African Vaccine Regulatory Forum (AVAREF)

CLINICAL ASSESSMENT

Study Full Title	
Short Title	
Protocol No.	
Version No.	
Study Drug	
Date of review	
Name of reviewers	

1.1 Background information

1.1.1 Trial category

1.1.1.1 **For low-intervention clinical trials only**

If the trial is low interventional, **briefly** describe the justification (as provided by the sponsor):	
The justification for a low-intervention clinical trial as provided by the sponsor is acceptable (in compliance with guideline/regulation XXX) Yes ☐ No ☐ **If No - tick appropriate box** below and **provide comment**	
The investigational medicinal products used in the study, excluding placebos, are not authorised	☐
The investigational medicinal products **are not used** in accordance with the terms of the marketing authorisation and the use of the investigational medicinal products **is not** evidence-based	☐
The additional diagnostic or monitoring procedures **pose more than minimal additional risk or burden to the safety** of the subjects compared to normal clinical practice in any Member State concerned	☐
Workspace:	
Assessor's comment:	

1.1.1.2 **Phase of trial**

Workspace:
Assessor's comment if disagreement with the study phase proposed

1.1.2 Therapeutic condition

Workspace:
Brief description of the disease:

1.1.3 Mechanism of action, Drug class

Workspace:
Brief description

1.2 Status of development

Workspace:
Brief discussion of clinical pharmacokinetic data, efficacy and safety data described in the IB from previous trials /previously investigated indications(s) for the IMP(s). Non-clinical studies may also be discussed for early or FIH clinical trials. Consideration should be given to the justification provided based on the non-clinical data, for the proposed starting dose, dose steps, and maximum exposure **Assessor's discussion on the clinical development**:

1.3

1.4 Proposed clinical trial

1.4.1 Clinical trial Rationale

Is the rationale for the trial provided by the sponsor acceptable? Yes ☐ No ☐
Workspace:
Assessor's comment:

1.4.2 Primary objective(s) and endpoint(s)

List of primary objective(s):	
The primary objective(s) are clearly defined and measurable and are acceptable.	Yes ☐ No ☐
List of primary endpoint(s):	
The primary endpoint(s) are acceptable.	Yes ☐ No ☐
Workspace:	
Assessor's comment:	

1.4.3 Secondary objective(s) and endpoint(s)

List of secondary objective(s):	
The secondary objective(s) are clearly defined and measurable and are acceptable.	Yes ☐ No ☐
List of secondary endpoint(s):	
The secondary endpoint(s) are acceptable.	Yes ☐ No ☐
Workspace:	
Assessor's comment:	

1.4.4 Study population as per the study protocol

Healthy volunteers/ patients	Healthy volunteers ☐ Patients ☐
Age	Adults ☐ Children/adolescents ☐ Age group if children/adolescents proposed:
Gender	M ☐ F ☐
Workspace:	
Assessor's comment:	

1.4.5 Inclusion criteria

List of inclusion criteria:	
The inclusion criteria are rationally defined, representative of the target population and are acceptable.	Yes ☐ No ☐
Workspace:	
Assessor's comment:	

1.4.6 Exclusion criteria

List of exclusion criteria:	
The exclusion criteria are rationally defined and in accordance with IMP/comparator's safety profile.	Yes ☐ No ☐
Workspace:	
Assessor's comment:	

1.4.7 Vulnerable populations and clinical trials in emergency situations

Vulnerable populations are included in the study ☐ **If yes,** specify which population(s):	
The inclusion of the vulnerable population(s) is **justifiable** and the **benefit/risk profile** is acceptable (this should be defined in a guideline/regulation).	Yes ☐ No ☐ NA ☐
For emergency clinical trials: Does the trial provide clinically relevant direct benefit to subjects?	Yes ☐ No ☐ NA ☐
Workspace:	
Assessor's comment:	

1.4.8 Study plan and design

Brief description of the study plan and design, and include where possible a diagram/flow chart:	
Is the proposed study plan and design acceptable?	Yes ☐ No ☐
Workspace:	
Assessor's comment:	

1.4.9 Study treatment

1.4.9.1 **Investigational medicinal/medical product(s) (IMP(s))**
(Copy and repeat this section as necessary)

Summary of proposed use of the IMP in this trial:
Is the justification for the dose(s)/dose steps, dose rationale, route of administration, schedule, treatment duration, and dose modifications of the IMP acceptable? Yes ☐ No ☐ Other, comment ☐
Workspace:
Assessor's comment:

1.4.9.2 **Comparator IMP(s)/placebo/Auxiliary medicinal product(s)**
(Copy and repeat this section as necessary)

Comparator IMP(s)

The study protocol proposes the use of a **comparator IMP** ☐
Brief information on the comparator:
The comparator is a standard therapy as per; • The SmPC ☐ • International or national guidelines ☐ • Scientific publications ☐
The use of the comparator is justified and is acceptable: Yes ☐ No ☐
Workspace:
Assessor's comment:

Placebo

The study protocol proposes the use of a **Placebo** ☐
The use of a placebo controlled design is sufficiently justified. Yes ☐ No ☐
Workspace:
Assessor's comment:

Auxiliary medicinal product(s)

The study protocol proposes the use of an auxiliary medicinal product(s). ☐
The use of auxiliary medicinal products in the trial is justified and acceptable. Yes ☐ No ☐
Workspace:
Assessor's comment:

1.4.9.3 **Additional considerations for trials involving a medical device**

The trial includes the investigation of a medical device(s) which is considered acceptable. Yes ☐ No ☐
Workspace:
Assessor's comment

1.4.9.4 **Additional considerations for specific medicinal products (e.g. advanced therapy medicinal products or radiopharmaceuticals)**

Workspace:
Assessor's comment:

1.4.10 Safety: List of important safety risks associated with trial treatments (IMP/comparator/auxiliary medicinal products/medical devices)

Workspace:
Brief description of the important safety risks associated with trial treatments identified in any previous clinical trials, and as outlined in the IB or SmPC, or from another source: **Assessor's comment:**

1.4.11 Blinding and unblinding-clinical aspects (where applicable)

The procedure for emergency unbinding is described in the protocol and is acceptable. Yes ☐ No ☐
In the case where a particular laboratory finding or a specific adverse reaction might reveal the treatment allocation, there are additional measures in place to protect the blinding. Yes ☐ No ☐
Workspace:
Assessor's comment:

1.4.12 Contraception measures

The risk to embryo and/or foetus:

Overall risk category

As based on non-clinical (see section 4.4.6.3 in non-clinical section) and clinical data, the risk of teratogenicity/fetotoxicity in early pregnancy is:

Demonstrated/suspected ☐ Possible ☐ Unlikely ☐

Are contraceptive measures adequately defined and acceptable? Yes ☐ No ☐

If No - tick appropriate box below and **provide comment**

Method of contraception proposed for WOCBP in the study is insufficient or an effective method is listed as a highly effective method (e.g. double barrier)	☐
Contraception for male participants is required but is not included or is insufficient in the protocol	☐
Contraception after the end of treatment is not included in the protocol or the duration of this contraception is insufficient	☐
Pregnancy testing at screening is not included or there is an inappropriate interval from time of pregnancy test to start of treatment	☐
Insufficient frequency of pregnancy tests during the study (as per CTFG guidelines)	☐
Definition of WOCBP or postmenopausal woman is not included in the study protocol or is inadequate	☐
Other issue:	☐

Workspace:

Assessor's comment:

1.4.13 Discontinuation criteria for study subjects and study stopping criteria

Discontinuation criteria for study subjects (either from treatment or from the trial) and procedures for collection of data relating to withdrawn subjects are included in the protocol and are acceptable.	Yes ☐ No ☐
Clinical trial termination criteria are included in the protocol and are acceptable.	Yes ☐ No ☐

Workspace:

Assessor's comment:

1.4.14 Other concomitant therapy

A description of permitted medications is included in the study protocol and is acceptable.	Yes ☐ No ☐

A description of prohibited medications is included in the study protocol and is acceptable.	Yes ☐ No ☐
Workspace:	
Assessor's comment:	

1.4.15 Safety and Monitoring

1.4.15.1 **Study procedures, visits and monitoring of subjects, and follow up**

Are the study procedures, study visits, monitoring of subjects, risk minimization measures and follow up adequately described and acceptable? **If No - tick appropriate box** below and **provide comment**	Yes ☐ No ☐
The frequency of the study visits/monitoring is insufficient	☐
The relevant targets are not monitored	☐
The proposed risk minimization measures and risk management guidelines (including monitoring, treatment modifications in case of toxicities) are not acceptable	☐
Risks associated with the study procedures including diagnostic procedures are unacceptable	☐
The follow-up period after the treatment is completed or after adverse reactions is insufficient	☐
Other issues:	☐
Workspace:	
Assessor's comment:	

1.4.15.2 **Reference Safety Information**

Reference Safety Information (RSI) is included in the SmPC or IB	SmPC ☐ IB ☐ **Version, Date and Section of IB**:
The document proposed as the RSI (SmPC or IB) is acceptable	Yes ☐ No ☐
The format of the RSI is acceptable (where IB is used)	Yes ☐ No ☐
The list of the proposed ARs declared as "expected" is acceptable (where IB is used)	Yes ☐ No ☐
Workspace:	

Assessor's comment:

1.4.15.3 **Data Safety Monitoring Committee (if applicable)**

The trial has a data safety monitoring committee.	Yes ☐ No ☐
Where the trial has a DSMC are the arrangements considered acceptable?	Yes ☐ No ☐
Workspace:	
Assessor's comment:	

1.4.16 Definition of the end of the trial

Definition of the end of trial is provided and it is acceptable.	Yes ☐ No ☐
Workspace:	
Assessor's comment:	

1.4.17 Biological samples used in the study (if applicable)

Procedures for the collection, storage and future use of biological samples are **not** described adequately or are **not** acceptable.	☐
Workspace:	
Assessor's comment:	

1.4.18 Data protection

The data protection policies as described in the protocol are **not** acceptable. **If No - tick appropriate box** below and **provide comment**	☐
Organisational and technical arrangements to avoid unauthorised access, disclosure, dissemination, alteration or loss of information and personal data processed are **insufficiently described or are unacceptable**	☐
Measures to ensure confidentiality of records and personal data of subjects are **insufficiently described or are unacceptable**	☐

Measures that will be implemented in case of data security breach are **insufficiently described or are unacceptable**	☐
Other issues:	☐
Workspace:	
Assessor's comment:	

1.4.19 Recruitment and informed consent procedures

Recruitment and informed consent procedure as described in the study protocol are **not** acceptable and/or **not** in compliance with the requirement of Chapter V of the Regulation (taking the study population into consideration).	☐
Workspace:	
Assessor's comment:	

1.5 Benefit/Risk assessment

1.5.1 Benefit/risk assessment in accordance with Chapter V of the Regulation

The protocol contains an acceptable evaluation of the anticipated benefits and risks of participation in the trial.	Yes ☐ No ☐
Measures to address the known and potential risks of trial participation and to protect subjects are acceptable. **If No - tick appropriate box** below and **provide comment**	Yes ☐ No ☐
Based on medical and ethical principles the **anticipated benefits** to the subjects or to public health **do not justify the foreseeable risks and inconveniences**, or compliance with this condition is not constantly monitored	☐
Rights of the subjects to physical and mental integrity, and privacy **are insufficiently safeguarded** in the study	☐
The clinical trial **has not been designed** to involve as little pain, discomfort, fear and any other foreseeable risk as possible, or both the risk threshold and the degree of distress **are not defined** in the protocol or are not monitored	☐
Workspace:	
Assessor's comment on benefit risk:	

1.6 Assessor's Overall Conclusions on the Clinical Part

The clinical aspects of the application are acceptable	☐

Supplementary information needs to be provided (refer to the list of requests for additional information)	☐
Workspace:	
Overall comment/ conclusion on the clinical assessment:	

1.6.1 REQUESTS FOR ADDITIONAL INFORMATION: CLINICAL: