Healthy GateWays

Co-funded by
the Health Programme
of the European Union

PREPAREDNESS AND RESPONSE TO CASES OF COVID-19 AT POINTS OF ENTRY IN THE EUROPEAN UNION (EU)/EEA MEMBER STATES (MS)

Considerations for implementing a common strategy for testing of travellers for SARS-CoV-2 at international airports in EU MS

REPORT Version 2

17 October 2020

The EU HEALTHY GATEWAYS Joint Action has received funding from the European Union, in the framework of the Third Health Programme (2014-2020). The content of this document represents the views of the author only and is his/her sole responsibility; it cannot be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency (CHAFEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

Table of Contents

This report was prepared after a request from the European Commission's Directorate-General for Health and Food Safety (DG SANTE). An ad-hoc working group was established with members from the EU HEALTHY GATEWAYS joint action consortium. The names and affiliations of the working group members who prepared this document are listed at the end of the document.

1. Summary

- The International Health Regulations (IHR) 2005 requires that public health measures implemented must be commensurate to the risk and avoid unnecessary disruption to international traffic and trade. Efforts by governments should ensure protection of public health, allowing at the same time societal and economical activities. Attempts are needed to lift restrictions of free movement which lead to huge financial consequences to countries' economies.
- Lack of a common, coordinated, evidence-based approach at European level for implementing laboratory testing of incoming travellers at airports causes unnecessary disruption to the free movement of citizens in the EU MS, is a barrier for travellers from third countries to travel to the EU, and may create confusion among the travelling public.
- This report suggests implementation of laboratory testing for incoming travellers according to the risk zone (red, orange, grey) of countries visited 14 days prior to travel, as a supplementary measure and after ensuring that essential prerequisites are in place and implemented strictly, such as comprehensive follow-up of travellers who test negative.
- Testing incoming travellers can identify a proportion of infectious cases, preventing introduction and further spread to the receiving country to some extent. When using a test with sensitivity of 80% and specificity of 98%, the false negative results are expected to be 32 per 100 000 population coming from a red zone, and 10 and 5 per 100 000 population coming from an orange and green zone respectively. Assuming that the actual cumulative rate of cases in the community is five times more than the reported rate, then false negative results are expected to be 150 per 100 000 population coming from a red zone, and 50 and 25 per 100 000 population coming from an orange and green zone respectively.
- This report further provides an analysis of options for laboratory testing methods (PCR, antigen rapid tests), timing of laboratory testing of travellers including advantages and limitations, practicalities regarding triage of passengers, and how to get information about orientation of passengers and setting up "corridors" according to the risk zones (green, orange, red, grey).

2. Rational

2.1. Problem analysis

In response to the novel coronavirus disease 2019 (COVID-19) pandemic, European Union (EU) Member States (MS) as well as other countries worldwide, have implemented border closures and other public health measures resulting in restrictions of movement on citizens, in an attempt to prevent spread of the disease. In our modern world where the transport sector provides people with the ability to travel for meeting family and friends, for business or for leisure and also serves essential trade activities, most economies greatly rely on ensuring continuation of air, sea and land transport operations.

The International Health Regulations (IHR) 2005 requires that public health measures implemented must be commensurate to the risk and avoid unnecessary disruption to international traffic and trade. Efforts by governments should ensure protection of public health, allowing at the same time societal and economical activities. Mandatory quarantine of all incoming travellers from certain countries

discourages travelling for business, for leisure or for other purposes and causes significant interference with international traffic and trade. Attempts are needed to lift restrictions of free movement which lead to huge financial consequences to countries' economies.

The COVID-19 pandemic adversely impacted countries' economies and caused enormous financial losses for various industries, especially the travel and tourism sectors. According to the joint industry letter from Airports Council International (ACI), Airlines for Europe and the International Air Transport Association (IATA), "*Europe's aviation sector is suffering dramatically financially with total industry revenue losses of approximately €140 billion during 2020 for airlines, airports and Air Navigation Service Providers*" (1). In the European Union, significant efforts have been made by various organizations including the European Union Aviation Safety Agency (EASA), to facilitate the aviation industry to continue operating normally as far as possible, taking essential measures to ensure protection of the health of the travelling public and transport workers (2).

In an attempt to detect infectious incoming travellers, many EU MS require as a condition for entry into the country COVID-19 diagnostic laboratory testing prior to travel, or implement laboratory testing to incoming travellers at the borders (3). Lack of a common, coordinated, evidence-based approach at European level for implementing such measures causes unnecessary disruption to the free movement of citizens in EU MS, is a barrier for travellers from third countries to travel to the EU, and may create confusion among the travelling public.

According to the proposal for a recommendation of the Council of the European Union, "*a coordinated approach among Member States requires joint efforts on the following key points: the application of common criteria and thresholds when deciding whether to introduce restrictions to free movement, a mapping of the risk of COVID-19 transmission based on an agreed colour code, and a coordinated approach as to the measures, if any, which may appropriately be applied to persons moving between areas, depending on the level of risk of transmission in those areas*" (4).

The purpose of this report is to describe the feasibility, the prerequisites and the potential approaches for implementing a common testing strategy at airports in the EU which can be used within strategies to re-launch the transport sector, and specifically the aviation sector.

2.2. Evidence about the effectiveness of SARS-CoV-2 testing at borders

Screening measures on travellers at airports have been applied in response to the COVID-19 pandemic by many countries worldwide (3, 5). Screening may involve body temperature measurement, visual checks for symptoms, assessment of exposure to COVID-19 cases and laboratory testing of clinical specimens.

During August and September 2020, targeted laboratory testing conducted at points of entry in 396,624 incoming travellers to Greece by reverse transcriptase polymerase chain reaction (RT-PCR) identified 1,332 COVID-19 cases (3.4 per 1000 RT-PCR tests) (6). In Norway, 8,607 persons have been tested by PCR at airports; of those 20 have been positive since August (Governmental press conference 25/08). In Lithuania, 3,354 incoming travellers were tested at airports and 57 COVID-19 cases were identified; 9,033 incoming travellers were tested at ports and 16 COVID-19 cases were identified (Personal communication, 15 October 2020). One airport in Central Europe had a rate of up to 1.1% of positive PCR-results from tourists returning home (Personal communication, 13 October 2020).

European Centre for Disease Prevention and Control (ECDC) guidelines for the implementation of non-pharmaceutical interventions against COVID-19, after considering modelling studies suggested that "*targeted screening of travellers from areas of high community transmission at points of entry, with laboratory tests for active infection (PCR or antigen detection) at destination airports, appears to yield notable numbers of cases*" (7).

Responses to the enquiry made by ECDC in July 2020 to the extended network of 53 countries within the EU/EEA and UK, as well as select non-EU countries included the following (8): "*Luxembourg has a large cross-border commuter population with over 200 000 incoming travellers every day. The objective of testing commuters at entry sites (airport, stations, and international entry points) was to identify cases and control the epidemic. Cross-border workers accounted for 16% of infections, with limited evidence of spread in the workplace setting itself. The Republic of Korea also performs temperature screening and testing of all incoming travellers on Day 3 and Day 14 of mandatory quarantine. Some travellers have been found positive on Day 14. Based on preliminary analysis, the proportion of asymptomatic cases confirmed among travellers is lower than the proportion of asymptomatic cases in community outbreaks and further analysis is ongoing to determine the underlying factors. Cases in travellers tended to be in younger age groups than cases in the general population. There is an ongoing evaluation of the results of this testing strategy"* (8).

In conclusion, there are currently limited data available to allow for assessment of the effectiveness of COVID-19 testing strategies at points of entry. Testing incoming travellers can identify a proportion of infectious cases, preventing introduction and further spread to the receiving country to some extent. If testing takes place before travelling, then further spread will be prevented during travel at the points of entry (ports, airports, ground crossings) and on board conveyances (airplanes, ships, means of ground transportation); moreover, contact tracing and quarantine of contacts' co-travellers will not be necessary. The benefits and limitations of testing approaches are described in paragraph 2.4 and in Table 1.

2.3. Legal issues about SARS-CoV-2 testing at borders

2.3.1. IHR, WHO temporary recommendations and costs

The World Health Organization (WHO) currently has not included laboratory testing at borders as a condition of entry in the list of temporary recommendations.

Despite this, countries have the right to perform SARS-CoV-2 testing to incoming travellers at borders as an additional health measure and provided that the related provisions of IHR Article 43 are implemented. According to IHR Article 23, countries may require for public health purposes, on arrival or departure a non-invasive medical examination. Moreover, on the basis of evidence of a public health risk obtained through the previously mentioned measures provided on arrival or departure, "…States Parties may apply additional health measures, in accordance with IHR, in particular, with regard to a suspect or affected traveller, on a case-by-case basis …".

According to IHR Article 40 *"No charge shall be made by a State Party for: any medical examination under IHR, or any supplementary examination which may be required by that State Party to ascertain the health status of the traveller examined. No charge shall be made by a State Party for: appropriate isolation or quarantine requirements of travellers; any certificate issued to the traveller specifying the measures applied and the date of application..."*. Therefore, in regards to payment for laboratory tests conducted, it seems that payment should not be made by a traveller to a State Party for laboratory testing, however, IHR Article 40 further states that "*Nothing in IHR shall preclude States Parties from seeking reimbursement for expenses incurred in providing the health measures in paragraph 1 of this Article: (a) from conveyance operators or owners with regard to their employees; or (b) from applicable insurance sources*".

2.3.2. EU legislations and obligations for consulting and reporting of public health measures among the EU MS

According to Article 4 of Decision 1082/2013/EU, MS and the European Commission shall consult each other within the Health Security Committee (HSC) to coordinate their efforts to: develop, strengthen

and maintain their capacities for the monitoring, early warning and assessment of, and response to, serious cross-border threats to health.

According to Articles 9 and 11 of Decision 1082/2013/EU, where a Member State intends to adopt public health measures to combat a serious cross-border threat to health (fulfilling criteria to notify an alert to EWRS), it shall, before adopting those measures, inform and consult the other Member States and the Commission on the nature, purpose and scope of the measures, unless the need to protect public health is so urgent that the immediate adoption of the measures is necessary.

2.4. Possibility for a common testing strategy at airports in EU MS - benefits and limitations

WHO has not issued a temporary recommendation about laboratory testing of travellers at borders as a condition of entry/exit to/from countries, nor mandatory quarantine of all incoming travellers without prior case-by-case assessment for exposure (9). ECDC, in the current epidemiological situation does not recommend that travellers should be systematically tested when crossing internal or external administrative borders (10). However, ECDC describes a proposed testing approach with the specific objective and for an exceptional situation, when a country or region has achieved consistent sustained control of the virus, as demonstrated by the effective implementation of population-based surveillance described above (10).

For the reasons described in paragraph 2.1 “Problem analysis”, a common laboratory testing strategy for COVID-19 at airports in EU MS can be decided as a supplementary measure to information strategies, epidemiological investigation, contact tracing, isolation of confirmed cases and quarantine of contacts and laboratory support, in order to achieve a comprehensive case/outbreak management response (11). Laboratory testing should be considered as an attempt to facilitate the safe start of lifting travel restrictions at the external borders of EU MS, as well as restrictions of movement between the EU MS. However, since laboratory testing at borders cannot detect incubating travellers, has several limitations (Table 1) and the residual risk for introduction of new cases in one country is still considerable, essential prerequisites (see paragraph 3.1) must be in place and strictly implemented before determining and setting up laboratory testing for incoming travellers.

Table 1: Benefits and limitations of a common laboratory testing strategy for COVID-19 at airports in EU MS

Benefits	Limitations
- Identify a proportion of infectious travellers and prevent introduction of new cases to a country and/or transmission during transportation - Ensure mutual recognition of test results conducted in one EU MS by the other EU MS, and avoid repetition of testing the same traveller more than one time during the journey and avoid unnecessary costs - Help to avoid unnecessary disruption of the free movement of citizens in EU MS - Ensure safe start of lifting the travel restrictions at the external borders of EU MS - Avoid confusion caused by different requirements for testing of travellers from third countries who travel to EU MS - Ensure contact tracing of confirmed cases identified by obtaining contact information of travellers through the Passenger Locator Form - Facilitate rapid and appropriate isolation, and if needed clinical care for infected travellers - Relieve political and social pressure, and limit negative economic consequences from travel and trade restrictions - Link the traveller with public health authorities to facilitate health monitoring and prompt referral for care if they became ill - Help to avoid major economic and social impacts of a possible future bankruptcy of airlines and related sectors - Discourage ill persons from travelling - Preserve public confidence and reduce the fear of becoming infected while travelling	- Unable to detect individuals incubating the disease during the phase when the virus is not detectable - False sense of security to people tested negative, resulting in non-compliance with personal protection and hygiene measures (use of masks, hand washing, social distancing etc.) - Limitations of the laboratory technique (sensitivity) - Limitations/difficulties of the sampling procedure - Highly resource demanding - Countries may divert resources from other essential activities

3. Potential approaches for implementing common laboratory COVID-19 testing strategies at airports in EU MS

3.1. Essential measures in place as prerequisites for laboratory testing

Laboratory testing of incoming travellers is unable to detect individuals incubating the disease during the phase when the virus is not detectable. Moreover, laboratory testing may give a false sense of security to people tested negative, resulting in their non-compliance with personal protection and hygiene measures (use of masks, hand washing, social distancing etc.). Furthermore, laboratory results should be interpreted with caution since a small proportion of false negative and false positive results may occur (see paragraph 4 and the Annex) (12).

Before deciding on and implementing laboratory testing, the following measures must be in place and strictly implemented:

i. Communication strategy targeting incoming travellers and informing them about: a) recognition of the signs and symptoms compatible with COVID-19; b) procedures that should be followed when a traveller displays signs and symptoms indicative of COVID-19 (i.e. self-isolation, contact number to report to authorities and arrange laboratory testing) and any possible consequences of non-compliance according to the country rules and regulations; c) rules/advice applied to the country of destination regarding social and physical distancing measures, use of face masks; d) appropriate hand hygiene, respiratory etiquette and avoidance of touching the eyes, nose or mouth with hands, waste disposal; e) avoid being in public crowed places and limit contact with other persons.

ii. Comprehensive follow-up of incoming travellers tested negative by advising departing travellers who have been tested to report any symptoms to local public health authorities. If the testing is conducted on arrival, all travellers should be provided with an emergency phone number in case symptoms develop. A relevant case management protocol should be followed in case of a positive test (12). Travellers should self-monitor for the potential onset of symptoms on arrival for 14 days, report symptoms and travel history to local health facilities and follow national protocols (12).

iii. If a person develops symptoms upon arrival at the destination, testing, diagnosis, isolation and contact tracing should take place in accordance with local practice, and entry should not be refused. For contact tracing purposes, information about cases detected upon arrival should immediately be shared with public health authorities of countries where the person concerned resided during the period they were infectious, using the Early Warning and Response System (EWRS) (4).

iv. Member States should provide relevant stakeholders and the general public with clear, comprehensive and timely information about any restrictions to free movement, any accompanying requirements (for example negative tests for COVID-19 infection or Passenger Locator Forms), as well as the measures applied to travellers travelling from higher risk areas, as early as possible before new measures come into effect (4). As a general rule, this information should be published 24 hours before the measures come into effect, taking into account that some flexibility is required for epidemiological emergencies (4). In particular, Member States should as quickly as possible, inform the public of any newly introduced or lifted restrictions, communicated to other Member States and the Commission (4). This information should also be made available on the 'Re-open EU' web platform, which should contain a cross-reference to the map published regularly by ECDC (4). The substance of the measures, their geographical scope and the categories of persons to whom they apply should be clearly described.

v. A common European Passenger Locator Form should be developed for possible use by Member States. Wherever possible, a digital option for passenger locator information should be used in order to simplify processing, while ensuring equal access to all citizens (4).

vi. Crowd control should be put in place to prevent transmission in areas where travellers congregate (12).

vii. Countries must follow the special considerations for travellers under the IHR (2005), including treating travellers with respect for their dignity, human rights and fundamental freedoms and minimizing any discomfort or distress associated with any health measures applied to them (12).

3.2. Public health objectives

At EU level, the public health objectives are to prevent introduction of new COVID-19 cases to the EU MS, to prevent transmission of the virus during travel on board aircrafts or at airports, and to ensure coordinated efforts among EU MS to prevent re-introduction into regions/countries with sustained control of the virus.

3.3. Targeting the travelling population for testing for SARS-CoV-2

The Council of the European Union proposal for a recommendation seeks to ensure increased coordination among Member States considering the adoption of measures restricting free movement on grounds of public health. To limit restrictions to what is strictly necessary, Member States should, in a non-discriminatory manner and as much as possible, apply those restrictions to persons coming from specific areas or regions particularly affected rather than to the entire territory of a Member State (4).

The proposal for a recommendation further states that a coordinated approach among Member States requires joint efforts on the following key points: the application of common criteria and thresholds when deciding whether to introduce restrictions to free movement, a mapping of the risk of COVID-19 transmission based on an agreed colour code, and a coordinated approach as to the measures, if any, which may appropriately be applied to persons moving between areas, depending on the level of risk of transmission in those areas (4). Restrictions on free movement should only be considered when Member States have sufficient evidence to justify such restrictions in terms of their benefit for public health and they have reasonable grounds to believe that the restrictions would be effective (4). To limit the disruption to the internal market and family life while the pandemic is on-going, travellers with an essential function or need, such as workers or self-employed persons exercising critical occupations, cross-border workers, transport workers or transport service providers, seafarers, and persons travelling for imperative business or family reason, including members of cross-border families travelling on a regular basis, should not be required to undergo quarantine.

Member States could require persons entering their territory to submit Passenger Locator Forms in accordance with data protection requirements. A common European Passenger Locator Form should be developed for possible use by Member States. Wherever possible, a digital option for passenger locator information should be used in order to simplify processing, while ensuring equal access to all citizens. Decisions about the travellers to be tested could be made based on the information recorded in the Passenger Locator Form, regarding the areas that travellers have stayed in or passed through in the 14 days prior to travel.

Taking the above into consideration the working group suggests the approach described in Table 2 to targeting the travelling population (internally in the EU MS as well as travellers from third countries outside the EU) for laboratory testing, in addition to any traveller detected at a point of entry or on

board an aircraft with COVID-19-compatible symptoms, or any traveller who had been in contact with a confirmed COVID-19 case at any point in the previous 14 days.

3.4. Timing of testing

The timing of testing can determine the probability of detecting an infected traveller in the infectious phase. Testing can take place before travelling or upon arrival at the destination airport, or for travellers coming from outside of the EU, upon arrival at the first airport in an EU MS. Each option has advantages and limitations. Table 3 presents the advantages and disadvantages of each method.

Timely notification of laboratory results should be available via automated processes, mobile apps, and/or other electronic means (10).

3.5. Proof of laboratory testing

To avoid each traveller being tested more than once by different authorities during the same journey, the traveller should be provided a paper version or an electronic version of the test conducted and the test results, which can be demonstrated to the arriving country. It is preferable for the laboratory test result document to be available in the English language as well. Methods for authentication are needed to ensure that the document demonstrated is valid and authentic.

4. Testing technology for SARS-CoV-2

The available testing technology for SARS-CoV-2 includes: a) the reverse transcriptase polymerase chain reaction (RT-PCR) that detects the RNA of the virus; b) the antigen tests that detect the presence of the viral antigen and c) the antibody tests that detect the presence of antibodies generated against SARS-CoV-2. This category has not been described in this paragraph since there are uncertainties about the immune response to SARS-CoV-2 (e.g. duration of human antibodies), as well as the performance of available specific antibody testing methods (laboratory based and point-of-care); therefore, antibody tests cannot be used at this point for inclusion or exclusion of a traveller.

4.1. Nucleic acid tests

RT-PCR can be used to detect on-going infection and it is the method accepted by WHO to consider a COVID-19 case as confirmed. Results of the test are available within a few hours, however the cost is much higher than the antigen test.

4.2. Antigen tests

SARS-CoV-2 Ag-RDTs that meet the minimum performance requirements of ≥80% sensitivity and ≥97% specificity compared to a NAAT reference assay(1) can be used to diagnose SARS-CoV-2 infection in a range of settings where NAAT is unavailable, or where prolonged turnaround times preclude clinical utility. 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 the onset of symptoms (13).

Testing 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 (17), though in this situation a negative Ag-RDT should not exclude a close contact from quarantine requirements (13).

According to WHO, use of Ag-RDTs is not recommended in settings or populations with low expected prevalence of disease (e.g. screening at points of entry including airports, blood donation, elective

surgery), especially where confirmatory testing by NAAT is not readily available. Such use will not be possible until more data from high-quality studies is available confirming high specificity (>99%) of one or more of the commercialized Ag-RDT test kits (13).

The antigen (rapid) test format is based on the detection of viral protein in respiratory sample materials. Fluorescence- or chemiluminescence-based tests, which require an evaluation device, as well as lateral flow tests for immediate visual evaluation, are currently available in the point-of-care format.

If defined requirements are met, antigen tests can represent a useful addition to the existing SARS-CoV-2 PCR test where an initial (pre-) decision about the possible existence of a transmission-relevant early phase of the infection in a person is possible (14). For example, if the antigen test is positive the person should be considered infectious; if it is negative, the person should be considered non-infectious, but not necessarily non-infected. It is also noteworthy to recognize that in the early phase of an infection, antigen tests will not indicate the infection for a very short time, possibly for a day or so, while PCR would.

The prerequisite for this is a sensitivity of the antigen test that indicates an infection from the beginning of the (transmission-relevant) excretion of the virus to the end of the contagiousness of the person concerned. The results of comparative studies (PCR / AG test / virus cultivation; minimum Positive Percent Agreement; minimum Negative Percent Agreement) or clinical studies in the test's practical application are decisive regarding this.

Due to the test principle, antigen tests' analytical sensitivity is usually below the analytical sensitivity of PCR, which is considered the reference method. Information on how sensitively an antigen test detects viral proteins and further information on protein concentration (pg / µl) or on infectious particles (tissue culture infection dose 50, TCID50; plaque forming units, PFU) are used. The clinical validation must meet a number of requirements according to the *WHO Instructions and requirements for Emergency Use Listing (EUL) submission guidelines (13)*. Independent validations of antigen tests are currently being carried out at several centers, the results of which are publicly available (see Foundation for Innovative Diagnostics: https://www.finddx.org).

For quality-assured diagnostics, it will be necessary to routinely perform appropriate quality controls for antigen detection (detection of SARS-CoV-2 or selected virus proteins, e.g. using antigen-POCT) and for the indirect detection of anti-SARS-CoV-2 antibodies to be included in diagnostics. Calibrants which contain the virus/antigen or the antibody in a buffer solution in a defined concentration/number of particles are often used as QC controls. To check for possible matrix effects, e.g. the influence of components of the test material on the detection method, matrix reference materials are used that contain the named analytes in the real matrix (e.g. virus/antigen or antibodies in serum or other clinical matrices) (15).

WHO has recently received two EUL submissions for two immunochromatographic tests for rapid qualitative detection of the SARS-CoV-2 virus antigen. The Panbio COVID-19 Ag Rapid Test Device (Nasopharyngeal) manufactured by Abbott Rapid Diagnostics Jena GmbH and the STANDARD Q COVID-19 Ag Test manufactured by SD Biosensor, Inc. Both are rapid, visually-read antigen detection assays, which do not require a specialized reader for result interpretation. Both products are intended for the qualitative detection of SARS-CoV-2 antigen (Ag) in human nasopharyngeal swab specimens.

4.2.1. Panbio™ COVID-19 Ag Rapid Test Device

Abbott claims the following sensitivity and specificity vs PCR using Nasopharyngeal swabs for its Panbio™ COVID-19 Ag Rapid Test Device, based on a clinical study performed by Abbott in the following population: 241 individuals, including 60 PCR-positives and 181 PCR-negatives:

Sensitivity: 93.3% (98.2% for samples with Ct values ≤33)

Specificity: 99.4%

A study by Linares et al. (16) published as preprint, including 185 symptomatic and 72 patients compared the Panbio™ COVID-19 Ag Rapid Test with RT-PCR Allplex SARS-CoV-2 assay (Seegene, Seoul, South Korea). The authors found that the Panbio™ COVID-19 AG Rapid Test Device can rapidly identify SARS-CoV-2-infected individuals with moderate to high viral loads.

They found that out of 60 (23.5%) positive RT-qPCR samples and 44 (17.2%) were detected by the Panbio™ COVID-19 Ag Rapid Test. Overall, amongst the 60 positive samples, the Ct value was detected for gene N in 53 samples. For samples with Ct < 25 (n = 33), <30 (n = 7), <35 (n = 2) and <40 (n=1), Panbio™ COVID-19 Ag Rapid Test had a sensitivity of 100%, 87.5%, 25% and 25% respectively. The overall sensitivity in this study population is 73.3% (95% IC: 62.2–83.8). Considering only symptomatic patients with less than seven days since onset, Panbio™ COVID-19 Ag Rapid Test reaches a sensitivity of 86.5% (95% CI: 75.0-97.0).

4.2.2. STANDARD Q COVID-19 Ag Test

According to SD Biosensor, Inc.: The prospective diagnostic evaluation of STANDARD Q COVID-19 Ag Test was conducted by FIND with collaborators in Germany and Brazil with a total number of enrolled individuals of 1659. The sensitivity and specificity of the STANDARD Q COVID-19 Ag Test was compared to the site-specific RT-PCR method. The pooled sensitivity in Germany was 76.6% (62.8-86.4%) and the pooled specificity was 99.3% (98.6-99.6%). The sensitivity observed in the testing clinic in Brazil was at 88.7% (81.3-93.4%) and the pooled specificity was 97.6% (95.2-98.8%). (https://www.who.int/diagnostics_laboratory/eual/eul_0563_117_00_standard_q_covid19_ag_ifu.pdf?ua=1)

However, in other documentation by SD Biosensor based on 115 positive samples from Brazil and India (https://www.aidian.eu/uploads/NO-Dokumenter-og-materiell/ES-Products/SD-Biosensor/9159-01NO-SD-Biosensor-Standard-Q-COVID-19-Ag-Rapid-Test-IFU-copy-NO-version-out-of-ES-original_web.pdf) a sensitivity of 96.52% (95% CI: 91.33 – 99.04%) and a specificity of 99.68% (95% CI: 98.22 – 99.99%) were reported.

5. Resources needed and practical arrangements at airports

Testing measures for SARS-CoV-2 as part of public health measures at the airports requires detailed planning, with careful execution to ensure consistent application by all staff involved and to all targeted travellers (11). The timing, testing methods, technology and tools, human resources and training issues should be considered in preparedness and response plans. Training of staff is an important component especially with regards to specimen collection and the laboratory testing.

Appropriate space must be available at the facilities of the airport as required by the IHR 2005. Further essential resources include capacities for laboratory diagnosis, quarantine, isolation and treatment of possible, exposed or affected travellers. Laboratory testing should be part of a broader set of measures. Both the public and the private sectors, the transport industry, airport administrations and actors at all levels, from the local point of entry to the national, EU and international level should be involved.

Other issues for consideration are the methods for targeting travellers through the Passenger Locator Forms and/or review of itineraries.

Suggested practical arrangements for implementing different options of testing travellers at airports including triage, identification of passengers' orientation, and setting up corridors according to the risk zones (green, red, orange/grey) are presented in Table 4. Adequate resources should be available to ensure timely and accurate results including staff, laboratory reagents, safe pretesting of storage equipment and maintenance of laboratory equipment (14). Changes to the airport infrastructure will be needed in order to conduct triage of incoming travellers and set up "corridors" depending on the orientation of travellers (Table 4). If laboratory testing will be conducted at airports, then biosafety rules should be applied in regards to training and practices of staff, as well as space arrangements and set up of equipment.

6. Conclusion

To date, published data are only available for a few antigen assays (16-18). Data on the performance of the antigen tests for practical use in asymptomatically infected or pre-symptomatic persons are not yet available. Before independent validation studies are carried out, use of antigen tests in these groups of people should be interpreted very carefully, as the meaning of a negative finding is unclear. However, for the reasons analysed previously and considering the available data and the benefits and limitations presented in Table 1 and Table 3, until additional evidence becomes known, the working group recommends the following approach for the type of testing (Table 2).

For countries belonging to the "orange" category, there are two options: a) not to perform any test or b) optionally to perform antigen rapid testing using the technology recorded in the WHO list of Emergency Use Listing products eligible for procurement (19), and any positive results to be confirmed by RT-PCR. Prevalence of COVID-19 in areas fulfilling the "orange" category is not high and therefore, the number of positive infectious cases that will be missed is expected to be low. The cost of antigen rapid tests is considerably lower than RT-PCR. It should be noted that the Positive Predictive Value (PPV) will be low due to the low prevalence of the disease and the specificity of the antigen test around 98%, and for this reason we recommend the confirmation of the positive results with RT-PCR. However, the Negative Predictive Value (NPV) is close to 100%, which means that those who will be allowed to travel are really negative/healthy (see Annex).

For areas under the "red" category where prevalence of COVID-19 is expected to be higher, it is recommended to perform RT-PCR testing that has high sensitivity, in order to ensure that as far as possible, all infectious COVID-19 cases will be detected. Examples of calculating the expected numbers of sensitivity, specificity, PPV and NPV among travellers who are coming from areas with different prevalence of COVID-19 are provided in the Annex.

Pooling of five samples from asymptomatic persons per pool before RNA extraction and RT-PCR amplification could be considered (according to the guidance provided from international organizations) after proper validation in the laboratory. This can increase testing capacity with existing equipment. If there is a positive result from a pooled sample then PCR must be repeated for the individual samples within this pool to identify the infected person(s), thus potentially substantially reducing the number of tests needed (20).

Table 2: Suggested approach for targeting the travelling population for testing for SARS-CoV-2

Epidemiological criteria in the area where incoming persons to the EU MS stayed 14 days prior to travel		Target population*	Type of laboratory test	Timing
(a) green	if the 14-day cumulative COVID-19 case notification rate is less than 25 and the test positivity rate of tests for COVID-19 infection is less than 4%	No testing recommended	Not applicable	Not applicable
(b) orange	if the 14-day cumulative COVID-19 case notification rate is less than 50 but the test positivity rate of tests for COVID-19 infection is 4% or more, or, if the 14-day cumulative COVID-19 case notification rate ranges from 25 to 150 but the test positivity rate of tests for COVID-19 infection is less than 4%	No testing recommended OR Optionally all incoming travellers from orange areas	No testing recommended OR Optionally antigen rapid test using technology recorded in the WHO list of Emergency Use Listing products eligible for procurement (19). Any positive antigen rapid test result should be confirmed by RT-PCR.	For travellers travelling between the EU MS: when starting the journey at the departing airport For travellers traveling to an EU MS from a third country: a) optionally within 24-72 hours before departure; b) obligatory when first arriving at the airport (transit or final destination) of an EU MS
(c) red	if the 14-day cumulative COVID-19 case notification rate is 50 or more and the test positivity rate of tests for COVID-19 infection is 4% or more, or if the 14-day cumulative COVID-19 case notification rate is more than 150 per 100 000 population	All incoming travellers from red areas	Testing by RT-PCR	
(d) grey	if insufficient information is available to assess the criteria in points (a) to (c) or if the testing rate is 300 or less COVID-19 tests for infection per 100 000 population	All incoming travellers from grey areas	Depending on the available resources, RT-PCR or antigen rapid test using technology recorded in the WHO list of Emergency Use Listing products eligible for procurement (19). Any positive antigen rapid test result should be confirmed by RT-PCR.	

*Persons coming from specific areas or regions particularly affected rather than to the entire territory of a Member State

Table 3: Options for timing of laboratory testing of travellers, including advantages and limitations

Option	Advantages	Limitations
Testing travellers (intra and extra EU) at the country of origin and before starting travel (at the airport or in the laboratory in the community 24-72h before travel)	- Quarantine burden for the receiving country will be avoided since the infectious traveller can be quarantined at home - Any possible transmission during the journey on board aircrafts or at the airport will be prevented - Contact tracing of co-travellers on the same airplane/s and quarantine of contacts' co-travellers will be avoided - Detection of a proportion of incoming infectious travellers, isolation and treatment, and prevention of introduction of new cases in the receiving country/area	- The traveller may be incubating the disease during the phase where SARS-CoV-2 is not detectable at the time of testing, but may become infectious during travel - Testing should take place at reliable accredited laboratories, but this is difficult for the destination country to verify - The country of origin may not have the laboratory capacity to test outgoing travellers - The traveller may be exposed to the virus after the test has been performed and become infectious during travel at the destination country
Testing travellers (intra and extra EU) upon arrival at the final destination airport	- Detection of a proportion of incoming infectious travellers, isolation and treatment, and prevention of introduction of new cases in the receiving country/area	- Highly resource demanding for the country - Requires capacities for case and contact management - The traveller may be infectious and transmit the disease in the timeframe waiting for the laboratory results - The traveller might be infectious during travel and contact tracing will be essential - A number of positive travellers will not be detected if they are in the incubation period

Table 4: Suggested practical arrangements for implementing different options of testing travellers at airports

Option about timing of testing	Triage of passengers	
	How to get information about orientation of passengers	Setting up "corridors"* according to the risk zones (green, orange, red, grey)
Testing travellers (intra and extra EU) at the country of origin and before starting travel (at the airport or in the laboratory in the community 24-72h before travel)	Information about the countries visited/stayed in during the previous 14 days can be obtained through: 1. Digitised Passenger Locator Form (dPLF) The traveller can complete a European dPLF before going to the departing airport. If a QR code is used, then by scanning the QR code the information about the country zone can be obtained and the traveller can be guided to the respective corridor for testing or asked to provide proof of laboratory testing. 2. Hard copy Passenger Locator Form (PLF) The traveller can complete a PLF before going to the departing airport. Once arriving at the airport, the completed PLF can be reviewed and depending on the countries stayed/visited, the traveller can be guided to the respective corridor for testing or providing proof of laboratory testing. 3. Interview/ form Interviewing or asking the passenger to complete a form at the entrance of the airport and before checking in. Depending on the replies, the traveller can be guided to the respective corridor for testing or providing proof of laboratory testing.	Corridor 1: symptomatic travellers guided to isolation facility Corridor 2: passengers from red and grey zones guided to the airport facilities for laboratory testing; if tested positive then they will be guided to the isolation facility, if tested negative they will be given instructions as per paragraph 3.1 for comprehensive follow-up and then continue their travel Corridor 3: passengers from orange zone guided to the airport facilities for laboratory testing; if tested positive then they will be guided to the isolation facility, if tested negative they will be given instructions as per paragraph 3.1 for comprehensive follow-up and then continue their travel Corridor 4: passengers from green zone continue their travel or passengers who have valid proof of laboratory testing continue their travel
Testing travellers (intra and extra EU) at the airport upon arrival at	Information about the countries visited/stayed in during the previous 14 days	Corridor 1: symptomatic travellers guided to isolation facility

the final destination airport	can be obtained through: 1. Digitised Passenger Locator Form (dPLF) The traveller can complete a European dPLF before going to the departing airport. If a QR code is used, then by scanning the QR code the information about the country zone can be obtained and the traveller can be guided to the respective corridor for testing. 2. Hard copy Passenger Locator Form (PLF) The traveller can complete a PLF before boarding the airplane. Once arriving at the destination airport, the completed PLF can be reviewed and depending on the countries stayed/visited, the traveller can be guided to the respective corridor for testing. 3. Interview/ form Interviewing or asking the passenger to complete a form once on board and present to authorities after disembarking at the destination airport. The traveller depending on the replies can be guided to the respective corridor for testing.	Corridor 2: passengers from red and grey zones guided to the airport facilities for laboratory testing; if tested positive then they will be guided to the isolation facility, if tested negative they will be given instructions as per paragraph 3.1 for comprehensive follow-up and then continue their travel Corridor 3: passengers from orange zone guided to the airport facilities for laboratory testing; if tested positive then they will be guided to the isolation facility, if tested negative they will be given instructions as per paragraph 3.1 for comprehensive follow-up and then continue their travel Corridor 4: passengers from green zone continue their travel

Measures at "corridors"* according to the risk zones

- Travellers should be given clear instructions about the measures in place.
- Travellers should be guided to the respective corridor after triage, and monitored until exiting corridors 1,2,3.
- Any symptomatic traveller should be immediately transferred to the temporary isolation facility of the airport and should not wait together with other travellers at the airport.
- Crowd control should be put in place to prevent transmission and physical distancing should be maintained.
- Infection control measures must be in place.
- It is preferable to share any documents in an electronic format.

* The term "corridor" is used to describe permanent or temporary portable/movable arrangements at the airport or just routeways that travellers need to pass after triage.

7. Annex

Examples of calculating the expected numbers of false negative infectious cases who are coming from areas with different cumulative COVID-19 case notification rates (red, orange and greenzones), and according to test performance criteria of sensitivity 80% and specificity 98%.

<table>
<tr><th>Indicators</th><th>Example 1
Area with cumulative COVID-19 case notification rate of 160/100,000 population</th><th>Example 2
Area with cumulative COVID-19 case notification rate of 50/100,000 population</th><th>Example 3
Area with cumulative COVID-19 case notification rate of 25 /100,000 population</th></tr>
<tr><td>True Positive (TP), False Positive (FP), True Negative (TN), False Negative (FN)</td><td>
<table>
<tr><th></th><th>Disease</th><th>No disease</th><th>Total</th></tr>
<tr><td>Test +</td><td>128 (TP)</td><td>1997 (FP)</td><td>2125</td></tr>
<tr><td>Test -</td><td>32 (FN)</td><td>97843 (TN)</td><td>97875</td></tr>
<tr><td>Total</td><td>160</td><td>99840</td><td>100000</td></tr>
</table>
</td><td>
<table>
<tr><th></th><th>Disease</th><th>No disease</th><th>Total</th></tr>
<tr><td>Test +</td><td>40 (TP)</td><td>1999 (FP)</td><td>2039</td></tr>
<tr><td>Test -</td><td>10 (FN)</td><td>97951 (TN)</td><td>97961</td></tr>
<tr><td>Total</td><td>50</td><td>99950</td><td>100000</td></tr>
</table>
</td><td>
<table>
<tr><th></th><th>Disease</th><th>No disease</th><th>Total</th></tr>
<tr><td>Test +</td><td>20 (TP)</td><td>2000 (FP)</td><td>2020</td></tr>
<tr><td>Test -</td><td>5 (FN)</td><td>97975 (TN)</td><td>97980</td></tr>
<tr><td>Total</td><td>25</td><td>99975</td><td>100000</td></tr>
</table>
</td></tr>
<tr><td>Positive predictive value</td><td>6.02%</td><td>1.96%</td><td>0.99%</td></tr>
<tr><td>Negative predictive value</td><td>99.97%</td><td>99.99%</td><td>99.99%</td></tr>
</table>

Examples of calculating the expected numbers of false negative infectious cases, who are coming from areas of the red and orange zones, assuming that the actual cumulative COVID-19 case notification rates are five times more than the reported rates (since sero-epidemiological studies have suggested five to ten times higher incidence than the notification rate (21)), and according to test performance criteria of sensitivity 80% and specificity 98%.

<table>
<tr><th>Indicators</th><th>Example 1
Area with cumulative COVID-19 case notification rate of 750/100,000 population</th><th>Example 2
Area with cumulative COVID-19 case notification rate of 250/100,000 population</th><th>Example 3
Area with cumulative COVID-19 case notification rate of 125 /100,000 population</th></tr>
<tr><td>True Positive (TP), False Positive (FP), True Negative (TN), False Negative (FN)</td><td>
<table>
<tr><th></th><th>Disease</th><th>No disease</th><th>Total</th></tr>
<tr><td>Test +</td><td>600 (TP)</td><td>1985 (FP)</td><td>2585</td></tr>
<tr><td>Test -</td><td>150 (FN)</td><td>97265 (TN)</td><td>97415</td></tr>
<tr><td>Total</td><td>750</td><td>99250</td><td>100000</td></tr>
</table>
</td><td>
<table>
<tr><th></th><th>Disease</th><th>No disease</th><th>Total</th></tr>
<tr><td>Test +</td><td>200 (TP)</td><td>1995</td><td>2195</td></tr>
<tr><td>Test -</td><td>50 (FN)</td><td>97755</td><td>97805</td></tr>
<tr><td>Total</td><td>250</td><td>99750</td><td>100000</td></tr>
</table>
</td><td>
<table>
<tr><th></th><th>Disease</th><th>No disease</th><th>Total</th></tr>
<tr><td>Test +</td><td>100 (TP)</td><td>1998 (FP)</td><td>2098</td></tr>
<tr><td>Test -</td><td>25 (FN)</td><td>97878 (TN)</td><td>97903</td></tr>
<tr><td>Total</td><td>125</td><td>99875</td><td>100000</td></tr>
</table>
</td></tr>
<tr><td>Positive predictive value</td><td>23.21%</td><td>9.11%</td><td>4.77%</td></tr>
<tr><td>Negative predictive value</td><td>99.85%</td><td>99.95%</td><td>99.97%</td></tr>
</table>

8. Reference list

1. Airports Council International, Airlines For Europe, International Air Transport Association. COVID-19 Testing and the Recovery of Travel & Tourism. Urgent need for a common EU Testing Protocol for Travel. 2020 1 October Report No.

2. European Union Aviation Safety Agency. Coronavirus COVID-19 2020 [cited 2020 11 October]. Available from: https://www.easa.europa.eu/the-agency/coronavirus-covid-19.

3. European Union. Re-open EU 2020 [cited 2020 11 October]. Available from: https://reopen.europa.eu/en.

4. Council of the European Union. Proposal for a Council recommendation on a coordinated approach to the restriction of free movement in response to the COVID-19 pandemic: - Presidency compromise text. Brussels: Council of the European Union, 2020 12 October 2020. Report No.: Contract No.: 2020/0256(NLE).

5. Mouchtouri VA, Bogogiannidou Z, Dirksen-Fischer M, Tsiodras S, Hadjichristodoulou C. Detection of imported COVID-19 cases worldwide: early assessment of airport entry screening, 24 January until 17 February 2020. Trop Med Health. 2020;48:79.

6. Organization HNPH. Reports for COVID-19: August and September 2020 [cited 2020 13 October]. Available from: https://eody.gov.gr/epidimiologika-statistika-dedomena/ektheseis-covid-19/.

7. European Centre for Disease Prevention and Control. Guidelines for non-pharmaceutical interventions to reduce the impact of COVID-19 in the EU/EEA and the UK. Stockholm: ECDC, 2020 24 September Report No.

8. European Centre for Disease Prevention and Control (ECDC). Population-wide testing of SARS-CoV-2: country experiences and potential approaches in the EU/EEA and the United Kingdom. . 2020 19 August. Report No.

9. World Health Organization. COVID-19 IHR Emergency Committee 2020 [cited 2020 17 October]. Available from: https://www.who.int/groups/covid-19-ihr-emergency-committee.

10. European Centre for Disease Prevention and Control. COVID-19 testing strategies and objectives. Stockholm: ECDC, 2020 15 September Report No.

11. Mouchtouri VA, Christoforidou EP, An der Heiden M, Menel Lemos C, Fanos M, Rexroth U, et al. Exit and Entry Screening Practices for Infectious Diseases among Travelers at Points of Entry: Looking for Evidence on Public Health Impact. Int J Environ Res Public Health. 2019;16(23).

12. World Health Organization. Public health considerations while resuming international travel. 30 July 2020. COVID-19 Travel Advice 2020 [cited 2020 17 October]. Available from: https://www.who.int/news-room/articles-detail/public-health-considerations-while-resuming-international-travel.

13. World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays. Interim guidance. 2020 11 September. Report No.

14. World Health Organization. Laboratory testing strategy recommendations for COVID-19. Interim guidance. . 2020 21 March 2020. Report No.

15. Zeleny R, Schimmel H. Influence of the approach to calibration on the accuracy and the traceability of certified values in certified reference materials. TrAC, Trends in analytical chemistry (Regular ed). 2012;33:107-16.

16. Linares M, Pérez Tanoira R, Romanyk J, Pérez García F, Gómez-Herruz P, Arroyo T, et al. Panbio antigen rapid test is reliable to diagnose SARS-CoV-2 infection in the first 7 days after the onset of symptoms. medRxiv. 2020:2020.09.20.20198192.

17. Diao B, Wen K, Chen J, Liu Y, Yuan Z, Han C, et al. Diagnosis of acute respiratory syndrome coronavirus 2 infection by detection of nucleocapsid protein. medRxiv. 2020.

18. Dinnes J, Deeks JJ, Adriano A, Berhane S, Davenport C, Dittrich S, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database Syst Rev. 2020;8:CD013705.

19. World Health Organization. In vitro diagnostics and laboratory technology. List of Emergency Use Listing products eligible for procurement 2020 [cited 2020 12 October]. Available from: https://www.who.int/diagnostics_laboratory/eual/listing/en/.

20. Lohse S, Pfuhl T, Berkó-Göttel B, Rissland J, Geißler T, Gärtner B, et al. Pooling of samples for testing for SARS-CoV-2 in asymptomatic people. The Lancet Infectious Diseases.

21. Bogogiannidou Z, Vontas A, Dadouli K, Kyritsi MA, Soteriades S, Nikoulis DJ, et al. Repeated leftover serosurvey of SARS-CoV-2 IgG antibodies, Greece, March and April 2020. Eurosurveillance. 2020;25(31):2001369.

Working group members

Barbara Mouchtouri[1], Martin Dirksen-Fischer[2], Jörn Klein[3], Mauro Dionisio[4], Katarina Bitenc[5] Brigita Kairiene[6], , Janusz Janiec[7], Sotirios Tsiodras[8], Christos Hadjichristodoulou[1]

1. Laboratory of Hygiene and Epidemiology, Faculty of Medicine, University of Thessaly, Larissa, Greece
2. Institute for Hygiene and Environment of the Hamburg State Department for Health and Consumer Protection, Hamburg, Germany
3. University of South-Eastern Norway, Faculty of Health and Social Sciences, Department of Nursing and Health Sciences, Norway
4. Italian Ministry of Health, Rome, Italy
5. National Institute of Public Health, Ljubljana, Slovenia
6. National Public Health Centre under the Ministry of Health, Klaipeda, Lithuania
7. National Institute of Public Health-National Institute of Hygiene, Poland
8. National and Kapodistrian University of Athens, Medical School, Athens, Greece

For any questions or support related to the points of entry, please email info@healthygateways.eu