SeroNet
Template for SARS-CoV-2 post-vaccine surveillance studies in cancer/immunocompromised individuals

Purpose:
Provide a common study template that could be used within SeroNet and beyond for the serosurveillance of cancer/immunocompromised patients receiving a SARS-CoV-2 vaccine. The template could be applicable to prospective interventional trials when investigators have access to vaccines for experimental use, or for observational studies where individuals receive vaccines as they become available in the community.

Population can include:
- Newly diagnosed cancer patients
- Patients currently undergoing treatment for cancer, including chemotherapy, radiation therapy, immunotherapy, targeted therapy, or combinations of therapies
- Individuals with a history of cancer/cancer survivors
- Immunocompromised individuals
- Individuals with autoimmune diseases

This document is intended to be agnostic as to which vaccination individuals receive and will provide recommendations for:
- Population
    - Recommend focus on a particular population if possible. For example, a specific cancer type, autoimmune disease, or individuals treated with certain therapeutics.
    - Inclusion of a control group, or consideration for an external control group using the same timepoints and assays.
- Specimen selection and collection
    - Timepoints for vaccination and collection
    - Specimen types
    - Specimen collection protocols
    - Key determinants to be considered
- Assays
    - Type
    - Benchmarking/standardizing
    - Standard protocols where available
- Data collection and common data elements (CDEs)
    - Demographics
    - Clinical characteristics
        - Including cancer CDEs as well as for other co-morbidities
    - Vaccine kinetics

Design Considerations:

- Vaccine responses can be influenced by a number of factors and conditions
    - Cancer and autoimmune disease and their treatments could affect immunocompetence and therefore vaccination responses.
    - What is this impact of cancer and/or cancer therapy on response to the vaccine and conversely, what is the impact of the vaccine on cancer treatment or cancer progression?
    - Individuals with cancer are a complex and extremely diverse population and there are a multitude of considerations, including approaches to capturing the appropriate clinical information regarding an individual's cancer type, subtype, stage, treatments/regimen (chemotherapy, radiation therapy, immunotherapy, surgery), time since diagnosis, timing of therapy, etc.
    - Individuals with autoimmune diseases could experience flareups or other adverse reactions following vaccination.
- Recommendations for when specimens should be collected for optimal tracking of the vaccine induced immune response vs. those timepoints that are important from a cancer treatment perspective.
    - Inclusion of additional sampling timepoints following a documented infection (positive PCR) after vaccination.
    - Inclusion of additional sampling timepoints when adverse events are observed.
- The inclusion of a healthy control group within the study, or identification of an external control group using similar collection and testing procedures.
- Collection of non-cancer related clinical data performance status, chronic diseases and specific therapies, co-morbidities, tobacco history (particularly lung cancer), alcohol history, other medications, etc.
- Collection of quality-of-life considerations and patient reported outcomes

Scientific and Clinical Questions

- Anamnestic response is likely to be blunted in cancer/immunocompromised population as measured by antibody titer.
    - The degree of compromise in antibody responses and decay is unknown.
    - Specific populations and treatments should be correlated with antibody kinetics.
- Changes in incidence of adverse events (vaccine or cancer related).
- Considerations for the spacing of vaccine doses or need for an additional boost to confer protective "titers".

Timeline and specimen collection

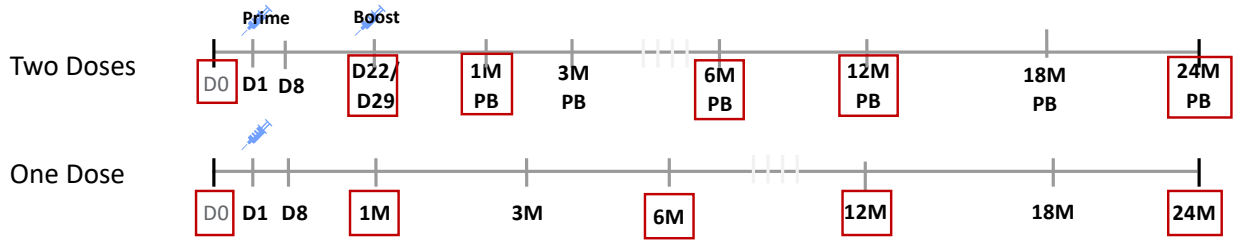

***Figure 1**. Recommended timepoints for the collection of biospecimens following vaccination with a two dose or single dose vaccine. The red box indicates the recommended minimal timepoints for specimen collection to measure vaccine immune kinetics.*

Dependent upon the needs of the study, this template provides guidance about the core or minimum number of timepoints and sample types to collect post-vaccination for meaningful interpretation of the immune response to the vaccine. Note that the D0/D1 timepoint is intended to establish a baseline and samples should be collected prior to vaccination. This sample collection can occur on the same day as the vaccination, or up to one week before a planned vaccination.

It is also recommended to collect a nasal swab at the time other specimens are collected for measuring active infection/viral shedding.

***Table 1**. Recommended collection timepoints per specimen type. PB denotes post-boost timing, for single dose vaccines the timepoints PB should be considered as well (1-, 3-, 6-, 12-, 18-, and 24-months post vaccination). The timepoints highlighted in red and with an X denote the minimum recommended specimen collection per timepoint. Other sample collection timepoints within the table are recommended for additional collections based on study aims.*

Sample Type	D0/D1 (Prime)	D4	D8	D22/29 (Boost)	1M (PB)	3M (PB)	6M (PB)	12M (PB)	18M (PB)	24M (PB)
Serum										X
Plasma										
PBMC	X			X	X					
DBS										
Saliva										
Nasal Swab	X			X	X		X	X		X

Table 2. *Recommended assays per timepoint following vaccination. X denotes the minimum recommended timepoints per assay type. Other sample collection timepoints within the table are recommended for additional assays depending on study aims.*

Assay Type	D0/1D1 (Prime)	D4	D8	D22/29 (Boost)	1M PB	3M PB	6M PB	12M PB	18M PB	24M PB
Serology (LBA)										X
Serology (Neutralization Assay)	X			X	X			X		
Immune Cell Repertoire	X	X	X	X	X					
ELISPOT	X		X	X	X	X				
Intracellular Cytokine Staining	X		X	X	X	X				
Assays for innate immunity	X	X	X							

Table 3. *Immune assays by sample type*

Assay	Serum	Plasma	PBMC	DBS	Saliva	Nasal Swab
Serology (LBA)						
Serology (Neutralization Assay)	X	X			X	
Immune Cell Repertoire			X			
ELISPOT			X			
Intracellular Cytokine Staining			X			
Assays for innate immunity	X	X	X			
SARS CoV 2 Diagnostic Test						X

Assay Types

The SeroNet Operations (Ops) groups will be key to collecting information about assays that are used by SeroNet investigators, including validation and regulatory status, and the intended use for clinical or research studies with the goal of developing standard or harmonized assays to enable cross-laboratory and study analyses. The Serology Assays Ops group is currently planning on conducting a comparative study for high-throughput immune monitoring assays, in particular ligand binding assays (LBA), to determine assay performance characteristics and evaluate the suitability for the intended use.

Sample collection/preparation protocols are dependent upon the assay type. The attached documents provide standard procedures from the FNL Serology Lab for:

- Serum biospecimen processing
- PBMC isolation and cryopreservation

It is recommended to use assays that have been well characterized and validated. Below is a list of recommended assay types and protocols as available at the time of document completion.

- **Serology (LBA):** To distinguish natural infection from vaccine induced immunity we recommend performing an IgG LBA against both the Spike (natural infection and vaccine-mediated) and N (natural infection) proteins.
  - It is recommended to perform an FDA EUA quantitative assay.
  - When using an in-house assay provide information about the sensitivity and specificity of the assay compared to the National standard available from the FNL Serology Lab.
- **Serology (neutralization assay):** To determine the presence and magnitude of functional, neutralizing SARS-CoV-2 antibodies as well as correlation with ligand binding assay results. This is a more laborious assay and can be considered at limited timepoints or in limited subsets.
- **Immune cell assessments:** Disease related abnormalities and treatments for cancer and autoimmune disease can impact immune cell populations/ immunocompetence and potentially affect the response to vaccination. Therefore, especially a baseline immune assessment will be critical for the correlation of immune kinetics to immune status.
  - Assay types can include flow-cytometry and CyTOF.
- **ELISPOT**: Quantitative assay that measures cytokines released from antigen stimulated T cells.
- **Intracellular cytokine staining (ICS):** Flowcytometry-based assay that allows for simultaneous cellular phenotyping and single cell cytokine detection used to assess T cell responses.
- **Innate immune cell measurement assays**:
  - This template does not make specific assay recommendations to measure the innate immune response (note that the immune cell repertoire profiling can include assessment of innate immune cell populations).
- **SARS-CoV-2 diagnostic test**: PCR-based assay to detect viral RNA.
  - Recommend using an FDA EUA assay.

Common Data Elements

To facilitate SeroNet-wide data analyses the use of a minimum set of common data elements (CDEs) are recommended. Some data elements are recommended to be collected at each timepoint/encounter if feasible, others can be collected following consent at the beginning of the study. CDEs are roughly divided by:

- Demographics
- Clinical characteristics

- Patient reported outcomes
- Assay results

See the spreadsheet for draft SeroNet Common Data Elements