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Information and criteria for prioritizing diagnostic tests for SARS-CoV-2 in order to address the procurement needs of health systems

Questions and Answers

- *What type of in vitro diagnostics should the countries prioritize for determining infection by SARS-CoV-2, the causative agent of COVID-19?*

Countries should prioritize tests that are based on detecting nucleic acids (RT-PCR tests), whether they use open or closed platforms. Due to their nature, tests of this type are highly sensitive and specific (depending on their design, sample taking, and the operator).

- *What are the limitations of the so-called “rapid tests”? What might they be used for?*

It is important to clarify that there are two types of so-called “rapid tests”: those that detect antigens (proteins from the virus) and those that detect antibodies (IgM/IgG). The ones that detect antigens can be useful for confirming whether the virus was present at the time when the sample was taken. However, those that detect antibodies only confirm previous contact with the virus. They cannot either confirm or rule out whether the virus was present when the sample was taken; thus, special caution should be used in interpreting their results, taking into consideration the phase of the infection.

The rapid tests are generally not highly sensitive, meaning that a negative result does not rule out infection. At present, therefore, they are not recommended for COVID-19 diagnosis, and, more particularly, they are not recommended as a tool for ruling out cases of acute infection. The presence of antibodies does not indicate absence of the virus (the time at which the sample was taken is a relevant factor), nor does it necessarily indicate protection against the virus.

These tests, if available, may be useful for epidemiological research or to infer seroprevalence in a given location or area. Their use in adapting public health measures is also of interest, and their potential deserves strong consideration. Although PAHO monitors, on a daily basis, products being placed on the market, and evaluates their potential uses and applications, it is important

for each country to conduct its own tests to validate tests of this type before implementing them, using a panel of previously characterized samples for the purpose, and carrying out the process under appropriate laboratory conditions.

- *Are all of the products (kits and/or reagents) for the detection of SARS-CoV-2 nucleic acid similar?*

Not necessarily. The products can vary depending on the manufacturer and on the equipment needed for the test, among other factors. The reagents and protocols that PAHO has recommended to date for use in public health laboratories underwent a rigorous process of validation. PAHO also offered countries support for implementing these tests within their official laboratory networks. These tests are considered “RUO” products (for research use only) – a category used for *in vitro* tests developed non-commercially for health surveillance and/or diagnosis of emerging diseases. Their optimization requires a certain level of experience, and they are normally used in countries’ public health laboratories, rather than in conventional clinical diagnostic laboratories.

Given that demand is increasing, and that there is a need for more diagnostic centers within the countries’ national territories, countries might consider procuring commercial products that use a similar technology. These kits generally allow for use by clinical laboratories that have the necessary equipment and the required biosafety conditions but that are not necessarily part of the network of specialized laboratories.

A growing number of *in vitro* diagnostic kits on the market today make it possible to detect viral nucleic acid over open platforms (using a piece of equipment known as a thermocycler, and employing the technique of RT-PCR amplification). Kits are also available today that require little manipulation by laboratory personnel, and that function by using specifically designed laboratory equipment, the so-called closed platforms.

- *How can the quality and performance of commercial products be evaluated?*

When a country decides to acquire commercial *in vitro* diagnostic tests, the first criterion should be the product’s regulatory status. The authorities responsible for regulating drugs and other health technologies should have quality control and performance evaluation processes for these products in order to ensure a range of specificity and sensitivity adequate for clinical use, as well as a level of consistency from lot to lot that ensures the comparability of results. If the authorities require international references as an input to their process of authorizing diagnostic products for the national market, they can institute regulatory reliance processes using the decisions of

authorities with a recognized track record for these technologies (see “SRA,” or Stringent Regulatory Authority, considerations below). Another alternative is to use the WHO list of products for emergency use (EUL, or Emergency List Use; see below). Lastly, WHO and the FIND Collaborating Center for diagnostic tests – FIND being the Foundation for Innovative New Diagnostics, a non-profit organization devoted to improving access to *in vitro* diagnoses at the global level – are collaborating on an initiative to determine the performance of COVID-19 molecular and immunological tests. The results of the first round of evaluations will be published shortly (for more information see <https://www.finddx.org/covid-19/>).

- *In the COVID 19 context, what options do countries have to gain more rapid access to quality products?*

During emergencies in which countries face a new pathogen, and where their markets therefore lack products with proven performance, selecting *in vitro* diagnostic products becomes more complex. National authorities’ adoption of emergency authorization processes must strike a balance between the need for timely access to these technologies and a quality control process based on risk analysis. Thus, authorities can and should create emergency authorization mechanisms that – due to their own resources or based on decisions by other regulatory authorities that are considered reference (or reliable) entities with regard to the regulation and control of *in vitro* diagnostics – establish a list of products approved for purchase and use by health systems. Information from the WHO EULs and results of evaluations by FIND (see above) can also be useful sources when authorizing or selecting these products.

- *What regulatory authorities does WHO consider to be reference entities for the regulation and monitoring of in vitro diagnostics in the context of the COVID-19 pandemic?*

For its abbreviated process of prequalifying *in vitro* diagnostic tests, WHO recognizes, as SRAs (Stringent Regulatory Authorities), a group of authorities. These authorities maintain close relations with WHO, permitting the exchange of information and technical consultation. The authorities recognized by WHO¹ for this purpose are as follows:

¹ The list of regulatory authorities is provided in the document *Abridged Prequalification Assessment*, which can be accessed at: <https://apps.who.int/iris/bitstream/handle/10665/259172/WHO-EMP-RHT-PQT-2017.08-eng.pdf;jsessionid=E94795813D36205EA97EA1E75F2761DD?sequence=1>.

NOTE A: Although it is regarded as an SRA, the European Union (EU) has not been included in this list, since at this time it is accepting products for market that are vouched for only by their manufacturers’ statements, without any EU evaluation taking place prior to their being put on the market.

| Regulatory Authority | Country | Website |
|--|--------------------------|---|
| Food and Drug Administration (FDA) | United States of America | https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd |
| Health Canada | Canada | https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/covid-19/diagnostic-devices-authorized.html |
| Therapeutic Goods Administration | Australia | https://www.tga.gov.au/covid-19-test-kits-included-artg-legal-supply-australia |
| Ministry of Health, Labour and Welfare | Japan | https://www.mhlw.go.jp/english/ https://www.who.int/diagnostics_laboratory/200402_imdrf_collated_table_2_april_2020.pdf?ua=1 |
| Health Sciences Authority (see note B) | Singapore | https://www.hsa.gov.sg/announcements/regulatory-updates/hsa-expedites-approval-of-covid-19-diagnostic-tests-in-singapore-via-provisional-authorisation |

During the COVID-19 emergency, these authorities have implemented emergency authorization processes to ensure the availability of *in vitro* diagnostics that can be used in a variety of contexts. Since these procedures are not as exhaustive as the usual registration and authorization processes, the authorities also implement post-marketing surveillance procedures to ensure that the performance of these products within the health system can be monitored, and that any necessary corrective measures, or actions to remove a product from the market, can be undertaken.

- *What constitutes the WHO emergency use list (EUL)?*

During health emergencies, WHO activates a mechanism known as an EUL, in order to recommend new products that are critical for health systems. With the declaration of the COVID-19 emergency, WHO put out a call for producers of SARS-CoV-2 molecular tests (i.e., nucleic acid detection tests). This process is different from prequalification (PQ), which is an exhaustive process that takes months or years. The EUL is a review process that makes it possible to issue recommendations more quickly, as is appropriate for emergency situations. The products in the

NOTE B: WHO is working on updating this document. The new version's list is expected to include the regulatory authority of Singapore (the Health Sciences Authority). The reference document can be accessed at: https://www.who.int/diagnostics_laboratory/pqdx_173_draft_abridged_pq_assessment_for_public_comment_with_annex.pdf?ua=1.



PAHO

EUL are recommended for the procurement systems both of the UN and of the countries' health systems.

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