Summary of WHO Interim Guidance (11 Sept, 2020)

[Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays]

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STANDARD F COVID-19 Ag FIA

This document is a summary of WHO interim guidance for the use of rapid immunoassays in the diagnosis of SARS-CoV-2 Infection. WHO has currently updated guidance on the use of Ag-RDTs, and this will be helpful information while using STANDARD F COVID-19 Ag FIA to set up the adequate protocol in your country.

1. General Recommendation

No.	WHO recommendations	STANDARD F COVID-19 Ag FIA
1	SARS-CoV-2 Ag RDTs that meet the minimum performance requirements of ≥80% sensitivity and ≥97% specificity compared to a NAAT reference assay.	According to clinical evaluations conducted in nine different counties around the world, total clinical sensitivity & specificity of STANDARD F COVID-19 Ag FIA is **94.09%** and **98.52%** respectively.
2	To optimize performance, testing with Ag-RDTs should be conducted by trained operators in strict accordance with the manufacturer's instructions and **within the first 5-7 days following onset of symptoms.**	Distributors of STANDARD F should note that selection of sample or patient group is very important when conducting the performance evaluation of STANDARD F COVID-19 Ag FIA. **Nasopharyngeal or Nasal specimen from patients within the first 5-7 days following onset of symptoms must be included**, and **distinguish this group of sample when you analysis of final data.**
3	Appropriate scenarios for use of COVID-19 Ag RDTs include the followings: • Use RDTs to respond to suspected outbreaks of COVID-19 in remote setting, institutions and semi-closed communities where NAAT is not immediately available	If you have multiple positive results in a certain group, it can be an evidence of a COVID-19 outbreak. In this case, all samples giving positive results should be transported to laboratory for NAAT testing.
	• To support outbreak investigations (e.g. in closed or semi-closed groups including schools, care-homes, cruise ships, prisons, work-places and dormitories, etc.)	In NAAT-confirmed COVID-19 outbreaks, F Ag FIA could be use : • **to screen at-risk individuals** • **rapidly isolate positive cases** • **prioritize sample collection from F-Ag negative individuals for NAAT**
	• To monitor trends in disease incidence in communities, and particularly among essential workers and health workers during outbreaks	STANDARD F COVID-19 Ag FIA can be offered to **hospital groups or industries for the purpose of daily screening.**
	• Where there is widespread community transmission, RDTs may be used for early detection and isolation of positive cases in health facilities, COIVD-19 testing centers/sites, care homes, prisons, schools, front-line and health-care workers and for contact tracing.	**A negative result cannot completely exclude an active COVID-19 infection**, and, therefore, repeat testing or preferably confirmatory testing (NAAT) should be performed whenever possible, particularly in symptomatic patients**.**

	• Testing of asymptomatic contacts of cases may be considered even if the Ag-RDT is not specifically authorized for this use, since **asymptomatic cases have been demonstrated to have viral loads similar to symptomatic cases.**	In this situation, a negative Ag-RDT should not be remove a contact from quarantine requirements.
4	For initial introduction of Ag-RDTs into clinical use, countries should consider selecting some settings where NAAT confirmatory testing is currently available.	• Confirm performance of the selected product • Troubleshoot any implementation issues encountered • **The samples for the two tests should be collected at roughly the same time, or at most within a period of less than 2 days.**
5	In situations where confirmatory testing with NAAT is not feasible, any indications that results may be incorrect should raise suspicions about validity.	In such situations below, **considerations should be given to repeating the test**, especially if there is also any uncertainty about the visual result (faint bands) or adequacy of sampling. • Patients who are Ag-positive but have a clinical syndrome not consistent with COVID-19 • Patients with a positive test detected in a low-prevalence setting • Patients who are Ag-negative but have a classical syndrome • Patients who are close contacts of a case or are in a high-prevalence setting
6	Use of Ag-RDTs is not recommended in settings or populations with low expected prevalence of disease, especially where confirmatory testing by NAAT is not readily available.	(e.g.) • Screening at points of entry • Blood donation • Elective surgery

2. Selection of tests for procurement and implementation

No.	WHO recommendations	STANDARD F COVID-19 Ag FIA
1	There are a number of factors to consider when selecting Ag-RDTs for use in the scenarios presented above, in the recommendations section. These Include : • **Quality of available data used to validate the test.** - The reference standard used - The type of specimen - The delay between sample collection days since symptom onset - Test execution and the number of days since symptom onset - The number of subjects enrolled - The setting of enrolment - The concentration of virus in specimen (the greatest predictor of test sensitivity) - The selection of patients and study sites	While planning for the evaluation of STANDARD F COVID-19 Ag FIA, those factors should be considered and be listed in the final report. It is better to **include specimen from patients within the first 5-7 days following onset of symptoms** as many as possible, and **final results should be sorted by the Ct value of reference method(NAAT).** **Note that prospective clinical studies are generally superior to retrospective studies.**

	• **Reported Performance** Given the **relatively low prevalence** of active SARS-CoV-2 infections even in settings with community transmission:	High specificity (minimum ≥97% and ideally ≥99%) is necessary to avoid many false positive results.
	Sensitivity will depend on the status of patients studied (degree of illness, days since onset of symptoms, etc.)as well as the product quality, but should reach a minimum of ≥80%. A useful assessment is the sensitivity of the test in patients with a rRT-PCR cycle threshold(Ct) below a specific value (e.g. 28 or 30), because the virus is expected to be abundant in respiratory samples when the test is in this range, and test sensitivity correspondingly high.	Recommended criteria using Ct value of rt-PCR method for the evaluation of STANDARD F COVID-19 Ag FIA: • **< 20** • **20 – 25** • **25 – 28(or30)** • **28(or 30) – 35** • **> 35**
2	**Manufacturing quality and regulatory status** Test should be procured from manufacturers who work under a quality management system (e.g. ISO 13485) and with at least local regulatory approval or right of free sale granted by the country of manufacturer. RDTs, as all in vitro diagnostics intended for clinical use, should undergo a rigorous and transparent regulatory review. Approval or authorization by a stringent regulatory body and/or Emergency Use Listing by WHO should be available at the time of procurement.	• All products are produced under ISO 13485 • CE approved • KFDA (in progress – estimated Oct 2020) • FDA (in progress – estimated Dec 2020) • Free sales certificate is available
3	**Manufacturing capacity and further evidence of quality** Many new companies without a history of success in the manufacture, sales and support of in vitro diagnostics are entering the market with SARS-CoV-2 Ag-RDTs. Procurers should consider the range of other products offered by the company (especially lateral flow tests), what regulatory approvals they have for non-emergency diagnostic products, and their manufacturing and post-market surveillance capacity. Many companies are able to manufacture high-quality prototypes or completed tests at low volume but may have difficulty when scaling up manufacturing to meet global needs.	• Check SD BIOSNESOR's company profile via website (www.sdbiosensor.com). • SD BIOSENSOR's manufacturing capacity of IVD products : **- Current annual capacity : 432 million tests** (from Korea & India factories) **- Target capacity in 2021 : 1.14 billion tests** (After opening a new factory in Indonesia)
4	**Distribution and technical support** Consideration should be given to a supplier's distribution and product support capacity, especially in low and middle-income countries. This is particularly true for tests that require additional equipment like readers.	• If you are a end user, please contact your local sales representative. • SD BIOSENSOR Headquarter contact information ✓ Inquiries for F COVID-19 Ag FIA (Application Specialists) - Travis Ahn / travis@sdbiosensor.com - Heeeun Heo / heeeun.heo@sdbiosensor.com ✓ Inquires for STANDARD F Analyzer (Technical Service Engineers) - David Jeon / minhyeok.jeon@sdbiosensor.com - Chuck Lee/ seungmok.lee@sdbiosensor.com
5	Shipping and storage conditions and shelf-life. The capacity to withstand temperature stress and having an extended shelf-life are critical to the ease-of-use of Ag-RDTs. With new products, **shelf-life must be estimated based on accelerated stability studies** (usually at higher temperatures), but **target shelf-life should be at least 12-18 months at 30˚C and ideally 40˚C**. A cold chain requirement for shipping and/or storage would significantly increase the cost and complexity of procurement and distribution.	• Shelf-life of STANDARD F COVID-19 Ag FIA : **18 months** If ambient temperature is 30℃ and the accelerated storage temperature is 55℃, △T is 25 °C. If △T is 25°C, accelerated stability predictions would be 22.5 (5.66). We have performed the accelerated stability test using 3 batches at 55°C up to 13 weeks. If the test kit is stable at 55°C up to 13 weeks, then the predicted stability would be 73 weeks (13 weeks x 5.66 fold). As the STANDARD™ F COVID-19 Ag FIA was stable at 55°C (55±10%) up to 13 weeks when stored unopened. The predicted stability is 73 weeks (18months). • Storage condition of STANDARD F COVID-19 Ag FIA **: 2 – 30 °C (36 – 86 °F)**

6	**Specimen collection requirements** SARSCoV-2 Ag-RDTs vary in their requirements for specimen type, number of processing steps, need for accurate timing, instrumentation and interpretation of results, which will influence the extent of training and supervision required. For this reason, an ease-of-use assessment is an important consideration along with test performance.	• **Specimen type : Nasopharyngeal, Nasal swab and VTM** • Please check the test procedure from the Instructions for use of STANDARD F COVID-19 Ag FIA
7	**Contents of test kit** Standard kit contents do not necessarily include everything required to perform and quality control the test, and this must be verified prior to purchase. Several commercially available Ag-RDTs for SARSCoV-2 utilize a reading instrument.	**[Kit contents]** • Test device x 25 • Extraction buffer tube x 25 • Nozzle cap x 25 • Sterile swab x 25 • Instructions for use x 1 ☞ Quality controls are not included in the test kit, but are separately available.
8	**The cost of the test** The cost of tests will vary according to the test and the volume to be purchased. In general, they should be less expensive than PCR tests. The cost of transportation, import tariffs, storage, end-user training (and supervision) and post-purchase quality control testing activities required to support quality implementation of RDTs must also be considered.	• Please contact your local distributors to get the quotation for STANDARD F COVID-19 Ag FIA and the analyzer.
9	**Availability, completeness and clarity of instructions for use** These should be clear, contain illustrations and be user-friendly for a non-laboratory specialist.	• Instructions for use is included in the package of STANDARD F COVID-19 Ag FIA in the form of multi-language. Please request pdf version of the Instructions for use if needed.