Medicine Evaluation; Non-Clinical Studies

FINAL

1 PRODUCT DETAILS

File number:	TT50-10853
Product name:	Comirnaty (COVID-19 mRNA vaccine) (Pfizer-BioNTech) 0.5 mg/mL concentrate for injection (TT50-10853).
Dose form:	Concentrate for injection
Drug substance and strength:	BNT162b2 [mRNA], 0.5 mg/mL (as 225 µg/0.45 mL) Each 0.3 mL dose of the diluted vaccine delivers 30 µg drug substance.

Evaluator: s 9(2)(g)(ii) [redacted]

By email to s 9(2)(g)(ii) [redacted]**, Acting Manager Product Regulation, Medsafe 28 Jan 2021 12:27 am**

Peer reviewer: s 9(2)(g)(ii) [redacted]

By email to s 9(2)(g)(ii) [redacted]**, Acting Manager Product Regulation, Medsafe 28 Jan 2021 10:32 am**

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Limited glossary / abbreviations

Abbreviation	Expansion
ACE2	Angiotensin Converting Enzyme 2 Receptor for
ADE	Antigen Dependent Enhancement
ALC-0159	2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide
ALC-0315	((4-hydroxybutyl) azanediyl) bis (hexane-6,1-diyl) bis(2-hexyldecanoate)
Bw;bwt	Bodyweight
DART	Developmental and Reproductive Toxicity
EM	Electron Microscopy
GMT	Geometric Mean Titre
HEK	Human Embryonic Kidney Cells
HCS	Human Convalescent Serum
IM	Intra muscular injection
IFN	Interferon
IL	Interleukin
LNP	Lipid Nano-Particles (specifically LNP8 unless otherwise specified)
MACS	Magnetic Antigen Cell Separation
MOE	Margin of Exposure
mRNA	messenger Ribonucleic acid
modRNA	nucleoside modified mRNA
OP	OroPharyngeal
P2	two proline mutations
pVN_{50}	A measure of the serum antibody Titre (The reciprocal of the serum dilution resulting in a 50% neutralization of a pseudo-virus). A higher value indicates a greater response/titre
pVNT	Pseudo Virus Neutralisation Titre
q.s.	Quatum satis
QSAR	Quantative Strutural Activity Relationship
RNA	Ribonucleic acid
RBD	Receptor Binding Domain
S protein	SARS-CoV-2 spike glycoprotein
TGA	Therapeutic Goods Administration (Australia)
Th1	T helper type 1 cells
Th2	T helper type 2 cells
TNF	Tumour Necrosis Factor
TTC	Threshold of Toxicological Concern
V8&9	Viral variants of SAR-CoV-2
VAERD	vaccine-associated enhanced respiratory disease

Non-Clinical Assessment

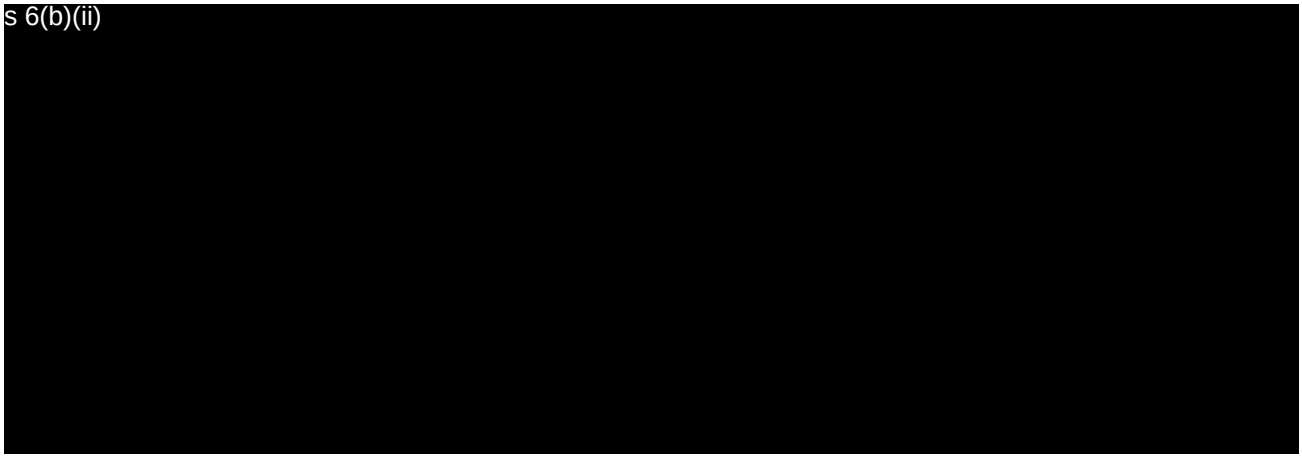
1 INTRODUCTION

This new medicine application is for a new biological entity, BNT162b2 [mRNA], hereafter referred to as BNT162b2 (BioNTech code number BNT162, Pfizer code number PF-07302048), developed by Pfizer and BioNTech. The drug product (COMIRNATY) is an RNA-based vaccine indicated for the active immunisation of individuals aged 16 (originally 18 in the TGA application but amended by the applicant) years and over against COVID-19 disease caused by the SARS-CoV-2 virus.

The vaccine will be administered intramuscularly (IM) in the upper arm (deltoid muscle) as a series of two 30 µg doses of the diluted vaccine solution (0.3 mL each) according to the following schedule: a single 0.3 mL dose followed by a second 0.3 mL dose 21 days later (prime/boost regimen).

The drug substance is a nucleoside-modified mRNA that encodes a prefusion stabilised full-length variant of the SARS-CoV-2 spike (S) glycoprotein and is manufactured by a cell-free *in vitro* transcription process. The final clinical variant and related developmental variant RNAs were encapsulated lipid nanoparticles (LNPs), which facilitate entry of the RNA into host cells. The RNA is translated in the host cells to the S protein, which induces a protective immune response in the vaccinated individual. The vaccine is formulated as a preservative-free concentrated suspension for injection, presented in a multi-dose vial. The product is supplied frozen (-80°C to -60°C) and must be thawed and diluted with sterile sodium chloride (0.9%) solution prior to administration.

s 6(b)(ii)



The LNP component of the Pfizer vaccine formulation contains two novel excipient lipids, ALC-0159 (2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide) and ALC-0315(4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate). These lipids are a key aspect of the formulation contributing both to the particle size of LNPs and the stability of the mRNA in the formulation.