FAQ: On the Use of Samples/Materials Associated with SARS-CoV-2 (or the COVID-19 Virus)

Question 1: What is the difference or relationship between 2019-nCoV, SARS CoV-2 and COVID-19 virus?

These are different names given to the same strain of coronavirus at different time points.

When the virus was first isolated from pneumonia cases in Wuhan, China in December 2019, it was named 2019 novel coronavirus (2019-nCoV). As more information and genetic analyses became available, the virus was given the official name of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee for Taxonomy of Viruses, while the WHO named the disease caused by the virus, Coronavirus disease 2019 (COVID-19).

Question 2: Is SARS-CoV-2/COVID-19 virus listed as a scheduled biological agent under the Biological Agents and Toxins Act (BATA)?

SARS-CoV-2/COVID-19 virus is listed as a BATA First Schedule Part II biological agent as of 30 Jan 2020. An approval to possess from MOH is required for facilities to possess/handle the virus or any samples/materials known to contain the virus unless viral inactivation (see Qn 10 for information related to inactivation) has been performed.

If the possession/use/handling of such samples is solely for the purpose of diagnosis, the facility will be exempted from BATA but may have to comply with the Private Hospitals and Medical Clinics (PHMC) Act.

For more details, please see:

a) Qn3 for BATA’s definition of “diagnosis”;
b) Qn4 for the conditions apply to diagnostic activity; and
c) the Ministry of Health “Interim Biosafety Guidelines for Laboratories and Personnel Handling Samples/Materials Associated with 2019-nCoV” for information regarding the transport and processing of diagnostic samples. Click here for the Guidelines.

Question 3: What is the BATA’s definition of “diagnosis”?

Diagnosis is defined in the BATA (Section 2) as “any activity undertaken solely with the intention of analysing any specimen from a person or an animal in which a biological agent is or is suspected of being present for the purpose of:

a) determining the cause of any disease suffered by any person or animal;
b) assessing the clinical progress of any person or animal;
c) carrying out the clinical management of any person or animal; or
d) determining the cause of death of any person or animal in an autopsy”.

Updated on 5 June 2020
Question 4: What are the requirements or conditions for conducting diagnostic activities involving samples/materials associated with SARS-CoV-2/COVID-19 virus?

Diagnostic activities shall be carried out according to “MOH Circular 34/2006 on Interpretation of Diagnosis”. All samples positive for SARS-CoV-2/COVID-19 virus, including virus isolated from the clinical samples and the clinical samples where the virus were isolated from, **MUST be inactivated as part of the diagnostic process, destroyed or transferred** to a facility that has been granted an approval to possess the virus as soon as possible after confirmation of diagnostic test results. Click [here](#) for details of the Circular.

MOH Biosafety Branch shall be notified of transfer(s) of virus (including associated materials/derivatives) via email at moh_biosafety@moh.gov.sg. All inventory records and transfer documents shall be kept up to date.

Question 5: Can a diagnostic laboratory retain residual SARS-CoV-2/COVID-19 virus-positive clinical samples as positive controls?

For safety purposes, diagnostic laboratories are strongly advised to **use non-infectious materials** (e.g. synthetic or plasmid DNA) or inactivated materials as positive controls.

Residual samples may be retained as positive controls only if they have undergone inactivation. Laboratories **MUST use a validated inactivation method** to render the residual samples non-infectious and non-replicable under any conditions. The inactivation method must be validated to be effective, and approved by the Biosafety Committee (with the appropriate expert committee members) or personnel with good biosafety and microbiology knowledge and experience. Information or supporting documents on the effectiveness of the inactivation method shall be kept and be made available when requested by MOH.

*Please see Qn 10 for examples of inactivation methods.*

Question 6: Can a diagnostic laboratory retain residual SARS-CoV-2/COVID-19 virus-positive clinical samples for evaluation of diagnostic kits?

A diagnostic laboratory can obtain a **conditional approval** to store and handle residual SARS-CoV-2/COVID-19 virus-positive clinical samples for the evaluation of diagnostic kits, by submitting a declaration to moh_biosafety@moh.gov.sg. Click [here](#) for more information on the specified conditions and the declaration form.

Question 7: What are the requirements for the importation, handling and/or storage of samples from clinical trial participants that are known or suspected to have SARS-CoV-2/COVID-19 virus for laboratory safety testing?

The requirements for such activities related to **non-COVID-19 clinical trials** are specified in [this guidance document](#).

For COVID-19 related clinical trials, please consult Biosafety Branch prior to the commencement of such activities.
Question 8: What are the requirements for conducting non-diagnostic activities involving samples/materials associated with SARS-CoV-2/COVID-19 virus?

Non-diagnostic activities refer to activities which do not fall under diagnosis (see Qn 3) or any BATA exempted purposes. Examples of non-diagnostic activities include (but are not limited to) the storage of samples, virus culture (see Qn 9 for additional conditions), virus neutralization assay, development of diagnostic assay, full genome sequencing, evaluation of new diagnostic kits (see Qn 6 for information related to conditional approval for diagnostic laboratories), identification of disease biomarkers, generation of antibodies against SARS-CoV-2/COVID-19 virus, laboratory testing for clinical trials (see Qn 7 for more information).

Facilities intending to engage in non-diagnostic activities (other than those specified in Qn 6 and 7) involving non-inactivated samples of SARS-CoV-2/COVID-19 virus MUST satisfy the requirements for the possession of BATA First Schedule Part II biological agents prior to the commencement of work, regardless of the type of laboratory (e.g. diagnostic or otherwise) where such activities are carried out. See detailed requirements in Table 1. Non-diagnostic activities involving inactivated samples can be carried out in a BSL2 lab with due precautions. Please see Qn 10 for examples of inactivation methods.

Prior to the commencement of any activities involving samples/materials associated with SARS-CoV-2/COVID-19 virus (whether inactivated or otherwise), individual facilities shall perform a thorough risk assessment and implement appropriate risk mitigation measures, which must be reviewed and approved by the Biosafety Committee (if performed in a BSL3 facility) or personnel with good biosafety and microbiology knowledge and experience. In addition, the facilities shall implement a robust inventory system and document all movement (or transfer) of the samples. Facilities are also required to notify MOH of any adverse incident involving the handling of such samples.

Table 1 below serves as a guide for facilities handling samples/materials for non-diagnostic activities.

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1 BATA exempted purposes listed under Section 4 include:
   a) the disposal of any biological agent or toxin by a hazardous waste contractor
   b) the handling of any biological agent or toxin in the course of carrying out a diagnosis or an autopsy;
   c) the collection of food samples or samples from the environment for the purpose of carrying out any laboratory analysis to determine or identify, for public health purposes, the nature of any biological agent or toxin that is present in such samples or in the environment from which such samples have been taken; or
   d) the use or possession by any of the following persons of any finished cosmetic or medicinal product consisting of any toxin:
      (i) any person lawfully manufacturing, supplying, selling or dispensing the finished cosmetic or medicinal product;
      (ii) any registered medical practitioner using the finished cosmetic or medicinal product in the course of treating another person;
      (iii) any person using the finished cosmetic or medicinal product for the cosmetic or medical purposes for which it is intended.
Table 1: Requirements for handling samples/materials associated with SARS-CoV-2/COVID-19 virus, for non-diagnostic activities

<table>
<thead>
<tr>
<th>Sample Types</th>
<th>Requirements</th>
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<tbody>
<tr>
<td><strong>1</strong> Samples confirmed or known to contain infectious/replicative SARS-CoV-2/COVID-19 virus</td>
<td>(a) Handle in a BSL3 facility with requisite approvals for the virus; (b) All work procedures, risk assessments and safety measures shall be approved by the facility’s Biosafety Committee; and (c) Can only be handled outside of a BSL3 facility after inactivation of the materials using a validated method. Please refer to Qn 10 for more information regarding inactivation.</td>
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<td>(a) SARS-CoV-2 isolate (or culture)</td>
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<tr>
<td>(b) Clinical samples from COVID-19 patients (e.g. respiratory samples, blood, urine, bodily fluids, stool)</td>
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<tr>
<td><strong>2</strong> Samples/materials with high potential to contain infectious/replicative SARS-CoV-2/COVID-19 virus or where the absence of infectious/replicative SARS-CoV-2/COVID-19 virus has not been confirmed</td>
<td>(c) Can only be handled outside of a BSL3 facility after inactivation of the materials using a validated method. Please refer to Qn 10 for more information regarding inactivation.</td>
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<tr>
<td>(a) Samples from individuals who are close contacts of confirmed COVID-19 individuals;</td>
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<tr>
<td>(b) Environmental samples collected from areas or isolation ward where COVID-19 patients reside</td>
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<tr>
<td><strong>3</strong> Samples/materials from individuals who have recovered from COVID-19</td>
<td>Can be handled outside of a BSL3 facility as per risk assessment. If any downstream activities suggest the presence of infectious/replicative SARS-CoV-2/COVID-19 virus in the sample/material, a) MOH Biosafety shall be informed immediately; and b) Facilities are to secure and handle the sample/material in accordance with the BATA, i.e. to destroy or transfer it to a facility with an approval to possess the virus.</td>
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<tr>
<td>i.e. samples collected from COVID-19 patients who have been cleared for discharge and</td>
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<td>(a) are clinically well by Day 21 of onset of illness; OR (a) for those with a history of being immunocompromised, tested SARS-CoV-2/COVID-19 virus PCR negative, twice consecutively at least 24 hours apart.</td>
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<tr>
<td><strong>4</strong> Environmental samples with low potential to contain infectious/replicative SARS-CoV-2/COVID-19 virus</td>
<td>Can be handled outside of a BSL3 facility but facilities are required to ensure that: (a) The method used for inactivation is validated and effective, and approved by the Biosafety Committee (if performed in a BSL3 facility) or personnel with knowledge and expertise on biosafety and microbiology;</td>
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<tr>
<td>Example: Samples (environmental swab or air sampling medium) collected from common areas accessible by public.</td>
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<td><strong>5</strong> Samples/materials where the presence of infectious/replicative SARS-CoV-2/COVID-19 virus have been ruled out</td>
<td>Can be handled outside of a BSL3 facility but facilities are required to ensure that: (a) The method used for inactivation is validated and effective, and approved by the Biosafety Committee (if performed in a BSL3 facility) or personnel with knowledge and expertise on biosafety and microbiology;</td>
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<tr>
<td>Examples: (a) Inactivated SARS-CoV-2/COVID-19 virus culture;</td>
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<tr>
<td>(b) Inactivated clinical samples of COVID-19 patients;</td>
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### Sample Types and Requirements

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<tr>
<td>(c) Inactivated environment samples collected from the ward/isolation area where a COVID-19 patient resided; and (d) RNA extract from (1), (2), (3), and (4)</td>
<td>(b) Personnel are properly trained and competent to perform the inactivation process; and (c) Personnel strictly adhere to the procedures (which may include the equipment(^2) used, the concentration of the chemical and contact time with the chemical or the temperature used) of the inactivation method.</td>
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</tbody>
</table>

Please refer to Qn 10 for more information regarding inactivation.

In addition, facilities are advised to:

(a) Handle inactivated samples/materials as potentially infectious;
(b) Ensure that a thorough risk assessment is performed for activities involving inactivated samples/materials; and
(c) Ensure that risk mitigation measures are implemented for the safety of personnel and environment.

### Question 9: Are there any restrictions to the volume of SARS-CoV-2/COVID-19 virus that can be cultured?

As the risk of the activity will increase with the volume of the sample/virus handled, facilities are strongly advised to keep the volume of virus culture to laboratory scale (up to a maximum of 100mL) at any one time. Facilities shall perform a thorough risk assessment and implement appropriate (and additional, if needed) risk mitigation measures, and these MUST be reviewed and approved by the Biosafety Committee.

Additional requirements (e.g. engineering controls, laboratory design, policy and procedures) may be required if culture volume is beyond laboratory scale. Please consult MOH in such instances.

### Question 10: What are the methods and/or criteria for inactivating samples/materials containing or highly suspected to contain SARS-CoV-2/COVID-19 virus?

Methods employed for the inactivation of samples/materials containing or highly suspected to contain SARS-CoV-2/COVID-19 virus shall be validated against SARS-CoV-2/COVID-19 virus or related coronavirus (i.e. SARS CoV or MERS CoV). Facilities are advised to carry out validation of the inactivation in-house, or to adopt a well-established inactivation procedure validated by others.

Samples that may require inactivation (see Qn 8 above): Virus culture; Clinical samples (examples include but are not limited to: blood, serum, plasma, urine, tears, stool, tissue); and Environmental samples (examples include but are not limited to: surface swab, air sampling filters, suspension from air sampling).

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\(^2\) E.g. water bath versus heating block
Inactivation of SARS-CoV-2/COVID-19 virus can be achieved through a number of methods, examples can be found below. Individual facilities are advised to assess the appropriateness of the respective inactivation method for their sample types / materials and to ensure that inactivation procedures are closely adhered to, so as not to compromise the efficacy of the inactivation process.

<table>
<thead>
<tr>
<th>Examples of Inactivation Method</th>
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<tbody>
<tr>
<td><strong>Heat inactivation</strong></td>
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<tr>
<td>Example: Heat at 60°C or higher temperature for a specified minimum duration.</td>
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<tr>
<td><strong>Chemical Inactivation</strong></td>
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<tr>
<td>Examples: Acetone, formaldehyde, glutaraldehyde, Trizol.</td>
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<tr>
<td><strong>Solvent/Detergent</strong></td>
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<tr>
<td>Examples: Triton X, Tween 80 of appropriate concentration and duration of incubation.</td>
</tr>
</tbody>
</table>

**Note:**
The presence of certain substances, such as protein in the samples may affect the effectivity of the inactivation process. Facilities shall conduct their own risk assessment to evaluate the appropriateness of the chosen inactivation method. If in doubt, facilities should consider conducting in-house validation of the inactivation method.

The Biosafety Committee is responsible for ensuring that the inactivation procedures are reliable, that the inactivation procedures are strictly adhered to, and are carried out by properly trained and competent laboratory personnel. The Biosafety Committee is also advised to ensure that personnel handling the inactivated materials will **treat the materials as potentially infectious and take appropriate precautions when handling the materials.**

**Question 11: Are there any other biosafety guidelines and resources for laboratories handling samples/materials associated with SARS-CoV-2/COVID-19 virus?**

The following international biosafety guidelines on the safe handling of samples/materials associated with COVID-19 virus may be useful for laboratories:

a) World Health Organization – **Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans**
b) Public Health England – **Guidance for health professionals**
c) European Centre for Disease Prevention and Control – **COVID-19 Guidance and Technical Reports**
d) Centers for Disease Control and Prevention – **Information for Laboratories (2019-nCoV)**
e) Australian Government Department of Health – **Coronavirus (COVID-19) resources**

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References for inactivation methods include:

f) WHO (2003b) First data on stability and resistance of SAR coronavirus compiled by members of WHO laboratory network.