MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

ADVERSE EVENT and POST-MARKETING VIGILANCE REPORTING of MEDICAL DEVICES and IVDs

This guideline is intended to provide recommendations to Manufacturers, Importers, Exporters, Distributors and Holders of Certificate of Registration (HRC) of medical devices and IVDs. It represents the Council's current thinking on the safety, quality and performance of medical devices and IVDs. It is not intended as an exclusive approach. The council reserves the right to request any additional information to establish the safety, quality and performance of a medical device or IVD in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. The Council is committed to ensure that all registered medical devices and IVDs will be of the required quality, safety and performance. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Guidelines and application forms are available from the office of the Registrar and the website.

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REGISTRAR OF MEDICINES

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GUIDELINE FOR THE REPORTING OF ADVERSE EVENTS &POST-MARKETING VIGILANCE OF MEDICAL DEVICES AND IVDs

NOTE: This guideline outlines the format and data requirements for reporting of adverse events and post-marketing vigilance and monitoring requirements for Medical Devices and IVDs, and should be read in conjunction with the Medicines and Related Substances Act, 1965 (Act 101 of 1965), and the Regulations to this Act

1 INTRODUCTION

The registration of medical devices and IVDs in South Africa is governed by the provisions and requirements of the Medicines and Related Substances Control Act No. 101 of 1965, (hereafter 'the Act') and the Regulations and Guidelines published in terms thereof.

Copies of the legislation can be obtained from the Department of Health website <http://www.doh.gov.za> or the MCC website www.mccza.com

This guideline provides a reference document detailing the regulatory requirements for reporting of adverse events and post marketing vigilance and monitoring requirements for medical devices and IVDs in South Africa and describes the information to be supplied to the Regulatory Authority in South Africa.

The information submitted will be evaluated in terms of the provisions of the Act.

The aim of these Guidelines is to assist licensed manufacturers, importer, distributors and wholesalers and the holders of registration certificates in the reporting of adverse events and in the post-marketing vigilance and monitoring of medical devices or IVDs. The types of medical devices or IVDs include all products classified as per the different Classes based on a risk assessment and intended use.

All medical device or IVDs for supply in South Africa must continue to meet all the regulatory, safety and performance requirements and any applicable standards.

Whenever there is doubt, applicants are advised to consult the Council (MCC) for confirmation and/or clarification regarding reporting; refer to the website for contact details. Applicants should always refer to the **current** version of the relevant ***GUIDELINE FOR THE REPORTING OF ADVERSE EVENTS & POST-MARKETING VIGILANCE OF MEDICAL DEVICES AND IVDs*** and the Addenda thereto when reporting.

Guidelines are constantly evolving as a result of scientific developments and harmonisation of the requirements of regional and international regulatory authorities. The Council (MCC) endeavours to regularly update the guidelines to reflect current thinking and keep its technical requirements and evaluation policies in line with “best international medical device and IVD regulatory practice”.

2 GENERAL

2.1 SCOPE

A medical device and IVD is defined as per the provisions of the Medicines and Related Substances Act, 1965 (Act 101 of 1965 as amended). Legislation requires that the a medical device or IVD shall comply with the Essential Principles of Safety and Performance of Medical Devices and IVDs which include requirements for quality, safety and performance as determined by Council.

2.1 Scope - continued

This guideline is intended to assist Licence Holders and Holders of a Certificate of Registration of Medical Devices and IVDs in

- the reporting of adverse events associated with the use of medical devices and IVDs, and
- the post-marketing vigilance for medical devices and IVDs. This includes the management of safety data which arises during post-registration and post-marketing performance and clinical trials.

If there is a problem with a medical device or the way in which it is being used, the Holder of the Certificate of Registration (HRC) and the manufacturer or distributor will first conduct an analysis and make a decision on the appropriate action. One of these actions may require notifying or obtaining further advice from the Council. Some actions that may need to be taken could include to:

- follow corrective actions / preventive actions procedures under the manufacturer‘s / distributor’s quality management system,
- inform the users of the device or IVD,
- make corrections to the device or IVD,
- remove the medical device or IVD from the market.

Council has established procedures for the ongoing monitoring and vigilance for medical devices and IVDs supplied in South Africa.

These guidelines are relevant only to medical devices and IVDs. Separate guidelines apply to the reporting of adverse events and pharmacovigilance of human medicines including biological and complementary medicines.

2.2 DEFINITIONS

Recall - means the removal of specific batch/batches or lot/lots of a medical device or IVD from the market for reasons relating to deficiencies in the quality, safety or performance.

Withdrawal - means the total withdrawal of a medical device or IVD from the market

Holder of a Certificate of Registration (HCR) - means a person in whose name a registration certificate has been granted and who is responsible for all aspects of the medical device or IVD, including quality and safety and compliance with conditions of registration.

3 VIGILANCE

The purpose of medical device vigilance is to improve the health and safety of patients, users, and others by reducing the likelihood of adverse events being repeated. This can be achieved by:

- evaluating reported adverse events
- disseminating information that could be used to prevent or minimise the consequences of adverse events, where appropriate
- modifying the device or IVD
- removing the medical device or IVD from the market
- Action is undertaken by the Council and the HRC and/or manufacturer after any party becomes aware of information about a medical device or IVD supplied in South Africa, such as:

- adverse event reports
- malfunctions
- results of testing
- any other information

The HRC or manufacturer must inform the Council of all reportable adverse events, within the appropriate timeframes. They must also ensure timely and appropriate action is taken.

To improve the monitoring of the performance of devices supplied in South Africa, the Council encourages the reporting of adverse events by users of medical devices and IVDs.

3.1 VIGILANCE EXCHANGE

Through various Mutual Recognition Agreements for medical device and IVD regulation, the Council has an obligation to exchange vigilance information with other national regulatory authorities. Information will be exchanged on incidents and events where:

- corrective action, including a recall, is to be taken
- there is a serious risk to the safety of patients or other users, but where the corrective action is still being determined.

The Council will consult the HRC or manufacturer when preparing a vigilance report to be sent to other regulatory authorities. It is the responsibility of the HRC or manufacturer to ensure that the primary manufacturer is aware of the Council vigilance report, and that any comments that are made by the primary manufacturer are submitted to the Council for consideration.

Regulatory authorities generally use discretion where a manufacturer takes corrective action that is not considered to be essential to protect the safety of patients or others. Examples of this are minor improvements to current devices and updates of user information. In the case of doubt, however, a regulatory authority will generally disseminate information.

4 ADVERSE EVENTS

The Licence holder and HRC are legally responsible for the supply of the medical devices and IVDs in South Africa, including the receipt and handling of complaints and adverse events. The Licence holder and or HRC may receive event reports from users, the Council, the manufacturer or other sources, e.g., literature, consumer bodies, professional bodies. The Licence holder and HRC must forward copies of all reports to the manufacturer and copies of all reportable adverse event reports to the Council.

The manufacturer and distributor must maintain records of any complaints/incidents that occur involving a medical device or IVD that they manufacture that is supplied in South Africa. The manufacturer must inform the Authorised Representative and HRC of any reports from users or other information that indicates there is a possible problem with a device supplied in South Africa.

The Council must be notified of any incidents that occur in South Africa and that are considered adverse events (see below for an explanation of what is considered an adverse event). The Council will forward details of incident and the device in the reports from users to the Licence holder, Authorised Representative and or HRC of the device.

4.1 REPORTABLE ADVERSE EVENTS

Any event that meets three basic reporting criteria, even if it does not involve a patient or user, should be reported to the Council:

- an adverse event has occurred
- the Licence holder's and manufacturer's medical device is associated with the adverse event
- the event led to or might lead to (often referred to as a near adverse event) death or serious injury, or might lead to death or serious injury if it were to occur again.

An adverse event is an event that may lead to:

- death, or
- a serious injury or serious deterioration to a patient, user or other person, including
  - a life-threatening illness or injury
  - permanent impairment of a body function
  - permanent damage to a body structure
  - a condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

A 'near adverse event' is an event that might have led to a death or serious injury. It may be that due to the timely intervention of a healthcare practitioner a death or serious injury did not occur. For an event to be defined as a near adverse event, it is sufficient that:

- an event associated with the device happened
- if the event occurred again, it might lead to death or serious injury
- testing or examination of the device or the information supplied with the device, or scientific literature indicated some factor that could lead to a death or serious injury.

Typical adverse events are as follows:

Event or cause of an adverse event	Description
Malfunction or deterioration in the characteristics or performance of a medical device	Failure of a device to perform in accordance with its intended purpose when used in accordance with the manufacturer's instructions *Please note: intended purpose means the intended use according to the data supplied by the manufacturer on the labelling, in the Instructions for Use and/or in advertising materials*
Inadequate design or manufacture of a device	Design or manufacturing of a device is found deficient
Inaccuracy in the labelling, *Instructions for Use* and/or promotional materials	Inaccuracies include omissions and deficiencies Omissions do not include the absence of information that should generally be known by the intended users
Significant public health concern	Can include an event that is of significant and unexpected nature that becomes a potential public health hazard, for example, human immunodeficiency virus (HIV) or Creutzfeldt–Jacob Disease (CJD) The Council, Authorised Representative, or the manufacturer may identify these concerns

Event or cause of an adverse event	Description
Other information becoming available	Can include: • information from the literature or other scientific documentation • the results of testing performed by the manufacturer on its products • reports from the user prior to the device being used on the patient

4.2 REPORTING INCIDENTS WITH MEDICAL DEVICES

The reporting requirements for Authorised Representative, HRC or Manufacturers are conditions on the sale of medical devices or IVDs in South Africa. Breaching conditions may lead to suspension or cancellation of the sale of device as well as constituting an offence (Regulation 26 of the Act).

The Authorised Representative or HCR is responsible for forwarding reports of all incidents to the manufacturer or distributor for assessment under the manufacturer's and distributor's surveillance systems.

It is possible that the HCR will not have enough information to decide if the problem should be reported to the Council. The Authorised Representative and HCR should make reasonable efforts to obtain additional information to assist in making this decision. In assessing the link between the device and the event, the Authorised Representative and or HCR should take into account:

- the opinion, based on available information, from a health professional
- information concerning previous, similar events
- other information held by the Authorised Representative, or HCR, manufacturer and distributor.

In complex situations, it should be assumed that the device was associated with the event. If there is any doubt about whether a report should be submitted, the report should be submitted.

Where possible, the Authorised Representative/HCR /manufacturer/distributor should consult with the user and/or medical practitioners or other healthcare professionals involved, and do their utmost to retrieve the particular device.

Reporting of events or near events by users is voluntary. The Council promotes and encourages users to report. Device users are encouraged to report events associated with the use of a medical device to the HRC and the Council.

EXAMPLES OF REPORTABLE ADVERSE EVENTS

- The premature revision of an orthopaedic implant due to loosening or fracture
- An infusion pump stops, due to a malfunction, but fails to give an alarm. The patient receives an under-infusion of needed fluids
- During the use of an external defibrillator on a patient, the defibrillator failed to deliver the programmed level of energy due to a malfunction
- An intravenous set separates and the comatose patient's blood leaks onto the floor, resulting in significant blood loss

EXAMPLES OF REPORTABLE ADVERSE EVENTS INVOLVING PUBLIC HEALTH CONCERNS

- Fatigue testing performed on a commercialised heart valve bioprosthesis demonstrates premature failure, which would indicate that a risk to public health could occur

4.2 Reporting Incidents with Medical Devices - continued

- After delivery of an orthopaedic implant, errors were discovered in heat treatment records raising questions about the effectiveness of the implant's materials that would create a risk to public health
- A manufacturer provides insufficient details on cleaning methods for reusable surgical instruments used in brain surgery, despite the obvious risk of transmission of CJD

Only adverse events that occur in South Africa are required to be reported to the Council. Adverse events that occur overseas for devices supplied in South Africa do not need to be reported to the Council. However, records of these events should be available if requested. Also, any remedial action that arises overseas for devices supplied in South Africa should be reported.

4.3 EXEMPTIONS FROM REPORTING ADVERSE EVENTS TO THE COUNCIL

There are eight exemption rules that can apply (see table of exemption rules overleaf). However, these rules do NOT apply when:

- a device, event or issue specifically identified by the Council as an issue that requires close monitoring—applicants of devices that are affected will be notified by the Council when this occurs
- an adverse event normally subject to a reporting exemption, where a change in trend (usually an increase in frequency) or pattern is identified
- adverse events associated with user error, as the Council may use this data to identify trends with similar products that may lead to recommendations for:
  - corrective action for the device
  - revising the labelling or *Instructions for Use*
  - identifying a need for increased user education.

If a manufacturer believes an exemption rule applies to reporting an adverse event, the reasons for not reporting the event should be documented.

EXEMPTION RULES FROM REPORTING ADVERSE EVENTS TO THE COUNCIL

Rule No.	Exemption Rule	Examples of adverse events exempt from reporting
1	Deficiency of a new device found by the user prior to its use Regardless of the existence of provisions in the Instruction for Use provided by the manufacturer, deficiencies of devices that will be always detected by the user and where no serious injury has occurred, do not need to be reported. *Please note: If the device is used the exemption does not apply—the event must be reported*.	A user performs an inflation test (standard procedure) prior to inserting the balloon catheter in the patient as required in the *Instructions for Use* accompanying the device. Malfunction on inflation is identified. Another balloon is used. Patient is not injured. Sterile single-use device packaging is labelled with the caution '*do not use if package is opened or damaged'*. Open package seals are discovered prior to use, device is not used. An intravenous administration set tip protector has fallen off the set during distribution resulting in a non-sterile fluid pathway. The intravenous administration set was not used.
2	Adverse event caused solely by patient conditions When the manufacturer has information that the root cause of the adverse event is due to patient condition, the event does not need to be reported. These conditions could be pre-existing or occurring during device use. To justify not reporting, the manufacturer should have information available to conclude that the device performed as intended and did not cause or contribute to a death or serious injury. A person qualified to make a medical judgement would accept the same conclusion.	An orthopaedic surgeon implants a hip joint and warns against sports-related use. Patient chooses to go water skiing and subsequently requires premature revision. The early revision of an orthopaedic implant due to loosening caused by the patient developing osteoporosis. A patient died after dialysis treatment. The patient had end-stage-renal disease and died of renal failure.
3	Service life of the medical device The service life is defined as '*the time or usage that a device is intended to remain functional after it is manufactured, placed into use, and maintained as specified'*. The service life must be specified by the device manufacturer and included in the master record (technical file). When the only cause for the adverse event was that the device exceeded its service life and the failure mode is not unusual, the adverse event does not need to be reported. Assessment of whether an event is exempt from reporting under this rule must be based on the information in the master record, on the label or in *Instructions for Use* for the device.	Loss of sensing after a pacemaker has reached its end of life. The elective replacement indicator has shown up in due time according to the device specification. Surgical explanation of pacemaker is required. A drill bit was used beyond the end of its specified life. It fractured during invasive operation. Operation time was prolonged due to the difficulty to retrieve the broken parts.

Rule No.	Exemption Rule	Examples of adverse events exempt from reporting
4	Protection against a fault functioned correctly Adverse events that did not lead to serious injury or death, because a design feature protected against a fault becoming a hazardous situation (in accordance with relevant standards or documented design inputs) do not need to be reported.	An infusion pump stops, due to a malfunction, but gives an appropriate alarm (for example, in compliance with relevant standards) and there was no injury to the patient. Microprocessor-controlled radiant warmers malfunction and provide an audible appropriate alarm, in compliance with relevant standards and there was no injury to the patient. During radiation treatment, the automatic exposure control is engaged and the treatment stops. Although the patient receives less than an optimal dose, the patient is not exposed to excess radiation.
5	Remote likelihood of occurrence of death or serious injury Adverse events that could lead, but have not yet led, to death or serious injury, but have a remote likelihood of causing death or serious injury, and which have been established and documented as acceptable after risk assessment do not need to be reported. If an adverse event resulting in death or serious injury occurs, the adverse event is reportable and a reassessment of the risk is necessary. If reassessment determines that the risk remains remote, previous reports of near incidents of the same type do not need to be reported retrospectively. Decisions not to report subsequent failures of the same type must be documented. Please note: A change in the trend (usually an increase in frequency) of these non-serious outcomes must be reported.	The manufacturer of a pacemaker supplied to the market identified a software bug and determined that the likelihood of occurrence of a serious injury with a particular setting is remote. No patients experienced any adverse health effects. The manufacturer of blood donor sets obtains repeated complaints of minor leaks of blood from these sets. No patient injuries from blood loss or infections of staff have been reported. The chance of infection or blood loss has been re-evaluated by manufacturer and deemed remote.
6	Expected and foreseeable side effects that are documented in manufacturer's Instructions for Use or labelling Side effects that are clearly identified in the manufacturer's labelling or are clinically well known as being foreseeable and having a certain functional or numerical predictability when the device was used as intended need not be reported. Some of these events are well known in the medical, scientific, or technology fields. Others may have been clearly identified during clinical investigation and labelled by the manufacturer. Documentation, including the risk assessment, for the particular side effect	A patient receives a second-degree burn during the use of an external defibrillator in an emergency. The risk assessment documents that such a burn has been accepted in view of the potential patient benefit and a warning is provided in the *Instructions for Use*. The frequency of burns is occurring within range specified in the device master record. A patient has an undesirable tissue reaction that is previously known and documented in the device master record. A patient who has a mechanical heart valve developed endocarditis ten years after implantation and then died.

Rule No.	Exemption Rule	Examples of adverse events exempt from reporting
	should be available in the device master record prior to the occurrence of adverse events. The manufacturer cannot conclude in the face of events that they are foreseeable unless there is prior supporting information.	Placement of central line catheter results in an anxiety reaction and shortness of breath. Both reactions are known and labelled side effects.
7	Adverse events described in an advisory notice Adverse events that occur after the manufacturer has issued an advisory notice need not be reported individually if they are specified in the notice. Advisory notices include removals from the market, corrective actions, and product recalls. The manufacturer should provide a summary report, the content and frequency of which should be agreed with the Council.	A manufacturer issued an advisory notice and undertook a recall of a coronary stent that migrated due to inadequate inflation of an attached balloon mechanism. Subsequent examples of stent migration were summarised in quarterly reports required for the recall action and individual adverse events did not have to be reported.
8	Reporting exemptions granted by the Council Upon request by the applicant, common and well-documented events may be exempted by the Council from reporting or changed to periodic reporting on a case by case basis.	

4.4 TIMEFRAMES FOR SUBMITTING ADVERSE EVENTS REPORTS TO COUNCIL

With reference to Regulation 24 of the Act, the period in which a person in relation to whom a kind of medical device is included in the Register must give information to the Council is:

- if the information relates to an event or other occurrence that represents a serious threat to public health-48 hours after the person becomes aware of the event or occurrence; and
- if the information relates to an event or other occurrence that led to the death, or a serious deterioration in the state of health, of a patient, a user of the device, or another person-10 calendar days after the person becomes aware of the event or occurrence; and
- if the information relates to an event or other occurrence a recurrence of which might lead to the death, or a serious deterioration in the state of health, of a patient, a user of the device, or another person-30 days after the person becomes aware of the event or occurrence.

4.5 DETAILS TO BE INCLUDED IN AN ADVERSE EVENT REPORT

The following information to be included in the adverse event report form:

- data relating to the Authorised Representative or HRC's:
  - name
  - address
  - telephone number
  - fax number
  - Email address
- the date when the incident came to the knowledge of the:
  - manufacturer
  - distributor
  - Authorised Representative/HRC
- information about the device including the:
  - kind of medical device
  - commercial name
  - catalogue number
  - Medical Device or IVD registration number (if applicable)
  - model number
  - serial number
  - batch number
  - lot number
  - software version (if applicable)
- if implantable, date of implant and if applicable, date of explant
- any associated devices and/or accessories involved in the incident
- the known details of the event, including the date and patient or user outcome
- the current known location of the medical device involved in the event

4.5 Details to be included in an Adverse Event Report - continued

- the contact point of the user where the event occurred. The patient's full identity should not be reported. The contact point need not necessarily be a person who actually witnessed the event.
- any manufacturer, distributor and HRC comments
- the action taken or proposed action and timeframe
- a statement of whether the manufacturer, distributor and HRC are aware of the same type of events having an impact on the current report. The statement should include the:
  - names of any other regulatory authorities to which these events have been reported
  - date of the reports
  - number of similar events
  - number of devices supplied
  - rate of similar events, if available
  - any other countries in which the medical device is known to be on sale or supplied

Reports should be submitted to the Registrar of Medicines, private Bag X828, Pretoria.

The report should not be unduly delayed if the information is incomplete. It is important to get this process underway as additional information can be provided later.

4.6 ACCESS TO MEDICAL DEVICES INVOLVED IN ADVERSE EVENTS

Where possible, a manufacturer and distributor, Authorised Representative and HRC, should consult with the medical device user about the event before a report is submitted to the Council. The manufacturer may also wish to have access to the medical device involved in the event to help decide whether the event should be reported to the Council. Such access would be at the discretion of the user or healthcare facility concerned, but they are encouraged to assist the manufacturer to determine the root cause of the incident.

If the manufacturer has access to the medical device, and the initial assessment or cleaning or decontamination process will involve altering the device in a way that may affect subsequent analysis, the manufacturer should, through the Authorised Representative or HRC, inform the Council before proceeding.

The Council encourages release of the medical device to the manufacturer so that they can complete their analysis.

The outcome of any investigation may include one or more:

- referral to other areas of Council for regulatory actions, such as auditing of the manufacturer
- recall of the devices to:
  - remove the devices from supply in South Africa
  - allow correction at the user's site
- the issue of a Safety Alert where there is a need to reinforce the manufacturer's *Instructions for Use* to those responsible for the use of the device or those affected by the problem
- product improvement for problems that are not safety-related - carried out by the manufacturer
- report on the Council website and/or appropriate communication

5 QUALITY DEFECTS OF MEDICAL DEVICES AND IVDS

If the applicant or manufacturer is contemplating any of the following:

- correcting product on the market
- removing product from the market, or
- advising users of an issue with a medical device

contact the Vigilance Unit at the office of the Registrar for advice.

When the need for a recall of a medical device supplied in or exported from South Africa has been established, the applicant of the affected device is responsible for the recovery of the devices.

Please refer to the MCC Guideline addressing Recalls to guide on the process and requirements to conduct a recall i.e. the current version of Guideline ***5.07 Recalls***

6 NON-RECALL ACTIONS FOR MEDICAL DEVICES & IVDS

Where the HRC is unsure of the appropriate action to be taken, and particularly in cases where patient safety may be a consideration, the issues involved should be discussed with the office of the Registrar of Medicines: Recall officer.

Other action may be taken by the HRC voluntarily that is not considered to be a recall:

Action	Description
Safety Alert	Intended to provide information on safe use of devices, as distinct from recall action, which addresses product deficiencies Issued to provide additional advice to health professionals in situations where the device, although meeting all specifications and therapeutic indications, its use could present an unreasonable risk of substantial harm if certain specified precautions or advice are not observed. For example, specific precautions about the longevity of an implanted medical device
Product Notification	Issue of precautionary information about a device in a situation that is unlikely to involve significant adverse health consequences
Product Withdrawal	HRC's removal from supply or use of devices for reasons not related to their quality, safety or performance
Product Recovery	The HRC recovers devices that have been manufactured or imported but not yet supplied to the market. For example, recovery of devices in a warehouse
User information	Generally conducted by the HRC in response to issues with the use of a medical device Includes in-house sessions, seminars and improved educational materials such as posters

7 UPDATE HISTORY

Date	Reason for update	Version & publication
Aug 2015	First publication for comment	v 1, Sept 2015
30 November 2015	Due date for comment	