South African Health Products Regulatory Authority
Building A
Loftus Park
Arcadia
Pretoria

Communication to Stakeholders 1 September 2020

MD022: Application for clinical evaluation of a medical device/*in-vitro* diagnostic (IVD)

BACKGROUND

1. The Medicines and Related Substances Act, 1965 (Act 101 of 1965) as amended, read in conjunction with the General Regulations on Medical Devices, published in Government Gazette Notice 40480, No.1515 of 9 December 2016, provides for the regulatory oversight of Medical Devices including In- Vitro Diagnostics (IVDs) in South Africa.

2. In terms of Regulation 16 of the General Regulations on Medical Devices, published in Government Gazette Notice 40480, No.1515 of 09 December 2016—
   16(4) A clinical investigation and a clinical trial or a clinical performance assessment for an IVD must be conducted in accordance with the guidelines for good clinical practice determined by the Authority; and
   16(5) A person may not conduct a clinical investigation, a clinical trial or a clinical performance assessment for an IVD without the authorisation of the Authority.

3. A clinical evaluation, including a clinical investigation, clinical trial and/or clinical performance assessment of a medical device and/or IVD may not be initiated prior to obtaining authorisation from SAHPRA.

4. Application must be made to SAHPRA to obtain authorisation to conduct a clinical evaluation of a medical device and/or IVD.

SUBMITTING AN APPLICATION FOR A NEW/AMENDMENT TO A CLINICAL EVALUATION OF A MEDICAL DEVICE/IVD

5. Applications must be submitted via email to **khanyisile.nkuku@sahpra.org.za** only. Applications submitted by any other means or to any other email address will not be processed.

6. The fee for a new or amendment to a clinical evaluation application is payable upon application and proof of payment should be submitted together with the completed application. Note: Fees may be updated from time to time. The onus is on the applicant to ensure that payment is made in line with the current fees structures, as published in the Government Gazette.
   a. Fee for application for a new clinical evaluation (Companies): R 9 900
   b. Fee for application for a new clinical evaluation (Institutions): R 4 950
   c. Fee for application for a technical amendment of a clinical evaluation: R 2 310
   d. Fee for application for a administrative amendment of a clinical evaluation: R 715

7. Supportive documents, as listed in the table below, must be provided by the applicant for each medical device/IVD to be evaluated in the clinical evaluation.

TIMELINES FOR PROCESSING APPLICATIONS FOR CLINICAL EVALUATION OF A MEDICAL DEVICES/IVD

8. Applications for clinical evaluations of medical devices and IVDs made to SAHPRA will be processed within 6 - 8 weeks.

9. An observation letter will be sent to the applicant in the event that an application does not meet the evaluation criteria. The deficiencies identified within the application will be documented in the observation letter.

10. The applicant is required to respond to the deficiencies noted in the observation letter **within five working days.**

11. NOTE: Only 2 cycles will be permitted, i.e. the applicant will have two opportunities to address the deficiencies identified in the application by submitting a response to SAHPRA within the defined timelines.

12. If the response/s (limited to a maximum of two cycles) from the applicant does not adequately address the deficiencies identified in the application, the application will not be recommended and the application process will be concluded.

PART 1: GENERAL INFORMATION			
Applicant			
Name:			
Address:			
Contact person:			
Telephone no.:			
Cell no.:			
E-mail address:			
Sponsor:			
Date of application:			
Protocol			
Study title			
Protocol no.		Version no.	
Investigational medical device/IVD			
Name of product			
South African risk classification of medical device/IVD			
Original manufacturer of investigational medical device/IVD			
Manufacturer name:			
Address:			
Name of authorised representative:			
Contact number of authorised representative:			
Email address of authorised representative:			
SAHPRA licence number (where relevant):			

PART 2: CHECKLIST -*Documents Submitted with Application (Circle or shade applicable)*	
Cover letter date	*YES / NO*
Application form	*YES / NO*
Checklist completed	*YES / NO*
Protocol (version and date)	*YES / NO*
Clinical investigation plan or clinical trial or clinical performance assessment for the medical device/IVD protocol	*YES / NO*
Investigator Brochure	*YES / NO*
Informed consent documents	*YES / NO*
Instructions for use	
Curriculum vitae of the investigator/s (SAHPRA format)	*YES / NO*
Investigator/s proof of GCP training certificates (not more than 3 years old)	*YES / NO*
Investigator/s proof of current malpractice insurance (Certificate/ Card)	*YES / NO*
Signed declaration by investigator/s	*YES / NO*
National Principle Investigator (CV/GCP/Malp/Declaration)	*YES / NO*
Participant insurance & expiry date (where relevant)	*YES / NO*
Proof of sponsor indemnity for investigators and trial sites	*YES / NO*
Proof of application to register the trial/investigation/performance assessment on SANCTR	*YES / NO*
Workloads for investigators	*YES / NO*
Copy of ethics approval	*YES / NO*
Copy of letter submitted to Ethics Committee	*YES / NO*
Reimbursement for patients	*YES / NO*
Remuneration to investigators	*YES / NO*
Study budget	*YES / NO*
Patients questionnaire(s)	*YES / NO*
Proof of registration with Professional Statutory Body(ies)	*YES / NO*
Additional information, i.e. Cert. of analysis (where relevant)	*YES / NO*

PART 3: DETAILS OF EVALUATION & SITES	
Details of Site(s) (Name of site, physical address, contact details, contact person)	
Details of how sites were selected	
Details of investigators and staff (Investigators, staff, number of staff, names, qualifications, experience)	
Details of capacity of site(s): (site facilities, equipment, emergency facilities, other relevant infrastructure and investigator workload documents)	
Details and evidence of competence of the laboratories (where relevant): • Collection and processing of samples for shipping to centralised testing facilities (include conditions of shipping) • Bedside/point-of-contact testing and details of training of staff • Screening and safety testing of clinical samples during the trial • Specialised end-point testing (virology, immunology, cytokine analysis)	

PART 4: REGULATORY DETAILS	
Name other Regulatory Authorities/ Ethics Committees to which application to do this evaluation have been submitted, and/or approved	
If the evaluation is to be conducted in SA and not in the host country of the applicant / sponsor, provide an explanation	
Name other Regulatory Authorities or Ethics Committees which have rejected this evaluation protocol and give reasons for rejection	
If applicable, details of and reasons for this evaluation having been halted at any stage by other Regulatory Authorities	

PART 5: INFORMATION SUMMARY CONTAINED IN CLINICAL INVESTIGATION PLAN OR CLINICAL TRIAL OR CLINICAL PERFORMANCE ASSESSMENT FOR MEDICAL DEVICE/IVD PROTOCOL	
Number of human or animal subjects involved in the clinical investigation, clinical trial or clinical performance assessment	
Name of investigator/s	
Quantity of the investigational medical device/IVD units to be used	
Information in respect of design, manufacture and expected performance of the medical device/IVD	

PART 6: INVESTIGATIONAL IVD INFORMATION TO BE PROVIDED	
Intended purpose or use of the investigational medical device/IVD in the proposed clinical trial	
The population and indications for which the investigational medical device/IVD is intended	
Name and number of the model or type including software version and accessories if any to permit full identification	
A descriptor as to how traceability is to be achieved during and after the clinical investigation e.g. assignment of lot numbers, batch number or serial number	
Labelling with name and address of the premises where the clinical trial is to carried out	
Labelled with clause “For research use only” and “For investigational use only”	

PART 7: BACKGROUND INFORMATION	
Disease / problem in South African context (e.g. local epidemiology)	
Overall rationale for the study summarised	
Rationale for the study in the South African context	

PART 8: STUDY OBJECTIVES AND ENDPOINTS (with justifications)	
Primary objectives and endpoints	
Secondary objectives and endpoints	
Exploratory objectives and endpoints	
Safety objectives and endpoints	
Other objectives	

PART 9: STUDY DESIGN AND METHODOLOGY	
Study Design (with justifications) • choice of design • randomisation • blinding	
Duration of the study	
Planned start and stop date of the study	
Participant numbers (local and worldwide) include participant numbers per site in South Africa	
Provide information indicating potential of each site to recruit required number of patients within envisaged duration of trial	

PART 10: ELIGIBILITY CRITERIA (with justification for each criterion)	
Inclusion criteria	
Exclusion criteria	

PART 11: STATISTICAL MEASURES	
Provide method of sample size determination (justification of the power of the study in relation to the outcomes measures)	
Provide statistical method(s) and analysis of qualitative and/or quantitative measures with appropriate, clear justification	

Details of data processing • how • where • when • who	

PART 12: ETHICAL AND ADMINISTRATIVE ISSUES	
Justification for deviation from current SA GCP guidelines	
Provide details of capacity building and transformation at all sites	
Provide details of insurance (including title, protocol, dates, policy #, amount, local vendor)	
Provide details of indemnity for investigators and trial site	
Ensure Instructions for Use (IFU) and Informed Consent / Assent includes: • latest ABPI and SA GCP guidelines • written in appropriate level of education /English • explains possible benefits / risks • ensuring patient rights • SAHPRA and Ethics contact names and numbers • Other details as per ICH GCP • Confirm translations available	
Provide separate IFUs and informed consent forms for any proposed • archiving of blood specimens for later research • genetics research • HIV testing • any other	
Provide details of publication policy	
Provide details of remuneration and other benefits for participants	
Provide details of remuneration of investigators or site	

Provide a list of Ethics Committees which will be involved in approving the study	
Provide details of possible conflict of interest of any person(s)/ organisation(s) who/which will be involved in the trial	
Provide updated proof of GCP training for staff involved in this trial (done in the past three years)	
Provide details on treatment and/or management of participants and their disease condition(s) after completion of trial (Post trial)	

PART 13: ADDITIONAL COMMENTS	
Provide any additional information that may be relevant to the study	

DR B SEMETE-MAKOKOTLELA
CHIEF EXECUTIVE OFFICER OF SAHPRA
1 September 2020

Annexure 1

DECLARATION BY APPLICANT

I/We, the undersigned have submitted all requested and required documentation, and have disclosed all information which may influence the approval of this application.

I/We, the undersigned will ensure that if the above-said clinical trial/investigation/performance assessment is approved, it will be conducted according to the submitted protocol and South African legal, ethical and regulatory requirements.

_____ _____

1st Applicant (local contact) Date

_____ _____

Alternative (local contact) Date

Declaration by National Principal Investigator

I, the undersigned as National Principal Investigator agree that I have reviewed the application and protocol and will ensure that if the above-said clinical trial/investigation/performance assessment is approved, it will be conducted according to the submitted protocol and South African legal, ethical and regulatory requirements.

_____ _____

National Principal Investigator / Other (state designation) Date

Annexure 2

STANDARDISED WORDING TO BE ADDED TO INSTRUCTIONS FOR USE (IFU)

If you have questions about this trial, you should first discuss them with your doctor or the Ethics Committee (contact details as provided on this form). After you have consulted your doctor or the Ethics Committee and if they have not provided you with answers to your satisfaction, you should write to the South African Health Products Regulatory Authority (SAHPRA) at:

The Chief Executive Officer

South African Health Products Regulatory Authority

Private Bag X828

PRETORIA

0001

E-mail: Boitumelo.Semete@sahpra.org.za

Annexure 3

SAHPRA FORMAT FOR CVs OF INDIVIDUALS PARTICIPATING IN THE CONDUCT OF CLINICAL TRIALS IN SOUTH AFRICA

1. Trial/Investigation/Performance Assessment:	
2. Protocol:	
3. Designation: (e.g. National Principal Investigator, Investigator (Principal, Co- or sub-), Study Co-ordinator, Regional Monitor, Local Monitor, Contract Research Affiliate)	
4. Personal Details	
Name:	
Work Address:	
Telephone Number:	
Cell-phone Number:	
E-mail address:	
5. Academic and Professional Qualifications	
6. Professional Statutory body registration number i.e. HPCSA, SAPC, SANC, etc.	
7. Current personal medical malpractice insurance details (all investigators)	
8. Relevant related work experience (brief) and current position	

9. Participation in clinical trials research in the last three years (title, protocol number, designation) [If multiple trials, only list those with relevance to this application, or in the last years.]
10. Peer-reviewed publications in the past 3 years
11. Date of last GCP training (as a participant or presenter)
12. Any additional relevant information supporting abilities to participate in conducting this trial. [briefly]

13. Signature:	Date:

Annexure 4

DECLARATION BY CO- AND PRINCIPAL INVESTIGATOR	
Name: **Title of Trial/Investigation/Performance Assessment:** **Protocol:** **Site:**	
1. I have read and understood 'Responsibility of The Principal Investigator (PI) and Participating Investigators' of the current Good Clinical Practice Guidelines of the National Department of Health. 2. I have notified the South African Health Products Regulatory Authority (SAHPRA) of any aspects of the above guidelines with which I do not / am unable to, comply. (If applicable, this may be attached to this declaration.) 3. I have thoroughly read, understood, and critically analysed (in terms of the South African context) the protocol and all applicable accompanying documentation, including the investigator's brochure, instructions for use and informed consent form(s). 4. I will conduct the trial/investigation/performance assessment as specified in the protocol. 5. To the best of my knowledge, I have the potential at the site(s) I am responsible for, to recruit the required number of suitable participants within the stipulated time period. 6. I will not commence with the trial before written authorisations from the relevant ethics committee(s) and SAHPRA have been obtained. 7. I will obtain informed consent from all participants or if they are not legally competent, from their legal representatives. 8. I will ensure that every participant (or other involved persons, such as relatives), shall at all times be treated in a dignified manner and with respect. 9. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial. *[Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.]** *Modified from: Davidoff F, *et al.* Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001) 10. I have* / have not (delete as applicable) previously been the principal investigator at a site which has been closed due to failure to comply with Good Clinical Practice. (*Attach details.) 11. I have* / have not (delete as applicable) previously been involved in a trial/investigation/performance assessment which has been closed as a result of unethical practices. (*Attach details) 12. I will submit all required reports within the stipulated time-frames.	
Signature:	Date:
Witness:	Date:

Annexure 5

JOINT DECLARATION BY SPONSOR (OR REPRESENTATIVE) AND PRINCIPAL INVESTIGATOR (OR NATIONAL PRINCIPAL INVESTIGATOR) CONCERNING SUFFICIENT FUNDS TO COMPLETE STUDY*
Title: Protocol:
I, <full name>, representing <sponsor or representative) And I, <full name>, Principal Investigator/National Principal Investigator Hereby declare that sufficient funds have been made available to complete the above-identified study. Signed: Date: SPONSOR (or alternative) Name: Address: Contact details: Signed: Date: PRINCIPAL INVESTIGATOR (or National PI) Name: Address: Contact details:

Annexure 6

PROVISIONAL DECLARATION BY SUB-INVESTIGATORS AND OTHER STAFF INVOLVED IN A CLINICAL TRIAL/INVESTIGATION/PERFROMANCE ASSESSMENT	
Name: Title of Trial/Investigation/Performance Assessment: Protocol: Principal Investigator's Name: Site: Designation:	
1. I will carry out my role in the trial/investigation/performance assessment as specified in the protocol. 2. I will not commence with my role in the trial/investigation/performance assessment before written authorisations from the relevant ethics committee(s) and South African Health Products Regulatory Authority (SAHPRA) have been obtained. 3. If applicable to my role in the trial/investigation/performance assessment, I will ensure that informed consent has been obtained from all participants or if they are not legally competent, from their legal representatives. 4. I will ensure that every participant (or other involved persons, such as relatives), shall at all times be treated in a dignified manner and with respect. 5. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial/investigation/performance assessment. *[Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.]** *Modified from: Davidoff F, *et al.* Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001) 6. I have* / have not *(delete as applicable)* previously been involved in a trial/investigation/performance assessment which has been closed due to failure to comply with Good Clinical Practice. *(*Attach details)* 7. I will submit all required reports within the stipulated time-frames.	
Signature:	Date:
Witness:	Date:

Annexure 7

DECLARATION BY REGIONAL MONITOR	
Name: Title of Trial/Investigation/Performance Assessment: Protocol: Principal Investigator's Name: Site: Designation:	
1. I have read and understood "The Monitor" of the current Clinical Trials Guidelines of the National Department of Health. *2.* I have notified the South African Health Products Regulatory Authority of any aspects of the above guidelines with which I do not / am unable to, comply. *(If applicable, this may be attached to this declaration.)* 3. I will carry out my responsibilities as specified in the trial protocol and according to the current Good Clinical Practice Guidelines of the Department of Health. 4. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial/investigation/performance assessment. [*Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions*.]* *Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001) 5. I have* / have not *(delete as applicable)* previously been the monitor at a site which has been closed due to failure to comply with Good Clinical Practice. *(*Attach details.)* 6. I have* / have not *(delete as applicable)* previously been involved in a trial/investigation/performance assessment which has been closed as a result of unethical practices. *(*Attach details)* 7. I will submit all required reports within the stipulated time-frames.	
Signature:	Date:
Witness:	Date:

Annexure 8

WORDING FOR THE SPONSOR INDEMNIFICATION FOR SITES AND INVESTIGATORS

In consideration of the {PI's / Institution's / Research Unit's] participation in the trial/ investigation/ performance assessment, we shall indemnify and hold harmless [Name of PI / Institution / Research Unit] and its employees from any legal liability for costs or damages for death or personal injury which may result from the administration of [Name of compound] pursuant to the said trial/investigation/performance assessment. This indemnity does not apply to the extent that such death or personal injury arises out of any negligent act, default or omission of [Name of PI / Institution / Research Unit] or its employees. Furthermore, this indemnity is subject to the condition that the trial/investigation/performance assessment is carried out in accordance with the Protocol approved by us in writing, that [Name of Sponsor] is notified immediately on receipt of any claim, that [Name of Sponsor] shall have full control of the management and defence of any such claim and that no offer to compromise or settle any claim is made without the written agreement of [Name of Sponsor].

Note: The wording for Sponsor Indemnification for investigators and sites serves as a guide and is not an exclusive approach.

Annexure 9

WORKLOAD TABLE				
Date:				
Title:				
Protocol number:				
Investigator (Title, Name and Designation i.e. PI, Co-PI or sub-I):				
Primary Employer *e.g* University, Research Unit, CRO, Private Practice of the investigator:				
Area of expertise of Investigator:				
Area of Study Research (*e.g*. oncology, cardiology):				
NUMBER OF CURRENT CLINICAL TRIALS OF INVESTIGATOR'S INVOLVEMENT				
Role (Principal Investigator/Co-PI or Sub-Investigator)	**Number of participants responsible for in actively recruiting clinical trials**	**Number of participants responsible for in follow-up clinical trials**	**Number of actively recruiting clinical trials**	**Number of clinical trials in follow-up clinical trials**
Principal /Co-Principal Investigator				
Sub-Investigator				
ESTIMATED TIME PER WEEK				Hours
Clinical trials		Clinical work (patient contact)		
		Administrative work		
Organisation 1 (e.g. Private practice / University / Governmental)		Clinical / Routine work		
		Teaching/Research		
		Administrative work		
Organisation 2 (e.g. Private practice / University / Governmental), if applicable		Clinical / Routine work		
		Teaching / Research		
		Administrative work		
		Clinical / Routine work		

Organisation 3 (e.g. Private practice / University / Governmental), if applicable	Teaching / Research	
	Administrative work	
Total		
Investigator Signature:		**Date:**