Dear scientific boards managers (all pharmaceutical companies):

Greetings to all of you..

According to the Saudi Food & Drug Authority (SFDA) regulation which issued by the Royal act No. (M/6) on the date of (25/1/1428 H), and to the regulation of Pharmaceutical Facilities and Products which was issued by the Royal act No. (M/31) on the date of (1/6/1425 H.), we would like to inform you about the following:

First: All clinical trials must be registered at the Saudi Food and Drug Authority, Drug sector, Clinical Trials Department according to the pharmaceutical products clinical trials Memo No.3476 on the date of (13/1/1431 H).

Second: Approving the applications of conducting the clinical trials:

1- According to the SFDA requirements that mentioned in the attachment (1), the researcher, sponsor of the trial or the Clinical Trial Monitoring Center (CTMC) must register all clinical trials. The registration of the trial does not mean that the application has been approved.
2- According to the Royal act No. (M/59) on the date (14/9/1431 H), the researcher, sponsor of the trial or CTMC must be committed to the Law of Bioethical Research on Living Creatures.
3- According to the memo No (3993/ E) on (15/10/1430), the sponsor of the trial or the follow-up center of clinical trial must pay to the SFDA a 15000 S.R as a fee for any clinical trial protocol evaluation procedure.
4- Clinical trials on registered drugs at SFDA:

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An approval letter from the SFDA is required in the following cases:

- ✓ Using drugs for unregistered indication.
- ✓ Change in dosage regimen or treatment options.
- ✓ Off label indication.

- According to the attachment (1), it is satisfactory to notify the SFDA about the clinical trial and then to submit the file (application) of clinical trials requirements.
- The researcher can starts his/her trial after having the acceptance of Ethics Committee (ECs)/ or Institutional Review Board (IRB) at the clinical trials site, except the three above mentioned cases.

5- <u>Clinical trials on unregistered drugs at SFDA:</u>

- An approval letter from the SFDA is required for each clinical trial site of these trials.
- All SFDA requirements which mentioned in the attachment (1) must be obligated.
- In the case of clinical trials that uses registered products by the United States-Food and Drug Administration (US-FDA) or European Medicinal Agency (EMA), the product registration application must be submitted by the company to the SFDA within 6 months from the date of approval letter.
- In the case of clinical trials that uses non-registered products by the FDA or EMA, the company is required to submit an Investigational New Drug (IND) application according to the registration requirements at SFDA. Taking into consideration that the SFDA will receive the IND application in the following cases:

  - ✓ The application is submitted by a local company.

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- ✓ The clinical trial must be a Multi- center trials and reached the phase 2 or phase 3. Also, the propuse of this trial must be conducting trials on medication which intended to be used in treating AIDS, Cancer or Epidemic diseases.

6- <u>If the application file included all requested documents, the target performance needed to reply for the researcher or the sponsor company of the trial are:</u>

- 10 working days for clinical trials on registered drugs at the SFDA.
- 30 working days for clinical trials on unregistered drugs at the SFDA while they are registered by the FDA and EMA.
- 180 working day for the for clinical trials on unregistered drugs at the SFDA, FDA and EMA.

<u>Third: Importing drugs used in clinical trials:</u>

1- According to the SFDA importing requirements, Importing drug samples which will be used in the clinical trial needs approval from the Central Clearance Unit-Drug Sector at the SFDA after the issuing of approval letter from Clinical Trial department.

<u>Forth: Sending Biological samples outside the clinical trials locations:</u>

1- According to the Royal act No. (M/59) on the date (14/9/1431 H) which organizing the interaction with the Biological samples, the

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researcher, sponsor of the trial or CTMC must be committed to the Law of Bioethical Research on Living Creatures.

2- If the protocol of the clinical trial stipulate on sending the Biological samples to a laboratories outside Kingdom of Saudi Arabia, the researcher or sponsor of the trial or the follow-up center of clinical trial must get the permission of SFDA to send these samples. The researcher must submit an application including the following:

- The quantity and expected sending date of the Biological samples.
- The destination (receiver) which will receive the Biological samples, with no conflict with what was mentioned in the trial protocol.
- The researcher must pledge that the sent samples will be used for trial purpose according to what was mentioned in the trial protocol.

Fifth: Adverse Events handling:

1- It is essential to inform the SFDA about all expected and unexpected (not serious) adverse events for drugs used in the trial within 15 days. In case of serious adverse events that might lead to (death, life threatening, hospitalization, disability or birth defect), the SFDA must be informed immediately within 7 days.

Sixth: Dealing with a suspended trial by the SFDA:

1- According to the attachment (2), the researcher, sponsor of the trial or CTMC must be committed to the SFDA requirements.

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Seventh: Dealing with completed trials:

1- According to the attachment (2), the researcher, sponsor of the trial or the follow-up center of clinical trial must be committed to the SFDA requirements.

Eighth: The qualifications of clinical trials researchers:

1- Starting from 1/1/1433H, the SFDA will request from the researchers to provide any documents which proves that they get the proper training on the (GCP) for every researcher who wants to participate in any clinical trials.

For any further inquires or questions, kindly contact us through the following:

- E-mail: CT.Drug@sfda.gov.sa
- Phone number: 01-2759222 ext: 2318 or 2339 (clinical trials unit).

With my best regards...

Vice-President for Drug Affairs.

Professor: Saleh Abdullah Bawazir

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Attachment number (1)

SFDA requirements for clinical trial approval

Requirement	Registered Drug	Unregistered Drug	
		Registered in FDA/EMA	Unregistered in FDA/EMA
Headed Letter to SFDA.	✓	✓	✓
Bank Transfer Payment.	✓	✓	✓
Confidentiality Agreement.	✓	✓	✓
Trial Application Form.	✓	✓	✓
Trial Protocol.	✓	✓	✓
Informed Consent Form.	✓	✓	✓
IRB/EC Approval.	✓	✓	✓
Investigator Brochure.	✓	✓	✓
Financial Disclosure of Principal Investigator.	✓	✓	✓
GMP Certificate.	x	✓	✓
Certificate of Analysis of Study Drug.	x	✓	✓
Sample of Label of Study Drug.	✓	✓	✓
IMP Labeling & Packaging	x	✓	✓
Samples of drug	x	✓	✓
Clinical Trial Agreement.	✓	✓	✓
CVs of Principal Investigator & Coordinator.	✓	✓	✓
IND application	x	x	✓
Saudi Drug Registration application	x	✓	x

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Attachment number (2)

SFDA requirements for clinical trial during Conducting, Completion and Termination

	Title of Document	Purpose	Located in Files of Investigator/ Sponsor Institution	
8.3.1	Investigator's Brochure updates	To document that investigator is informed in a timely manner of relevant information as it becomes available	X	X
8.3.2	Any revisions to: Protocol/amendment(s) and CRF -Informed consent form - Any other written information provided to subjects - Advertisement for subject recruitment (if used)	To document revisions of these trial-related documents that take effect during trial	X	X
8.3.3	Dated, document approval/favorable opinion of (IRB)/(IEC) of the following: - protocol amendments - Revision(s) of: -informed consent form -Any other written information to be provided to the subject -Advertisement for subject recruitment (if used) - Any other document given approval/favorable opinion - Continuing review of trial (see section 3.1.4)	To document that the amendment(s) and/or revision(s) have been subject to IRB/IEC review and were given approval/favorable opinion. To identify the version number and date of the document(s)	X	X

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8.3.4	SFDA authorizations/approval /notifications where required for: -Protocol amendment(s) and other document	To document compliance with applicable regulatory requirements	X (where required)	X
8.3.5	Curriculum vitae for new investigator(s) and/or sub investigators	(see section 8.2.10)	X	X
8.3.6	Updates to normal value(s)/range(s) for medical laboratory/technical procedure(s)/test(s) included in the protocol	To document normal values and ranges that are revised during the trial (see section 8.2.11)	X	X
8.3.7	Updates of medical/laboratory/tech nical/procedures/tests -Certification or -Accreditation or -Established quality control and/or external quality assessment or -Other validation (where required)	To document that tests remain adequate throughout the trial period (see section 8.2.12)	X (where required)	X
8.3.8	Documentation of investigational product(s) and trial-related materials shipment	(See section 8.2.15)	X	X
8.3.9	Certificate(s)of analysis for new batches of investigational products	(See section 8.2.16)		X
8.3.10	Monitoring visit reports	To document site visits by, and findings of, the monitor		X
8.3.11	Relevant communications other than site visits -letters -meeting notes -Notes of telephone calls	To document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting	X	X
8.3.12	Signed informed consent forms	To document that consent is obtained in accordance with GCP and protocol and dated prior to participation of each subject in trial. Also to document direct access permission (see section 8.2.3)	X	

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8.3.13	Source documents	To document the existence of the subject and substantiate integrity of trial data collected. To include original documents related to the trial, to medical treatment, and history of subject	X	
8.3.14	Signed, dated, and completed case report forms (CRFs)	To document that the investigator or authorized member of the investigators staff confirms the observations recorded	X (copy)	X (original)
8.3.15	Documentation of CRF corrections	To document all changes/ additions or corrections made to CRF after initial data were recorded	X (copy)	X (original)
8.3.16	Notification by originating investigator to sponsor of serious adverse events and related reports	Notification by originating investigator to sponsor of serious adverse events and related reports in accordance whit 4.11	X	X
8.3.17	Notification by sponsor and/or investigator, where applicable, to SFDA and IRB(s)/IEC(s) of unexpected serious adverse drug reactions and of other safety information	Notification by sponsor and/or investigator, where applicable, to SFDA and IRB(s)/IEC(s) of unexpected serious adverse drug reactions in accordance with 5.17 and 4.11.1 and of other safety information in accordance with 4.11.2 and 5.16.2	X (where required)	X
8.3.18	Notification by sponsor to investigators of safety information	Notification by sponsor to investigators of safety information in accordance with 5.16.2	X	X
8.3.19	Interim or annual reports provided to IRB/IEC and authority(ies)	Interim or annual reports provided to IRB/IEC in accordance with 4.10 and to authority(ies) in accordance with 5.17.3	X	X (where required)

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8.3.20	Subject screening log	To document identification of subject who entered pretrial screening	X	X (where required)
8.3.21	Subject identification code list	To document that investigator/ institution keeps a confidential list of names of all subject allocated to trial numbers on enrolling in the trial. Allows investigator/institution to reveal identity of any subject	X	
8.3.22	Subject enrollment log	To document chronological enrollment of subject by trial number	X	
8.3.23	Investigational products(s) accountability at the sits	To document that investigational products(s) have been used according to the protocol	X	X
8.3.24	Signatures sheet	To document signatures and initials of all persons authorized to make entries and/or corrections on CRFs	X	X
8.3.25	Record of retained body fluids/tissue samples (if any)	To document location and identification of retained samples if assays need to be repeated	X	X

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After completion or termination of the trial, all of the documents identified in section 8.3 should be in the file together with the following:

	Title of Document	**Purpose**	**Located in Files of** Investigator/ Institution	Sponsor
8.4.1	Investigational product(s) accountability at site	To document that the investigational product(s) have been used according to the protocol . To document the final accounting of investigational product(s) received at the site, dispensed to subjects, returned by the subjects, and returned to sponsor	X	X
8.4.2	Documentation of investigational product(s) destruction	To document destruction of unused investigational product(s) by sponsor or at site	X (if destroyed at site)	X
8.4.3	Completed subject identification code list	To permit identification of all subjects enrolled in the trial in case follow-up is required. List should be kept in a confidential manner and for agreed upon time	X	
8.4.4	Audit certificate (if required)	To document that audit was performed (if required) (see section 5.19.3(e))		X
8.4.5	Final trial close-out monitoring report	To document that all activities required for trial close-out are completed, and copies of essential document are held in the appropriate files		X
8.4.6	Treatment allocation and decoding documentation	Returned to sponsor to document any decoding that may have occurred		X

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8.4.7	Final report by investigator/institution to IRB/IEC where required, and where applicable, to the SFDA (see section 4.13	To document completion of the trial	X	
8.4.8	Clinical study report (see section 5.22)	To document results and interpretation of trial	X (if applicable)	X

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