Summary report on the

Meeting of directors of national influenza centres in the Eastern Mediterranean Region

WHO-EM/CSR/520/E

Virtual meeting
15 July 2021

World Health Organization
REGIONAL OFFICE FOR THE Eastern Mediterranean

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1. Introduction

The WHO Regional Office for the Eastern Mediterranean held a virtual regional meeting of the directors of national influenza centres (NICs) and national influenza laboratories in the WHO Eastern Mediterranean Region on 15 July 2021. The meeting was attended by directors of NICs and other national influenza laboratories from 22 countries/territories, along with representatives from WHO Collaborating Centres (WHO CCs), partners and other global experts. The meeting provided an opportunity to review the functioning of NICs in the Region, strengthen collaboration and information-sharing among countries and identify gaps, suggest possible solutions and formulate plans for 2021–2022 in strengthening and maintaining laboratory capacity for the detection of influenza, SARS-CoV-2 and other respiratory viruses.

The meeting's objective were to:

- identify and discuss current challenges in the detection and characterization of influenza and respiratory viruses and share new laboratory techniques and methodologies for influenza and respiratory virus detection and characterization;
- discuss and agree ways to strengthen consistent and timely influenza reporting, virus-sharing and data utilization in the Region;
- debate and agree on expediting the integrated surveillance of influenza and SARS-CoV-2 from detection to sequencing; and
- critically analyse and evaluate current knowledge on influenza virology, WHO tools, detection and characterization methods for influenza and respiratory viruses, approaches to implementing antigenic and genetic characterization and antiviral resistance surveillance, and external quality assessment (EQA).

The meeting was inaugurated by Dr Abdinasir Abubakar, Manager, Infectious Hazard Prevention and Preparedness, WHO Regional Office for the Eastern Mediterranean, who welcomed participants and noted the

importance of the meeting, last held in 2019. He outlined the many changes to operations that had taken place during the COVID-19 pandemic and thanked NIC directors, staff and other influenza laboratories for their good work, emphasizing the need to share experiences, particularly regarding the achievements made during the pandemic.

He expressed his appreciation for the efforts of the NICs during the pandemic, which were the first to detect the SARS-COV-2 in the Region, noting that currently over 600 laboratories were engaged in this task. The laboratory network and capacity in the Region had grown over time. However, it was noted that there had been a general repurposing of NICs due to the COVID-19 pandemic leading to an increasing workload for staff and some requirements for influenza not being fulfilled; testing for influenza had now been reactivated since it remains a major threat in the Region. The importance of enhancing testing capacities such as for real-time polymerase chain reaction (RT-PCR), cell culture and sequencing, leveraging the Global Influenza Surveillance and Response System (GISRS) platform was emphasised.

He noted that the NICs in the Region had been acknowledged in 2019 for their contribution towards global vaccine selection through the sharing of a large number of viruses and their testing capacity. He encouraged participants to document the lessons learned during the COVID-19 pandemic, including the role NICs and GISRS. Participants were encouraged to reflect on the recommendations made in 2019 during the last meeting of NICs, as they remained relevant. He congratulated and welcomed on board the new NICs designated in 2019 (occupied Palestinian territory) and 2020 (United Arab Emirates) and highlighted the need to have further NICs designated, especially in those countries in the Region without one.

2. Summary of discussions

Overview: Regional situation, activities and issues

The Region has 18 NICs in 17 countries and four national influenza laboratories that also conduct SARS-CoV-2 detection, excluding those in the Islamic Republic of Iran and Lebanon. Some countries in the Region did not have PCR capacity before the COVID-19 pandemic but have now been able to introduce it, such as Somalia which now has six laboratories with PCR capacity and is beginning surveillance and testing for severe acute respiratory infections (SARI) and influenza-like illnesses (ILI). Djibouti has one national laboratory for COVID-19 but not for influenza. National influenza laboratories and NICs have different capacities in terms of detection, sequencing and virus isolation. The Region has no WHO CC for influenza but does have a WHO CC for emerging and re-emerging infectious diseases in Oman (designation ongoing) and two WHO COVID-19 reference laboratories in Abu Dhabi, United Arab Emirates, and Oman, which help other countries with SARS-CoV 2 sequencing.

The COVID-19 pandemic caused a drop in the testing and reporting of influenza cases from 137 511 in 2019 to 65 121 in 2020. The sharing of influenza virus and positive samples by NICs in the Region with WHO CCs decreased due to travel restrictions brought about by the pandemic. WHO has developed country profiles for the import and export of laboratory reagents and specimens in each country, including a list of contacts/companies capable of transportation, clearance and delivery into and out of each country.

Due to the COVID-19 pandemic, only 15 countries participated in the WHO external quality assessment programme (EQAP) for influenza in 2020, mainly due to travel restrictions and denial of customs permits for EQAP material shipments in some countries. Currently, 14 out of 22

countries/territories in the Region have the capacity to conduct genomic surveillance, while eight have no national genomic capacity but are external users of the Abu Dhabi regional sequencing laboratory and other private laboratories. WHO will expand and implement sequencing capacity using Oxford Nanopore Technology in those countries/territories experiencing complex emergencies.

Update from the February 2021 WHO vaccine composition meeting

Highlights from the February 2021 WHO vaccine composition meeting were described, including the following recommendations.

- For the northern hemisphere 2021/2022, it was recommended that egg-based vaccines be used, namely: A/Victoria/2570/2019 (H1N1)pdm09-like virus (new), A/Cambodia/e0826360/2020 (H3N2)-like virus (new), B/Washington/02/2019 (B/Victoria lineage)-like virus and B/Phuket/3073/2013 (B/Yamagata lineage)-like virus. It is noted that the recommendation for H1N1 pdm09 for the southern hemisphere has not changed from 2021 but A/Victoria/5270/2019 is a new recommendation for the northern hemisphere.

- It was noted that H3N2 viruses were in circulation in Bangladesh, Cambodia and West Africa. The viruses circulating in Bangladesh, in particular, are antigenically different from previously circulating viruses. The viruses circulating in Cambodia are somewhat different from the previous main groups and are genetically closer to the Bangladesh group, hence it was recommended that an A/Cambodia/e0826360/2020 (H3N2)-like virus be used in vaccines.

- Considering influenza B viruses, all the viruses analysed in the 2020/2021 northern hemisphere season B belonging to the Victoria lineage were in circulation in north and south China, most having HA1

substitutions N150K, G184E, N197D (-CHO) and R279K in HA1. It was also noted that a few B/Yamagata lineage viruses were detected, one being reported in the Islamic Republic of Iran, but no virus isolate was made; B/Washington/02/2019 has been retained as the vaccine virus as candidate vaccine viruses were not fully developed.

- Considering B/Yamagata lineage viruses, no new viruses were analysed and although a case was reported in the Islamic Republic of Iran, no virus was available. The older analysed viruses during the period were still in clade 3 and were still recognized well by antisera raised against B/Phuket/3073/2013 propagated either in eggs or in tissue culture.

Looking forward: GISRS +

The objectives of the global influenza strategy (2019–2030) are to: (1) promote research and innovation to address unmet public health needs; (2) strengthen global surveillance, monitoring and data utilization; (3) expand seasonal prevention and control policies and programmes to protect the vulnerable; and (4) Strengthen pandemic preparedness and response for influenza to make the world safer. The envisaged outcomes are to lead to better global tools and stronger country capacities, with the goals of a reduced burden of seasonal influenza, minimized risk of zoonotic influenza and mitigated impact of pandemic influenza. GISRS+ aligns with the vision of the global influenza strategy and will remain the backbone for pandemic preparedness and response.

The interim lessons learned during the COVID-19 pandemic are currently being reviewed and will be applied to influenza. The aim is to have a broader view of respiratory pathogen preparedness and response without losing sight of the ongoing threats and specificities of influenza, coronaviruses and respiratory syncytial virus (RSV).

Existing systems and platforms will be built upon, country ownership is emphasized for sustainability and national priorities should be set within the context of global needs following a country-led approach.

Capacity-building for GISRS+ should meet global needs for influenza, SARS-CoV-2, MERS-CoV-2, RSV and other respiratory viruses, should not disrupt well-established and functioning influenza systems, and must be done in a purposeful, measured and sustainable way outlining the broader package of laboratory, epidemiology and bioinformatics technical assistance and support. The emphasis should be on quality rather than quantity.

The multi-year roadmap for GISRS+ outlines the development of a coordinated approach in technical capacity-building by identifying gaps, opportunities, goals and areas for future investments. The development of an options paper for overall GISRS+ structure, coordination, terms of reference, roles and responsibilities at sentinel sites is key to its success.

In addition to building capacities for other respiratory viruses with epidemic and pandemic potential, the integration of laboratory and epidemiological capabilities, building upon the success of the existing GISRS infrastructure and avoiding the creation of parallel systems in regions and countries, is key. A survey has been sent out to surveillance teams, epidemiologists and laboratory staff who are participating in GIRS to collect feedback on how they could be better served.

Integration of influenza and SARS-CoV-2

Integrated surveillance for influenza and SARS-CoV-2 using the existing high-functioning influenza systems is important to address both COVID-19 and other illnesses simultaneously. Since March 2021,

SARS-CoV-2 has been integrated in GISRS, following a standardized algorithm, quantitative guidance and standardized tools.

Key points for NICs on integrated surveillance include:

- sampling: a weekly minimum of 50–100 specimens (ILI, SARI, acute respiratory infection (ARI) case definitions) using innovative sourcing for the purposes of representativeness;
- testing: utilize multiplex reagents kits from international reference reagents for GISRS and ancillary reagent support from WHO;
- focus on quality not quantity;
- sequencing: a weekly minimum of 15 sentinel viruses of SARS-CoV-2 from the above sources should be sequenced either in-house or after shipping to reference laboratories with support from WHO;
- data reporting: should be timely and consistent;
- surveillance (influenza and SARS-CoV-2) weekly reporting to FluMart by Thursday of the following week;
- genetic sequence data provided quickly and regularly, e.g. weekly or fortnightly, to GISAID or another publicly accessible database (tick "sentinel surveillance" under the sampling strategy field in the GISAID platform);
- provide technical advice and rationales for adjusting policies;
- prepare for seasonal influenza epidemics, which might occur at any time, and conduct out-of-season surveillance, shipping viruses to WHO CCs; and
- support (technical and financial) is available from WHO and partners, but NICs must demonstrate feasibility and must be models for the development of GISRS+.

Influenza remains among the top threats to global public health and this has not changed despite the ongoing COVID-19 pandemic. It is important to use existing systems for the integrated surveillance of influenza and other respiratory viruses, and the way forward for GISRS

is to build a global system for influenza as demonstrated for SARS in 2002, RSV since 2015 and now SARS-CoV-2, in combination with research and development on phenotypic assays that have a potential for rollout in GISRS, depending on public health needs arising from the evolution of SARS-CoV-2.

Whole genome sequencing of influenza and SARS-CoV-2 viruses, algorithm and sample selection, quality assurance, bioinformatic tools

An update was provided on current protocols for whole genome sequencing of influenza and SARS CoV 2, the influenza A and influenza genome sequencing pipeline and mobile influenza analysis, and harmonizing the different steps for all platforms to have same workflow. The United States Centers for Disease Control and Prevention (CDC) influenza genomics team is cross-training on the CDC SARS-CoV-2 genomic pipeline and PCR detection for SARS-CoV-2 in influenza genomic surveillance using automated data flagging with Kraken 2, but also taking note of the SARS-CoV-2 spike for a surveillance pipeline using only Oxford Nanopore Technologies and Mia, with a simple two pair amplification strategy.

Development of an influenza A, influenza B and SARS-CoV-2 multiplex rRT-PCR assay (influenza/SARS-CoV-2)

The rationale for the development of multiplex assays is that the SARS-CoV 2, influenza A and influenza B viruses are respiratory pathogens that present with similar symptoms. National public health laboratories, the US Association of Public Health Laboratories and the WHO global influenza programme have all highlighted that the challenges associated with SARS-CoV-2 testing include a reduction in or cessation of influenza testing during the COVID-19 pandemic and that data on

influenza viruses in circulation with SARS-CoV-2 is needed to better understand co-circulation and epidemiological trends.

The advantages of the CDC Influenza SARS-CoV-2 (Flu SC2) Multiplex Assay include: approximately threefold increases in testing capacity over the current CDC diagnostic panel, from 30 to over 90 samples per plate; reduced use of testing equipment, reagents and staff; reduced time to result; and identification of coinfections with influenza and SARS-CoV-2, which is important in clinical management. The ultimate goal was to develop a multiplex assay that simultaneously detects influenza A, influenza B, SARS-CoV-2 (SCV2) and human RNA transcript (control). The assay has been cleared by the US Food and Drug Administration and verified by CDC for use for Applied Biosystems 7500 Fast, BioRad CFX 96 and Thermo Quant Studio equipment.

CDC update on influenza and other respiratory pathogens

Within CDC's National Center for Immunization and Respiratory Diseases, the international influenza division has responsibility for: building capacity of ministries of health; analysing and sharing data and specimens with GISRS; global situational awareness; candidate vaccine virus selection; conducting research to inform public health policy and support policy development and influenza prevention and control policies and programmes; and ensuring greater health security within and outside the United States of America. Currently, the division is re-evaluating itself to strengthen its ability to influence policies and practices for influenza, SARS-CoV-2 and other respiratory viruses by optimizing the GISRS platform, surveillance and data to inform policy and action. The goals of CDC's international influenza programme include: establishing bilateral cooperative agreements (5 years in length); developing and/or optimizing technical partnerships; providing required strategic technical assistance; and conducting regional or multiregional

training. A new CDC office has been opened in the WHO Eastern Mediterranean Region, in Oman, to bring services closer to countries.

Update from the PIP Secretariat

An update was provided on the implementation of the Pandemic Influenza Preparedness (PIP) Framework's benefit-sharing system among Member States, the sharing of influenza viruses with pandemic potential with GISRS, assessing risk and taking preparedness measures (e.g. developing candidate vaccine viruses and other materials) and encouraging manufacturers to use materials to develop vaccines, antivirals and diagnostics, with a commitment to donate vaccines and other supplies during pandemics. Based on lessons from the 2009 H1N1 pandemic, the PIP Framework Advisory Group in 2013 identified five 10-year objectives for improving PIP through two high-level implementation plans (HLIP), including:

- all countries to have in place well established core capacities for surveillance, risk assessment and response at the local, intermediate and national levels, as required by the IHR (2005);
- all countries to have access to a NIC laboratory – the backbone of GISRS;
- to establish a clearer picture of the health burden that influenza imposes on different populations;
- all countries to have access to pandemic influenza vaccines and antiviral medicines to help reduce pandemic-related morbidity and mortality; and
- all countries to have improved capacities to carry out effective risk communications at the time of a pandemic.

Achievements have included: 131 countries have either started or improved laboratory and surveillance systems for participation in GISRS; 11 new NICs have been designated and recognized; 43 countries

(including 29 low- and middle-income countries) have published burden of disease estimates; three countries reported COVID-19 data to an established influenza platform at least once in 2020 (out of the 123 countries participating in GISRS); most NICs are serving as national COVID-19 laboratories; and at the country level, expertise has been built to estimate influenza morbidity and mortality that can be used to gain a better understanding of the COVID-19 burden.

However, there have been challenges to the implementation of the PIP Framework, including review indicators and milestones being found to be no longer fit for purpose, regional activities that are too complex to capture and measure, and the need to regularly inform stakeholders about information available on resource allocation and financial implementation.

Nevertheless, the response to the COVID-19 pandemic has presented opportunities and lessons regarding the monitoring of the current pandemic landscape, new ways of responding to a pandemic, linking to independent reviews of preparedness to provide an overview of country and regional preparedness, and mapping Partnership Contribution investments for pandemic influenza preparedness in the context of the broader preparedness landscape. Recommendations on opportunities to catalyse pandemic preparedness in the light of COVID-19 will inform adjustments in the 2022–2023 HLIPII (e.g. pilot projects to integrate ARI surveillance systems and strengthen data management), which in turn will inform the design of HLIPIII, taking into consideration COVID-19 lessons learned to inform future implementation.

Global RSV surveillance update

The WHO Global Influenza Programme's RSV surveillance project focuses on infants aged two years and over (RSV causes the greatest number of hospitalizations of infants). The project was disrupted by the

COVID-19 pandemic, which led to a reduction in the sourcing of specimens as patients avoided or delayed seeking care, sentinel hospitals were repurposed as COVID-19 treatment centres, staff were reassigned and there was a shortage of laboratory supplies. Additionally, the RSV case definition changed. Despite this, there have been a number of achievements, with 16 of 25 countries maintaining their RSV surveillance (although others could not initiate it or had to suspend it due to the COVID-19 pandemic), and countries participated in the EQAP for RSV detection and typing, sequencing protocols for RSV were implemented and the GISAID epiRSV platform was launched in June 2021. Plans for 2021–2022 include: multiplex RT-PCR assays for influenza (A, B), RSV (typing) and SARS-CoV-2; EQA for RSV sequencing protocols; and hands-on trainings in bioinformatics and other analytic tools.

Group discussion

Through group discussion, participants identified some of the achievements in the Region, including:

- most countries have participated in the EQAP;
- influenza surveillance systems were leveraged for the COVID-19 response;
- most countries are achieving 150 specimens per week;
- most countries are using multiplex Flu/SC2 kits;
- respiratory viruses other than SC2 (FlA, FlB, RSV, AdV, PIV, hMPV and rhino viruses) are being tested;
- viruses have been shared in a timely manner in most countries, which has had a positive impact on influenza detection;
- most countries are reporting data regularly to FluNet or EMFLU;
- genomic surveillance capacities developed for SC2 can be utilized for influenza; and
- countries are starting to work on the regular reporting and timely processing of ILI/SARI.

However, challenges were also identified, including:

- government policy to prioritize SARS-CoV-2 testing;
- lack of structured SARI/ILI surveillance;
- some countries have lost sentinel sites due to COVID-19 pressures;
- reagents or kits delivered in poor condition and global transportation issues;
- limited number of kits available to order at CDC International Reagent Resources (IRR);
- staff turnover leading to increased workloads;
- lack of functioning vertical surveillance systems for influenza and laboratory equipment;
- procurement processes taking a long time;
- inadequate funding for influenza activities;
- national and international challenges to the shipment of specimens;
- a severe need for capacity-building and staff recruitment to compensate for the high turnover; and
- lack of laboratory supplies and consumables.

In discussion on plans for 2021–2022, it was noted that countries are working on integrating national surveillance systems for SARS-CoV-2, influenza and other respiratory viruses, recruiting more staff and building the capacities of laboratory personnel. WHO support was requested to help initiate sentinel site influenza surveillance systems in Djibouti, Iraq, Libya and Somalia, facilitate the procurement and shipping process for countries, train newly-recruited staff and provide refresher training in bioinformatics. Ensuring the availability of needed laboratory supplies from CDC IRR was seen as important.

3. Conclusions

NICs and other national influenza laboratories have been facing numerous challenges in maintaining routine influenza surveillance

during the COVID-19 pandemic due to the prioritizing of SARS-CoV-2 and a shortage of laboratory staff, supplies and sentinel sites, among other things. There is a need to maintain influenza activities and capacities during the pandemic and to extend them for other respiratory viruses.

4. Recommendations

To Member States

1. NICs and other influenza laboratories should consider implementing or continuing influenza and SARS-CoV-2 testing through implementation of multiplex kits for testing of both using the WHO recommended algorithm.
2. WHO recommends at least 50 to 100 clinical specimens (and ideally 150 specimens) per week be collected from sentinel systems and tested for both influenza and SARS-CoV-2.
3. Wherever resources allow, laboratories should consider genomic sequencing of all SARS-CoV-2 PCR-positive sentinel specimens with a RT-PCR Ct value of ≤ 30.
4. NICs and other influenza laboratories should report in a timely manner and consistently to FluNet/EMFLU.
5. Representative influenza specimens should be shipped to WHO CC by 15 August 2021 for the September 2021 vaccine composition meeting and by 15 January 2022 for the February 2022 vaccine composition meeting and all specimens should have been tested for SARS-CoV-2 with a negative result.
6. Quality should be prioritized over quantity.

To WHO

7. Provide technical support to NICs for a testing strategy to integrate multiplex methods into a sampling strategy, laboratory protocols and testing algorithms.
8. Ensure the availability of kits for selected countries adopting the multiplex methodology (including preparation for the next season).
9. Support countries reporting separate sentinel and non-sentinel surveillance data for both influenza and SARS-CoV-2 to adapt to FluMart requirements for differentiation between types and sources of samples, processing and denominators.
10. Support the procurement of laboratory supplies and reagents, where needed, for enhancing and sustaining laboratory testing of ILI and SARI clinical specimens in complex emergency countries.
11. Support countries to enhance NIC capacities for sequencing and phylogenetic analysis of sequences, the identification and interpretation of influenza virus sequence mutations, and sharing and submission to public databases such as the GISAID platform.

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