

**Draft Guide to
Distribution of Medical Devices, including *in vitro* diagnostic Medical Devices**

DRAFT



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1 SCOPE

The purpose of this document is to provide guidance to industry in the area of **distribution of medical devices**, *in vitro* medical devices and their accessories for human use in Ireland. For the purpose of this document, all such medical devices shall be referred to collectively as 'medical devices' unless otherwise specified.

2 INTRODUCTION

The quality and performance of medical devices directly affects patients' safety and health. The range of medical devices available is vast and they are used by a broad variety of users from the general public in their homes to the most critically ill patients in specialist clinical settings. Patients using devices include extremely vulnerable groups such as neonates and infants, the elderly, disabled and other patients who are particularly susceptible to diseases. Medical devices may also be used in high risk surgical procedures and intensive care settings, where improper storage along the supply chain, amongst other aspects, may lead to undesirable, and in some cases extremely serious, consequences.

Two EU Regulations (together known as 'the Regulations') are in draft at the time of writing, one for medical devices and one specifically for *in-vitro* diagnostic medical devices. They are:

- 'Proposal for a Regulation of the European Parliament and of the Council on medical devices and amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation 1223/2009'. Ref - COM (2012) 542 ['the medical device Regulation']
- 'Proposal for a Regulation of the European Parliament and of the Council on *in vitro* diagnostic medical devices' Ref - COM (2012) 541 ['the IVD Regulation']

When legally applicable, these two Regulations will replace the current European Directives for medical devices; including Council Directives 90/385/EEC and 93/42/EEC and 98/79/EC. It is anticipated that requirements relating to distribution of devices will be essentially the same in both Regulations.

This is a best practice guidance document published in advance of the final adoption of the new Regulations placing legal obligations on the distributors of medical devices. It is anticipated that the requirements for distributors will essentially constitute good distribution practice (GDP) for medical devices. This document aims to provide supplementary guidance to distributors in that regard taking into account the proposed obligations for medical device distributors in the two Regulations. It sets out the Health Products Regulatory Authority's (HPRA) recommendations for best practice and other considerations for distributors of medical devices.

3 LEGISLATIVE BASIS

At European level, the legislative basis for distribution of medical devices will be based on two Regulations. At the time of writing, the proposed definitions relevant to medical device distributors are identified in table 1 below.

Table 1: Proposed definitions

Term	Definition
Distributor	Means any natural or legal person in the supply chain, other than the manufacturer or the importer, who makes a device available on the market up until the point of putting into service
Manufacturer	means a natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under its name or trademark
Importer	means any natural or legal person established within the Union that places a device from a third country on the Union market
Authorised representative	means any natural or legal person established within the Union who has received and accepted a written mandate from a manufacturer, located outside the Union, to act on the manufacturer's behalf in relation to specified tasks with regard to the latter's obligations under this Regulation
Making available on the market	means any supply of a device, other than an investigational device, for distribution, consumption or use on the Union market in the course of a commercial activity, whether in return for payment or free of charge
Placing on the market	means the first making available of a device, other than an investigational device, on the Union market
Putting into service	means the stage at which a device, other than an investigational device, has been made available to the final user as being ready for use on the Union market for the first time for its intended purpose

References to proposed Regulations within the document

Article 14¹ of the proposed Regulations describes the obligations of medical device distributors. Article 25 of the medical device Regulation (corresponding to Article 22 of the IVD Regulation) describes the obligations relating to identification within the supply chain. The identification relates to the medical device, suppliers and customers. At the time of writing, the proposed obligations relating to distributors are indicated in table 2 below. This guidance document is intended to describe how a medical device distributor can meet the requirements.

Table 2: Proposed distributor obligations
(further details of the Articles referenced in this table can be found in Section 1 of Appendix 1)

Article 14	Obligation
Paragraph 1	When making a device available on the market, distributors shall, in the context of their activities, act with due care in relation to the requirements applicable.
Paragraph 2	<p>Before making a device available on the market, distributors shall verify that all of the following requirements are met:</p> <ul style="list-style-type: none"> (a) the device has been CE marked and that the EU declaration of conformity of the device has been drawn up; (b) the device is accompanied by the information to be supplied by the manufacturer in accordance with Article 10(11) [<i>Article 10(10) of the IVD Regulation</i>]; (c) for imported devices, the importer has complied with the requirements set out in Article 13(3); (d) that, where applicable, a UDI has been assigned by the manufacturer. <p>In order to meet the requirements referred to in points (a), and (b) and (d) of the first subparagraph the distributor may apply a sampling method representative of devices supplied by that distributor.</p> <p>Where a distributor considers or has reason to believe that a device is not in conformity with the requirements of this Regulation, it shall not make the device available on the market</p>

¹ Please note that the numbering of the articles in the draft Regulations may change when the Regulations are published in the Official Journal of the European Union. This guide will then be updated accordingly.

Article 14	Obligation
	<p>until it has been brought into conformity, and shall inform the manufacturer and, where applicable, the manufacturer's authorised representative, and the importer. Where the distributor considers or has reason to believe that the device presents a serious risk or is a falsified device, it shall also inform the competent authority of the Member State in which it is established.</p>
Paragraph 3	<p>Distributors shall ensure that, while the device is under their responsibility, storage or transport conditions comply with the conditions set by the manufacturer.</p>
Paragraph 4	<p>Distributors that consider or have reason to believe that a device which they have made available on the market is not in conformity with this Regulation shall immediately inform the manufacturer and, where applicable, the manufacturer's authorised representative and the importer. Distributors shall co-operate with the manufacturer and, where applicable, the manufacturer's authorised representative, and the importer, and with competent authorities to ensure that the necessary corrective action to bring that device into conformity, to withdraw or to recall it, as appropriate, is taken. Where the distributor considers or has reason to believe that the device presents a serious risk, it shall also immediately inform the competent authorities of the Member States in which it made the device available, giving details, in particular, of the non-compliance and of any corrective action taken.</p>
Paragraph 5	<p>Distributors that have received complaints or reports from healthcare professionals, patients or users about suspected incidents related to a device they have made available, shall immediately forward this information to the manufacturer and, where applicable, the manufacturer's authorised representative, and the importer. They shall keep a register of complaints, of non-conforming devices and of recalls and withdrawals, and keep the manufacturer and, where available, the authorised representative and the importer informed of such monitoring and provide them with any information upon their request.</p>
Paragraph 6	<p>Distributors shall, upon request by a competent authority, provide it with all the information and documentation that is at their disposal and is necessary to demonstrate the conformity of a device.</p> <p>Distributors shall be considered to have fulfilled the obligation referred to in the first subparagraph when the manufacturer or, where applicable, the authorised representative for the device in</p>

Article 14	Obligation
	question provides the required information. Distributors shall cooperate with competent authorities, at their request, on any action taken to eliminate the risks posed by devices which they have made available on the market. Distributors, upon request by a competent authority, shall provide free samples of the device or, where that is impracticable, grant access to the device.

Article 25 (corresponding to Article 22 of the IVD Regulation)	Obligation
Paragraph 1	Distributors and importers shall co-operate with manufacturers or authorised representatives to achieve an appropriate level of traceability of devices.
Paragraph 2	<p>Economic operators shall be able to identify the following to the competent authority, for the period referred to in Article 10(8) [<i>Article 10(7) of the IVD Regulation</i>]:</p> <ul style="list-style-type: none"> (a) any economic operator to whom they have directly supplied a device; (b) any economic operator who has directly supplied them with a device; (c) any health institution or healthcare professional to which they have directly supplied a device.

4 IMPLEMENTATION OF A QUALITY SYSTEM

In order to meet the legislative requirements and to ensure that only medical devices that comply with the legislation are made available for supply, it is recommended that distributors have a quality system in place. An effective quality system provides assurance that only medical devices which comply with legislative requirements are distributed, that non-compliant, defective or unsuitable medical devices can be detected, that traceability is maintained and that non-conformances and the introduction of changes are controlled.

The quality system is the responsibility of the organisation's management and requires their leadership and active participation and should be supported by staff commitment. A person responsible should be appointed by the management who should have clearly specified authority and responsibility for ensuring that a quality system is implemented and maintained. A quality manual or equivalent should be established in which all distribution activities should be clearly defined and systematically reviewed. All critical steps of the distribution process and significant changes should be justified and where relevant, validated.

Traceability of medical devices are fundamental to protecting public health in ensuring that full reconciliation is achievable in case of the need for prompt removal of defective or unsuitable medical devices from stock that has been distributed or remains stored in the warehouse. The operation of an effective quality system for the distribution of medical devices can help maintain the integrity of the supply chain and ensure patient safety in the distribution of medical devices.

Some of the key components of a quality system are outlined below and further discussed throughout this document:

- Quality Management
- Personnel and Staff Training
- Documentation and Record keeping
- Medical Device Receipt, Storage and Supply
- Management of Returned Medical Devices
- Falsified Medical Devices
- Medical Device Recalls
- Outsourced Activities
- Transportation

Standard operating procedures (SOPs) should be established to clearly describe how key activities are carried out. Forms, which are controlled documents, should be used to capture relevant information such as goods receipt checks. In addition to this guidance document, distributors may wish to refer to ISO 13485 which provides information on quality systems for suppliers of medical devices and is more specific than the general requirements of quality systems specified in ISO 9001. Not all sections will be applicable to medical device distributors, but in particular, references to management responsibility, product identification and traceability, corrective and preventative actions and handling, storage, packaging, preservation and delivery may be useful.

Distribution of documents to staff should be controlled in a manner such that only up-to-date and approved documents are available in relevant areas and obsolete copies should not be accessible. This may be achieved by maintaining a distribution list with records of procedures issued and retrieved, including the dates on which these activities took place. Superseded master copies of procedures should be maintained for a period of at least 6 years.

In order to ensure that procedures are maintained and are reflective of current requirements, a periodic review should be performed. This review should be documented and any recommendations should be implemented.

It is particularly important that SOPs relating to activities in certain areas (e.g. receipt of material at the goods inwards area) are available to staff in the relevant area for reference as required.

SOPs should describe the different operations which may affect the quality of the medical devices.

In addition, there should be procedures in place for:

- Training
- Documentation control
- Approval of suppliers and customers
- Order processing and deliveries
- Waste management
- Self-inspection
- Change control
- Management review
- Quality risk management
- Deviation management
- Corrective and preventive actions

Any distributor operating to accredited quality standards should ensure that its operation also complies with the legislative parameters governing the distribution of medical devices. In such cases the distributor should perform a gap analysis of the specific requirements relating to the distribution of medical devices against its current operational standard. Differences in approach or gaps identified should be addressed through the introduction of additional procedures within the quality system as required.

4.1 The role of management

The role of management within the distribution operation should not be underestimated. The distribution of medical devices is the responsibility of the organisation's management and requires their leadership and active participation. It is imperative that management is involved, provides adequate resources and maintains oversight of distribution compliance. There should be a formal process for reviewing the quality system on a periodic basis. Senior management should be involved and the review should include a measurement of the achievement of the objectives of the quality system, assessment of performance indicator that can be used to monitor the effectiveness of the quality system (e.g. complaints, deviations and corrective and preventative actions).

4.2 Change control

The purpose of a change control system is to enable distributors to identify, document and assess changes which may impact on compliance and quality of the device. Such changes may include, for example: a change in the settings of a heating system or the relocation of a medical device storage area within a warehouse. Such changes may have a significant impact and may have the potential to affect the quality of medical device distributed. Therefore it is vital that the change is conducted in a controlled manner.

A change control procedure and associated forms should be implemented and appropriately documented. Its purpose should be to ensure that all changes to the operation are fully evaluated in terms of impact on the medical device quality and traceability. The evaluation process should identify the areas impacted by the change, including processes, equipment, personnel, training, validation, quality system and regulatory implications. The required actions to give full effect to the change and ensure its implementation should be identified. In addition, changes should be formally approved by the relevant managerial representative of the areas of the operation impacted by the change prior to implementation. Changes should also be subjected to periodic review to ensure completion of actions which had been identified as required during the change control process. The principles of quality risk management should be built into the change control process. Each change should be considered and a decision taken as to whether a risk assessment is required prior to approval of the change for implementation. The requirement for a risk assessment to be considered should be documented on the change control form.

4.3 Quality risk management

Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the medical device. It is a valuable component of an effective quality system. Risk management may be used to assess the risk posed to the medical device as a result of a deviation from normal practices or to justify a proposed deviation from accepted practice. The use of risk management should be based on scientific knowledge, reason and practices. The level of detail contained within the risk management process should be reflective of the level of risk to the medical device. Implications for medical device quality, security, traceability and follow up actions should be detailed. Risk assessments should be carried out by competent personnel and should be reviewed and approved by the relevant responsible personnel.

Companies should have a procedure in place and training should be provided. All documentation for risk assessments performed should be available to an inspector during the course of an inspection.

While there is no specific guidance or standard relevant to risk management in this circumstance, more information on risk management and performing risk assessments, can be found in the ISO14971 'Medical devices – application of risk management to medical devices' and in the ICH Harmonised Tripartite Guideline entitled 'Quality Risk Management – Q9'. This document is available for download on the ICH website. Whilst not all aspects will be relevant to distributors, there are concepts and methodologies that can be applied to medical device distributors.

4.4 Deviations, investigations and corrective and preventive actions (CAPA)

Deviations are non-conformances with the Regulations or internal procedures. A procedure should be in place outlining the process for identifying, documenting, investigating and

closing deviations which occur and the timelines involved. An assessment should be performed to determine medical device quality implications and/or impact on the quality system.

It is important to note that distributors should commence the documentation of investigations immediately upon a potential deviation or incident being identified. Should the outcome of an investigation conclude that no deviation has occurred, then the documentation of the investigation should still be maintained and available to an inspector. An example of this may be where an investigation is commenced into stock discrepancies identified during stock counts where the outcome of the investigation is the location of the missing stock.

Deviation investigations should aim to identify the root cause of the deviation. Corrective and preventive actions (CAPAs) may arise as a result of deviations, self-inspections, observations or from other incidents.

A log of deviations and suspected deviations should be maintained and all investigations, root cause identifications and resulting CAPAs documented. CAPAs should be subjected to regular review to ensure their full implementation and they should be subject to formal checks of their effectiveness.

The principles of quality risk management should be built into the deviation process. Each deviation should be considered and a decision taken as to whether a risk assessment is required. The requirement for a risk assessment to be considered should be documented on the deviation form.

4.5 Complaints

According to the proposed Regulations, distributors who have received complaints or reports from healthcare professionals, patients or users about suspected incidents related to a device they have made available, shall immediately forward this information to the manufacturer and, where applicable, his authorised representative and the importer. They shall keep a register of complaints, of non-conforming products and of product recalls and withdrawals, and keep the manufacturer and, where available, the authorised representative and the importer informed of such monitoring and provide them with any information upon their request.

A procedure should be in-place describing the process to be followed upon receipt of a complaint, an event or incident report. A complaint, event and incident report log should be established.

All complaints, events or incidents received should be investigated and categorised into either a quality, technical/service, vigilance or distribution related complaint depending on the nature of the report.

The decisions and actions taken as a result of a complaint, event or incident should be justified and recorded. Where complaints are not reported to the manufacturer or authorised representative/importer, this should be justified and documented.

The procedure established should clearly define the criteria that if met requires an incident to be reported to the HPRA or other national competent authority of another EEA member state.

The customer should be informed of the outcome of the complaint and all communications documented.

5 PERSONNEL AND STAFF TRAINING

Personnel involved in the distribution of medical devices should have the appropriate training and experience to adequately conduct their assigned duties. Training should be documented and recorded. Reporting structures and role profiles should be clearly established. There should be sufficient competent personnel to carry out all the tasks for which the distributor is responsible.

5.1 Key personnel

It is suggested that each distribution centre appoint a person of appropriate training and experience that has primary responsibility for ensuring that due care is met and that the quality system is effective. This person may also serve as the primary contact between the competent authority and the distributor.

Other duties that need to be carefully controlled and assigned to key personnel of appropriate training and experience include the segregation, storage and release of returned stock to saleable stock and the handling of product recalls and field safety notices.

5.2 Training

Training is a key component of any quality system.

The training and skills necessary to carry out the various unit operations should be clearly established. A training plan should be in place for each staff member to ensure that they receive induction training, task specific training and on-going training relevant to their role profile. This ongoing training should include training on updated SOPs.

The effectiveness of training should be determined and before taking on any role, staff should have shown the competency needed. Evidence to this effect must be recorded and maintained.

All training events should be documented and it should be ensured that the details with respect to the objective of the training event, a description of the training, its duration and location, the training provider and the outcomes are recorded in sufficient detail that upon examination of the record it can be determined what training was given, who was trained and whether the trainee received the required level of competence. For training on documents the revision number of the document should be included.

Both trainer and trainee should sign-off on all training records.

Training could include but is not limited to:

- defined responsibilities for personnel
- access to and training on documentation relevant to their role
- storage requirements
- labelling checks
- reporting of non-compliances
- operation of segregated areas to minimize the risk of mix-ups
- recall/withdrawal procedures
- complaints procedures
- regulatory requirements and related guidance documents

6 DOCUMENTATION AND RECORD KEEPING

Article 25 of the medical device Regulation (corresponding to Article 22 of the IVD Regulation) relates to the obligations of distributors to achieve an appropriate level of traceability of medical devices it distributes.

Distributors should keep adequate records, including records of customers and suppliers to and from whom medical devices have been distributed. This includes but is not limited to medical device name and/or code, batch or lot number, quantities and delivery date. This information is especially important in the event of a recall/withdrawal from the market. In the event that a recall of a particular batch/lot is required, failure to record the batch/lot numbers involved in transactions may result in a full product recall being required.

Records to be maintained by the distributor could include:

- copies of invoices relating to the receipt and supply of a medical device
- copies of orders relating to the receipt and supply of a medical device
- a list of approved medical device suppliers and details of the relevant medical devices
- customer list to include contact details of all customers to whom medical devices were supplied
- records of checks carried out at receipt (for example labelling checks for CE marks) and the approval of medical device into saleable stock

These records should be kept for up to 6 years following the date of receipt of the last batch/lot and may be requested by the HPRA.

7 MEDICAL DEVICE RECEIPT, STORAGE AND SUPPLY

7.1 New medical device introduction

A robust system for approval of new medical device suppliers is a key component in the prevention of falsified medical devices entering the supply chain. Distributors should have a procedure in place relating to the introduction of new medical devices to their inventory. This procedure should include a requirement to assess and document the regulatory system under which a new product has been classified (e.g. medical device, medicinal product, food supplement, cosmetic, biocidal product). For medical devices, the required storage and transport conditions and any additional requirements relating to their distribution should be documented. Distributors should consult with their suppliers with respect to the classification of new medical devices. Documentation should be available for review relating to each new medical device introduction.

It is recommended that a distributor of medical devices has a technical agreement in place with their supplier. The technical agreement serves as a basis for defining the division of responsibilities between the parties. However, it is important to highlight that each distributor retains ultimate responsibility for ensuring that the operations are compliant with legal requirements. A technical agreement between a distributor and their supplier should include but is not limited to:

- relationship of parties and relevant contact details
- devices covered by the agreement and any specific requirements (e.g. storage conditions)
- transport specifications
- device traceability requirements
- responsibilities and procedural aspects in terms of recall/withdrawal procedures, handling returns, complaints (distribution-related and/or device quality related)
- review provision for ensuring the agreement maintains relevance to the ongoing operation

Distributors receiving medicinal products directly from operators in a country outside of the European Economic Area may be considered to be an importer. According to the proposed legislation, importers have specific legal obligations in addition to a distributor's obligations. The Regulations also propose that where a distributor performs certain activities, they may assume the responsibility of a manufacturer. These activities include where a distributor:

- makes a device available on the market under their name, registered trade name or registered trade mark,
- changes the intended purpose of the device already placed on the market or put into service,

- modifies a device already placed on the market or put into service in such a way as to affect the compliance of the device.

7.2 Receiving

It is recommended that deliveries are examined at receipt to include checking for damage (including any breaches to sterile packaging) and appropriate remaining shelf life. A written SOP should be in place to enable any non-conforming or defective product to be detected and quarantined.

There should be a system in place to enable the distributor to meet the requirements of Article 14 paragraph 2 of the Regulations. Before making the medical device available on the market, the distributor must verify that certain minimum requirements are met. This includes checking for the presence of a CE mark and that a declaration of conformity of the device has been drawn up. This check should be performed on a sample from each batch of each medical device received. Batch/lot numbers and expiry dates should also be checked at this stage to ensure that expired medical devices are not supplied. These checks should be recorded.

In addition, distributors must also verify that the following requirements are met:

- the medical device is accompanied by the information to be supplied by the manufacturer in accordance with Article 10(11) of the medical device Regulation (corresponding to Article 10(10) of the IVD Regulation) (i.e. labelling and instructions for use). A risk-based sampling approach can be used for this check;
- for imported devices, the importer has complied with the requirements set out in Article 13(3) of the Regulations (i.e. importers contact details);
- where applicable, a Unique Device Identifier (UDI) has been assigned by the manufacturer.

The verification checks should also be recorded.

The process for handling of non-conforming goods at goods-in should be described in a procedure and should include where the medical device is stored, what documentation is completed and how the stock is controlled on the warehouse management system (if applicable).

At the goods-in stage, it should be verified that all goods have been received from an approved supplier. To ensure this, goods-in personnel should have access to the list of suppliers approved under the company's quality system. Alternatively, an inventory management system may be used which permits medical devices to be booked onto the inventory system only if the supplier is approved to supply that medical device.

Specific checks should be performed on medical devices requiring refrigerated storage. These checks should include, but are not limited to: checking that cold chain conditions were

maintained during transportation; checking that the consignment(s) were received within the validated transportation time if received in qualified cold-chain shippers.

If a medical device is received under quarantine status, there should be systems and procedures in place to ensure that it is not released into saleable stock until all necessary conditions, including formal release, have been met.

Where a distributor considers or has reason to believe that a device is not in conformity with the requirements of the Regulations, they shall not make the device available on the market until it has been brought into conformity. It is also a requirement that in this case, the distributor informs the manufacturer and, where applicable, the authorised representative and the importer.

Where the distributor considers or has reason to believe that the medical device presents a serious risk or is falsified, they shall also inform the HPRA. If the distributor has made a medical device that poses a serious risk available in other markets within the EEA, the distributor is also required to inform the national competent authority in each of those markets. This requires that the distributor needs to have a documented system in place relating to identification of serious risk and of falsified medical devices.

Records should be available of all checks performed at receipt and these should be available to the HPRA during an inspection.

7.3 Traceability

Article 25 of the medical device Regulation (corresponding to Article 22 of the IVD Regulation) describes the obligations relating to identification within the supply chain. Medical device traceability is achieved through maintaining adequately detailed records in relation to the sourcing and supply of medical devices. In the event of a product recall it may be necessary to determine the customers that received a specific batch/lot of a medical device which was affected by the recall. In such cases, the maintenance of a system which includes tracking by batch/lot number is most valuable in terms of assisting and ensuring the swift conduct of the recall and limiting it to the affected batch/lot only. The system used to maintain product traceability should be challenged periodically to ensure that it is capable of determining stock location.

7.4 Storage

According to Article 14(3) of the Regulations, distributors shall ensure that, while medical devices are under their responsibility, storage or transport conditions comply with the conditions set by the manufacturer. Storage conditions are normally specified on the containers, for example 'Store between 2 and 8°C', 'Store at -20°C' or 'Do not store above 25°C'. Medical devices must be stored in accordance with the labelled conditions, including

potential relative humidity conditions. Where there are no specified storage conditions, there are no restrictions on the temperatures at which medical devices may be stored.

Continuous temperature monitoring must be performed and documented in order to ensure that the appropriate conditions are maintained, if applicable. This applies to all areas where medical devices are stored (e.g. bulk storage, pick-face, quarantine and returns areas). At a minimum, a calibrated max/min type thermometer should be used. The maximum and minimum temperatures reached should be recorded every day and the thermometer reset after the readings have been taken.

Temperature monitoring records should be reviewed and approved regularly to ensure compliance with the required conditions. Temperature excursions should be investigated immediately and documented. Consideration should be given to the potential impact that the excursion may have had on devices stored during that time period. In the event that there are multiple temperature excursions across a time period, the impact of the multiple excursions on the devices should be considered. The manufacturer of the medical device should be consulted to ascertain the effect of any excursions from the labelled storage conditions. The method for investigating excursions should be described in a procedure.

Calibration certificates for temperature monitoring devices should be reviewed by the distributor to ensure that the accuracy of the devices is acceptable. Documentation should be available for inspection demonstrating that this review has occurred.

Temperatures should also be monitored during periods when temperature measuring devices used routinely are being recalibrated. This may mean that auxiliary temperature measuring devices are required. These devices should also be calibrated.

For detailed information on temperature monitoring and mapping requirements refer to the HPRA document entitled 'Guide to Control and Monitoring of Storage and Transportation Temperature Conditions for Medicinal Products and Active Substances', please see the 'Publications and Forms' section of www.hpra.ie. Although the document refers to medicinal products, the principles are the same for medical devices.

Adequate rotation of stock is advised to ensure that a 'first expired first out' (FEFO) or similar stock rotation system is applied. As such the expiry date should be checked at goods put away and routinely checked during product storage to ensure that stock with the shortest remaining expiry is supplied first.

Quarantined stock should be kept separate from approved stock. There should be a system in place to ensure that quarantined stock is not available for picking or returned to saleable stock inadvertently. An inventory should be maintained of all quarantined medical devices and should include details such as date quarantined, batch/ lot numbers, expiry dates, quantities, reason for quarantining, disposition (i.e. approved for sale, rejected or intended for

destruction) and date removed from quarantine. This inventory may also be maintained on a warehouse management system.

Care should be exercised by the distributors to ensure that where segregation is achieved by only using a computerised system that this system should be at least as effective as if devices were physically segregated. This is to ensure that devices which have been deemed as not suitable for saleable stock (e.g. falsified, recalled or defective medical device) are not supplied to customers.

7.5 Pest control

A pest control programme should be in place. At a minimum this should include rodent control. Further controls may be required for birds and flying and crawling insects and may include electrical fly killers, glue traps etc. Rodent control should cover both internal and external locations.

The programme should be described in a procedure. A bait map should show the locations of all pest control monitoring stations and should be approved by the distributor.

Any recommendations made by a pest control service provider should be completed and recorded. If recommendations are not completed, an explanation should be recorded. All pest control records should be approved by the distributor and maintained.

7.6 Medical device disposal

All medical devices that are rejected in-house, rejected when received as a return from a customer or recalled stock should, if instructed accordingly, be destroyed in an appropriate and timely manner and in accordance with waste legislation. The decision to dispose of medical devices should be documented and recorded.

There should be an inventory of medical devices placed into waste. Records and certificates of destruction should be maintained.

Service level agreements should be in place with third party contractors.

7.7 Promotional samples/sales representatives

A procedure should be in place describing the controls and traceability system in place for promotional samples and samples maintained by sales representatives.

Ensure that batch details and quantities of medical devices supplied to sales representatives are recorded and are included in any recall action which may arise. All samples received by sales representatives should be stored and transported in accordance with the labelled conditions.

7.8 Validation and qualification

All critical steps of distribution processes and significant changes should be justified and where relevant validated.

Validation of critical processes

The distributor should first identify the critical steps within the process. Such steps may include goods-in, storage, order processing and dispatch. The distributor may further subdivide these steps into the critical sub-steps involved in each individual process. For example, goods-in may be subdivided into receipt on-site, delivery checking and acceptance, placing of goods into the goods-in area, detailed checking of medical devices, medical device acceptance/rejection and finally removal of goods to storage/picking/rejection area.

Once the distributor has identified the critical steps, a decision should be taken as to which steps require validation (or indeed whether all steps require validation). A risk management approach should be applied. Risks may be calculated by identifying the risk event (error) which may occur and then assessing the probability of occurrence, severity of occurrence (consequence/impact) and the degree of detectability of the event. In order to validate a process the distributor should first clearly describe/map the process (including the use of diagrams/flowcharts where relevant). Each individual step within the process should then be tested to verify if it is achieving its desired effects and operating correctly. This may include the following:

- Does the process as described within the procedure comply with legislation and guidance?
- Are the required actions being carried out as per the procedure?
- Are there any additional actions being conducted that are not in the procedure?
- Do the records (either paper or electronic) capture the data required by the procedure?
- Are personnel trained on the process?
- Are there delegated personnel to conduct the activity in the event of an absence?
- Is the equipment used for the process calibrated, maintained and operational?
- Is the correct equipment being used?
- Does each individual step allow the following step to proceed correctly?
- What could go wrong with the process and are there plans in place to provide for such eventualities?

Validation of processes should include an entire run through of a system from start to completion to ensure that each individual process does not have a negative impact on the following process.

Process validation should be completed prior to the distribution and sale of the medical device (prospective validation). In exceptional circumstances, where this is not possible, it may be necessary to validate processes during routine distribution (concurrent validation). Processes in use for some time should also be validated (retrospective validation).

Computer validation

Before a computerised system (relating to distribution processes) is brought into use, it should be demonstrated, through appropriate validation or verification studies, that the system is capable of achieving the desired results accurately, consistently and reproducibly. The level of validation required will depend on the complexity of the system, whether it is a bespoke or 'off-the-shelf' system, and also the level of customisation performed on the system. The distributor should examine its systems and decide on the level of validation required using a risk management approach. There should be documentation available describing the computerised systems in use and the level of validation performed or planned to be performed.

Equipment qualification

In order to qualify a piece of equipment, a written protocol should be generated outlining how the qualification will be conducted. The protocol should describe the piece of equipment along with its critical functions and attributes. The protocol should describe how the correct operation of these critical functions and attributes will be verified along with acceptance criteria. The protocol should be reviewed and approved by the company.

Following completion of the qualification exercise a report which cross-references the qualification and/or validation protocol should be prepared, summarising the results obtained, commenting on any deviations observed, and drawing the necessary conclusions, including recommending changes necessary to correct deficiencies.

8 THE MANAGEMENT OF RETURNED MEDICAL DEVICES

A medical device should be considered to be a 'return' once it has left the premises of the supplying distributor and subsequently returned to that premises. This may include the following examples:

- where a distributor supplies a customer with the incorrect medical device which is subsequently returned
- where a customer returns a medical device to a distributor which they ordered in error
- where a medical device is received back to the premises of a distributor having never been received by the customer (e.g. because the customer's premises was closed)

Distributors should be extremely vigilant in their assessment of the suitability of returned medical devices to be placed back into saleable stock. Once the returned medical device has been placed back into saleable stock it may not be possible to distinguish between the returned medical device and the remainder of the stock even if the batch/lot number of the returned medical device was recorded. The distributor must be extremely confident that the quality of the medical device has not been affected in any way whilst the medical device has been out of their care.

When a return is received back it should be placed in a separate area so that there is no risk that it would be returned to saleable stock prior to assessment in error. This separate area should be clearly segregated from saleable stock (either by physical means or by a validated computerised system).

All stages of the returns process should be documented. This documentation should allow all stages of the returns process to be traced including the person conducting each stage/activity.

A suitably competent person should perform the checks on returned medical devices. If the medical device is to be rejected then it should be placed into a reject area.

Personnel involved in the returns process should receive appropriate training and should have sufficient experience in relation to the handling of medical devices to increase their ability to identify falsified medical devices.

The distributor must ensure that the correct storage conditions have been maintained during the period the medical device was outside of the distributor's control. There must be no reasonable possibility that the storage conditions have been compromised during this period.

There should be a register or log of returns in place which should include all medical device details and reasons for their return. The assessment performed on returned medical device should be documented and should include the final disposition (i.e. approved for sale, quarantined, rejected or intended for destruction).

Special care must be exercised with the return of any medical devices requiring storage at low temperatures and sterile medical devices. Should a distributor decide to accept returns of medical devices requiring storage at low temperatures the criteria for accepting these should be strictly adhered to and clearly described within a procedure. The distributor must have documented evidence available for review confirming that the medical device was maintained within the cold chain for the entire time period during which it was outside of its control.

It is considered best practice if sterile medical device stock is only returned to saleable stock where there is no reasonable possibility that sterility has been compromised. If there is any doubt about their storage then they must not be returned to saleable stock. Stocks of sterile products with broken seals, damaged packaging or suspected of possible contamination must not be returned to saleable stock.

Distributors should be aware of the potential for falsified medical devices to enter the supply chain through the returns process. All relevant staff members should be made aware of this.

9 FALSIFIED MEDICAL DEVICES

It is imperative that all distributors operate using good governance and display vigilance in their efforts to prevent falsified medical devices from being traded with other distributors or placed on the market.

Distributors must:

- have a procedure in place detailing the processes to be followed in the event of identifying a suspected falsified medical device or of being notified that a (suspected) falsified medical device has been received.
- be aware of the possibility of falsified medical devices being supplied inadvertently through legitimate sources.
- have robust systems for ensuring the legitimacy of their suppliers and ensure that this is regularly reviewed.
- maintain a list of approved suppliers and ensure that medical devices are only sourced directly from these approved suppliers. In this regard it is imperative that the approval process includes assessment of the authority of the supplier to supply medical devices.
- be familiar with the history of the supply chain for medical devices received and question previous stages in the supply chain, if deemed necessary.
- train staff to be aware of falsified medical devices and what to look out for.
- ensure that the goods-in procedure involves a detailed inspection of medical devices received which is capable of identifying changes or unusual aspects to the appearance and packaging of medical devices.
- treat any offer of lower-cost medical device with suspicion. As such, distributors should be familiar with the market price of the medical devices they source and normal fluctuations in this price. Offers below expected fluctuation should be treated cautiously and investigated to ensure these are genuine.
- be vigilant and do not allow themselves to be used by counterfeiters to 'launder' falsified medical device.
- be aware of the possibility of falsified medical device entering the supply chain through returns.
- be knowledgeable of medical devices at risk of counterfeiting. Purchasers for the distributor should also be made aware of these medical devices.

A distributor in possession of a medical device that is found to be (or suspected of being) falsified is responsible for the removal and quarantine of the medical device from saleable stock. If a distributor is suspicious that a medical device which is being offered or has been received is not genuine then the HPRA should be informed immediately. Received medical devices which are suspected of being falsified should never be returned to the supplier without the consent of the HPRA.

Any suspicious approaches or activities noticed by a distributor should be reported to the HPRA without delay (devices@hpra.ie).

10 MEDICAL DEVICE RECALLS

The distributor should have a recall procedure in place. This is to enable the swift and effective recall from the marketplace of defective and/or potentially harmful medical devices. In the event of a recall the responsibility of the distributor will depend on where in the supply chain they act for the medical device in question.

The recall procedure should include, at a minimum, the following:

- the role of the management
- nominated responsibilities for coordination of the recall action
- contact numbers for the company (at least three personnel) and the HPRA (vigilance@hpra.ie)
- requirement to discuss with the manufacturer and agree any action with the HPRA before recall action or communication to other customers is carried out
- description of the batch/lot traceability system and method of identification of medical device recipients within the distribution chain
- method of handling recalled medical devices currently in-house and those received back
- arrangements to ensure segregation of recalled medical devices from saleable medical device
- arrangements for return of recalled medical device to the manufacturer or for destruction
- investigation and reconciliation reports
- procedure to be followed in the event of a quality defect being discovered on-site

There should be an efficient and effective method for identifying customers supplied with a medical device subject to a recall along with templates of forms and letters for the execution of a recall.

The recall procedure should be regularly challenged (at least once per year) to ensure that the process is effective and capable of tracing all customers and medical devices in the event of a recall in a timely manner. This challenge may involve identifying a particular batch of a medical device and reconciling quantities received with those in stock and distributed to customers. A mock recall need not be carried out where the company has participated in an actual recall during the previous year which has utilised the same traceability system.

11 OUTSOURCED ACTIVITIES

Technical agreements should be in place for all outsourced activities relating to distribution of medical devices. The technical agreements should at least describe the roles and responsibilities of both parties including details on transportation arrangements, receipt of goods, batch release arrangements, customer approval, documentation, recalls, returns, customer complaints, suspected falsified medical devices, and management of deviations and changes. The technical agreement serves as a basis for defining the division of activities and responsibilities between the parties. However, it is important to highlight that the distributor retains ultimate responsibility for ensuring that the operations conducted are compliant with

legal requirements. Technical agreements and procedures covering delegated activities may be reviewed during the course of a HPRA inspection.

12 TRANSPORTATION

Medical devices must be transported appropriately and in accordance with labelled storage conditions (including sterile conditions if applicable) and written procedures. Where contract service providers are used, the distributor must make itself aware of the operating procedures of that party (e.g. by audit). This assessment should include examination of the transportation methods and routes. The distributor should be fully aware of, and agree to, any operations subcontracted to another party by the contract service provider. The contracted arrangements for transportation should be documented in a service level agreement, and should include details of any sub-contracting.

The distributor must ensure that medical devices are not subjected to prolonged periods of storage during transportation.

For guidance on the transportation of medical devices requiring storage at low temperatures refer to the HPRA document entitled 'Guide to Control and Monitoring of Storage and Transportation Temperature Conditions for Medical devices and Active Substances' available on the 'Publications and Forms' section of www.hpra.ie. Although the guidance document refers to medicinal products and active substances, the principles are applicable to medical devices.

13 SELF-INSPECTIONS

In order to ensure and determine the effectiveness and compliance of the business with its quality system and legislation a self-inspection programme should be established. To this end, a risk based self-inspection plan should be prepared that covers all the unit operations carried out in the course of business over a defined period of time. Any self-inspection plan should be realistic and capable of achieving its objectives. Self-inspections may cover individual unit operations (and be conducted more frequently) or numerous operations within their scope.

A self-inspection log should also be established to record the scope of any self-inspections carried out, the outcomes of any self-inspection carried out and the actions (corrective and preventative) arising from any self-inspection carried out. A self-inspection log capturing such detail should prove useful with respect to trending the effectiveness of the quality system and determining the content of future self-inspection plans.

For all self-inspections carried out, a detailed report should be prepared and any non-conformances identified should be closed out in a timely manner.

14 FURTHER INFORMATION

For queries on the distribution of medical devices in Ireland, contact the Health Products Regulatory Authority at the following address:

Compliance Department
Health Products Regulatory Authority
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
Dublin 2

Telephone: +353-1-6764971

Fax: +353-1-6764061

E-mail: compliance@hpra.ie

Information is also available on the HPRAs website at www.hpra.ie

APPENDIX 1 FURTHER GUIDANCE

1 Selection of Articles from the Regulations

Medical Device Regulation

Article 10 (8)

Manufacturers shall keep the technical documentation, the EU declaration of conformity and, if applicable, a copy of any relevant certificate, including any amendments and supplements, issued in accordance with Article 56, available for the competent authorities for a period of at least ten years after the last device covered by the EU declaration of conformity has been placed on the market. In the case of implantable devices, the period shall be at least 15 years after the last device has been placed on the market.

Upon request by a competent authority, the manufacturer shall, as indicated therein, provide that technical documentation in its entirety or a summary thereof.

A manufacturer with a registered place of business outside the Union shall, in order to allow its authorised representative to fulfil the tasks mentioned in Article 11(3), ensure that the authorised representative has the necessary documentation permanently available.

Article 10 (11)

Manufacturers shall ensure that the device is accompanied by the information set out in Section 23 of Annex I in an official Union language(s) determined by the Member State in which the device is made available to the user or patient. The particulars on the label shall be indelible, easily legible, clearly comprehensible to the intended user or patient.

Article 13 (3)

Importers shall indicate on the device or on its packaging or in a document accompanying the device their name, registered trade name or registered trade mark, their registered place of business and the address at which they can be contacted, so that their location can be established. They shall ensure that any additional label does not obscure any information on the label provided by the manufacturer.

IVD Regulation

Article 10 (7)

Manufacturers shall keep the technical documentation, the EU declaration of conformity and, if applicable, a copy of the relevant certificate, including any amendments and supplements, issued in accordance with Article 51, available for the competent authorities for a period of at least ten years after the last device covered by the EU declaration of conformity has been placed on the market.

Upon request by a competent authority, the manufacturer shall, as indicated therein, provide that technical documentation in its entirety or a summary thereof.

A manufacturer with a registered place of business outside the Union shall, in order to allow its authorised representative to fulfil the tasks mentioned in Article 11(3), ensure that the authorised representative has the necessary documentation permanently available.

Article 10 (10)

Manufacturers shall ensure that the device is accompanied by the information set out in Section 20 of Annex I in an official Union language(s) determined by the Member State in which the device is made available to the user or patient. The particulars on the label shall be indelible, easily legible and clearly comprehensible to the intended user or patient.

The information supplied in accordance with Section 20 of Annex I with devices for self-testing or near-patient-testing shall be easily understandable and provided in the official Union language(s) determined by the Member State in which the device is made available to the user or patient.

Article 13 (3)

Importers shall indicate on the device or on its packaging or in a document accompanying the device their name, registered trade name or registered trade mark, their registered place of business and the address at which they can be contacted, so that their location can be established. They shall ensure that any additional label does not obscure any information on the label provided by the manufacturer.

2 Field safety corrective actions

An incident report can lead to the need for a Field Safety Corrective Action (FSCA) to be taken. An FSCA is an action taken by a manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. A FSCA can result in:

- The return or recall of a medical device to the supplier/manufacturer
- Modification of the medical device
- Modification to the clinical management of patients
- Exchange of the medical device
- Destruction of the medical device
- Retrofit by the purchaser of the manufacturer's modification or design change
- Advice or a Field Safety Notice given by the manufacturer regarding the use of the device (e.g. where the device is no longer on the market or has been withdrawn but could still possibly be in use as in the case of implants, or where there is a change in analytical sensitivity or specificity for diagnostic devices)

Distributors should note that a device modification can include permanent or temporary changes to the labelling or instructions for use, software upgrades including those carried out by remote access and advice relating to a change in the way the device is used (e.g. when an IVD manufacturer advises of a revised quality control procedure such as the use of third party controls or more frequent calibration or modification of control values for IVDs).

It is the manufacturer's responsibility under the legislation to inform member states of a FSCA. A field safety notice (FSN) is a communication sent by a manufacturer to users or customers (including distributors) in relation to a field safety corrective action. Nonetheless, a documented procedure for handling FSCAs notified by the manufacturer should be in-place. In addition, the system established should be capable of handling the reporting of FSCAs where the distributor is responsible for initiating or reporting a FSCA. The document should clearly outline the various responsibilities with respect to the planning, conducting and reporting of the corrective action taken. The procedure should also clearly stipulate that the HPRA should be notified before any FSCA is undertaken and/or communicated onward.