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

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EMERGENCY PROCEDURES FOR CLINICAL TRIAL SITES

This document highlights the importance of having emergency standard operating procedures in place during the conduct of clinical trial at sites and includes the minimum requirements for emergency procedures. This guideline represents the South African Health Product Regulatory Authority's (SAHPRA) current thinking on the measures to be taken to ensure that patients gain access to emergency procedures during the conduct of clinical trial. SAHPRA reserves the right to request any additional information and may make amendments in keeping with the knowledge which is current.

Document History

Final Version	Reason for Amendment	Effective Date
1	Document 9.60 for implementation, Version 1	July 2015
2	Replacement of 9.60 with guideline 2.41, change in title Amendment of sections 1, 2, 5, 9 (old 7) Addition of sections 7 & 8	May 2019
3	Administrative changes Change of document number from 2.41 to SAHPGL-CEM-CT-03	August 2022

DR BOITUMELO SEMETE-MAKOKOTLELA
CHIEF EXECUTIVE OFFICER

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1. BACKGROUND

Clinical trials involve the use of predominantly unregistered drugs in human participants. The potential associated risks are often not well known, especially in phase I and II studies. Although efforts are made to control risks to clinical trial participants, some risks may be unavoidable because of the uncertainty inherent in clinical research.

For this reason, trial protocols should incorporate a clear guideline for medical emergencies, including the following mandatory requirements:

- An emergency standard operating procedure for medical emergencies;
- Participant post-dose observational period on the trial site;
- A resuscitation trolley that provides the required equipment and recommended medicines;
- The provision of suitably trained personnel; and
- A written procedure for rapidly identifying a 'blinded' investigational product in an emergency.

While this guideline aims to improve participant protection, there may be instances where sites may not meet or need to meet these minimum requirements. Clear justification would be required in such instances, and this will be reviewed on a case-by-case basis to ensure that participant safety is not compromised. Further information may be required in such instances. Sites that comply with the guidelines will not require any further information to be provided.

2. STANDARD OPERATING PROCEDURE TO DEAL WITH MEDICAL EMERGENCIES

All clinical trial sites should have an emergency standard operating procedure in place that should be available for inspection by the South African Health Product Regulatory Authority (SAHPRA). Additional emergency equipment and/or medicines listed below may be appropriate depending on the nature and scope of the trial.

3. LOCATION OF THE RESUSCITATION/EMERGENCY TROLLEY

The resuscitation trolley should be located within the clinical trial unit where any invasive protocol defined procedures are conducted and/or investigational product (IP) administered and be under the control of a designated person at the clinical trial site.

4. MONITORING

Monthly checks of the resuscitation trolley, including availability of equipment and/or medicines as well as expiry dates, should be performed by a suitably qualified member of the research team, and documentation of these checks should be maintained, and be made available for SAHPRA inspection.

5. RESUSCITATION/EMERGENCY TROLLEY EQUIPMENT

There are a number of different national and international bodies which set the minimum recommended contents of a resuscitation trolley for areas of a hospital other than the Emergency Centre, or for use in general

practice rooms, including the Emergency Medicine Society of South Africa. There are, however, no such provisions for clinical trial units. It is thus recommended that the minimum requirements for clinical trial units be adapted from the minimum requirements of the Emergency Medicine Society of South Africa, Practice Guideline EM006 (2008). These are the essential basic minimum items recommended but more items may be needed depending on clinical requirement:

DEVICES TO OPEN AND PROTECT AIRWAY	
Laryngoscope set	Handle with adult and/or paediatric blades, spare bulbs and spare batteries
Tracheal tubes	Uncuffed and/or cuffed; available sizes dependent on population seen in unit
Tape or equivalent to tie tube in place	
Oropharyngeal airways	Available sizes dependent on population seen in unit
Pulse Oximeter	
EQUIPMENT FOR DIFFICULT INTUBATION	
Introducers for ET tubes	Available sizes dependent on population seen in unit
Magill's forceps	Adult and/or paediatric
Laryngeal masks	Available sizes dependent on population seen in unit
DEVICES TO DELIVER OXYGEN AND TO VENTILATE PATIENTS	
Bag valve ventilation devices	With oxygen reservoir and adult and/or paediatric masks
Oxygen delivery devices	
Oxygen supply	
EQUIPMENT TO DIAGNOSE AND TREAT CARDIAC DYSRHYTHMIAS	
Defibrillator or Automated external defibrillator	With conductive paste or pads, paddles, electrodes in appropriate sizes dependent on population seen in unit
DEVICES TO GAIN INTRAVASCULAR ACCESS	
IV cannulae (various)	Available sizes dependent on population seen in unit
Needles and syringes (various)	Available sizes dependent on population seen in unit
Sharps container	
IV administration sets	Available sizes dependent on population seen in unit
EQUIPMENT FOR MONITORING AIRWAY, BREATHING AND CIRCULATION	

Stethoscope	Available sizes dependent on population seen in unit
Non-invasive blood pressure monitoring device	Available cuff sizes dependent on population seen in unit
Thermometer	
Glucometer	
APPROPRIATE HARDWARE	
Drip stand or equivalent hanging device	
Suction devices and suction catheters	
Universal precautions	Gloves *etc.*
ESSENTIAL MEDICINES	
Adrenaline (Epinephrine)	
Antihistamine (*e.g.* promethazine)	
Aspirin	
Atropine	
Dextrose 50 % IV	
Diazepam	
Hydrocortisone	
Lignocaine IV	
IV SOLUTIONS	
Ringer's lactate or	
0,9 % NaCl (sodium chloride)	

6. ADEQUATELY TRAINED STAFF

Each clinical trial unit should have adequately trained investigators (at least one on site where and when investigational product is administered) and staff to manage medical emergencies with relevant expertise in the area of study.

The investigators should be trained to use the equipment and medicines that they have available in the trolley.

There must be an emergency 24-hour contact number for trial participants that may experience an unexpected adverse event.

Phase I sites may require additional emergency facilities and resources in addition to those discussed in this document.

7. EMERGENCY UNBLINDING

The investigators must have a written procedure for rapidly identifying a 'blinded' investigational product in

an emergency. The procedure must be secure, readily available at all times during the trial, and not allow breaks of the blinding to go undetected. It is of importance that an investigator may immediately unblind a participant's treatment allocation, without having to first contact the Sponsor or trial staff.

8. RECORD KEEPING

All medical emergencies occurring at a trial site must be recorded in detail in an appropriate minute book and be available for SAHPRA inspection.

9. REFERENCES

The following related documents are referenced:

1. EMSSA Practice Guideline EM006. 2008. Available from [https://emssa.org.za/wp-content/uploads/2017/10/em006.pdf] Accessed 25 July 2022.

2. ABPI. Guidelines for phase 1 clinical trials. 2018 edition. Available from [https://www.abpi.org.uk/publications/guidelines-for-phase-i-clinical-trials-2018-edition/] Accessed 12 July 2022.

10. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces Emergency Procedures for Clinical Trial Sites, old document number 2.41. It will be reviewed on this timeframe or as and when required.