IMSTA feedback on HPRA Draft Guide to Distribution of Medical Devices, including *in vitro* diagnostic Medical Devices public consultation

Prepared by IMSTA Regulatory Working Group, May 2017

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Summary

IMSTA welcomes the introduction of the HPRA Guide on Good Distribution Practice (GDP) for Medical devices to clarify and support best practice implementation. IMSTA believes the guidance will support the industry to develop and improve standards in the medical device supply chain. The IMSTA regulatory working group following consultation with the membership would like provide the following feedback on the draft guidance document in advance of publication in its final form to ensure a practical and economically viable implementation of the coming years. IMSTA also recommends that HPRA consult with other stakeholders such as the customer e.g. HSE so they are also aware of knock-on implications of the new Regulations and HPRA guidance on the customer experience. IMSTA understands HPRA will update the guidance prior to publication to ensure it is line with the final approved Regulations text as published on May 6th 2017.

To assure fair and equitable application of the Regulations and guidance, IMSTA would also like to reiterate our requests for HPRA certification of compliance or equivalent such that distributors may provide as evidence to customers such as HSE for example during the tender process of an assured and compliant supply chain. Such certification would also encourage the broader distributor base to comply both with the upcoming Registration programme and ultimately the implementation of Good Distributor Practice for Medical Devices.

It would also be useful for a definition of distributor to be included in the guidance to better understand where the guidance is applicable. Distributors can vary from those who are part of the same corporate group as the manufacturer, those exclusively representing the manufacturer, those in a wholesaling arrangement, buying and selling based on customer demand or those performing a virtual transaction only. Similarly a distributor may supply other distributors or economic operators or directly to the consumer or patient. The practical implication of the requirements in the guidance document would vary depending on the nature of the distribution arrangement. Further guidance on the requirements of importer would also be welcomed in this document. From previous communications, IMSTA also understands the HSE National Distribution Centre (NDC) will be considered an economic operator under the new MDR and hence this guidance is also applicable to the NDC.

On a general point, IMSTA notes many similarities with the existing GDP for medicinal products many of which are valuable. However, we wish to highlight the differences in medical devices where the CE is a pan-European accreditation versus typically a national authorisation for a medicinal product and hence the requirement for certain checks at national level such as checks for certification and accompanying information for all batches are considered unnecessary and indeed challenging in the absence of availability of documentation on EUDAMED database.

Finally IMSTA seeks clarification on the regulatory application of the guidance document including timing and in particular the impact on futureinspection findings e.g. are inspection findings/non-conformances restricted to non-conformances with the Regulation clauses only rather than recommendations from this guidance document?

The following sections highlight feedback to a number of aspects of the HPRA guidance for HPRA consideration. Members' specific responses are included in the Appendices.

Quality Management Systems (QMS)

Emphasis on a number of specific standards such as ISO 13485 and 14971 may be confusing to distributors as these standards are typically considered product and/or manufacturing related. ISO 9001 is an existing well established and understood standard to the majority of distributors. IMSTA considers that this standard is well suited to distributor requirements and aligns with customer requirement and supports the awareness and application of external/regulatory requirements on the QMS. The latest ISO 9001:2015 standard, required to be implemented by 2018, has additional focus and requirements regarding statutory/regulatory requirements, planning of changes and risk management which support these elements as outlined in the Draft guidance document – see related updated clauses below:

- 4.1 UNDERSTANDING THE ORGANISATION AND ITS CONTEXT
- 4.2 UNDERSTANDING THE NEEDS AND EXPECTATIONS OF INTERESTED PARTIES
- 4.3 DETERMINING THE SCOPE OF THE QUALITY MANAGEMENT SYSTEM
- 6.1 ACTIONS TO ADDRESS RISKS AND OPPORTUNITIES
- 6.3 PLANNING OF CHANGES
- 8.4 CONTROL OF EXTERNALLY PROVIDED PROCESSES, PRODUCTS AND SERVICES

To support distributor understanding of the guidance document and minimise confusion with manufacturer responsibilities, IMSTA request that HPRA include some distributor examples or case studies to explain new concepts such as risk management, change control and validation. Further guidance on Computer system validation versus verification requirements would also be valuable. To be consistent and maximise understanding of certain QMS elements, IMSTA also recommend that terms such as self-inspection and deviations/non-compliances should be replaced with more recognised terms such as internal audits and non-conformances in line with the ISO 9001 standard.

CE Mark and documentation verification

The new Regulation calls for distributors to verify that devices are CE-marked with EU declarations of conformity plus the requirement to check for appropriate accompanying information supplied by the manufacturer and the UDI. The Regulation draft text indicates that a sampling method approach representative of devices supplied by that distributors may be taken.

In reviewing the HPRA guidance document, the sampling approach is indicate at a batch level e.g. Sections 7.1, S. 7.2 rather than a broader portfolio level sampling approach indicated by the Regulations text. The requirement to check for the above at a batch level is potentially very onerous and challenging for distributors for the following reasons:

- Deliveries may include multiple batches and may not be packed by batch by the supplier or itemised at this level on delivery documentation.
- Declarations of conformity (DoC)are available at a product level and not batch level
- Certificates of conformity (CoC) are batch level certificates but are not routinely provided by all manufacturers on a batch basis nor are Certificates of conformity mandatory for all Devices

Classes e.g. Class 1. Manufacturers may not provide such documentation readily if the distributor is non-exclusive partner.

- Distributors do currently not have the regulatory expertise nor do they routinely classify in ERP systems medical devices by Class (e.g. I, Is, IIa, IIb, III, General IVD etc.) to enable assessment of manufacturer documentation for compliance.
- A small to medium scale distributor may have thousands of product lines/skus with a large scale distributor having tens of thousands of lines/skus on their ERP systems with up to 10,000 active lines at any one time. The volume of activity to complete CE, DoC and/or CoC checks on all products and batches is not economically viable so a risk based approach as per the Regulations draft text would be welcomed to ensure stock availability for Irish patients is not compromised.
- Distributors do not have access to the Technical file to determine what information should be supplied with a product to complete this check and may not have an exclusive partnership with manufacturers where they may be prepared to supply the approved documents to check against.
- Additionally Distributors would have to open packaging in order to check for Instructions for Use (IFU) etc. to perform this check which is destructive and hence such samples could not be sold. For higher cost items this may not economically viable and may also be the case if high samples volumes are expected to be taken.
- The EUDAMED database (unlike similar tools in pharma such as the HPRA website access to Summary of Products Characteristics or EudraGMDP for supplier bona fides) will not be available for the implementation deadline of the MDR to facilitate access to regulatory documentation.
- UDI requirements will be phased in and as indicated above, distributors will need to implement device classification by Class in order to configure ERP systems and/or manually to enable implementation of UDI checks at the appropriate timeframe.

Batch traceability

It is unclear from the document if HPRA expects full batch traceability on all medical devices as in Section 6, it is included as a record to be check and retained whereas section 7.3 indicates tracking by batch is more valuable rather than mandatory. Similarly requirements for certain documentation at batch level at receipt also indicates an expectation of batch level traceability. The Regulations allow for "appropriate level of traceability" so IMSTA would welcome a more open approach to risk-based batch tracking. The minimum should be traceability of product to customer (while customer term should be defined, see later in this document and traceability to the end users, who is not a healthcare professional, is not planned in MDR/IVDR) level which enables recall of all batches of a particular product to the receiving customers. Also in terms of Goods in checks outlined in the guidance, multiple batches may be received in any one delivery which will add significant labour time to any CE mark or documentation checks at batch level.

Supplier and Product Due diligence

As highlighted above, supplier and product level checks will be onerous and challenging as these are not routinely performed nor is there ready access to such data esp in the absence of EUDAMED. The volume of product lines and codes for medical devices is significant and will significantly increase workload and time to set-up products which may compromise timely patient access. There is also a high reliance on cooperation of the supplier to guide the distributor on the documentation applied and the nature and classification of the products.

There is a recommendation for a technical agreement to be in place with the supplier. Clarification is sought under which circumstances this is expected as many distributors operate trading relations with suppliers rather than exclusive arrangements (aka primary wholesaling) where a TA may be feasible. The concept of technical clauses in a commercial agreement is also recommended by IMSTA as an alternative but again in exclusive rather than trading partnerships. The Draft Guidance advises that documentation should be available relating to each new medical devices introduction – this is not in lien with eh Regulations sampling approach.

Customers

The guidance contains requirements concerning customer details including SOPs for customer approval. As customers may be end user and/or patients, it is unclear what customer requirements are to set-up and what contact details may be possible to hold. Therefore IMSTA requests that HPRA defined the customer set and hence we request that the term customers is replaced by economic operators.

Personnel & Training

Clarification on expectations of training and personnel role profiles would be welcomed. Standards such as ISO 9001 include such requirements and IMSTA would recommend HRPA advice if these standards are acceptable and whether additional requirements as has been seen in pharma are expected e.g. annual GDP training. Similarly qualifications and expertise for certain roles and activities are not specified and as there is no regulated role for distributors such as Responsible Person outlined in the Regulations, is HPRA open to distributor decisions in this regard. Expectations of HPRA around “suitably competent person” to perform returns checks is also requested.

Receiving

HPRA clarification on the expectation on how checks are expected to be recorded is requested. Will SOPs describing checks supported by electronic or manual signatures on receipt documentation be considered adequate? See above for feedback on batch level checks for CE market, certification, labelling and UDI.

Returns

Impact of returns formal assessments esp. for cold chain and sterile products is likely to restrict medical devices returns in future and the HSE as a key customer needs to be made aware that the medical device industry will be require to implement such requirements.

Transportation

Medical device manufacturer's storage instructions appear not to be as tightly regulated as in other industries such as Pharma and can tend to be based on long term storage rather than inclusive of e.g. transportation time. Similarly manufacturers' validation and cold chain processes may not currently provide adequate guidance to distributors on maximum transport times or the impact of excursions. Hence education and activity across global medical device manufacturers is required to support distributors in this regard including provision of supplier documentation to assure transportation. Reference in made in Section 12 to sterile conditions as a transportation arrangement; please clarify what is meant by the statement e.g. robust shippers/packaging? IMSTA considers that manufacturers are responsible for ensuring medical device packaging is adequate to maintain product integrity and hence sterile conditions and that this is not a distributor responsibility except to check for outer carton damage etc.

Paragraph 3 of the Regulations only requires Distributors to be responsible o transport under their responsibility and hence transport from supplier to distributor may be challenging for the distributor to control esp. in a trading rather than a partnership relationship.

Complaints/Incidents management

Distributors have a responsibility to inform their suppliers/manufacturers of complaints and other incidents/reports which may affect product quality or patient safety. However there is an additional requirement in the draft guidance to notify the competent authority if a distributor is concerned about serious risk. Serious risk requires further definition as vigilance assessment is a manfacturer responsibility and hence the expertise is not available at the distributor to make this assessment in the absence of further direction.

Comment [PhS1]: There is no ment that ALL suspected incidents must be communicated immediately to manufacturers, which would generate unnecessary data flow and workload. It also will implicitly enforce distributor' installed base disclosure, which my lead competitive advantage loss and manufacturer dominant position.

Recalls

IMSTA recommends that term recall is replace with Field Safety Corrective Actions as this is the currently used terminology for medical devices. Similarly the requirement to agree any action with HPRA has not traditionally been seen as a mandatory requirement for manufacturers and distributors generally have not been involved in such communications directly. Can HPRA clarify the expectation in this regard for distributors and what are mandatory vs desirable? Regarding template recall forms and letters at distributor level, these are from our members' experience provided by the

manufacturer on a case by case basis and not documents generally developed by distributors so IMSTA query the inclusion of this requirement.

Outsourced arrangements

Batch release arrangements are not normally defined in outsource activities for a distributor as the distributor only receives finished released goods and hence the inclusion of this activity in Section 11 is confusing. Similarly as outlined previously the requirement to define customer approval activity is not clear as we are not aware of customer restrictions to receive medical devices unlike pharma.

Importers

As Distributors may not be aware of the new definition of importer as an economic operator, IMSTA requests additional information on the Importer and the requirements to be included including some examples. Can HPRA also clarify on whether importation relates to sourcing outside EU or EEA as this remains unclear. Similarly for potential manufacturer activities such as making a device under distributor own name may not be fully understood and further guidance is requested (ref Section 7.1).

Record keeping

The guidance references 6 years record keeping which may prove confusing as many distributors already retain pharma distribution records for 5 years and/or implants may require 15 years traceability records with financial records up to 7 years. It is also unclear if retention periods may vary with record type.

Further detailed guidance is requested for areas such as pest control, disposal and validation.