SWISS SOCIETY FOR MICROBIOLOGY
SOCIÉTÉ SUISSE DE MICROBIOLOGIE
SOCIETÀ SVIZZERA DI MICROBIOLOGIA
SCHWEIZERISCHE GESELLSCHAFT FÜR MIKROBIOLOGIE

Recommendations of CCCM-SSM SARS-CoV-2 diagnostics working group on indications and limitations of the SARS-CoV-2 PCR testing from saliva

Gilbert Greub[1], Reto Lienhard[2], and Adrian Egli[3] for the Coordinated Commission for Clinical Microbiology of the Swiss Society of Microbiology (CCCM-SSM)*

Date & versions:
First draft prepared on 06.12.2020; shared to FOPH on 18.12.2020 after consultation with all SSM members.
According to comments of the FOPH and given the emergence of the UK variant, the recommendation has been slightly adapted on 21.12.2020 (Version: 2.0, with (i) removal of the proposal to shorten the quarantine based on a negative PCR tests 5 to 7 days' post exposure to an infected individual, (ii) change of the time of the investigation of the contact in quarantine, and (ii) addition of a short paragraph regarding the UK variant).

Content and focus of this document
The first version of these recommendations have been written by the Coordinated Commission for Clinical Microbiology of the Swiss Society of Microbiology (CCCM-SSM) on Sunday 6th December. This version 2 (21th December) has been revised according to the comments received from the FOPH on 21th December. These recommendations focus on SARS-CoV-2 PCR testing from saliva, their usage in specific cohorts, sensitivity, specificity, indications, availability and limitations and provide minimal acceptance criteria for technical validation.

Background
Overall, the COVID-19 situation remains worrisome due to the high dynamic of SARS-CoV-2 transmission, the high prevalence, and the healthcare system under constant pressure. For these reasons a broad testing strategy with diverse SARS-CoV-2 specific tests is critical to (i) rapidly and reliably identify infected individuals and (ii) to interrupt transmission chains.

The current gold standard for virus diagnostics is the RT-PCR (1). Swiss diagnostic laboratories have been highly active since early January 2020, when it became obvious that SARS-CoV-2 will have the potential to spread in Europe, including Switzerland. Thus, in-house developed RT-PCRs tests were rapidly introduced at all University hospital centers and were utilized to validate and implement new commercially RT-PCRs tests.

In Switzerland, diagnostics of pathogens is only performed in laboratories with experienced technical personnel, respective laboratory equipment and infrastructure for diagnostics, e.g. safety bench for potential contagious materials, a quality assurance concept, and also access to samples for verification and validation. This situation is not the case outside of such laboratory dedicated to diagnostics.

SARS-CoV-2 specific RT-PCR from Saliva

Nasopharyngeal swabs are considered the optimal material for detection of SARS-CoV-2 (1, 2). However, saliva is another interesting sample to be used for mass testing for various reasons. Saliva can easily be collected, and the collection procedure is more comfortable. Especially specific cohorts can more easily be accessed such as children or the elderly. The collection of saliva also does not require specifically trained personnel. RT-PCR performed on self-made saliva represents a very good solution to decrease the workload of testing centers and to increase accessibility and acceptance of tests (see below). Samples can be easily transported to a laboratory for RT-PCR testing by surface mail as any other patient sample (UN3373 standard).

Symptomatic patients. Recently, RT-PCR testing from saliva has been used in clinical studies from Lausanne and Zürich (3, 4). When sampling is done properly, this approach may exhibit sensitivities of 95% (4) in patients with acute symptoms of COVID-19 (fever, cough, and onset of symptoms within one week). Moreover, this approach still exhibits more than 99.9% specificity. Of note, the viral load in saliva is of about 100-fold lower compared to nasopharyngeal material (3, 4). Thus, RT-PCR from saliva will detect subjects that exhibits more than 10'000 copies/ml in nasopharyngeal swabs and still exhibiting about a 100-fold better sensitivity as compared to antigen test on nasopharyngeal samples (4).

Less or asymptomatic individuals. Due to the high sensitivity of RT-PCRs, this approach is also suitable to test any subjects with more than 7 days of symptoms, as well as asymptomatic individuals, whereas antigen tests due their lower sensitivity have been only considered for symptomatic patients during the first 4 days of symptoms (5).

Sample collection in practice. For the collection and transport specific tubes should be used. The Institute of Medical Virology of the University of Zurich has developed a guidance document how to collect saliva samples (https://www.virology.uzh.ch/de/services/SARS-CoV-2-Diagnostik.html, top right on the web page). Depending on the scenario, where the sample is collected, proper labelling of sample and an order sheet should be prepared to reduce later problems of identification in the laboratory, where the PCR is conducted.

Sample collection may be performed with certain assistance/supervision, in e.g. test centers, nursing homes, or pharmacies, but also self-collection at home may likely be done safely with sufficient quality sampling. Due to variable pre-analytical quality, self-collection should not be recommended when the test is intended to reduce the quarantine. After the sample is collected, the sample should ideally be transported within 24h to a testing laboratory.

Noteworthy, only laboratories that have performed a validation of the PCR on saliva samples may propose these RT-PCR on saliva. Rapid PCR tests that are based on microfluidics may not be suitable to be used on saliva samples and the CCM-SSM recommend to mainly perform RT-PCR on saliva using more robust approaches, that have been already shown to be compatible with different sample types, such as Cobas 6800 or the Magnapure RNA extraction followed by a Quanstudio RT-PCR for example .

Recommended test indications for RT-PCR from saliva:

Nasopharyngeal RT-PCR remains the gold standard for patient who requires hospitalization or are critical ill in order to provide a precise diagnosis. Saliva-based PCR assays are predominantly suited for outpatient scenarios or specific symptomatic and asymptomatic cohorts:

- **Any symptomatic outpatient**, especially when symptoms started more than 7 days ago; even if the symptoms started less than 4 days ago, a PCR test should be preferred to the antigen test for individuals exposed to vulnerable subjects (person living in the same household or healthcare workers).
- Diagnosis of symptomatic **pediatric outpatients**
- **Any subject exposed to a confirmed patient (contact)**, at day 5 after exposure, in order to triage between isolation and quarantine for 10 days
- **Screening tool at borders** for symptomatic and asymptomatic person entering Switzerland from a country with higher prevalence (except commuters), to avoid un-necessary quarantine
- **Asymptomatic persons**, for instance in pharmacy, physician or dedicated testing centers or by self saliva collection using pre-prepared kits, available in pharmacies, train stations, ski resorts, and other touristic locations.
- **Subjects at risk of infection with the UK variant.** The saliva and nasopharynx PCR are especially recommended (over antigen testing) for any subject that has travelled to an area endemic for the UK variant or exposed to someone infected by the UK variant, since (i) antigen tests when performed using the “dry swab” approach does not provide access to material for further sequencing, and (ii) antigen tests are more likely than PCR to give false negative results since they generally rely on a single antigen (often the spike protein).
- To increase acceptance, **to anyone** (fulfilling criteria of an antigen but) **preferring a saliva PCR test** in order to avoid nasopharyngeal sample (and to get a better sensitivity)

References

1.
Caruana G, Croxatto A, Coste AT, Opota O, Lamoth F, Jaton K, Greub G.
Diagnostic strategies for SARS-CoV-2 infection and interpretation of microbiological results.
Clin Microbiol Infect. 2020 Jun 25;26(9):1178-82.

2.
WHO. Target product profiles for priority diagnostics to support response to the COVID-19 pandemic v.1.0. Geneva, 2020 Sep 29.

3.
Large parallel screen of saliva and nasopharyngeal swabs in a test center setting proofs utility of saliva as alternate specimen for SARS-CoV-2 detection by RT-PCR
Michael Huber, Peter W. Schreiber, Thomas Scheier, Annette Audigé, Roberto Buonomano, Alain Rudiger, Dominique L. Braun, View ORCID ProfileGerhard Eich, Dagmar Keller, Barbara Hasse, Christoph Berger, Amapola Manrique, Huldrych F. Günthard, Jürg Böni, Alexandra Trkola
https://www.medrxiv.org/content/10.1101/2020.12.01.20241778v1
doi: https://doi.org/10.1101/2020.12.01.20241778

4.
Jean Marc Schwob, Alix Miauton, Dusan Petrovic, Jean Perdrix, Nicolas Senn, Katia Jaton, Opota Onya, Alain Maillard, Gianni Minghelli, Jacques Cornuz, Gilbert Greub, Blaise Genton, Valérie D'Acremont. Antigen rapid tests, nasopharyngeal PCR and saliva PCR to detect SARS-CoV-2: a prospective comparative clinical trial.
https://www.medrxiv.org/content/10.1101/2020.11.23.20237057v1.article-info
doi: https://doi.org/10.1101/2020.11.23.20237057

5.
Adrian Egli, Reto Lienhard & Gilbert Greub for the Coordination Committee of Clinical Microbiology of the Swiss Society of Microbiology (CCM-SSM). Recommendation regarding antigen tests. Swiss Laboratory medicine, in press.

Members of CCMC of the Swiss Society of Microbiology (in bold the members who have written this recommendation; *members who have endorsed the present recommendation) **Prof. Adrian Egli* (president)** Prof. André Burnens* Dr. Hans Fankhauser Dr. Meri Gorgievski* **Prof. Gilbert Greub*** Dr. Eric Grueter (Swissmedic) Dr. Nadia Liassine* Reto Lienhard* Dr. Gladys Martinetti-Lucchini Dr. Martin Risch* Prof. Jacques Schrenzel Marie-Lise Tritten* Prof. Reinhard Zbinden