Guidelines relating to good distribution practice for distributors of medical devices.

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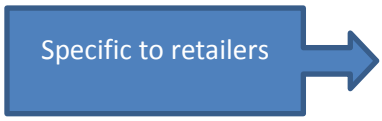
INTRODUCTION

The aim of this document is to allow for a high level of quality to be maintained throughout the medical device distribution network and the supply chain and to harmonise procedures for the inspection of distributors who distribute or deliver medical devices. All of the measures taken by operators applying the recommendations that appear in the guide aim to minimise the presence of non-compliant and of counterfeit medicinal devices in the distribution chain.

This guide applies to all distributors. However, specific information is provided to retailers who distribute medical devices exclusively to private individuals (see the definition at the end of this guide). This specific information can be identified in this guide by the following logo.



This guide supplements the legislation, which must be respected at all times, on the distribution of medical devices by distributors. This law may be consulted on the FAMHP website or in the Moniteur belge.

CHAPITRE 1 - QUALITY ASSURANCE SYSTEM

1.1 Distributors of medical devices must put in place and maintain a quality assurance system that covers distribution activities in the aim of maintaining a high level of quality across the whole medical device distribution network.

1.2 The quality assurance system entails having a sufficient number of qualified staff and a suitable and appropriate storage space, as well as suitable equipment and infrastructures.
The quality assurance system must ensure that:

- only compliant medical devices are distributed;
- the responsibilities for materiovigilance and of the quality manager are clearly defined;
- the distribution circuit is respected;
- appropriate procedures are drawn up;
- corrective and preventive actions (or CAPA) are taken to correct and prevent non-compliance.

1.3 The size, structure and complexity of the distributor's activities must be taken into consideration in the development or modification of a quality assurance system.

CHAPITRE 2 - STAFF

2.1 Wherever distribution activities are performed, a person responsible for quality and a person responsible for materiovigilance must be appointed. The same person may be appointed for both of these responsibilities. The company management shall also offer a back-up if there is more than one person working at the company.

2.2 The quality manager is responsible for at least the following tasks:

- Guaranteeing that the quality management system is implemented and maintained.
- Managing the activities for which a registration has been submitted to the FAMHP, and the accuracy and quality of the documentation.
- Ensuring that initial and continuous training programmes are implemented and maintained.
- Coordinating and immediately carrying out recall campaigns for medical devices.
- Guaranteeing that customer complaints relating to the quality of medical devices are properly handled.
- Guaranteeing that the suppliers are registered with the FAMHP.
- Guaranteeing that the customers benefit from the required level of professional quality.

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As retailers only distribute to private individuals, they do have to perform customer inspections.

- Approving possible outsourced activities likely to affect the quality of the medical devices.
- Guaranteeing that internal audits/self-assessments take place at suitable and regular intervals, according to a pre-determined schedule, and that useful corrective measures are taken.
- Keeping a detailed record of delegated tasks.
- Deciding on the final destination of medical devices that have been sent back, declined, recalled or falsified.
- Approving the reintegration of saleable medical devices into the stock.
- Guaranteeing that any supplements to the legislation, applicable for certain products, are respected.

2.3 The materiovigilance manager is responsible for at least the following tasks:

- Reporting any incidents to the manufacturers or their representatives, and to the FAMHP.
- Taking part in inquiries carried out by the FAMHP and in works relating to the safety of medical devices.
- Assessing according to current procedure and recording any incident or risk of incident that may be attributable to a medical device.
- Recording any measures to be taken following the reporting of an incident.
- Ensuring that all users are aware of materiovigilance-related problems.
- Distributing the information received to the users concerned.

2.4 The responsibilities of all staff members who take part in the distribution of medical devices must be laid down in writing.

2.5 Staff members who take part in the storage and distribution of medical devices must have the appropriate skills and experience to ensure that the medical devices are stored and handled correctly.

2.6 Staff must have followed training on allocated tasks; a record of this training must be kept in a register.

CHAPITRE 3 - DOCUMENTATION

3.1 Documentation includes all procedures, instructions, agreements, data and registers in written form, either on paper or in electronic format. The documentation must be available or recoverable immediately.

3.2 It must contain enough information on the extent of the distributor's activities and must be written in a language that can understood by the staff. The document must also be error-free and written in clear, unambiguous language.

3.3 Any changes made to the documentation must be signed and dated; the change must have been made in such a way that the original information is still legible. If necessary, the reason for the change will be mentioned.

3.4 All employees must have direct access to all necessary documentation relating to the tasks carried out under their responsibility.

3.5 The documents must always comply with legal and ethical requirements. They must be adjusted to compensate for any changes. The documents must be kept for at least five years, in accordance with legal provisions, and must be made immediately available to the competent authorities.

Procedures

3.6 The medical device distributor must have procedures and work instructions including a detailed description of the distribution activities that affect the quality of medical devices.

3.7 The FAMHP counts on at least the following procedures being part of the quality manual: receipt and delivery of medical devices (including counterfeit checks), storage, cleaning and maintenance of the storage facilities (including pest control), recording of storage conditions, traceability, processing of returned products, complaints management, recall plans and incident reports, corrective and preventive actions taken.

3.8 The procedures in question may be described in a single procedure (e.g. temperature control, cleaning and pest control in the same procedure) or interdisciplinary (e.g. not having a specific traceability procedure as it may be covered in several other procedures)

3.9 The procedures must have been approved, signed and dated by the quality manager and may not be modified without his or her approval.

3.10 An operating method aimed at preventing uncontrolled copies must be in place.

3.11 It is vital to ensure that sound and approved procedures are applied. Procedures must be reviewed and updated on a regular basis. Procedures must be subject to a version control system. After a procedure has been reviewed, a system preventing the accidental use of an obsolete version must be available. Obsolete procedures must be deleted from work stations and archived.

Records and registers

3.12 Each time an activity (purchase and supply, maintenance and inspection of storage facilities, complaints, feedback and recalls) is carried out, clearly noted records must be kept up to date so that any notable activities or incidents are traceable.

3.13 For any purchase or supply transaction, registers containing the following information must be kept: purchase or delivery date, name of medical device, batch/series number (if applicable), expiry date (if applicable), quantity received or delivered, legal manufacturer's name, the name and address of the supplier (if different to the legal manufacturer) or of the recipient. Records must ensure the traceability of the product's origin and of the destination of the products so that all suppliers or users of a medical device are identifiable.

Specific to retailers → As retailers only distribute to private individuals, they do not have to record supply transactions.

CHAPITRE 4 - SUITABLE FACILITIES

4.1 Medical devices must be stored under the conditions recommended by the manufacturer, if necessary in a humidity and temperature-controlled environment. The storage method must prevent any means of contamination. Storage conditions must be inspected and the corresponding data must be recorded. The data must be evaluated on a regular basis by the quality manager.

4.2 To assess if a facility is suitable for the storage of medical devices, the following three parameters must be taken into account:

- The **condition of the facilities**: the facilities must be suitable and sufficiently clean to ensure the proper storage and distribution of medical devices. The storage infrastructures must be clean and litter and dust-free. The facilities must be have sufficient lighting to enable work to be carried out safely. Unsuitable objects that may negatively affect the quality of the medical devices may not be found in the storage facilities. Goods must be stored in such a way as to prevent moisture from penetrating (no direct contact with the floor or with the wall). The facilities must be adequately maintained.

- **Medical device storage conditions**: medical devices must be stored under the conditions recommended by the manufacturer, if necessary in a humidity and temperature-controlled

environment. It must also be ensured that the medical devices are not exposed to direct sunlight or are not directly near a heating or cooling device.

Examples of packaging symbols concerning storage conditions (according to ISO 15223-1): Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements):

-  temperature limit
-  air humidity limit
-  keep out of sunlight
-  keep dry

Storage conditions must be inspected and the relevant data must be recorded. The data must be regularly evaluated by the quality manager.

- **Pest control**: a preventive pest control system must be in place, both from crawling and flying insects and for rodents.

4.3 Measures will be in place in case of any deviation from the storage conditions.

4.4 A system for the organisation of stock renewal must be in place, e.g. according to the FEFO (First Expired, First Out) principle, in which the products closest to their expiry date are the first to be delivered. Regular inspections must be carried out at adequate intervals to ensure this system is working correctly.

4.5 Medical devices that have exceeded their expiry date must be physically separated from stock approved for supply and cannot be distributed.

4.6 Medical devices intended for purposes other than supply must be kept separate from saleable stock. They may not, under any circumstance, enter the distribution circuit or be supplied to the patient/customer and must be correctly labelled to avoid any return to saleable stock. Ideally, they shall be placed in a specific cordoned-off zone. These zones may be flexible in the sense that their size may vary. Examples: quarantine zone, recall zone, destruction zone, zone for articles pending VAT control, zone for demonstration equipment, zone for samples, rental zone, equipment calibration zone, etc.

4.7 If the storage of medical devices is outsourced, the distributor must ensure that the sub-contractor is aware of the suitable storage conditions and complies with them. The backer and the sub-contractor must draw up a written quality agreement, clearly establishing each party's tasks.

CHAPITRE 5 - ACTIVITIES

Reception

5.1 Unloading areas for medical devices must protect the deliveries from bad weather during unloading.

5.2 The reception area must be separate from the storage area, in order to establish a visual distinction between products that have just been delivered and have yet to be inspected on one hand, and already approved products in stock on the other hand.

5.3 The distributor must receive their supply from a legal manufacturer or a supplier registered with the FAMHP.

5.4 The products must be examined upon receipt to verify that:

- the products received are not damaged;
- any anti-tamper seals are present and do not show any signs of falsification or tampering;
- all obligatory legal mentions appear on the packaging (outer packaging and/or immediate packaging and/or package leaflet), namely:
  - EC marking,
  - the number of the notified organism (if applicable),
  - the product name,
  - the manufacturer's name and address,
  - the authorised representative's name and address (if applicable),
  - the expiry date (if applicable),
  - the batch/series number (if applicable),
  - the temperature conditions (if applicable),
  - conditions relating to humidity levels (if applicable),
  - sterility + sterilisation method (if applicable).
- the instructions provided to patients/customers are written in at least the three national languages (French, Dutch, German), unless the medical device is only intended for use by professionals. In this case, the instructions must be provided in the users' national language, unless otherwise agreed in writing with the manufacturer, their representative or the official distributor of medical devices.
- The medical devices received are not counterfeit. N.B.: Particular attention should be paid to changes made to aspects of the packaging, which may be a sign of counterfeit.
- To comply with these requirements, the distributors may use a sampling method which is representative of the products purchased by them.

5.5 The distributor must have free access to or must be in possession of all compliance statements and, where applicable, to the EC certificates of the medical devices they distribute/sell.

5.6 Medical devices requiring special storage conditions (e.g. temperature and humidity conditions) must be immediately identified and stored in accordance with these requirements.

5.7 If the distributor suspects that a medical device acquired by them is counterfeit, they must immediately separate it from the stock destined for supply and inform the competent authority.

5.8 Non-compliant products must be identified, inspected and placed in quarantine to avoid any further distribution or supply. Data relating to subsequent actions must be documented on a case by case basis and be made directly accessible to the FAMHP.

Delivery

5.9 The distributor is required to carry out customer inspections. In particular, they must request and verify a distributor's registration, the APB number of public pharmacies, the INAMI number of the professionals and the hospital pharmacy's accreditation.

As retailers only distribute to private individuals, they do not have to perform customer inspections.

5.10 The medical devices must be transported under the conditions recommended by the manufacturer. The transport mode must not affect the quality of the medical devices.

5.11 Each delivery must be accompanied by a delivery note or by a dated invoice, a description of the medical device, if applicable with the batch/series number, the quantity delivered, and the name and address of the supplier and of the recipient. Warning: in case of supply to a hospital, the delivery note must be addressed to the hospital pharmacist.

As retailers only distribute to private individuals, they do not have to write delivery notes or invoices.

5.12 If the transportation of medical devices is sub-contracted, the distributor must ensure that the sub-contractor is aware of the suitable transport conditions and complies with them. The backer and the sub-contractor must draw up a written quality agreement, clearly establishing each party's obligations and responsibilities.

Traceability

5.13 Any purchase and any supply, as well as any other activity and notable event (storage, consignment, returns, recalls, samples, loans of demonstration equipment, equipment rental, etc.) must be recorded in writing and/or in electronic format, in such a way that the origin and the destination of the medical devices can be found. Likewise, the date of the action, the name of the medical device, the quantity received or supplied, and the name and address of the supplier or of the customer will be mentioned along with the batch number and expiry date if a legal obligation exists.

As retailers only distribute to private individuals, they must only guarantee the traceability of the purchase and of the storage, but not of the supply.

5.14 For Class III implantable medical devices, a traceability system must be provided for the batch/series number and the expiry date of these articles.

5.15 The traceability system must allow the company to identify and immediately contact all recipients of the medical device, e.g. in case of recall. From this point of view, it is very beneficial to record the batch/series numbers for all articles, both at the time of purchase and of supply.

As retailers only distribute to private individuals, they do not have to guarantee the traceability of supply.

5.16 The same system must be able to be used in the event of delivery abroad (outside of Belgium).

5.17 The traceability system must be tested annually by means of a simulation.

CHAPITRE 6 - RETURNS, COMPLAINTS AND RECALLS

Returns

6.1 Medical devices returned by customers must be marked as such and placed in quarantine pending a more in-depth examination or sample from the distributor/manufacturer.

6.2 Medical devices that have left the distributor's premises or which have been removed from saleable stock may only be placed back into the stock approved for supply if the following elements have been confirmed:

- The medical device is in its original, unopened container, unused and in good condition;
- The user can demonstrate that the medical device has been continuously stored and handled under the intended conditions;
- The medical device has an acceptable life span;

- The batch/series number and the expiry dates have been checked in order to verify whether the returned medical device has actually previously been sold.

6.3 Only the quality manager can authorise the reintegration of medical devices into saleable stock. The medical devices must be reintegrated into saleable stock in such a way as to allow the effective operation of the stock renewal system.

6.4 Returned medical device registers must be kept up to date. For each return, the documentation must contain the following information:

- name and address of the recipient returning the medical device;
- name or designation of the medical device, batch/series number and quantity returned;
- reason for return;
- use or elimination/destruction of the returned medical device and details on the assessment performed.

Complaints

6.5 All oral or written complaints must be recorded in order to analyse complaint trends, the frequency of complaints related to product quality and the seriousness of the complaints, in view of taking additional measures and, if necessary, immediate corrective measures. These records must be made available during inspections by the competent authorities.

6.6 The complaints records must include the following information:

- name and address of the person making the complaint;
- nature of the complaint, including the name of the medical device with batch/series number (if applicable);
- date the complaint was received;
- measures taken;
- response given to the person making the complaint, including the date on which it was sent;
- final decision taken for the medical device.

6.7 In situations likely to cause or having caused the death or serious deterioration of a patient or user's health, the local, national or international authorities must be informed and consulted for their opinion. (see chapter 7 - materiovigilance).

Recalls

6.8 The recall procedure must indicate how a recall process is initiated, who has to be informed and how the recalled products must subsequently be processed. A given person (normally the quality manager) must be appointed to implement and coordinate the recall campaign.

6.9 At the same time, the procedure must also allow the company to take stock, quickly and accurately, per product ("reconciliation"):

- number of products purchased (or manufactured) and supplier;
- number of products in stock and stock location;

- number of products delivered;
- number of products recovered from customers following recall.

to create an accurate and detailed image of the location of each product.

6.10 A letter template must be prepared for recalls and, if necessary, filled in with the relevant information (product, manufacturer, batch/series number concerned, etc.). This document will be used to immediately inform all customers (other distributors, hospital pharmacists and others) who appear to have purchased the medical device. This document shall also provide the customer with instructions to follow.

As retailers only distribute to private individuals, they do not have to guarantee the traceability of supply.

6.11 Each recall must be recorded internally as soon as it takes place. This record must be made available to the FAMHP.

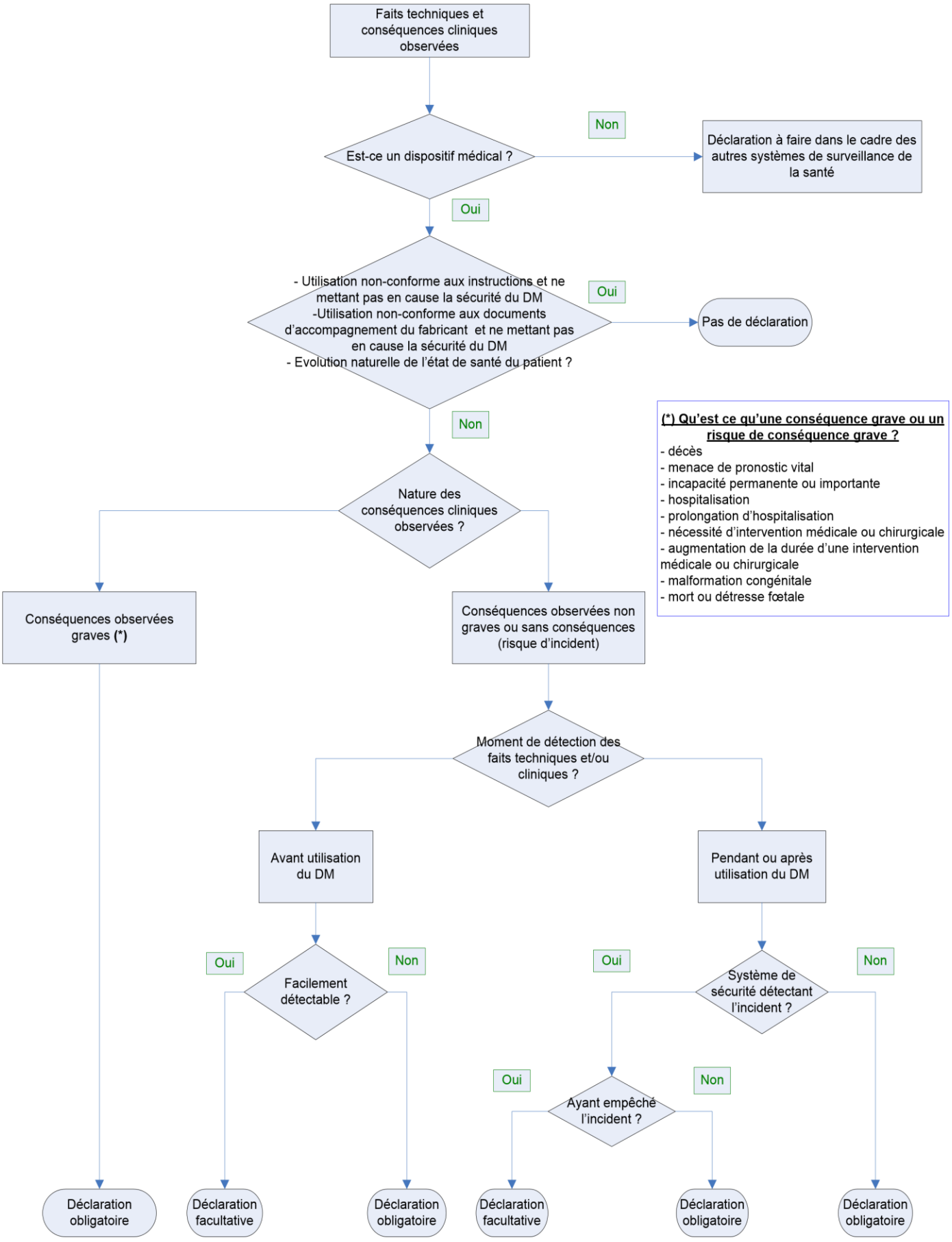
CHAPITRE 7 - MATERIOVIGILANCE

7.1 The materiovigilance contact person within the company must inform the manufacturer/distributor and the FAMHP immediately of any incident, including recalls concerning the medical devices they distribute.

7.2 The attached decision tree can be used to determine if an incident must be reported. This decision tree can also be consulted on the FAMHP website or via the FAMHP portal.

7.3 Any communication regarding incidents can be made to the *meddev@fagg-afmps.be* email address (general address for medical devices) using the standard form published on the FAMHP website.

7.4 Incidents can also be (voluntarily) reported using the standard form published by the European Commission: http://ec.europa.eu/health/medical-devices/documents/guidelines/index_en.htm


Faits techniques et conséquences cliniques observées
Est-ce un dispositif médical ?
Non
Déclaration à faire dans le cadre des autres systèmes de surveillance de la santé
Oui
- Utilisation non-conforme aux instructions et ne mettant pas en cause la sécurité du DM
-Utilisation non-conforme aux documents d'accompagnement du fabricant et ne mettant pas en cause la sécurité du DM
- Evolution naturelle de l'état de santé du patient ?
Oui
Pas de déclaration
Non
(*) Qu'est ce qu'une conséquence grave ou un risque de conséquence grave ?
- décès
- menace de pronostic vital
- incapacité permanente ou importante
- hospitalisation
- prolongation d'hospitalisation
- nécessité d'intervention médicale ou chirurgicale
- augmentation de la durée d'une intervention médicale ou chirurgicale
- malformation congénitale
- mort ou détresse fœtale
Nature des conséquences cliniques observées ?
Conséquences observées graves (*)
Conséquences observées non graves ou sans conséquences (risque d'incident)
Moment de détection des faits techniques et/ou cliniques ?
Avant utilisation du DM
Pendant ou après utilisation du DM
Oui
Facilement détectable ?
Non
Oui
Système de sécurité détectant l'incident ?
Non
Oui
Ayant empêché l'incident ?
Non
Déclaration obligatoire
Déclaration facultative
Déclaration obligatoire
Déclaration facultative
Déclaration obligatoire
Déclaration obligatoire

ANNEXE - DEFINITIONS

Good Distribution Practice (GDP): GDP is part of the quality guarantee that ensures that the quality of the medical devices is maintained throughout all phases of the distribution chain, from manufacture to delivery.

CAPA: Corrective and Preventive Actions

Retailer: distributor supplying medical devices to consumers, in other words any physical person acquiring or using medical devices for non-professional purposes only.

Medical device: any instrument, device, equipment, software, material or other article, used alone or in association, including the software intended by the manufacturer to be used specifically for diagnostic and/or therapeutic purposes, and necessary for its correct operation, intended by the manufacturer to be used on human beings for the purposes of:

- diagnosis, prevention, control, treatment or alleviation of an illness,
- diagnosis, control, treatment, alleviation or compensation of an injury or of a handicap,
- study or replacement or modification of the anatomy or of a physiological process,
- to control conception,

and of which the primary intended action in or on the human body is not obtained by pharmacological or immunological means nor by metabolism, but of which the function may be assisted by such means.

Distribution: the availability, on a paid or free basis, of a medical device in view of its distribution or of its use to other Member States of the European Union or States which are part of the European Economic Community, whether the medical device is new or refurbished.

Distributor: any physical or legal person that is part of the supply chain, other than the manufacturer or importer, who makes a medical device available on the market

Counterfeit: A counterfeit product is a product that has been falsely labelled regarding its identity or to its source. The counterfeit may concern the brand or the products, and it may apply to products containing the correct or incorrect components, giving the end consumer false expectations compared to the original/authentic products.

FEFO: First Expiry/First Out. Earliest expiry date distributed first.

FIFO: First In/First Out. First products received distributed first.

Supply: activity consisting of supplying, selling or giving medical devices.

Quality guarantee: all measures intended to guarantee the maintenance of the quality of the medical devices during storage and distribution. The quality guarantee notably includes good distribution practice.

Work instruction: Document which describes the way in which an operation is performed, as well as the means necessary to successfully accomplish it. The instructions are distinguished from the procedures by the fact that, generally speaking, they only concern a specific procedure, a service, a machine or a

Lot/batch: a pre-determined quantity of products manufactured in a single process or a single series of processes, in such a way as to assume homogeneity.

Materiovigilance: the study and monitoring of incidents that may result from the use of medical devices. It allows for the withdrawal from the market of dangerous devices and the elimination of faults from medical devices in view of progressively improving the quality of the devices and assuring the increased safety of the patients and of the users.

Corrective measure: a measure intended to prevent a problem from occurring in the future by correcting the cause of the problem.

Preventive measure: is a measure taken to eliminate the cause of an anomaly or any other undesirable situation, and to prevent their occurrence.

Non-compliant: a non-compliant medical device is a medical device that does not comply with the legal requirements for medical devices laid down in European and national legislation.

Procedure: Description according to a logical, coherent and detailed plan of operations to be carried out, measures to be taken, of technical methods and of the documentation to be used to assure an operation or series of operations in a reproducible manner. Insofar as possible, the procedures are expressed in document form.

Quality: The extent to which a collection of properties and characteristics comply with requirements (standards).

Quarantine: status of medical devices isolated physically or by other effective means pending a subsequent decision on their release, their destruction or their reprocessing.

Recall: the withdrawal of a medical device from the market by a recall organised by the distributor or manufacturer or upon request by the competent authorities.

European Representative (EU Rep): any physical or legal person established in the European Union and authorised in writing by a manufacturer to act on its behalf and in relation to the specific tasks set out in legislation concerning medical devices.

Traceability: Process of collection and recording of data to be able to quickly find the history, implementation or location of the thing that is being sought.

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