

## **EMA's Draft Guideline on Drug-Device Combinations Sheds Needed Light on Expectations for Device Assessment**

EMA's draft guideline on quality requirements for drug-device combination (DDC) products provides a template for the new concept of the notified body opinion (NBOp), intended to help ensure a consistent interpretation by individual assessors, notified bodies, and industry.

**As part of the effort to standardize expectations for combination products in the EU, the draft DDC guideline was released at the beginning of June for a 90-day consultation period ending August 31. The goal is for the comments to be collated and reviewed and the final guideline released by early next year, in advance of the implementation of the new EU medical device regulations in May 2020 (see [IPQ November 26, 2017](#)).**

In presentations at conferences and workshops over the last year, the evolution of the EMA guideline has been shared openly by regulators in the effort to garner industry input ahead of the formal consultation period.

EMA's joint Quality and Biological Working Party (QWP/BWP) engagement activities have also extended to direct discussions with notified bodies (NBs), the accredited third-party entities responsible for approving CE marking of higher risk medical devices in Europe. Reflective of these discussions, the template included in the guideline outlines the information that medicine assessors would find helpful from the NB device reviewers.

**At the CASSS EU CMC forum held in Seville, Spain in mid-May, the co-rapporteur for the guideline, HPRA Executive Pharmaceutical Assessor Nick Lee, highlighted its key concepts and structure, explaining the interaction with notified bodies, the new NBOp, and requirements for integral versus non-integral DDCs.**

Lee also explained the background thinking on key topics including: • platform technologies • quality aspects of bridging to pivotal clinical trials • lifecycle management, and • emerging technologies.

### **EMA is Looking for Coordinated Industry Input**

Lee's comments (*a link to his full presentation is provided below*) complemented those made the previous week by the guideline's lead rapporteur, MHRA Senior Pharmaceutical Assessor, Abigail Moran. She presented on the draft guideline at a DDC training course held at The Organisation for Professionals in Regulatory Affairs (TOPRA) headquarters in London.

The two speakers coordinated their presentations and stressed the same message to industry stakeholders – to continue working together toward providing a consolidated list of prioritized comments on the draft guideline, focusing on what is achievable rather than a broad wish list for a perfect guideline.

Both presenters recognized the usefulness of the dialogue with industry stakeholders and the reflection papers they had provided. They did note one hot topic on the industry wish list, however, that will not be possible to resolve at this point – the frequently raised request for a definition of “substantial change” and the specific expectations for handling post-approval lifecycle management.

**Other concerns that have been drawing a lot of attention are the resources and availability of NBs to fulfil the review requirements in time for the May 2020 compliance deadline, and how companies are preparing in highly uncertain times.**

The guideline is coming to the fore in the context of the stresses that notified bodies are feeling as a result of the demands and uncertainties surrounding their transition to the new requirements under the MDR. While the demands on the NBs are increasing, their numbers are actually shrinking as existing organizations opt not to pursue redesignation. *[Editor's Note: IPQ will be providing in-depth coverage of the current dialogue on post-approval changes and the NB role for DDCs, in upcoming stories.]*

On top of that is the disruption of Brexit and its implications for the engagement of both the MHRA and UK-based NBs, which have been playing an important role in the European system to date.

### **Major Comments from Concept Paper Addressed**

The guideline considers the interplay between the drug and device constituents and is the first foray by European medicine regulators into quality considerations for devices referenced in a drug Summary of Product Characteristics (SmPC). Throughout, the focus is on documenting that the DDC has been appropriately designed and controlled and can be used correctly in the intended clinical situations.

**EMA released a concept paper in February 2017 on “developing a guideline on quality requirements of medicinal products containing a device component for delivery or use of the medicinal product,” in view of the escalating number of marketing applications and requests for scientific advice for these products.**

The concept paper noted that – reflective of the web of legislation for different medicines and medical devices that comes into play, the wide diversity of devices supplied with medicinal products, and the continuous technological developments – the data supplied in the dossiers of marketing authorisation applications (MAAs) has been “inconsistent and often incomplete.”

In response to the concept paper, industry stakeholders commented that they have also been finding inconsistencies in approach and depth of questioning between assessors, depending on individual reviewer experience and interest in device components.

Also noted was that there was no mention of the impact of the incoming medical device regulation (MDR), finalized during evolution of the concept paper in 2016 and coming into force in May 2020.

**The MDR brings in requirements for an opinion from a notified body (NBOP) on the safety and performance of integral device components, such as pre-filled syringes and auto-injectors, for all new MAAs submitted after May 2020.**

The new device regulation places the notified bodies much more squarely into the review process for drug-device combination and in vitro diagnostic (IVD) products. The requirement for an NBOP will mean that drug manufacturers and other companies that have not previously intersected with the NBs will now have to do so. *[See [IPQ November 26, 2017](#) for background on the increasing focus in Europe on combination product regulation.]*

### **EMA Expanding Guidance Support**

EMA publications over the last few years have increasingly been recognizing that usability and functionality of medical device components have an important role in minimization of medication errors, and that what have previously been considered container closure systems for the drug product may have dual functions as delivery devices that need accounting for in terms of safety and performance.

**Also, with the new MDR and IVDR come new responsibilities for EMA and for national competent authorities.**

EMA has brought in a medical device expert from the Irish Health Products Regulatory Authority (HPRA), and in February 2019 published a medical device page on its website. In the news release for the webpage, the increasing convergence of medicines and medical devices was noted, along with the intention to provide a number of guidelines to help stakeholders navigate the regulatory expectations. *[A link to the news release is provided below.]*

The first publication, a Q&A in February 2019, outlines the procedural requirements for MAAs submitted after May 2020 for medicinal products integrating devices where an NBOP is required. The Q&A is a “living document,” EMA explains, and the intention is to adapt the guideline over time to reflect experience and address comments and questions from industry.

The second publication is the draft guideline on DDC quality requirements published in June.

In previewing the guideline at the CASSS meeting in May, Lee explained that it was a multi-EU member state effort – developed jointly by national agency expert members of the QWP and BWP from the UK, Ireland, Sweden, Austria, and the Netherlands, with support from a French representative at EMA.

He noted that the guideline was considered a priority topic by the EMA to prepare for the imminent new regulations, and therefore work was continuing despite the relocation of EMA from London to Amsterdam and related business continuity restrictions.

**Guideline Defines Drug-Device Combination Product**

In addition to addressing the concept paper feedback on consistency of approach and new requirements of the MDR, the draft DDC quality guideline also includes a working definition of “drug-device combination.” Acknowledging that there is no legal definition of a combination product in Europe, the guideline defines a DDC as: “A medicinal product(s) with integral and/or non-integral medical device/device component(s) necessary for administration, correct dosing or use of the medicinal product.”

MHRA’s Moran noted in her TOPRA presentation that the definition was provided in response to the many comments that had been submitted on the concept paper about the title, scope, and need for a clear definition – and to make it easier to discuss the type of products covered – in the absence of a US-style legal definition of combination products.

**The types of DDCs within the scope of the guideline are “medical devices that are integral to the medicinal product, co-packaged with the medicinal product, or referenced in the medicinal product information and obtained separately.”**

The draft guideline covers dossier requirements for DDCs in the context of new marketing authorisation applications (MAAs) and changes to them.

**Integral vs. Non-integral DDC Products**

Central to discussions around combination product regulation in Europe has been the differentiation of integral versus non-integral devices. In Europe, this is currently the deciding factor for whether a device for delivery of the medicinal product (MP) is reviewed by a competent authority (CA) or a notified body.

**A list of the types of products falling under these categories and therefore covered in the guideline is given upfront in the introduction section.**

Examples listed of medical devices in integral DDCs include the more conventional devices for delivery of liquid MPs: ● the dropper on the top of the container with eye drops or the mouthpiece on the top of spray cans for throat sprays ● single dose pre-filled syringes, pens, and injectors, and ● multi-dose pens and injectors containing a pre-filled cartridge or designed for subsequent use with a new cartridge.

Other integral device examples given are: ● dry powder inhalers that are assembled with the medicinal component and ready for use with single or multiple doses, but that cannot be refilled when all doses are taken ● drug-releasing intra-uterine devices ● pre-assembled, non-reusable applicators for vaginal tablets ● implants containing medicinal products whose primary purpose is to release the medicinal product, and ● medicinal products with an embedded sensor.

Examples provided of medical devices in non-integral DDCs are: ● oral administration devices – for example, cups, spoons, syringes ● injection needles and filter needles ● refillable pens and injectors – for example, using cartridges ● reusable dry powder inhalers ● spacers for inhalation sprays ● nebulizers and vaporizers ● pumps for medicinal product delivery, and ● electronic tablet dispensers.

### **Consider Impact of Device on QTTP, CQA, and Control Strategy**

Traditionally, in Europe there have been two distinct regulatory review pathways for medical devices used to deliver specific medicinal products and for the MPs that are provided or marketed separately – those that are co-packaged or referenced in the summary of product characteristics (SmPC). Until now, a link between them has not been defined, leading to the perception of a ‘regulatory gap’ (*see IPQ November 26, 2017*).

The DDC guideline closes that gap, making clear that quality aspects of both integral and non-integral combination products are covered and that “the complexity of the device, relevant patient characteristics and clinical setting in which the DDC is to be used are also important aspects of the review process.”

There is an expectation for manufacturers to explain to medicines regulators how the device could impact the quality, safety, and efficacy profile of the medicinal product. Recognising the broad range of both integral and non-integral DDCs, the information provided will be dependent on the specifics of the device and potential risks to the patient.

**The guideline makes it clear that the MP dossier “should include full evaluation of the impact of the device on the quality target product profile (QTTP), critical quality attributes (CQA) and overall control strategy of the medicinal product.”**

The core precept underpinning the division of assessment work is that the medicinal product competent authority will evaluate the device-specific aspects of safety and performance relevant to quality, safety and efficacy of the MP, and that, as applicable, the notified body will assess the relevant general safety and performance requirements (GSPRs) outlined in Annex I of the MDR.

The guideline goes on to address: ● the application of relevant standards ● location and format of data in the submission dossier ● use of platform technologies, and ● the importance of scientific advice, particularly for complex or new and emerging technologies.

Both Lee and Moran stressed that providing relevant information in the correct sections of the dossier – in particular, P7 on the container closure system, and P3 on the manufacturing process – would be essential for efficient review, rather than assessors having to look for it in 3.2R.

They also emphasized that the guideline is focused on the combination product itself. There is no discussion of the requirements for the medical device component *per se* or the medicinal product formulation.

## **Notified Body Opinion is Critical**

A big question raised by industry groups including the European Biopharmaceutical Enterprises group of the European Federation for Pharmaceutical Industries and Associations (EBE/EFPIA), has been around timing of submission of the NBOp.

Lee noted that the quality guideline was “silent about submission strategy,” because it was considered it to be “more of a process issue.”

He said that additional guidance will be provided by EMA during the implementation phase, and went on to stress the importance of the NBOp, pointing out that, “if not provided, this lack of documentation would be considered a major objection. So you do need to remember that and understand that – because we cannot authorize a product without this information [NBOp] being present.”

### **At a DIA CMC Workshop in June 2018 in Basel, Lee presented on the early development of the guideline and the background and impact of the new medical device regulations.**

He described how the working party had reached out to The European Association of Medical Device Notified Bodies [TEAM-NB] to understand the NB role in CE marking of medical devices and discuss potential division of assessment responsibilities.

The notified bodies put forward for interaction with the EMA working party (WP), Lee pointed out, were DEKRA Certification B.V., based in The Netherlands, and TÜV SÜD Product Service, based in Germany. A sub-group of the EMA WP had been formed at that time and were already “looking into prioritizing roles and responsibilities”.

**“That is particularly important,” Lee continued, because “we don’t want to introduce unnecessary complexities. We don’t want to introduce unnecessary duplications. So what we are looking to do is to understand, in light of the regulation and Article 117, what we would expect to be presented.”**

In his May 2019 CASSS forum update, Lee explained that a series of subsequent teleconferences had taken place in which the medicines and devices reviewers discussed the format and length of the report as well as concerns about redundant or duplicated assessment. The output of those interactions is the suggested template for the NBOp provided in Annex I of the draft guideline.

## **Content and Consistency of the NBOp at Issue**

The NBOp annex of the guideline begins with the requirement for a clear statement from the NB whether, in their opinion, compliance of the integral device constituent with the general safety and performance requirements (GSPRs) is acceptable or not. A brief summary is then called for highlighting the basis of the opinion and any relevant constraints or considerations.

Next, the NBOp will focus in more detail on: ● a description of the device components and intended use ● a list of the applicable GSPRs, and ● an assessment report to confirm that the safety and performance requirements are met, with justification for any omissions.

**Notably, the NB is required to describe any changes made to the device during pivotal clinical trials and to discuss the impact on relevant GSPRs.**

One of the discussion points at public forums has been the length and detail of the NBOp. Lee noted in his CASSS presentation that, from experience as a reviewer of drug substances used in medical devices, where notified bodies consult with medicine CAs, the feedback from NBs was that “they don’t appreciate a four-page document, but equally they don’t really appreciate 100 pages. So we have to find a balance, and that balance needs to be agreed upon.”

At the TOPRA event, MHRA's Moran explained that different views on the length of the report had been expressed across the working party, with the final agreement being a summary report, saying: "This is what we looked at. This is our decision."

### **Article 117 Taskforce Convened**

Concerns about the consistency of approach of the different notified bodies across Europe – as yet an unknown number after MDR re-designation – were discussed at an inter-regulatory and stakeholder workshop on combination products held in late November 2018 in Brussels, which was cosponsored by TOPRA and RAPS.

DEKRA RA Manager and President of TEAM-NB Guy van Buijzen provided background to the regulation of medical devices and the role of the association subgroups in promoting high standards and consistency across member organizations. At the workshop, Buijzen committed to forming a sub-group on Article 117 implementation.

**Despite huge pressure as notified bodies deal with re-designation under the MDR, the work has been prioritised and an Article 117 task force has now been set up. It is co-chaired by DEKRA's Petra van Leeuwen, who provided NB input to the QWP/BWP guideline, and TÜV SÜD's combination product team manager, Julia Frese.**

In an email communication, van Leeuwen confirmed that the notified bodies have been involved in commenting on the draft NBOp template, and would be discussing the content and strategies to avoid overlap and duplication at a face-to-face meeting with representatives from medicines CAs and industry in early July.

Some of the goals identified for the NB taskforce are: ● to give consolidated comments to the EMA guideline from the NB perspective ● to prepare a gap assessment between the guideline and further guidance required, and ● to prioritize needs. The guideline will be developed by, and for, NBs for consistent assessment and expectations among them. Industry can then extract from this guideline what they have to do to be in compliance.

**One of the topics for the taskforce will be the suggestion from the pharma industry and device suppliers that a US-style device master file (DMF) could be helpful for devices used in multiple products.**

Platform technologies are defined in the DDC guideline as where the device "has already been approved for use in another medicinal product and therefore been (at least) partially characterized previously." In the Annex II template cover sheet for the NBOp, two options are given: ● for a stand-alone medicinal product to be completed by the marketing authorization holder (MAH), and ● where an application is made that utilizes a platform technology.

For platform technologies, the guideline explains that it is the technology owner who completes this section – "effectively providing a letter of authorization to the MAH to use the data, similar to the approach used where a CEP [Certificate of Suitability] holder authorizes the use of the active substance in an EU procedure."

### **DDC Guideline Reflects Proactive Stakeholder Engagement**

The aim of the DDC guideline is two-fold: ● to ensure consistent expectations for documentation between companies and assessors, and ● to prepare for a new regulatory paradigm in advance of legislation changes. As such, proactive engagement with stakeholders by members of the drafting team has been a salient part of its development.

**In discussing the plans for the guideline at a DIA CMC workshop in June 2018, Lee recognized that, based on the experience with other guidelines, there would be a lot of learning along the way and no doubt some surprises. He cautioned that "we really have to be cognizant of that and be aware that there are potentially a lot of unintended consequences in terms of the way that we act and the way we go forward from here."**

He stressed the message that care had to be taken not to introduce new complexities – a concern shared by both co-presenters and attendees in the DDC-specific session. The session was led by Novartis' Head of Quality Intelligence, Ursula Busse. Co-presenters giving a notified body and industry perspective, respectively, were TÜV SÜD's Global Focus Teams VP Bassil Akra and Novartis New Technologies Head Marc Rohrschneider.

Referencing Donald Rumsfeld's famous quote, Lee pointed out that "it is clear from Bassil's presentation and also from Marc's that there are lots of known knowns and there are also an awful lot of known unknowns, because there are lot of questions still to be answered – and my feeling is that, as we go through the implementation of the MDR, these unknown unknowns will pop-up. What we don't want," he continued, is "what Virgil had to say about 'the road to hell being paved with good intentions.'"

**At the DIA meeting, Lee noted that, "if we think perhaps not philosophically but in a slightly different way, for any drug-device combination product, you need to consider three main areas: • the formulation and medicinal product aspect • the medical device component, and • also system challenges that you have, using the system as a whole."**

The plea at that time to the workshop delegates from industry, Lee continued, was about preparation – "about doing the risk assessments on your products, trying to work out which ones are the priority products, what are the most critical, what would the impact be on potential public health if there is an issue," and then starting to initiate the discussions with the relevant organizations in order to prevent shortages and products not being available on the market.

At the CASSS, DIA, and TOPRA/RAPS events, Lee and Moran extended an invitation to stakeholders to take the opportunity to share informal, as well as formal, feedback with regulators, including suggestions for further workshops. "I think that is one of the things that is really necessary," Lee stressed at the CASSS forum, "and will help make us as regulators better understand an alternative position."

### **MHRA Experience Helped Inform EMA Draft Guideline**

Speaking to 36 delegates at the May TOPRA training event – rather than the audience of over 300 Lee was addressing at the CASSS Europe forum – afforded Moran the opportunity to have a more interactive discussion that drew in informed co-presenters and industry stakeholders. Presenters included AstraZeneca Devices and Combination Products Head Tim Chesworth, Amgen Medical Devices and Combination Products Regulatory Affairs Manager April Kent, and Corvus Device Principal Consultant Mark Chipperfield, who previously headed up device development for biologics at Roche – all of whom have been active contributors to industry publications shared with the regulators.

In response to a question from the audience asking about the UK leadership of the EMA working party, Moran explained that MHRA had extensive experience and in-house DDC guidance already, on which the EMA guideline drew. The UK leadership would continue prior to leaving the EU, she said, with participation in the WG thereafter dependant on the terms of the withdrawal.

Moran also offered some insight into the complex environment and number of different European bodies involved in preparation and approval of the guideline, with drafts being reviewed multiple times before final release, including legal review for consistency with other relevant regulations.

**She stressed the value of applicants providing samples if possible – noting that the guideline recommends doing so, especially for emerging technologies.**

"The provision of a sample or samples of the DDC to the assessors in order to simulate use is strongly encouraged to aid assessment and minimise queries relating to hands-on, practical aspects of use," the guideline states.

## **DDC Lifecycle Management Linked to ICH Q12**

Both Lee and Moran addressed the issue of lifecycle management – a hot topic whenever combination products are discussed due to the different regulatory strategies applicable to medicinal products and medical devices.

Recognizing that the current EU variations regulation and classification guideline do not convey well to device changes, both Lee and Moran explained that there were no plans currently to re-open the EU variations guideline.

While the core expectation is that the current variation categories are applicable, the DDC guideline recommends that the scope and impact of the change should be considered – with changes to the device that impact any DDC critical quality attributes [CQAs] or elements of the overall control strategy, potentially warranting a higher category of variation.

The guideline recommends addressing any queries about the need for, or category of, variation to the medicines competent authority (CA) that issued the original authorization.

**In the Q&A at the TOPRA event, AZ’s Chesworth asked whether there would be a definition of “substantial change” and whether there would be any information regarding the need to consult a notified body.**

Moran explained that it was decided that it wasn’t appropriate to include that in the guideline, since it was more of a procedural consideration to be addressed by EMA. She added that there were not many examples in the guideline, but it was planned that additional information and guidance could be provided in annexes and Q&As from EMA during the implementation phase.

Moran and Chesworth discussed the current situation regarding ICH Q12 – which now encompasses combination products – and whether that would lead to opening of the EU variations guideline. Both said they understood that the European Commission, which is responsible for the variations guideline, had no plans to re-open it, and agreed this resulted in challenges for DDCs as well as alignment with ICH Q12.

**According to Moran, the advanced therapy medicinal products (ATMP) wording was difficult to agree on and an area in which they expect to see changes. She noted that AGES’ Ilona Reischl, who co-chairs the EMA Committee on Advanced Therapies (CAT) and is an active participant in the DDC discussions at the CASSS CMC forums, is providing expertise as a member of the DDC quality guideline drafting group.**

In the panel discussion that followed Lee’s presentation at the May CASSS Europe forum, Reischl commented that the DDC guideline is applicable to ATMPs, “but only in the situations where you are talking about the container closure system, not when talking about the combined ATMP. For the combined ATMPs, it is the ATMP regulation that needs to be followed. And because that does not, per definition, require a notified body opinion, this is why we need to be specific in the guideline.”

## **Applying Both Drug and Device Standards Is Challenging**

The potential conflicts of applying both European drug monographs and medical device standards has been a key topic of discussion at the recent meetings.

**Lee pointed out at the June 2018 DIA meeting that there are “different manufacturing standards and processes being applied. The device might be referencing engineering standards or other ISO standards, whereas, with the manufacturing process for a medicinal product, you will be referencing the [EMA] guidelines that exist and the GMPs.”**



In the panel discussion that followed Lee's presentation at the DIA meeting, a comment was made that the European Pharmacopeia has several texts and chapters on materials and containers used as primary packaging for medicinal products. TÜV SÜD's Akra asserted that notified bodies will be looking for compliance with "harmonized standards, common specifications, and guidance related to medical devices in Europe." If a standard is not used, "you are going to get an opinion from our side," but the final decision is taken by the medicinal product competent authorities.

Confinis' Beat Steffen added that the monographs of the European Pharmacopeia (PhEur) were considered to be equal to harmonized standards.

The new guideline clarifies that where both PhEur monographs and ISO standards may be applicable, the PhEur standards will take precedence. In response to a question at the TOPRA event, Moran clarified that justification for taking a different approach could be acceptable, as with all guidelines, but advised that if a PhEur standard exists, assessors will generally be looking for compliance with it.

### **Plea Made to Industry Stakeholders for Consolidated Comments**

Moran affirmed that the drafting team was looking forward to receiving comments on the draft guideline. Recognizing that a three-month consultation period provides limited time for industry to respond, she explained that it would allow the team "more time to make it right at the end." She emphasised that providing "consolidated feedback as much as possible as an industry would be really useful."

What is sought is "a priority list of what you are particularly concerned about ... focusing on what can be changed, rather than something that is just there, and we can't do anything about it at the moment."

Concluding her presentation in the same way as Lee, Moran implored stakeholders to "take the opportunity to talk to us. If you consider that it would be really useful to have some sort of collaboration, to talk about a particular issue, then say that." She acknowledged that with the current EMA climate and its business continuity plan, it may not be possible to organize any stakeholder workshops in the autumn, and she was not aware of any plans currently to do so.

She advised that if there were particular topics to discuss that are critical to industry, to give as much evidence as possible for why that is the case. "Certainly, the drafting group would appreciate being able to talk things through."

In the Q&A discussion, Chesworth referred to the TOPRA/RAPS November 2018 workshop in which Moran participated and agreed was "really useful." These types of forums, Moran commented, were what the drafting group were using to have interaction and share feedback with stakeholders.

Also highlighted were the successful cross-industry collaborations leading to publication of reflection papers and joint letters to the Commission, EMA, Heads of Medicines Agencies (HMA), and Competent Authorities for Medical Devices (CAMD).

**Again stressing the benefit of consolidated comments from industry stakeholder groups working together, Moran cited how the EU member states had worked together to provide consolidated comments to the ICH Q12 guideline. The individual members, she said, put in their comments, then had a meeting to grade them and agree on priorities, and what they could live with.**

The chair of the TOPRA event, IPQ's European editor and former MHRA quality reviewer Janine Jamieson, suggested that companies submit comments via an industry trade organization rather than individually in order to reduce the number of comments received that need to be addressed.

It was also proposed that smaller companies submit comments via consultants who are actively involved in the DDC regulatory discussions alongside industry groups, such as EBE/EFPIA, that are welcoming input from non-members with appropriate expertise.

From an industry point of view, Chesworth added, aligning across all the different industry associations has a kind of “force multiplier effect,” indicating “not only the content of what we are saying, but that this is really important – this is what we have all agreed we want to say.”

**Bringing the discussion on the DDC guideline at the TOPRA event to a close, major concerns were expressed around notified body availability and readiness to provide the required NBOp for MA applications submitted around the May 2020 implementation date.**

Referring to the on-going, well-publicized issue of re-designation of NBs, Biogen Medical Devices and Combination Products Regulatory Affairs Director Steve Dew and AZ’s Chesworth shared the industry perspective on how they were preparing.

Dew explained that notified bodies have different codes that they can apply, covering the range of medical devices that they have appropriate expertise to review. At the moment, he said, “manufacturers are powerless to work out exactly what codes individual notified bodies will be approved for.”

But, he advised, “manufacturers should be reaching out to notified bodies, asking them if they are intending to be accredited to similar codes to those under the MDD.... Sitting around and waiting to find out may be too late.”

Chesworth confirmed that this outreach is important, adding that, although the aim was to publish the guideline before May 2020, “industry has already had to make decisions about what we are going to do – because EMA is very clearly saying [the MDR] will be applicable on that date. So we had to start ages ago, making risk-based assumptions and hoping those assumptions will get us into a good place.”

**“But that is where there will have to be some level of flexibility from the regulatory agency’s point of view – to recognize that we have been working a little bit in the dark. We have done our best to make what we think are reasonable assumptions. So don’t be too harsh on us if we are not meeting all your expectations straight away after May 2020.”**

Moran acknowledged that this was a valid point and commented that it would be interesting to see how many NBs were eventually willing and able to give opinions – because the queues could potentially be “huge.”

***[[CLICK HERE](#) for Lee’s presentation at the CASSS strategy forum.]***

**LINKS:**

- [EMA News release on medical devices](#)
- [EMA guideline on quality requirements for drug-device combinations](#)



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