHR indicator 3.2.1: Of 194 countries, data for the IHR indicator were not available for 12 (6%) countries: 7 (15%) of AFR countries; 3 (6%) of EUR; 1 (5%) of EMR; and 1(3%) of AMR. These 12 countries were represented as having missing or no data. The reasons for missing data were not explored systematically, but likely vary, e.g. some countries may lack the capacity while others may have the capacity, but chose not to respond to the IHR survey.

IHR indicator data are voluntary, self-reported data and as such are subject to several limitations: understanding or interpretation of the question may vary among respondents; standardization of data across respondents is difficult, especially when open-ended questions are used; inaccuracies in reporting may result when data are not independently verified; and results can be biased if there are systematic differences between countries that did and did not respond.

NIC: There are currently 141 NICs in 111 countries. Some countries that lack a NIC may not have the required capacity. In other instances, the required capacity is available, but health authorities have not requested that their national influenza laboratory be recognized as a member of GISRS; in this situation, the "NIC score" does not reflect actual capacity.

PCR: Data on reliable PCR capacity were derived from the WHO EQAP. The EQAP was established in 2007 to monitor the quality of GISRS laboratories and other national influenza reference laboratories that perform PCR diagnosis, to identify gaps in PCR testing in these laboratories and provide guidance to laboratories as needed. The EQAP is open to all NICs and national influenza reference laboratories in countries without NICs with PCR capacity in place. Participation in this project is

voluntary for NICs and other national laboratories. There may be instances in which countries with reliable PCR capacity were incorrectly categorised as having no reliable PCR capacity due to lack of participation in the WHO EQAP.

2.2. Methodology to develop the gap analysis for "monitoring"

The following four factors (two for virological surveillance and two for disease surveillance) were used to assess and analyse **monitoring** capacity. Due to the complexities of evaluating the quality, efficiency and adequateness of ILI and SARI surveillance systems, however, no scoring system was used.

Virological surveillance
- Presence of a WHO-recognized NIC in the country [factor short name: NIC];
- Adequate PCR-capacity defined as scoring 80% accuracy in the WHO EQAP [factor short name: PCR].

Disease surveillance
- Capacity to conduct ILI or respiratory disease surveillance [factor short name: ILI];
- Capacity to conduct SARI surveillance or monitoring of severe cases [factor short name: SARI].

The data for ILI and SARI surveillance were collected by regional offices (RO), provided to WHO headquarters (HQ) and reviewed by experts in both HQ and the ROs. The consultation process was essential as there is no database that integrates data for these two factors. Country capacities for disease surveillance were classified into four groups as follows:

- **Unknown:** No information was available on the current status of ILI or SARI surveillance;
- **None**: ILI or SARI surveillance not in place or in the very early stages of implementation;
- **Partial**: ILI or SARI surveillance in place but reporting inconsistent, irregular or incomplete, e.g. laboratory testing inconsistently performed;
- **Full**: ILI and SARI surveillance both in place and of good quality; includes countries that perform regular monitoring of pneumonia or hospitalized case with acute respiratory infection and testing for influenza.

Table 2: Summary of MONITORING CAPACITY factors, sources of data and limitations

FUNCTION	CAPACITY	Factor	Source	Limitations
MONITOR	Laboratory capacity to identify circulating viruses	Existence of a NIC	GISRS data	Covers only countries participating in the GISRS network
	Good laboratory analysis capacity	Adequate PCR	GISRS data	Covers only countries participating in EQAP
	Capacity to follow trends of disease and assess morbidity	ILI surveillance	Assessment by WHO experts (HQ and ROs)	WHO expert assessment based on available information
	Capacity to monitor severe outcomes and impact of influenza on health care system	SARI surveillance	Assessment by WHO experts (HQ and ROs)	WHO expert assessment based on available information

MONITORING data limitations by factor

Table 2 provides a summary of capacities, factors, data sources and limitations for assessing monitoring capacities, as more fully developed below.

NIC: described previously in data limitations for detection.

PCR: described previously in data limitations for detection.

ILI and SARI surveillance: WHO has recently published interim standards for influenza epidemiological surveillance in an attempt to standardize practices globally. However, many pre-existing systems persist, some of which have been in use for decades, and multiple types of data are collected creating a diverse assortment of global data which are very often not comparable. The assessment of disease surveillance, particularly for SARI surveillance capacity, is difficult. Countries monitor severe disease activity on a voluntary basis; there is no mandatory reporting of these data. SARI surveillance, which includes more epidemiological data collection, is a recent introduction and has been adopted by a limited number of countries. Many countries, however, have systems that serve approximately the same purpose by monitoring hospitalizations for pneumonia, admissions to intensive care units, or some other proxy for severe respiratory disease in near real time. These are largely used by wealthier, developed countries that have electronic reporting. Interest in monitoring for severe disease has increased following the H1N1 pandemic. Several countries have recently started monitoring SARI activity; however, these systems are difficult to sustain consistently and are often dependent on external funding.

Data for ILI and SARI were missing for 10% and 9%, respectively of 194 countries. The classification of country capacity was based on a WHO expert assessment of qualitative information. ROs may have used different criteria when evaluating disease surveillance; it is not possible, therefore, to make comparisons between regions. Data within a given region are assumed to have been derived in a consistent manner.

2.3 Methodology to develop the gap analysis for "sharing of viruses and information"

Influenza data sharing is conducted through a number of platforms.

- FluNet: FluNet was launched in 1997 as the GISRS tool for virological surveillance. In recent years data were not only provided by GISRS laboratories but also by other national influenza reference laboratories collaborating actively with GISRS.

- FluID: FluID is a platform for global sharing of epidemiological data. The system was brought online in 2010.

- EZCollab: GISRS has an informal communication platform based on EZCollab for sharing information and experiences, discussing issues and problems, and finding solutions among GISRS members. The platform is most useful in emergency situations for rapid access to technical information e.g. diagnostic protocols.

The following three factors were used to assess countries' capacity to **share influenza viruses and information:**

- submission of viruses from countries to WHO Collaborating Centres (WHO CC);
- reporting virological information to regional or global databases;
- reporting epidemiological data to regional or global databases.

No scoring system was used due to the complexities of quantifying individual factors in a meaningful way to reflect the capacity to share viruses and information. Sharing of viruses and information is dependent on influenza activity in a specific season and varies from country to country, region to region, and year to year; e.g. a country may share few viruses or data in a given year if seasonal influenza activity is low.

Table 3: Summary of VIRUS/INFORMATION SHARING CAPACITY factors, sources of data and limitations

FUNCTION	CAPACITY	Factor	Source	Limitations
Sharing of viruses and information	Sharing of viruses	Submission of viruses from countries to WHO CCs	Shipping fund project	1) virus activity; 2) capacity to collect and do PCR testing of specimens; 3) financial resources to ship to a CC or to access funds thru the shipping fund project
	Sharing of virological information	- Reporting to regional or global databases	FluNet	Mandatory only for NICs in GISRS
		- Informal exchange of virological data within GISRS	GISRS/EZCollab	Voluntary participation
	Sharing of epidemiological information	Reporting to regional or global databases	FluID	Voluntary participation of countries

## 2.4. Methodology to prioritize countries to receive PC resources

All countries were assessed for their "detection", "monitoring" and "sharing" capacities using the factors described above and placed in a matrix stratified by region. The matrix was used as a tool to identify countries most in need.

The gap analyses were not the only source of information to prioritize countries to receive PC resources. Regions took into account several additional elements to further refine the prioritization of countries:

- **Country development status**: For purpose of this analysis, a definition of "developing country" was developed to take into account three important developmental factors: income status, human development index and "least developed country" classification. The resulting country development status factor gives primary focus to low/lower-middle income resource countries, but allows other countries to be considered for capacity building activities under the PIP Framework (see Annex 1 for further details). Of 194 countries, 106 are categorised as "developing" and therefore eligible for support with PC resources. The proportion of countries that are "developing" varies by WHO region (Figure 2). On a global level, 70% of the world's population lives in developing countries: 38% of those are n SEAR; 32% in WPR; and 18% in AFR (Table 4).
- **"H5N1 vulnerability"**[12] : Countries with laboratory confirmed cases of H5N1, or influenza virus with human pandemic potential, were classified for vulnerability as follows (see Annex 1 for more details):
    - **High risk countries for sporadic human infections**: Countries with laboratory confirmed human case due to H5N1 or infection with influenza viruses of pandemic potential in the last 5 years; and/or countries with H5 or influenza viruses with pandemic potential viruses currently circulating in poultry.
    - **Medium risk countries for sporadic human infections**: Countries which have had one or fewer laboratory confirmed human cases of H5N1 or infection with influenza viruses of pandemic potential in the last 5 years. These countries may or may not have reported sporadic outbreaks of influenza in animals (including H5 and H7) to the World Organisation for Animal Health (OIE) in the past 5 years.
- **Total population size of each country;** see Table 4.
- **Other factors including:**
    - On-going donor funding and investments in a country;
    - Absorptive capacity of a country;
    - Geographical location of a country in the region/sub-region (notably for island states);
    - Interest of a country/Ministry of Health to work in influenza;
    - Ability of countries to build on existing capacities to produce influenza surveillance data which could be shared with neighbouring countries;
    - The political and social stability of the country, the existence of other source of funding for influenza laboratory and surveillance activities.

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[12] Derived from definition of "affected country"; see PIP Framework Section 4.4.

Figure 2: Number of developing, and non-developing countries, by WHO region
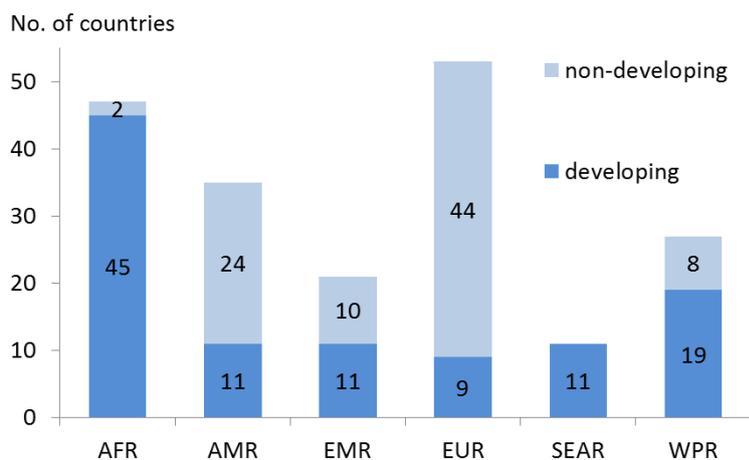
SEAR has the highest percentage of developing countries (100%), followed by AFR (96%), WPR (70%), EMR (52%), AMR (31%) and EUR (17%).

**Table 4: Number of countries, developing countries and population, in 2012, by WHO region**

WHO region	Number of countries	Number of developing countries	Population of the region	Population in developing countries
AFR	47	45	857,382,404	855,988,903
AMR	35	11	938,647,212	73,049,106
EMR	21	11	559,842,894	418,936,833
EUR	53	9	899,442,387	104,615,400
SEAR	11	11	1,830,361,233	1,830,361,233
WPR	27	19	1,800,262,924	1,563,880,484
Total	**194**	**106**	**6,885,939,054**	**4,846,831,959**

## 3. ANALYSIS AND FINDINGS

3.1 Detection capacity

At the global level, of the 182 countries with available data, 98 countries have a detection capacity score above or equal to the median value of 8 (Figure 3).

Figure 3. Frequency distribution of detection scores (N=182 countries with available data)
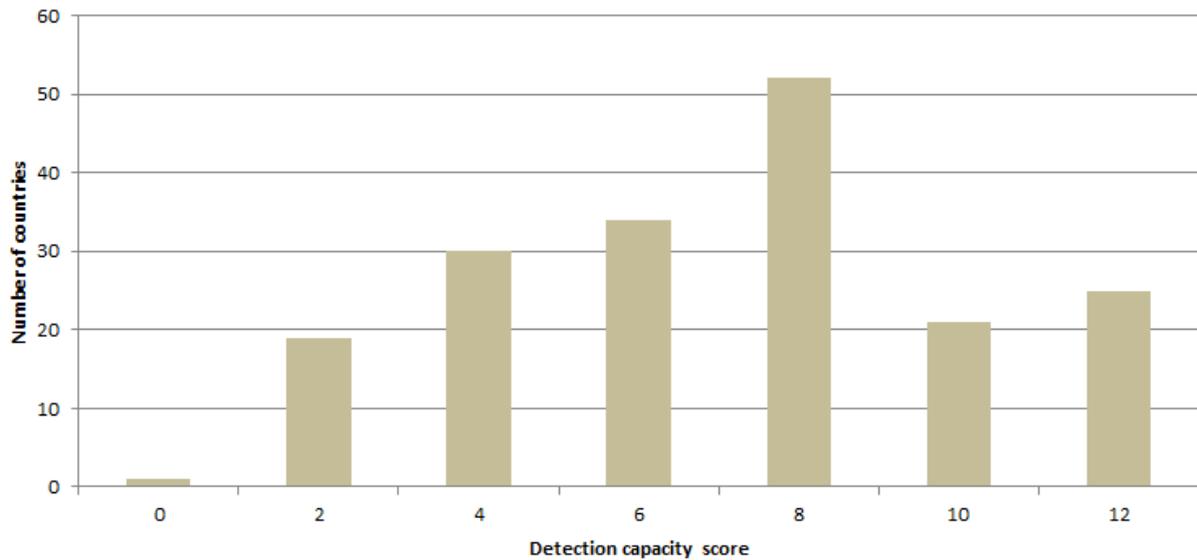
The distribution of scores differs by region (Figure 4): of the 40 countries in AFR with data, 39 (98%) score below or equal the global median); AMR, EMR, EUR and SEAR have a median score equal to the global median.

Figure 4. Distribution of detection capacity scores, by WHO region (N=182 countries with available data)
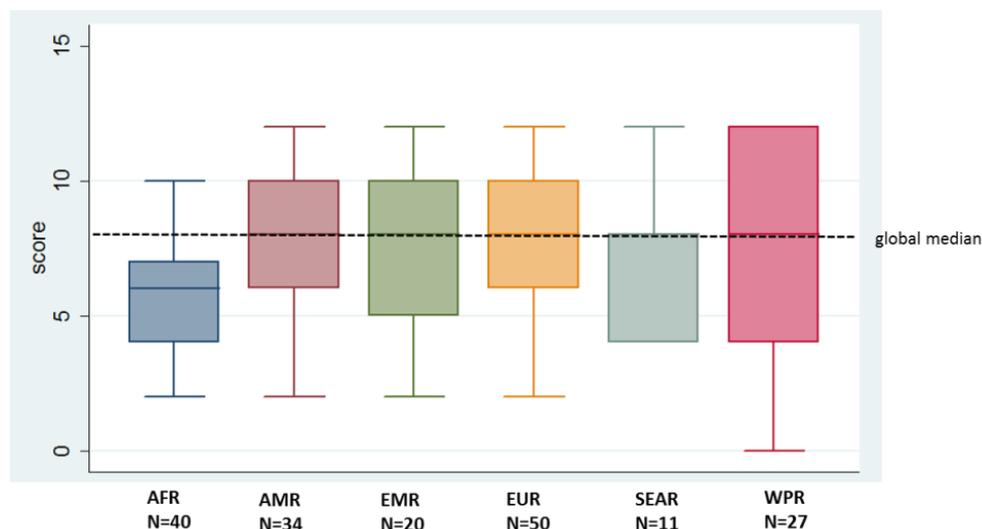
Based on the tabulated detection capacity score, countries were placed into one of the four levels of capacity. In this way, the level of support needed for detection capacity in each WHO region could be distinguished.

In general detection capacity is low or weak (Figure 5). Overall, 50 (26%) countries have low (level 1) capacity; 86 (44%) weak (level 2); 21 (11%) moderate (level 3); and 25 (13%) high (level 4). Data were missing for 12 (6%) countries.

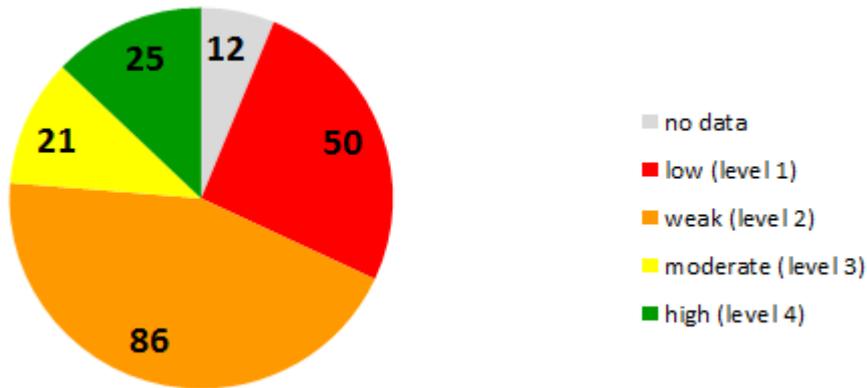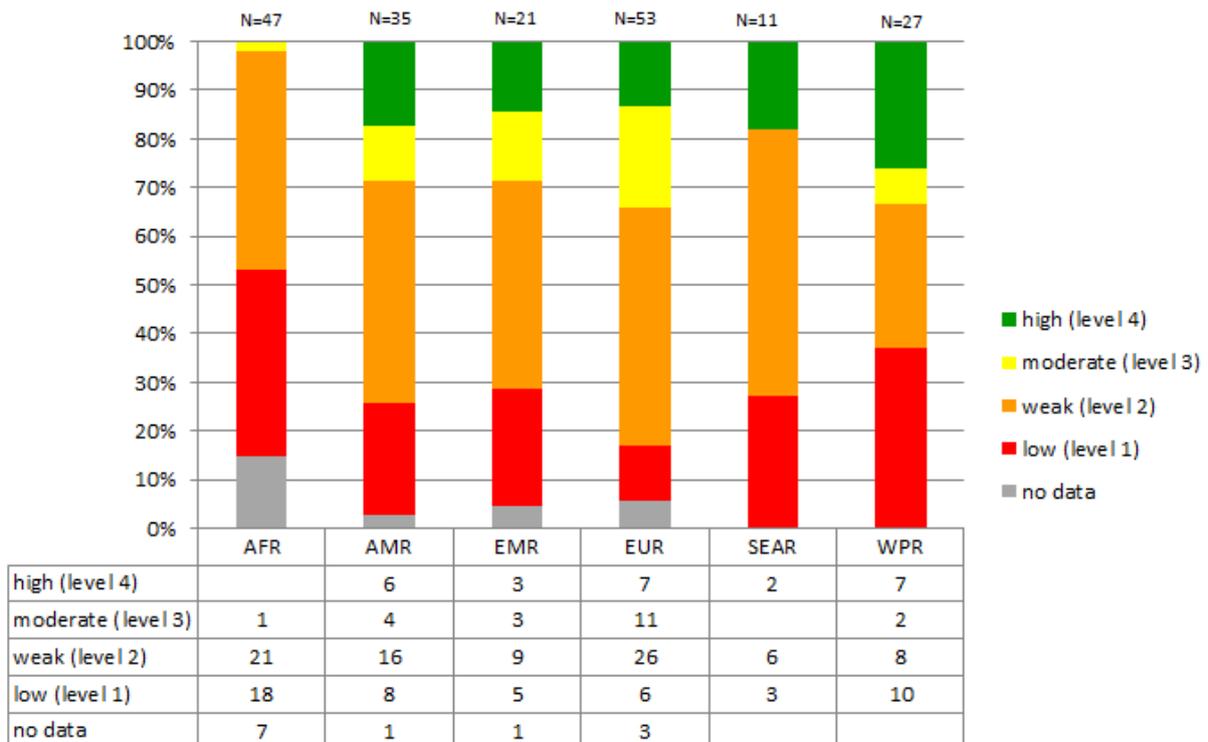**Figure 5: Global detection capacity level (N=194 countries)**

Figure 6: Detection capacity level, by WHO region

	AFR	AMR	EMR	EUR	SEAR	WPR
high (level 4)		6	3	7	2	7
moderate (level 3)	1	4	3	11		2
weak (level 2)	21	16	9	26	6	8
low (level 1)	18	8	5	6	3	10
no data	7	1	1	3		

Of the 194 countries, 70% have low or weak capacity (level 1 or level 2). Detection capacity varies by region (Figure 6); 17% to 26% of countries in three WHO regions (AMR, SEAR, and WPR) have a high capacity (level 4) while only 13% and 14% of countries in EUR and EMR, and 0% in AFR have this level of capacity.

AFR has the highest proportion of countries with level 1 or level 2 capacity (83%), followed by SEAR (82%), AMR (77%), WPR (67%), EMR (67%), and EUR (60%).

The percentage of developing countries with low or weak capacity (level 1 or level 2) is about 78% globally. AFR and WPR have the highest percentage of developing countries with low or weak capacity (level 1 or level 2) [84% in both regions], followed by AMR and SEAR (82% in both regions), EMR (64%), and EUR (56%). However, in terms of number of countries, AFR has the highest number of developing countries with low or weak capacity (level 1 or level 2) [N=38].

The capacity to detect was also compared with the vulnerability to A(H5N1).

Table 5. Detection capacity among countries considered at <u>high</u> risk for H5N1, by WHO region

Region	Capacity				
	Low (level 1)	Weak (level 2)	Moderate (level 3)	High (level 4)	total
EMR	0	2	0	0	2
SEAR	0	2	0	2	4
WPR	0	1	1	1	3
Total	**0**	**5**	**1**	**3**	**9**

Table 6: Detection capacity among countries considered at <u>medium</u> risk for H5N1, by WHO region

Region	Capacity					
	No data	Low (level 1)	Weak (level 2)	Moderate (level 3)	High (level 4)	total
AFR	0	1	4	0	0	5
AMR	0	0	0	0	1	1
EMR	0	2	1	1	2	6
EUR	2	0	3	4	2	11
SEAR	0	1	2	0	0	3
WPR	0	0	2	0	3	5
Total	**2**	**4**	**12**	**5**	**8**	**31**

Influenza surveillance detection capacity is weak (level 2) for 56% of the nine countries at high risk for H5N1 (Table 5): 2 countries in EMR and SEAR each and 1 in WPR have weak capacity (level 2). All nine "at risk" countries are developing countries.

Of 31 countries at medium risk for H5N1 (Table 6), 16 have low or weak (level 1 or level 2) influenza detection capacity (5 in AFR, 3 in EMR, 3 in EUR, 3 in SEAR and 2 in WPR); 12 of the 16 are developing countries. Globally, 42% of the countries considered to be at medium risk for H5N1 have a moderate or high detection capacity (level 3 or level 4).

Summary of findings

Detection capacity is unevenly distributed worldwide. Gaps exist in all WHO Regions, in particular in AFR and SEAR.

- 136 (70%) of countries have low or weak (level 1 or level 2) detection capacity.
- The percentage of countries with low or weak (level 1 or level 2) capacity is as follows:
    - AFR (83%)
    - SEAR (82%)
    - AMR (77%)
    - WPR (67%)
    - EMR (67%)
    - EUR (60%).
- AFR has the greatest number of countries with low or weak (level 1 or level 2) capacity.
- Among the 50 countries with low (level 1) capacity, 35 (70%) are developing countries.
- From the perspective of H5N1 vulnerability, 5 of the 9 countries at high risk for H5N1 have weak (level 2) capacity.

3.2. Monitoring capacity

3.2.1. Virological surveillance – Presence of a NIC

As illustrated on the map and detailed in Figure 7, EUR has the largest percentage of countries with a WHO-recognized NIC (41 of 53 countries or 77%), followed by SEAR (8 of 11 or 73%), EMR (15 of 21 or 71%), AMR (21 of 35 or 60%), WPR (14 of 27 or 52%), and AFR (12 of 47 or 26%).
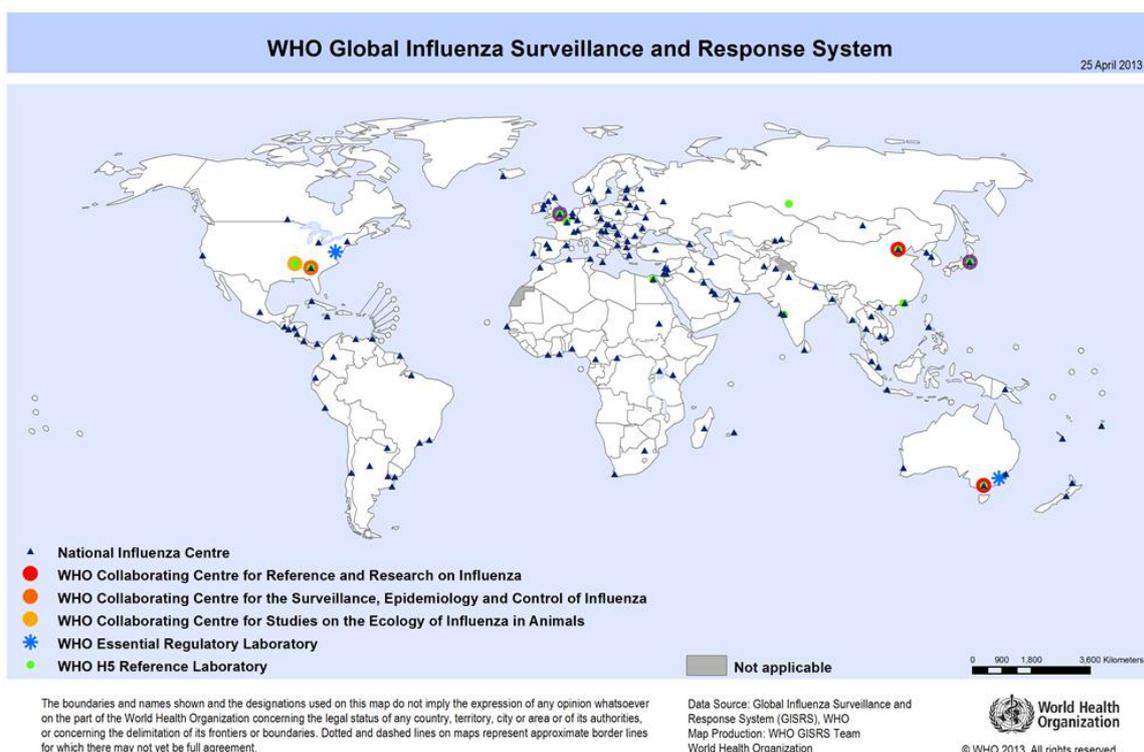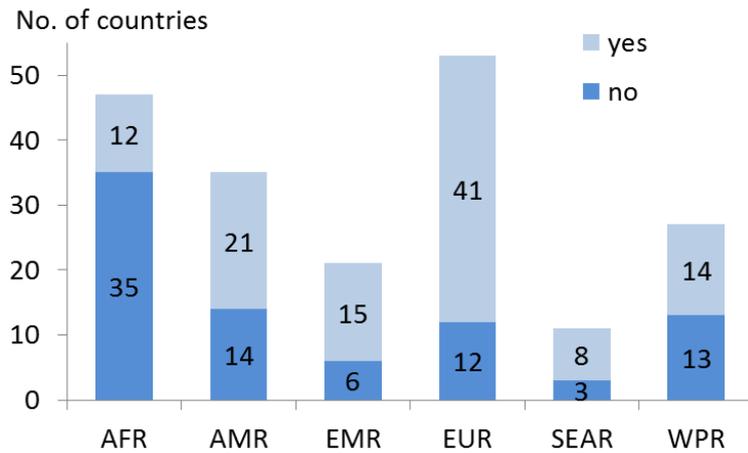
Figure 7: Number of countries with a WHO-recognized NIC, by WHO region


3.2.2. Virological surveillance – PCR capacity

Real time PCR is the most widely used technology for influenza virus detection. Most countries have the ability to perform PCR. However, in many countries where PCR is available, the number, quality, and representativeness of specimens for testing is limited. This is partly reflected in the number of virus detections reported to FluNet per year. Of those countries reporting to FluNet (2011-2013), 17% detected fewer than 150 viruses per year, a level below which it is difficult to interpret seasonality and other aspects of influenza activity. Countries with the weakest capacity for PCR are located primarily in Africa and Central Asia (see map below).
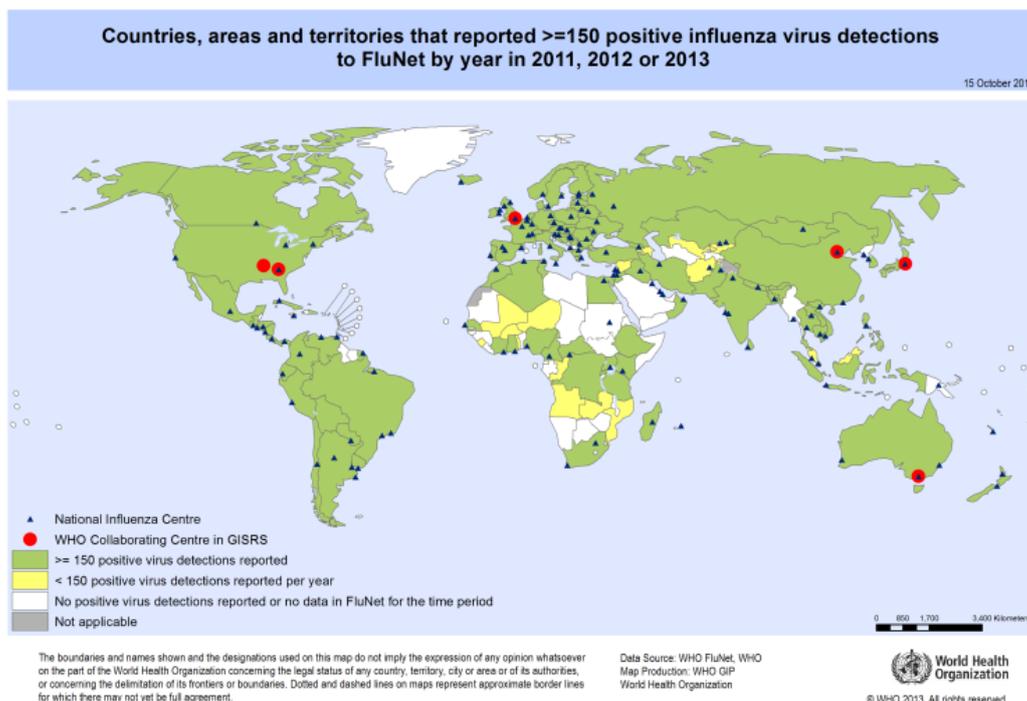
The quality of PCR was also examined using the results of the WHO EQAP.[13] In 2013, 170 laboratories from 130 countries reported results. Figure 8 displays the regional distribution of countries with laboratories that achieved 100% accuracy for detection of H5 viruses in the WHO EQAP in 2012 and 2013. Globally, 55% of all countries correctly identified all H5 influenza test sample viruses, and regional averages ranged from 40% to 64%.

Figure 8: Number of countries with at least one laboratory that reported all correct results for influenza A(H5) in 2012 and 2013 (panels 11 and 12), by WHO region
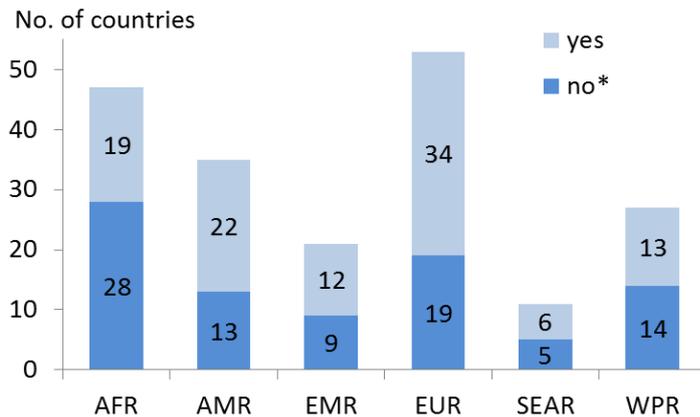
* no or not participating.

Figure 9: Number of countries with adequate (80% correctness) PCR capacity (panels 11 and 12), by WHO region
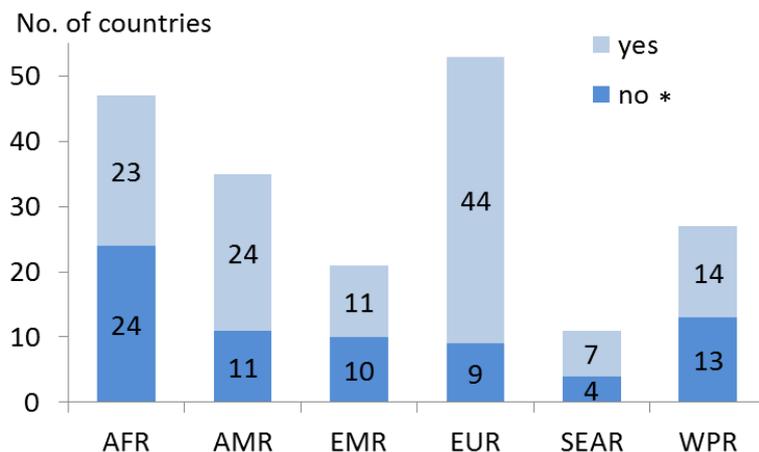
* no or not participating.

Based on figure 9 above, globally 123 (64%) countries have adequate (80% correctness in EQAP) PCR capacity. EUR has the highest percentage of countries (83%) with adequate PCR capacity, followed by AMR (69%), SEAR (64%), EMR (52%), WPR (52%) and AFR (49%).

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[13] http://www.who.int/influenza/gisrs_laboratory/external_quality_assessment_project/en/

3.2.3. Disease surveillance

Currently, most countries do some kind of surveillance for ILI and these systems form the basis for the virus sampling that is reported to FluNet. SARI surveillance, which includes more epidemiological data collection, is a recent introduction and has only been adopted by a small number of countries. Many countries, mainly developed countries with electronic reporting, have systems that serve approximately the same purpose by monitoring hospitalizations for pneumonia, admissions to the intensive care unit, or some other proxy for severe respiratory disease in near real time.

The distribution of capacities to conduct ILI and or SARI surveillance by region, and findings are presented in Figures 10a – 10f).

**AFR:** In AFR, there is no ILI and SARI surveillance or information about such surveillance is unknown for almost half (44% for ILI and 53% for SARI) of the countries; in countries with ILI and SARI surveillance, more than half of these represent partial surveillance.
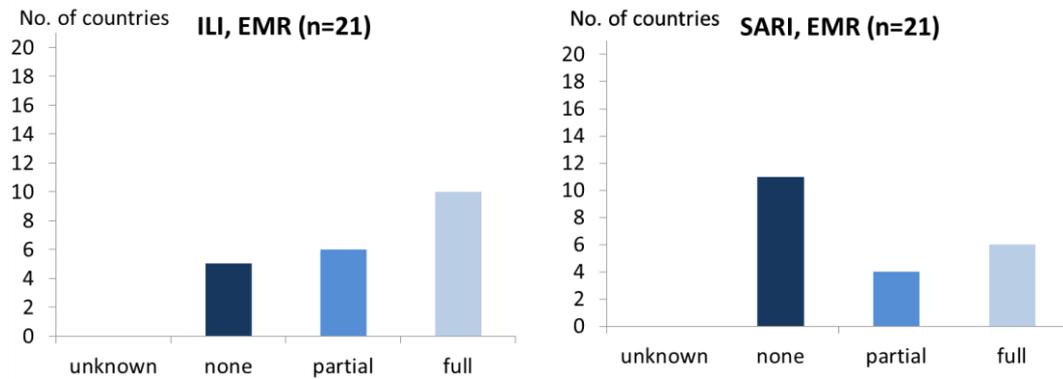
Figure 10a.
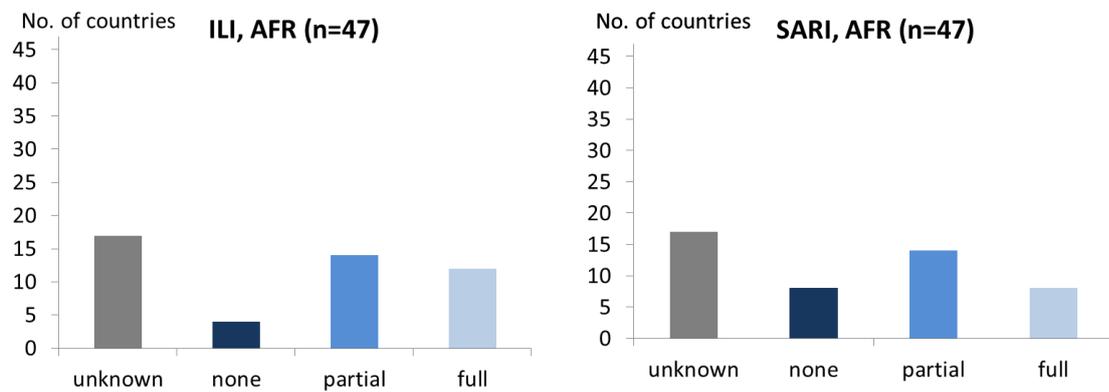
AMR: In AMR, 97% and 82% of countries have partial or full ILI and SARI surveillance capacity, respectively.

Figure 10b.

24
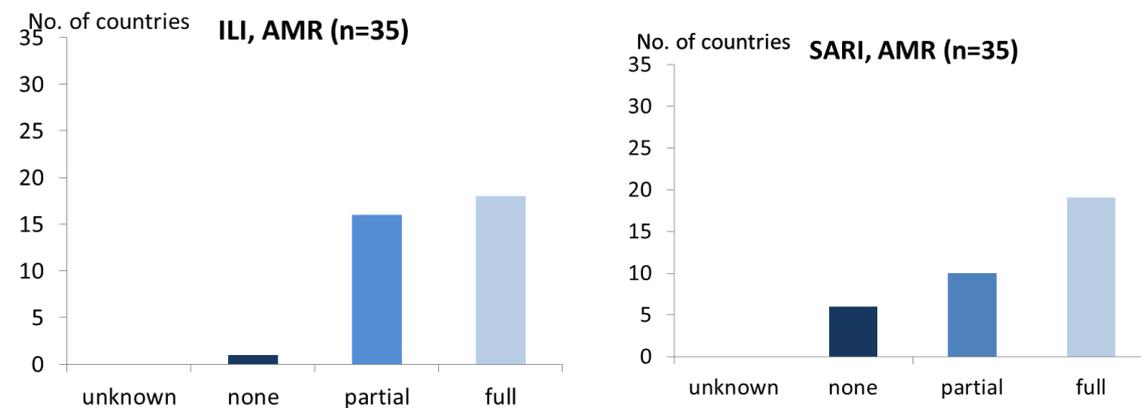
EMR: In EMR, 23% of countries have no ILI surveillance capacity and 52% have no SARI surveillance capacity.

Figure 10c.

EUR: In EUR, 92% of countries have partial or full   ILI surveillance in place while only 34% of countries have partial SARI surveillance in place.

Figure 10d.
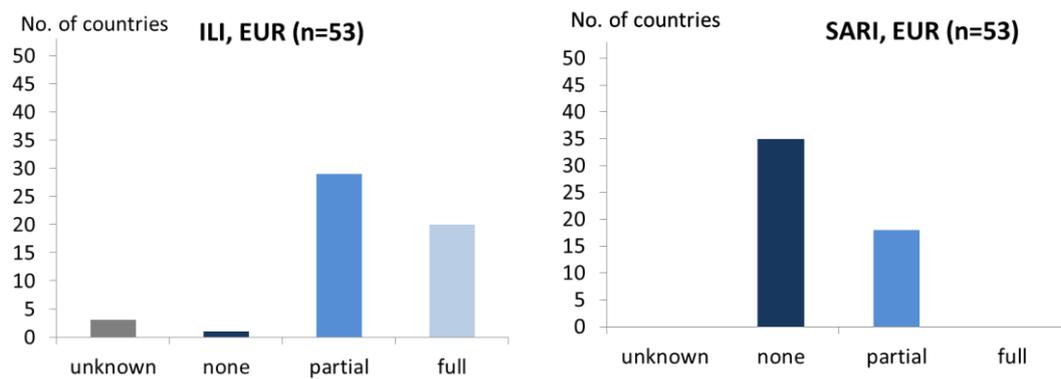
SEAR: In SEAR 100% of countries   have ILI surveillance capacity, but most (81%) countries have partial surveillance; similarly, 91% of countries have SARI surveillance capacity but most (72%) countries have partial surveillance.

Figure 10e.

25

WPR: In WPR 100% of countries have ILI surveillance capacity; only 7% of these are countries with partial surveillance; 44% of countries have SARI surveillance capacity, evenly split between partial and full surveillance.
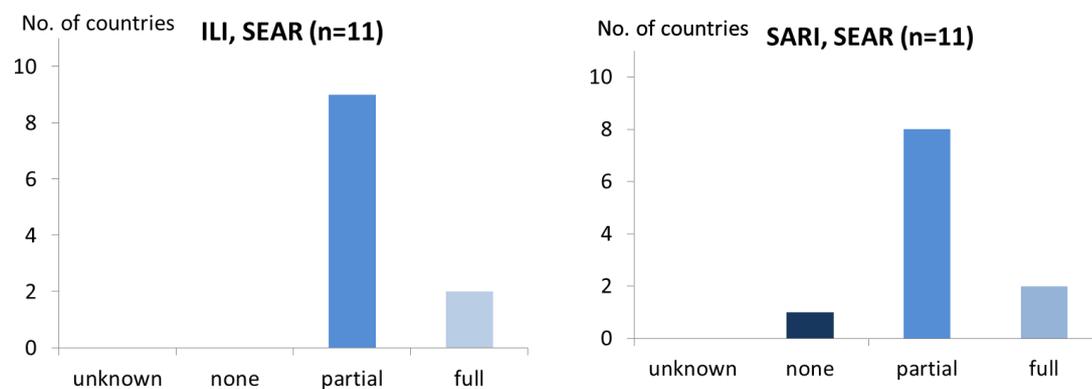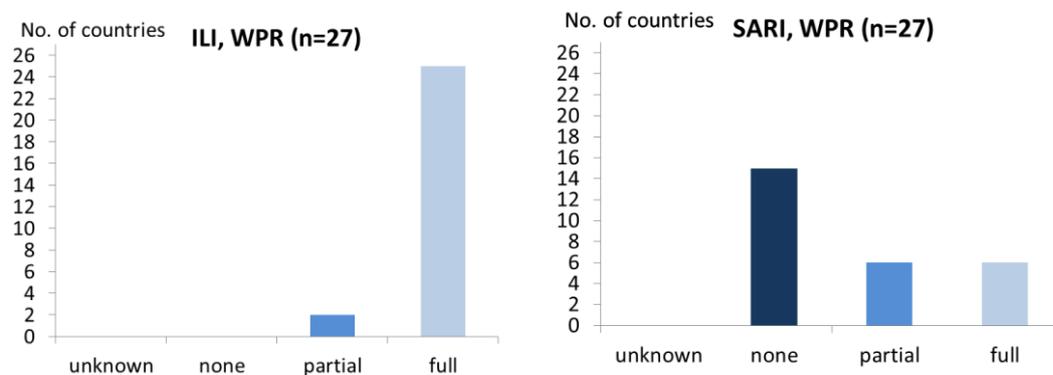
Figure 10f.

Summary of findings

- Monitoring capacity in the world is unevenly distributed with virological surveillance more systematically functioning than disease surveillance.
- Virological surveillance capacity is weakest in AFR: 40% of countries are able to detect all H5 viruses in EQAP, and 51% of countries do not have adequate PCR capacity in place.
- Diseases surveillance capacity is weakest also in AFR. In all 6 regions, ILI surveillance and to a lesser extent SARI surveillance capacity exists, but the majority of surveillance is partial.

3.3. Virus and information sharing capacity

3.3.1. Virus sharing

Most countries send representative specimens to WHO CCs for further characterization. Countries in AFR, however, are largely underrepresented in this process as many do not submit any samples at all (Figure 11). As stated above, this may be a function of: 1) virus activity; 2) capacity to collect and do PCR testing of specimens; 3) financial resources to ship to a CC or to access funds through the shipping fund project or some combination of all three.

Figure 11
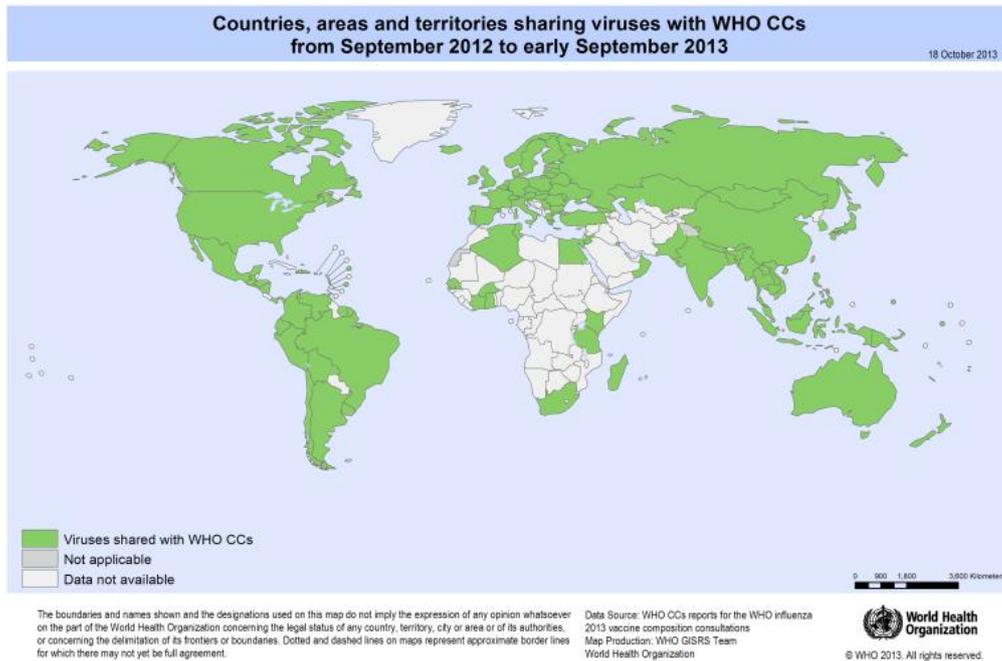
From September 2012 to September 2013, nearly half (49%) of all countries shared influenza viruses with WHO CCs. In AMR, EUR and WPR, 63%, 62% and 63% of countries respectively shared viruses, while only 23% of countries in AFR did so during this period. In fact, a majority of viruses submitted to the WHO CC for annual vaccine strain selections come from a small subset of countries. Most countries that submit viruses, submit a relatively small number, meaning that data derived from these viruses have limited representativeness.

Shipping specimens to centres where advanced characterization can be performed is very expensive; since 2007, 96 (49.5%) of all countries have relied on the global shipping fund project for support. Figure 12 illustrates influenza virus shipments from 2007 – 2013.

Figure 12

Countries, areas and territories that shipped clinical samples and/or viruses to WHO Collaborating Centres in the WHO Global Influenza Surveillance and Response System (GISRS) from 2007 to 2013
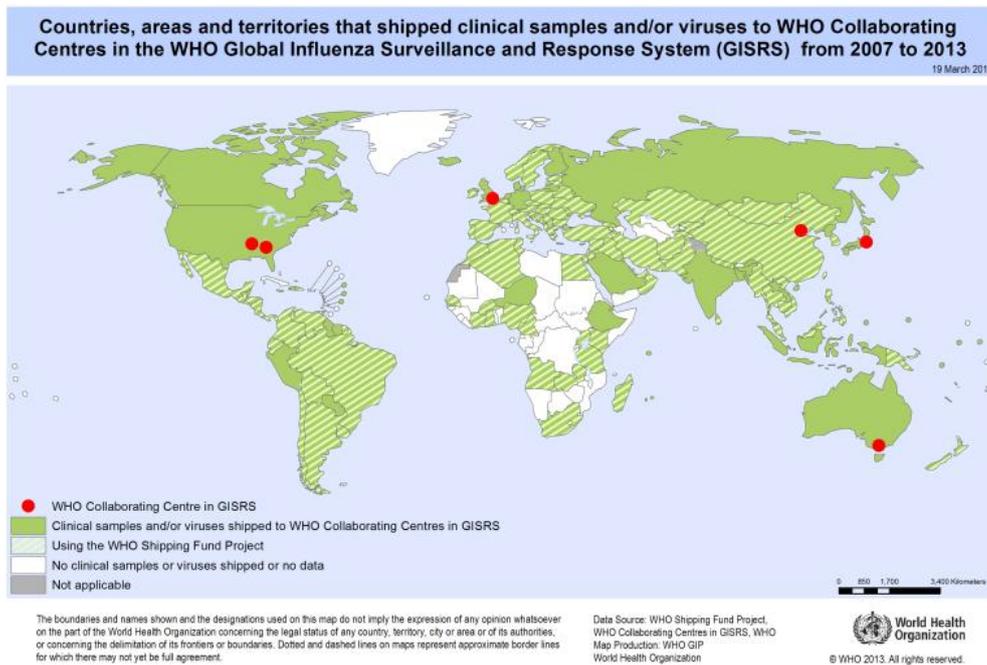
3.3.2. Sharing of virological and epidemiological information

FluNet

Since 2011, 124 countries (64% of all countries) regularly contributed to FluNet during their influenza season, although reporting was late and inconsistent at times. The highest coverage is from EUR (85% of its countries) and the least is from WPR (48% of its countries), where the majority of countries not reporting are small islands.

EZCollab

Currently, 100 countries have NICs or influenza reference laboratory staff registered in the GISRS EZCollab platform (Figure 13): 16 from AFR (34% of AFR countries), 14 from AMR (40% of AMR countries), 13 from EMR (62% of EMR countries), 38 from EUR (72% of EUR countries), 7 from SEAR (64% of SEAR countries) and 12 from WPR (44% of WPR countries).

Figure 13

Countries, areas and territories with National Influenza Centres (NICs) or other influenza reference laboratories staff registered to the GISRS EZcollab platform (as of 10 June 2013)
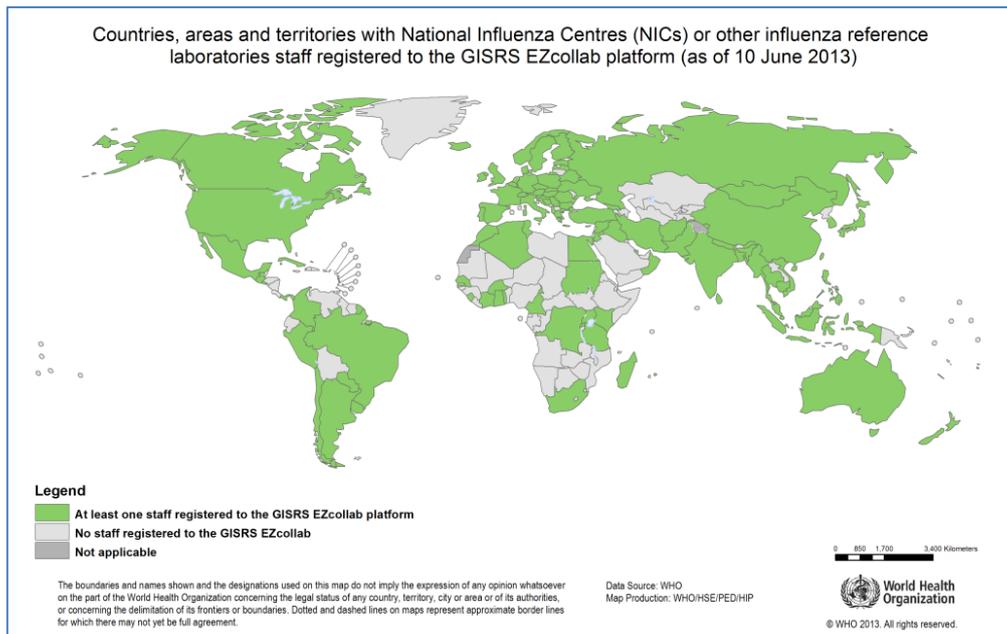
FluID

Since its implementation in 2010, 87 (52%) of all countries have reported data to FluID. The majority of participants are in EUR and AMR; there is limited participation in other regions (4 countries/territories in AFR; 3 in SEAR; and 3 in EMR. While all 87 countries or territories have contributed at least once, only 57 contributed in 2013. Currently no WPR countries report to FluID.

Figure 14

Countries, areas or territories with data available in FluID
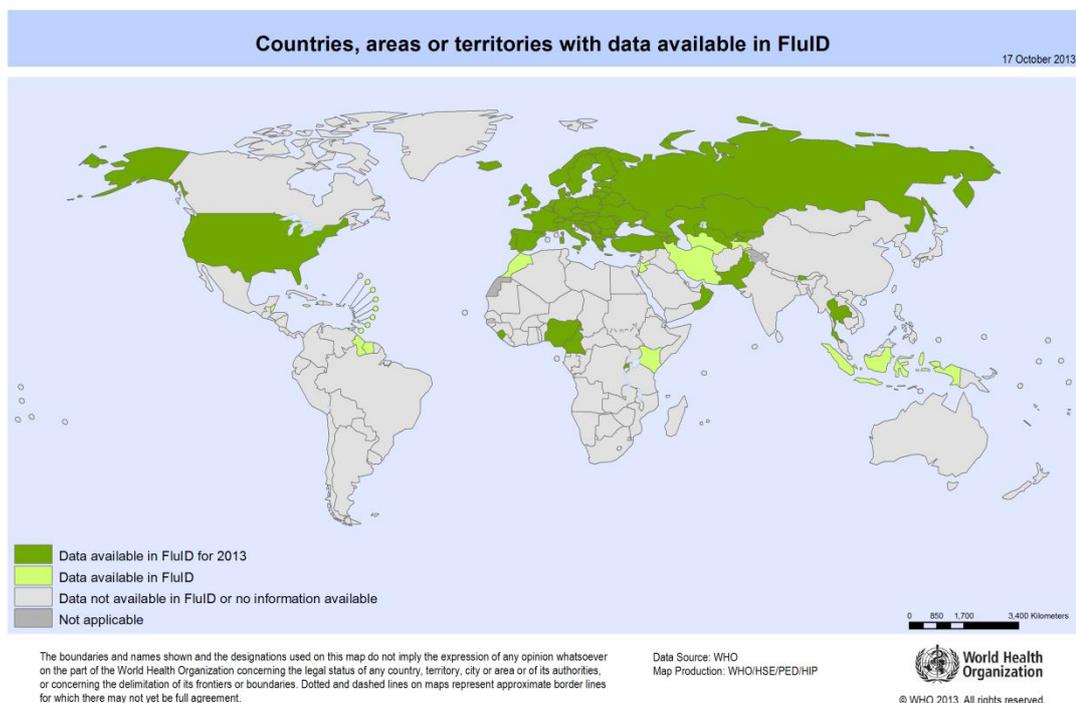
EUR has a regional network through which the NICs in the region report. The network is linked directly to the global FluNet and FluID databases. In AMR and AFR, surveillance data are collected from countries directly through weekly submissions to ROs. Data sharing in AMR is consistent, regular and includes nearly all countries that have surveillance systems.

<u>Summary of findings</u>

Sharing of viruses and information is the key output of national laboratory and surveillance capacity building under the PIP Framework.

- There are gaps in availability of both virological and disease surveillance information: globally 64% of countries report to FluNet and 52% report to FluID. Of the 111 countries that have a WHO recognized NIC, 104 (94%) share data through FluNet since 2011.
- Half (49.5%) of all countries have relied on the global shipping fund project to share influenza viruses with WHO CCs.
- Representativeness of virus sharing is suboptimal with the biggest gap in AFR.

4. CONCLUSIONS

The analyses have provided a snapshot of current global laboratory and surveillance capacity by WHO Region. Laboratory and surveillance capacities are sub-optimal in all WHO regions. AFR has the biggest gaps in nearly every aspect that was examined. The indicators used in this analysis are critical capacities that must be in place for effective detection of outbreaks, identifying emerging novel viruses of pandemic potential, monitoring the evolution of influenza viruses, establishing baseline of influenza activity, identifying risk groups and generating scientific evidence for policy making. The gaps in these critical capacities vary from country to country and from region to region.

Appropriate allocation of resources will need to include careful consideration of the specific needs of each Region and country. In addition, some countries with greatest need have limited capacity to absorb and effectively use resources. Actual country selection for receiving PC will therefore depend on multiple other considerations including absorption capacity, political will, and the presence of on-going conflict.

For further readings and references, see Annex 2.

CHAPTER 2

Burden of Disease

The burden of disease related to influenza remains unknown in most of the world. Most of the available burden information and vaccine cost effectiveness data derives from a few countries located in temperate climates, which likely are not representative of the majority of countries in the developing world.[14] This lack of data makes it difficult to prioritize influenza prevention and control measures against other competing health issues in countries where resources are most limited.

There are also a number of specific gaps in the understanding of the influenza disease burden and the factors that affect it. It is uncertain, for example, if climate might positively or negatively affect rates of severe illness. Other factors that might influence burden include:

- *Social structure*: School-aged children are thought to be the primary vectors for influenza transmission in any community but the largest burden of severe disease is in the elderly. It is unclear what impact a different social structure might have on burden, for example, in countries where extended families tend to live together versus countries where generations are more dispersed geographically.
- *Seasonality:* In most temperate countries of the world, winter tends to coincide with the school season and the two conditions likely work to amplify transmission. This is not the case in many tropical areas of the world and it is unclear if lower grade transmission might impact burden of severe disease.
- *Prevalence of chronic medical conditions:* Many chronic illnesses are associated with an increased risk for severe complications from influenza. However, the prevalence of these conditions, such as HIV, tuberculosis, diabetes, and atherosclerosis, varies markedly from region to region. The impact and interplay that these conditions have on burden are unknown.
- *Non seasonal influenza viruses:* Some influenza viruses circulating in animals can cross the species barrier to infect humans, with varying disease severity. The prevalence and distribution of these infections is essentially unknown on a global level, although it is likely that these infections contribute to influenza morbidity and mortality, on both a sporadic and continuous basis.

The lack of understanding the impact these factors have on disease burden has been largely due to a lack of adequate data with which to estimate disease burden. However, recent developments in surveillance capacity now provide an opportunity to expand our understanding of influenza disease burden into previously underrepresented areas of the world. Specifically, a description of disease burden is needed that will address gaps in understanding of mortality, morbidity, high risk groups and economic impact.

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[14] WHO. *Vaccines against influenza WHO position paper – November 2012.* WER No. 47, 2012, 87, 461–476

Mortality

National estimates of influenza mortality and/or severe influenza associated respiratory disease are available for a very limited number of wealthy countries. When global estimates or individual national estimates for less wealthy countries are produced, data from wealthy countries are used and extrapolated, resulting in estimates that are based on a large number of assumptions rather than data. A recent review of respiratory disease in children, for example, attempted to use existing data from developing countries to produce a global estimate of influenza-associated child mortality, and only found one study from a single surveillance project in India upon which to base global estimates.[16] Due to the limited number of national estimates especially from lower-resourced countries and the tropics, reliable global estimates of influenza mortality are limited and incomplete.

There are several obstacles to producing national mortality estimates including the lack of vital statistics data in many non-industrialized nations; the lack of technical capacity to apply the models that are typically used for mortality estimates, and the fact that the models have primarily been developed for countries where influenza and mortality both have a marked seasonal variation and have not been validated in tropical areas of the world where influenza transmission is often year-round. There is a need to develop new techniques for mortality estimation using available data.

Morbidity

Influenza morbidity, including hospitalization burden, is difficult to assess because of the lack of specific symptoms and the need to use sophisticated protocols including laboratory confirmation. However, once produced, these estimates have the advantage of being based on laboratory confirmed cases and reflect the impact and demand on health care resources more directly than mortality. A recent review attempted to estimate childhood morbidity associated with influenza using meta-analysis techniques that combined data from a number of different studies.[15] This study found that for children under the age of five, about 20 million cases of acute lower respiratory infection and 1 million cases of *severe* acute lower respiratory infection occur annually, placing it on the same level of magnitude as pneumococcus and *Hemphophilus influenza* associated disease. However, the authors noted that their estimates required a great deal of extrapolation and a number of assumptions due to the lack of data. No similar estimates exist for other high risk groups, such as pregnant women, who were identified in a WHO position paper as a primary target group, and the elderly.[15]

The challenges for estimating the hospital burden related to influenza are similar than for mortality but exacerbated by the fact that even countries with national vital statistics data do not generally have the same data for hospitalizations. However, because admission to hospital for influenza-related complications is much more common than death from influenza, it is feasible to derive hospitalization figures from surveillance data representing relatively small populations.

The recent increase in hospital-based surveillance activities around the world in the years leading up to the 2009 pandemic has resulted in a substantial body of hospital surveillance data that was not

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[15] Nair H, Brooks WA, Katz M, Roca A, Berkley JA, Madhi SA, et al. Global burden of respiratory infections due to seasonal influenza in young children: a systematic review and meta-analysis. Lancet 2011;378(9807):1917-30.

previously available. WHO has produced a manual with a detailed methodology[16] for developing population-based estimates of influenza-associated hospitalizations using hospital surveillance data.

Disease burden in high-risk groups

Several populations have long been recognized to be at increased risk for severe complications due to influenza; these same groups were observed to have an increased risk of hospitalization and death during the pandemic.[17] High-risk groups include persons at the extremes of age, both infants and the elderly; pregnant women, particularly in the 3rd trimester; and persons with pre-existing chronic medical conditions. Marked differences were seen between countries during the 2009 pandemic in the risk associated with some of these conditions, most notably with pregnancy. Determining if these differences are real and understanding what factors contribute to an increased risk for severe outcomes among pregnant women will facilitate the development of country-specific intervention strategies. The other risk group for which very few data are available is infants under the age of 2 years.

Economic Burden

In addition to the morbidity and mortality burden of seasonal influenza, costs to the economy, the health care system, and the individual are important factors influencing the adoption of intervention strategies. Two types of costs can be described as economic burden; direct medical costs, which are related directly to care of the patient, and indirect costs related to missed work and lost productivity. The relative impact of each of these costs on the individual varies depending on the social support structure of their country. In countries with strong social security systems, most of the healthcare costs are directly financed by a third party payer (national insurance, occupation based social security schemes); the direct impact on individual households may be minimal because the burden is shared. In countries that do not have such support mechanisms, the burden of a disease can be significant for households.

Indirect costs: For industrialized countries, indirect costs related to work absenteeism rather than direct medical costs account for the largest share of total influenza economic impact representing 60 to 90% of total burden.[18,19,20,21,22,23,24,25,26,] Indeed, influenza is one of the leading causes of absence

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[16] Final document in clearance.

[17] Van Kerkhove MD, et al., Risk factors for severe outcomes following 2009 influenza A (H1N1) infection: a global pooled analysis. PLoS medicine, 2011. 8(7): p. e1001053.

[18] Molinari N-A M, et al.. The annual impact of seasonal influenza in the US: measuring disease burden and costs. Vaccine 25 (2007) 5086–5096.

[19] Kressin, BKW, et al. Influenza: Ökonomische Bedeutung der Schutzimpfung. Deutsches Ärzteblatt (1999): Archiv 96(6);pp A342-3 Available at: http://www.aerzteblatt.de/v4/archiv/artikel.asp?id=15507.

[20] Newall, AT, et al.. Influenza-related disease: the cost to the Australian healthcare system. Vaccine (2008) Dec. 9;26(52);6818-23.

[21] Simmerman JM, et al., The cost of influenza in Thailand. Vaccine (2006) 24(20): 4417-4426.

[22] Cohen JM, et al. Ecogrippe 2006 : combien coûte la grippe. Presented at: XII ème Journée Nationale des GROG - Paris, le 15 novembre 2007. Available at: http://www.grog.org/documents/jour_2007/Ecogrippe.pdf.

[23] Cohen JM, La surveillance de la grippe en France. MEDECINE/SCIENCES 2003 ; 19 : 239-42. Available at : http://www.erudit.org/revue/ms/2003/v19/n2/000694ar.pdf

from work in these countries, representing 10 to 20% of the yearly total, with a large share linked to missed work related to the care of sick children by working parents.[27,28,29] Because influenza infects all age groups, working adults will also miss work due to their own illness and to care for a sick child. As a result, indirect costs for influenza are higher compared to other respiratory pathogens that primarily infect only children, such as Respiratory Syncytial Virus (RSV); indirect costs were found to be €223 per case for influenza vs. €163 for RSV[30] and AU$904 for influenza vs. AU$304 for RSV[31] by investigators in Germany and Australia, respectively. During the winter 2005/2006 epidemic season in France, 70% of working adults took 5 days off from work for their own treatment and a quarter of households with a child took 3 days off; both cost the sickness-leave fund at least the same amount as direct costs over that season (US$180 million).[22,23] In Germany, over a third of absenteeism in the winter season is influenza- related, making influenza the leading cause of sickness absence episodes during that time of the year. Sickness leave absences for influenza tend to be relatively short, with a typical episode lasting 4-6 days, however, case volume results in a large impact, particularly during the epidemic season.

Direct Health Care related costs: Influenza and influenza-related diseases represent between 0.1 and 0.5 % of total healthcare expenditure, costing US$4 - 35 per inhabitant yearly.[18,19,20,21,23,24,25,26] The primary driver of influenza-related costs to an industrialized nation's health care systems is hospitalizations, costing over half the total and accounting for 0.1% to 1% of total hospital expenditures. Although treatment in the outpatient setting costs far less than hospital treatment for individual cases, total medical outpatient setting costs remain high because of the large number of cases. Influenza and ILI visits represent between 1 and 4% of total outpatient visits, costing between 0.1 and 0.5 % of total outpatient expenditures. Influenza is the most costly cause of ARIs amongst other viruses in the outpatient setting, costing more than double per case on average.[32] Medication represents 1/3 of total influenza medical expenditure, whether delivered in the hospital or the outpatient setting.

[24] Levy E. French economic evaluations of influenza and influenza vaccination. PharmacoEconomics 9 Suppl 3 (1996): 62-66.

[25] Belousov YB, et al. [Economic analysis of Influenza in Children and Adolescents]. Russian Medical Journal. Available at: http://www.rmj.ru/articles_5534.htm.

[26] Lucioni C, et al. I costi dell'influenza in Italia. Farmeconomia e percorsi terapeutici 2001,2:11-8.

[27] O', Reilly F.W., et al.. Sickness absence due to influenza. Occupational Medicine 52 (August 2002): 265-269.

[28] Pedersen C. [Convalescence and sick leave after influenza]. Ugeskrift for Laeger 171, no. 40 (Septembre 28, 2009): 2913-2915.

[29] Keech M, et al.. The impact of influenza on working days lost: a review of the literature. PharmacoEconomics 26, no. 11 (2008): 911-924.

[30] Ehlken B, et al.. Economic impact of community-acquired and nosocomial lower respiratory tract infections in young children in Germany. Euro J of Pediatrics 164, no. 10 (October 2005): 607-615.

[31] Lambert SB et al. The cost of community-managed viral respiratory illnesses in a cohort of healthy preschool-aged children. Respiratory Research 9 (2008): 11.

[32] Lambert SB, et al., "The cost of seasonal respiratory illnesses in Australian children: the dominance of patient and family costs and implications for vaccine use," Communicable Diseases Intelligence 28, no. 4 (2004): 510-516.

Gaps in knowledge: As with other measures of influenza disease burden, most economic impact data comes from industrialized countries. The available data do not give a clear indication of the impact felt by developing countries, either to the individual or society as a whole. As third party health care coverage is much less common in developing nations, much more of the cost for medical care due to influenza-related illness is likely borne directly by the patient. In addition, the indirect costs to developed economies are not directly applicable to economies that are largely informal.

Vaccine supply and demand

Globally, seasonal influenza vaccine usage is largely associated with economic development and wealth. Although, many countries of the world have vaccination programmes for seasonal influenza vaccine, currently 75-80% of the global influenza vaccine supply is used by in the Americas and Western Europe.[33]

Preparation for the next pandemic will require increased global vaccine production capacity much in excess of what is currently available. The stated goal of the WHO Global Action Plan for influenza vaccines is "By 2015, produce enough vaccine to immunize two billion people", well more than double the current global production capacity. Strategies have been developed for increasing global production capacity. However, the success of these plans will largely depend on increasing global demand for vaccine, particularly in areas of the world where vaccine is currently not widely used. Adoption of seasonal vaccine in these areas will also likely have significant impact on the numbers of respiratory deaths, particularly in the most vulnerable of populations. The adoption of vaccine by these countries will require disease burden data which helps national policy makers to rationalize the use of limited resources by allowing meaningful comparisons of burden related to influenza with other health priorities. This goal has also been clearly articulated in the WHO Global Action which includes as a primary objective the development of tools for estimating influenza impact and the cost effectiveness of vaccination.

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[33] Palache A. *Seasonal influenza vaccine provision in 157 countries (2004–2009) and the potential influence of national public health policies.* Vaccine 29 (2011) 9459– 9466

CHAPTER 3

Regulatory Capacity

Since the 1990's, the WHO programme on regulatory systems strengthening (RSS) has implemented a capacity building model with the goal of aiding countries meet and sustain regulatory functionality for medicines and other health products as per established WHO indicators[34]. A guiding principle is that to sustainably strengthen regulatory capacity, simultaneous attention must be given to the oversight of specific health products. Additionally, proper establishment of national regulatory systems enables countries to respond better to public health emergencies.

Experts at the '*Workshop on international regulatory capacity enhancement for influenza vaccines'*, 8-10 June 2011, São Paulo, Brazil,[35] indicated that robust regulatory capacity is unquestionably essential to achieve the WHO global health agenda, the millennium development goals (MDG), the Decade of Vaccines goals and a number of vaccine-specific initiatives. Regulators and policymakers from across the world met to discuss ways to build regulatory capacity in developing countries. The workshop served as a catalyst to initiate and strengthen partnerships and coordination between governments, Ministries of Health, National Regulatory Authorities (NRAs), regulatory networks, and international organizations.

Challenges faced and lessons learnt by technical partners, National Regulatory Authorities (NRA), and policy makers in enhancing regulatory capacity for pandemic influenza response were documented. Capacity for drug regulation including vaccines, available expertise, and resources vary amongst NRAs in developing countries. No single regulatory model can fit all countries or be directly integrated into a NRA due to different political, legal, public health, techno-scientific, and socio-cultural-economic contexts. Progress in regulatory capacity building requires mutual understanding and appreciation for each stakeholder's roles and responsibilities; political and resource commitments to coordinate efforts, as well as maintain effective lines of communication between all stakeholders, are also necessary.

In order to address regulatory gaps for influenza vaccines, the experts advised that:

- A percentage of the grants countries receive to build manufacturing capacity should be allocated for National Regulatory Authority (NRA) capacity building[36];

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[34] Vaccine regulation, http://www.who.int/immunization_standards/vaccine_regulation/nra_rp_info/en/index.html, accessed 24 October 2013.

[35] Workshop on International Regulatory Capacity Enhancement for Influenza Vaccines (WIRCEIV) http://www.who.int/influenza_vaccines_plan/objectives/workshop_WIRCEIV_8_10_June_2011/en/index.html

[36] Funding grants for regulatory capacity building should be similar to grants provided to manufacturers through the WHO technology transfer initiative. This measure would ensure balanced capacity building for both manufacturing and regulation.

- Support should be provided to strengthen regional regulatory partnerships, approaches, and networks, and particularly models that address the specific regulatory needs of developing countries;
- Enhancing pharmaco-vigilance and monitoring of adverse events following immunization in countries with and without influenza vaccine manufacturing capacity should be undertaken;
- Support should be provided to strengthen the evaluation of clinical trial data for regulatory registration; and,
- Support should be provided to implement WHO regulatory capacity building initiatives and recommendations, including the Regulatory Systems Strengthening (RSS) Programme, the medicines and health products prequalification programme, the NRA Strategic Forum of Regulatory Agencies for Vaccines, the Global Learning Opportunities for Vaccine Quality, and the Global Action Plan (GAP) for Influenza Vaccines.

These recommendations informed the review and refinement of the second WHO consultation on the GAP for Influenza Vaccines (GAP II) in July 2011.

The '*Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine deployment initiative*'[37] were discussed at a WHO consultation of more than 50 representatives from donor and recipient governments, international organizations and vaccine manufacturers on 13-15 December 2010 in Geneva. Experiences and challenges with crucial aspects of the process to deploy 78 million doses of pandemic H1N1 vaccine[38] to 77 of the poorest countries in the world were shared and recommendations on improving the process were formulated.

Review of the deployment process showed that national regulatory requirements constituted a significant limiting factor in the optimal deployment of pandemic vaccines. Although it was recognized that countries have unique regulatory requirements, it was suggested that a harmonized approach to importing, distributing and registering vaccines during pandemic events could ease deployment. Seeking early engagement with, and approval by, NRAs would ease the process of legally releasing imported vaccines or other medicines for prompt shipment. For the most part, WHO prequalification of influenza vaccines aided in reducing or eliminating country-specific regulatory delays in many countries. Having established legal agreements between donors and beneficiary countries ahead of a pandemic would have significantly reduced deployment time as well. Finally, it was recognized that keeping national deployment plans (NDP) up to date would reduce time for country planning.

Donor commitments in support of the 2009 H1N1 pandemic-related WHO Deployment Initiative were generous; a broad range of vaccine source, presentation and availability times were available to WHO. The first WHO prequalified vaccine was released in December 2009 for deployment to countries that satisfied three major prerequisites:

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[37] Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine deployment initiative, Meeting report, http://whqlibdoc.who.int/publications/2012/9789241564342_eng.pdf, accessed 18 June 2013.
[38] Securing donor commitments, prequalifying vaccines, helping countries to satisfy the prerequisites for supply and managing global deployment.

- A Letter of Intent (LOI) from the government to WHO officially expressing the Member State's wish to obtain vaccine donation;
- A Letter of Agreement (LOA) between the Member State and WHO encompassing legal agreement on multifaceted issues requiring government clearance i.e. national regulatory registration, a waiver of liability for donated vaccine; and,
- National deployment plan (NDP) developed and in place.

The LOI was the easiest prerequisite to satisfy while the LOA and NDP were more challenging.

In January 2010, vaccine deliveries started; the number of monthly doses requested and supplied gradually declined by the time a second pandemic peak appeared in August 2010. The targeted priority groups for immunization included pregnant women, health-care workers, children and people with underlying conditions; in some countries, 100% of persons in these groups were covered by vaccination campaigns.

Participants at the WHO consultation[39] underscored that similar future health emergencies will occur and cooperation among international partners is essential for preparedness and response efforts.

Review of the pandemic influence deployment process found that national regulatory requirements had a significant impact. Each country has unique regulatory requirements and a harmonized approach to importing, distributing and registering vaccines during pandemic events is highly desirable. Seeking early engagement with and approval by NRAs would ease the process of legally releasing imported vaccines and medicines for prompt shipment. WHO prequalification of influenza vaccines aided in reducing or eliminating country-specific regulatory delays in many, but not all, countries; the establishment of legal agreements between donors and beneficiary countries in advance of the pandemic would have significantly reduced deployment time. Maintaining an up-to-date NDP would also be expected to reduce time for country planning.

For influenza antivirals, the medicines and other health technologies prequalification programme has developed a collaborative procedure to fast track the national registration of prequalified medicines. Early engagement of Member States in this procedure would achieve rapid registration of key antivirals, such as oseltamivir and zanamivir during pandemics. The presence of an internationally accepted pharmacopeial standard for a medicinal product also facilitates the entry of additional manufacturers into the supply chain, which increases availability and reduces cost of the medicine. Currently, the WHO Essential Medicines Safety and Vigilance has published a monograph for oseltamivir active pharmaceutical ingredient (API) . The development and publication of monographs for zanamivir API and finished pharmaceutical product (FPP) as well as oseltamivir FPP would also aid in rapid registration of these antivirals.

Regulation of influenza diagnostics is very limited worldwide and the prequalification requirements of priority kits and solicit applications from manufacturers for the prequalification of influenza diagnostics products must be defined by the prequalification programme of the WHO medicines and other health technologies. There is a need for strengthening regulation of influenza diagnostics

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[39] Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine deployment initiative, Meeting report, http://whqlibdoc.who.int/publications/2012/9789241564342_eng.pdf, accessed 18 June 2013.

including laboratory capacity and outbreak/pandemic response via institutional development plans (IDPs) in priority countries with follow up on agreed training, guidance and technical support. It would be expected that NRAs in priority countries would develop capacity to assess WHO prequalified influenza diagnostics.

In short, the evidence, experience and consensus of international experts from countries indicate that national regulatory preparedness for influenza products including vaccines, antivirals and diagnostics in response to a pandemic should be a priority area for investment of PIP contributions. The recommendations of the PIP Advisory Group are fully consistent with the findings and priorities identified through the international consultations mentioned.

In addition to the expert consultations described above, WHO conducted a gap analysis to determine the priority countries to be targeted for technical support and training for regulators under the PIP Framework.

A cumulative scoring system and selection criteria were developed to rank countries. Country information was obtained from publically available as well as WHO RSS databases. In addition to the selection criteria recommended by the AG, countries were scored, ranked and selected according to the following criteria:

- Population[40] and economic development status[41];
- On-going regulatory capacity building efforts in vaccines, antivirals and/or diagnostics [42].
- Existing National Regulatory Authority (NRA) Institutional Development Plans (IDP) in the databases of the WHO Regulatory Systems Strengthening (RSS) Programme;[43];
- Interest to donors i.e. Global Alliance for Vaccine and Immunization (GAVI) graduating[44] and eligible countries[45];
- Countries without licensed pre-qualified vaccines, with local production not existing[46],; and with production capacity not existing[47];
- Countries with existing national control laboratories[48];
- Countries with newly introduced or with the plan to introduce new vaccines (as of 2012)[49];

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[40] United Nations Statistic Division, Social indicators, http://unstats.un.org/unsd/demographic/products/socind/population.htm, accessed 25 June 2013
[41] The World Bank list of economies, http://data.worldbank.org/about/country-classifications/country-and-lending-groups#Low_income, accessed 24 June 2013
[42] As per documented consultations within WHO HQ and Regional Offices
[43] WHO regulatory systems strengthening databases, https://workspace.who.int/sites/nra_database/Update/IDP_Analysis.xlsx, accessed 15 July 2013
[44] http://www.gavialliance.org/support/apply/graduating-countries/, plus India and China, accessed 25 June 2013
[45] http://www.gavialliance.org/support/apply/countries-eligible-for-support/; accessed 25 June 2013
[46] http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html, accessed 25 June 2013
[47] WHO NRA systems strengthening databases, https://workspace.who.int/sites/nra_database/Update/nra%20functions%20statts2011_revised%20by%20Ali_ver2.xls, accessed 15 July 2013
[48] WHO NRA system strengthening databases, https://workspace.who.int/sites/att/NRAs%20contacts/Forms/AllItems.aspx, accessed 15 July 2013

- Regulatory history during the 2009 H1N1 pandemic-related WHO Deployment Initiative[50]; and,
- Countries in the GAP for Influenza Vaccines[51].

Countries (N=194) were sorted from highest to lowest as per cumulative score. With 50% of the countries (n=97) chosen as the cut-off point, the percentage distribution of countries amongst WHO Regions was determined (Table 1). The results indicated AFR to be the region with largest proportion of countries (39%) scoring high followed by EMR (15%), EUR (12%); WPR (11%), EMR (11%) and SEAR (10%) for priority intervention.

In order to keep geographical balance, focusing on regions where regulatory capacities are weakest, countries with highest scores can be recommended for capacity building under the PIP Framework.

WHO Region	No. of countries with highest score at 50% cut off point	% of countries with highest score at 50% cut off point	No. of highest scoring countries for PIP implementation
AMR	11	11%	2
AFR	38	39%	6
EUR	12	13%	2
EMR	15	16%	2
SEAR	10	10%	2
WPR	11	11%	2
No. of countries at 50% cut off point	97	100%	15

[49] WHO NRA systems strengthening databases,
https://workspace.who.int/sites/nra_database/useful_documents/Strengthening%20NRAs/Country-Vaccines.xlsx. accessed 15 July 2013
[50] Main operational lessons learnt from the WHO pandemic influenza A(H1N1) vaccine deployment initiative, Meeting report, http://whqlibdoc.who.int/publications/2012/9789241564342_eng.pdf, accessed 18 June 2013
[51] http://www.who.int/influenza_vaccines_plan/objectives/projects/en/index.html, accessed 25 June 2013

CHAPTER 4

Risk Communications

Effective risk communications is a critical and complex part of the management of any public health emergency, especially one as widespread and complex as a pandemic. The explosion of real-time information sources, especially social media, has created enormous demands for effective, coherent and credible communications during emergencies.

Preparation for communicating during pandemics – communicating risk to health, communicating about actions the public can take to protect their and their families' health (including to support the uptake of vaccines), and dealing with rumours and perceptions – requires developing or strengthening capacities and maintaining those capacities during the relatively long periods between pandemics. A pandemic is a public health event of international concern (PHEIC) and is detected, defined and responded to under the International Health Regulations (2005). Therefore the IHR form the basis for pandemic communications and risk communications. As all States Parties are obliged to develop capacities under the IHR, there is an opportunity to engage with them in strengthening or building specific pandemic communications capacities.

Using the nine requirements of national risk communications capacities strengthening as defined by the *IHR Monitoring Framework: Checklist and Indicators for monitoring progress on the implementation of the IHR Core capacities in States Parties, WHO, 2011*[52]*,* is an efficient and effective way to strengthen and monitor risk communications capacities for a pandemic response. While this monitoring document is not legally binding, it represents a consensus of technical expert views drawn globally from WHO Member States, technical institutions, partners, and from within WHO. It forms part of the regular monitoring process for IHR capacities and is thereby a good measure of capacity building progress made in countries.

Many countries, however, are still lacking in this essential capacity. In the 2012 report by the Director-General on the Implementation of the International Health Regulations (IHR), countries reported the on their capacities in risk communications. According to the latest data obtained from the reporting database in September 2013, 139 Member States provided self-assessments on their risk communications capacities. Analysis of the data reveals that:

- 55 Member States did not report on their risk communications capacity;
- 56 reported less than 60% of required risk communications capacity;
- 41 others reported less than 50% of the required risk communications capacity.

This means that 28% did not report on their risk communications capacities. Of those who reported, 29% reported less than 50% of required capacity.

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[52] See Annex 3.

Risk communications capacity building related to pandemic preparedness is aimed at ensuring that countries have policies, procedures, skills and other core elements in place for communicating to national and international audiences during public health emergencies of international concern. The work outlined in this plan will carry out activities to (a) support *all* countries, and (b) provide intense support for at least 30 priority countries to ensure that the baseline communication needs are met during an influenza pandemic or other public health crisis and can be sustained beyond the three-year scope of this project.

The implementation plan for risk communications capacity building is anchored in the recommendations in the 2012 report by the Director-General on the Implementation of the IHR and in the review of the Organization's response to the 2009 H1N1 Influenza pandemic. It builds upon extensive work already carried out by the WHO Secretariat, including its newly established Emergency Communications Network (ECN). The ECN is a pre-selected, pre-trained and assessed group of communications experts from within and outside WHO who are ready to be deployed to countries to provide support in the area of risk, pandemic and crisis communications. The plan will also strengthen collaboration with partner institutions already working to strengthen global communications capacity, including the US Centers for Disease Control and Prevention (CDC), the Public Health Agency of Canada, Public Health England, and the European Centre for Disease Control (ECDC).


Analysis of existing data

Of the 194 WHO Member States, 136 reported on the progress in implementation of the risk communications capacities required under the International Health Regulations(IHR 2005), in 2012. This report is based on Member States' self-assessment of their risk communications capacity in preparation for, and to respond to a public health emergencies.

The nine areas of work that need to be met and maintained to establish and maintain risk communications capacity to deal with public health emergencies including pandemics, include:

1. identification of risk communications partners and stakeholders ;
2. development of risk communications plan ;
3. Implementation and test of the risk communications plan through an actual emergency or a simulation exercise, and updated in the last 12 months;
4. development of policies, standard operating procedures (SOPs) or guidelines on the clearance and release of information during a public health emergency);
5. accessibility of regularly updated information sources provided to the media and the public for information dissemination;
6. accessibility of relevant information, education and communication (IEC) materials tailored to the needs of the population;
7. provision of information on at least three recent real or potential risk of a national or international public health emergency to the population and partners within 24 hours of confirmation;
8. conduct an evaluation of the public health communication after emergencies, for timeliness, transparency and appropriateness of communications; and
9. share results of the evaluations of risk communications efforts during public health emergencies with the global community.

The act of self-reporting is an important one as this confers ownership of the capacity building on the countries and thereby increases the relevance and the sustainability of the capacity.

Figure 1: Overview of risk communications capacities: self-reporting by Member States , 2012
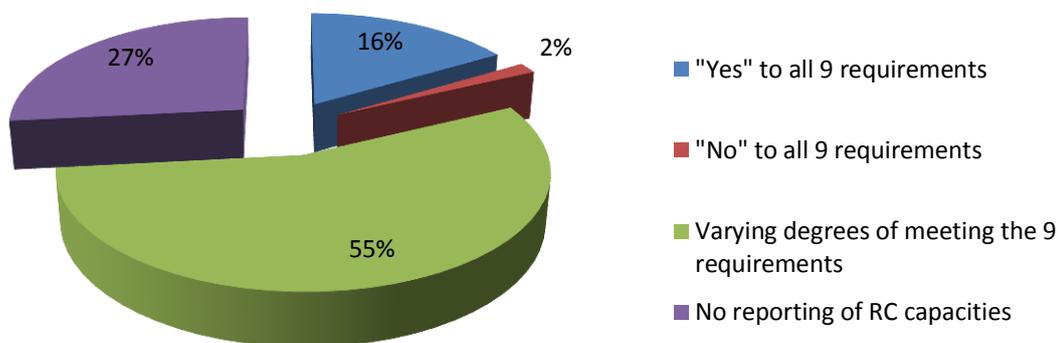
As shown in Figure 1, in 2012, only 16% of the 139 Member States reporting on their risk communications capacity felt they had met all 9 requirements. More than half reported that they were still short of meeting the full set of requirements. There were 55% that feel that they are (to varying degrees) not yet able to deal with all pre-defined aspects. Another 2% even state to be unable to meet any of the above requirements. The fact that 55 Member States did not report on their risk communications capacities point to one of two possibilities:

a) The Member State did not wish to report on this capacity for reasons unknown to the Secretariat, or
b) The Member State did not have the basic ability and/or information to provide information to the Secretariat.

The following additional factors were considered in order to prioritize countries for intense support:

Primary factors
- Countries with low capacity or for which there was no information on capacity for IHR implementation;
- Commitment and requests from Ministries of Health;
- Countries at significant risk of disease outbreaks and other public health emergencies;
- Countries where other IHR capacity building work is already being carried out, with the aim of building synergies, cost-effectiveness, and/or achieving stronger results.

Secondary factors
- Assessment of the country's ability to sustain capacities;
- Regional representation;
- Ability to build in-country collaboration – bringing partners together;
- Countries with unstable public health/political/social infrastructure, but which are able to absorb risk communications support;
- Countries with varying levels of capacity required under the IHR (e.g. surveillance, laboratory, points of entry, etc.);
- Countries with a recent event of poor transparency.

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Annexes

ANNEX 1

Description and scoring of factors for laboratory and surveillance

Factor	**IHR Indicator 3.2.1 - Event-based surveillance is established and functioning**
Definition	Implementation status of IHR Indicator 3.2.1 "Event-Based Surveillance is established and functioning under "Core Capacity 3 Surveillance, Component 3.2 Event-Based Surveillance".
	<u>As per 2012 questionnaire, 15 questions support Indicator 3.2.1:</u>
01: Has unit(s) responsible for event-based surveillance been identified?
02: Are country SOPs and/or guidelines for event based surveillance available?
03: Have SOPs and guidelines for event capture, reporting, confirmation, verification, assessment and notification been implemented, reviewed and updated as needed?
04: Have information sources for public health events and risks been identified?
05: Is there a system or mechanism in place at national and/or sub-national levels for capturing and registering public health events from a variety of sources?
06: Is there active engagement and sensitization of community leaders, networks, health volunteers, and other community members to the detection and reporting of unusual health events?
07: Has the community/primary response level reporting been evaluated and updated as needed?
08: Are country experiences and findings on implementation of event-based surveillance, and the integration with indicator based surveillance, documented and shared with the global community?
09: Are there arrangements with neighbouring countries to share data on surveillance and the control of public health events that may be of international concern?
10: Is the decision instrument in Annex 2 of the IHR used to notify WHO?
11: Have all of events that meet the criteria for notification under Annex 2 of IHR been notified by the IHR NFP to WHO within 24 hours of conducting risk assessments over the last 12 months?
12: Have all events identified as urgent within the last 12 months been assessed within 48 hours of reporting?
13: Has the IHR NFP responded to all verification requests from WHO within 24 hours in the last 12 months?
14: Has the use of the decision instrument been reviewed and procedures for decision making updated on the basis of lessons learnt?
15: Are country experiences and findings in notification and use of Annex 2 of the IHR documented and shared globally?
Source	IHR core capacity monitoring framework: questionnaire for monitoring progress in the implementation of IHR core capacities in State Parties. 2010-2013 data (use of latest available data).

WHO International Health Regulations. Data accessed in October 2013.
Link: http://www.who.int/ihr/en/ |
| Scoring | 0-49% implementation progress= 0 point
50-89% implementation progress = 2 points
90-99% implementation progress = 4 points
100% implementation progress = 6 points |

Factor	**WHO-recognized National Influenza Centre**
Definition	WHO-recognized NIC in country.
	NICs collect virus specimens in their country and perform preliminary analysis. They ship representative clinical specimens and isolated viruses to WHO Collaborating Centres (CCs) for advanced antigenic and genetic analysis. The results form the basis for WHO recommendations on the composition of influenza vaccine each year, as well as relevant risk assessment activities of WHO. NICs are national institutions designated by Ministries of Health and recognized by WHO. They form the backbone of the WHO's Global Influenza Surveillance and Response System (GISRS).
Source	WHO/PED/GIP, GISRS and laboratory, October 2013. Link: http://www.who.int/influenza/gisrs_laboratory/national_influenza_centres/en/
Scoring	No NIC = 0 point NIC = 2 points

Factor	**Adequate (80%) PCR Capacity**
Definition	Country that has a NIC/other influenza laboratory that has achieved 80% accuracy in RT-PCR detection of influenza viruses under WHO EQAP in the past 2 years (panels 11-12).
	The WHO External Quality Assessment Project (EQAP) was established in 2007 to monitor the quality of GISRS and other national influenza reference laboratories that perform PCR diagnosis and to identify gaps in PCR testing in these laboratories. Influenza viruses are constantly evolving and timely adjustments in PCR testing is required to maintain robust laboratory diagnostic capacity. By monitoring quality and standards of performance, the EQAP plays a key role in strengthening the GISRS diagnostic capacity and preparedness to effectively respond to influenza outbreaks world-wide. The overall goal of this project is to improve the global laboratory capacity for influenza diagnosis by the detection of influenza virus type A by PCR and the promotion of good laboratory practices. In 2010 the programme was extended to include detection of influenza B viruses. The EQAP is open to all NICs with PCR capacity and candidate NICs that are willing to participate.
Source	WHO/PED/GIP, GISRS and laboratory, external quality assessment project, October 2013. Link: http://www.who.int/influenza/gisrs_laboratory/external_quality_assessment_project/en/
Scoring	Non adequate PCR capacity / not participating in EQAP = 0 point 80% PCR capacity = 2 points

Factor	**Shipping capacity**
Definition	Capacity for shipping specimens/viruses in accordance with international standards and regulations is met if one of the following four indicators is met: • Country uses the WHO Shipping Fund Project for shipping influenza viruses to GISRS WHO CCs and H5 Reference Laboratories (since 2005) • Country has laboratory staff that have received WHO training on shipping of infectious substances (since 2007) • Country has laboratory staff that have received WHO training and have a currently valid certificate for shipping of infectious substances (a valid certificate requires mandatory training every 24 months) • Country has a NIC/other influenza laboratory that shares influenza viruses globally with GISRS WHO CCs and H5 Reference Laboratories (since 2007).
Source	WHO/PED/GIP, GISRS and laboratory, logistics activities, October 2013. Link: http://www.who.int/influenza/gisrs_laboratory/logistic_activities/en/
Scoring	No shipping capacity = 0 point Shipping capacity = 2 points

Factor	**Influenza-like illness or respiratory disease surveillance**
Definition	Country carries out Influenza-like illness (ILI) or respiratory disease surveillance.
Source	WHO technical experts, October 2013.
Classification	• **Unknown:** No information was available on the current status of ILI surveillance • **None**: ILI surveillance not in place or in the very early stages of implementation • **Partial**: ILI surveillance in place but reporting inconsistent, irregular or incomplete, e.g. laboratory testing inconsistently performed • **Full**: ILI surveillance both in place and of good quality.

Factor	**SARI surveillance**
Definition	Country carries out severe acute respiratory infection (SARI) surveillance.
Source	WHO technical experts, October 2013.
Classification	• **Unknown:** No information was available on the current status of SARI surveillance • **None**: SARI surveillance not in place or in the very early stages of implementation • **Partial**: SARI surveillance in place but reporting inconsistent, irregular or incomplete, e.g. laboratory testing inconsistently performed • **Full**: SARI surveillance both in place and of good quality; includes countries that have regular monitoring of pneumonia or hospitalized case with acute respiratory infection and testing for influenza

Developing Countries

The developing countries category is an aggregation of the income status, human development index and least developed countries classifications.
Primary focus is given to low resources countries (low / lower middle income countries), but also to upper middle income or high income countries that:
- have a low or medium human development index; or
- are least developed.

Classification	Income Status
Definition	Economies are divided according to 2011 gross national income (GNI) per capita, calculated using the World Bank Atlas method. The groups are: - low income: $1,025 or less - lower middle income: $1,026 - $4,035 - upper middle income: $4,036 - $12,475 - high income (non OECD and OECD): $12,476 or more.
Source	World Bank, July 2012 Link: http://data.worldbank.org/about/country-classifications and http://data.worldbank.org/about/country-classifications/country-and-lending-groups
Focus	Low and lower middle income countries

Classification	Human Development Index
Definition	The human development index (HDI) was created to emphasize that people and their capabilities should be the ultimate criteria for assessing the development of a country, not economic growth alone. HDI measure uses three components to derive a single statistic that measures social and economic development: health (measured by life expectancy at birth), education (measured by mean and expected years of schooling), and living standards (measured by gross national income per capita). The HDI categories are: - very high human development - high human development - medium human development - low human development.
Source	United Nations Development Programme, 2012 Link: http://hdr.undp.org and http://hdr.undp.org/en/statistics/hdi/
Focus	Low and medium human development countries

Classification	**Least Developed Countries**
Definition	The least developed countries represent the poorest and weakest segment of the international community. Their low level of socio-economic development is characterized by weak human and institutional capacities, low and unequally distributed income and scarcity of domestic financial resources. They often suffer from governance crisis, political instability and, in some cases, internal and external conflicts. Their largely agrarian economies are affected by a vicious cycle of low productivity and low investment. They rely on the export of few primary commodities as major source of export and fiscal earnings, which makes them highly vulnerable to external terms-of-trade shocks. Only a handful has been able to diversify into the manufacturing sector, though with a limited range of products in labour-intensive industries, i.e. textiles and clothing. These constraints are responsible for insufficient domestic resource mobilization, low economic management capacity, weaknesses in programme design and implementation, chronic external deficits, high debt burdens and heavy dependence on external financing that have kept LDCs in a poverty trap.
Source	UN-OHRLLS, 2012 Link: http://www.unohrlls.org/ and http://unstats.un.org/unsd/methods/m49/m49regin.htm#ftnc
Focus	Least developed countries

H5N1 vulnerability or "Affected country" as defined in PIP Framework Section 4.4

Definition	Country with laboratory confirmed cases of H5N1, or influenza virus with human pandemic potential. • **High risk** countries for sporadic human infections Countries with laboratory confirmed human case due to H5N1 or infection with influenza viruses of pandemic potential in the last 5 years; and/or countries with H5 or influenza viruses with pandemic potential viruses currently circulating in poultry. • **Medium risk** countries for sporadic human infections Countries which have had one or fewer laboratory confirmed human cases of H5N1 or infection with influenza viruses of pandemic potential in the last 5 years. These countries may or may not have reported sporadic outbreaks of influenza in animals (including H5 and H7) to the World Organisation for Animal Health (OIE) in the past 5 years.
Source	WHO, Influenza at the Human-Animal Interface, June 2012 Link: http://www.who.int/influenza/human_animal_interface

Total Population

Data year	2011
Definition	The 2010 Revision of the World Population Prospects is the twenty-second round of global demographic estimates and projections undertaken by the Population Division of the United Nations Department of Economic and Social Affairs of the United Nations Secretariat. The world population prospects are used widely throughout the United Nations and by many international organizations, research centres, academic researchers and the media.
Source	United Nations, Department of Economic and Social Affairs, Population Division, World Population Prospects: The 2010 Revision, New York, 2011. Link: http://esa.un.org/unpd/wpp

ANNEX 2

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ANNEX 3

Requirements for national risk communications capacities

IHR Monitoring Framework: Checklist and Indicators for monitoring progress on the implementation of the IHR Core capacities in States Parties, WHO, 2011

1. identification of risk communications partners and stakeholders ;
2. development of risk communications plan ;
3. Implementation and test of the risk communications plan through an actual emergency or a simulation exercise, and updated in the last 12 months;
4. development of policies, standard operating procedures (SOPs) or guidelines on the clearance and release of information during a public health emergency);
5. accessibility of regularly updated information sources provided to the media and the public for information dissemination;
6. accessibility of relevant information, education and communication (IEC) materials tailored to the needs of the population;
7. provision of information on at least three recent real or potential risk of a national or international public health emergency to the population and partners within 24 hours of confirmation
8. conduct an evaluation of the public health communication after emergencies, for timeliness, transparency and appropriateness of communications; and
9. share results of the evaluations of risk communications efforts during public health emergencies with the global community.