Coalición Interamericana de Convergencia Regulatoria
SECTOR DE TECNOLOGÍA MÉDICA

Coalizão Interamericana de Convergência Regulatória
SETOR DE TECNOLOGIA MÉDICA

Inter-American Coalition for Regulatory Convergence
MEDICAL TECHNOLOGY SECTOR

Dear Coalition Members:

Please, find below some information regarding the "Use of tests for detection of antigens / antibodies" of SARS-CoV-2 which can help in discussions related to the topic.

The World Health Organization (WHO)[1] and the Pan American Health Organization (PAHO)[2], **at this moment** (04/10/2020), have been advising against the use of tests for detection of antigens / antibodies for COVID-19. Such position is founded on two issues:

1. The possibility of cross-reaction with other coronavirus that are normally present in the community, making difficult the results interpretation[3].
2. The dynamics of the human organism's response in the production of antibodies is not well known yet. Some studies show that only 40% of the patients develop antibodies for the first 6 or 7 days after onset of symptoms[4].

Therefore, negative results obtained with the use of serological tests would not be an adequate tool to eliminate the possibility of infection on the first days of the disease. Positive results must be evaluated in conjunction with other symptoms, since there is possibility of cross-reaction with other coronavirus.

The position of WHO/PAHO leads us to reflect on the role of *in vitro* diagnostic (IVD) products. These products include reagents, instruments and systems for testing samples collected from the body and intended for use in a broad spectrum of healthcare applications, among them the early detection of diseases and conditions and the generation of risk related medical information required for the clinical action.[5]

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[1]WHO. Advice on the use of point-of-care immunodiagnostic tests for COVID-19.Availabe in: https://www.who.int/news-room/commentaries/detail/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19

[2] PAHO. Laboratory Guidelines for the Detection and Diagnosis of COVID-19 Virus Infection. Available in https://www.paho.org/en/documents/laboratory-guidelines-detection-and-diagnosis-covid-19-virus-infection

[3] Meyer B, Drosten C, Müller MA. Serological assays for emerging coronaviruses: challenges and pitfalls. Virus Res. 2014 Dec 19;194:175-83.

[4] Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. medRxiv. 2020:2020.03.02.20030189.

[5] The Lewin Group, Inc. The Value of Diagnostics Innovation, Adoption and Diffusion into Health Care. July 2005. Available in https://dx.advamed.org/sites/dx.advamed.org/files/resource/Lewin%20Value%20of%20Diagnostics%20Report.pdf

IVD products available in the market detect the genetic material of the virus, through molecular biology techniques (Polimerase Chain Reaction - PCR), detect the presence of antigens or the presence of antibodies (serological tests). Each of these methods has its own characteristics and limitations, and it is necessary to use "the right test, on the right patient, in the right setting, at the right time."

In this sense, with the objective of expanding the access of the population to testing for COVID-19, several countries have established guidelines for the use of tests for detection of antigens and for detection of antibodies. The testing strategy can vary, not only among countries but also within the country.

In the United States, the Food and Drug Administration (FDA), through procedure called "Emergency Use Authorizations (EUA)" published the "Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency"[6].

In accordance with this document, serological tests, intended for the detection of antibodies for SARS-CoV-2, which have been validated and notified to the FDA in the EUA, must contain in their instructions for use warnings that:

- This test has not been reviewed by the FDA.
- Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic should be considered to rule out infection in these individuals.
- Results from antibody testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status.
- Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.

In addition to the guidelines in instructions for use, the manufacturer must provide, through informational pamphlets directed to healthcare service providers and patients, information regarding known potential risks and benefits of use of products authorized for emergency use.

6 FDA. Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency. March 2020. Available in https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-diagnostic-tests-coronavirus-disease-2019-during-public-health-emergency

Warnings and recommendations were also announced by the FDA in a letter addressed to healthcare service providers. Among them, the FDA instructs that the services continue to use serological tests, provided that they are aware of their limitations[7].

The CDC has guidelines regarding who musts be tested, but the decisions on testing remains at the discretion of state or local health departments and/or of individual clinics[8].

An additional resource is the *Toolkit Covid-19*[9], a collection of resources compiled and curated by AdvaMed to guide messaging and communications efforts. The publication includes actions taken by the Association in response to the crisis, with a focus on the production and distribution of medical devices, including personal protective equipment, ventilators and diagnostic kits. The list of products that received EUA for Covid-19 in the United States is included in Toollkit Covid-19.

In Spain, the "Guide for the use of Rapid Tests for Covid-19 Antibodies"[10], published by the Ministry of Health, instructs on the use of rapid tests for detection of COVID-19 inside and outside hospitals and in penal institutions.

In Brazil, the "COVID-19 COE Bulletin number 12" published by the Ministry of Health[11], contemplates information regarding laboratory epidemiological surveillance, bringing the history of implementation of diagnosis of COVID-19, in the country, from its initial phases up to the current moment.

The Ministry of Health recommends the use of serological test to "the entire population which presents condition of flu syndrome and pertains to one of the following categories:

- active healthcare and safety professionals.
- person who resides in the same address of an active healthcare and safety professional.

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[7]FDA. Important Information on the Use of Serological (Antibody) Tests for COVID-19 - Letter to Health Care Providers. April 2020. Available in https://www.fda.gov/medical-devices/letters-health-care-providers/important-information-use-serological-antibody-tests-covid-19-letter-health-care-providers

[8] CDC. Testing for COVID-19. Available in https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/testing.html.

[9] TOOLKIT COVID-19 – A collection of resources compiled and curated by AdvaMed to guide messaging and communications efforts. Available in : https://www.advamed.org/sites/default/files/resource/covid19-toolkit-042020.pdf

[10]Guía para la utilización de tests rápidos de anticuerpos para Covid-19. Available in: https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov-China/documentos/Guia_test_diagnosticos_serologicos_20200407.pdf

[11] Brazil. Boletim COE COVID-19. Semana epidemiológica 17(19 – 25/04). Available in: https://portalarquivos.saude.gov.br/images/pdf/2020/April/19/BE12-Boletim-do-COE.pdf

- people aged 60 years or more.
- carriers of chronic health conditions, and
- economically active population.

The test, used by the Ministry of Health was validated by the National Institute for Quality Control in Health (INCQS) of Fundação Osvaldo Cruz, must be done after the seventh day from the onset of the symptoms. Recommendations regarding the interpretation of the test result are brought by the document, as well as the ongoing indication of validation alternatives of the available tests, which will be worth as reference, through organized entities under the "SARS-CoV-2 Diagnostic Kits Validation Program" (SBPC/ML, SBAC, ABRAMED and CBDL).

Finally, we conclude that, despite the limitations for use of serological tests (antibodies) pointed out by the World Health Organization, these tests could be decisive for making of clinical and epidemiological decisions in the pandemic confrontation process, provided that its implementation is well established.

Links for query of documents

Due to the evolution and advancement of the Coronavirus pandemic, the documents related to the theme have undergone constant update, in this manner, we opted for annexing the links of the current documents on this date 04/20/2020.

Updates to this document will be continuously incorporated when relevant information becomes available.

1. TOOLKIT COVID-19 – A collection of resources compiled and curated by AdvaMed to guide messaging and communications efforts.: https://www.advamed.org/sites/default/files/resource/covid19-toolkit-042020.pdf
2. Advice on the use of point-of-care immunodiagnostic tests for COVID-19 : https://www.who.int/news-room/commentaries/detail/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19
3. Laboratory Guidelines for the Detection and Diagnosis of COVID-19 Virus Infection. : https://www.paho.org/en/documents/laboratory-guidelines-detection-and-diagnosis-covid-19-virus-infection

4. FDA. Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency:https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-diagnostic-tests-coronavirus-disease-2019-during-public-health-emergency
5. FDA. Important Information on the Use of Serological (Antibody) Tests for COVID-19 - Letter to Health Care Providers: https://www.fda.gov/medical-devices/letters-health-care-providers/important-information-use-serological-antibody-tests-covid-19-letter-health-care-providers
6. Brazil. COE COVID-19 Bulletin. Epidemiological week. 17(19 – 25/04): https://portalarquivos.saude.gov.br/images/pdf/2020/April/19/BE12-Boletim-do-COE.pdf
7. Guide for the use of Rapid Tests for COVID-19 Antibodies: https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov-China/documentos/Guia_test_diagnosticos_serologicos_20200407.pdf