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COVER NOTE

From:	Secretary-General of the European Commission, signed by Ms Martine DEPREZ, Director
date of receipt:	18 October 2021
To:	Mr Jeppe TRANHOLM-MIKKELSEN, Secretary-General of the Council of the European Union
No. Cion doc.:	COM(2021) 649 final
Subject:	ANNEXES to the Report from the Commission to the European Parliament and the Council pursuant to Article 16(1) of Regulation (EU) 2021/953 of the European Parliament and of the Council on a framework for the issuance, verification and acceptance of interoperable COVID-19 vaccination, test and recovery certificates (EU Digital COVID Certificate) to facilitate free movement during the COVID-19 pandemic.

Delegations will find attached document COM(2021) 649 final.

Encl.: COM(2021) 649 final

EUROPEAN
COMMISSION

Brussels, 18.10.2021
COM(2021) 649 final

ANNEXES 1 to 2

ANNEXES

to the

Report from the Commission to the European Parliament and the Council pursuant to Article 16(1) of Regulation (EU) 2021/953 of the European Parliament and of the Council on a framework for the issuance, verification and acceptance of interoperable COVID-19 vaccination, test and recovery certificates (EU Digital COVID Certificate) to facilitate free movement during the COVID-19 pandemic.

ANNEX I

Detailed breakdown of number of EU Digital COVID Certificates issued (by 13 October 2021)

	Vaccination certificates issued	Test cert. issued (NAAT[1])	Test cert. issued (RAT[2])	Recovery certificates issued	Total issued
Austria	11.125.292	10.872.756	20.482.546	577.981	**43.058.575**
Belgium*	17.440.792	5.822.096		608.250	**23.871.138**
Bulgaria	1.372.297	307.779	705.533	37.251	**2.422.860**
Czechia	7.199.918	1.935.056	3.413.355	377.589	**12.925.918**
Denmark**					
Germany***	119.750.418	1.629.445	1.267.528	607.075	**123.254.466**
Estonia*	662.125	3.073		63.597	**728.795**
Ireland	3.978.823	186.203	37.461	69.317	**4.271.804**
Greece	3.419.809	17.064	200.551	471.751	**4.109.175**
Spain*	25.371.410	809.495		515.562	**26.696.467**
France	72.186.091	24.593.086	38.226.112	1.896.065	**136.901.354**
Croatia	1.600.824	17.241	597.661	126.353	**2.342.079**
Italy	72.726.630	7.078.397	15.092.611	2.160.524	**97.058.162**
Cyprus	739.837	14.118	314.614	76.179	**1.144.748**
Latvia	1.387.323	270.523	21.397	77.337	**1.756.580**
Lithuania	1.770.546	3.501.075	358.855	333.994	**5.964.470**
Luxembourg	1.363.875	621.868	138.140	46.493	**2.170.376**
Hungary	4.746.433	183.653	79.521	356.155	**5.365.762**
Malta*	282.886	619		145	**283.650**
Netherlands****	42.179.079				**42.179.079**
Poland*	14.098.319	307.336		495.632	**14.901.287**
Portugal	7.147.103	81.387	178.954	227.940	**7.635.384**
Romania	4.726.990	61.642	98.909	111.190	**4.998.731**
Slovenia	4.170.614	473.674	1.582.643	561.128	**6.788.059**
Slovakia	4.623.889	933.324	1.046.082	214.011	**6.817.306**
Finland	1.820.819	202.113	5.386	28.533	**2.056.851**
Sweden*	4.857.039	143.834		1.573	**5.002.446**
Iceland	538.095	73.760	148.121	3.431	**763.407**
Lichtenstein	47.288	21.975	13.830	1.322	**84.415**
Norway****	6.175.000				**6.175.000**
Total EU/EEA	**437.509.564**	**60.162.592**	**84.009.810**	**10.046.378**	**591.728.344**

* Combined total for NAAT and RAT test certificates

** Figures not available

*** Reporting for RAT tests issued only as of 27 September 2021

**** Total number issued for all three types of certificates

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1 'Nucleic acid amplification test', such as reverse transcription polymerase chain reaction (RT-PCR), loop-mediated isothermal amplification (LAMP) and transcription-mediated amplification (TMA) techniques, used to detect the presence of the SARS-CoV-2 ribonucleic acid (RNA).

2 'Rapid antigen test', that is, a test that relies on detection of viral proteins (antigens) using a lateral flow immunoassay that gives results in less than 30 minutes.

ANNEX II

Guidance provided by the European Centre for Disease Prevention and Control

Possible issuance of certificates of recovery based on rapid antigen test results

Appropriately validated rapid antigen detection tests (RADTs) can be used for issuing the recovery certificates for the purposes of the EU DCC. According to the Council Recommendation on a common framework for the use and validation of rapid antigen tests, the mutual recognition of COVID-19 test results in the EU (2021/C 24/01) and the common list of COVID-19 rapid antigen tests that are considered appropriate for use in the context of the situations described in the Council Recommendation. Self-test RADTs should NOT be used for the purpose of issuing a formal certificate such as testing, or recovery certificates. Proper sampling is one of the most crucial steps for SARS-CoV-2 diagnosis and, if performed incorrectly, a reliable test result cannot be assured[3].

The RADTs have generally lower sensitivity but high specificity. The use of RADTs is primarily intended to detect individuals with an ongoing SARS-CoV-2 infection, i.e. while they are most infectious. The use of RADTs is appropriate in settings with high COVID-19 prevalence when a positive result is likely to indicate true infection, as well as in low prevalence settings for rapid identification of highly infectious individuals. However, in low prevalence settings, the use of RADTs could result in false positive test results. The lower the prevalence in the population to be tested, the higher the likelihood of false positive test results. This means that there could be a proportion of people certified to have recovered, whereas they are still susceptible (i.e. people with a false positive RADT result for COVID-19). This is true for all test types.

All COVID-19 tests, including NAATs, have the risk of producing false positive test results, but this proportion may be higher for RADTs than for RT-PCR if the clinical performance (i.e. specificity level) of the used test is lower. If RADTs of lower specificity are used, this should be taken into consideration, especially in low prevalence settings when these tests are used for screening of asymptomatic individuals and where the positive predictive value of the RADTs would thus be low. The validity period of the recovery certificate would be the same for positive RADTs and positive NAAT.

The list of mutually recognised RADTs is regularly updated by the Technical working group on COVID-19 diagnostic tests and agreed by the Health Security Committee.

[3] ECDC (2021). Considerations on the use of rapid antigen detection (including self-) tests for SARS-CoV-2 in occupational settings. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/Considerations-on-use-of-rapid-antigen-detection-tests-for-SARS-CoV-2-in-occupational-settings.pdf

Possible issuance of certificates of recovery based on antibody test results

Regarding antibody tests, the European Centre for Disease Prevention and Control (ECDC) and the Joint Research Centre (JRC) have produced technical notes[4] where the main points for consideration are listed, namely:

- Antibody tests are currently mostly used in research studies (sero-epidemiological studies) of population rather than for individual diagnosis of COVID-19 cases.
- The detection and quantification of antibodies cannot be used as a direct indication of protective immunity.
    - A positive antibody test result can be a proof of a past infection but is not an absolute proof that a person is not infectious and/or protected against a new infection and cannot transmit the virus further.
    - So far, it is not known which antibody levels would protect against re-infection.
    - Conversely, individuals that have recovered may not test positive to serological tests (over an extended period).
    - Moreover, not all antibodies induced by a SARS-CoV-2 infection neutralise the virus effectively.
    - Most antibody tests available cannot assess if the antibodies detected offer effective protection.
- Antibody tests cannot define the time of infection.
    - Antibody tests cannot give any indication about the time of the infection, so without any additional evidence, e.g. NAAT and/or RAT test performed at the time of infection, it is impossible to determine the validity period of the recovery certificate.
    - It may well be that soon after a positive antibody test, the antibodies become undetectable.
- There is a risk that the antibodies detected by currently used commercial tests do not prevent infection with newly emerging SARS-CoV-2 variants.
    - Current testing systems are not validated against new variants.
- When a serological test results positive, this does not necessarily mean the individual has recovered from SARS-CoV-2.
    - For example, patients that have received one dose of a vaccine may develop antibodies similar to the ones present in recovered patients and this category would represent 'false positive results'.
    - There is evidence of high risk of false positive results in areas of low SARS-CoV-2 prevalence.
    - Regional differences in the prevalence of SARS-CoV-2 infections may have an impact on the (positive/negative) predictive value of serological tests.
    - Antibodies presented in autoimmune diseases (e.g. rheumatoid factors) might give a positive result without ever having the infection.

[4] https://www.ecdc.europa.eu/sites/default/files/documents/Use-of-antibody-tests-for-SARS-COV-2-in-the-context-of-Digital-Green-Certificates.pdf

- There is a variety of antibody tests and a comparison of their results is extremely difficult due to this variety and the lack of standardisation.
    - Antibody tests currently used in Member States are not harmonised/ standardised and results are not comparable.
    - Laboratory methods may target different antibodies (IgM / IgG), which may also recognise different parts of the virus.
    - Most commercially available tests only provide qualitative results (presence or absence of antibodies).
    - These qualitative antibody tests are useful from a population, rather than individual perspective.
    - Quantitative detection kits are primarily used for research purposes but the comparability between laboratories is hindered by the lack of available reference material
    - Therefore, it may not be possible to propose a single list of recommended serological tests to be applied across the EU.
- Use of certificates issued on the basis of positive antibody tests (IgM and IgG) in the context of public health measures.
    - It is possible that individuals with certificates issued on the basis of a positive antibody test may be falsely reassured that they can relax attitudes towards behaviours that are essential to limiting risk of infection and onwards transmission, such as physical distancing, mask use and hand washing. As mentioned above, whilst a positive antibody test result may be suggestive of prior infection, it may not guarantee protection from reinfection, or to newly emerging variants with possible immune-escape potential.
    - Any implementation of certificates based on a positive antibody test should be carefully considered and be accompanied by strong public messages and relevant communication about the importance of both vaccination and public health measures to reduce SARS-CoV-2 transmission.

After reviewing the technical notes and the evidence published later, we conclude that currently available antibody tests are not suitable for the assessment of the time of infection and immunity status of an individual. Therefore, the positive antibody test results are not considered sufficient for issuing of a recovery certificate that would exempt the holder from certain public health measures.

ECDC and JRC will continue their monitoring of antibody tests and their usage, including via the "COVID-19 Diagnostic Testing database" of the JRC and the sero-epidemiological study network in the WHO European Region that is coordinated jointly by ECDC and the WHO Regional Office for Europe.

Validity period of certificates of recovery

Evidence on duration of immunity for recovered individuals is ideally drawn from longitudinal cohorts comparing infection risk amongst naïve and recovered individuals at 3- or 6-monthly intervals. Unfortunately, such studies are sparse. A systematic review of 11 key studies conducted by Health Information and Quality Authority in Ireland suggests that reinfection risk amongst recovered individuals is low (absolute rate 0%–1.1%), with protection maintained for up to 10 months post initial infection [1]. More recently, Vitale *et al.* observed protection from reinfection for recovered individuals for a period of at least 12 months [2]. However, a critical limitation of these studies, is that their observation periods predate the emergence and subsequent dominance of the B.1.617.2 (Delta) SARS-CoV-2 variant of concern (VOC) across the EU/EEA.

Preliminary analysis of national surveillance data from the UK indicates that recovered individuals have an increased risk of reinfection with Delta compared to the previously dominant B.1.1.7 (Alpha) strain, with the overall odds around 46% higher [3]. The Public Health England analysis included 83,197 individuals ≥15 years, who became SARS-CoV-2 PCR positive during an 11-week observation period (12 April and 27 June 2021), of whom 980 (1.2%) were possible reinfections. The adjusted odds ratio of reinfection with the Delta variant was 1.46 (95% CI 1.03 to 2.05) compared to the previously dominant Alpha variant. The **risk of reinfection** was not elevated for Delta if the primary infection was <180 days (adjusted odds ratio = 0.79, 95% CI 0.49 to1.28) but was **higher for those with a prior infection ≥180 days earlier** (adjusted odds ratio = 2.37, 95%CI 1.43 to 3.93). This finding has not yet been replicated in other settings, and additional age-stratified data on reinfection risk over time, specifically in the context of Delta, is needed.

Table 7: Multivariable logistic regression model of the risk of reinfection with alpha and delta variants during a period of emergent delta infection in England

			Risk of reinfection-week 2021-15 to 2021-25		
		Totals	Crude OR	aOR (95% CI)*	aP-Value
Definition of reinfection applied	All possible reinfections	980 (1.2%)			
	All first infections	82,217 (98.8%)			
All possible reinfections arising at least 90 days after prior infection	Alpha variant	83/14,509 (0.6%)	1	1	
	Delta variant	897/68,688 (1.3%)	2.30 (1.84 to 2.88)	1.46 (1.03 to 2.05)	0.031
Possible reinfections arising between 90-179 days after prior infection	Alpha variant	54/14,480 (0.4%)	1	1	
	Delta variant	243/68,034 (0.4%)	0.96 (0.71to 1.29)	0.79 (0.49 to1.28)	0.342
Possible reinfections arising at least 180 days after prior infection	Alpha variant	29/14,455 (0.2%)	1	1	
	Delta variant	654/68,445 (1.0%)	4.80 (3.31 to 6.96)	2.37 (1.43 to 3.93)	0.001

*adjusted for age group (<30 years, 30+years), sex, Region, vaccination status (any vaccine at least 14 days earlier vs no vaccine), ethnicity and week

Source: Public Health England [3].

In the absence of a universal immune correlate which can be measured in recovered individuals to infer protection, the virus-neutralising capability of serum antibodies provide the best current indication of protection from reinfection. Whilst the majority of SARS-CoV-2 infected individuals will develop serum antibodies, recovered individuals demonstrate highly variable antibody dynamics over time [4], with waning of neutralising antibodies widely documented [5]. In a key study by Planas *et al.*, sera collected from 56 convalescent individuals 6 months post symptom onset were shown to be four-fold less potent against the Delta variant relative to the Alpha variant. The authors also observed a similar four-fold reduction in a separate cohort of 26 convalescent individuals evaluated 12 months post symptom onset, stressing that neutralisation activity was globally low by month 12 [6]. Waning of serum antibodies may be entirely mitigated by the presence of SARS-CoV-2-specific memory B cells, which can rapidly expand when supported by SARS-CoV-2-specific memory T cells. Memory T cells may also contribute to protection and recovery from infection by directly lysing SARS-CoV-2 infected cells. However, specific T cell correlates remain elusive.

Conclusions

- Duration of immunity is a complex issue and to date the correlation between measured immunity and clinical protection from SARS-CoV-2 infection still needs to be established.
- The validity of the recovery certificates depends on the emerging scientific evidence on the duration of protective immunity after natural infection and effectiveness of the previous infection in the presence of current and potential future variants, which is a dynamic process changing on a regular basis.
- Taken together, in absolute terms, the risk of reinfection with Delta variant remains low at 180 days post infection, albeit with evidence of an increased risk relative to to the previously circulating Alpha variant. Given these factors, there is currently insufficient evidence to support an increase of the recovery certificate validity period beyond 180 days.
- ECDC will continue to regularly monitor the relevant new scientific evidence in this area in order to provide updates on the duration of immunity following natural infection.

References

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