

ECDC TECHNICAL REPORT

Guidance for COVID-19 quarantine and testing of travellers

12 March 2021

Summary

Travel measures, such as quarantine and testing of travellers, are designed to reduce the likelihood of SARS-CoV-2 transmission prior to, during, and after travel. This document summarises the current scientific evidence to support decision-making with regard to quarantine and testing of travellers, taking into consideration the emergence of SARS-CoV-2 variants of concern (VOC) and the current epidemiological situation in the EU/EEA. ECDC will continue monitoring the epidemiological situation and this guidance will be updated with all relevant evidence accordingly.

- The further transmission of new VOCs to a geographical area may to some extent be delayed by reducing the movement of people i.e. by reducing non-essential travel. Travel measures, such as quarantine and testing, can help to further delay the importation and spread of the virus. However, once a VOC is established and widespread in a community, the impact of travel measures is limited.
- When deciding on the implementation of travel measures, countries should carefully weigh the expected public health benefit against the public health resources required to implement them and the socially and economically disruptive effects they may cause.
- To respond to the emergence of VOCs, ECDC recommends strengthening of all public health measures, including those relevant to travel, taking into account the epidemiological situation at both the points of departure and arrival. These strengthened measures should remain in place until very high vaccination coverage of high-risk groups and healthcare workers has been achieved, and sufficient sequencing capacity is in place for Member States to rapidly detect VOCs and take appropriate action to reduce the risk of their further spread.
- As a general measure, anyone who develops symptoms of COVID-19 or is in quarantine should refrain
 from travelling. In addition, at this stage of the pandemic, non-essential travel should be avoided as part
 of the non-pharmaceutical interventions (NPIs) designed to prevent crowding and delay the introduction
 and/or spread of VOCs.
- When travel measures are being considered, current evidence supports a combined approach to
 quarantine and testing of travellers i.e. a pre-departure test (or test directly upon arrival) combined with
 quarantine and a further test five to seven days after arrival to confirm the possibility of being released
 from quarantine if the test is negative.
- For individuals that have recovered from a laboratory-confirmed SARS-CoV-2 infection within 180 days prior to travel, it can be considered to ease quarantine and testing requirements. However, it is still unclear whether a prior infection with one variant protects against other variants.
- At this stage, it also remains uncertain whether vaccinated individuals are capable of transmitting the infection.
- It is therefore important that both individuals having recovered from a COVID-19 infection in the last 180 days and those who have been vaccinated continue to adhere to all other preventive measures, such as wearing a face mask and respecting the need for physical distancing during travel.

Suggested citation: European Centre for Disease Prevention and Control. Guidance for COVID-19 quarantine and testing options for travellers. 12 March 2021. ECDC: Stockholm; 2021.

Scope of this document

This document provides guidance based on scientific evidence regarding quarantine and testing of travellers in EU/EEA countries in the context of the emergence of SARS-CoV-2 variants of concern (VOCs). It follows the provisions of the Council Recommendation (EU) 2021/119 of 1 February 2021 amending Recommendation (EU) 2020/1475 on a coordinated approach to the restriction of free movement in response to the COVID-19 pandemic.

Target audience

This document is intended to support decision-makers in EU/EEA countries, including public health authorities and transportation authorities, in adopting strategies for the quarantining and testing of travellers at the current stage of the pandemic, and in light of the VOCs currently in circulation.

Context

In the context of SARS-CoV-2, one approach to delaying the introduction of the virus into new settings during the first stages of the pandemic was to recommend avoiding international, European, national and regional travel. However, once the virus has become established and widespread in a community such approaches (i.e. restricting travel) are considered to have limited impact.

As a general measure, travel should not be undertaken by people who are ill or who have had recent contact with COVID-19 cases. Furthermore, at the time of writing this guidance, ECDC recommends that non-essential travel should be avoided as one of several non-pharmaceutical interventions (NPIs) designed to prevent crowding and delay the introduction and/or spread of VOCs. In time, vaccination programmes will enable the easing of NPIs.

To respond to the emergence of VOCs that are not yet widespread in the community, ECDC recommends strengthening all public health measures in place. These measures should remain in place until very high vaccination coverage of high-risk groups and healthcare workers has been achieved, and Member States have sufficient sequencing capacity to rapidly detect VOCs and take appropriate action to reduce the risk of their further spread [1]. The actions adopted by Member States should include measures to reduce the risk of virus importation from travellers.

International/cross-border travel restrictions are regulated under the International Health Regulations (IHR) [2] and EU law. Free movement within the EU is one of the fundamental principles of the Treaty on the Functioning of the European Union [3]. Under both legal frameworks, public safety and health threats related to infectious disease outbreaks are considered reasonable grounds for countries to restrict free movement across borders.

In response to the COVID-19 pandemic, EU/EEA countries have implemented various travel-related measures to reduce the likelihood of SARS-CoV-2 transmission prior to, during, and after travel at the point of departure, on the conveyance itself, as well as at the points of entry. These measures include:

- individual-level and community level NPIs (e.g. physical distancing, hand hygiene, use of face masks, environmental cleaning, ventilation) [4-7];
- monitoring of symptoms before, during and after travel;
- quarantine of travellers;
- testing of travellers when leaving or entering an area or a country;
- management of travellers and their contacts when a positive case is identified.

To support EU/EEA countries, ECDC, the European Union Aviation Safety Agency (EASA), the European Maritime Safety Agency (EMSA) and the European Union Agency for Railways (ERA) have developed guidance on safe travel by promoting the implementation of NPIs and public health measures [8-11]. For more details on the national recommendations in place please see the ECDC-JRC response measures database [12] or ECDC's weekly Country Overview [13].

The travel measures adopted by EU/EEA countries in the context of the COVID-19 pandemic have varied significantly. Most EU/EEA countries have developed national criteria to determine the need for testing and/or voluntary or mandatory quarantine of incoming travellers. Due to the rapidly evolving epidemiological situation, travel measures have been modified frequently. Quarantine and testing of travellers can, however, only complement, and not replace, the necessary individual and community measures (such as NPIs, testing according to ECDC recommendations [14,15], contact tracing, isolation of cases and quarantining of their contacts). The effectiveness of entry screening methods, such as temperature screening and health questionnaires, is not supported by evidence [16].

The provision of timely information to travellers on the disease, the epidemiological situation in the destination country and the measures in place are all very important and should be part of an established risk communication strategy. This information can be delivered by the relevant travel companies in cooperation with public health authorities. Travellers using their own means of transport need to obtain the appropriate information before beginning

their journey. In addition, Passenger Locator Forms (PLFs), preferably in a digital format (dPLFs) are recommended as an important tool for facilitating prompt contact tracing in the destination country.

On 30 June 2020, the Council of the European Union adopted Recommendation (EU) 2020/912 on the temporary restriction on non-essential travel into the EU and the possible lifting of such restriction [17]. This Recommendation was amended on 2 February 2021 (2021/132) [18].

On13 October 2020, the Council of the European Union adopted Recommendation (EU) 2020/1475 on a coordinated approach to the restriction of free movement in response to the COVID-19 pandemic, aiming to avoid fragmentation and disruption, and to increase harmonisation, transparency and predictability for EU/EEA citizens and businesses [19]. This Recommendation was amended on 1 February 2021 by means of Council Recommendation (EU) 2021/119 [20], in light of the emergence of new VOCs and the observed increase in case incidence.

The updated Recommendation 2021/119 [20] provides a categorisation of geographical areas/countries based on the level of ongoing virus circulation and presence of VOCs. Based on these categories, the updated Recommendation presents travel measures according to the incidence at the place of departure and the place of arrival. It strongly discourages all non-essential travel, especially to and from high-risk areas, until the epidemiological situation has considerably improved, particularly in the light of the outbreak of new VOCs. It further highlights the need for a SARS-CoV-2 test before departure, combined with quarantine, for people travelling for non-essential purposes from areas where the virus is circulating at very high levels. The Recommendation also presents considerations for shortening the length of quarantine to five-to-seven days based on a negative test. It also addresses the issue of people travelling for essential versus non-essential purposes as well as those travelling to and from areas with different levels of virus circulation. For a detailed description of the recommended approaches please refer to the Council Recommendation [20].

At the time of writing, three VOCs with an important public health impact have already emerged and been described (P.1 first described in Brazil; B.1.351 first described in South Africa and B.1.1.7 first described in the United Kingdom). New VOCs derived from the previous ones will continue to emerge, be detected and characterised. The characterisation and epidemiological investigation of the VOCs is therefore essential to understand their transmissibility, virulence and impact on vaccine effectiveness [21,22]. The ability to identify and define the extent to which a VOC is spread in an area depends on the sensitivity and representativeness of surveillance systems with integrated sampling strategies for virus sequencing. This, in turn, depends on the sequencing capacity of the different EU/EEA countries. Other approaches, such as sequencing of convenience samples and sampling from clusters and outbreaks of SARS-CoV-2, provide complementary information, but cannot replace representative sampling in the community. As at the beginning of the COVID-19 pandemic in 2020, the emergence and further transmission of new VOCs to a geographical area may be delayed by a combination of strong surveillance systems and measures to reduce the spread through movement of people. Travel measures (as listed above), can therefore be an important part of the overall strategy to delay the importation and spread of VOCs. However, once a VOC is established in a community the impact of travel measures becomes limited. Furthermore, the VOCs currently circulating in the EU/EEA countries are characterised by increased transmissibility, and they may rapidly become the dominant circulating variant virus in the community they are affecting.

This document provides EU/EEA countries with scientific evidence on quarantining and/or testing of travellers, taking into account the overall ECDC advice to strengthen public health measures to delay the spread of VOCs. For further information on other travel-related measures please refer to other relevant ECDC guidance [4,8,9,11].

Travel-related risks in the COVID-19 pandemic, in light of VOCs

Travel-related SARS-CoV-2 introduction and tourism-related spread within the EU/EEA contributed substantially to the transmission across and within countries during the early phase of the COVID-19 pandemic [23-29]. As mentioned above, since late 2020, new VOCs have emerged and, as during the early phase of the COVID-19 pandemic, some of them have spread worldwide due to their increased transmissibility and the movement of people within and between countries.

Modelling studies assume that the prevalence of COVID-19 in travellers is close to that estimated in the general population and much lower than that in high-risk contacts of COVID-19 cases [30,31]. Given that individuals are restricted from travelling if they exhibit COVID-19-like symptoms prior to departure, or if they have been identified as a high-risk contact of a case, travellers could be considered as a non-symptomatic sub-population whose probability of being infected with COVID-19 is potentially lower, than that of the general population in the country of origin. With regard to limiting non-essential travel as a means of reducing the (re)-importation¹ of the virus and/or VOCs, modelling studies indicate that this approach will delay the importation [32]. The delay of importation can help in decreasing the level of virus transmission at the place of arrival, as long as other community-based NPIs and measures are in place. By decreasing the case load as well as the extent of community transmission, travel measures may subsequently be of value in reducing the burden on healthcare systems. As discussed above, travel measures for COVID-19 are unlikely to completely prevent the (re)-introduction of SARS-CoV-2 and/or VOCs in a community, with the exception of particular locations, such as island states.

Quarantine and testing of travellers

At this stage of the pandemic, quarantine and testing can be considered for travellers coming from areas with a high level of viral community transmission with the presence of one or more VOCs, in order to delay the importation and spread of these VOCs in an area where they are not widely circulating. Quarantine and testing can also be considered for travellers coming from areas with a high level of SARS-CoV-2 community circulation, but where the extent of VOC circulation is unknown.

Travel measures can play a role for cross-border travel or journeys at local and regional level. Depending on the epidemiological situation, national authorities could consider implementing similar measures at sub-national level. Monitoring the implementation and compliance with travel measures should be part of the response in any setting. Any travel-related measure should be based on the epidemiological situation in the countries/areas of departure and arrival [1].

Although when introducing travel measures it is important to consider their effectiveness, compliance with and acceptance of these measures also needs to be taken into account. Moreover, countries should carefully weigh the expected public health benefit against the public health resources required to implement such measures and the socially and economically disruptive effects they may cause.

When introducing travel measures, it is important to establish a functioning link with the local, regional, and/or national authorities, as well as the appropriate liaison with international health bodies, in order to ensure rapid referral and management of travellers and/or their contacts if they develop symptoms during travel, after arrival and/or test positive through the testing mechanism.

Finally, it is important to highlight that any quarantine and/or testing strategy leaves a residual risk of viral importation into an area or country. EU/EEA countries should assess the residual risk that they are prepared to accept, and subsequently manage potential imported cases accordingly at the national level and through their public health infrastructure (e.g. by testing suspected cases, contact tracing and isolation and provision of healthcare services).

Quarantine of travellers

At this stage of the pandemic, reducing and/or delaying the importation of virus variants is of the utmost importance in order to allow public health authorities to vaccinate the highest possible number of individuals at risk and healthcare workers. New VOCs will continue to emerge in the future and the identification and understanding of the extent to which a VOC is established in an area is linked to the area's capacity to identify VOCs.

In the absence of testing, the current evidence from modelling studies supports a quarantine period for travellers of 14 days upon arrival. This quarantine duration ensures that almost anyone infected upon arrival will not further transmit the virus at the place of arrival, assuming full compliance. Countries implementing quarantine of travellers can consider exploring quarantine monitoring measures, such as regular health checks, or follow-up calls, according to their national capacities.

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¹ (Re)-importation refers here to the re-importation of SARS-CoV-2 to geographical areas where the viral circulation in the community has been reduced to very low levels or the importation of VOCs to geographical areas where the VOCs are not yet circulating.

Compliance with the quarantine period will be of the utmost importance for the success of the measure. Although reducing the duration of quarantine could facilitate compliance, a balance between compliance and the residual risk of missing potential cases needs to be considered. Data on compliance with quarantine rules for travellers in EU/EEA countries are not readily available. Data on compliance with quarantine rules for contacts of cases shows low compliance in asymptomatic persons [33,34]. Moreover, there are currently no empirical data available on the effectiveness of shortened quarantine duration in the absence of testing. At this point, only modelling studies (some of which are still in pre-print) provide information on the effectiveness of different durations of quarantine, alone or in combination with testing, to prevent the importation of COVID-19 cases [35-37].

Testing of travellers

In the context of the COVID-19 pandemic, the testing of travellers before and/or after travel aims to identify individuals testing positive, in order to:

- prevent viral transmission during travel by reducing the number of potentially infectious cases in transit;
- delay the (re)-introduction and further spread at the place of arrival, by isolating positive travellers and initiating the tracing of contacts;
- monitor the introduction and further spread of VOCs at the place of arrival.

If testing for SARS-CoV-2 is implemented, the limited available evidence [1,10,38] currently supports a combination of pre-departure and post-arrival testing for travellers. Specifically:

1. A pre-departure test, at the earliest 48 hours before departure or at the point of departure. If this is difficult or not feasible (e.g. for short business or personal trips or for any non-residents at the place of departure), this could be replaced by a test performed immediately upon arrival at the destination, followed by contact tracing in the event of a positive test.

The rationale is the following:

- testing travellers at the earliest 48 hours before travel or at the point of departure allows for the identification of SARS-CoV-2-positive individuals, preventing their travel and thus preventing the risk of travel-related transmission. This would decrease the proportion of infectious cases in transit as well as at the place of arrival;
- testing directly upon arrival will identify individuals that might have been infectious in transit, allowing for rapid contact tracing [39] which would also help to prevent further community transmission at the place of arrival.
- 2. Testing five to seven days after arrival.

The rationale is the following:

• combined with quarantine, this would allow the quarantine period to be shortened (to five to seven days).

The best effect, as suggested in a recent pre-print modelling study, would be achieved by applying a combination of all the testing approaches – i.e. requiring a pre-departure test as well as a test directly upon arrival and followed by a test five to seven days after arrival in combination with quarantine (see below) [38]. However, the resources required for such an approach would be extensive, as would the social and economic disruption, and therefore any such approach would need to be carefully considered and balanced against the expected public health gain.

In addition to previous modelling studies [35-37], the recent pre-print modelling study mentioned above [38] showed how combining pre-travel and post-travel testing could reduce the risk of importation of SARS-CoV-2 by 40-66%, with the timing of testing playing an important role. As described below in the section 'Combination of quarantine and testing of travellers', the authors reported a further reduced risk of SARS-CoV-2 being introduced if testing were combined with symptom monitoring and quarantine of travellers.

Practical requirements for testing

To secure the expected quality of the test and for safety reasons, testing should always be conducted in accordance with the manufacturer's instructions. When testing is performed, trained healthcare staff, laboratory staff, and/or trained operators are needed to carry out sampling, testing, test analysis and to report test results to clinical staff and public health authorities at local, regional, national and international level. Furthermore, an established link and collaboration with public health authorities at all levels is required to ensure appropriate and immediate action when necessary. Professional sampling by trained personnel is particularly important in the context of testing with rapid antigen detection tests (RADTs), as these tests lack a control to indicate that sampling has been successful. Testing of travellers should take into account the availability and prioritisation of all prerequisite resources, including appropriate human resources.

Finally, implementing a testing procedure at any point of departure and/or entry will increase crowding, thus creating further opportunities for SARS-CoV-2 transmission. It is therefore crucial that the logistics for testing are carefully organised in order to ensure physical distancing among travellers and the protection of staff at all times.

Test validity

No diagnostic test has 100% sensitivity and 100% specificity. Test performance depends on factors such as the quality of the sample, the technical characteristics of the test, the prevalence of the infection in the target population, the timing of testing, the person's infection and immune status, and the transport of specimens [40].

Test performance characteristics (sensitivity/specificity) and the prevalence of COVID-19 in the target population (in this case, travellers) play a pivotal role in determining the validity (i.e. ability to detect true positives and true negatives) of the test results in different settings and for different purposes. In a low-prevalence population such as travellers, there will be individuals presenting false negative² and false positive³ results. This will have an impact on the transmission of SARS-CoV-2 and/or requirements for public health resources to manage individuals testing positive.

Testing methods used for the diagnosis of COVID-19 include molecular tests - e.g. reverse transcription polymerase chain reaction (RT-PCR) or reverse transcription loop-mediated isothermal amplification (RT-LAMP), and RADTs. Molecular tests detect SARS-CoV-2 genomic material in a sample and RADTs detect viral antigens. Further information on testing methods can be found in Annex 1.

It is important to underline that whilst RADTs and regular RT-PCR will detect a SARS-CoV-2 infection, they will not distinguish SARS-CoV-2 variants (including VOCs). Specialised RT-PCR tests are able to discriminate the presence of known variants and can be used if available. RADTs can help to reduce further transmission of SARS-CoV-2 or SARS-CoV-2 VOCs through early detection of highly infectious cases, enabling immediate isolation and the rapid commencement of contact tracing. At the time of writing this report, the UK had evaluated five RADTs (targeting the nucleocapsid protein) and they all detected cases that later on were identified as carrying the variant B.1.1.7/501Y.V1 [41]. Further validation of RADTs is needed to ensure that they also detect future/emerging variants.

To be able to confirm infection with a specific variant, sequencing of the whole SARS-CoV-2 genome, or at least whole or partial sections of the genome, is required. For an early detection and prevalence calculation of known VOCs, alternative methods can be valuable, such as using diagnostic screening PCR-based assays that generate results in a few hours, with subsequent verification/confirmation by sequencing.

Combination of quarantine and testing of travellers

Quarantine and testing of travellers are effective public health measures if implemented comprehensively and very early in the evolution of the epidemic. They can also be effective if implemented very soon after the emergence of VOCs, or when a country has consistently reduced the transmission in the community.

The combination of guarantine and testing of travellers aims to:

- prevent viral transmission during travel, by reducing the number of potentially infectious cases in transit;
- delay the (re)-introduction and further spread at the place of arrival, by isolating travellers who may become symptomatic or otherwise be infectious, during the quarantine and by triggering the tracing of contacts if symptoms or infection develop;
- monitor the introduction and further spread of VOCs at the place of arrival:
- reduce the time in quarantine to minimise its personal, social and economic impact.

When implementing a combined approach to quarantine and the testing of travellers, based on the evidence available through modelling studies, the best result with a reasonable balance of resource use and effectiveness, may be obtained by testing prior to departure or directly upon arrival, combined with quarantine and a further test five to seven days after arrival to enable release from quarantine if the test is negative⁴.

The rationale is the following:

- requiring a test five to seven days after arrival will identify travellers who are positive and would be potentially
 infectious at the place of arrival;
- combining testing with quarantine would allow the quarantine period to be shortened whilst delaying and reducing (re)-introduction and/or transmission of SARS-CoV-2 and/or VOCs at the place of arrival:
- if accurate contact information is collected for travellers upon arrival, the combination of testing prior to departure or upon arrival, with quarantine and a further test five to seven days after arrival, would enable follow-up if required:
- this combination could offer a reasonable balance of risks and benefits as an alternative to longer quarantine
 without testing. With every testing and/or quarantine strategy, there is a residual risk of (re)-importation of
 SARS-CoV-2 and/or VOCs. It is ultimately the responsibility of EU/EEA countries to assess the residual risk linked
 to a shorter quarantine period with or without testing depending on the local situation and the potential
 impact on the public health system.

² Refers to a test result indicating that the disease is not present when the person actually does have the disease.

³ Refers to a test result indicating that the disease is present when the person actually does not have the disease.

⁴ A shortened quarantine, even if combined with a negative test, will leave a residual risk of (re)-importation of SARS-CoV-2 and/or VOCs (as with every quarantine and/or testing strategy). In order to decrease this residual risk, depending on the local situation and the potential impact of (re)-importation of SARS-CoV-2 and/or VOCs on the public health system, EU/EEA countries can consider extending the duration of quarantine (e.g. to seven to ten days) before asking for a negative test to enable release.

Specific traveller populations

Individuals who have recovered from a COVID-19 infection

For individuals who have recently recovered from a COVID-19 infection, a certificate confirming their recovery within the last 180 days (issued no sooner than eleven days after a person has received their first RT-PCR, LAMP or RADTs SARS-CoV-2 positive test result) could be accepted as the equivalent of the SARS-CoV-2 negative test that is required for travellers.

This is based on that fact that individuals may remain RT-PCR positive for 10 days after diagnosis, but it is unlikely that they will carry infectious viral particles after 10 days.

Requiring a RADT at the earliest 48 hours in advance of travel may also be considered for this group of travellers as a means of confirming that that they are not infectious with SARS-CoV-2 at the time of travel since these tests will rule out individuals with a high viral load (i.e. the most infectious cases; see Annex 1). This approach may be considered to account for the possibility of being re-infected with VOCs.

Evidence from observational and immunological studies points towards a protection against reinfection or an immunological memory in the range of three to eight months following infection [42-44]. However, more longitudinal observational studies are needed to better define the actual protection provided by the immune response against reinfection and the duration of such protection.

In light of the available evidence, it is reasonable to consider easing the requirements for quarantine and testing in individuals that have recovered from a laboratory-confirmed SARS-CoV-2 infection within the previous 180 days. However, evidence on the protection of prior immunity against the various VOCs is currently lacking and this advice may change when such evidence becomes available.

Therefore, it is important that individuals who can provide reliable proof of having recovered from a COVID-19 infection in the previous 180 days continue to adhere to all other preventive measures. Such measures would be the wearing of a face mask, respecting physical distancing rules during travel, and not travelling if experiencing COVID-19 compatible symptoms, or if having recently been in contact with a positive case. At present, it would also be prudent to continue to require such travellers to follow NPIs following arrival and to monitor for symptoms and seek testing if they develop.

ECDC recommends that Member States continue to monitor VOCs and their characteristics (ability to evade immunity, transmissibility, etc.), including the emergence of new VOCs, and subsequently revise recommendations for travellers that have recovered from COVID-19 within the 180 days prior to travel when required.

Vaccinated individuals

Evidence on the efficacy of the vaccine products currently available in protecting against infection and onward transmission is still incomplete. A recent pre-print of a cohort study conducted in Scotland shows a promising effect of two of the currently authorised vaccines in the EU/EEA against COVID-19 related hospitalisation. The study refers to a vaccine effectiveness of 85% (95% CI 76-91) for COVID-19 related hospitalisations after a first dose of the Pfizer-BioNTech vaccine and a 94% (95% CI 73-99) vaccine effectiveness for COVID-19 related hospitalisations after a first dose of the Oxford-AstraZeneca vaccine [45]. The first published post-marketing effectiveness study shows a 92% effect against documented SARS-CoV-2 infection seven days after administering the second dose of the Pfizer-BioNTech vaccine [46]. More studies will probably continue to become available on different vaccines and their effect on various disease outcomes. Studies looking at vaccine effectiveness against asymptomatic cases will be of particular relevance. Such studies will require active follow-up of vaccinated individuals with repeated testing, irrespective of symptoms, and collection of their exposure history ahead of testing. Other relevant studies will be those assessing the infectiousness of vaccinated individuals developing SARS-CoV-2 infection.

There have been reports of decreased vaccine efficacy against some of the VOCs, and this seems to differ by vaccine product. In addition, there is currently no evidence on the duration of protection following immunisation. Therefore, it remains uncertain whether vaccinated individuals are capable of transmitting the infection to others and it will take some time before this evidence is available for all authorised vaccine products.

As more data becomes available, it will be possible to estimate the degree of protection offered by the different vaccine products against infection and, subsequently assess the potential for fully-vaccinated individuals to further transmit the virus, including VOCs. In the context of travel, at the time of writing of this guidance, the European Commission is working on a proposal for a common framework for the issuance, verification and acceptance of interoperable certificates on COVID-19 vaccination to ensure the security and cross-border verifiability of the certificates issued.

Limitations

The uncertainty surrounding the findings presented in this document are mainly related to the following:

- much of the evidence currently available on the effectiveness of travel measures on SARS-CoV-2 (re)introduction and transmissibility of VOCs is based on preprint manuscripts, which have not yet completed the
 peer-review process;
- there are currently no empirical data available on the effectiveness of quarantine and testing of travellers. There
 are only modelling studies available (some of which still in pre-print) to provide information on the effectiveness
 of different durations of quarantine, alone or in combination with testing, to delay the importation of COVID-19
 cases:
- changes in individual behaviour, compliance with measures, and cultural, societal, and economic factors all play
 a role in the transmission dynamics of SARS-CoV-2 and/or VOCs and the effectiveness of implemented NPIs and
 travel measures;
- there is no evidence on the role of natural immunity against newly-emerging VOCs;
- there is incomplete evidence on the effectiveness of the various vaccine products against infection and further transmission of SARS-CoV-2.

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Acknowledgments

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Annex 1. Tests for SARS-CoV-2 detection

Molecular tests

Reverse transcription polymerase chain reaction (RT-PCR) remains the gold standard in terms of SARS-CoV-2 testing.

RT-PCR has the characteristics set out below:

- It detects the genetic material of the SARS-CoV-2 virus.
- It is a diagnostic test with high sensitivity, usually higher than 95%, and very high specificity (99–100%).
- A SARS-CoV-2 positive RT-PCR test does not necessarily mean that the tested person is infectious since
 recovering cases can remain RT-PCR positive for weeks after recovery, due to the prolonged existence of viral
 genetic material.
- False negative RT-PCR results (i.e. the test misses a positive case) are rare but can occur in cases with low viral load or due to improper pre-analytical conditions (e.g. sampling technique or poor swab quality).
- False positive RT-PCR results (i.e. the test misses a negative case) are rare but can occur, for example in the event of sample contamination.
- As new variants of the virus emerge, the ability of RT-PCR assays to identify the virus in a sample needs to be
 assessed. Certain mutations might affect the RT-PCR result, for example causing a false negative result if the
 virus genome has changed so much that the RT-PCR does not identify the genetic material of the virus [22].
- RT-PCR can also be used to screen/indicate the prevalence of certain VOCs. For example, the variant B.1.1.7, which holds a deletion in the S-gene, may cause certain RT-PCR assays targeting that specific S-gene to produce a negative result (so-called S-gene target failure) [22]. This characteristic can be used as an indicator for the B.1.1.7 and similar variants in SARS-CoV-2 positive persons tested with RT-PCR. However, to be able to confirm infection with any new variant, sequencing of the whole SARS-CoV-2 genome is needed.

Reverse transcription loop-mediated isothermal amplification (RT-LAMP) technique has emerged as an alternative molecular detection method for the detection of SARS-CoV-2. RT-LAMP technique has some advantages, such as fast test results and the need for fewer resources, while maintaining high sensitivity and specificity [47]. Proper clinical validation studies are needed to evaluate this new technique and assess the potential role it could play in the travel setting.

Rapid Antigen Detection Tests (RADTs)

Rapid Antigen Detection Tests (RADTs) have the following characteristics [15]:

- RADTs detect the presence of viral antigen in a sample.
- RADTs can provide a result within 10–30 minutes, allowing rapid turnaround of results and shortening the time before further contact tracing and self-isolation can begin.
- RADTs perform best in cases with high viral load, in pre-symptomatic and early symptomatic cases up to five days from symptom onset [15].
- Some RADTs require a laboratory instrument for the analysis, but others do not, as the analysis is performed using a hand-held cartridge with visual readout.
- When compared with RT-PCR, RADTs exhibit lower sensitivities and specificities, which also depend on the time of sampling [15].
- RADTs should be able to rule out the most infectious cases. Using them to screen travellers prior to departure
 would therefore specifically prevent transmission during travel and directly upon arrival, as it would stop highly
 infectious individuals from travelling. RADTs may miss individuals with low viral loads, for example during the
 pre-symptomatic phase and/or towards the end of the active infection.
- A positive test with an RADT will need confirmation by RT-PCR.
- As new variants of the virus emerge, the ability of RADTs to identify the infectious individuals needs to be assessed. At the time of writing, there was no indication that the RADTs could not identify the VOCs that are currently in circulation [41].
- RADTs are not suitable for screening incoming travellers to prevent virus (re-)introduction in regions/countries that have achieved very low levels of transmission. In these situations (i.e. in a low to very low prevalence population), RT-PCR should be used to reduce the risk of false negative results.
- A <u>Common list of COVID-19 rapid antigen tests</u>, including validated RADTs at EU/EEA level, was published by the Commission on 17 February 2021.