Medical Information for Medical Devices: Understanding requirements; Anticipating needs; Delivering services

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With the increasing diversity and volume of medical devices, there is a growing need for the provision of medical information to support their use. While devices are sometimes used independently, they are more commonly used in combination with other devices or licensed medicines, or sometimes designed to enhance the lifecycle of the medicine. Through this article, I share an insight to the legal framework, including the imminent European Medical Device Regulation, and challenges of delivering Medical Information for medical devices with some proposals for practical application.

Background, Definition and Classification:

In 2013, I had the privilege to lead the revision and publication of the PIPA UK Guidelines for the Pharmaceutical Industry Medical Information Departments. At that time, we chose to broaden the scope to include medical devices. This decision was catalysed by the publication of the first Association of British Healthcare Industries Code of Business Practice (http://www.abhicodeofpractice.org.uk/multimedia/New%20Folder/ABHI%20CoBP%20-%20March%202016.pdf) in 2012, the update to the European Commission Guidelines regarding the Medical Device Vigilance System in 2013 (MEDDEV 2.12-1 rev8 - (http://ec.europa.eu/DocsRoom/documents/15506/attachments/1/translations) and also in recognition of the increasing volume of medical device and hybrid medical device / licensed medicine enquiries being received across our membership. Similar to the European Directive 2001/83/EC (http://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf) relating to medicinal products, the longer standing 93/42/EEC (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1990L0385:20071011:en:PDF) relating to medical devices made only limited reference to the provision of information on request. However, it is clear that patients and healthcare professionals expect and require ready access to quality, up-to-date balanced information to facilitate the safe and effective use of medical devices.

The draft European Medical Device Regulation (http://data.consilium.europa.eu/doc/document/ST-10728-2016-INIT/en/pdf) has just been published (Feb 2017). This is set to replace 93/42/EEC and the related 90/385/EEC (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1990L0385:20071011:en:PDF) (active implantable devices), with adoption forecast in May/June 2017 and transition to full implementation over the next 3 years. This new Regulation, extending to a massive 566 pages, is a major development. It should support medical device innovation, with greater emphasis on safety – including quality assessment and management, market surveillance, traceability (a new international Unique Device Identification (UDI) system), clinical investigation and documentation. Progression of the Eudamed regional database of medical devices and the Medical Device Coordination Group appear key.

The 'Medical Device' definition is very wide and included within Article 1 of 93/42/EEC (2007 update). It has been further modified and broadened within Article 2 of the draft 2017 Regulation:

any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- *diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*
- *investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*
- *providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,*

and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.

The following products shall also be deemed to be medical devices:

- *devices for the control or support of conception;*
- *products specifically intended for the cleaning, disinfection or sterilisation of devices as referred to in Article 1(4) and of those referred to in the first subparagraph of this point.*

Both the 93/42/EEC directive and draft 2017 Regulation advise that, where a device is used to administer medicines, 2001/82/EC is also relevant for the medicinal component. However, for an integrated presentation of a device and medicine, the single product is governed by 2001/82/EC with device safety and performance considerations from 93/42/EEC, transitioning to Annex 1 of the Regulations (once implemented).

Devices are categorized as Class I, IIa, IIb or III, where Class III products carry the greatest clinical impact and risk. For example, products that include a human blood derivative or come in to contact with the CNS are Class III whereas non-invasive devices which only contact intact skin are Class I. This classification is not printed on the label but is indicative of the documentation, safety monitoring and quality assessment criteria.

CE marking of devices is necessary for marketing within Europe and indicates that they have been formally assessed against Class-specific quality assurance criteria and an appropriate EC Declaration of Conformity to the Medical Device Directive has been made.

Every device label must carry specific information to support its safe and appropriate use. While all licensed medicines have a 'Summary of Product Characteristics', not all devices are required to have an informative, structured 'Instructions For Use' (IFU) - for full details, see 93/42/EEC Annex 1 Clause 13.6 or Chapter III of the draft 2017 Regulation. Class IIb and Class III devices must be supplied with an IFU, however this is not always necessary or available for simpler Class I and IIa devices. Also, even when an IFU is available, the level of detail can vary. While all licensed medicines have a defined 'Indication' it is only necessary for the 'Intended Purpose' of a device to be shown on the label or IFU when this is not obvious. The variability of information available can sometimes, in itself, drive enquiries as well as impact the ease to which enquiries can be answered.

The draft 2017 Regulation has rich content and, from a Medical Information perspective, paragraphs 43, 48 and 74 of the formal introduction especially caught my attention:

> *43 - Transparency and adequate access to information, appropriately presented for the intended user, are essential in the public interest, to protect public health, empower patients and healthcare professionals and to enable them to make informed decisions, to provide a sound basis for regulatory decision-making and to build confidence in the regulatory system.*
>
> *48 – For implantable devices and for Class III devices, manufacturers should summarise the main safety and performance aspects of the device and the outcome of the clinical evaluation in a document that should be publicly available.*
>
> *74 – Manufacturers should play an active role during the post-market phase by systematically and actively gathering information… /…manufacturers should establish a comprehensive post-market surveillance system…*

It is important to understand how Eudamed will develop to support 43 and 48, and clarify the role of company Medical Information functions, both internally and customer-facing, for all three aspects.

For those involved in Promotional Compliance medical review, Article 7 of the draft 2017 Regulation also lays out the expectation not to mislead, to stay in line with the 'intended purpose' of the device and to include information about likely risks.

Anticipating Device Enquiries:

There is some cross-over and predictability between the style of medicine and device enquiries. For medicines, the focus is typically efficacy, dose, adverse events,

Reprint from PIPELINE Issue 52, April 2017
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excipients, release specifications, clinical studies, interactions etc. However, device enquiries are also relatively easy to anticipate:

- *excipients and specification of components e.g. latex, plasticisers,*
- *evidence of validation and verification for CE-marked medical software,*
- *provision or discussion of IFU documents (sometimes explaining why they are not available and providing alternatives),*
- *clinical data supporting the 'Intended Purpose' or contra-indications,*
- *method of assembly and use,*
- *specification and explanation of device accuracy,*
- *pharmaceutical compatibility with named medicines,*
- *device performance concerns (with possible escalation for Quality data collection).*

Some will be simple while others will be extremely complex, especially when there is limited information or the clinical setting is unfamiliar.

Interestingly, both the 2007 update to 93/42/EEC and the draft 2017 Regulation specify that, for single use devices, manufacturers must include their rationale for this designation and the risks of multi-use on any IFU or, when there is no IFU, provide this on request. Of course, Medical Information are the ideal function to fulfill this mandatory requirement.

Market Surveillance for devices is included in the European Commission guidance (http://ec.europa.eu/DocsRoom/documents/15506/attachments/1/translations) relating to the Medical Device Vigilance System. This is likely to be further advanced through the transition to the new Regulation (for example, clause 76 highlights the need for Member States to raise awareness of the importance of reporting incidents). Medical Information is likely to receive reportable incidents that need to be appropriately escalated and also serve as a professional contact route for Field Safety Corrective Actions and Field Safety Notices.

Many devices are used in direct combination or at the same time as medicines. Sometimes these are from different companies and it is important to liaise efficiently, especially for any escalation and transfer of potential issues to Vigilance or Quality.

Healthcare Professional and Patient Awareness, Needs and Expectations:

From experience, enquirers do not always know that the product they want to discuss is a device rather than a medicine. For example, most Pharmacists are trained that all injectables are licensed medicines, so there is surprise when manufacturers provide some pre-filled intravenous flushes as devices. Their questions and service expectations are guided by clinical need, not the legal classification or with consideration that there is a combination of products.

Also, as devices have come into scope for promotional compliance guidelines, the scientific rigor of devices, with access to greater product detail and clinical/functional evidence, has been highlighted. Initially, this was UK-specific (with the 2012 ABHI Code of Business Practice, last updated in 2016) (http://www.abhicodeofpractice.org.uk/multimedia/New%20Folder/ABHI%20CoBP%20-%20Advertising%20&%20Promotion%20Guidelines%20March%202016.pdf). However it was interesting to note that human drugs, devices and biological products as well as animal drugs are all in scope for the draft 2017 FDA guidance (https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm537130.pdf) "Medical Product Communications That Are Consistent With the FDA-Required Labelling – Questions and Answers, Guidance for Industry".

As the comprehensive 2017 Regulation is adopted and implemented, it is reasonable to anticipate raised awareness and more requests from healthcare professionals and patients to the manufacturing or distributing company.

Practical Proposals:

I'm a great believer in keeping things simple and avoiding undue complexity.

As enquirer service level expectations are similar, the style of questions is broadly the same (with some relating to the combined use of a device with a medicine), and there is a requirement to escalate product incidents, it is probably best to adopt the same process for medicines and devices. Any significant differences can be managed by exception (for example, you may have a different escalation path for device incidents).

You could also extrapolate many of your usual operational management approaches to the devices – for example: periodically reviewing past enquires to identify trends, resourcing gaps and training needs, considering assigning a subject matter expert for key devices. If device enquiry levels are low, consider if this is a missed opportunity.

You may find it useful to explore within your company how other functions are preparing for the transition to the 2017 Regulation. For example, how will UDI be

implemented and what are the relevant changes to the Quality Management System including the post-market surveillance system?

These proposals will also hopefully assist building or growing the professional support for your medical devices:

- *Explore 93/42/EEC and the draft 2017 Regulation,*
- *List your medical devices, including their site of manufacture and key contacts for support,*
- *Understand the sales profile and forecast (including any major supply chain issues) to anticipate changes in enquiry activity,*
- *Maintain access to an up-to-date source of label artwork, IFU, Class designation, Declaration of Conformity and CE-certificates, and other supporting documents (eg manuals),*
- *View and handle the key devices (or at least collect annotated pictures),*
- *Obtain a sample of your complex devices (to help you understand and manage the questions),*
- *Clarify the style of questions in scope for your function and what would be transferred.*

In summary, although document names may differ, the principles and needs are broadly the same and Medical Device Medical Information should be delivered to similar standards and processes as Medicinal Product Medical Information.

Follow the discussion online:

http://www.pipaonline.org/Discussion-Forums/Discussion-Forum/540-PIPELINE-ARTICLE-DISCUSSION-Medical-Information-for-Medical-Devices

References:

ABHI Code of Business Practice - http://www.abhicodeofpractice.org.uk/multimedia/New%20Folder/ABHI%20CoBP%20-%20March%202016.pdf

European Directive 2001/83/EC - http://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf

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Guidelines on a Medical Devices Vigilance System – MEDDEV2.12-1 rev 8 http://ec.europa.eu/DocsRoom/documents/15506/attachments/1/translations

Draft 2017 FDA guidance - Medical Product Communications That Are Consistent With the FDA-Required Labelling – Questions and Answers, Guidance for Industry - http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm537130.pdf

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