Process Validation Plan
For
Covid-19 Vaccine (PF-07302048, BNT-162) Drug Product – Phase I

AUTHOR:

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NAME	JOB TITLE	SIGNATURE & DATE

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1. Introduction

1.1 Purpose

This document describes the holistic process validation approach for Phase 1 of Covid-19 Vaccine (PF-07302048, BNT-162) drug product formulation and fill/finish processes in PGS Puurs, PGS Kalamazoo, Dermapharm and Polymun CMO to support potential emergency use of supplies. The following supply nodes are in scope of this document:

- Supply 1 (PGS Puurs): Formulation in Vaccine Cell 2 (booth 3 and 4), Filling at Focus Cell 2, Inspection at Focus Cell 2, packaging in Focus Cell area and freezing in Logistics 2
- Supply 2: Formulation by Polymun, transport to PGS Puurs, sterile filtration in formulation booths 7 or 10, Filling on WSL5, Inspection and packaging on IL7 and freezing in Logistics 2
- Supply 3: Formulation by Dermapharm, transport to PGS Puurs, sterile filtration in formulation booths 7 or 10, Filling on WSL5, Inspection and packaging on IL7 and freezing in Logistics 2
- Supply 4 (PGS Kalamazoo): Formulation in Biologics Operations, Filling at Line 8, Inspection at Line 9, packaging at Line 82 and freezing in Building 41 Warehouse
- Supply 5 (PGS Kalamazoo): Formulation in Biologics Operations, Filling at Line 18, Inspection at Line 12, packaging at Line 82 and freezing in Building 41 Warehouse

The project described is the first phase of the validation of these different supply nodes for manufacturing the Covid-19 Vaccine. The first phase includes manufacturing of 1 batch of each supply node. In a later phase, the full validation of all supply nodes will be completed. The phased approach is established to ensure having process validation data of each individual supply node as soon as possible that can support the 'Emergency Use Authorization' (EUA) and conditional approval applications. The Phase I and Phase II process validation campaigns are separated by continued EUA manufacturing. Changes in between Phase I and Phase II will be assessed through change management procedures.

The project described is covered by the referenced CRFs (cf. ref. 1-3).

1.2 Project Scope

1.2.1. General description

The scope of the validation is covered by the different CRFs (cf. ref 1-3). This Validation plan provides the rationale for the validation approach. A summary of the process in scope can be found in the process definition document (cf. Ref 4) and is shown in Table 1.

The BNT162b2 drug product is prepared as a preservative-free, sterile, multi-dose concentrate of RNA-containing lipid nanoparticles (LNP) formulated in phosphate-buffered saline and 300 mM sucrose at pH 7.4 to be diluted for intramuscular administration. The drug product is filled at 0.45 mL/vial (0.5 mg/mL) into 2 mL glass vials which are stoppered and capped to provide total of 225 μg of the RNA in a multi-dose vial. At the administration site, the vaccine drug product is diluted with 0.9% sodium chloride and is intended to supply 5 doses per vial at 30 μg/dose.

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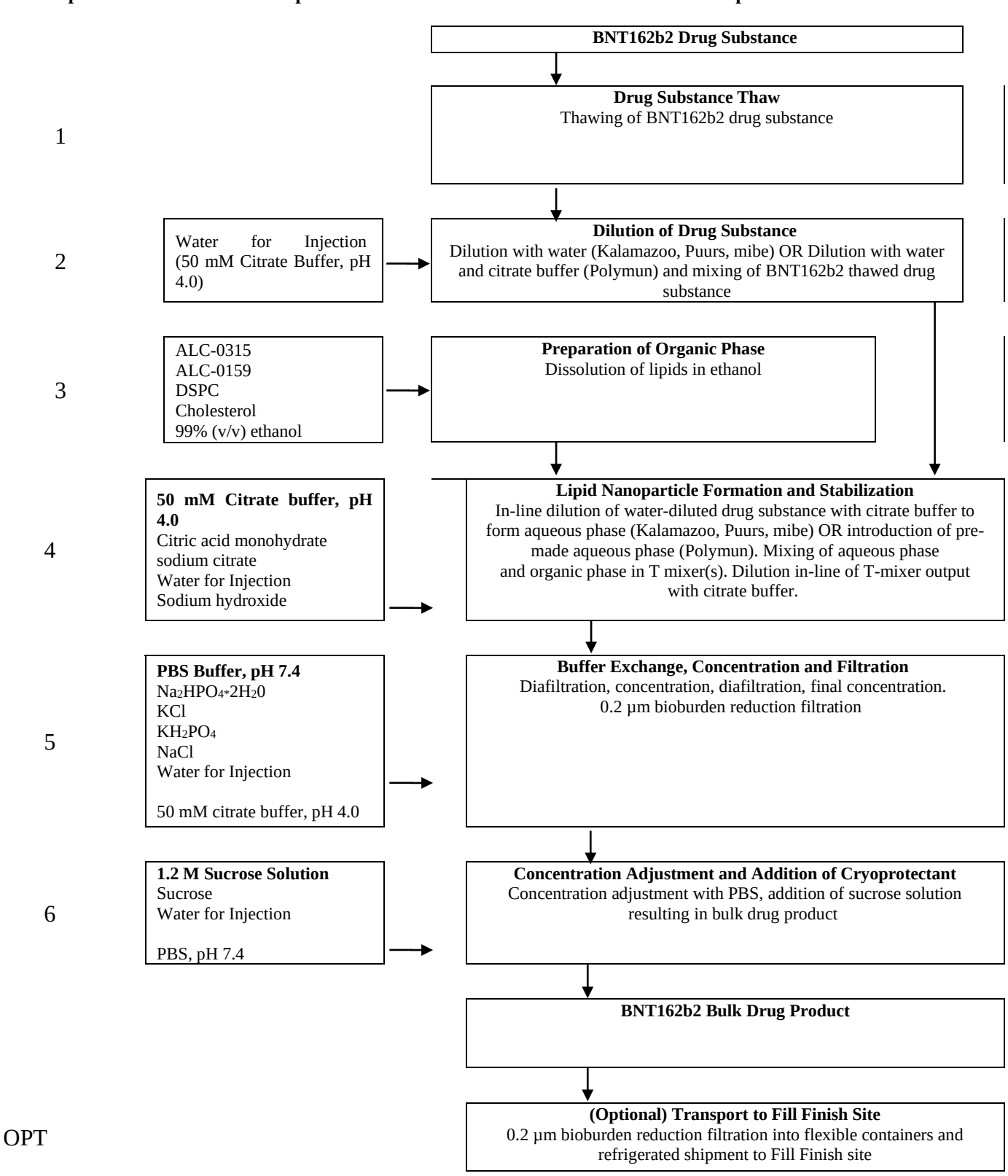
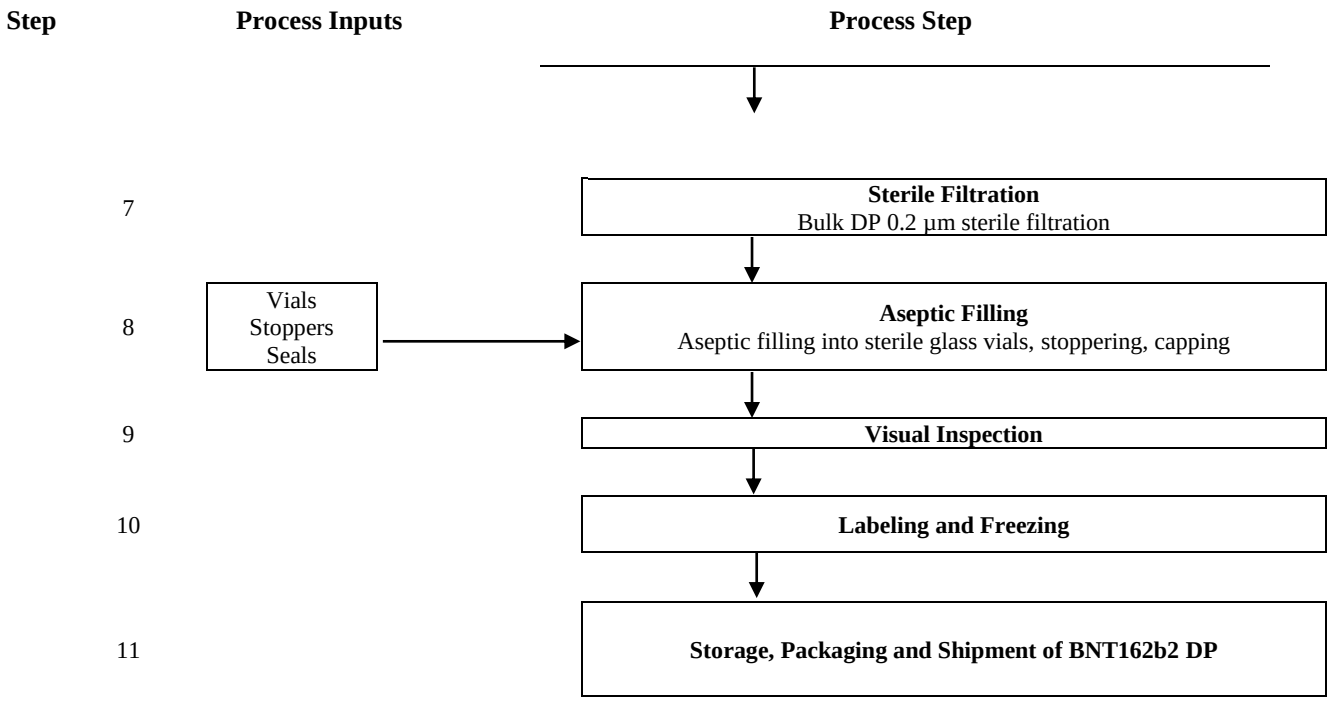
Table 1: Process overview





1.2.2. Out of Scope

Validation activities for introduction of the product into other areas are out of scope of this document.

2. References

This validation plan is aligned with the SOP 51080 (Puurs), and SOP 25091 (Kalamazoo) and the therein-referenced quality standards.

The project is covered by the following documents:

Table 1: List of references

Ref N°	Document ID	Document	Approval date	Author	Location	Remarks
Ref. 1	CRF PR4953874	Introduction of COVID-19 Vaccine PF-07302048	14/08/2020	Dries Van Hemelryk	gQTS	NA
Ref. 2	CRF PR5336199	Validation of the manufacturing with supplied Covid vaccine Bulk Product at PGS Puurs	17/11/2020	Elize Van Driessche	gQTS	NA

Ref N°	Document ID	Document	Approval date	Author	Location	Remarks
Ref. 3	CRF PR5351233	Pfizer Kalamazoo Drug Product Project Validation Plan BNT162b2 Drug Product Formulation, Filtration, Filling, Inspection, Packaging and Freeze Storage	03/11/2020	Timothy Wang	gQTS	NA
Ref. 4	INX100426829 v3.0	Process Definition Document for PF-07302048 BNT162b2 Vaccine (SARS-CoV-2 full spike protein S-P1 variant)	22/10/2020	Piet Renard	GDMS	NA
Ref. 5	20043-COVAL-RAT0-A2	Rational for Concurrent Validation Approach for Covid-19 Vaccine	19/11/2020	Wendy De Keyzer & Elize Van Driessche	QA archive	NA
Ref.6	SOP 25091 v18.0	Process Validation Requirements	28/07/2020	David P. Walch	PDOCS	NA

3. Validation strategy

3.1 Assessment

This initial validation requires one Process Validation (PV) batch per supply node (cf. section 1.1) performed at Puurs and Kalamazoo on different filling lines. The PV batches hence cover all current drug product processes and incoming materials. An overall summary report will be issued after completion of all PV batches in order to assess comparability between all the different drug product nodes, demonstrate that the manufacturing process has the appropriate controls, demonstrate that the sites manufacture a product that complies with its specifications and that the product produced is comparable across sites. The summary report will include an evaluation of all prerequisites. Deviations towards this validation plan will also be discussed and assessed in the summary report.

An overview of the validation strategy is shown in Table 2 and includes an indication of the hold time challenges, the origin and batches of both drug substance and lipids. More details on the prerequisites, activities, sampling and acceptance criteria will be documented in the protocols.

A concurrent validation approach will be used and this is supported by rational for concurrent validation. (cf. Ref. 5 and 6)

Table 2: PV justification to support emergency use submissions

PV batch	PV 1	PV 2	PV 3	PV 4	PV 5	Remarks/ justification
Supply node in scope	Puurs – Formulation in VC2 and filling in FC2	Puurs – Formulation by DER and filling on WSL5	Puurs – Formulation by PLY and filling on WSL5	Kalamazoo – Filling on Line 8	Kalamazoo – Filling on Line 18	Different supply nodes are covered by performing the validation across the different sites. In Phase 1, only 1 batch per drug product supply node will be manufactured to support emergency use submissions In Phase 2, process validation will be completed to support commercial licensure.

PV batch	PV 1	PV 2	PV 3	PV 4	PV 5	Remarks/ justification
Protocol	Puurs Protocol (20043-COVID-PRP0-A1)			Kalamazoo protocol (PR 5370247)		1 protocol will be written per site.
	Puurs Protocol (20043-COVID-PRP0-A1)	Dermapharm protocol (V-PS-118-02)	Polymun protocol (BCV/VP/003-01)	Polymun protocol (BCV/VP/003-01)		
Drug substance origin	BioNTech, Mainz + Rentschler (purification) (BNT)			Pfizer Andover (ACMF)		Both drug substance suppliers are included.
Drug substance batch	BNT 1	BNT 2	BNT 2	ACMF 1	ACMF 2	2 batches per drug substance supplier are included.
Micro hold times challenge for buffers	Yes	No	No	No	Yes	Buffer hold times > 24 h will be evaluated once per formulation area. Polymun has already qualified the buffer hold times which will be covered in the protocol and report. For Dermapharm, the buffer hold times do not exceed 24 hours.
Micro hold time challenge before BBRF	No	No	No	No	No	Hold times prior to bioburden reducing filtration will not be challenged but are monitored via sampling and testing for bioburden and endotoxins. The microbiological growth in the different phases is expected to be limited, as the hold times do not exceed 24 hours. Additionally, part of this hold time is in presence of ethanol, which does not promote the growth and there is no sucrose present in the formulation yet.

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PV batch	PV 1	PV 2	PV 3	PV 4	PV 5	Remarks/ justification
						Monitoring through sampling is therefore the suggested approach for the batches in scope.
Micro hold time challenge before sterile filtration	Yes	No	Yes	No	Yes	The hold time before the sterile filtration will be challenged once for every facility where the filtration process is being performed
Batch consistency	Yes	Yes	Yes	Yes	Yes	During all process validation batches, samples will be taken throughout the filling process to demonstrate batch homogeneity.
Product hold times challenge dilution – freeze	No	No	No	No	No	Product hold time targets have been defined (cfr the individual protocols). From previous manufacturing experience, it has been dictated that all product release testing is performed at the end of process hold times for each batch. Hence, forced product hold challenges as part of phase 1 PV is not seen as necessary
Stability studies	Yes	Yes	Yes	Yes	Yes	All PV batches will be put on stability. A detailed stability study protocol will be available prior to start of stability studies.

Detailed sampling plan and test conditions will be described in the separate validation protocols.

A concurrent validation approach will be used due to the urgent need for this product. The rationale for this approach is documented (cf. Ref 5 and 6). This concurrent approach requires interim reports to be documented for each individual validation run.

3.2 Validation Deliverables

The deliverables are identified in the table below. The validation plan requires one process validation protocol per site to be issued prior to start of the batches in scope of each protocol. The concurrent validation approach dictates an interim report for each PV batch. An overall report per site will be compiled that summarizes all evaluations and contains a comparability assessment of the data of all batches manufactured. Finally, a concluding report linked to this plan will be written that summarizes al findings from the different validation reports.

Table 3: List of deliverables

Document ID	Document	Due Date/ Approval date	Author	Location	Remarks
20043-COVID-PRP0-A1	Process Validation Protocol For Introduction of Covid-19 Vaccine (PF-07302048, BNT-162) into PGS Puurs	Before start of PV in PGS Puurs	Elien Rosier	TBD	NA
PR 5370247	Process Validation Protocol For Introduction of Covid-19 Vaccine (PF-07302048, BNT-162) into PGS Kalamazoo	Before start of PV in PGS Kalamazoo	TBD	TBD	NA
V-PS-118-02	Process validation protocol for Dermapharm	Before start of PV in Dermapharm	TBD	TBD	NA
BCV/VP/003-01	Process validation protocol for Polymun	Before start of PV in Polymun	TBD	TBD	NA
20043-COVID-PRR1/2/3-A1	Process validation Interim Reports for Introduction of Covid-19 Vaccine (PF-07302048, BNT-162) into PGS Puurs (Phase I)	Prior to release of the PV batch in scope of the interim report	TBD	TBD	NA
PR 5370247	Process Validation Interim Reports For Covid-19 (Pf-07302048, BNT-162) In Pfizer Kalamazoo (Phase 1)		TBD	TBD	NA
20043-COVID-PRRA-A1	Process validation Report for Introduction of Covid-19 Vaccine (PF-07302048, BNT-162) into PGS Puurs (Phase I)	TBD	TBD	TBD	NA
PR 5370247	Process Validation Report For Covid-19 (Pf-07302048, BNT-162) In Pfizer Kalamazoo (Phase 1)	TBD	TBD	TBD	NA
V-PS-118-02	Process validation report for Dermapharm	TBD	TBD	TBD	NA
BCV/VR/003-01	Process validation report for Polymun	TBD	TBD	TBD	NA
TBD	Summary process validation report Covid-19 Vaccine (PF-07302048, BNT-162) Drug Product (Phase I)	TBD	TBD	TBD	NA

An overview of the documentation deliverables is shown in Figure 1.

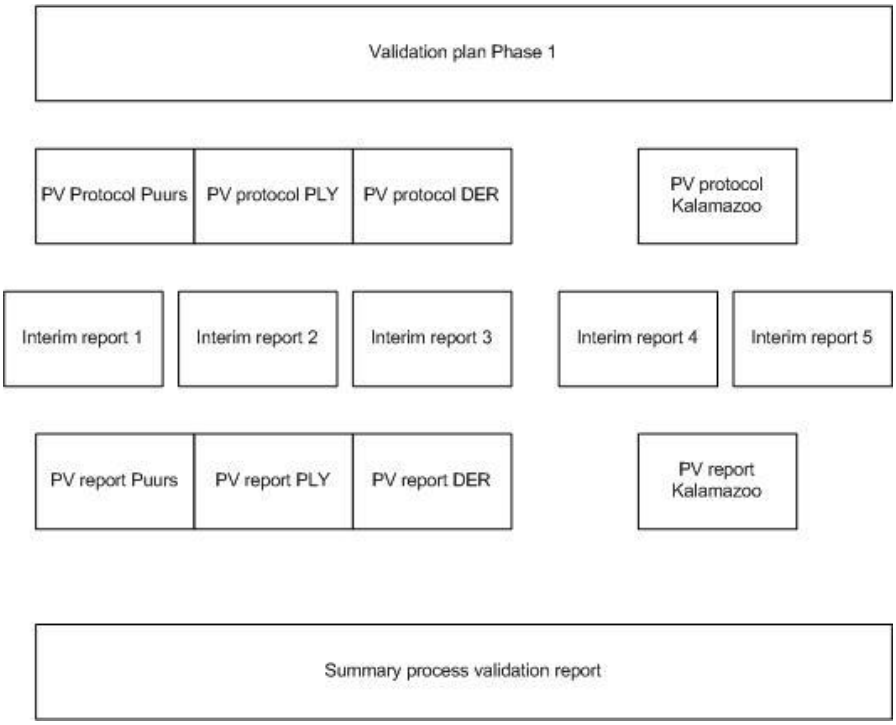

Figure 1: Overview of deliverable documents in scope of this validation plan.

4. Glossary

ACMF	Andover Clinical Manufacturing Facility
BLA	Biologics license application
BNT	BioNTech
CMO	Contract Manufacturing Organisation
CRF	Change Request Form
DER	Dermapharm
EUA	Emergency Use Authorization
FC	Focus Cell
LNP	Lipid Nano Particles
MAA	Marketing Authorization Application
PGS	Pfizer Global Supply
PLY	Polymun
PV	Process validation
SOP	Standard Operating Procedure
VC	Vaccine Cell

5. Attachments

Attachment 1 – Signed approval page from the external company

6. Document History

Version:	Author:	Last edited on:
1.0	*Heleen Dhondt*	*19/11/2020*
Initial Document		

DocUUID : 8dadc2d1-bfdf-4856-b44f-7e8a97a70049

Status	Effective	Effective Date	-	Version	5.0	Doc Name	FORM-26097
Title	FORM: Process Validation Plan						
Doc Alias	F(2)-19-002-Validation Plan			Site Code / Department		Puu / Validation Master Plan	

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BIONTECH	Patricia Aldaz Senior Regulatory Project Manager	19/NOV/2020
BIONTECH	Dr. Andreas Kirscht QA Manager	19/Nov/2020
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NAME	JOB TITLE	SIGNATURE & DATE

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Heleen Dhondt

Heleen Dhondt 19 Nov 2020 15:07:026-0500

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Product/Process:	Document ID:
Process Validation Plan For Covid-19 Vaccine (PF-07302048, BNT-162) Drug Product – Phase I	VAL100130986