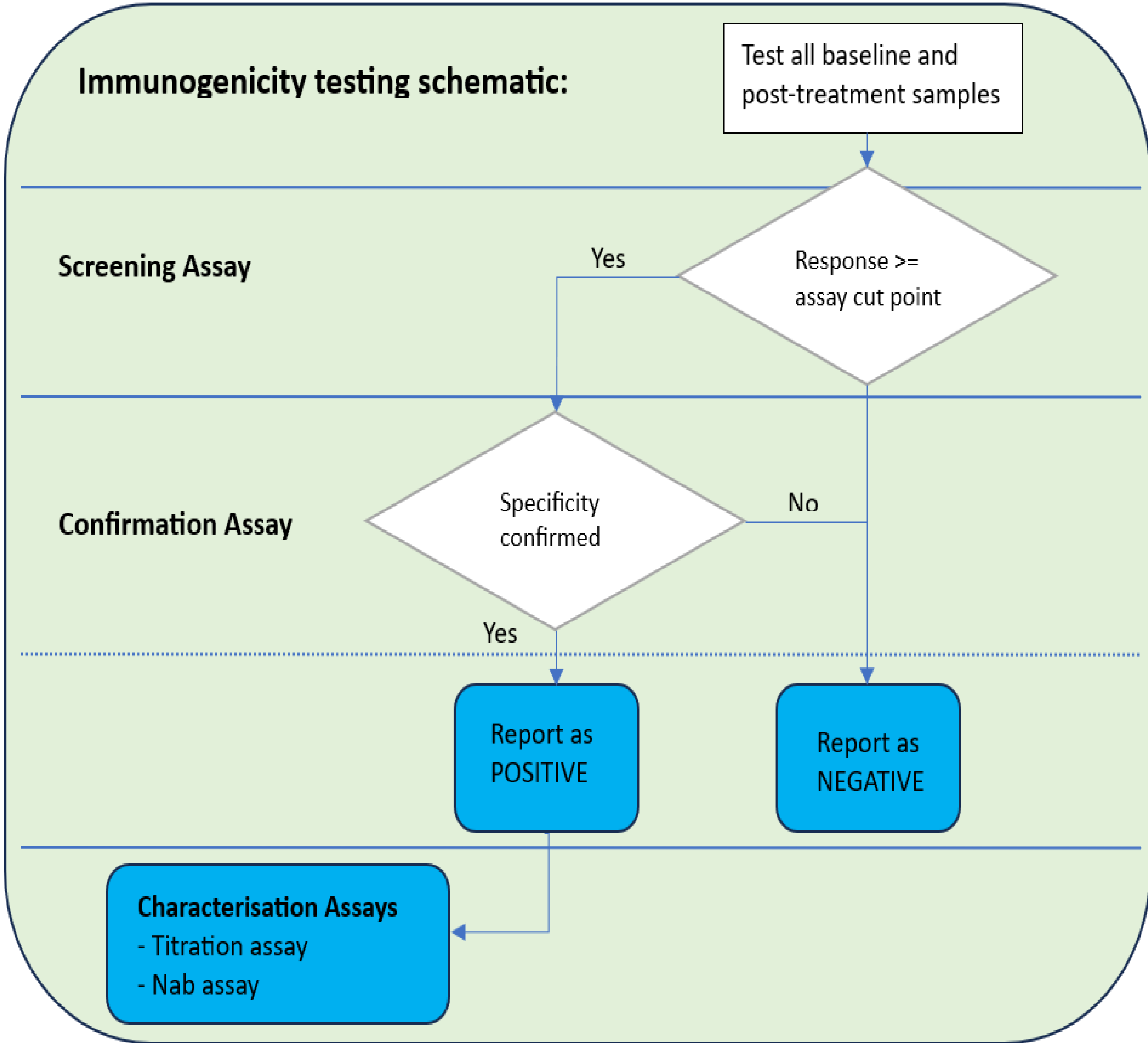




Analysis and Reporting of Immunogenicity Data

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Immunogenicity is a measure of the immune response to a therapeutic drug resulting in generation of anti-drug antibodies (ADAs, also known as anti-therapeutic antibodies (ATAs)). ADAs can be neutralizing and non-neutralizing. Clinical samples are usually tested for non- neutralizing ADAs in a sequence of assays: screening, confirmation, and titration. Neutralizing only employ a screening assay.



IS SDTM

Information included:

SCREENING ASSAY:

Informs if **ADA** is present (POSITIVE) or not (NEGATIVE).

Informs if **NAb** is present (POSITIVE) or not (NEGATIVE), if measured.

CONFIRMATION ASSAY:

Confirms if ADA is present (POSITIVE) or not (NEGATIVE).

TITRATION ASSAY: Each positive sample from the confirmation assay is usually assessed using serial dilution to provide a titer, corresponding to the highest dilution factor that still yields a positive test result.

WHAT DO WE NEED FOR ANALYSIS?

- Overall sample status:** For ADA, this will be the confirmation assay result, if available, otherwise screening.
- Negative Inconclusive/conclusive:** Uses PK drug concentration and a validated screening assay drug tolerance value. For ADA negative samples post baseline, compare the drug concentration with tolerance value. Sample is inconclusive if the drug concentration is > tolerance value and conclusive if the drug concentration is <= tolerance value.
- Treatment-induced ADA:** Participant with at least one post-baseline ADA-positive sample and an ADA negative or missing baseline sample.
- Treatment-boosted ADA:** A participant with an ADA-positive baseline sample, in which at least one post-baseline sample titer value is four-fold greater than the baseline titer value or if no titers to compare, where baseline is ADA-positive and there is at least one ADA-positive sample post-baseline.
- Treatment-unaffected ADA:** A participant with an ADA-positive baseline sample, in which all post-baseline sample titer values are less than or equal to a four-fold increase in titer values relative to the baseline titer value or was ADA-negative at all timepoints post-baseline.
- Duration of ADA:** Time between first and last ADA-positive sample for treatment-induced ADA participants. Only required for Treatment-induced participants.
- Drug Concentration:** As measured by Pharmacokinetics, provides the level of drug in the body at the time the ADA sample was taken.

ADIS ADaM

PARAMCD=ADBABDSS AVALC=Positive or Negative

PARAMCD=ADBABDSS

AVALC=Negative Conclusive or Negative Inconclusive

TRTINDFL=Y for all records for the participant

TRTBSTFL=Y for all records for the participant

TRTUNFFL=Y for all records for the participant

PARAMCD=DURADA AVALC=XX
AVALC=1 Timepoint only
AVALC=XX – Last Timepoint

PARAMCD=DRGCONC From PC SDTM, matching on participant and timepoint:
AVAL=PC.PCSTRESN

Information carried over from SDTM:

SCREENING ASSAY – PARAMCD=ADBABDS
CONFIRMATION ASSAY – PARAMCD=ADBABDC
NEUTRALISING SCREENING ASSAY – PARAMCD=ADBNABDC
TITER – PARAMCD=ADBABTT

Immunogenicity in other ADaMs:

ADAE – AE Overview by Participant ADA Status
ADEFF – Efficacy Measure by Participant ADA Status
ADPP – Influence of ADA on PK Parameters