

COVID-19 vaccine breakthrough case investigation

Information for public health, clinical, and reference laboratories

Objective

Investigate SARS-CoV-2 infections among people who received COVID-19 vaccine to identify trends or clustering in demographic, the administered vaccine, or the infecting virus.

Case definition

A person who has SARS-CoV-2 RNA or antigen detected on respiratory specimen collected ≥ 14 days after completing the primary series of an FDA-authorized COVID-19 vaccine.

Rationale and request for additional laboratory testing

- CDC and state/local health departments are investigating COVID-19 vaccine breakthrough cases.
- CDC would like to receive viral sequence data and respiratory specimens from COVID-19 vaccine breakthrough cases to assess the frequency of SARS-CoV-2 variant.
- When a case is identified, the health department will contact the laboratory to determine if there are residual specimens from the positive test (i.e., respiratory specimen) and request that those be held for shipment to CDC.
- The health department will also request the specimen ID numbers and the cycle threshold (Ct) value for positive RT-PCR results.
- If your laboratory identifies a COVID-19 vaccine breakthrough case, please report it to your state health department so they can initiate the investigation with CDC.

SARS-CoV-2 sequence data

- Some COVID-19 vaccine breakthrough cases will have SARS-CoV-2 sequencing performed at a clinical, public health, or commercial reference laboratory.
- For cases with sequence data that are already available, please provide the SARS-CoV-2 lineage and GISAID or GenBank accession number to the state health department.

Respiratory specimen for SARS-CoV-2 sequencing

- **Specimen selection**
 - Clinical specimens for sequencing should have an RT-PCR Ct value ≤ 28 .
 - If a Ct value is not available, specimens that are positive for SARS-CoV-2 RNA or antigen by another testing modality may be sent.
- **Specimen storage and labeling**
 - Store the specimens at -70°C or colder.
 - Use 1.0–2.0 mL O-ring screw cap microcentrifuge tubes.
 - Label each specimen with the “SPHL Submitter Specimen ID” or the “Original Submitter Specimen ID” (if no SPHL ID).
- **Fill in the following fields on the two forms for submitting specimens to CDC.**
 - *Global File Accessioning Template (GFAT) form*
 - Origin [Column D]: “**Human**”
 - Test order name [Column E]: “**SARS-CoV-2 whole genome sequencing**”
 - Suspected agent [Column F]: “**SARS-CoV-2**”
 - Specimen collected date [Column AC]
 - SPHL submitter ID [Column AN]



- SPHL submitter patient ID [Column BB]
 - SPHL submitter specimen ID [Column BD] – **This number should be reported by the state health department into the REDCap system.**
 - Comments [Column GM] **Please enter the COVID-19 Vaccine Breakthrough database ID that was assigned to this case.**
 - CDC event ID [Column IB]: **“1890”**
 - Event name [Column IC]: **“Vaccine breakthroughs”**
- *National SARS-CoV-2 Strain Surveillance (NS3) Supplementary Form*
 - Submitter specimen ID [Column B]
 - Reason for submission [Column C]: **“ES21-04 – Vaccine Breakthrough”**
 - Primary assay name [Column E]
 - Assay target [Column F]
 - Ct value [Column G]
 - Previously sequenced [Column Y]
 - GISAID accession [Column Z] – only if sequenced
 - GenBank accession [Column AA] – only if sequenced
- **Packaging specimens for shipment**
 - Package and ship all specimens as Category B infectious substances in compliance with IATA and US DOT (<https://www.cdc.gov/coronavirus/2019-ncov/lab/lab-biosafety-guidelines.html#specimen>).
 - Include a hard copy of the forms and/or specimen manifest in the package.
 - Include vaccine breakthrough case specimens with your weekly NS3 sample shipment but indicate the vaccine breakthrough specimens on the form.
- **Shipping specimen(s) to CDC**
 - Email both sarsseqshipping@cdc.gov and eocevent531@cdc.gov when you send the specimen.
 - Attach the completed GFAT and NS3 supplementary forms.
 - Include package tracking information.
 - Send specimens on a Monday or Tuesday.
 - Ship overnight on dry ice using your usual courier (e.g., FedEx, UPS).
 - Address the package to:

ATTN: STATT Lab: Unit 66 TRL
Centers for Disease Control and Prevention
1600 Clifton Road, NE
Atlanta, Georgia, 30333
Telephone: 404-639-3931
Email: sarsseqshipping@cdc.gov
- **Sequencing results**
 - Once CDC obtains genomic sequences and assesses them for quality, CDC will upload the consensus sequence data and release into GenBank and GISAID.
 - CDC will also send a report to the submitting and state public health laboratories.
 - SARS-CoV-2 variants are circulating in the United States and will cause some vaccine breakthrough cases. It is important to consider what SARS-CoV-2 variants are circulating in the community when evaluating variants found in breakthrough cases.