Drug-device products - and the impact of MDR

CASSS, Strategy Forum EU, DDC Session
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Some DDC products
Combining products
Combining products

1. Drug* + Device
   - **Combination Product** (Single-entity), CD/BER (+CDRH)
   - **Medicinal Product** (single integral-combined-nonreusable), CA†, No CE-mark
2. Drug* + Device
   - **Combination Product** (Single-entity), CDRH (+CD/BER)
   - **Medical Device** with ancillary substance, NB††, Class III, CE-mark
3. Drug* + Device
   - **Combination Product** (Packaged together), CD/BER (+CD/BER)
   - **Medical Device**, CE-mark
4. Drug* + Device
   - **Combination Product** (Packaged together), CDRH (+CD/BER)
   - **Medical Device**, CE-mark
5. Drug* + Device
   - **Combination Product** (Cross-labelled), CD/BER + CDRH
   - **Medical Device**, CE-mark

**Device Constituent:**

- **US-FDA Device Risk Classes:**
  - I
  - II
  - III

- **EU Device Risk Classes:**
  - I
  - Is
  - Im
  - Ir
  - IIa
  - IIb
  - III

††† Cross-labelled
Combining products brings different concepts into play

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...and several other ‘challenges’ of integration across the organisation, product development and documentation

• Terminology, vocabulary
• Disciplines
• Competences
• Intellectual Property
• Planning ‘touchpoints’
  – Trigger for a delivery device vs. Readiness for Phase III
  – Final formulation vs. Design Inputs for the delivery device
• Different services, contributors, suppliers
• Homogenous vs non-homogenous manufacturing
• ‘Reluctance’ to change vs continuous improvement
Products may be developed in many different ways... with significant implications for the developer

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Medical Device Regulation – Some hot topic areas...

• Quality System
  • How much does a Pharma need to conform with ISO 13485 or similar? For which areas?

• Clinical
  • Implications of including the device in Clinical Studies of the product
  • Clinical Evaluation of device constituent – when, why and how?
  • Clinical Investigation of device constituent – when, why and how?
  • Who reviews what? Who is best advised to guide through advice meetings?

• Documentation
  • MAA - How much info on the associated medical device is needed in the dossier for the particular combination to demonstrate safety and efficacy?
  • STED/TD - How much info on the associated medicinal product is needed for the particular combination to demonstrate safety, reliability and usability?
  • Can a line be drawn between drug and device data?
  • Who reviews what? How much is duplicated? Potential for misinterpretation?

• Change management
  • How should a device-change be notified? Who reviews?

• Post-Market Reporting
  • Should we use the mechanism associated with the original approval (PMOA, as for US)?
  • In all cases?
Medical Device Regulation – Article 117

• Art.117 ONLY applies to a:
  – single integral product, that IS...
  – intended exclusively for use in the given combination... AND that is...
  – not reusable

• All other combined drug delivery products fall into Medical Device or Medicinal Product

• Many open questions...
  – How is Device Risk Classification to be used to define requirements?
  – How are attributes such as measuring, sterile, active, implantable, to be used to define the applicability of MDR and other requirements.
  – Who is the NB opinion applicant - the device developer or the MAA applicant?
  – When is review needed relative to MAA submission?
  – How is the review of the product as a ‘system’ ensured?
  – When does a change prompt revisiting the NB opinion?
  – What are the ongoing ‘maintenance’ requirements for an NB opinion?
  – etc
Summary

• It’s not always as simple as “Is it a Medicine, or is it a Device?”

• Notified Body review, conformity assessment and CE-marking remain appropriate for standalone medical devices.

• There is huge diversity of combination configurations, and a sliding scale of drug-device interaction.

• MDR applicability to any form of combined product needs further clarification...
  – The role the delivery device plays should be more carefully considered and the application of regulation, the review process and the approval co-ordinated appropriately
  – The less ‘standalone’ the device, the more clarification is needed

• A more integrated approach is needed for more integrated products.
  – ... to recognise the complexities, permutations, configurations, and challenges ...
  – ... both for the developer and the reviewer.

• It is proposed that a formal review of industry concerns is performed and these be gathered, grouped and used to drive specific guidance appropriate to the different types and groups of products.
Q&A

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Different combinations – different models & interactions

- **Co-packed** products - Interact at point of use
  - Drug (MPD, PQS, cGMPs) + ‘off-the-shelf’ device (MDD/MDR, ISO) – most common
    - Pharma purchases and confirms suitability of selected device with drug. Studies interactions.
    - CE-mark independent of drug, Device manufacturer sells CE-marked devices to any buyer.
  - Drug (MPD, PQS, cGMPs) + ‘customised’ device (MDD/MDR, ISO)
    - Pharma defines changes, purchases, confirms suitability of selected device with drug.
    - Device producer/CMO customises and sells/provides specific versions to several Pharma.
    - CE-mark in/dependent of drug, CE-marking may be taken up by either.
  - Drug (MPD, PQS, cGMPs) + developed device (MDD/MDR, ISO) – least common
    - Pharma ‘designs’ (may outsource), confirms suitability of selected device with drug.
    - CMO manufactures and provides specifically to Pharma customer.
    - CE-mark in/dependent of drug, CE-mark may be taken up by either.

- **Integrated** products - Interact through life
  - Drug (MPD, PQS, cGMPs) + ‘off the shelf’ device – least common exc. container components e.g. PFS
    - Pharma purchases and confirms suitability of selected device with drug. Studies interactions.
    - Device manufacturer sells. No development or approval role responsibility. Approved WITH drug.
  - Drug (MPD, PQS, cGMPs) + ‘customised’ device – most common, often leveraging external platforms
    - Pharma defines changes, purchases, confirms suitability of selected device with drug.
    - Device producer/CMO customises and sells/provides. No development or approval responsibility. Approved WITH drug.
  - Drug (MPD, PQS, cGMPs) + developed device
    - Pharma ‘designs’ (may outsource), confirms suitability of selected device with drug.
    - CMO manufactures and provides. No development or approval responsibility. Approved WITH drug.