

2.3.S.4. CONTROL OF DRUG SUBSTANCE

This section contains information specific for presentation Comirnaty Original, which is discontinued. For information purposes, data/information supportive of the platform development approach for other presentations is maintained.

2.3.S.4.1. Batch Analyses

BNT162b2 drug substance batches used for nonclinical toxicology, clinical trials, process performance qualification (PPQ), emergency supply, and stability are summarized in [Section 3.2.S.4.4 Batch Analyses](#).

A full drug substance genealogy can be found in Section 3.2.S.2.6 Developmental History and Comparability. The analytical testing strategy applied to BNT162b2 drug substance has evolved throughout the development history. Information on the drug substance method evolution/testing strategy is provided in Section 3.2.S.2.6 Analytical Method Evolution.

2.3.S.4.2. Justification of Specification

The specification for BNT162b2 drug substance is based on an understanding of the control strategy and CQAs for the drug substance. The attributes tested and associated acceptance criteria ensure the consistency of drug substance and linkage to clinical experience. This specification was established to ensure the quality, purity, potency/biological activity and safety of the commercial drug substance at release and during storage. The specification was informed by:

- Development experience (manufacture and analytical) with BNT162b2 drug substance;
- Total BNT162b2 manufacturing experience, including drug substance batches used to manufacture drug product lots used in nonclinical and clinical studies, as well as drug substance process performance qualification batches;
- BNT162b2 drug substance process characterization studies and process validation data;
- The release and on-going stability data for drug substance.

2.3.S.4.2.1. Specification-Setting Strategy

A comprehensive panel of analytical procedures has been implemented along with corresponding acceptance criteria to monitor and control BNT162b2 drug substance quality at release and over shelf life.

Appropriate analytical procedures were established to monitor and assess BNT162b2 drug substance as detailed in Section 3.2.S.4.2 Analytical Procedures and Section 3.2.S.4.3 Validation of Analytical Procedures. **CCI**

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Because there are no significant trends that would impact the shelf life of the drug substance

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[REDACTED] the acceptance criteria used for stability over shelf life are the same as the acceptance criteria used for batch release. In summary, the acceptance criteria in the drug substance specification reflect the current understanding of criticality of quality attributes, their impact on product performance, their stability, and the quality of the product used in clinical trials.

A global approach to development has been undertaken across multiple manufacturing facilities in order to maximize vaccine production and availability. As such, information and analysis presented within Section 3.2.S.4.5 Justification of Specification reflects the global development effort, and the drug substance batches included in the specification analysis are not limited to those produced in market-specific registered manufacturing facilities. The batches included in the establishment of the commercial specification are presented in Section 3.2.S.4.5 Justification of Specification.

The analytical testing strategy applied to BNT162b2 has evolved during the development history for the molecule. Several drug substance analytical method changes have been made

during product development, particularly in preparation for process 2 manufacture. In preparing the analytical testing panel for setting of acceptance criteria, improved methods for the assessment of product quality have been introduced late in development prior to process validation. In addition to the BNT162b2 product-specific methods, standard compendial test methods are performed in accordance with the current requirements.

Method evolution and changes, with bridging information as appropriate, are described in detail Section 3.2.S.2.6 Analytical Method Evolution.

Please refer to Section 3.2.S.4.5 Justification of Specification for further information.

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