

16 November 2020
EMA/617752/2020
Human Medicines Division

EMA Product team peer review of the CMC Rolling Review reports for COVID-19 mRNA Vaccine BioNTech (covid-19 mrna vaccine (nucleoside-modified))

EMA Product team reviewers	GCP Inspections: Maria Antonietta Antonelli Paediatrics: Laura Fregonese GMP Inspections: Claudio Facchini RMP: Emil Cochino Quality: Ton van der Stappen Regulatory Affairs: Christelle Bouygues QRD: Monica Prizzi Scientific Advice Administrator: Efthymios Manolis Product Lead: Vanessa Seguin
Rapporteur	Filip Josephson
Co - Rapporteur	Alexandre Moreau
CHMP Peer Reviewer	Ingrid Wang
PRAC Co-Rapporteur	Ulla Wändel Liminga
PRAC Rapporteur	Menno van der Elst
Product lead	Vanessa Seguin
Procedure No.	EMA/H/C/005735/RR

Indication (4.1) Proposed by the applicant

SIAMED indication summary:

Active immunization against COVID-19 disease

SIAMED full indication:

The Agency comments on the (Co)Rapporteurs ARs are particularly made in relation to clarity and consistency of the "Overview and List of Questions".

The Agency comments should be **aimed at**:

Proposing improvements of the questions regarding clarity and format and proposing deletions of redundancies (including grouping /merging of questions) in the (Co) Rapporteurs' LoQ. Are the questions clear, such that the applicant would understand what sort of answer is expected?

Ensuring consistency between the ARs and the questions raised and vice versa

Ensuring that issues raised during presubmission (minutes) and validation (letter) have been adequately addressed in the assessment reports

Ensuring that (Co) Rapporteurs ARs follow the Day 80 templates and guidances, i.e. does it address all indents described by the Annex to the Directive? Check the legal basis of the application so as to ensure what sort of assessment to expect. Is the proposed legal status in agreement with similar approved products?

Drawing attention to relevant CHMP guidelines and Scientific Advice.

Drawing attention to contents of previous dossiers and questions raised on similar products in the Centralised Procedure (Memory Database).

Raising issues related to inspection (GCP, ethics) as appropriate.

Proposing improvement in the product information

1. General (with regard to previous submissions; templates and guidance etc)

1.1. Structure and Format of the Overview

2. List of questions (make reference to the number of the question in Rapp and CoRapps AR as appropriate)

2.1. Quality

GMP

General

RNA Integrity

According to the Company, the efficacy of the DP is dependent on the expression of the delivered RNA, which requires a sufficiently intact RNA molecule. The RNA integrity of the BNT162b2 DP is routinely tested at release and during stability. It is noted that there is an apparent lower %RNA integrity at the level of both DS and DP for the Clinical inventory, Emergency Supply and PPQ batches when compared

to the batches used in clinical trial (study C4591001); DS 62-75% (process 1) vs 77-86% (process 2), DP 55-63% vs 69-86%. It is stated that DP lot EE8493 (%RNA integrity: 55%) manufactured from the 20Y513C101 DS (process 2, %RNA integrity: 62%) has also been designated as for use as clinical material. Hence, DP for the clinical trial was manufactured using the classical processes. In the bridging part of trial, C4591001 evaluates material manufactured by the upscaled process employing Polymun for the LNP formulation and Pfizer, Puurs for fill and finish. The first doses from the Process 2 batch were dispensed on 19 October 2020, and the first subjects received dose 2 on 09 November 2020. As the cut-off date for the IA was prior to 09 November 2020, the IA doesn't include data from subjects dosed with Process 2 material, and the Company does not expect to have Process 2 included in the Final Analysis dataset either.

Met opmerkingen [vdST1]: But was first dose process 1 with higher %RNA integrity?

2.2. Non-clinical

Not applicable

2.3. Clinical

Not applicable

2.4. Risk Management Plan

Not applicable

3. Proposed improvements in the product information

Not applicable