

3.2.A.2. ADVENTITIOUS AGENTS SAFETY EVALUATION [PUURS]

Multiple mechanisms, procedures, and assays are used to minimize the entry of adventitious agents into the process stream and detect those agents that do enter the process stream. The adventitious agent control program includes the engineering systems of the facility and vessels, the control of the raw materials used in the process, various filtration steps to control microbial load in buffers and the process stream, and in-process and environmental testing to monitor the level of adventitious agents in and around the process stream.

3.2.A.2.1. Introduction

The main theoretical risk associated with these ingredients is a contamination of the product by Transmissible Spongiform Encephalopathy (TSE) agents. A multifaceted program has been established to ensure the viral safety of the drug product, including development of a formulation process that is devoid of human or animal proteins.

Management of transmissible spongiform encephalopathy (TSE)/ bovine spongiform encephalopathy (BSE) risks is part of the comprehensive adventitious agent control program for COVID-19 Vaccine.

All raw materials used in the production of BNT162b2 are evaluated as part of a comprehensive program to identify and manage TSE/BSE risks. Under this program, the risk of transmission of TSE/BSE through the use of animal-derived materials is managed by sourcing such materials in a manner consistent with the current industry guidelines including those from the European Medicines Agency (EMA), the Therapeutic Goods Administration (TGA), and the World Health Organization (WHO).

The conclusion from the TSE/BSE risk evaluations performed for raw materials is that the risk of transmitting TSE/BSE via BNT162b2 has been minimized.

Details of any material, reagent, or component containing material of animal origin including its source and preparation are discussed in the following sections. These products are commercially available and are not specially produced for the applicant.

Other materials from animal origin are used in the production of polymer for the filters, containers and/or filters components. These equipment components may contain traces of animal tallow derivatives. The tallow is processed under rigorous conditions and is considered compliant with the TSE note for guidance (EMA/410/01).

Moreover, equipment and materials are cleaned, sterilized and/or chemically decontaminated according to validated procedures.

3.2.A.2.2. Non-Viral Adventitious Agents

3.2.A.2.2.1. Raw Material Sourcing and Testing

Raw material vendors are qualified to sourcing materials from them for use in the manufacturing process. Raw material information is provided in 3.2.S.2.3 Control of Materials used in Manufacturing.

In particular, the human or animal-derived materials are provided in Table 3.2.A.2-1. All other materials are of synthetic and/or biological origin.

Table 3.2.A.2-1. Materials of Animal Origin Used in the Manufacture of BNT162b2 DP

Raw Material (Source ^a)	Manufacturing Process Stage (Use)	Country of Origin ^b	Comment (Certificate of Suitability availability, other significant safety details)
Tubing assembly	Drug product manufacturing	Not available	The materials of construction of these tubing assemblies are not of direct animal origin. However, polypropylene and polycarbonate used in the filter case may contain trace level of additives, derived from animal tallow. The polypropylene meets the requirements of the current guidance which gives specific consideration to tallow derivatives and states that they are unlikely to be infectious if processed under rigorous conditions.
Various filters	Drug product manufacturing	Not available	The materials of construction of these tubing assemblies are not of direct animal origin. However, polypropylene and polycarbonate used in the filter case may contain trace level of additives, derived from animal tallow. The polypropylene meets the requirements of the current guidance which gives specific consideration to tallow derivatives and states that they are unlikely to be infectious if processed under rigorous conditions.

a. Source as defined in supplier documentation.

b. Countries of origin as defined in supplier documentation.

3.2.A.2.3. Conclusion

In summary, a comprehensive, multifaceted program is in place to ensure that the risk, with respect to potential viral and non-viral adventitious agents contamination of drug product, is acceptable. Equipment is cleaned by validated cleaning procedures described in 3.2.A.1 Facility and Equipment – Puurs. In addition, sterility testing is performed on the final product, as described in 3.2.P.5.1 Specifications.