An Overview of EBE Advocacy Work on Drug/Biologics-Device Combination Products

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EU CMC Strategy Forum, May 14, 2018, Noordwijk, Netherlands
Background information on EBE DDC team

- DDC team formed early 2015
- Initially to address technical requirement for mAb’s in prefilled syringe / prefilled pens
  - **e.g.** Selection of primary/secondary pack components, Syringe/Stopper system incoming tests / Siliconisation control, Functional performance testing strategy, Shelf life setting/stability testing strategy, CCIT, PV for mechanical reiterative assembly process, appropriateness of ISO Standards, Stability control strategy, Device Change management post-approval
- **Then scope was expanded based on**
  - Discussion at EMA BWP IP meeting 2016 and 2017
  - **Scope expanded to emerging technologies e.g. LVD**
  - **Call for comment on EMA Concept Paper** on developing a guideline on Quality requirements of medicinal products containing a device component for delivery or use of the medicinal product (EMA/CHMP/QWP/BWP/661488/2016)
  - **Development and Publishing in the European Union Official Journal of the new Regulation on Medical Devices (MDR)**
  - **ICH Q12 – Step 2 - Technical and regulatory considerations for pharmaceutical product lifecycle 6 management (Draft)**
  - **ISO: Committee 84/ Working Group 15** “Change assessment of devices intended for administration of medicinal products
EBE DDC team Priorities 2018/2019

- Publish EBE reflection paper “Medicinal product incorporating a drug delivery device component: An Industry Perspective on the EU marketing application technical requirements, regulatory review “process and post-approval device related change assessment”

- Socialize key proposals from EBE reflection paper published in January 2018 at Industry/Regulator/NB forums:
  - smi prefilled syringe conference, London Jan 17-18, 2018,
  - EBE-DDC multi-stakeholder meeting TOPRA office London April 11, 2018,
  - DIA Europe meeting in Basel April 17-19 2018,
  - EU CMC Strategy forum, Netherland, May 14-16 2018
  - EMA BWP IP meeting, London, June 20, 2018
  - TOPRA/RAPS symposium Nov 2018
  - Short Article in IPQ journal and Medical Device Regulation journal
  - Other forums

- Support EMA/NB MDR pilot program and Regulator//Industry workshop as proposed in the paper
EBE DDC team Priorities 2018/2019

• Finalize and publish a position paper on “Medicinal product incorporating a drug delivery device component: An Industry Perspective on developing an efficient, ‘End To End’ Control Strategy”

• Develop, finalized and publish a position paper on “Medicinal product incorporating a drug delivery device component: An Industry Perspective on Article 117 of the EU Medical Device Regulation and the Impact on how Medicines are assessed”

• Support EFPIA TDEG DDC GMP team and EREG DDC team (e.g. joint quarterly alignment meetings)
Options on where to locate device and DDC product information and case study on the extent of device and DDC product information required in eCTD Module 3.

Reflection and position on involvement of Notified Body review (scope and timing) as will be required by MDR Art 117.

Position on a risk-based approach to classification of device post-approval change reporting level, discussing guiding principles for categorization of device variations and providing examples of variation requirements experienced by Industry.

Perspectives on dossier content and/or regulatory review issues on emerging technologies i.e; Large Volume Devices for high viscosity biological products, electromechanical devices and electronic add-ons to existing products (digital health).

→ Need for tripartite workshop (EMA/NB/Industry)

→ Need for MDR Art 117 EMA/NB Pilot Program toward an integrated review process
Industry would support EMA in setting up and coordinating a pilot program to explore the practical implications of MDR Article 117 implementation with complex and innovative DDC products under development.

This pilot would provide a framework for informal dialogue between key stakeholders; EMA, future marketing authorization applicants and selected Notified Bodies to address a range of procedural, technical and scientific questions in the context of the target DDC product profile, aligning and expectations and facilitating the implementation of an integrated and optimized review process.”
EBE position paper under development on MDR Art. 117 and the Impact on how Medicines are assessed (Paper 2)

- Technical and procedural concerns and challenges being discussed amongst industry relating to Art. 117
- Specifically what is the purpose of the Notified Body Assessment/opinion?
- Recognise that evaluating complex devices claiming compliance with multiple ISO Standards is typically outside the competence of any CA
- But, also recognition that the same level of assessment may not be applicable to all device-types, commensurate with overall risk of product?
- Concern about the efficiency of the process in relation to overall MAA review/approval process and timing
- Not wanting to delay/significantly impact product approvals based on overly-long NB assessments
- Being able to leverage assessments across products where appropriate to do so
- Recommendations from this second paper possibly helpful to develop future process-related guidances i.e. within NB group (akin to process NBs developed for competence to review substance based devices for Rule 21 of MDR) and/or EMA (i.e. future CHMP Quality guidance for DDCs)
4 key areas of discussion

- Regulatory review process & recommendation on how combined Advance Therapy Medicinal Product (cATMP) review process could be adapted
- Roles and responsibilities of key stakeholders
  - Recommended considerations for Notified Body, Manufacturers, Competent Authorities
- Review of products within scope of Article 117
  - Recommended risk approach to products where NB assessment required
- Technical and Quality requirements
  - Recommended scope of NB assessment vs. CA for MAA dossier

Publishing timeline: July 2018
Title: Medicinal product incorporating a drug delivery device component: An Industry Perspective on developing an efficient, ‘End To End’, Control Strategy

Summary:
- The paper seeks to demonstrate that, if an ‘end-to-end’ approach to drug product control has been applied, an acceptable Pharmaceutical Quality System (PQS) is in place and an appropriate risk profile has been established, a minimal approach can often be adopted for the testing of a finished DDC product.

Publishing timeline: Q3/Q4 2018
Topic Group members (EBE - blue and non EBE - orange)

- Serge Mathonet, Sanofi, Global Regulatory Affairs CMC Biologics
- Janine Jamieson, JCombinations AB Consultant, IPQ publication editor
- Feuerstein, Ulrike, Abbvie, Primary Packaging Development for parenterals ex CMC Submission groups for prefilled pens
- Carolin Gordon, Astra Zeneca, Regulatory CMC
- Stephanie Horn, Roche, Technical Regulatory Device
- April Kent, Amgen, Regulatory Device
- Andrew Lennard, Amgen Regulatory CMC
- Tim Chesworth, Astra Zeneca, Global Regulatory Affairs Medical Devices and Combination Products
- Amanda Matthews, Pfizer, Regulatory CMC
- Blake Green Amgen, Regulatory Device
- Michelle Czajkowski, GSK
- Vikas Jaiteley, Global Regulatory Affairs CMC
- Bjorg Hunter, Device engineering GSK
- Daniel Latham Novartis, Head of Device Development operations
- Manfred Maeder, Novartis, Device development and commercialization
- Florian. lengyel, boehringer-ingelheim, Biopharma CMC Project Mgmt + Tech RA
- Steve Dew, Biogen, Regulatory Affairs for combination products and devices
- Torsten Wollenberg, Bayer, Quality Assurance Medical Device
- Kriistina Rosin, Abbvie Regulatory Policy and Intelligence
- Elizabeth Bacou, Sanofi Global Regulatory Affairs Device
- Jannie Funch, Novo Nordisk Regulatory Affairs Device and Combination Products – Intelligence group
- Tine Juul, Novo Nordisk, Regulatory Affairs Device and Combination products
- Alice Maden BD MPS, Regulatory Affairs