HSA Proposed Minimum Data Requirement for Approval via the Pandemic Special Access Route [PSAR] for Supply of Emergency Therapeutic Products

1. Introduction

This is to be read in conjunction with the Guidance note on Pandemic Special Access Route [PSAR] for Supply of Emergency Therapeutic Products.

The interim authorisation provides flexibility in the level of evidence required for supporting the application and allows data to be submitted on a rolling basis. At the time of application, the company:

- may provide initial data that is available to initiate the review process and file information as data is accrued from on-going studies; and
- must submit a rolling submission plan outlining the sequence and timelines of the subsequent data submission.

The grant of interim authorisation depends on the timepoint where the amount of data accrued meets the minimum data requirements to allow for an initial benefit vs risk assessment.

2. Data Requirement for Interim Authorisation of a COVID-19 Vaccine Under PSAR

The minimum data requirements for supporting an interim authorisation for a COVID-19 vaccine under PSAR are outlined below:

a) Chemistry, Manufacturing & Controls (CMC)

Aspects	Minimum Data Requirements
Good Manufacturing Practice (GMP)	• Drug substance (DS) and drug product (DP) sites to demonstrate compliance with the Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP standards
Drug substance	• Physio-chemical and biological characterisation, in particular attributes that may impact performance and stability • History and qualification of cell/virus banks • Information on all animal-derived materials used in cell culture/virus growth, and/or as excipients • Evaluation of potential adventitious agents, including viral clearance studies, bioburden control, absence of mycoplasma, and transmissible spongiform encephalopathies (TSE) risk
DS/ DP Manufacturing controls	• Description of manufacturing process & process control parameters • Validation of critical process parameters & in-process controls • Full process validation data from the initial site* **Possible to leverage data from a site that is not intended for supply to Singapore* • Process validation data from a minimum of 1 lot from the proposed site, with comparability demonstrated between the initial and proposed sites

Aspects	Minimum Data Requirements
DS/ DP Product Quality	• DS/ DP specification & Certificate of Analysis (CoA) from the proposed site(s) • DS/ DP CoAs of lots to be supplied to Singapore • Method validation for critical parameters such as potency and impurities, as well as methods which are specific to the vaccine platforms (e.g. encapsulation efficiency for mRNA vaccines, viral vector aggregation, virus replication competency for viral vector vaccines)
DS/ DP Stability	• Stability data based on the proposed container closure system (CCS) and final formulation • Stability data from a non-proposed site can be considered if comparability is demonstrated • Real-time stability data to support long-term shelf-life • In-use stability data to support shelf-life after thawing, dilution, reconstitution, etc
Comparability	• Comparability data for sites, process, manufacturing scale and formulation changes, including characterisation, release, forced degradation and accelerated stability data

b) Non-Clinical

Aspects	Minimum Data Requirements
Toxicology	• General toxicology and local tolerance studies • Biodistribution and genotoxicity studies, if relevant • Developmental and Reproductive Toxicology (DART) studies, if intended for use in pregnant women
Pharmacology	• Immunogenicity data on antibody & cellular immune responses, including Th1/Th2 responses • Animal challenge studies assessing protection, risk of enhanced respiratory disease (ERD), nasal and lung viral loads, lung histopathology and clinical features, Th1/Th2 responses in relevant animal models

c) Clinical Efficacy

Aspects	Minimum Data Requirements
Efficacy	Vaccine efficacy data from pre-specified interim analysis of Phase III clinical studies, including vaccine efficacy against severe disease
Population subgroups	Vaccine efficacy data in different age cohorts and subgroups of interest (e.g., asymptomatic infection, high risk population seropositive at baseline), if available
Durability of immune responses	Data from Phase I and II clinical studies, if available

d) Clinical Safety

Aspects	Minimum Data Requirements
Safety	• Safety data from Phase I and II studies • Safety data from phase III studies with a median follow-up of at least 2 months
Median duration of follow-up	At least 2 months post vaccination with the proposed dose and regimen
Safety sample size	At least 3000 vaccine recipients receiving the proposed dose and regimen
Events	Local and systemic solicited adverse events (AEs), unsolicited AEs, serious AEs, AEs of special interest, deaths, severe COVID-19 cases
Subgroups	Subgroup analyses in different age groups, high risk population, etc, if available

3. Data Requirement for Interim Authorisation of a COVID-19 Therapeutic Monoclonal Antibody Under PSAR

The minimum data requirements for supporting an interim authorisation for a COVID-19 therapeutic monoclonal antibody under PSAR are outlined below:

a) Chemistry, Manufacturing & Controls (CMC)

Aspects	Minimum Data Requirements
Good Manufacturing Practice (GMP)	• Drug substance (DS) and drug product (DP) sites to demonstrate compliance with the Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP standards
Drug substance	• Physio-chemical and biological characterisation, in particular attributes that may impact performance and stability • History and qualification of cell banks • Information on all animal-derived materials used in cell culture growth, and/or as excipients • Evaluation of potential adventitious agents, including viral clearance studies, bioburden control, absence of mycoplasma, and transmissible spongiform encephalopathies (TSE) risk
DS/ DP Manufacturing controls	• Description of manufacturing process & process control parameters • Validation of critical process parameters & in-process controls • Full process validation data from the initial site* **Possible to leverage data from a site that is not intended for supply to Singapore* • Process validation data from a minimum of 1 lot from the proposed site, with comparability demonstrated between the initial and proposed sites
DS/ DP Product Quality	• DS/ DP specification & Certificate of Analysis (CoA) from the proposed site(s) • DS/ DP CoAs of lots to be supplied to Singapore • Method validation for critical parameters such as potency and impurities
DS/ DP Stability	• Stability data based on the proposed container closure system (CCS) and final formulation • Stability data from a non-proposed site can be considered if comparability is demonstrated • Real-time stability data to support long-term shelf-life and shelf life after thawing, if applicable • In-use stability data to support shelf-life after dilution, reconstitution, etc
Comparability	• Comparability data for sites, process, manufacturing scale and formulation changes, including characterisation, release, forced degradation and accelerated stability data

b) Non-Clinical

Aspects	Minimum data requirements
Toxicology	• Toxicology studies including safety, local tolerance and safety pharmacology • Tissue cross-reactivity studies/in silico analyses or equivalent analyses for potential cross-reactivity • Developmental toxicity studies (if available)
Pharmacology (*in vitro*)	• Binding and neutralisation assays (including variants if available) • Epitope mapping and binding site characterization and binding site conservation studies, characterisation of viral resistance (if available) • Effector function studies (Fc receptor and C1q binding, ADCC, CDC activity etc.,) • *In vitro* assays for antibody dependent enhancement (ADE)
Pharmacology (*in vivo*)	• Animal challenge studies on efficacy and potential risk of ADE • Exposure assessment data in animals

c) Clinical Efficacy

Aspects	Minimum Data requirements
Efficacy	Efficacy data from Phase II or Phase III studies
Population subgroups	Efficacy data in different age cohorts and subgroups of interest (e.g., high risk population), if available
Pharmacology	• PK studies • Dose response studies

d) Clinical Safety

Aspects	Minimum data requirements
Safety	• Safety data from Phase I/ II/III Studies • Anti-drug antibody data
Events	Treatment emergent adverse events (AEs); Hypersensitivity and infusion reactions, Serious AEs, deaths, AEs of special interest, Worsening of clinical symptoms
Subgroups	Subgroup analyses in different age groups, high risk population etc., if available