

ASEAN AGREEMENT ON MEDICAL DEVICE DIRECTIVE

The Governments of Brunei Darussalam, the Kingdom of Cambodia, the Republic of Indonesia, the Lao People's Democratic Republic, Malaysia, the Republic of the Union of Myanmar, the Republic of the Philippines, the Republic of Singapore, the Kingdom of Thailand and the Socialist Republic of Viet Nam, Member States of the Association of Southeast Asian Nations (hereinafter collectively referred to as “Member States” or singularly as “Member State”),

MINDFUL that in the year 1992, the ASEAN Heads of Government declared that an ASEAN Free Trade Area (AFTA) shall be established in the region and that in 1995, they agreed to accelerate its implementation to the year 2003;

NOTING the Agreement on the Common Effective Preferential Tariff (CEPT) Scheme for the AFTA signed on 28 January 1992 and its amending Protocols of 1995 and 2003, which provide for cooperation to supplement and complement the liberalisation of trade including, among others, the harmonisation of standards, reciprocal recognition of test reports and certification of products;

MINDFUL that the Declaration of ASEAN Concord II (Bali Concord II) adopted by the ASEAN Heads of Government during the 9th ASEAN Summit in Bali, Indonesia on 7 October 2003, commits ASEAN to deepen and broaden its internal economic integration and linkages, with the participation of the private sector, so as to realise an ASEAN Economic Community;

MINDFUL that the establishment of the ASEAN Economic Community has been accelerated from 2020 to 2015 which will create ASEAN as a single market and production base;

REITERATING their commitments to the Agreement on Technical Barriers to Trade of the World Trade Organisation, which encourages Contracting Parties to enter into negotiations for the

conclusion of agreements for the mutual recognition of results of each other's conformity assessment and mandates, among other matters, the elimination of unnecessary obstacles to trade including those relating to technical regulations;

RECALLING the ASEAN Framework Agreement for the Integration of Priority Sectors and the ASEAN Sectoral Integration Protocol for Healthcare signed on 29 November 2004 in Vientiane, Lao PDR; and

HAVING regard to the principles of harmonisation of medical device regulations, the harmonised common technical documents and the progress made in its implementation

HAVE AGREED as follows:

ARTICLE 1
GENERAL PROVISIONS

1. Member States shall undertake all necessary measures to ensure that only medical devices which conform to the provisions of this ASEAN Agreement on Medical Device Directive (hereinafter referred to as "Medical Device Directive") and its Annexes may be placed in the markets of Member States.

2. The natural or legal person or authorised representative responsible for placing the medical devices in any Member State shall register with the regulatory authority of each Member State.

3. The natural or legal person or authorised representative responsible for placing the medical device in one or more Member State shall apply for pre-market approval of the product to the regulatory authority of each Member State.

ARTICLE 2

DEFINITION AND SCOPE OF MEDICAL DEVICE

For the purpose of this Medical Device Directive, the terms:

1. “medical device” shall mean any instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent and calibrator, software, material or other similar or related article:
 - (a) intended by the product owner to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:-
 - (i) diagnosis, prevention, monitoring, treatment or alleviation of disease,
 - (ii) diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
 - (iii) investigation, replacement, modification, or support of the anatomy or of a physiological process,
 - (iv) supporting or sustaining life,
 - (v) control of conception,
 - (vi) disinfection of medical devices,

- (vii) providing information for medical or diagnostic purposes by means of *in vitro* examination of specimens derived from the human body; and
- (b) 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.
2. “Accessory” means an article intended specifically by its product owner to be used together with a particular medical device to enable or assist that device to be used in accordance with its intended purpose.
3. “Adverse event” means either a malfunction or a deterioration in the characteristics or performance of a supplied medical device or use error, which either has caused or could have caused or contributed to death, or injury to health of patients or other persons.
4. “Authorised representative” means any natural or legal person¹ established in a Member State who, explicitly designated by the product owner, acts and may be addressed by authorities and bodies in a Member State instead of the product owner with regard to the latter’s obligations under this

¹ The term “legal person” that appears here and in the other definitions of this document, includes legal entities such as a corporation, a partnership or association.

Medical Device Directive , and relevant laws and regulations of the Member State.

5. “Authorised distributor”, in relation to the placing on the market of a medical device, means any natural or legal person who has been authorised by the product owner or authorised representative to distribute the medical device in that Member State.

6. “Custom-made medical device” means any device specifically made in accordance with a duly qualified medical practitioner's written prescription which gives, under his responsibility, specific design characteristics and is intended for the sole use of a particular patient. For the purposes of this definition, a duly qualified medical practitioner is defined as a person who is duly qualified by the relevant laws and regulations of the member state where the custom-made medical device is fabricated, and by virtue of his professional qualifications, is authorised to carry out such investigation.

For purposes of clarity, , mass produced devices which need to be adapted to meet the specific requirements of the medical practitioner or any other professional user shall not be considered to be custom-made medical devices.

7. “Device intended for clinical investigation” means any device intended for use by a duly qualified medical practitioner when

conducting investigations as referred to in Annex 10, in an adequate human clinical environment. For the purposes of conducting of clinical investigation, a duly qualified medical practitioner is defined as a person who is duly qualified by the relevant laws and regulations of the member state where the clinical investigation is carried out, and by virtue of his professional qualifications, is authorised to carry out such investigation.

8. “Field Safety Corrective Action” means any action taken by a product owner to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device. This may include:
- (a) the return of a medical device to the product owner or its representative;
 - (b) device modification;
 - (c) device exchange;
 - (d) device destruction;
 - (e) advice given by product owner regarding the use of the device.

Such device modifications may include:

- (a) retrofit in accordance with the product owner's modification or design change;

- (b) permanent or temporary changes to the labelling or instructions for use;
 - (c) software upgrades including those carried out by remote access;
 - (d) modification to the clinical management of patients to address a risk of serious injury or death related specifically to the characteristics of the device.
9. “Intended purpose” means the use for which the medical device is intended according to the specifications of its product owner as stated on any or all of the followings:
- (a) the label of the medical device;
 - (b) the instructions for use of the medical device;
 - (c) the promotional materials in relation to the medical device
- (10) “*in vitro* diagnostic (IVD) product” means any reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination with any other reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, that is intended by its product owner to be used *in vitro* for the examination of any *specimen*, including any blood or tissue

donation, derived from the human body, solely or principally for the purpose of providing information:

- (a) concerning a physiological or pathological state or a congenital abnormality;
 - (b) to determine the safety and compatibility of any blood or tissue donation with a potential recipient thereof; or
 - (c) to monitor therapeutic measures; and
- includes a specimen receptacle.

(11) “manufacture”, in relation to a medical device, means to make, fabricate, produce or process the medical device and includes

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- (a) any process carried out in the course of so making, fabricating, producing or processing the medical device; and/or
 - (b) the packaging and labelling of the medical device before it is supplied.

(12) “Physical manufacturer”, in relation to a medical device, means any natural or legal person who performs the activity of manufacture.

(13) “Placing on the market” means the first making available in return for payment or free of charge of a device other than a device intended for clinical investigation, with a view to

distribution and/or use on the market of a Member State, regardless of whether it is new or fully refurbished.

- (14) “Product owner”, in relation to a medical *device*, means any natural or legal person who —
- (a) supplies the medical device under his own name, or under any trade mark, design, trade name or other name or mark owned or controlled by him; and
 - (b) is responsible for designing, manufacturing, assembling, processing, labelling, packaging, refurbishing or modifying the medical device, or for assigning to it a purpose, whether those tasks are performed by him or on his behalf.
- (15) “Putting into service” means the stage at which a device has been made available to the final user as being ready for use on the market of a Member State for the first time for its intended purpose.
- (16) “Regulatory authority” means the regulatory authority or entity of that Member State which exercises a legal right to control the import, manufacture, export, distribution, transfer, use and the sale of medical devices within that Member State’s jurisdiction and which may take regulatory action to ensure that the products marketed within its jurisdiction comply with regulatory requirements.”

- (17) Sponsor means an individual, corporate body, institution or organization that conducts a clinical investigation.

This Medical Device Directive shall not apply to the following:-

- (a) human blood, plasma or blood cells of human origin or to devices which incorporate at the time of placing on the markets of Member States such human blood, plasma or blood cells of human origin, except if it is incorporated in an in-vitro diagnostic product;
- (b) transplants or tissues or cells of human origin nor to products incorporating or derived from tissues or cells of human origin, except if it is incorporated in an in-vitro diagnostic product;
and
- (c) transplants or tissues or cells of animal origin, unless
- (i) it is incorporated in an in-vitro diagnostic product, or
 - (ii) it is a device manufactured utilizing animal tissue which is rendered non-viable or non-viable products derived from animal tissues or cells. “Non-viable” means in relation to a biological entity, an entity that is incapable of growth, development and reproduction.

ARTICLE 3
ESSENTIAL PRINCIPLES OF SAFETY AND
PERFORMANCE OF MEDICAL DEVICE

Medical devices shall meet the essential principles set out in Annex 1, which apply to them, taking account of the intended purpose of the device concerned.

ARTICLE 4
CLASSIFICATION OF MEDICAL DEVICES

(1) Medical devices shall be classified into the following four classes, in accordance with risk classification rules set out in Annex 2 and Annex 3:

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

(2) The classification rules are based on the vulnerability of the human body taking into account of the potential risks associated with the technical design and manufacture of the devices.

(3) In the event medical device may be assigned into 2 or more classes of medical devices, the Regulatory Authority of the

Member State shall assign the medical device into such of those classes as represents the highest health risk posed to an end-user of the medical device.

(4) In the event the medical device is designed to be used in combination with another medical device, each of the medical devices shall be classified separately.

(5) In the event the medical device has 2 or more intended purposes, the medical device shall, subject to Article 4(3), be assigned into a class of medical devices having regard to the most critical intended purpose of the medical device.

(6) In the event of a dispute in classifying a medical device resulting from the application of the classification rules, the regulatory authority of Member States shall decide on the proper classification or reclassification of the device concerned, where appropriate.

(7) Member state who reclassifies or differs in its application of the classification rules set out in Annex 2 and Annex 3 shall notify, with the reasons thereof, to the ASEAN Medical Device Committee (AMDC) of such measures taken.

ARTICLE 5

CONFORMITY ASSESSMENT OF MEDICAL DEVICES

- (1) A medical device shall be assessed by the regulatory authority of a Member State, or any appointed bodies recognized by a Member State, as the case may be, and should be in conformity and in compliance with the requirements laid down in this Medical Device Directive and other relevant laws and regulations of a Member State.
- (2) Member States shall put in place an appropriate system for assessment of medical devices.

ARTICLE 6

REGISTRATION AND PLACEMENT ON THE MARKET

- (1) A medical device which has been assessed by the regulatory authority of a particular Member State, and deemed to be in conformity and in compliance with the requirements laid down in this Medical Device Directive, and relevant laws and regulations of that Member State, may be placed on the market of that particular Member State.
- (2) A medical device to be placed on the market of a Member State shall be registered with or notified to, as the case may be, with the regulatory authority of that Member State. The regulatory authority of the Member State may exempt certain

Class A medical devices from the requirement for registration or notification.

- (3) Member States shall put in place an appropriate system for the registration or notification of medical devices, as the case may be, with the regulatory authority of that Member State.
- (4) Custom-made medical devices shall not be subjected to product registration requirements.
- (5) The regulatory authorities may authorize, on duly justified request or by their own, the use within the territory of the Member State concerned, of medical devices which have not undergone registration with the regulatory authority and the use of which is in the interest of protection of public health.

ARTICLE 7

REGISTRATION OF PERSONS RESPONSIBLE FOR PLACING MEDICAL DEVICES ON THE MARKETS OF MEMBER STATES

- (1) A product owner, under his own name, or his authorised representative or physical manufacturer, who is responsible for placing devices on the market and any other natural or legal person engaged in the activities referred to in Article 6, on the market of a Member State, shall register or notify, as the case may be, with the regulatory authority of that Member

State. The information shall include his registered place of business in that Member State and the description of the devices concerned.

- (2) Where a product owner who places devices referred to in paragraph 1 of this Article on the market of a Member State under his own name does not have a registered place of business in that Member State, he shall designate authorised representative(s) who is (are) established in that Member State. That person shall register or notify, as the case may be, with the regulatory authority of that Member State his registered place of business in that Member State and the devices concerned.
- (3) Member States shall put in place an appropriate system for registration or notification of persons responsible for placing medical devices on their markets.

ARTICLE 8

TECHNICAL DOCUMENTS FOR MEDICAL DEVICES

Member States shall undertake appropriate measures to adopt and implement the following common technical documents which is annexed to this Medical Device Directive: :-

- (a) ASEAN Common Submission Dossier Template (CSDT) (Annex 4);

- (b) Post Marketing Alerts System (PMAS) Requirements (Annex 5);
- (c) Harmonized set of elements for a Product Owner's or Physical Manufacturer's Declaration of Conformity (DoC) (Annex 6);
- (d) Component Elements of a "Dear Healthcare Professional" Letter (Annex 7);
- (e) Sample Template of Letter of Authorisation (Annex 8)

ARTICLE 9

REFERENCE TO STANDARDS AND RELEVANT DOCUMENTS

- (1) Member States shall presume compliance with the essential principles referred to in Article 3 in respect of devices which are in conformity with the relevant standards recognised by the AMDC or other standards accepted by the Regulatory Authority of that Member State for the medical device to be placed in the market of that Member State.
- (2) Member states may revise by consensus the standards and relevant documents, which form an integral part of this Medical Device Directive,. It is acknowledged that these revised documents are subject to periodical review, and shall become effective upon acceptance by all Member States.

ARTICLE 10

LABELLING

- (1) A medical device shall be labelled in accordance with the requirements of the Member State prior to placing on the market in that Member State.
- (2) Member States may set the labelling requirements for a medical device in accordance with Annex 9.
- (3) Member States may set the requirement for having the label of a medical device in their national languages.

ARTICLE 11

PRODUCT CLAIMS

- (1) Member States shall take all necessary measures to ensure that product claims of medical devices comply with the approved labelling, as approved by the regulatory authority. In general, product claims shall be subjected to regulatory control of Member States.
- (2) As a general rule, claimed benefits of a medical device shall be justified by substantial evidence and/or by the medical device composition/formulation or preparation itself. Claimed benefits of a medical device shall be justified by substantial evidence in accordance with the requirements as set out in Annex 1.

ARTICLE 12

POST-MARKETING ALERT SYSTEM

- (1) Member States shall take the necessary steps to ensure that any information brought to their knowledge, in accordance with the provisions of this Medical Device Directive , regarding the incidents involving a medical device as mentioned below is recorded and evaluated:-
- (a) any malfunction or deterioration in the characteristics or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;
 - (b) any technical or medical reason in relation to the characteristics or performance of a device for the reasons referred to in subparagraph (a), leading to product recall of devices of the same type by the product owner, authorised representative, authorised distributor or person responsible for placing medical device into the market.
- (2) After carrying out an assessment, if possible together with the product owner, a Member State may, without prejudice to Article 16, inform the other Member States of the incidents referred to in paragraph 1 for which relevant measures have been taken or are contemplated.

- (3) The physical manufacturer, authorised representative and authorised distributor of a medical device in a Member State:-
- (a) shall keep all relevant records pertaining to the traceability of the medical device, for such period and format as the regulatory authority in the Member State may stipulate;
 - (b) produce such records for inspection when required by the regulatory authority in the Member State;
 - (c) shall be bound to inform the Regulatory Authority, within the stated prescribed time and format of the Regulatory Authority in the Member State, where he becomes aware of any adverse event that has arisen or can arise from the use of the medical device placed on the market in the Member State; and
 - (d) shall be bound to inform the Regulatory Authority, within the stated prescribed time and format of the Regulatory Authority in the Member State, when he performs or intends to perform a field safety corrective action (FSCA) on a medical device placed on the market in the Member State.

ARTICLE 13

CLINICAL INVESTIGATION

Member States shall put in place an appropriate system for the conduct of clinical investigation of medical devices, taking into

account the Helsinki Declaration adopted by the 18th World Medical Assembly in Helsinki, Finland, in 1964, and any subsequent amendments or revisions to this Declaration by the World Medical Association. It is acknowledged that all measures relating to the protection of human subjects are required to carry out in accordance with the spirit of the Helsinki Declaration. This includes every step in the clinical investigation from first consideration of the need and justification of the study to publication of the results, which may include the following requirements:

- (a) In the case of medical devices intended for clinical investigation, the regulatory authority of the Member State may require the product owner, or his authorised representative, or the sponsor of the clinical investigation in a Member State, as the case may be, to follow the procedure referred to in Annex 10 and register or notify, as the case may be, with the regulatory authority of that Member State in which the investigations are to be conducted.
- (b) The regulatory authority of the Member State may require that the clinical investigations be conducted in accordance with the provisions of Annex 10.
- (c) The regulatory authority of that Member State may require the product owner or his authorised representative, or the sponsor of the clinical investigation in a Member State, as the case may be, to submit or make available on request, as deemed appropriate by, the report referred to in Annex 10.

- (d) Where a clinical investigation is refused or halted by a Member State, that Member State may communicate its decision and the grounds thereof to all Member States and the AMDC. Where a Member State has called for a significant modification or temporary interruption of a clinical investigation, that Member State may inform all Member States and the AMDC concerned about its actions and the grounds for the actions taken.
- (e) The regulatory authority of a Member State may require that the product owner or his authorised representative, or the sponsor of the clinical investigation in a Member State, as the case may be, to notify of the end of the clinical investigation, with justification(s) in case of early termination. In the case of early termination of the clinical investigation on safety grounds, this notification may be communicated to the regulatory authority of all Member States where the clinical investigation is carried out.

ARTICLE 14

INSTITUTIONAL ARRANGEMENTS

- (1) The ASEAN Medical Device Committee (AMDC) shall be established with the overall responsibility, which shall include the coordination, review and monitoring of the implementation of this ASEAN Medical Device Directive.

- (2) The ASEAN Consultative Committee for Standards and Quality (ACCSQ) and the ASEAN Secretariat shall provide support in coordinating and monitoring the implementation of this ASEAN Medical Device Directive and assist the AMDC in all matters relating thereto.
- (3) The AMDC may establish an ASEAN Medical Device Technical Committee (AMDTC) to assist the AMDC in reviewing the technical and safety issues. The AMDTC shall consist of representatives from the regulatory authorities, the industry and the academe.

ARTICLE 15
SAFEGUARD CLAUSES

- (1) A medical device placed on the market of Member States must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use, taking account, in particular, of the product's presentation, its labelling, instructions for its use and disposal, warning statements as well as any other indication or information provided by the product owner or his authorised representative or by any other person responsible for placing the product on the market. The provision of such warnings shall not, in any event, exempt any person from compliance with the other requirements laid down in this ASEAN Medical

Device Directive , and relevant laws and regulations of Member States.

- (2) Where a regulatory authority ascertains that a medical device placed on the market of a Member State, when correctly installed, maintained and used for their intended purpose, may compromise the health or safety of patients, users or, where applicable, other persons, it shall take all appropriate interim measures to withdraw such medical device from the market or prohibit or restrict their being placed on the market or put into service. That Member State shall immediately inform the other Member States of any such measures, indicating the reasons for its decision and, in particular, whether non-compliance with this ASEAN Medical Device Directive is due to:
- (a) failure to meet the essential principles set out in Annex 1;
 - (b) incorrect application of the standards referred to in Article 9, in so far as it is claimed that the standards have been applied; or
 - (c) inadequacies in the standards applied to demonstrate conformity to the essential principles.

ARTICLE 16

CONFIDENTIALITY

Without prejudice to the existing national provisions and practices on medical secrets, Member States shall ensure that all the parties

involved in the application of this ASEAN Medical Device Directive are bound to observe confidentiality with regard to all information obtained in carrying out their tasks. This does not affect the obligation of Member States with regard to mutual information and the dissemination of warnings, nor the obligations of the persons concerned to provide information under criminal law.

ARTICLE 17

SPECIAL CASES

- (1) A Member State may refuse to register or provisionally prohibit the marketing of a medical device, as it deem appropriate, in its market or subject it to special conditions, if that Member State finds out that on the basis of a substantiated justification, the medical device, although complying with the requirements of the ASEAN Medical Device Directive , represents a hazard to public health or for reasons specific to religious or cultural sensitivity. Certain product claims may be permitted or prohibited in accordance with national requirements. Furthermore, a Member State for reasons related to its local organization and laws, may designate a specific regulatory authority and subject to a different control, a specific medical device which comply with the requirements of this ASEAN Medical Device Directive and Annexes thereto.

- (2) A Member State who places a restriction or temporary ban on specific medical devices shall notify the other Member States with the reasons thereof, together with a copy to the AMDC of such measures taken.

ARTICLE 18

IMPLEMENTATION

- (1) Member States shall undertake appropriate measures to implement this ASEAN Medical Device Directive
- (2) Member States shall undertake appropriate measures to ensure that the technical infrastructures necessary are in place to implement this ASEAN Medical Device Directive
- (3) Member States shall ensure that the texts of such provisions of national laws, which they adopt in the field governed by this ASEAN Medical Device Directive are communicated to the other Member States with a copy to the ASEAN Secretariat, who shall promptly notify the AMDC.
- (4) Member States shall ensure that post marketing surveillance is in place and shall have full authority to enforce the law on medical devices found to be not complying with this ASEAN Medical Device Directive

- (5) The provisions of this Agreement may be amended by written agreement of all Member States. All amendments shall become effective upon acceptance by all Member States.

ARTICLE 19

DISPUTE SETTLEMENT

The ASEAN Protocol on Enhanced Dispute Settlement Mechanism signed on 29 November 2004 in Vientiane, Lao PDR and amendments thereto, shall apply to the settlement of disputes concerning the interpretation or implementation, of this Medical Device Directive .

ARTICLE 20

FINAL PROVISIONS

1. This ASEAN Medical Device Directive shall enter into force, after all Member States have ratified or notified the Secretary-General of ASEAN of the completion of their respective domestic requirements necessary for the entry into force of this ASEAN Medical Device Directive, which shall be no later than 31 December 2014.
2. Instruments of ratification or notification shall be deposited with the Secretary-General of ASEAN who shall promptly notify all Member States of each deposit.

3. Any Member State may propose amendment or modification to this ASEAN Medical Device Directive and its Annexes which shall be subject to agreement in writing by all Member States.

1. .

2. .

(2) 4. Member States shall make no reservation with respect to any of the provisions of this ASEAN Medical Device Directive .

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(3) This ASEAN Medical Device Directive shall be deposited with the Secretary-General of ASEAN, who shall promptly furnish each Member State a certified copy thereof.

IN WITNESS WHEREOF the undersigned, being duly authorised by their respective Governments, have signed this ASEAN Medical Device Directive .

DONE at [Venue], this [DD] of [Month] in the Year [Year], in a single copy in the English Language.

For Brunei Darussalam:

LIM JOCK SENG
Second Minister of Foreign Affairs and Trade

For the Kingdom of Cambodia:

CHAM PRASIDH
Senior Minister and Minister of Commerce

For the Republic of Indonesia:

DRAFT
MARI ELKA PANGESTU
Minister of Trade

For the Lao People's Democratic Republic:

NAM VIYAKETH
Minister of Industry and Commerce

For Malaysia:

TAN SRI MUHYIDDIN YASSIN

Minister of International Trade and Industry

For the Union of Myanmar:

U SOE THA
Minister for National Planning and Economic Development

For the Republic of the Philippines:

PETER B. FAVILA
Secretary of Trade and Industry

For the Republic of Singapore:

LIM HNG KIANG
Minister for Trade and Industry

For the Kingdom of Thailand:

PORNTIVA NAKASAI

Minister of Commerce

For the Socialist Republic of Viet Nam:

VU HUY HOANG
Minister of Industry and Trade

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ANNEX 1

Essential Principles of Safety and Performance of Medical Devices

General Requirements

1. Medical devices shall be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.
2. The solutions adopted by the product owner for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the product owner shall control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable. The product owner shall apply the following principles in the priority order listed:
 - identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse,
 - eliminate risks as far as reasonably practicable through inherently safe design and manufacture,
 - reduce as far as is reasonably practicable the remaining risks by taking adequate protection measures, including alarms,
 - inform users of any residual risks.

3. Devices shall achieve the performance intended by the product owner and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions within the scope of the definition of a medical device.

4. The characteristics and performances referred to in Clauses 1, 2 and 3 shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the product owner, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the product owner's instructions.

5. The devices shall be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected under transport and storage conditions (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the product owner.

6. The benefits must be determined to outweigh any undesirable side effects for the performances intended.

7. Every medical device requires clinical evidence, appropriate for the use and classification of the device, demonstrating that the device complies with the applicable provisions of the essential principles. A clinical evaluation shall be conducted.

Design and Manufacturing Requirements

8. Chemical, physical and biological properties

8.1 The devices shall be designed and manufactured in such a way as to ensure the characteristics and performance requirements referred to in Clauses 1 to 6 of the 'General Requirements' are met. Particular attention shall be paid to:

- the choice of materials used, particularly as regards toxicity and, where appropriate, flammability,
- the compatibility between the materials used and biological tissues, cells, body fluids, and specimens, taking account of the intended purpose of the device,
- the choice of materials used shall reflect, where appropriate, matters such as hardness, wear and fatigue strength.

8.2 The devices shall be designed, manufactured and packed in such a way as to minimise the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the product. Particular attention shall be paid to tissues exposed and to the duration and frequency of exposure.

8.3 The devices shall be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they shall be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use.

- 8.4 Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product/drug as defined in the relevant legislation that applies and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and usefulness of the substance shall be verified, taking account of the intended purpose of the device.
- 8.5 The devices shall be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that may leach or leak from the device.
- 8.6 Devices shall be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by the unintentional ingress or egress of substances into or from the device taking into account the device and the nature of the environment in which it is intended to be used.

9. Infection and microbial contamination

- 9.1 The devices and manufacturing processes shall be designed in such a way as to eliminate or to reduce as far as reasonably practicable and appropriate the risk of infection to patients, users and, where applicable, other persons. The design shall:
- allow easy handling,
- and, where necessary:
- reduce as far as reasonably practicable and appropriate any microbial leakage from the device and/or microbial exposure during use,
 - prevent microbial contamination of the device, or specimen where applicable, by the patient, user or other person, or contamination of the patient by the medical device, during its use.

- 9.2 Where a device incorporates substances of biological origin, the risk of infection must be reduced as far as reasonably practicable and appropriate by selecting appropriate sources, donors and substances and by using, as appropriate, validated inactivation, conservation, test and control procedures.
- 9.3 Products incorporating non-viable tissues, cells and substances of animal origin falling within the definition of a medical device, shall originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues. The product owner is required to retain information on the geographical origin of the animals. Processing, preservation, testing and handling of tissues, cells and substances of animal origin shall be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.
- 9.4 For products incorporating cells, tissues and derivatives of microbial or recombinant origin falling within the definition of a medical device, the selection of sources/donors, the processing, preservation, testing and handling of cells, tissues and derivatives of such origin shall be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.
- 9.5 For products incorporating non-viable human tissues, cells and substances falling within the definition of an in-vitro diagnostic product, the selection of sources, donors and/or substances of human origin, the processing, preservation, testing and handling of tissues, cells and

substances of such origin shall be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

- 9.6 Devices labelled as having a special microbiological state shall be designed, manufactured and packed to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the product owner.
- 9.7 Devices delivered in a sterile state shall be designed, manufactured and packed in a non-reusable pack, and/or according to appropriate procedures, to ensure that they are sterile when placed on the market and remain sterile, under the transport and storage conditions indicated by the product owner, until the protective packaging is damaged or opened.
- 9.8 Devices labelled either as sterile or as having a special microbiological state shall have been processed, manufactured and, if applicable, sterilised by appropriate, validated methods.
- 9.9 Devices intended to be sterilised shall be manufactured in appropriately controlled (e.g. environmental) conditions.
- 9.10 Packaging systems for non-sterile devices shall keep the product without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilised prior to use, minimise the risk of microbial contamination; the packaging system shall be suitable taking account of the method of sterilisation indicated by the product owner.

- 9.11 The packaging and/or label of the device shall distinguish between identical or similar products placed on the market in both sterile and non-sterile condition.

10. Manufacturing and environmental properties

- 10.1 If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system shall be safe and shall not impair the specified performance of the devices, or equipment with which it is used. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use.

- 10.2 Devices shall be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate:
- the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features;
 - risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, pressure, humidity, temperature or variations in pressure and acceleration;
 - the risks connected to their use in conjunction with materials, substances and gases with which they may come into contact during normal conditions of use;
 - the risks of accidental penetration of substances into the device;
 - the risk of incorrect identification of specimens;
 - the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given;

- risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.

10.3 Devices shall be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition. Particular attention shall be paid to devices whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.

10.4 Devices must be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.

11. Devices with a diagnostic or measuring function

11.1 Devices with a measuring function, where inaccuracy could have a significant adverse effect on the patient, shall be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose of the device. The limits of accuracy shall be indicated by the product owner.

11.2 Diagnostic devices shall be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended use, based on appropriate scientific and technical methods. In particular the design shall address sensitivity, specificity, trueness, repeatability, reproducibility, control of known relevant interference and limits of detection, as appropriate.

11.3 Where the performance of devices depends on the use of calibrators and/or control materials, the traceability of values assigned to such

calibrators and/or control materials shall be assured through a quality management system.

- 11.4 Any measurement, monitoring or display scale shall be designed in line with ergonomic principles, taking account of the intended purpose of the device.
- 11.5 Wherever possible values expressed numerically shall be in commonly accepted, standardised units, and understood by the users of the device.

12. Protection against radiation

12.1 General

- 12.1.1 Devices shall be designed and manufactured and packaged in such a way that exposure of patients, users and other persons to any emitted radiation shall be reduced as far as practicable and appropriate, compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.

12.2 Intended radiation

- 12.2.1 Where devices are designed to emit hazardous, or potentially hazardous, levels of visible and/or invisible radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent in the emission, it shall be possible for the user to control the emissions. Such devices shall be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.

12.2.2 Where devices are intended to emit potentially hazardous, visible and/or invisible radiation, they shall be fitted, where practicable, with visual displays and/or audible warnings of such emissions.

12.3 Unintended radiation

12.3.1 Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as practicable and appropriate.

12.4 Instructions for use

12.4.1 The operating instructions for devices emitting radiation shall give detailed information as to the nature of the emitted radiation, means of protecting the patient and the user and on ways of avoiding misuse and of eliminating the risks inherent in installation.

12.5 Ionising radiation

12.5.1 Devices intended to emit ionising radiation shall be designed and manufactured in such a way as to ensure that, where practicable, the quantity, geometry and energy distribution (or quality) of radiation emitted can be varied and controlled taking into account the intended use.

12.5.2 Devices emitting ionising radiation intended for diagnostic radiology shall be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose whilst minimising radiation exposure of the patient and user.

12.5.3 Devices emitting ionising radiation, intended for therapeutic radiology shall be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy and where appropriate the energy distribution of the radiation beam.

13. Requirements for medical devices connected to or equipped with an energy source

13.1 Devices incorporating electronic programmable systems, including software, shall be designed to ensure the repeatability, reliability and performance of these systems according to the intended use. In the event of a single fault condition in the system, appropriate means shall be adopted to eliminate or reduce as far as practicable and appropriate consequent risks.

13.2 For devices which incorporate software or which are medical software in themselves, the software shall be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification.

13.3 Devices where the safety of the patients depends on an internal power supply shall be equipped with a means of determining the state of the power supply.

13.4 Devices where the safety of the patients depends on an external power supply shall include an alarm system to signal any power failure.

13.5 Devices intended to monitor one or more clinical parameters of a patient shall be equipped with appropriate alarm systems to alert the

user of situations which could lead to death or severe deterioration of the patient's state of health.

13.6 Devices shall be designed and manufactured in such a way as to reduce as far as practicable and appropriate the risks of creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.

13.7 Devices shall be designed and manufactured in such a way as to provide an adequate level of intrinsic immunity to electromagnetic disturbance to enable them to operate as intended.

13.8 Protection against electrical risks

13.8.1 Devices shall be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks during normal use and in single fault condition, provided the devices are installed and maintained as indicated by the product owner.

14. Protection against mechanical risks

14.1 Devices shall be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with, for example, resistance to movement, instability and moving parts.

14.2 Devices shall be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.

14.3 Devices shall be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.

14.4 Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle shall be designed and constructed in such a way as to minimise all possible risks.

14.5 Accessible parts of the devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings shall not attain potentially dangerous temperatures under normal use.

15. Protection against the risks posed to the patient by supplied energy or substances

15.1 Devices for supplying the patient with energy or substances shall be designed and constructed in such a way that the delivered amount can be set and maintained accurately enough to guarantee the safety of the patient and of the user.

15.2 Devices shall be fitted with the means of preventing and/or indicating any inadequacies in the delivered amount which could pose a danger. Devices shall incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy from an energy and/or substance source.

15.3 The function of the controls and indicators shall be clearly specified on the devices. Where a device bears instructions required for its

operation or indicates operating or adjustment parameters by means of a visual system, such information shall be understandable to the user and, as appropriate, the patient.

16. Active implantable medical devices

16.1 An active implantable medical device shall display an identifier that can be used to identify:-

- the type of medical device;
- the product owner of the medical device; and
- the year of manufacture of the medical device.

16.2 The identifier shall be readable without the need for surgery to the person in whom the medical device is implanted.

17. Protection against the risks posed to the patient for devices for self-testing or self-administration

17.1 Such devices shall be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to users and the influence resulting from variation that can reasonably be anticipated in user's technique and environment. The information and instructions provided by the product owner shall be easy for the user to understand and apply.

17.2 Such devices shall be designed and manufactured in such a way as to reduce as far as practicable the risk of use error in the handling of the device and, if applicable, the specimen, and also in the interpretation of results.

17.3 Such devices shall, where reasonably possible, include a procedure by which the user can verify that, at the time of use, that the product will perform as intended by the product owner.

18. Information supplied by the product owner

18.1 Users shall be provided with the information needed to identify the product owner, to use the device safely and to ensure the intended performance, taking account of their training and knowledge. This information shall be easily understood.

19. Clinical Investigation

19.1 Clinical investigations on human subjects shall be carried out in accordance with the spirit of the Helsinki Declaration. This includes every step in the clinical investigation from first consideration of the need and justification of the study to publication of the results.

ANNEX 2

Risk Classification Rules for Medical Devices other than in-vitro diagnostic products

1. DEFINITIONS

ACTIVE MEDICAL DEVICE: Any medical device, operation of which depends on a source of electrical energy or any source of power other than that directly generated by the human body or gravity and which acts by converting this energy. Medical devices intended to transmit energy, substances or other elements between an active medical device and the patient, without any significant change, are not considered to be active medical devices.

NOTE: Standalone software (to the extent it falls within the definition of a medical device) is deemed to be an active device.

ACTIVE THERAPEUTIC DEVICE: Any active medical device, whether used alone or in combination with other medical devices, to support, modify, replace or restore biological functions or structures with a view to treatment or alleviation of an illness, injury or handicap.

ACTIVE DEVICE INTENDED FOR DIAGNOSIS: Any active medical device, whether used alone or in combination with other medical devices, to supply information for detecting, diagnosing, monitoring or to support in treating physiological conditions, states of health, illnesses or congenital deformities.

BODY ORIFICE: Any natural opening in the body, as well as the external surface of the eyeball, or any permanent artificial opening, such as a stoma or permanent tracheotomy.

CENTRAL CIRCULATORY SYSTEM: For the purpose of this document, central circulatory system means the major internal blood vessels including

the following:

- arteriae pulmonales (pulmonary artery);
- aorta ascendens (ascending aorta);
- arteriae coronariae (coronary artery);
- arteria carotis communis (common carotid artery);
- arteria carotis externa (external carotid artery);
- arteria carotis interna (internal carotid artery);
- arteriae cerebrates (cerebella arteries);
- truncus brachiocephalicus (brachiocephalic trunk);
- venae cordis (cardiac veins);
- venae pulmonales (pulmonary vein);
- venae cava superior (superior vena cava);
- venae cava inferior (inferior vena cava);
- arcus aorta (aortic arch);
- thoracica aorta (thoracic aorta);
- abdominalis aorta (abdominal aorta);
- ilica communis (common iliac arteries and veins);
- aorta descendens to the bifurcatio aortae. (descending aorta to the bifurcation of aorta)

CENTRAL NERVOUS SYSTEM: For the purpose of this document, central nervous system refers to the brain, meninges and spinal cord.

CONTINUOUS USE: in relation to a medical device, means

- the uninterrupted use of the medical device, not including any temporary interruption of its use during a procedure or any temporary removal of the medical device for purposes such as cleaning or disinfection; or
- the accumulated use of the medical device by replacing it immediately with another medical device of the same type, as intended by its product owner;

DURATION OF USE

- **TRANSIENT:** Normally intended for continuous use for less than 60 minutes,
- **SHORT TERM:** Normally intended for continuous use for between 60 minutes and 30 days
- **LONG TERM:** Normally intended for continuous use for more than 30 days.

HAZARD: Potential source of harm.

IMMEDIATE DANGER: A situation where the patient is at risk of either losing life or an important physiological function if no immediate preventative measure is taken.

IMPLANTABLE DEVICE: Any medical device, including those that are partially or wholly absorbed, which is intended: -

- to be totally introduced into the human body or,
 - to replace an epithelial surface or the surface of the eye,
- by surgical intervention which is intended to remain in place after the procedure.

NOTE: *Any medical device intended for partial introduction into the human body through surgical intervention and intended to remain in place after the procedure for at least 30 days is also considered an implantable device.*

INTENDED PURPOSE: The use for which the medical device is intended according to the specifications of its product owner as stated on any or all of the following:

- the label of the medical device;

- the instructions for use of the medical device;
- the promotional materials in relation to the medical device.

INVASIVE DEVICE: A medical device, which, in whole or in part, penetrates inside the body, either through a body orifice or through the surface of the body.

LIFE SUPPORTING OR LIFE SUSTAINING: A medical device that is essential to, or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life.

MEDICAL DEVICE: means a medical device as described in the ASEAN Medical Device Agreement.

REUSABLE SURGICAL INSTRUMENT: Instrument intended for surgical use by cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or other surgical procedures, without connection to any active medical device and which are intended by the product owner to be reused after appropriate procedures for cleaning and/or sterilisation have been carried out.

RISK: Combination of the probability of occurrence of harm and the severity of that harm.

SURGICALLY INVASIVE DEVICE: An invasive medical device that penetrates inside the body through the surface of the body, with the aid or in the context of a surgical operation.

NOTE: *Medical devices other than those referred to in the previous subparagraph and which produce penetration other than through a natural body orifice, should be treated as surgically invasive devices.*

2. RISK CLASSIFICATION FOR MEDICAL DEVICES OTHER THAN IN-VITRO DIAGNOSTIC PRODUCTS

RULES
NON-INVASIVE DEVICES
Rule 1. All non-invasive devices which come into contact with injured skin: - are in Class A if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates only, i.e. they heal by primary intent; - are in Class B if they are intended to be used principally with wounds which have breached the dermis, including devices principally intended to manage the microenvironment of a wound. Unless they are intended to be used principally with wounds which have breached the dermis and can only heal by secondary intent, in which case they are in Class C.
Rule 2. All non-invasive devices intended for channelling or storing <ul style="list-style-type: none">• body liquids or tissues,• liquids or• gases for the purpose of eventual infusion, administration or introduction into the body are in Class A, Unless they may be connected to an active medical device in Class B or a higher class, in which case they are Class B; Unless they are intended for use of <ul style="list-style-type: none">• channeling blood, or• storing or channeling other body liquids, or• for storing organs, parts of organs or body tissues, in which case they are Class B. Unless they are blood bags, in which case they are Class C.

Rule 3. All non-invasive devices intended for modifying the biological or chemical composition of

- blood,
- other body liquids, or
- other liquids

intended for infusion into the body are in Class C,

Unless the treatment consists of filtration, centrifuging or exchanges of gas or of heat, in which case they are in Class B.

Rule 4. All other non-invasive devices are in Class A.

INVASIVE DEVICES

Rule 5. All invasive devices with respect to body orifices (other than those which are surgically invasive) and which:

- are not intended for connection to an active medical device, or
- are intended for connection to a Class A medical device only.

- are in Class A if they are intended for transient use;

Unless they are intended by its product owner for use on the external surface of any eyeball; or it is liable to be absorbed by the mucous membrane, in which case they are in Class B.

- are in Class B if they are intended for short-term use;

Unless they are intended for short-term use in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in a nasal cavity, in which case they are in Class A,

- are in Class C if they are intended for long-term use;

Unless they are intended for long-term use in the oral cavity as far as the pharynx, in an ear canal up to the ear-drum or in a nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are in Class B.

All invasive devices with respect to body orifices (other than those which are surgically invasive) that are intended to be connected to an active medical device in Class B or a higher class, are in Class B.

Rule 6. All surgically invasive devices intended for transient use are in Class B,

Unless they are reusable surgical instruments, in which case they are in Class A; or

Unless intended to supply energy in the form of ionising radiation, in which case they are in Class C; or

Unless intended to have a biological effect or be wholly or mainly absorbed, in which case they are in Class C; or

Unless intended to administer medicinal products by means of a delivery system, if this is done in a manner that is potentially hazardous taking account of the mode of application, in which they are in Class C; or

Unless they are intended specifically for use in direct contact with the central nervous system, in which case they are in Class D; or

Unless intended specifically to diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with these parts of the body, in which case they are in Class D.

Rule 7. All surgically invasive devices intended for short-term use are in Class B,

Unless they are intended to administer medicinal products, in which case they are in Class C; or

Unless they are intended to undergo chemical change in the body (except if the devices are placed in the teeth), in which case they are in Class C; or

Unless they are intended to supply energy in the form of ionising radiation, in which case they are in Class C; or

Unless they are intended to have a biological effect or to be wholly or mainly absorbed, in which case they are in Class D; or

Unless they are intended specifically for use in direct contact with the central nervous system, in which case they are in Class D;

Unless they are intended specifically to diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact

with these parts of the body, in which case they are in Class D.
Rule 8. All implantable devices, and long-term surgically invasive devices, are in Class C,
Unless they are intended to be placed into the teeth, in which case they are in Class B; or
Unless they are intended to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are in Class D; or
Unless they are intended to be life supporting or life sustaining, in which case they are in Class D; or
Unless they are intended to be active implantable medical devices, in which case they are Class D; or
Unless they are intended to have a biological effect or to be wholly or mainly absorbed, in which case they are in Class D; or
Unless they are intended to administer medicinal products, in which case they are in Class D; or
Unless they are intended to undergo chemical change in the body (except if the devices are placed in the teeth), in which case they are in Class D; or
Unless they are breast implants, in which case they are in Class D.
ACTIVE DEVICES
Rule 9(i). All active therapeutic devices intended to administer or exchange energy are in Class B,
Unless their characteristics are such that they may administer or exchange energy to or from the human body in a potentially hazardous way, including ionising radiation, taking account of the nature, the density and site of application of the energy, in which case they are in Class C.
Rule 9(ii). All active devices intended to control or monitor the performance of active therapeutic devices in Class C, or intended directly to influence the performance of such devices, are in Class C.
Rule 10(i). Active devices intended for diagnosis are in Class B:

- if they are intended to supply energy which will be absorbed by the human body (except for devices used solely to illuminate the patient's body, with light in the visible or near infra-red spectrum, in which case they are Class A), or

- if they are intended to image *in vivo* distribution of radiopharmaceuticals, or

- if they are intended to allow direct diagnosis or monitoring of vital physiological processes,

Unless they are specifically intended for:

- monitoring of vital physiological parameters, where the nature of variations is such that it could result in immediate danger to the patient, for instance variations in cardiac performance, respiration, activity of central nervous system, or
- diagnosing in clinical situations where the patient is in immediate danger, in which case they are in Class C.

Rule 10(ii). Active devices intended to emit ionising radiation and intended for diagnostic and/or interventional radiology, including devices which control or monitor such devices, or those which directly influence their performance, are in Class C.

Rule 11. All active devices intended to administer and/or remove medicinal products, body liquids or other substances to or from the body are in Class B,

Unless this is done in a manner that is potentially hazardous, taking account of the nature of the substances involved, of the part of the body concerned and of the mode and route of administration or removal, in which case they are in Class C.

Rule 12. All other active devices are in Class A.

ADDITIONAL RULES

Rule 13. All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product (as defined by the Member State), and which is liable to act on the human body with action ancillary to that of the devices, are in Class D,

Unless the incorporated substance is a medicinal product that is exempted from the medicinal product registration requirements of the Member State, in which case they are in Class B.

Rule 14. All devices manufactured from or incorporating

- animal cells, tissues and/or derivatives thereof, rendered non-viable, or
- cells, tissues and/or derivatives of microbial or recombinant origin

are Class D,

Unless such devices are manufactured from or incorporate non-viable animal tissues or their derivatives that come in contact with intact skin only, where they are in Class A.

Rule 15. All devices intended specifically to be used for sterilising medical devices, or disinfecting as the end point of processing, are in Class C.

Unless they are intended for disinfecting medical devices prior to end point sterilisation or higher level disinfection, in which case they are in Class B; or

Unless they are intended specifically to be used for disinfecting, cleaning, rinsing or, when appropriate, hydrating contact lenses, in which case they are in Class C.

Rule 16. All devices used for contraception or the prevention of the transmission of sexually transmitted diseases are in Class C,

Unless they are implantable or long-term invasive devices, in which case they are in Class D.

ANNEX 3

Risk Classification Rules for *In-Vitro* Diagnostic Products

1. DEFINITIONS

ACCESSORY: means an article is intended specifically by its product owner to be used together with a particular medical device to enable or assist that device to be used in accordance with its intended purpose.

EXAMINATION: Set of operations having the object of determining the value of a property.

NOTE: *Examination of an analyte in a biological sample is commonly referred to as a test, assay or analysis.*

HAZARD: Potential source of harm.

INSTRUMENT: Equipment or apparatus intended by the product owner to be used as IVD medical device.

IN VITRO DIAGNOSTIC (IVD) PRODUCT: means any reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination, that is intended by its product owner to be used *in vitro* for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information:-

- concerning a physiological or pathological state;
- concerning a congenital abnormality;
- to determine the safety and compatibility of donations, including blood and tissue donations, with potential recipients; or
- to monitor therapeutic measures, and

includes a specimen receptacle.

IVD MEDICAL DEVICE FOR SELF-TESTING: Any IVD medical device intended by the product owner for use by lay persons.

LAY PERSON: Any individual who does not have formal training in a relevant field or discipline.

NEAR PATIENT TESTING: Any testing performed outside a laboratory environment by a healthcare professional not necessarily a laboratory professional, generally near to, or at the side of, the patient. Also known as Point-of-Care (POC).

REAGENT: Any chemical, biological or immunological components, solutions or preparations intended by the product owner to be used as IVD medical devices.

RISK: The combination of the probability of occurrence of harm and the severity of that harm.

SELF-TESTING: Testing performed by lay persons.

SPECIMEN RECEPTACLE: An IVD medical device, whether vacuum-type or not, specifically intended by their product owner for the primary containment of specimens derived from the human body.

TRANSMISSIBLE AGENT: An agent capable of being transmitted to a person, as a communicable, infectious or contagious disease.

TRANSMISSION: The conveyance of disease to a person.

2. CLASSIFICATION RULES FOR IN-VITRO DIAGNOSTIC PRODUCTS

RULE 1: IVD medical devices intended for the following purposes are classified as Class D:

- devices intended to be used to detect the presence of, or exposure to, a transmissible agent in blood, blood components, blood derivatives, cells, tissues or organs in order to assess their suitability for transfusion or transplantation, or
- devices intended to be used to detect the presence of, or exposure to, a transmissible agent that causes a life-threatening, often incurable, disease with a high risk of propagation.

Rationale: The application of this rule as defined above should be in accordance with the rationale that follows: IVD medical devices in this Class are intended to be used to ensure the safety of blood and blood components for transfusion and/or cells, tissues and organs for transplantation. In most cases, the result of the test is the major determinant as to whether the donation/product will be used. Serious diseases are those that result in death or long-term disability, which are often incurable or require major therapeutic interventions and where an accurate diagnosis is vital to mitigate the public health impact of the condition.

Examples: Tests to detect infection by HIV, HCV, HBV, HTLV. This Rule applies to first-line assays, confirmatory assays and supplemental assays.

RULE 2: IVD medical devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation, are classified as Class C, except for ABO system [A (ABO1), B (ABO2), AB (ABO3)], rhesus system [RH1 (D), RH2 (C), RH3 (E), RH4 (c),

RH5 (e)], Kell system [Kel1 (K)], Kidd system [JK1 (Jka), JK2 (Jkb)] and Duffy system [FY1 (Fya), FY2 (Fyb)] determination which are classified as Class D.

Rationale: The application of this rule as defined above should be in accordance with the following rationale: A high individual risk, where an erroneous result would put the patient in an imminent life-threatening situation places the device into Class D. The rule divides blood-grouping IVD medical devices into two subsets, Class C or D, depending on the nature of the blood group antigen the IVD medical device is designed to detect, and its importance in a transfusion setting.

Examples: HLA, Duffy system (other Duffy systems except those listed in the rule as Class D) are in Class C.

RULE 3: IVD medical devices are classified as Class C if they are intended for use:

- in detecting the presence of, or exposure to, a sexually transmitted agent (e.g. Sexually transmitted diseases, such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*).
- in detecting the presence in cerebrospinal fluid or blood of an infectious agent with a risk of limited propagation (e.g. *Neisseria meningitidis* or *Cryptococcus neoformans*).
- in detecting the presence of an infectious agent where there is a significant risk that an erroneous result would cause death or severe disability to the individual or fetus being tested (e.g. diagnostic assay for CMV, *Chlamydia pneumoniae*, Methycillin Resistant *Staphylococcus aureus*).
- in pre-natal screening of women in order to determine their immune status towards transmissible agents (e.g. Immune status tests for Rubella or Toxoplasmosis).
- in determining infective disease status or immune status, and where there is a risk that an erroneous result will lead to a patient management

decision resulting in an imminent life-threatening situation for the patient (e.g. Enteroviruses, CMV and HSV in transplant patients).

- in screening for selection of patients for selective therapy and management, or for disease staging, or in the diagnosis of cancer (e.g. personalised medicine).

NOTE: Those IVD medical devices where the therapy decision would usually be made only after further investigation and those used for monitoring would fall into class B under rule 6.

- in human genetic testing (e.g. Huntington's Disease, Cystic Fibrosis).
- to monitor levels of medicines, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in an immediate life-threatening situation for the patient (e.g. Cardiac markers, cyclosporin, prothrombin time testing).
- in the management of patients suffering from a life-threatening infectious disease (e.g. HCV viral load, HIV Viral Load and HIV and HCV geno- and subtyping).
- in screening for congenital disorders in the fetus (e.g. Spina Bifida or Down Syndrome).

Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: IVD medical devices in this Class present a moderate public health risk, or a high individual risk, where an erroneous result would put the patient in an imminent life-threatening situation, or would have a major negative impact on outcome. The IVD medical devices provide the critical, or sole, determinant for the correct diagnosis. They may also present a high individual risk because of the stress and anxiety resulting from the information and the nature of the possible follow-up measures.

RULE 4: IVD medical devices intended for self-testing are classified as Class C, except those devices from which the result is not determining a medically critical status, or is preliminary and requires follow-up with the appropriate laboratory test in which case they are Class B.

IVD medical devices intended for blood gases and blood glucose determinations for near-patient testing would be Class C. Other IVD medical devices that are intended for near patient should be classified in their own right using the classification rules.

Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: In general, these IVD medical devices are used by individuals with no technical expertise and thus the labelling and instructions for use are critical to the proper outcome of the test.

Example for Self-testing Class C: Blood glucose monitoring,

Example for Self-testing Class B: Pregnancy self test, Fertility testing, Urine test strip.

RULE 5: The following IVD medical devices are classified as Class A:

- reagents or other articles that possess specific characteristics, intended by the product owner to make them suitable for in vitro diagnostic procedures related to a specific examination.
- instruments intended by the product owner specifically to be used for in vitro diagnostic procedures.
- specimen receptacles.

NOTE: *Any product for general laboratory use not manufactured, sold or represented for use in specified in vitro diagnostic applications are not deemed to be IVD medical devices.*

Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: These IVD medical devices present a low individual risk and no or minimal public health risk.

Examples: Selective/differential microbiological media (excluding the dehydrated powders which are considered not to be a finished IVD medical device), identification kits for cultured microorganisms, wash solutions, instruments and plain urine cup.

NOTE: The performance of software or an instrument that is specifically required to perform a particular test will be assessed at the same time as the test kit.

NOTE: The interdependence of the instrument and the test methodology prevents the instrument from being assessed separately, even though the instrument itself is still classified as Class A.

RULE 6: IVD medical devices not covered in Rules 1 through 5 are classified as Class B.

Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: These IVD medical devices present a moderate individual risk as they are not likely to lead to an erroneous result that would cause death or severe disability, have a major negative impact on patient outcome or put the individual in immediate danger. The IVD medical devices give results that are usually one of several determinants. If the test result is the sole determinant however other information is available, such as presenting signs and symptoms or other clinical information that may guide a physician, such that classification into Class B may be justified. Other appropriate controls may also be in place to validate the results. This Class also includes those IVD medical devices that

present a low public health risk because they detect infectious agents that are not easily propagated in a population.

Examples: Blood gases, *H. pylori* and physiological markers such as hormones, vitamins, enzymes, metabolic markers, specific IgE assays and celiac disease markers.

RULE 7: IVD medical devices that are controls without a quantitative or qualitative assigned value will be classified as Class B.

Rationale: For such controls, the user, not the product owner, assigns the qualitative or quantitative value.

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ANNEX 4

ASEAN Common Submission Dossier Template

1. INTRODUCTION

The Common Submission Dossier Template (CSDT) will harmonize the differences in documentation formats that presently exist in different ASEAN jurisdictions. The adoption of this guidance document in ASEAN will eliminate the preparation of multiple dossiers, arranged in different formats but with essentially the same contents, for regulatory submission to different regulatory authorities.

2. SCOPE

The CSDT applies to all products that fall within the definition of a medical device.

The format of the CSDT recommended herein is based upon the goal of both regulators and product owners to strive for the least burdensome means to demonstrate conformity to the Essential Principles for all classes of medical devices.

Requirements for post-market vigilance or adverse event reporting are outside the scope of this document.

3. EXECUTIVE SUMMARY

An executive summary shall be provided with the common submission dossier template, which shall include the following information:

- an overview, e.g., introductory descriptive information on the medical device, the intended uses and indications for use of the medical device, any novel features and a synopsis of the content of the CSDT;
- commercial marketing history;

- intended uses and indications in labelling;
- list of regulatory approval or marketing clearance obtained;
- status of any pending request for market clearance; and
- important safety/performance related information.

4. ELEMENTS OF THE COMMON SUBMISSION DOSSIER TEMPLATE

4.1. Relevant Essential Principles and Method Used to Demonstrate Conformity

The CSDT should identify the Essential Principles of Safety and Performance of Medical Devices that are applicable to the device. The CSDT should identify the general method used to demonstrate conformity to each applicable Essential Principle. The methods that may be used include compliance with recognized or other standards, state of the art or internal industry methods, comparisons to other similar marketed devices, etc. The CSDT should identify the specific documents related to the method used to demonstrate conformity to the Essential Principles.

4.1.1. Essential Principles and Evidence of Conformity

The evidence of conformity can be provided in tabular form with supporting documentation available for review as required.

For example, a completed Essential Principles conformity checklist can be used to demonstrate that a recognized test standard was used as part of the method to demonstrate conformity to one Essential Principle. As such, CSDT would then include a declaration of conformity to the standard, or other certification permitted by the Regulatory Authority, and a summary of the test data, if the standard does not include performance requirements. When the **product owner** uses international or other standards to demonstrate conformity with the Essential Principles, the CSDT should identify the full title

of the standard, identifying numbers, date of the standard, and the organization that created the standard.

When the **product owner** uses other means, such as internal standards, the CSDT should describe the means. Not all the essential principles will apply to all devices and it is for the **product owner** of the device to assess which are appropriate for his particular device product. In determining this, account must be taken of the intended purpose of the device.

4.2. Device Description

4.2.1. Device description & features

Besides a general description of the device, a more detailed description of the device attributes is necessary to explain how the device functions, the basic scientific concepts that form the fundamentals for the device, the component materials and accessories used in its principles of operation as well as packaging. A complete description of each functional component, material or ingredient of the device should be provided, with labelled pictorial representation of the device in the form of diagrams, photographs or drawings, as appropriate.

4.2.2. Intended use

This means the use for which the medical device is intended, for which it is suited according to the data supplied by the **product owner** in the instructions as well as the functional capability of the device.

4.2.3. Indications

This is a general description of the disease or condition that the device will diagnose, treat, prevent, cure or mitigate and includes a description of the target patient population for which the device is intended.

4.2.4. Instructions of use

These are all necessary information from the **product owner** including the procedures, methods, frequency, duration, quantity and preparation to be followed for safe use of the medical device. Instructions needed to use the device in a safe manner shall, to the extent possible, be included on the device itself and/or on its packaging by other formats / forms.

4.2.5. Contraindications

This is a general description of the disease or condition and the patient population for which the device should not be used for the purpose of diagnosing, treating, curing or mitigating. Contraindications are conditions under which the device should not be used because the risk of use clearly outweighs any possible benefit.

4.2.6. Warnings

This is the specific hazard alert information that a user needs to know before using the device.

4.2.7. Precautions

This alerts the user to exercise special care necessary for the safe and effective use of the device. They may include actions to be taken to avoid effects on patients/users that may not be potentially life-threatening or result in serious injury, but about which the user should be aware. Precautions may also alert the user to adverse effects on the device of use or misuse and the care necessary to avoid such effects.

4.2.8. Potential adverse effects

These are potential undesirable and serious outcomes (death, injury, or serious adverse events) to the patient/user, or side effects from the use of the

medical device, under normal conditions.

4.2.9. Alternative therapy

This is a description of any alternative practices or procedures for diagnosing, treating, curing or mitigating the disease or condition for which the device is intended.

4.2.10. Materials

A description of the materials of the device and their physical properties to the extent necessary to demonstrate conformity with the relevant Essential Principles. The information shall include complete chemical, biological and physical characterization of the materials of the device.

4.2.11. Other Relevant Specifications

The functional characteristics and technical performance specifications for the device including, as relevant, accuracy, sensitivity, specificity of measuring and diagnostic devices, reliability and other factors; and other specifications including chemical, physical, electrical, mechanical, biological, software, sterility, stability, storage and transport, and packaging to the extent necessary to demonstrate conformity with the relevant Essential Principles.

4.2.12. Other Descriptive Information

Other important descriptive characteristics not detailed above, to the extent necessary to demonstrate conformity with the relevant Essential Principles (for example, the biocompatibility category for the finished device).

NOTE: For simple, low risk devices, the above information will typically be contained in already existing sales brochures, instructions for use, etc.

4.3. Summary of Design Verification and Validation Documents

This section should summarize or reference or contain design verification and design validation data to the extent appropriate to the complexity and risk class of the device:

Such documentation should typically include:

- declarations/certificates of conformity to the “recognized” standards listed as applied by the product owner; and/or
- summaries or reports of tests and evaluations based on other standards, manufacturer methods and tests, or alternative ways of demonstrating compliance.

EXAMPLE: The completed Table of Conformity to the Essential Principles that a recognized test standard was used as part of the method to demonstrate conformity to one Essential Principle.

Section 3.0 of the CSTD would then include a declaration of conformity to the standard, or other certification permitted by the relevant Regulatory Authority, and a summary of the test data, if the standard does not include performance requirements.

The data summaries or tests reports and evaluations would typically cover, as appropriate to the complexity and risk class of the device:

- a listing of and conclusions drawn from published reports that concern the safety and performance of aspects of the device with reference to the Essential Principles;
- engineering tests;
- laboratory tests;
- biocompatibility tests;
- animal tests;

- simulated use;
- software validation.

4.3.1. Pre-clinical Studies

Details must be provided on all biocompatibility tests conducted on materials used in a device. At a minimum, tests must be conducted on samples from the finished, sterilized device. All materials that are significantly different must be characterized. Information describing the tests, the results and the analyses of data must be presented.

Complete pre-clinical physical test data must be provided, as appropriate. The report must include the objectives, methodology, results and **product owner's** conclusions of all physical studies of the device and its components. Physical testing must be conducted to predict the adequacy of device response to physiological stresses, undesirable conditions and forces, long-term use and all known and possible failure modes.

Pre-clinical animal studies used to support the probability of effectiveness in humans must be reported. These studies must be undertaken using good laboratory practices. The objectives, methodology, results, analysis and **product owner's** conclusions must be presented. The study conclusion should address the device's interactions with animal fluids and tissues and the functional effectiveness of the device in the experimental animal model(s). The rationale (and limitations) of selecting the particular animal model should be discussed.

4.3.1.1. Software Verification and Validation Studies (if applicable)

The correctness of a software product is another critical product characteristic that cannot be fully verified in a finished product. The **product owner** must provide evidence that validates the software design and development

process. This information should include the results of all verification, validation and testing performed in-house and in a user's environment prior to final release, for all of the different hardware configurations identified in the labelling, as well as representative data generated from both testing environments.

4.3.1.2. Devices Containing Biological Material

Results of studies substantiating the adequacy of the measures taken with regards to the risks associated with transmissible agents must be provided. This will include viral clearance results for known hazards. Donor screening concerns must be fully addressed and methods of harvesting must also be fully described. Process validation results are required to substantiate that manufacturing procedures are in place to minimize biological risks.

4.3.2. Clinical Evidence

This section should indicate how any applicable requirements of the Essential Principles for clinical evaluation of the device have been met. Where applicable, this evaluation may take the form of a systematic review of existing bibliography, clinical experience with the same or similar devices, or by clinical investigation. Clinical investigation is most likely to be needed for higher risk class devices, or for devices where there is little or no clinical experience.

4.3.2.1. Use of Existing Bibliography

Copies are required of all literature studies, or existing bibliography, that the **product owner** is using to support safety and effectiveness. These will be a subset of the bibliography of references. General bibliographic references should be device-specific as supplied in chronological order. Care should be taken to ensure that the references are timely and relevant to the current application.

Clinical evidence of effectiveness may comprise device-related investigations conducted domestically or other countries. It may be derived from relevant publications in a peer-reviewed scientific literature. The documented evidence submitted should include the objectives, methodology and results presented in context, clearly and meaningfully. The conclusions on the outcome of the clinical studies should be preceded by a discussion in context with the published literature.

4.4. Device Labelling

This is the descriptive and informational product literature that accompanies the device any time while it is held for sale or shipped, such as any physician's manuals, pack labeling, promotional material and product brochures etc. This section should summarize or reference or contain the following labelling data to the extent appropriate to the complexity and risk class of the device, which is generally considered as "labelling":

- Labels on the device and its packaging
- Instructions for use
- Any information and instructions given to the patient, including instructions for any procedure the patient is expected to perform (if applicable).

4.4.1. Samples of Labels on the Device and its Packaging

This is the printed, written or graphic product information provided on or attached to one or more levels of packaging, including the outer packaging or the outside container wrapper. Any pack labelling, which is not provided on the outer packaging must be easily legible through this outer packaging. If it is physically impossible to include samples of labels (e.g. large warning labels affixed onto an X-ray machine), alternative submission methods (e.g. photographs or technical drawings), to the extent appropriate, will suffice to meet the requirements of this section.

4.4.2. Instructions for Use

The instructions for use is commonly referred to as the physician's manual, user manual, operator's manual, prescriber's manual or reference manual. It contains directions under which the physician or end-user can use a device safely and for its intended purpose. This should include information on indications, contraindications, warnings, precautions, potential adverse effects, alternative therapy and the conditions that should be managed during normal use to maintain the safety and effectiveness of the device.

4.5. Risk Analysis

This section should summarize or reference or contain the results of the risk analysis. This risk analysis should be based upon international or other recognized standards, and be appropriate to the complexity and risk class of the device.

4.5.1. Results of Risk Analysis

A list of possible hazards for these devices must be prepared. Indirect risks from medical devices may result from device-associated hazards, such as moving parts, which lead to sustained injury, or from user-related hazards, such as ionizing radiation from an X-ray machine. The evaluation of these risks against the claimed benefits of the device and the method(s) used to reduce risk to acceptable levels must be described. The individual or organization that carries out the risk analysis must be clearly identified. The technique used to analyze risk must be specified, to ensure that it is appropriate for the device and the risk involved.

4.6. Manufacturer Information

This section should summarize or reference or contain documentation related to the manufacturing processes, including quality assurance measures, which

is appropriate to the complexity and risk class of the device.

4.6.1. Manufacturing Process

Manufacturing process for the device should be provided in the form of a list of resources and activities that transform inputs into the desired output.

EXAMPLE: The manufacturing process should include the appropriate manufacturing methods and procedures, manufacturing environment or condition, and the facilities and controls used for the manufacturing, processing, packaging, labeling, storage of the device. Sufficient detail must be provided to enable a person generally familiar with quality systems to judge the appropriateness of the controls in place. A brief summary of the sterilization method and processing should be included, if any.

If multiple facilities are involved in the manufacture of device, the applicable information (e.g. quality assurance certificates issued by an accredited third party inspection body) for each facility must be submitted. Firms that manufacture or process the device under contract to **the product owner** may elect to submit all or a portion of the manufacturing information applicable to their facility directly to the Regulatory Authority in the form of a master file. The **product owner** should inform these contractors of the need to supply detailed information on the device. However, it is not the intent of this section to capture information relating to the supply of sub-components (i.e. unfinished medical device) that contributes towards the manufacture of the finished device itself.

ANNEX 5

Post Marketing Alert System (PMAS) Requirements

1. INTRODUCTION

1.1. Purpose

This document aims to provide guidance on the post-market obligations of companies or persons who place medical devices on the markets of ASEAN Member States.

1.2. Background

This document is intended to provide guidelines on the following post-market alerting system requirements:-

- Distribution records
- Complaint records
- Adverse event (AE) reporting criteria and reporting format
- Field Safety Corrective Action (FSCA) reporting format

The Regulatory Authorities in the Member States may adopt the recommended post-market alerting system requirements in this Annex or prescribe their own post-market alerting system requirements.

Distribution records

Traceability is not only a requirement of an effective quality system but also the requirement of regulatory bodies around the world. Keeping proper and appropriate distribution records is an important component of ensuring traceability of products in the market.

Complaint records

An effective complaint handling system is an important part of any quality system. Any complaint received on a medical device should be evaluated and

if necessary, thoroughly investigated and analysed, and corrective actions should be taken. The results of the evaluation should lead to a conclusion regarding whether the complaint was valid, the causes of the complaint, and what actions were necessary to prevent further occurrences.

Physical Manufacturers, authorised representative and authorised distributors of medical devices are to:-

- maintain records of complaint reports and of actions taken in response to these reports, and produce such records for inspection by the Regulatory Authority in the Member State or an enforcement officer as and when required; and
- establish and implement documented procedures to conduct effective and timely investigations of reported problems.

Adverse events

A number of post-marketing risk assessment measures to ensure the continued safe use of medical devices. These measures include reporting from healthcare professionals, mandatory reporting from medical device dealers, and exchange of regulatory information with other medical device regulatory agencies.

The mandatory reporting of AEs by medical device dealers is an important part of the post-market surveillance system. The objective of AE reporting and subsequent evaluations is to improve protection of the health and safety of patients, users and others by disseminating information that may reduce the likelihood of, or prevent repetition of AEs, or alleviate consequences of such repetition.

Field Safety Corrective Action (FSCA)

A FSCA is required when it becomes necessary for the product owner of the medical device to take action (including recall of the device) to eliminate, or

reduce the risk of, the hazards identified.

A FSCA may still be necessary even when the medical device is no longer on the market or has been withdrawn but could still possibly be in use (e.g. implants).

A FSCA only applies to a medical device that has already been distributed by the product owner. It does not arise when a product owner is exchanging or upgrading medical devices in the absence of a safety risk or when removals from the market are for purely commercial reasons.

The physical manufacturer, authorised representative or authorised distributor in the Member State shall be responsible for physically performing and completing the FSCA in the Member State.

1.3. Scope

This document applies to all medical devices, including in-vitro diagnostic products.

1.4. Definitions

MEDICAL DEVICE: means a medical device as described in the ASEAN Medical Device Agreement (AMDD).

PRODUCT OWNER: means a natural or legal person who supplies a medical device under his own name, or under a trade-mark, design, trade name or other name or mark owned or controlled by the person, and who is responsible for one or more of the following activities:- designing, manufacturing, assembling, processing, labelling, packaging, refurbishing or modifying the device, or for assigning to it a purpose, whether those tasks are performed by that person or on his behalf.

AUTHORISED REPRESENTATIVE (as set out in the AMDD): in relation to a registered health product, means the person who applied for and obtained the registration of the health product under the AMDD.

CUSTOMER COMPLAINT: any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety or performance of a medical device that has been placed on the market.

IN-VITRO DIAGNOSTIC PRODUCT (also referred to as 'IVD medical device'): means any reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination with any other reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, that is intended by its product owner to be used *in vitro* for the examination of any specimen, including any blood or tissue donation, derived from the human body, solely or principally for the purpose of providing information —

- concerning a physiological or pathological state or a congenital abnormality;
 - to determine the safety and compatibility of any blood or tissue donation with a potential recipient thereof; or
 - to monitor therapeutic measures; and
- includes a specimen receptacle;

ADVERSE EVENT: Is either a malfunction or a deterioration in the characteristics or performance of a supplied medical device or use error, which either has caused or could have caused or contributed to death, or injury to health of patients or other persons.

FIELD SAFETY CORRECTIVE ACTION: an action taken by a product owner to reduce a risk of death or serious deterioration in the state of health

associated with the use of a medical device. This may include:-

- the return of a medical device to the product owner or its representative;
- device modification;
- device exchange;
- device destruction;
- advice given by product owner regarding the use of the device.

Such device modifications may include:-

- retrofit in accordance with the product owner's modification or design change;
- permanent or temporary changes to the labelling or instructions for use;
- software upgrades including those carried out by remote access;
- modification to the clinical management of patients to address a risk of serious injury or death related specifically to the characteristics of the device.

In assessing the need of the FSCA, the product owner is advised to use the methodology described in ISO 14971:2007.

FIELD SAFETY NOTICE (FSN): A communication sent out by a product owner or its representative to the device users in relation to a FSCA.

PHYSICAL MANUFACTURER: means a physical manufacturer as described in the ASEAN Medical Device Agreement (AMDD).

AUTHORISED REPRESENTATIVE: means an authorised representative as described in the ASEAN Medical Device Agreement (AMDD).

AUTHORISED DISTRIBUTOR: means an authorised distributor as described in the ASEAN Medical Device Agreement (AMDD).

2. DISTRIBUTION RECORDS

2.1. Responsibility for keeping distribution records

The physical manufacturer, authorised representative and authorised distributor in the Member States shall be required to:-

- establish and implement documented procedures for distribution records;
- maintain a distribution record of each medical device.

Distribution records should be maintained for all medical devices, including low risk medical devices that may be exempted from product registration.

2.2. Necessity of distribution records

Keeping distribution records will facilitate the accountability and traceability of a medical device. This ensures that the medical device distribution channels in Member States.

Distribution records of the medical devices are required to:-

- expedite any recalls of batches of the medical devices;
- identify the manufacturer of each batch of the medical devices;
- identify where each batch of the medical devices is supplied.

2.3. Information to be retained as distribution records

The distribution record should contain sufficient information to permit complete and rapid withdrawal of the medical device from the market, where necessary.

Information may include:-

- name and address of initial consignee;
- identification and quantity of medical devices shipped;
- date shipped;

- any control number(s) used, including lot / batch / serial number of the medical device.

2.4. Retention period for distribution records

The distribution record maintained with respect of a medical device should be retained for the longer of one of the following:-

- the projected useful life of the medical device as determined by the product owner;
- two years after the medical device is shipped.

NOTE: The projected useful life of a medical device may be based on technical, legal, commercial or other considerations. Product owners may refer to ISO/TR 14969 Medical devices - Quality management systems - Guidance on the application of ISO 13485:2003 for some of the considerations when defining the lifetime of their medical device.

For medical devices that are imported for export only, it is two years after the date the medical device is shipped out of the Member State.

2.5. Records maintenance

Distribution records should be maintained in a manner that will allow their timely retrieval.

2.6. Records of implant

The distribution record maintained should also contain a record of the information of the implant when supplied by a healthcare facility.

3. COMPLAINT RECORDS

The records on complaints related to a medical device may include the following information:-

- the device brand name, licence number, model/catalogue number or bar code, control/serial/lot number and any other means of identification of the device;
- the name(s) and address(es) of the manufacturer, importer, wholesaler and/or registrant;
- records pertaining to the problem investigation.

All actions taken by the physical manufacturer, authorised representative, and authorised representative in response to the problems and complaints must be kept on record. These actions include any communications with the reporter/complainant, the evaluation of the problem/complaint, and any steps taken to correct the problem or prevent the recurrence of the problem. Such steps might include increased post-market surveillance of the medical device, corrective and preventive action with respect to the design and manufacture of the medical device, or product recall.

Attention should also be given to identifying the development of patterns or trends in problems with medical devices. The report of an isolated incident would assume much greater significance if other similar occurrences were reported.

3.1. Complaint handling procedure

Physical manufacturers, authorised representative and authorised distributors should have in place a written procedure for complaint handling that outlines the steps to be taken once a complaint report is received. The procedure should identify the personnel involved, and describe their functions and responsibilities.

In addition, the procedure should explain how to maintain records of the complaint reports, and where appropriate, how to assess these records and a reasonable time frame for completion of the investigation.

The procedure may contain the following:-

- determination of whether there is a health hazard associated with the medical device;
- determination of whether the medical device fails to conform to any claim made by the manufacturer, importer, wholesaler or registrant relating to its effectiveness, benefits, performance characteristics or safety;
- determination of whether the medical device fails to meet any legislative requirements;
- determination of the most appropriate preventive/corrective action; and
- justification when no action is taken, for example, in the case of receiving an unfounded or invalid complaint.

3.2. Retention of complaint records

Complaint records maintained with respect to a medical device should be retained for a period of five years on top of the projected useful life of the medical device as determined by the product owner. For example, if the projected useful life of the medical device is one year, the complaint records should be kept for six years.

4. ADVERSE EVENTS

4.1. Adverse event (AE) reportability criteria

As a general principle, there should be a pre-disposition to report rather than not to report in case of doubt on the reportability of an AE. Any AE, which meets the three basic reporting criteria listed below, is considered as a reportable AE. The criteria are that:-

- an AE has occurred;
- the medical device is associated with the AE;
- the AE led to one of the following outcomes;
 - a serious threat to public health;
 - death of a patient, user or other person;
 - serious deterioration in state of health, user or other person;
 - no death or serious injury occurred but the event might lead to death or serious injury of a patient, user or other person if the event recurs.

An event or other occurrence relating to a medical device represents a serious threat to public health if one or more of the following occur:-

- the event or other occurrence is a hazard arising from a systematic failure of the medical device that becomes known to the manufacturer, importer or wholesaler of the medical device;
- the event or other occurrence may lead to the death of, or a serious injury to, a patient, a user of the medical device or any other person;
- the probable rate of occurrence of or degree of severity of harm caused by the hazard was not previously known or anticipated by the product owner of the medical device;
- it becomes necessary for the product owner of the medical device to take prompt action (including the recall of the medical device) to eliminate or reduce the risk of the hazard.

A serious deterioration in state of health can include:-

- life-threatening illness or injury;
- permanent impairment of a body function or 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.

Not all AEs that should be reported involve a death or serious deterioration in health that actually occurred. The non-occurrence of an adverse effect might have been due to other fortunate circumstances or to the timely intervention of health-care personnel. In such cases, it is sufficient that either:-

- an AE associated with a medical device happened, and the AE was such that, if it occurred again, it might lead to death or serious deterioration in health; or
- testing, examination of the medical device, information supplied with the medical device, or any scientific literature indicated some factor (e.g. a deterioration in characteristics or performance, or a shortcoming in the information) which could lead to an AE involving death or serious deterioration in health.

For In Vitro Diagnostic (IVD) medical devices, it would be sufficient that:-

- an AE associated with an IVD medical device occurred, and
- the AE might lead to death or serious deterioration in health if it happens again;

for the adverse event to become reportable.

In assessing the type of AE, medical practitioner involved or other health-care professional should be consulted wherever practicable.

All persons who place medical devices on the markets of Member States should be vigilant for any changes in trends or frequency of occurrences of AEs with regards to medical devices they deal in.

4.2. Adverse events involving In vitro diagnostic devices

Most IVD medical devices do not come into contact with patients and so it is not easy to establish direct harm to patients, unless the IVD medical device itself causes deterioration in the state of health in a patient. However, an adverse event involving an IVD medical device could result in indirect harm as a result of an action taken or not taken on the basis of an incorrect reading obtained with an IVD medical device.

There should always be a predisposition to report even though it may not be easy to establish that a serious deterioration in the state of a patient's health was the result of an erroneous test result obtained with an IVD medical device, or if the harm was the result of an error by the user or third party.

Information supplied by the product owner when inadequate, can lead users, patients or third parties to harm and should be reported. For self-testing IVD medical devices, where a medical decision may be made directly by the user who is the patient, insufficient information on the product presentation could lead to an incorrect use of the IVD medical device or a misdiagnosis. Hence, AEs involving IVD medical devices will most likely result from a consequence of a medical decision or action taken, or not taken, on the basis of result(s) provided by the IVD medical device.

Examples of these types of AEs include (non-exhaustive list):-

- misdiagnosis;
- delayed diagnosis;
- delayed treatment;

- inappropriate treatment;
- transfusion of inappropriate materials.

AEs for IVD medical devices may arise due to (non-exhaustive list):-

- shortcomings in the design or manufacture of the IVD medical device itself;
- inadequate instructions for use;
- inadequate servicing and maintenance;
- locally initiated modifications or adjustments;
- inappropriate user practice;
- inappropriate management procedures;
- inappropriate environment in which an IVD medical device is used or stored;
- selection of the incorrect IVD medical device for the purpose.

4.3. Adverse Event Reporting Timeline

All AEs should be reported immediately and

- not later than 48 hours for events that represents a serious threat to public health;
- not later than 10 days for events that has led to the death, or a serious deterioration in the state of health, of a patient, a user of the medical device or any other person;
- not later than 30 days for events where 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 medical device or any other person

The clock for reporting starts as soon as any personnel of the medical device dealers, including sales representatives, is made aware of the AE. If there is uncertainty about whether the AE is reportable, dealers should still submit a report within the timeframe stipulated.

Dealers should not unduly delay the reporting of AE(s) if information is incomplete. The initial report of an AE should contain as much relevant detail as is immediately available, but should not be delayed for the sake of gathering additional information.

Dealers of medical devices are to follow up with a final report within 30 days of the initial reports, detailing the investigation into the AE. If the final report is not available within 30 days, a follow-up report is to be submitted. Follow-up reports may be requested as and when necessary.

4.4. Reporting obligations

All physical manufacturers, authorised representative and authorised distributors shall be required to report AEs involving medical devices, which they have placed on the market in the Member State.

Reports should be submitted using the prescribed format of the regulatory authority of the Member State, which may follow the ASEAN AE Report Form (Reference No. ASEAN-MDAR).

5. FIELD SAFETY CORRECTIVE ACTION (FSCA)

5.1. Determining the need for a field safety corrective action

The product owner of the medical device in question is responsible for determining the need for a FSCA. In accessing the need for an FSCA, the product owner should perform a risk assessment in accordance to ISO 14971:2007. If the risk assessment performed by the product owner is deemed deficient by the regulatory authority of the Member State, the regulatory authority of the member state may instruct the relevant companies and persons who placed the medical device in the market of the Member State to take additional measures to safeguard public health.

FSCA may be triggered when information from the product owner's post market surveillance (including product complaints, adverse incidents, etc) indicates an unacceptable increase in risk.

On occasions, the regulatory authority may advise product owners or their representative to implement a FSCA in relation to a medical device due to risk of serious injury or death to patients, users or others. Such risks are usually identified through adverse events reports or other means.

In certain cases it may be necessary to use precautionary measures in the interest of public health and restrict or prohibit products subject to particular requirements. In other cases, for safety reasons, it may be necessary to remove a medical device from the market.

5.2. Notification of field safety corrective action

When the product owner or its representative decides to initiate a FSCA, he shall notify the regulatory authority.

The time frame for notification of an FSCA shall be prescribed by the regulatory authority of the Member State.

All notification and reports are to be submitted in the manner that the regulatory authority prescribes.

5.3. Information to be provided

When the need for an FSCA has been established, the product owner or its representative should gather all relevant information on incident reports, the product and its distribution, and the action proposed. Some information may not be available immediately (e.g. distribution chains, batch size etc). Notification to the regulatory authority in the Member State should not be delayed pending collation of these data.

Reports should be submitted using the prescribed format of the regulatory authority of the Member State, which may follow the ASEAN FSCA Report Form (Reference No. ASEAN-MDFR).

5.4. Closure of FSCA

On completion of a FSCA, the product owner or its representative should provide details to the regulatory authority of the Member State of the proposed corrective action to prevent recurrence of the problem that give rise to the FSCA.

The FSCA will only be closed when all appropriate corrective actions have been undertaken, subject to the concurrence of the regulatory authority of the Member State.

ANNEX 6

Components Elements of a Product owner's Declaration of Conformity (DOC)

1. COMPONENTS OF A DECLARATION OF CONFORMITY

The DOC shall contain the following information:-

- an attestation that each medical device that is subject to the declaration
 - complies with the applicable Essential Principles for Safety and Performance, and
 - has been classified according to the classification rules;
- information sufficient to identify the device/s to which the DOC applies;
- the risk class allocated to the device/s after following the guidance found in Principles of Medical Device Classification;
- the date from which the DOC is valid;
- the name and address of the product owner;
- quality management standards;
- medical device standards (product standards²);
- the name, position and signature of the responsible person who has been authorised to complete the DOC upon the product owner's behalf.

2. RESPONSIBILITY FOR PREPARING THE DECLARATION OF CONFORMITY

The product owner of the medical device or a person authorised by the product owner is responsible for preparing and signing the DOC. The hardcopy of the DOC should be signed and dated. The signed and dated hardcopy should be part of product registration. The original signed copy of the DOC should be made available to the regulatory authority of a Member

² Standards may include international (e.g. ISO, IEC), regional (e.g. CEN) and national (e.g. SS, ASTM, BS) standards.

State upon request. A Member State may impose additional measures (e.g. legalisation or notarisation) to be undertaken to ensure the authenticity of a DOC submitted to the regulatory authority of that Member State.

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3. TEMPLATE FOR DECLARATION OF CONFORMITY

[To be printed on Company Letterhead of Product Owner]

Name and Address of Product Owner:

We hereby declare that the below mentioned devices have been classified according to the classification rules and conform to the Essential Principles for Safety and Performance as laid out in the *[state the applicable statute of the Member State]*.

Authorised Representative (if required by a particular Member State):

< Local authorised representative responsible for placing the medical device on the market of the ASEAN Member State >

Manufacturing Site:

< Person responsible for manufacturing the medical device >

Medical Device(s):

< e.g. product name and model number >

Risk Classification: e.g. Class B, rule

< Class of Device according to the classification rule, and the rule used to determine the classification >

Quality Management System Certificate:

< Certification Body and Certificate Number, issue date, expiry date >

Standards Applied:

< International standards; OR Regional Standard; OR See Attached Schedule for multiple standards >

This declaration of conformity is valid from <Day Month Year>

Authorised Signatory:

Name, Position

Date

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ANNEX 7

Component Elements Of A Dear Healthcare Professional Letter

1. DEFINITIONS

“DEAR HEALTHCARE PROFESSIONAL” LETTER: A letter drafted by dealers of medical devices addressed to doctors, pharmacists, and healthcare professionals regarding important new medical device issues, e.g., new warnings, other safety information, or other important changes to the prescribing information (labelling). In essence, it is commonly issued to communicate risk to medical device users, typically in response to an adverse event or to provide an update on safer use of medical device. Such letters may also be known as “Dear Doctor” letters.

2. COMPONENT ELEMENTS OF A “DEAR HEALTHCARE PROFESSIONAL” LETTER

The following components shall be included in a “Dear Healthcare Professional” letter:-

2.1. Name of product owner

The product owner is the natural or legal person with responsibility for the design, manufacture, packaging and labelling of a medical device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party.

2.2. Name & Contact Details of the Authorised Representative

An authorised representative is any natural or legal person established in an ASEAN member state who, explicitly designated by the product owner, acts on behalf of the product owner to fulfill regulatory obligations.

In cases where the product owner is based outside a Member State, the Regulatory Authority has to be able to contact an entity or person who is based within that Member State, and who has been appointed by the product owner to act on his behalf.

Contact information of the product owner or authorised representative should be provided to allow recipients to obtain any additional information.

2.3. Affected Medical Device Proprietary Name

Medical Device Proprietary Name is the name of the medical device as it appears on the medical device label.

2.4. Affected Device Intended Use and Indications

This paragraph should contain the statement of intended use and any indications relevant to the adverse event. In addition, it should contain relevant information on the device family or models affected, batch number, etc.

2.5. Subject Matter of the Letter

Association of [Medical Device Proprietary Name] with [specific adverse event].

2.6. Problem Identified & Description of Health Risk

This paragraph should contain a description of the health risk and any problems identified thus far. For example, it can contain:-

- any adverse events reported;
- their seriousness (e.g., hospitalisation, transplantation, fatality, etc);

- the rationale for suspecting a causal relationship or causative factor (e.g., pharmacodynamic mechanism, temporal relationship, etc);
- whether the event is linked to an “unapproved” indication or “unapproved” condition of use;
- specify what is known about the adverse event and how likely sensitive populations within the general public (e.g., children or the elderly) are affected;
- indicate how reliable the knowledge is on which the communication is based;
- indicate whether the quality of this knowledge is expected to improve (e.g. through further research) and who is responsible for improving it;
- provide a qualitative description of the uncertainties that may exist in the base of knowledge from which the content of the communication is drawn. Indicate what further steps may reduce these uncertainties;
- provide a qualitative and quantitative description of the estimates of probability; and
- the number of events of interest reported domestically and internationally with estimations of patient exposure.

NOTE: This is not an exhaustive list.

2.7. Suggested Actions & Recommendations

This paragraph recommends actions to be taken, and should provide justifications (if any) for these recommendations:-

- highlight contraindications relevant to the adverse event(s);
- reinforce warnings relevant to the adverse event(s), (e.g., comprehensive list of signs, symptoms, laboratory findings, clinical outcome, laboratory monitoring, risk factors);
- provide an extended list of possible known adverse reactions to be expected or likely to occur;

- provide information for the consumer (e.g., description of risk and possible consequences, warnings regarding prodromal symptoms);
- indicate what is thought to be an acceptable level of risk for the issue described in the communication. Provide a justification for this acceptable level; and
- provide a clear description of the actions taken to mitigate the risk. Provide a compelling justification for the action that was taken;
- provide details on any ongoing or pending field safety corrective action(s) (if any), as well as issues (if any) related to modification, replacement, medical device update, warranty, etc.

Generally, this paragraph should include additional detailed instructions on how to use the current disseminated safety or therapeutic effectiveness information.

2.8. Signatory for the Letter

The letter should be dated and should contain the name and designation of the signatory.

ANNEX 8

Sample Template of Letter of Authorisation

[To be printed on Company Letterhead of Product Owner]

To: [Regulatory Authority of Member State]
[Medical Device Centre]
[Medical Device Authority]

[Date]

Dear Sir/Madam,

Subject: Letter of Authorisation for *[name of Registrant]*

We, *[name of Product owner]*, as the Product owner, hereby authorise *[name of Authorised Representative in a Member State]*, as the Authorised Representative to prepare and submit applications for the evaluation and registration of medical devices to the *[name of Regulatory Authority of a Member State]* on our behalf.

This authorisation shall apply to the following medical devices:

[List containing product names of medical devices]

We also authorise *[name of Authorised Representative in a Member State]* to make declarations and to submit documents on our behalf, regarding the above medical devices, in support of this application. These declarations and submissions are made pursuant to the requirements of the ASEAN Medical Device Agreement, the *[state the applicable statute of the Member State]* and any other applicable laws that may also be in force.

Yours Sincerely,

[Signature]

[Full Name and Title of Senior Company Official]

[Company stamp]

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ANNEX 9

Labelling Requirements

1. DEFINITIONS

CLINICAL INVESTIGATION: Any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device.

Explanation: This term is synonymous with 'clinical trial' and 'clinical study'. Clinical investigations include feasibility studies and those conducted for the purpose of gaining market approval, as well as investigations conducted following marketing approval.

Routine post market surveillance may not constitute a clinical investigation (e.g. investigation of complaints, individual vigilance reports, literature reviews).

LABEL: Written, printed or graphic information provided upon the medical device itself. Where physical constraints prevent this happening, this term includes information provided on the packaging of each unit or on the packaging of multiple devices.

LABELLING: Written, printed or graphic matter

- affixed to a medical device or any of its containers or wrappers, or, accompanying a medical device,
- related to identification, technical description, and use of the medical device, but excluding shipping documents.

INSTRUCTIONS FOR USE: Information provided by the product owner to inform the device user of the product's proper use and of any precautions to

be taken.

INTENDED PURPOSE: The use for which the medical device is intended according to the specifications of its product owner as stated on any or all of the following:

- the label of the medical device;
- the instructions for use of the medical device;
- the promotional materials in relation to the medical device.

MEDICAL DEVICE: means a medical device as described in the ASEAN Medical Device Agreement.

PERFORMANCE EVALUATION: Review of the performance of a medical device based upon data already available, scientific literature and, where appropriate, laboratory, animal or clinical investigations.

REFURBISHED MEDICAL DEVICE: a medical device of which the whole or any part thereof has been substantially rebuilt, whether or not using parts from one or more used medical devices of that same kind, so as to create a medical device that can be used for the purpose originally intended by the product owner of the original medical device, and which may have had the following work carried out on it:

- stripping into component parts or sub-assemblies;
- checking their suitability for reuse;
- replacement of components/sub-assemblies not suitable for reuse;
- assembly of the reclaimed and/or replacement components/sub-assemblies;
- testing of the assembled device against either original or revised release criteria; or
- identifying an assembled medical device as a refurbished medical device.

RESEARCH USE ONLY: Research use only is where the device is made available to institutions/laboratories to be subject to studies intended for collation of data only. The product is not intended for any medical purpose or objective.

2. LABELLING REQUIREMENTS

2.1 General Requirements

- As far as it is practical and appropriate, the information needed to identify and use the device safely should be provided on the device itself, and /or on the packaging for each unit (primary level of packaging), and / or on the packaging of multiple devices (secondary level of packaging). If individual packaging of each unit is not practicable, the information should be set out in the leaflet, packaging insert or other media supplied with, or applicable to, one or multiple devices.
- Where the product owner supplies multiple devices to a single user and/or location, it may be sufficient and appropriate to provide with them only a single copy of the instructions for use. In these circumstances the device user should have access to further copies upon request.
- The medium, format, content, readability and location of labelling should be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use should be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams. Some devices may require separate information for the healthcare professional and the lay user.
- Instructions for Use (IFU) may not be needed or may be abbreviated for devices of low or moderate risk if they can be used safely and as intended by the product owner without any such instructions.
- Paper versions of all labelling must accompany the product.

- Any residual risk identified in the risk analysis should be reflected as contraindications or warnings within the labelling.
- The use of internationally recognised symbols is encouraged provided that device safety is not compromised by a lack of understanding on the part of the patient or user. Where the meaning of the symbol is not obvious to the device user, e.g. for a lay-user or for a newly introduced symbol, an explanation should be provided.
- All characters on labelling must be of adequate size and legibly printed.

2.2 Content of Labelling

2.2.1 Primary and Secondary Levels of Packaging

Contact Information

It is mandatory to include the name and contact details (address and/or phone number and/or fax number and/or website address to obtain technical assistance) of the product owner on the labelling.

General

The labelling for all medical devices should bear the following:

- Sufficient details for the user to identify the device and, where these are not obvious, its intended purpose, user and patient population of the device; also, where relevant, the contents of any packaging.
- An indication of either the batch code/lot number (e.g. on single-use disposable devices or reagents) or the serial number (e.g. on electrically-powered medical devices), where relevant, to allow appropriate actions to trace and recall the devices.
- An unambiguous indication of the date until when the device may be used safely, expressed at least as the year and month (e.g. on devices supplied sterile, single-use disposable devices or reagents), where this is relevant. Where relevant, the storage conditions and shelf life following the first opening of the primary container, together with the storage conditions and

stability of working solutions. For devices other than those covered by the above, and as appropriate to the type of device, an indication of the date of manufacture. This indication may be included in the batch code/lot number or serial number.

- The information needed to verify whether the device is properly installed and can operate correctly and safely, including details of the nature, and frequency of preventative and regular maintenance, where relevant any quality control, replacement of consumable components, and calibration needed to ensure that the device operates properly and safely during its intended life.
- Any warnings, precautions, limitations or contra-indications.
- The performance intended by the product owner and, where relevant, any undesirable side effects.
- An indication on the external packaging of any special storage and /or handling conditions that applies.
- Details of any further treatment or handling needed before the device can be used (e.g. sterilization, final assembly, calibration, preparation of reagents and/or control materials, etc.) where relevant.

The inclusion of the manufacturing site of the medical device and contact information of the importer is optional.

*NOTE: Please note that "manufactured/made in Country X" or other similar wording can only be printed on the labels if there is significant processing of the products in Country X. The following are **excluded**: simple operations consisting of removal of dust, sifting or screening, sorting, classifying, matching (including the making up of sets of articles), washing, painting, cutting up; changes of packing and breaking up and assembly of consignments; simple placing in bottles, flasks, bags, cases, boxes, fixing on cards or boards, and all other simple packing operations; the affixing of marks, labels or other like distinguishing signs on products or their packaging; etc.*

Additional Requirements

The labelling for some medical devices should contain the following additional information:

- If the device is **sterile**, an indication of that condition and necessary instructions in the event of damage to sterile packaging and, where appropriate, description of methods of re-sterilization.
- If the device has been specified by the product owner as intended for **single-use only**, an indication of that state.
- If the device is **reusable**, information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging and, where appropriate, the method of re-sterilization and any restriction on the number of reuses. Where a device is supplied with the intention that it is sterilized before use, the instructions for cleaning and sterilization should be such that, if correctly followed, the device will still perform as intended by the product owner and comply with the *Essential Principles of Safety and Performance of Medical Devices* in the ASEAN Medical Device Agreement (AMDD).
- If the device is a **refurbished** device, identification of the device as a refurbished device.
- If the device is for use by a single individual and has been manufactured according to a written prescription or pattern (i.e. it is **custom-made**), an indication of that state.
- If the device is intended for **clinical investigation** or, for in vitro diagnostic medical devices, **performance evaluation** only, an indication of that situation.
- If the device is intended for **research use** only, it must be labelled as “research use only”.
- If the device is intended for **presentation or demonstration purposes** only, it must be labelled as “for presentation or demonstration purposes only: not for use on humans”.

- If the device is **implantable**, information regarding any particular risks in connection with its implantation.
- If the device **emits radiation** for medical purposes, details of the nature, type and where appropriate, the intensity and distribution of this radiation.
- Information regarding the risks of reciprocal interference posed by the reasonably foreseeable presence of the device during specific investigations, evaluations, treatment or use (e.g. electromagnetic interference from other equipment).
- If the device is to be installed with or connected to other medical devices or equipment, or with dedicated software, in order to operate as required for its intended use, sufficient details of its characteristics to identify the correct devices or equipment to use in order to obtain a safe combination.
- If the device is an **in vitro diagnostic** medical device, it must be labelled as “in vitro diagnostic” or “IVD”.

2.2.2 Instructions For Use (IFU)/ Patient Information Leaflet

For medical devices where an IFU or a patient information leaflet is applicable, the following additional information should be contained therein:

- Date of issue or latest revision of the instructions for use and, where appropriate, an identification number.

The instructions for use should also include, where appropriate, details informing the users and/or patient and allowing the medical staff to brief the patient on any contra-indications, warnings and any precautions to be taken.

These details should cover in particular:

- Precautions and/or measures to be taken in the event of changes in the performance, or malfunction, of the device including a contact telephone number, if appropriate.
- Precautions and/or measures to be taken as regards exposure, in reasonably foreseeable environmental conditions, to magnetic fields,

external electrical influences, electrostatic discharge, pressure or variations in pressure, temperature, humidity, acceleration, thermal ignition sources, proximity to other devices, etc.

- If the device administers medicinal products, adequate information regarding any medicinal product(s) which the device in question is designed to administer, including any limitations in the choice of substances to be delivered.
- Any medicinal substances or biological material incorporated into the device as an integral part of the device.
- If the device has a measuring function, the degree of accuracy claimed for it.
- Any requirement for special facilities, or special training, or particular qualifications of the device user and/or third parties.
- Any precautions to be taken related to the disposal of the device and/or its accessories (e.g. lancets), to any consumables used with it (e.g. batteries or reagents) or to any potentially infectious substances of human or animal origin.
- Where relevant, for devices intended for lay persons a statement clearly directing the user not to make any decision of medical relevance without first consulting his or her health care provider.

In-vitro Diagnostic Products

For *in-vitro* diagnostic products, in addition to the information required above, directions/instructions for the proper use of *in vitro* diagnostic medical devices that should be contained in the labelling include:-

- (a) Intended purpose, including the following information:-
- Type of analyte or measurand of the assay.
 - Whether the test is quantitative or qualitative.
 - Role of the test in the clinical use e.g. screening, diagnostic or detection, aid to diagnostic, monitoring.

- Disease or condition that the test is intended for.
 - Type of specimen to be used e.g. serum, plasma etc.
 - The intended users (e.g. self-testing by lay person, near-patient by trained personnel or professionals).
 - Assay type e.g. immunoassay, chemistry, cytochemistry, image analysis, immunohistochemistry.
 - The specific name of the instrument required for the assay, if any.
 - For instruments, the intended use should also include the modes of operation for instruments e.g., random access, batch, stat, open tube, closed tube, automatic, manual.
- (b) Test principle.
- (c) Specimen type.
- (d) Conditions for collection, handling, storage and preparation of the specimen.
- (e) Reagent description and any limitation (e.g. use with a dedicated instrument only).
- (f) The metrological traceability of values assigned to calibrators and trueness-control materials, including identification of applicable reference materials and/or reference measurement procedures of higher order.
- (g) Assay procedure including calculations and interpretation of results.
- (h) Information on interfering substances that may affect the performance of the assay.
- (i) Performance characteristics (summarized analytical and diagnostic sensitivity, specificity, reproducibility, etc.),
- (j) Reference intervals.
- (k) Study design (population studies, N, type of sample, matrix, dilution, target concentrations, etc).

ANNEX 10

Clinical Investigation – Pre-market Clinical Investigation to Support Marketing Authorisation Application

1. INTRODUCTION

A clinical investigation is a systematic investigation or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device.”

The undertaking of a clinical investigation is a scientific process that represents one method of generating clinical data.

The objective of a clinical investigation is to evaluate whether the device is suitable for the purpose(s) and the population(s) for which it is intended.

In general, clinical investigations must take into account scientific principles underlying the collection of clinical data along with accepted ethical standards surrounding the use of human subjects. The clinical investigation objectives and design should be documented in a clinical investigation plan.

While clinical evidence is an essential element of the pre-market conformity assessment process to demonstrate conformity to Essential Principles, it is important to recognise that there may be limitations in the clinical data available in the pre-market phase. Such limitations may be due to, for example, the duration of pre-market clinical investigations, the number of subjects involved in an investigation, the relative homogeneity of subjects and investigators and the control of variables in the setting of a clinical investigation versus use in the full range of conditions encountered in general medical practice.

It is appropriate to place a product on the market once conformity to the relevant Essential Principles, including a favourable risk/benefit ratio, has been demonstrated. Complete characterization of all risks may not always be possible or practicable in the pre-market phase. Therefore, there may be questions regarding residual risks that should be answered in the post-market phase through the use of one or more systematic post-market clinical follow-up studies. Such studies are not intended to substitute or duplicate but rather supplement the pre-market clinical evaluation.

Post-market clinical follow-up studies are one of several options available in a post-market surveillance programme and contribute to the risk management process.

2. SCOPE

The primary purpose of this Annex is to provide guidelines in relation to:

- when a clinical investigation should be undertaken for a medical device to demonstrate compliance with the relevant Essential Principles (see Annex 1 “*Essential Principles of Safety and Performance of Medical Devices*”), and
- the general principles of clinical investigations involving medical devices.
- post-market clinical follow-up studies developed specifically for issues of residual risk (including those mandated by regulation).
- the circumstances where a post-market clinical follow-up study is indicated;
- the general principles of post-market clinical follow-up studies involving medical devices; and
- the use of study information.

This Annex is intended to apply to medical devices generally and the device component of combination products, to address the use of Clinical

Investigations to support a marketing authorization application. It is not intended to cover In Vitro Diagnostic products.

3. DEFINITIONS

CLINICAL DATA: Safety and/or performance information that are generated from the clinical use of a medical device.

CLINICAL EVALUATION: The assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the product owner.

CLINICAL EVIDENCE: The clinical data and the clinical evaluation report pertaining to a medical device.

CLINICAL INVESTIGATION: Any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device.

CLINICAL INVESTIGATION PLAN: Document that states the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical investigation.

CLINICAL PERFORMANCE: The ability of a medical device to achieve its intended purpose as claimed by the product owner.

CLINICAL SAFETY: The absence of unacceptable clinical risks, when using the device according to the product owner's Instructions for Use.

CONFORMITY ASSESSMENT: The systematic examination of evidence generated and procedures undertaken by the product owner, under

requirements established by the Regulatory Authority, to determine that a medical device is safe and performs as intended by the product owner and, therefore, conforms to the *Essential Principles of Safety and Performance for Medical Devices (Annex 1)*.

DEVICE REGISTRY: An organized system that uses observational study methods to collect defined clinical data under normal conditions of use relating to one or more devices to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure and that serves (a) predetermined scientific, clinical or policy purpose(s).

NOTE: *The term “device registry” as used here should not be confused with the concept of device registration and listing.*

ENDPOINT: Indicators measured or determined to assess the objectives of a clinical investigation, prospectively specified in the clinical investigation plan.

POST-MARKET CLINICAL FOLLOW-UP STUDY: A study carried out following marketing approval intended to answer specific questions relating to clinical safety or performance (i.e. residual risks) of a device when used in accordance with its approved labelling. These may examine issues such as long-term performance, the appearance of clinical events (such as delayed hypersensitivity reactions or thrombosis), or events specific to defined patient populations.

RESIDUAL RISK: Risk remaining after risk control measures have been taken (e.g. known or emerging risks, or potential risks due to statistical limitations).

RISK MANAGEMENT: The systematic application of management policies, procedures and practices to the tasks of analysing, evaluating, controlling and monitoring risk.

4. GENERAL PRINCIPLES WHEN CONSIDERING THE NEED FOR A CLINICAL INVESTIGATION

4.1. Circumstances Where a Pre-market Clinical Investigation is Needed

Clinical investigations are necessary to provide the data not available through other sources (such as literature or preclinical testing) required to demonstrate compliance with the relevant Essential Principles (including safety, clinical performance and acceptability of risk/benefit ratio associated with its use). When a clinical investigation is conducted, the data obtained is used in the clinical evaluation process and is part of the clinical evidence for the device.

Crucial steps in clarifying the need for clinical investigations

- (i) Identifying relevant clinical **Essential Principles** (for example, specifics of safety, clinical performance, acceptability of risk/benefit-ratio) for the device and its intended use/purpose(s) and use(s) (see Annex 1 – *Essential Principles of Safety and Performance of Medical Devices*);
- (ii) Perform **risk management** activities to help in identifying the clinical data necessary to control residual risks and aspects of clinical performance not completely resolved by available information e.g. design solutions, preclinical and material/technical evaluation, conformity with relevant standards, labelling, etc.;
- (iii) Conduct a proper **clinical evaluation** to demonstrate which clinical data are necessary and can be adequately contributed to by other methods, such as literature searching, prior clinical investigations or clinical experience, and which clinical data remain to be delivered by clinical investigation(s). Available clinical data for comparator devices should be

carefully examined for comparability and adequacy.

The steps are applicable for the introduction of a new device as well as for planned changes of a device, its intended use and/or claims.

4.2. Role of risk analysis

A properly conducted risk analysis is essential in determining what clinical evidence may be needed for a particular device. A clinical investigation may be required when the currently available data from preclinical testing, and any prior clinical investigations or other forms of clinical data are insufficient to demonstrate conformity with the Essential Principles. This would be the case when the product owner's risk analysis and the clinical evaluation of a medical device for a particular intended use, including new claims, shows that there are residual risks, including aspects of clinical performance, that have not been adequately addressed by the available data and cannot be addressed through other methods.

"Residual risk" refers to the risk remaining after risk control measures have been taken. Risk control measures include inherent safety by design, protective measures in the medical device itself or in the manufacturing process, and information for safety. The decision to use a medical device in the context of a clinical procedure requires the residual risk to be balanced against the anticipated benefits of the procedure. A clinical investigation may be used to further elucidate the risk/benefit ratio in a defined patient population. For instance, risk can be measured through safety endpoints, and benefits may be measured through assessments of clinical performance. Residual risks that could require the use of a clinical investigation might be an unknown rate of device failure.

For long established technologies, clinical investigation data that might be

required for novel technologies may not be necessary. The available clinical data in the form of, for example, published literature, reports of clinical experience, post-market reports and adverse event data should, in principle, be adequate to establish the safety and performance of the device, provided that new risks have not been identified, and that the indications for use have not changed.

Where uncertainty exists as to whether current data are sufficient to demonstrate conformity with the Essential Principles, discussion with regulatory authorities may be appropriate.

4.3. Justification for the Need for a Clinical Investigation

In order to be justified and to avoid unnecessary experimentation on human subjects, the clinical investigation(s) must:

- be necessary (as assessed above);
- be designed properly (see Section on “ General Principles of Clinical Investigation Design”);
- be ethical (see Section on “Ethical Considerations for Clinical Investigations”);
- follow a proper risk management procedure to avoid undue risks; and
- be compliant with all applicable legal and regulatory requirements.

4.4. General Principles of Clinical Investigation Design

The design of the clinical investigation, including the study objectives and statistical considerations, should provide the clinical data necessary to address the residual risks, including aspects of clinical performance. Some factors that may influence the extent of data requirements include, but are not limited to, the following:-

- type of device and/or regulatory classification;
- novel technology/relevant previous experience;

- clinical application/indications;
- nature of exposure to the product, e.g.: surface contact, implantation, ingestion;
- risks inherent in the use of the product, e.g.: risk associated with the procedure;
- performance claims made in the device labeling (including instructions for use) and/or promotional materials;
- component materials;
- disease process (including severity) and patient population being treated;
- demographic, geographic and cultural considerations (e.g.: age, race, gender, etc.);
- potential impact of device failure;
- period of exposure to the device;
- expected lifetime of the device;
- availability of alternative treatments and current standard of care; and
- ethical considerations.

As a general rule, devices based on new or “unproven” technology and those that extend the intended purpose of an existing technology through a new clinical use are more likely to require supporting clinical investigation data.

4.5. Specific Considerations for Device Study Designs

Device technologies have introduced a variety of complex challenges influencing the design of clinical investigations. Some of the factors that need to be considered include, for example:

- clear statement of objectives
- appropriate subject population(s)
- minimization of bias (e.g., randomization, blinding)
- identification of confounding factors (e.g., concurrent medications, co-morbidities)

- choice of appropriate controls (e.g., cohort, sham, historical), where necessary
- design configuration (e.g., parallel, crossover, factorial)
- type of comparison (e.g., superiority, non-inferiority, equivalence)
- Investigations should be planned in such a way as to maximize the clinical relevance of the data while minimizing confounding factors. Possible study designs include:
 - **randomized controlled trials** – clinical investigations where subjects are randomized to receive either a test or reference device or intervention and outcomes and event rates are compared for the treatment groups
 - **cohort studies** – data are obtained from groups who have and have not been exposed to the device (e.g. concurrent control) and outcomes compared
 - **case-control studies** – patients with a defined outcome and controls without the outcome are selected and information is obtained about whether the subjects were exposed to the device
 - **case series** – the device has been used in a series of patients and the results reported, with no control group for comparison
- In designing the study, statistical considerations should be prospectively specified and be based on sound scientific principles and methodology. Care must be taken in developing a statistical plan that includes consideration of, for example, the following:
 - clinically relevant endpoints
 - statistical significance levels, power
 - sample size justification
 - analysis methodology (including sensitivity and poolability analysis)
- The design should ensure that the statistical evaluation derived from the investigation reflects a meaningful, clinically significant outcome.

Discussion with regulatory authorities may be appropriate when there is

uncertainty as to whether the proposed clinical investigational plan is sufficient.

4.6. Conduct of Clinical Investigations

A properly conducted clinical investigation, including compliance to the clinical investigation plan and applicable local laws and regulations, ensures the protection of subjects, the integrity of the data and that the data obtained is acceptable for the purpose of demonstrating conformity to the Essential Principles.

4.7. Final Study Report

The outcome of a clinical investigation should be documented in a final study report. The final study report then forms part of the clinical data that is included in the clinical evaluation process and ultimately becomes integrated into the clinical evaluation report for the purposes of conformity assessment.

4.8. Ethical Considerations for Clinical Investigations

As a general principle, “the rights, safety and wellbeing of clinical investigation subjects shall be protected consistent with the ethical principles laid down in the Declaration of Helsinki”

Specific considerations may include:

- clinical investigations should be used only when appropriate data cannot be obtained through any other method, as it is desirable to minimize experimentation on human subjects;
- the design of the investigation and its endpoints should be adequate to address the residual risks including aspects of clinical performance;
- care must be taken to ensure that the necessary data are obtained through a scientific and ethical investigational process that does not expose

- subjects to undue risks or discomfort; and
- ethics review and regulatory body oversight occurs in conformity to local laws or regulations.

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5. CLINICAL INVESTIGATION - POST-MARKET CLINICAL FOLLOW-UP STUDIES

5.1. Circumstances Where A Post-Market Clinical Follow-Up Study Is Indicated

The need for post-market clinical follow-up studies should be determined from the identification of residual risks that may impact the risk/benefit ratio.

Circumstances that may result in the need for post-market clinical follow-up studies include, for example:

- innovation, e.g. where the design of the device, the materials, the principles of operation, the technology or the medical indications are novel;
- a new indication or claim has been approved;
- changes to device design or labelling;
- changes to medical practice;
- higher risk classification;
- high risk anatomical locations;
- severity of disease/treatment challenges;
- sensitivity of target population;
- identification of previously unstudied populations;
- risks identified from the literature or similar marketed devices;
- discrepancy between the pre-market follow-up time scales and the expected life of the product;
- unanswered questions of long-term safety and performance;
- results of any previous clinical investigation including adverse events identified or from post-market surveillance activities;
- questions of ability to generalise clinical investigation results; or
- emergence of new information relating to safety or performance.

Post-market clinical follow-up studies may not be required in cases where the

medium/long-term safety and clinical performance are already known from previous use of the device or where other appropriate post-market surveillance activities would provide sufficient data to address the risks.

5.2. Elements Of A Post-Market Clinical Follow-Up Study

Post-market clinical follow-up studies are performed on a device within its intended use/purpose(s) according to the instructions for use. It is important to note that post-market clinical follow-up studies must be conducted according to applicable laws and regulations, and should follow appropriate guidance and standards.

The elements of a post-market clinical follow-up study include:

- (a) clearly stated objective(s)
- a scientifically sound design with an appropriate rationale and statistical analysis plan
- a study plan
- implementation of the study according to the plan, an analysis of the data and appropriate conclusion(s)

5.2.1. The objective(s) of post-market clinical follow-up studies

The objective(s) of the study should be stated clearly and should address the residual risk(s) identified and be formulated to address one or more specific questions relating to the clinical safety or performance of the device.

5.2.2. The design of post-market clinical follow-up studies

Post-market clinical follow-up studies should be designed to address the objective(s) of the study. The design may vary based on the objective(s) and should be scientifically sound to allow for valid conclusions to be drawn.

The study design can take several forms, for example:

- the extended follow-up of patients enrolled in pre-market investigations;
- a new clinical investigation;
- a review of data derived from a device registry; or
- a review of relevant retrospective data from patients previously exposed to the device.

5.2.3. The post-market clinical follow-up study plan

All post-market clinical follow-up studies should have a plan appropriate for addressing the stated objectives. The study plan should justify, for example:

- the patient population;
- the selection of sites and investigators;
- the endpoints and statistical considerations;
- the number of subjects involved;
- the duration of the study;
- the data to be collected;
- the analysis plan including any interim reporting; and
- procedures for early study termination.

5.2.4. Implementation of the post-market clinical follow-up study, analysis of data and conclusion(s)

The study should:

- be executed with adequate control measures to assure compliance with the plan;
- include data analysis with conclusions drawn according to the analysis plan by someone with appropriate expertise; and
- have a final report with conclusions relating back to original objective(s).

5.3. The Use of Study Information

The data and conclusions derived from the post-market clinical follow-up

study are used to provide clinical evidence to support the post-market surveillance program. This process may result in the need to reassess whether the device continues to comply with the Essential Principles. Such assessment may result in corrective or preventive actions, for example, changes to the labelling/instructions for use, changes to manufacturing processes, or changes to the device design.

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