RISK MANAGEMENT PLAN – AUSTRALIA-SPECIFIC ANNEX

Active ingredient(s) (INN):	Not yet assigned. COVID-19 mRNA Vaccine is single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2.
Product name:	Comirnaty (proposed)
Pharmaco-therapeutic group (ATC Code):	J07BX03
Sponsor:	Pfizer Australia Pty Ltd
Regional Annex version number:	0.2
Regional Annex version date:	17 January 2021
Referenced EU RMP:	Version 1.0 dated 21 December 2020

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LIST OF ABBREVIATIONS

AE	adverse event
AESI	adverse event of special interest
ASA	Australian specific annex
CMI	consumer medicine information (Australia)
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 2019
CSR	clinical study report
DCA	data capture aid
DNA	deoxyribonucleic acid
eCTD	electronic common technical document
EU	European union
HLT	high-level term
mRNA	messenger ribonucleic acid
PhV	pharmacovigilance
PI	product information (Australia)
PSUR	periodic safety update report
RMP	risk management plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SOC	system organ class
TGA	therapeutic goods administration
VAED	vaccine-associated enhanced disease
VAERD	vaccine-associated enhanced respiratory disease

1. INTRODUCTION

This Australia-Specific Annex (ASA) relates to the approved EU Risk Management Plan (RMP) version 1.0 for COVID-19 mRNA vaccine dated 21 December 2020, with a data lock point of 17 December 2020.

Australian context is provided in this Addendum for the RMP sections identified in Table 1.

Table 1. Sections of the EU RMP

Part	Module/Annex	AUSTRALIA Context Included
Part I Product Overview		**See EU RMP**
Part II Safety Specification	SI Epidemiology of the Indications(s) and Target Population(s)	Yes – See Section 2.1
	SII Non-Clinical Part of the Safety Specification	**See EU RMP**
	SIII Clinical Trial Exposure	**See EU RMP**
	SIV Populations Not Studied in Clinical Trials	**See EU RMP**
	SV Post-Authorisation Experience	**See EU RMP**
	SVI Additional EU Requirements for the Safety Specification	**See EU RMP**
	SVII Identified and Potential Risks	**See EU RMP**
	SVIII Summary of the Safety Concerns	Yes – See Section 2.2
Part III Pharmacovigilance Plan (Including Post-Authorisation Safety Studies)		Yes – See Section 3
Part IV Plan for Post-Authorisation Efficacy Studies		**See EU RMP**
Part V Risk Minimisation Measures (Including Evaluation of the Effectiveness of Risk Minimisation Activities)		Yes – See Section 5
Part VI Summary of the RMP		**See EU RMP**

Table 1. Sections of the EU RMP

Part	Module/Annex	AUSTRALIA Context Included
Part VII Annexes to the Risk Management Plan	Annex 2 Tabulated Summary of Planned, On-going, and Completed Pharmacovigilance Study Programme	**See EU RMP**
	Annex 3 Protocols for Proposed, On-going, and Completed Studies in the Pharmacovigilance Plan	**See EU RMP**
	Annex 4 Specific Adverse Drug Reaction Follow-Up Forms	**See EU RMP**
	Annex 5 Protocols for Proposed and On-going Studies in RMP Part IV	**See EU RMP**
	Annex 6 Details of Proposed Additional Risk Minimisation Activities	**See EU RMP**
	Annex 7 Other Supporting Data	**See EU RMP**
	Annex 8 Summary of Changes to the Risk Management Plan over Time	**See EU RMP**

1.1. History of RMPs Submitted in Australia

COVID-19 mRNA vaccine will be included in the Black Triangle Scheme and the relevant text is included on the proposed Product Information (PI) and Consumer Medicine Information (CMI).

The history of EU RMPs submitted in Australia is provided in Table 2. This ASA is the first version for COVID-19 mRNA vaccine to be submitted in Australia.

Table 2. History of RMPs Submitted in Australia

EU RMP version	ASA version	Date Submitted	Application or Update	Major changes to the ASA/EU RMP from previous version
EU RMP v 0.1	N/A	10 December 2020	PM-2020-05461-1-2	N/A Proposed EU RMP
EU RMP v 1.0	ASA v 0.1	11 January 2021	PM-2020-05461-1-2	Initial version of the ASA EU RMP updated as per *Annex 8. Summary of Changes to the Risk Management Plan over Time*

2. SAFETY SPECIFICATION

2.1. Epidemiology of the Indication(s) and Target Population(s)

There are no significant differences between epidemiological information presented in the EU RMP Module SI *Epidemiology of the Indication(s) and Target Population (s)* compared to those applicable to the Australian population. Please refer to the EU RMP Part II- Module SI.

2.2. Summary of the Safety Concerns

The safety concerns proposed in the COVID-19 mRNA vaccine EU RMP (version 1.0, dated 21 December 2020) are presented in Table 3.

Table 3. Summary of Safety Concerns in the EU RMP

Important Identified Risks	Anaphylaxis
Important Potential Risks	Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)
Missing Information	Use in pregnancy and while breast feeding
	Use in immunocompromised patients
	Use in frail patients with co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders)
	Use in patients with autoimmune or inflammatory disorders
	Interaction with other vaccines
	Long term safety data

There are no safety concerns for Australia that are additional to those proposed in the EU RMP.

2.2.1. Australia Specific Safety Concerns

Not applicable.

2.2.2. Proposed Changes to the Australia-specific Safety Concerns

Not applicable.

3. PHARMACOVIGILANCE PLAN

3.1. Routine Pharmacovigilance Activities in Australia

All routine pharmacovigilance (PhV) activities in the EU RMP will be implemented in Australia. Refer to Part III, Section III.1 *Routine Pharmacovigilance Activities* of the EU RMP.

Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection are planned to be implemented in Australia.

Data Capture Aids have been created for this vaccine. They are intended to facilitate the capture of clinical details about:

- the nature and severity of COVID-19 illness in individuals who have received the COVID-19 mRNA vaccine and is anticipated to provide insight into potential cases of vaccine lack of effect or VAED. The DCA is provided in Annex 4 of the EU RMP;

- potential anaphylactic reactions in individuals who have received the COVID-19 mRNA vaccine. This DCA was internally approved on 22 December 2020.

Routine signal detection activities for the COVID-19 mRNA vaccine will include routine and specific review of AEs consistent with the Adverse Events of Special Interest (AESI) list provided in the EU RMP PART II.SVII.1.1 *Risks not considered important for inclusion in the list of safety concerns in the RMP*.

Concise, critical analyses of adverse events (AEs) for COVID-19 mRNA vaccine will be conducted and provided in the Periodic Safety Update Report (PSUR) in accordance with the TGA requirements.

In addition to routine 6-monthly PSUR production, monthly summary safety reports will be compiled to support timely and continuous benefit risk evaluations. Topics covered by monthly summary safety reports will include:

- Interval and cumulative number of reports, stratified by report type (medically confirmed/not) and by seriousness (including fatal separately);
- Interval and cumulative number of reports (serious and non-serious), overall and by age groups and in special populations (e.g. pregnant women);
- Interval and cumulative number of reports per HLT and SOC;
- Number of reports in Australia and Global;
- Exposure data, stratified by country, age groups, race and ethnicity;
- Changes to reference safety information in the interval;
- Summary of the designated medical events;
- Ongoing and closed signals in the interval;
- Reports on number and relevant cases, including time-to-onset and Observed/Expected analyses for the following:
    a. List of AESI
    b. RMP safety concerns
- Fatal reports – numbers and relevant cases, including observed/expected analyses;
- Number and relevant cases:
    a. Vaccination failure/lack of efficacy (including confirmed and suspected cases);
    b. Vaccination errors;
    c. Potential interaction with other vaccines/concomitant treatments
- Summary of any outcomes of routine pharmacovigilance activities (as presented in the EU RMP Part III and applied in the Australian context) that have a potential impact on the benefit/risk balance and or of the vaccine should be included for the purpose of rapid signal detection and communication activities.

- Risk/benefit considerations.

Monthly reports and PSURs will include results of the observed versus expected analysis for AESI as appropriate, including cases of Bell's palsy and will present the results and details of the statistical approach.

3.2. Additional Pharmacovigilance Activities

All the additional pharmacovigilance activities for COVID-19 mRNA vaccine included in the EU RMP are considered to apply to Australia.

3.2.1. Australia-Specific Additional Pharmacovigilance Activities

Not applicable.

4. CLINICAL STUDY PLAN FOR PROVISIONAL REGISTRATION

As agreed with the TGA at the pre-submission meeting held 18 September 2020 to discuss the proposed application to register COVID-19 mRNA vaccine, data are being provided on a rolling basis as it becomes available.

The pivotal trial Study C4591001 is an ongoing Phase 1/2/3, placebo-controlled, randomised, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals.

The primary efficacy analysis was efficacy against COVID-19 at least 14 days after the last dose of vaccine in participants without evidence of prior SARS-CoV-2 infection at baseline.

The Phase 2/3 part of Study C4591001 commenced on 27 July 2020 and had met its primary end points as at 14 November 2020. An interim clinical study report (CSR) comprising final analysis for efficacy and safety data 1 month after Dose 2 for 37,586 participants with a median of at least 2 months of follow-up, and available safety data for all 43,252 participants was submitted 10 December 2020.

The final C4591001 CSR with supplemental follow-up is expected to be available for submission by the end of 2023.

The study protocol for Study C4591001 is provided in Module 5.3.5.1 of the eCTD dossier.

5. RISK MINIMISATION PLAN

5.1. Routine Risk Minimisation Activities in Australia

The planned routine risk minimisation activities for COVID-19 mRNA vaccine applicable to Australia are consistent with those detailed in *Part V, Section V.1 Routine Risk Minimisation Measures* of the EU RMP.

The routine risk minimisation activities planned in Australia are described in Table 4.

Table 4. Routine Risk Minimisation Activities

Safety Concern	Routine Risk Minimisation Activities	Differences Between EU RMP and Australia Activities with Justification
Important Identified Risks		
Anaphylaxis	Local Product Information: Section 4.4 Special warnings and precautions for use Section 4.8 Adverse effects (undesirable effects)	None
Important Potential Risk		
Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)	None	None
Missing Information		
Use in Pregnancy and while breast feeding	Local Product Information: Section 4.6 Fertility, pregnancy and lactation	None
Use in immunocompromised patients	Local Product Information: Section 4.4 Special warnings and precautions for use Section 5.1 Pharmacodynamic properties	None
Use in frail patients with co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders)	Local Product Information: Section 5.1 Pharmacodynamic properties	None
Use in patients with autoimmune or inflammatory disorders	None	None
Interaction with other vaccines	Local Product Information: Section 4.5 Interactions with other medicines and other forms of interactions	None
Long term safety data	None	None

5.2. Additional Risk Minimisation Activities

There are no additional risk minimisation activities referenced in *Part V, Section V.2 Additional Risk Minimisation Measures* of the EU RMP. No risk minimisation activities additional to the routine risk minimisation activities described in Table 4 are currently planned to be undertaken in Australia.

5.3. How Additional Risk Minimisation Activities will be Evaluated in Australia

Not applicable. There are no additional risk minimisation activities being undertaken in Australia.

6. SUMMARY OF THE RMP IN AUSTRALIA

Table 5. Summary of the RMP in Australia

Safety concern		Routine pharmacovigilance activities	Additional pharmacovigilance activities	Routine risk minimisation activities	Additional risk minimisation activities
Important identified risks	*Anaphylaxis*	Data Capture Aid	Studies: • C4591001 • C4591010 • C4591011 • C4591012 • ACCESS/VAC4EU	Local Product Information: Section 4.4 Special warnings and precautions for use Section 4.8 Adverse effects (undesirable effects)	None
Important potential risks	*Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)*	Data Capture Aid	Studies: • C4591001 • C4591011 • C4591012 • ACCESS/VAC4EU	None	None
Missing information	*Use in Pregnancy and while breast feeding*	None	Studies: • C4591010 • C4591011 • C4591015 • ACCESS/VAC4EU	Local Product Information: Section 4.6 Fertility, pregnancy and lactation	None
	Use in immunocompromised patients	None	Studies: • BNT162-01 Cohort 13 • C4591018 • C4591011 • C4591012 • ACCESS/VAC4EU	Local Product Information: Section 4.4 Special warnings and precautions for use Section 5.1 Pharmacodynamic properties	None
	Use in frail patients with co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders)	None	Studies: • C4591001 • C4591011 • C4591012 • ACCESS/VAC4EU • Safety and immunogenicity in high risk adults	Local Product Information: Section 5.1 Pharmacodynamic properties	None

Table 5. Summary of the RMP in Australia

Safety concern		Routine pharmacovigilance activities	Additional pharmacovigilance activities	Routine risk minimisation activities	Additional risk minimisation activities
Missing information	*Use in patients with autoimmune or inflammatory disorders*	None	Studies: • C4591011 • C4591012 • C4591018 • ACCESS/VAC4EU	None	None
	Interaction with other vaccines	None	Study: Co-administration study with seasonal influenza vaccine	Local Product Information: Section 4.5 Interactions with other medicines and other forms of interactions	None
	Long term safety data	None	Studies: • C4591001 • C4591010 • C4591011 • C4591012 • ACCESS/VAC4EU	None	None