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

Ref: IA-G0004-x

Summary

DCC Vital welcomes the new draft guidance which will provide clarity in respect of distribution of medical devices. However, as a licensed pharmaceutical wholesaler that also works under similar GDP guidelines for medicinal products, we understand the significant differences in the devices vs the medicinal products market and hence the challenges with applying many of the guidance requirements to the devices setting. In particular devices manufacturers need to be significantly more aligned to the requirements in order to enable distributors to be compliant. It is unclear how such requirements will be communicated to manufacturers and whether the new MDR itself will ensure this and indeed what transition period may be required before manufacturers can themselves be compliant. It is therefore recommended that HPRA take the context into consideration in the guidance and apply this in practice in an inspection setting and clearly differentiate between a gap in applying best practice versus a non-conformance with the MDR itself. We suggest an additional section is added on HPRA inspections covering the transition period and beyond the implementation of the MDR from June 2020 and the impact of the requirements of this guidance on inspection outcomes in this regard. Similar to our IMSTA company members, we would also request that HPRA introduce a certification system to recognise compliance with the GDP guidance and/or the MDR clauses such that compliant companies are incentivised and non-compliant companies would not be permitted to continue breaching requirements. The following table includes specific comments on each section of the Guidance document.

Reference	Statement	Comment
Section 3	**Table 1:** *Placing on the Market* means the first making available of a device, other than an investigational device, on the Union market	Can HPRA clarify what is meant in practice by import? Is a number of distributors import the same product from the non-EU manufacturer which one is determined to be the importer or are all considered importer and each must apply their own details to the batches/stock they import? If one distributor assumes the position of importer, can other distributors import that product direct from the manufacturer with that importers details rather than their own?
Section 3	**Table 2:** **Article 14, Paragraph 2** 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.	The opportunity to sample here across the range of devices imported seems to be broader than HPRA interpretation later in the document which requires sampling with a batch rather than across a range. The MDR approach is more practical in the context of distributor.
Section 3	**Table 2:** **Article 14, Paragraph 6** 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 question provides the required information.	Can HPRA expand on how this is expected to be fulfilled? Whilst agreements may be in place which could stipulate this responsibility back on the manufacturer where a distributor is exclusive for that manufacturer, many distributors are in buy/sell arrangements to meet customer requirements and such agreements would not be viable in practice.
Section 3	**Table 2:** **Article 25, Paragraph 1** Distributors and importers shall co-operate with manufacturers or authorised representatives to achieve an **appropriate level of traceability** of devices.	Can HPRA clarify that batch traceability is not required for all medical devices once all recipients of a device can be contacted in the case of e.g. recall/FSCA.

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Section 4	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.	Can HPRA confirm they do not expect medical device distributors to seek the ISO 13485 standard?
Section 4	Superseded master copies of procedures should be maintained for a period of at least 6 years.	GDP guidelines for pharma require 5 years record-keeping. 6 years may add some level of confusion for those distributors distributing pharma and medical devices. Is 6 years regulated by the MDR itself or the HPRA guidance only?
Section 4	- Deviation management - Also in Section 4.4	Deviation is not a term generally used in distribution. Perhaps a broader explanation would be helpful or use of the term non-conformance instead? In section 4.4 there does not seem to be reference to other types of non-conformances e.g. product quality issues determined prior to distribution for example. The term incident and stock discrepancies are used as examples but it is not clear how these are deviations from the definition given ("non-conformances with the Regulators or internal procedures"). Non-conforming products appear to be covered under the definition of complaints which is usually reserved for complaints from customer or complaints to suppliers and doesn't ordinarily cover other non-confirming goods found e.g. internally.
Section 5	**PERSONNEL AND STAFF TRAINING** Reporting structures and role profiles should be clearly established.	At what levels would HPRA expect to see role profiles and what expectations around these documents does HPRA have?

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Section 5.1	**Key personnel** 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.	Can key personnel include non-management warehouse staff if appropriately trained?
Section 5.2	**Training**	Is there HPRA expectation of GDP training similar to pharma on annual basis? How is effectiveness of training expected to be demonstrated in practice?
Section 5.2	Both trainer and trainee should sign-off on all training records.	Is self-training permitted for minor updates e.g. of SOPS?
Section 6	**DOCUMENTATION AND RECORD KEEPING** This includes but is not limited to medical device name and/or code, batch or lot number, quantities and delivery date.	Based on the MDR paragraph stating "appropriate level of traceability", can HPRA confirm that batch or lot number records are not mandatory once traceability of customers is possible?
Section 6	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	Can HPRA confirm that electronic records e.g. on SAP/ERP system are acceptable? With regard to records for checks for CE marks on product, can HPRA advise how they would expect this check to be recorded in practice? If the requirement is in the SOP and the operator signs the delivery dockets are part of other checks e.g. quantity, lot etc., is this adequate? Unlike pharma where a product has a specific licence number a CE in and of itself gives limit info to check/record. Similarly on approval into saleable stock, would an electronic confirmation be adequate?

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Section 6	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.	Again reference to 6 years vs 5 years traditionally used in pharma distribution. Also the 6 years refers to from date of receipt rather than distribution which could be challenging to measure. If lot traceability is not practice (as not mandatory according to Article 25, paragraph 1) how can the 6 years be measured for any particular product?
Section 7	**7.1 New medical device introduction** 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.	HPRA should be aware that medical device distributors do not generally have access to regulatory expertise and hence the reliance on the supplier to assign classifications for products will be needed. The requirement of documentation of each new medical device appears onerous as thousands of products can be set up during a period with multiple codes within each product type vs a much smaller volume in pharma distribution. The MDR refers to a sampling approach under Article 14 Paragraph 2 rather than each new introduction. Can HPRA advise if sampling is acceptable in new medical device set-up e.g. setting up products from a new supplier? Distributors that are buy/selling may be sourcing once-off products and hence the investment in set-up time may make this activity unviable. In addition, manufacturers are not accustomed to providing Declarations of conformity etc. for products and this may be a challenge for distributors to obtain and may impact on availability of medical devices. Please note also the expertise to read and understand a Declaration of conformity or a CE certificate and associate it appropriate against a product is not a current skill set in devices distribution. For example not all products will have a CE cert due to their class, how can distributors be assured the DoCs or CE certs are valid etc.? It is unlike in pharma where the Summary of Product Characteristics (SPC), lists the licence number on a particular packaging and where this SPC is available online from HPRA etc.

Reference	Statement	Comment
Section 7	**7.1 New medical device introduction** It is recommended that a distributor of medical devices has a technical agreement in place with their supplier.	As mentioned earlier, this may be possible in an exclusive arrangement between the distributor and manufacturer but many distributors do not operate in this way. Similarly, exclusive distributors who then sell on the device to another distributors would not ordinarily have any agreements in pace as it is a fee trade arrangement. How therefore can this be applied in practice in all such situations or can this be restricted to exclusive or primary distribution settings. Please note the practice of technical agreements within medical devices by manufacturers is not well established unlike in pharma and will likely take some time to implement in practice and education of manufacturers is similarly required.
Section 7	**7.2 Receiving** 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.	The use of the term declaration of conformity here is confusing. This is a document in the technical file and not batch related and hence would not be expected x to be received at Goods in. Indeed it may be challenging to get such documentation as manufacturers are not accustomed to providing it and it may compromise market availability. Certs of conformity are batch related but not required for Class 1 products and this may be confusing at distributor level to understand what is available where. Again the volume and range of device products received by a typical device distributor is substantial and this level of checking may be unviable in many settings. Will HPRA accept a sampling approach as indicated by the MDR Article 14 Paragraph 1. In Pharma, the Batch release certificates (BRC) are only required to be checked when sourcing from outside of Ireland – can a similar pragmatic approach to be applied? If there is a Technical agreement in place with the manufacturer covering this requirement, can this check be the responsibility of the manufacturer rather than distributor? Please note there is some concern that this requirement for documentation may be so onerous and challenging that it may impact on the viability of some distribution and hence impact availability on the market.

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Section 7	**7.2 Receiving** 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.	HPRA guidance is allowing a risk based sampling approach for the verification steps only whereas the MDR appears to indicate a broader sampling approach which would be more practical in practice. How does HPRA anticipate distributors can verify the labelling and IFUs are fit for purpose without access to the technical file, regulatory expertise and without opening the packaging which would compromise the integrity of the product? This requirement is more onerous that pharma where only a licence number and in some circumstances BRC is needed. Would HPRA be open to this check being done off-line away from Goods –in perhaps sampling on a periodic basis? Please note also this relies on the cooperation of the manufacturer which may be challenging particular in a non-exclusive distribution situation or a longer supply chain e.gh. distributor to distributor. The UDI will be phased in so distributors will need to be aware of the timelines and will need to start classifying products by the classifications in order to know when it may apply. This is an extra layer of classification than that outlined in Section 4. Verification records are required and again if a sampling approach is acceptable for all verification elements this will be more practical to record in more detail outside a Goods in check. Goods in documentation is usually signed/initialled but the detail of what is being signed for is detailed in the related SOP – is this considered acceptable to HPRA for any checks to be conducted at Goods in?
Section 7	**7.2 Receiving** 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.	HPRA should be aware that cold chain validation is not as advanced in medical devices as in pharma. Manufacturers do not have the same disciplines of validation including validation time etc. as in pharma and therefore a substantial education is required across Europe in this regard by competent authorities and in particular Notified Bodies. Many cold chain products are indeed received in ambient conditions for storage under refrigerated conditions? Will HPRA accept if distributors receive manufacturer statements from manufacturers in this regard that such transportation is acceptable?

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Section 7	**7.2 Receiving** 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.	What is meant by "formal release" in this statement? Are routine procedure checks by Goods in staff and release on to the ERP system considered acceptable?
Section 7	**7.2 Receiving** 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.	Can HPRA please provide more guidance on what is considered to be a serious risk and reportable directly by the distributor (rather than the manufacturer)?
Section 7	**7.2 Receiving** Records should be available of all checks performed at receipt and these should be available to the HPRA during an inspection.	Not all documentation is routinely maintained for the 6 years indicated in this guidance? Are ERP records acceptable as evidence for the longer term as retaining such paper or indeed electronic scans would be onerous?
Section 7	**7,3 Traceability** 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.	As highlighted previously, it is unclear the level of traceability that is required e.g. by product by customer or by product by batch by customer.
Section 7	**7.4 Storage** Medical devices must be stored in accordance with the labelled conditions, including potential relative humidity conditions.	As HPRA are aware, labelled conditions for medical devices can vary significantly in nature and in many cases prove challenging in practice for example where a range is not give e.g. Store at 8^{o}C. Similarly manufacturers have not been particularly challenged on the rationale for labelled storage conditions to-date and have used legacy temperature ranges that are intended to reflect "ambient " but which in practice may be challenging to maintain esp. in transport e.g. 15 to 30^{o}C. On discussion with manufacturers e.g. in USA, they advise they have used these ranges for historical reasons rather than based on more scientific evidence. As the HPRA guidance is limited to Ireland, the power of an Irish distributor to work with a large manufacturer to change the labelled conditions to more practical ranges that meet with both the manufacturer and distributor needs will be challenging.

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Section 7	**7.4 Storage** 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.	DCC Vital request that HPRA update the referred guide to include medical devices or develop an equivalent document for medical devices as comparison to pharma is not always relevant. In particular relative humidity is not covered in the pharma document
Section 7	**7. Pest control**	Further guidance on the expectations for distributors on pest control would be valuable and expectations of HPRA e.g. who can approved the pest control records, what frequency of pest control visits is expected etc..
Section 7	**7.6 Medical device disposal**	Similarly further guidance on this area would be welcomed as the guide provides limited guidance.
Section 7	**7.7 Promotional samples/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.	As highlighted previously, it is unclear the level of traceability that is required e.g. by product by customer or by product by batch by customer. The same applies in terms of traceability to sales representative.
Section 7	**7.8 Validation and Qualification**	In general more information is requested to explain to distributors about validation vs qualification vs calibration and what should be included in a distribution setting to avoid confusion with the manufacturer setting. Also what are HPRA expectations in terms of SOPS, protocols, validation plans in respect of device distribution including the related scope e. steps/stages in supply chain, equipment, IT systems?
Section 7	**Computer validation** 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	The concept of CSV may be very new to device distributors and further guidance on what is expected including the level of documentation, testing etc. would be important to ensure compliance. Similarly on equipment qualification.

Reference	Statement	Comment
Section 8	**8 The Management of Returned Medical Devices** Distributors should be extremely vigilant in their assessment of the suitability of returned medical devices to be placed back into saleable stock. 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.	Whilst distributors will have a process for checking returned devices are fit for sale, the level of formalisation of this process including assessment documentation and sign off and by whom may vary widely. This process does not appear to be specifically covered in the new MDR under distributor requirements so it is unclear whether existing practices are acceptable and how onerous it may be for distributors to implement what appears to be a more pharma-like process for devices which are significant in number. Also to effectively assess a sterile or cold chain returned device may be difficult which may result in a blanket ban on such returns which may be uneconomical for ether the distributor or the customer resulting in patient supply being compromised. In this respect of a possible increase in restrictions on accepting returns, it is recommended that HPRA also engage with HSE in this regard to expect that returns and hence credit may not be available for returns of certain products e.g. sterile
Section 9	**Section 9 Falsified Medical Devices** 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.	In previous sections, we have commented on bona fides in the context for manufacturers but suppliers may also be other distributors/importers. Again this section this refers to bona fides which may be challenging esp. if products are being sourced from another distributor in another MS. How can an Irish distributor assess the authority of the supplier who is a distributor to supply medical devices? In reverse this is the same for distributors in other MSs, in the absence of a GDP certification from HPRA for Irish distributors how can distributors in other MSs assess Irish distributors?
Section 10	**10 Medical Device Recalls** requirement to discuss with the manufacturer and agree any action with the HPRA before recall action or communication to other customers is carried out. 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.	Currently distributors act on manufacturer instructions with regard to recalls/FSCAs (please note the FSCA is term normally used in devices). There is generally no involvement with HPRA not information provided on whether the manufacturer has informed HPRA. This is a manufacturer responsibility and it is unclear the role that a distributor can and should play in this regard. Similarly on letters and forms, these are usually provided by the manufacturer and it may cause confusion if the expectations is on distributors to generate such documentation esp. as they are not knowledge in the background to a particular product and the nature of the recall.

Reference	Statement	Comment
Section 11	**11 Outsourced activities** 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.	It is unclear the types of outsourced activities that are covered by this section and further elaboration would be useful. Also there is reference to responsibilities that are unexpected in the context of outsourcing distribution such as batch release. Distributors would not be involved in outsourcing batch release as this is a manufacturer responsibility.
Section 12	**12 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.	As above DCC Vital request that HPRA update the referred guide to include medical devices or develop an equivalent document for medical devices as comparison to pharma is not always relevant.
Section 13	**13 Self Inspections**	As most distributors will have an ISO 90001 system the term self-inspection is not well known so internal audits is considered a preferable term. It is unclear if the ISO 9001 standard in respect of internal audits is considered acceptable to meet this section of the guidance.