COMS Interim Policy on Multiplication or Amplification of SARS-CoV-2 Genes Utilized in University-Required SARS-CoV-2 Diagnostic Tests

I. Purpose

This policy outlines requirements for laboratories that perform certain laboratory techniques with nucleic acids representing the complete SARS-CoV-2 genome or portion(s) thereof in their research. It is meant to provide mechanisms for prevention of genetic element contamination within the laboratory and to mitigate the associated risks.

Research goals may require the multiplication or amplification of nucleic acids representing the complete SARS-CoV-2 genome or portion(s) thereof. This may be achieved by use of biological systems (e.g., multiplication of plasmids in *Escherichia coli*), *in vitro* nucleic acid amplification assays such as polymerase chain reaction (PCR), or other laboratory procedures. The number of copies of nucleic acid molecules representing SARS-CoV-2 genes can be greatly increased through the use of these techniques. If multiplied or amplified products are not handled carefully, large amounts of nucleic acid may be dispersed into the laboratory environment. Subsequent contamination of personnel or their personal belongings may potentially lead to positive results in COVID-19 tests that do not correspond to actual infection.

There are several risks associated with multiplication or amplification of any genes utilized in diagnostic tests required by Harvard University (University) for the health and safety protection of its community. The potential for multiple losses include, but are not limited to: 1) loss of researcher time for those who test positive and must isolate, as well as a loss of freedom for close contacts of such individuals who must quarantine; 2) loss of research integrity and progress on SARS-CoV-2 research due to nucleic acid contamination of the laboratory setting and cross contamination of laboratory samples, resulting in false positives, high background or skewed research results; 3) use of local occupational health and public health resources to retest and trace COVID-19 cases that may not be truly infectious; 4) a compromised testing frequency for those that test positive as there is currently a 90-day moratorium on testing an individual after a positive test; 5) perception and reputational risk due to external scrutiny of COVID-19 clusters in our laboratories; and 6) community health risk arising from individuals who may wrongfully dismiss positive test results as “false” and not take appropriate isolation or quarantine measures to protect the community.

To reduce the risk of nucleic acid contamination in the laboratory setting, personnel must adhere to the principles of biological containment, involving engineering, administrative, and personal protective equipment controls and behavior guidelines as outlined in this policy.

II. Applicability

All laboratory personnel (faculty, staff, trainees, students, visitors, and collaborators) that perform or oversee research activities that lead to the amplification or multiplication of nucleic acids representing any genes utilized in SARS-CoV-2 diagnostic tests required by Harvard University must follow this policy.

III. Definitions

Contamination:

For the purposes of this policy, contamination refers to known or suspected nucleic acids representing the complete SARS-CoV-2 genome or portion(s) thereof, found on a physical surface or item that is outside a contained vessel in the laboratory.

Environmental sampling:

The collection of dust and other particles from the environment. For the purposes of this policy, we are focused on sampling laboratory surfaces and personal belongings for laboratory workers handling nucleic acids representing the complete SARS-CoV-2 genome or portion(s) thereof. Sampling may also include the lab benches, desks, and personal belongings of co-workers not directly handling SARS-CoV-2 nucleic acids. The sampling method and number of samples collected will be determined by the circumstances of the potential contamination.

IV. Implementation Procedures

Mechanism for compliance:

PI must register all work involving multiplication or amplification of any genes utilized in University-required SARS-CoV-2 diagnostic testing through a protocol submission or amendment to an existing protocol in eCOMS. COMS will review and approve all multiplication or amplification of nucleic acids representing the complete SARS-CoV-2 genome or portion(s) thereof utilized in University-required SARS-CoV-2 diagnostic testing. An approval letter will be provided, and committee discussion will be documented in the meeting minutes. COMS approval will be based on the risk assessment of the institutional biosafety officer (BSO) and will include recommendations and requirements for the laboratory handling of this material. See references for specific guidance. Laboratories must follow all safety requirements incorporated into their COMS protocol approval letter.

Oversight and Monitoring

In addition to the safety recommendation and requirements for multiplication or amplification of nucleic acids representing any portion(s) of the SARS-CoV-2 genome utilized in University-required SARS-CoV-2 diagnostic testing by laboratories, the following institutional oversight will occur:

a. Online laboratory questionnaire (available here) must be completed by all PIs of laboratories in possession of any nucleic acids representing the SARS-CoV-2 genome or portion(s) thereof.

b. On-site and/or record-keeping inspections of the laboratory (announced or unannounced), as needed.
c. Institutional biosafety officers will investigate reports of known or suspected contamination.
d. Institutional biosafety officers will report the outcome of their investigation to COMS.
e. The outcome of the investigations may mandate sampling and testing.
Environmental sampling and testing for contamination, as needed:
Testing may be required for laboratories that focus on the multiplication or amplification of any genes utilized in University-required SARS-CoV-2 diagnostic testing. If required, laboratories must complete their own sampling and testing, and provide testing results to their institutional biosafety officer at a frequency indicated in their COMS approval letter, for review and monitoring. Repeat and more frequent sampling by laboratories may be required based on risk assessment of the work completed in the laboratory (e.g. opening of sample tubes) or in response to incidents of contamination. Laboratories that have environmental sampling requirements must consult with their institutional biosafety officer on how to conduct sampling and testing in their laboratory.
f. COMS will review investigation reports submitted by institutional biosafety officers and will discuss all incident and investigations with COMS leadership and/or at subsequent COMS meetings.

Risk Assessment

The containment level of the work for COMS review is as follows:

a. Laboratory techniques that lead to multiplication or amplification of SARS-CoV-2 sequences (risk assessment determined on a case-by-case basis)

Special practices

The special practices to address lab and personnel contamination from multiplication or amplification of nucleic acids representing the complete SARS-CoV-2 genome or portion(s) thereof include:

a. Requirements and recommendations provided by the institutional BSO
b. Institutional requirements may vary. Please reference the following documents for your institution as follows:

Institution	Document Title	Where to find document
Harvard University (all schools)	Harvard University Environmental Health and Safety: SARS-CoV-2 Genetics Elements:	https://www.ehs.harvard.edu/secure/node/8604

	Laboratory Contamination Prevention Guidelines	
Harvard University	SARS-CoV-2 Use Survey	https://www.ehs.harvard.edu/programs/covid-19sars-cov-2-research
Wyss	SARS-CoV-2 Amplicon Work at the Wyss	https://hu.sharepoint.com/sites/wyss/ehs/Shared%20Documents/SARS-CoV2%20Amplicon%20Work%20at%20the%20Wyss%20SOP.pdf

V. Authority

The Committee on Microbiological Safety shall enforce this policy. Should the policy not be followed, or approved safety requirements found to be not effective, COMS may require that the protocol be amended, suspended, or terminated. COMS may also require additional stipulations on the protocol related to work practices or other requirements. In some cases, reporting the incident to University administration or Local, State, or Federal Public Health offices may be warranted.

VI. References

Good Laboratory Practice to Avoid Contamination in Your qPCR Experiments

Biosafety Level 1 Laboratory Requirements for COMS -Approved Projects

Harvard University Environmental Health and Safety: SARS-CoV-2 Genetics Elements: Laboratory Contamination Prevention Guidelines

NIOSH Emergency Response Resources

Harvard COVID Testing and Tracing Policies