MDS – G20

Guidance on Requirements for Clinical Investigations of Medical Devices

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Introduction

Purpose

The purpose of this document is to clarify the requirements of conducting CIMD within the KSA.

Scope

This document is applicable to any party wishes to conduct CIMD within the KSA.

Background

SFDA/MDS has issued this guidance document in reference to Article Four of the "Medical Devices Interim Regulation" issued by Saudi Food and Drug Authority Board of Directors decree No. (1-8-1429) dated 29/12/1429 H and amended by Saudi Food and Drug Authority Board of Directors decree No. (4-16-1439) dated 27/12/2017 stipulating that the SFDA undertakes issuing the approval for conducting clinical investigations and clinical evaluation.

Requirements

General	1	Any CIMD within KSA shall be approved by SFDA before commencement.
	2	Investigational medical devices imported for clinical investigation may access KSA only if SFDA's importation approval is obtained.
	3	CIMD shall be approved by the EC that is registered at National Committee of Bio Ethics (NCBE).
Regulations and Standards	4	CIMD shall comply with the Law of Ethics of Research on Living Creatures.
	5	CIMD should be in accordance with: - Declaration of Helsinki - ISO 14155 (or any equivalent standard GCP)
Labeling Requirements	6	The labeling of the device shall comply with the requirements described in SFDA's guidance document entitled MDS – G10 Guidance on Labeling Requirements for Medical Devices
Reporting of Serious Adverse Event and Device Deficiency	7	The Sponsor shall report to the SFDA's NCMDR about any serious adverse events or device deficiencies that could have led to a serious adverse device effect, including serious health threat. This shall be reported without delay but not later than 15working days after the sponsor first knowing of the events.
Submitting Documents to SFDA	8	Sponsor (either located within the KSA, or outside the KSA through his AR) shall submit the required documents by email to MDCI@sfda.gov.sa as follows: 1. prior to CIMD, the required documents are specified in section (A) of "Required Documents". Once satisfied, SFDA will send a "No Objection Letter" to the applicant's email 2. during the CIMD, the required documents are specified in section (B) of "Required Documents". 3. at the end of the CIMD, the required documents are specified in section (C) of "Required Documents".
Inspection of the CIMD	9	SFDA has the right to inspect the CIMD without previous notification.
Reviewing Fees	10	No fees are required.

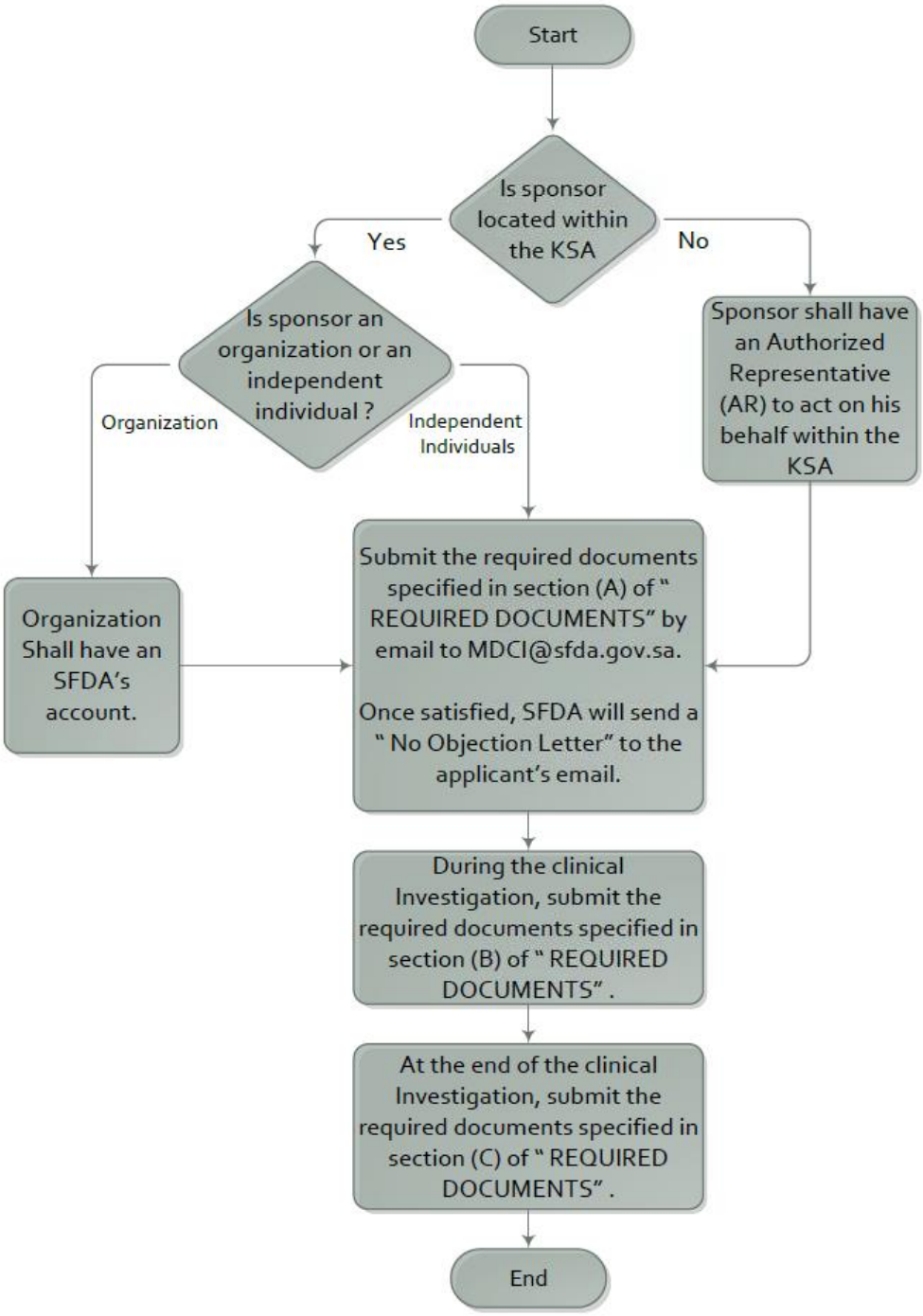
Required Documents

	Required Documents	Note
(A) Required documents prior to CIMD		
1	Application Form.	- See Annex (2) - See point (8) of "Requirements" - SFDA responds within a week in case of missing documents. - Application reviewing time is 60 working days.
2	Labelling of device.	- See point (6) of "Requirements"
3	Clinical investigation agreement between sponsor and clinical investigation site(s)/principal investigator(s)	-
4	Clinical investigation agreement between sponsor and CRO	- If applicable
5	EC approval letter	- It is required for each site - The EC shall be registered at National Committee of Bio Ethics (NCBE)
6	Clinical Investigation Plan (CIP)	-
7	Investigator's Brochure (IB)	- It is required only for premarket studies. - For post market studies, instructions for device use is required.
8	Informed consent	- It shall be in Arabic and English
9	Clinical investigation insurance for subjects	- It shall cover the cost of treatment of subjects in the event of injuries related to clinical investigation - for interventional studies
10	Curriculum Vitae of principal investigator(s) and investigator(s)	-
11	Disclosure of Principal Investigator Conflict of Interests	- See Annex (3) - It should be signed by PI
Note: Incomplete application will be deleted after 60 days.		

(B) Required documents during CIMD		
12	Progress Report	- It shall be submitted in yearly intervals, at least.
13	Change Form for amendments to any documents already approved by SFDA	- See Annex (4) - For non-substantial changes [e.g. minor logistical or administrative changes, change of monitor(s), telephone numbers, renewal of insurance] not affecting the rights, safety and well-being of human subjects or not related to the clinical investigation objectives or endpoints, a simple notification to SFDA can be sufficient*.
14	Change principal investigator	- The sponsor shall provide: 1. New PI CV 2. IRB approval of PI change 3. Any document and agreements signed by the previous PI need to be updated and submitted .
15	Withdrawal of EC approval	- Sponsor shall notify SFDA in case of withdrawal of EC approval or part of it, within five working days of receiving the withdrawal notice
16	Notification of suspension or premature termination of the clinical investigation.	- It shall be submitted to SFDA without delay but not later than: o five working days in case of suspension or premature termination because of safety grounds o 15 working days in case of reasons other than safety grounds . o Justification is requested in the case of premature termination, suspension and resuming after suspension.
17	Major deviations from the investigational plan that have a substantial impact on the safety or rights of subjects or on the robustness or reliability of the clinical data generated by the investigation	- It shall be submitted without delay but not later than five working days
18	Evaluation report of the serious adverse device events or device deficiencies that lead to serious adverse device effect.	- It shall be provided to the SFDA without delay but not later than 15 working days from the sponsor first knowing about the serious adverse event.

(C) Required documents at the end of the CIMD		
19	Notification of a clinical investigation completion.	- It shall be provided to the SFDA from the last patient follow up completed but not later than 10 working days.
20	Clinical investigation final report	- It shall be submitted to the SFDA without delay but not later than 12 months after the clinical investigation completion.

Flowchart


Start
Is sponsor located within the KSA
Yes
No
Is sponsor an organization or an independent individual ?
Organization
Independent Individuals
Sponsor shall have an Authorized Representative (AR) to act on his behalf within the KSA
Organization Shall have an SFDA's account.
Submit the required documents specified in section (A) of " REQUIRED DOCUMENTS" by email to MDCI@sfda.gov.sa.
Once satisfied, SFDA will send a " No Objection Letter" to the applicant's email.
During the clinical Investigation, submit the required documents specified in section (B) of " REQUIRED DOCUMENTS" .
At the end of the clinical Investigation, submit the required documents specified in section (C) of " REQUIRED DOCUMENTS" .
End

Annexes

Annex (1): Definitions and Abbreviations

KSA	Kingdom of Saudi Arabia
SFDA	Saudi Food and Drug Authority
MDS	Medical Devices Sector
GHTF	Global Harmonization Task Force
MDMA	Medical Devices Marketing Authorization
NCMDR	National Center for Medical Devices Reporting
AR	Authorized Representative
CIMD	Clinical Investigations of Medical Devices
CRO	Contract Research Organization
CIP	Clinical Investigation Plan
EC	Ethics Committee/Institutional Review Board
IB	Investigator's Brochure
NCBE	National Committee of Bio Ethics
GCP	Good Clinical Practice
Adverse Events (AE)*	any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device. Note 1: This definition includes events related to the investigational medical device or the comparator. Note 2: This definition includes events related to the procedures involved. Note 3: For users or other persons, this definition is restricted to events related to investigational medical devices.
Authorized Representative (AR)	means any natural or legal person established within the KSA who has received a written mandate from the manufacturer to act on his behalf for specified tasks, including the obligation to represent the manufacturer in its dealings with the SFDA.
Clinical Investigations* (of Medical Devices) (CIMD)	systematic investigation in one or more human subjects, undertaken to assess the safety or performance of a medical device. Note: “Clinical trial” and “clinical study” are synonyms for “clinical investigation”.
Clinical Investigation Plan (CIP)*	document that state(s) the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical investigation. Note: The term “protocol” is synonym for “CIP”. However, protocol has many different meanings, some not related to clinical

	investigation, and these can differ from country to country. Therefore, the term CIP is used in this International Standard.
Clinical Investigation Report*	document describing the design, execution, statistical analysis and results of a clinical investigation.
Contract Research Organization (CRO)*	person or organization contracted by the sponsor to perform one or more of the sponsor's clinical investigation-related duties and functions.
Deviation*	instance(s) of failure to follow, intentionally or unintentionally, the requirements of the CIP.
Device Deficiency*	inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. NOTE: Device deficiencies include malfunctions, use errors, and inadequate labeling.
Endpoint(s)*	⟨primary⟩ principal indicator(s) used for assessing the primary hypothesis of a clinical investigation.
establishment National Registry Number	means the number issued to a person by the SFDA under the establishment registration provisions of the Medical Devices Interim Regulation.
Ethics Committee (EC)*	independent body whose responsibility it is to review clinical investigations in order to protect the rights, safety and well-being of human subjects participating in a clinical investigation. Note 1: For the purposes of this International Standard, “ethics committee” is synonymous with “research ethics committee”, “independent ethics committee” or “institutional review board”. The regulatory requirements pertaining to ethics committees or similar institutions vary by country or region. Note 2: In the KSA, all local ECs supervising a clinical study have to be listed in The List of Registered Local Committees at the National Committee of Bioethics (NCBE) in King Abdulaziz City for Science & Technology (KACST): http://bioethics.kacst.edu.sa/LocalCommittees/What_are-the-local-committees.aspx
Informed Consent Process*	process by which an individual is provided information and is asked to voluntarily participate in a clinical investigation. Note: Informed consent is documented by means of a written, signed and dated informed consent form.
Investigation Site*	institution or site where the clinical investigation is carried out. Note: For the purpose of this International Standard, “investigation site” is synonymous with “investigation centre”.
Investigational Medical Device*	medical device being assessed for safety or performance in a clinical investigation.

	Note 1: This includes medical devices already on the market, that are being evaluated for new intended uses, new populations, new materials or design changes. Note 2: In this International Standard, the terms “investigational medical device” and “investigational device” are used interchangeably.
Investigator*	individual member of the investigation site team designated and supervised by the principal investigator at an investigation site to perform critical clinical-investigation-related procedures or to make important clinical-investigation-related decisions. Note: An individual member of the investigation site team can also be called “sub-investigator” or “co-investigator”.
Investigator's Brochure (IB)*	compilation of the current clinical and non-clinical information on the investigational medical device(s), relevant to the clinical investigation
Labelling	means written, printed or graphic matter Affixed to a medical device or any of its containers or wrappers. Information accompanying a medical device, related to identification, technical description. Information accompanying a medical device, related to its use, but excluding shipping documents.
Legally Authorized Representative*	individual or judicial or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical investigation.
Medical Device	means any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article: Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of: Diagnosis, prevention, monitoring, treatment or alleviation of disease, Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap, Investigation, replacement, modification, or support of the anatomy or of a physiological process, Supporting or sustaining life, Control of conception, Disinfection of medical devices, Providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body; And

	Which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means.
National Centre for Medical Device Reporting (NCMDR)	means an organization managing a database of information on safety and/or performance related aspects of medical devices and employing staff capable of taking appropriate action on any confirmed problems.
Objective*	main purpose for conducting the clinical investigation
Principal Investigator (PI)*	qualified person responsible for conducting the clinical investigation at an investigation site Note 1 If a clinical investigation is conducted by a team of individuals at an investigation site, the principal investigator is responsible for leading the team. Note 2 Whether this is the responsibility of an individual or an institution can depend on national regulations
Serious Adverse Event (SAE)*	adverse event that a) led to death, b) led to serious deterioration in the health of the subject, that either resulted in a life-threatening illness or injury, or a permanent impairment of a body structure or a body function, or in-patient or prolonged hospitalization, or medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, c) led to foetal distress, foetal death or a congenital abnormality or birth defect Note: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.
Adverse device effect (ADE)*	Adverse event related to the use of an investigational medical device Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device

Sponsor*	individual or organization taking responsibility and liability for the initiation or implementation of a clinical investigation NOTE When an investigator initiates, implements and takes full responsibility for the clinical investigation, the investigator also assumes the role of the sponsor and is identified as the sponsor-investigator.
Subject*	individual who participates in a clinical investigation NOTE A subject can be either a healthy volunteer or a patient.
Vulnerable Subject*	individual whose willingness to volunteer in a clinical investigation could be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or of retaliatory response from senior members of a hierarchy in case of refusal to participate example Individuals with lack of or loss of autonomy due to immaturity or through mental disability, persons in nursing homes, children, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving informed consent. Other vulnerable subjects include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the sponsor, members of the armed forces, and persons kept in detention.
* Source: ISO 14155:2011	

Annex (2): Application Form for CIMD

	Date Received		(For SFDA use only)
	CIMD Application Number		(For SFDA use only)
1. Status			
1.2	Aim of Study	☐ Pre-marketing approval for new device ☐ Pre-marketing approval for new claims ☐ Post-Marketing study ☐ Non Marketing study	
1.3	Type of Study	☐ Observational study ☐ Interventional study	
1.4	Does this clinical investigation involve first in human use?	☐ Yes ☐ No	
1.5	Will the investigational device be imported to KSA?	☐ Yes (SFDA importation license is required). ☐ No	
2. Sponsor details			
2.1	Type of Sponsorship	☐ Commercial ☐ Non-commercial	
2.2	Type of sponsor	☐ manufacturer ☐ AR ☐ Hospital ☐ Independent individuals ☐ Foundation ☐ University or Institution ☐ Other, please specify:	

2.3	Type of aid	☐ Material support ☐ Funding support ☐ Other, please specify: ……	
2.٤	Sponsor Details	Name SFDA's account (if applicable) Address Phone Fax E- mail Contact person name Contact person phone Contact person e-mail	
2.٥	Person responsible for completing the application.	Name Position Phone E-mail	
3. CRO Details (if applicable)			
3.1	CRO, if applicable	Name SFDA's license (if applicable) Address Phone Fax E- mail Contact person name Contact person phone Contact person e-mail	

4. Investigational Device Information			
4.1	Is the device registered at SFDA?	☐ Yes, where applicable: • MDMA Certificate No. : …… • SFDA registration No. : …… ☐ No, but registered in: ☐ Australia ☐ Canada ☐ Japan ☐ USA ☐ EU ☐ Other, please specify: ……..… ☐ Not registered anywhere	
4.2	Investigational Device Name		
4.3	Device Category	☐ Active implantable devices ☐ Anesthetic and respiratory devices ☐ Dental devices ☐ Electro mechanical medical devices ☐ Hospital hardware ☐ Non-active implantable devices; ☐ Ophthalmic and optical devices ☐ Reusable devices ☐ Single use devices ☐ Assistive products for persons with disability ☐ Diagnostic and therapeutic radiating devices ☐ Complementary therapy devices ☐ Biologically derived devices ☐ Healthcare e facility products and adaptations	

		☐ Laboratory equipment ☐ Other: ……..	
4.4	Does the device is an implantable?	☐ No ☐ Yes, brief description:…….. …… ➢ Is the device intended to remain permanently in patient: ☐ No ☐ Yes	
4.5	Whether the device intended to be used for cosmetic rather than medical purposes	☐ No ☐ Yes, Select: ☐ A non-corrective contact lens ☐ An implant for augmentation, fixation, or sculpting of body parts ☐ A facial or other skin filler ☐ Equipment for liposuction ☐ Surgical laser equipment	
4.6	Does the device incorporate, as an integral part or substance, a medicinal product in achieving its primary intended action?	☐ No ☐ Yes ➢ Brand name of drug: ……	
4.7	Does the device incorporate a substance of animal origin?	☐ No ☐ Yes ➢ Type of tissue, cell, or substance: …… ……	
4.8	Does the device incorporate human tissue, cell, or substance?	☐ No ☐ Yes ➢ Type of tissue, cell, or substance: …… ……	
4.9	Does the device incorporate cells or substance of microbial origin?	☐ No ☐ Yes ➢ Type of microorganism: …… ……	
4.10	The intended purpose of the investigational device		

5. Design of Clinical Investigation			
5.1	Clinical Investigational Plan (CIP) information	Scientific title	
5.2	Clinical Investigational Plan title	Abbreviated title	
		CIP number	
		CIP date	
		CIP version	
		Planned start date	
		Planned completion date	
5.3	Type of Design	☐ Open-label non-randomized clinical investigation ☐ Randomization, Randomized controlled clinical investigation o Parallel group: …… o Cross over: …… ☐ Blinding ☐ Single blinded ☐ Double blinded ☐ Other ☐ Comparator used ☐ Placebo ☐ Comparator device, identify: ……	
5.4	Does this study includes vulnerable subjects?	☐ No ☐ Yes	
5.5	Size of the sample population	Planned total number of subjects involved in the clinical investigation	
		Planned number of subjects involved in the KSA	
5.6	Number of study centers in the KSA		
5.7	Other countries where this clinical investigation is carried out		
5.8	Is there a Data Safety Monitoring Committee for this study?	☐ Yes ☐ No	

6. Investigation Site(s) in the KSA			
6.1	Site 1	Name	
		Address	
		Phone	
		E-mail	
		Name of principal investigator	
		EC name	
		EC address	
		EC phone	
		EC e-mail	
		Protocol number approved by HREC/EC	
6.2	Site 2	Name	
		Address	
		Phone	
		E-mail	
		Name of principal investigator	
		EC name	
		EC address	
		EC phone	
		EC e-mail	
		Protocol number approved by HREC/EC	
Add			

7. Declaration	
7.1	I'm the **sponsor** defined in this application,: ☐ undertake that I comply with the Law of Ethics of Research on Living Creatures. ☐ undertake that I will report to the SFDA's NCMDR any Adverse device effect of which I become aware of an investigational medical; without delay but not later than 10 working days of occurrence. ☐ undertake that I will provide the documents specified in sections (B) and (C) of "REQUIRED DOCUMENTS" in SFDA's guidance document entitled MDS – G20 Guidance on Requirements for Clinical Investigations of Medical Devices. ☐ undertake to notify ECs and principal investigators in case of withdrawal of SFDA's approval, or part of it, within five working days of receiving the withdrawal notice. ☐ undertake, under any request from the SFDA to respond by providing accurate, current, and complete information about any aspects of the study. ☐ declare that SFDA has the right to inspect the study at any time without previous notification. ☐ declare that all information provided in this application is true and complete. ☐ declare that I will maintain if applicable a proper safe return or disposal of investigational devices. Name: Position: Date: Signature:

Annex (3): Disclosure of Principal Investigator Conflict of Interests

Title of Clinical Invstigation Plan	
Date received:	(For SFDA use only)
CIMD Application Number:	(For SFDA use only)

I disclose the following regarding the involvement in the investigation in the submitted application:

- ☐ any significant payments of other type made from the sponsor, including but not limited to a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- ☐ any proprietary interest in the investigational product held by the clinical investigator;
- ☐ any considerable equity interest (including but not limited to any ownership interest, stock deal, or other financial interest) held by the clinical investigator in the sponsor of the covered study.

Details of the disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

Name of principal investigator:
Date:
Signature:

Note: In case of multicenter study, a separate form shall be filled for each principal investigator.

Annex (4): Change Form for CIMD

Date:	
CIMD Application Number:	
1. The document type where the change occur	
2. The original statement	
3. The changed statement	
4. Reason of change	