WHO STRATEGY FOR GLOBAL RESPIRATORY SYNCYTIAL VIRUS SURVEILLANCE PROJECT BASED ON THE INFLUENZA PLATFORM

-- Revised based on outcomes of the pilot phase --

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WHO Strategy for the Global Respiratory Syncytial Virus Surveillance based on Influenza Surveillance

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Contents

Abbreviations

ARI	Acute Respiratory Infection
CDC	Centers for Disease Control and Prevention, Atlanta
Ct	Cycle threshold
GIP	Global Influenza Programme
GISRS	Global Influenza Surveillance and Response System
ICD	International Classification of Diseases
ILI	Influenza-like Illness
NIC	National Influenza Centre
NICD	National Institute for Communicable Diseases
PHE	Public Health England
QCMD	Quality Control for Molecular Diagnostics
RSV	Respiratory Syncytial Virus
rRT-PCR	real-time reverse transcription polymerase chain reaction
SARI	Severe Acute Respiratory Infection
United Kingdom	United Kingdom of Great Britain and Northern Ireland
USA	United States of America
WGS	Whole Genome Sequencing
WHO	World Health Organization

WHO regions:

AFR	African Region
AMR	Region of the Americas
EMR	Eastern Mediterranean Region
EUR	European Region
SEAR	South-East Asia Region
WPR	Western Pacific Region

1. Introduction

Respiratory syncytial virus (RSV) has long been recognized as an important respiratory pathogen that often causes severe disease and mortality, particularly in very young children but also in other age and at-risk groups. The global burden of RSV-associated acute lower respiratory infections is estimated at 33 million annually, resulting in more than 3 million hospitalizations and 59 600 in-hospital deaths in children aged under 5 years. In infants under 6 months, RSV-associated acute lower respiratory infections account for about 1.4 million hospitalizations and 27 300 in-hospital deaths [1]. Many countries have recognized the importance of this pathogen and have established surveillance of RSV in certain settings.

WHO has conducted global surveillance of influenza for more than 60 years through a network of laboratories known as the Global Influenza Surveillance and Response System (GISRS). This long-established, well-functioning platform offers a cost-effective opportunity to leverage existing capacity to conduct surveillance for RSV without disturbing ongoing influenza surveillance. While there are differences in the epidemiology of influenza and RSV disease, the requirements for surveillance overlap, including sentinel sites, specimen source, laboratory diagnostics and personnel. For both infections the risks among children are of special interest.

WHO is committed to developing a surveillance system for RSV using the GISRS platform. In the long term, global RSV surveillance will provide a continuous, comprehensive and updated understanding of the epidemiology of this virus and the diseases it causes. Of interest are seasonal variations in RSV disease patterns in different countries and geographical regions, as well as the health-care burden due to RSV disease. Most importantly, RSV surveillance will help identify at-risk groups that will benefit most from immunization once vaccines become available. The RSV surveillance platform has the potential to provide a platform to evaluate vaccine impact following RSV vaccine introduction. RSV surveillance data can be used by health officials and decision-makers for evidence-based policy making.

Over a period of 3 years (2016-18), with support from the Bill & Melinda Gates Foundation and countries, appropriate and feasible processes for RSV surveillance with GISRS were established and evaluated in the RSV surveillance pilot. To achieve this, WHO regional offices identified two or three countries to participate in the pilot in each of the six regions where influenza surveillance was already established. Each country assigned RSV focal point representatives for laboratory and epidemiological aspects, and activities were conducted at selected laboratories and sentinel sites. The pilot was designed not to affect existing national surveillance systems; however, it was expected that national systems may benefit from the experiences and results of the pilot. Fourteen countries successfully participated in the pilot to evaluate whether RSV surveillance could be built on the well-established influenza surveillance conducted by the GISRS.

Countries used the extended criteria (not requiring the existence of fever) to existing SARI and ILI case-definitions to collect respiratory specimens from patients in all age-groups for the detection of RSV. Specimens were tested using standardized PCR assays for RSV. Most laboratories used a validated rRT-PCR assay developed and distributed by the CDC Atlanta. Laboratories using in-house detection or commercial assays were required to participate along with the other laboratories in an external quality assurance assessment for the molecular detection of RSV. The WHO FluMart data platform was adapted to receive case-based RSV laboratory and clinical data. At a meeting in Bangkok in October 2018, the outcomes of the two years of the pilot were reviewed, experiences exchanged, and lessons learnt discussed. The important outcomes from the pilot were:

1. Establishment of reference protocols for RSV detection
2. Establishment of the WHO RSV EQA 2019 for detection and typing

3. Testing the feasibility of leveraging the GISRS for RSV surveillance with marginal incremental costs without any significant adverse impact on influenza surveillance
4. Evaluation of the extended SARI and ARI case definition for detection of RSV infection
5. Assessment of seasonality of RSV epidemics in the participating countries

The meeting concluded with the decision to continue RSV surveillance for a further three years with the expansion of surveillance to low and middle-income countries (LMICs).

2. WHO RSV Surveillance – extension phase

The output from the pilot project establishes a solid RSV surveillance strategy with evidence-based standards and a tested mechanism for RSV surveillance based on the GISRS. The 3-year extension phase (Nov 2018 – Oct 2021) aims to consolidate the achievements of the original investment and proposes to (a) enhance the surveillance in infants and young children, (b) focus on the more severe disease requiring hospitalization, (c) expand virologic monitoring to differentiate virus types and to identify genetic groups, and (d) generate a better understanding of the seasonality, age groups at risk and disease burden among young children, particularly in LMICs representative in all WHO Regions.

Based on the key outcomes from the original pilot project, the extension phase (phase II) proposes to

1. Prioritize RSV surveillance in children less than two years of age
2. Focus on severe RSV disease that required hospitalization
3. Extend RSV surveillance with priority to Gavi-eligible countries and/or likely early recipient countries for RSV vaccines for deployment in national EPI programs
4. Implement methodologies to extrapolate RSV-associated hospitalization burden from routine surveillance
5. Develop considerations for ICD codes-based surveillance for RSV
6. Develop laboratory and surveillance guidance for RSV typing and genetic characterization
7. Enrich the genetic resource of RSV viruses in publicly accessible database(s), and
8. Extend the global RSV surveillance over at least three more seasons to better understand the epidemiology and global circulation of RSV strains.

Adjustments to Phase II include modifications of profiles of national and reference laboratory activities, and amendment in the sampling strategy (Table 1).

Table 1: Activities of participating countries and reference laboratories in Phase I and II

	Participating countries	Reference laboratories
Pilot Phase	• 14 countries • RSV detection all year round • 1000 specimens per year • all age-groups included	• standardized molecular detection of RSV in pilot countries • quality assurance of laboratory performance • technical support for countries • reagent support
Phase II	• 22 countries • RSV detection and typing all year round or if seasonality well defined then sampling during season • 400 specimens per year • age-restricted to <2-year-olds • periodic shipment of specimens to reference laboratories	• technical support for countries • standardized molecular detection and typing protocols • oversee preparation of the WHO RSV EQA 2019 • share protocols for sequencing between reference laboratories • perform genetic sequencing and analysis on specimens received from participating laboratories, and share results • select recent RSV isolates to create reference standards • establish genetic sequencing standards and information management • establish guidelines for selecting and sharing materials from participating laboratories

Countries in Phase II will work more closely with one of the reference laboratories of their choice for support in standardization of typing methodologies and sequencing of RSV viruses. Reference laboratories will take the lead in establishing sequencing protocols. In the first year of phase II, reference laboratories will establish protocols and a framework for sampling for sequence analysis using viruses collected during the pilot phase by countries (Table 2). In the second year, reference laboratories will complete the standardization of RSV sequencing protocols.