Cancer Association of South Africa (CANSA)

Fact Sheet
and Position Statement on
Non-Invasive Medical Devices

Introduction

According to the World Health Organization (WHO) a 'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for *in vitro* use, 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 medical purpose(s) of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- 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 by means of *in vitro* examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means. (World Health Organization).

[Picture Credit: Medical Devices]

Medical Devices in the United States

The United States Food and Drug Administration (FDA) defines a 'Medical Device' as an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including a component part, or accessory which is: recognised in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and

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which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolised for the achievement of any of its primary intended purposes.

Medical Devices in the United Kingdom

The Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom has issued updated guidance to help identify the health apps which are medical devices and make sure they comply with regulations and are acceptably safe.

Many apps and pieces of stand-alone software currently on the market are classified as medical devices. These are apps which gather data from the person or a diagnostic device, such as diet, heartbeat, or blood glucose levels and then analyse and interpret the data to make a diagnosis, prescribe a medicine, or recommend treatment.

It is important that apps which are medical devices comply with medical device regulation and work as expected. Apps that give incorrect diagnoses or prescribe inappropriate treatments may have severe, potentially life-threatening consequences.

We live in an increasingly digital world, both healthcare professionals, patients and the public are using software and stand-alone apps to aid diagnosis and monitor health.

Where apps or stand-alone software make a diagnosis, monitor, or recommend a treatment, people in the European Union should check for CE-marking before using their apps and developers should make sure they are complying with the appropriate medical device regulations.
(Gov.UK).

Medical Devices in South Africa

The registration of Medical Devices and *In Vitro* Diagnostic Devices (IVDs) in South Africa is governed by the provisions and requirements of the Medicines and Related Substances Control Act, 1965 (Act No. 101 of 1965), (hereinafter referred to as 'the Act'), the Regulations (hereinafter referred to as 'the Regulations), and the Guidelines (hereinafter referred to as 'the Guidelines), published in terms of the Act.

The aim of the Guidelines issued by the South African Health Products Regulatory Authority [SAHPRA] (previously Medicines Control Council (MCC)) is to assist manufacturers, importers, wholesalers, and distributors of Medical Devices, IVDs and Software regarding:

- Classification of Medical Devices and IVDs
- Manufacturing of Medical Devices and IVDs
- Distribution and sales of Medical Devices and IVDs
- Licensing of manufacturers, distributors, and wholesales of Medical Devices and IVDs
- Licensing of Medical Devices, IVDs and certain Software related to Medical Devices

- Registration of the different Classes of Medical Devices, IVDs, and Software is based on risk assessment and intended use.

Classes of Medical Devices:
The classes of Medical Devices are as follows, where risk relates to the health of the patient, the user or public health:

Class A - Low risk
Class B - Low to moderate risk
Class C - Moderate to high risk
Class D- High risk

Advertising of Medical Devices
The following requirements apply to an advertisement of a medical device or IVD:

- Only Class A and Class B medical devices and IVDs may be advertised to the South African public or lay persons

Licensing of Manufacturers, Wholesalers, or Distributors:
A manufacturer, wholesaler or distributor referred to in section 22C(1)(b) of the Act must, prior to commencing business, apply to the Medicines Control Council for:

- a manufacturer licence to manufacture, import or export medical devices or IVDs; or
- a distributor licence to import, export and distribute medical devices or IVDs; or
- a wholesale licence to act as wholesaler of medical devices or IVDs

Validity of Licences:
A licence (as mentioned above) issued in terms of the Regulations is valid for a period of five (5) years from the date of issue.
(Medicines Control Council; General Information on Medical Devices and IVDs).

Medical Apps to Diagnose Melanoma and non-Melanoma Skin Lesions
A variety of apps have become available to diagnose various health problems. It would appear, though that there is very little national and international oversight of such apps.

Chao, E., Mennan, C.K. & Ferris, L.K. 2017.
"With the advancement of mobile technologies, smartphone applications (apps) have become widely available and gained increasing attention as a novel tool to deliver dermatologic care. This article presents a review of various apps for skinmonitoring and melanoma detection and a discussion of current limitations in the field of dermatology. Concerns regarding quality, transparency, and reliability have emerged because there are currently no established quality standards or regulatory oversight of mobile medical apps. Only a few apps have been evaluated clinically. Further research is needed to evaluate the utility and efficacy of smartphone apps in skin cancer screening and early melanoma detection."

Singh, N. & Gupta, S.K. 2019..
BACKGROUND: The paper reviews the advancement of tools and current technologies for the detection of melanoma. We discussed several computational strategies from pre- to postprocessing image operations, descriptors, and popular classifiers to diagnose a suspected skin lesion based on its virtual similarity to the malignant lesion with known histopathology. We reviewed the current state of smart phone-based apps as diagnostic tools for screening.
METHODS: A literature survey was conducted using a combination of keywords in the bibliographic databases: PubMed, AJCC, PH2, EDRA, and ISIC melanoma project. A number of melanoma detection apps were downloaded for two major mobile operating systems, iOS and Android; their important uses, key challenges, and various expert opinions were evaluated and also discussed.
RESULTS: We have provided an overview of research on the computer-aided diagnosis methods to estimate melanoma risk and early screening. Dermoscopic images are the most viable option for the advent of new image processing technologies based on which many of the skin cancer detection apps are being developed recently. We have categorized and explored their potential uses, evaluation criteria, limitations, and other details.
CONCLUSION: Such advancements are helpful in the sense they are raising awareness. Diagnostic accuracy is the major issue of smart phone-based apps and it cannot replace an adequate clinical experience and biopsy procedures.

Ngoo, A., Finnane, A., McMeniman, E., Tan,J.M., Janda, M. & Soyer, H.P. 2018.
BACKGROUND/OBJECTIVES: Melanoma apps are smartphone applications that assess risk of pigmented lesions using a smartphone camera and underlying algorithm. We aimed to assess the capability of melanoma smartphone applications (apps) in making clinical decisions about risk, compared with lesion assessment by specialist trained dermatologists.
METHODS: A prospective study of 3 melanoma apps was conducted between 2015 and 2016, recruiting 30 patients with 57 pigmented lesions. Risk categories assigned by the apps were compared with the clinical decisions of two consultant dermatologists classifying lesions as 'suspicious' or 'benign'.
RESULTS: Of the 42 lesions deemed clinically suspicious to a dermatologist, from 9 to 26 were classified as suspicious by the apps; of the 15 clinically benign lesions 3 to 15 were correctly classified as benign by the apps. The apps' sensitivity and specificity ranged from 21 to 72% and 27 to 100.0%, respectively, when compared with the specialists' decisions. Two apps were unable to analyse 14 and 18% of lesions submitted, respectively. Interrater agreement between dermatologists and apps was poor (κ = -0.01 SE = 0.16; P = 0.97) to slight (κ = 0.16 SE = 0.09; P = 0.12).
CONCLUSIONS: None of the melanoma apps tested had high enough agreement with the dermatologist's clinical opinion to be considered to provide additional benefit to patients in assessing their skin for high-risk pigmented lesions. The low sensitivity in detecting lesions that are suspicious to a trained specialist may mean false reassurance is being given to patients. Development of highly sensitive and specific melanoma apps remains a work in progress.

Guidelines Regarding Medical Devices Issued by the South African Health Products Regulatory Authority [SAHPRA] (previously the Medicines Control Council)
If a device makes use of software to perform its purpose, the device is then classified as a medical device.

- Software that fits the definition of a medical device is also an active medical device since it relies on an energy source for its operation

- Software that is intended to make a device operate, control a device, or influence the functions of a device generally falls in the same classification as the device
- An active medical device for diagnosis is a device that is intended by the manufacturer to be used on a human being, either alone or in combination with another device, to supply information for the purpose of detecting, diagnosing, monitoring or treating physiological conditions, states of health, illness or congenital deformities

Provision of Information Regarding a Medical Device

Users of medical devices must be provided with information about the medical device. It should be noted that for many devices there may be more than one user, depending on circumstances. For example, when used in the hospital setting a urinary catheter is used by a healthcare professional in the course of treating the patient, but when used at home for self-catheterisation the user may be the patient or the patient's carer.

In accordance with Regulation 23 and Regulation 24 and Regulation 25 as applicable, of the Medicines and Related Substances Act, 1965 (Act 101 of 1965), all Medical Devices and IVDs must label a medical Device or IVD and must include an *Instructions for Use (IFU)* in the packaging. Applicants are requested to follow the format stipulated in the Regulations issued under the Act.

Instructions for Use should be typed in double-spaced text and should be in at least the English language.

The printing quality of the *Instructions for Use* insert should be clear to enable duplication, for inclusion into various documents, during the evaluation and registration process. The spelling and grammar in the *Instructions for Use* text should be checked thoroughly before submission of the application.

In the case of a Medical Device or IVD that requires assessment by the Council prior to being listed in the Medical Device or IVD Register, Council may request references for each statement on the *Instructions for Use (IFU)* insert. In such case the reference(s) for each statement should be included in a broad margin on the right hand side of each page of the IFU for this purpose. The exact page/s should be stated. No references should, however, be included in the finalised printed *Instructions for Use*.

Advertising

The Medicines and Related substances Act, 1965 (Act 101 of 1965) defines an advertisement as ***'advertisement'****, in relation to any medicine or Scheduled substance or medical device, and means any written, pictorial, visual or other descriptive matter or verbal statement or reference:*

(a) appearing in any newspaper, magazine, pamphlet or other publication; or
(b) distributed to members of the public; or
(c) brought to the notice of members of the public in any manner whatsoever,

which is intended to promote the sale of that medicine or Scheduled substance; and 'advertise' has a corresponding meaning".

Advertisement, therefore, includes any information including:

- product labels
- pamphlets
- instructions for Use
- promotional samples
- promotional seminars, demonstrations and displays
- advertorials
- advertisements for health services or treatments that identify a medical device

All advertising of medical devices and IVDs must comply with requirements of Regulation 22 of the General Regulations applicable to Medical Devices.

Software

Software operates as a controlling agent for an electronic device, e.g. a microcontroller or computer. Software is regulated in different ways depending on the manufacturer's intended purpose for the software and how it is supplied:

Type of Software:	How it is Used:	Some Examples:
Software that is part of a device and is supplied with a medical device	Part of the device	Pacemaker firmware Embedded patient monitor software
Software or an accessory to the device that is a device in its own right if it is supplied separately from the related device	A separate medical device	Image-processing software for use with an X-ray machine Pacemaker programmer and controller for use on a personal computer or laptop
Software that is used as a diagnostic or therapeutic tool	A Separate medical device	Oncology image-processing tool Radiation planning/treatment software
Upgrades to software supplied separately	A separate medical device	I[grade to image-processing software to add artificial colouring of images Upgrade to ultrasound equipment to allow 4-dimensional images
Corrections to software errors that have been supplied with a device Please note: must be a replacement part with no additional functionality	Not a medical device	Bug fix to stop infusion pump indicating incorrect drug administration values Stability fix to image processing tool to reduce incidence of crashing or freezing
Software that is used in combination with other equipment for handling general patient-related information	Not a medical device	Patient record management system (admission dates, case notes, contact details) Conversion, compression, and encryption functionality/tool Clinical Information System (CIS) without diagnostic or therapeutic functionality

The regulatory requirements apply to all forms of medical device software including software that is embedded (for example, firmware in hardware) such as:

- field-programmable gate arrays (FPGAs)

- electronic programmable read only memory (EPROM)
- flash memory
- static or dynamic random access memory (RAM)

Software often forms an integral part of an electronic device, for example, in a pacemaker or patient monitor. In these cases, the software is a part of the device and is not considered to be a separate or distinct device.

Software that fits the definition of a medical device in its own right requires separate entry on the South African Medical Device Register, which means that the prospective holder of the registration certificate must lodge an application with the Council to include the device in the Medical Device Register.
Some devices have more than one type of software residing within them. For example, an infusion pump monitor system may have software:

- to control the infusion parameters—Class C
- for the logging of patient data—Class A

If the device is supplied as a complete unit, the classification of the complete device is the highest classification—Class C. If the software is supplied separately, the individual classification of each device applies.

The international standard *IEC 62304 Medical device software—Software life cycle processes* addresses requirements that are specific to software, while the *IEC 62366 Medical devices—Application of usability engineering to medical devices* standard addresses usability engineering requirements to all devices, including those that are wholly or partially software-based. The Council considers these standards as representing the state-of-the-art for medical device software.

The labelling requirements apply to medical device software, regardless of whether it is downloaded from the Internet, installed from a CD, or pre-installed on a device.

Manufacturers need to ensure that the product information, such as the graphical user interface, screenshots, CD labels, and product demos meet the requirements of Essential Principle 13.

Cancellation of a Medical Device
The Council may cancel and remove a Medical Device from the SA Medical Device Register and IVD Register
(Medicines Control Council, General Information on Medical Devices and IVDs).

Requirements for Mole Mapping
Sophisticated digital mole mapping programmes should include the following:

- Risk evaluation i.e. age, medical and family history, skin typing, sun exposure
- Patient education regarding sun protection, moles and melanoma
- Skin examination by a health professional (usually a doctor or specially trained nurse)

- High quality digital images (photographs taken with a digital camera)
    - Standardised poses of the whole body, with lesions of concern carefully localised (this can require very accurate positioning and sophisticated computer programming if there are several similar moles in close proximity)
    - Close-up macro images of the lesions of concern
    - Dermoscopic images of lesions of concern
- Evaluation of the images by an expert in skin cancer, usually a dermatologist
- A report to the patient and/or referring health practitioner including suspected diagnoses and recommendations for treatment of lesions of concern
- Follow-up mole mapping in 3 to 6 months for lesions of concern that do not reach the threshold for excision
- Follow-up mole mapping of all imaged lesions at intervals of 1 to 2 years or as recommended by a doctor
- A secure database and transfer system to store the images and reports for future reference and comparison

Apps to Monitor (Diagnose) Mole Changes

From the above information contained in 'General Information on Medical Devices and IVDs', it is clear that apps downloaded onto another device, e.g. a mobile phone, is classified as a Medical Device by the Medicines Control Council, because its intended use is to monitor or diagnose (oncology image-processing) mole changes.

Registration of Medical Devices Based on Risk

Registration of the different Classes of Medical Devices, IVDs, and Software is based on risk assessment. Risk refers to:

- Possible incorrect interpretation of mole changes by a lay person.
- Possible delay in seeking medical advice because of non-recognition of changes within a mole by a lay person.
- Possible misinterpretation of information supplied to a lay person by the distributor.
- Possible severe, potentially life-threatening consequences that may result because of any of the aforementioned.

The **ABCDE** acronym applies when monitoring moles. The different letters of the acronym represents:

A - Asymmetry (one half of the mole doesn't match the other)
B - Border irregularity
C - Colour that is not uniform
D - Diameter greater than 6 mm — (about the size of a pencil eraser)
E - Evolving size, shape or colour.
(American Academy of Dermatology Inc; Skin Cancer Foundation; Melanoma Research Foundation).

The following are some examples of possible causes of misinterpretation/non-recognition of changes within a mole (by a lay person) when mole mapping is done with a device not specifically designed for the purpose:

- Possible different lighting sources or illuminance (measure of how much the incident **light** illuminates the surface) when consecutive images of moles are recorded that may result in non-recognition of colour changes and/or colour uniformity of a mole. Professional dermascopes have their own built-in light source, thereby ensuring the same lighting and illuminance during consecutive photographs of moles.

[Picture Credit: Dermascope]

- Possible errors in recognising the correct diameter, or change in diameter, of a mole because consecutive mole images may have been photographed at different distances from the mole. Professional dermascopes have a special built-in attach-ment that ensures photographs are always taken at the same distance from the lens.

The professional dermascope on the top right corner shows the built-in light source to ensure the same illuminance throughout all photographs of moles as well as the built-in facility that ensures that all photographs of moles are taken at the same distance from the lens.

Registration of Medical Devices on Intended Use

Registration of the different Classes of Medical Devices, IVDs, and Software is based on intended use. Intended use refers to:

- The purpose of the manufacturer of the app is to monitor and diagnose mole changes (oncology image-processing) – this being its intended use – makes it a Medical Device that must be approved and registered with the South African Health Products Regulatory Authority (SAHPRA).

Position of the Cancer Association of South Africa Regarding Medical Devices and Applications

The Position of the Cancer Association of South Africa (CANSA):

- CANSA recognise and accept the availability of applications that can be used to assist in identifying possible questionable skin lesions inclusive of Melanoma and non-Melanoma lesions.

- CANSA will only support the use of any application(s) which assists in identifying any possible questionable skin lesion(s) with an acceptable warning and disclaimer which forms part of the application's package to warn that possible false-positive and/or false-negative results may

be made following the use of such application and that CANSA advises a clinical skin examination once a year in the event of a negative result.

- In the event of a positive result, immediate follow-up should include a clinical skin examination by a medical practitioner and/or dermatologist.

- CANSA further strongly advises that individuals should request a clinical skin examination (as part of their annual medical check-up) at least once a year.

- CANSA fully subscribes to, and supports, the Regulations Relating to Medical Devices and *In Vitro* Diagnostic Devices (IVDs), Regulation No 1515 of 09 December 2016, as published in *Government Gazette* No 40480.

- CANSA may recognise, endorse, approve, or enter into a cause-related marketing agreement with an individual/organisation/business relating to a Medical Device approved by, and registered with, the Medicines Control Council.

- Notwithstanding the aforesaid, CANSA is not obliged to recognise, endorse, approve, or enter into a cause-related marketing agreement relating to any Medical Device merely based on the fact that it is approved by, and registered with, the Medicines Control Council.

- CANSA will, however, not entertain requests for recognition, endorsement, approval, cause-related marketing agreement or any other request pertaining to Medical Devices unless such Medical Device is approved by, and registered with the Medicines Control Council.

Medical Disclaimer

This Fact Sheet and Position Statement is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet and Position Statement. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet and Position Statement.

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