Manufacturers’ serialisation challenges with FMD & DR implementation

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Quality aspects of coding & serialisation - following the code end to end
Assumptions: Codes are printed online, there’s no aggregation

Master Data & Artwork management
- Verify correct master data available
- Defined and appropriate areas for the required print
- Consider space needed for multi-market packs. Consider pre-printed HRI* for GTIN**, NHRN*** and prefixes
- Blue box for centrally authorized products (multimarket packs - one or more codes?)

Process Order Created
- Create randomised number series
- Ensure sufficient amount of numbers available at line including additional quantity for rejects
- Interface to CMO (eg. send number series or CMO creates serial numbers...)

Start-up of packing line
- Download data elements to the line
- Check code and HRI print quality, content and readability before start up
- Ensure IPC* include coding & serialisation aspects
- Include information other than the unique identifier in the 2D barcode, eg. 6th data element’ per Art. 8

Pack Produced
- Verify 2D barcode and human readable text
- Commission (associate pack & serial number)
- 100% check or IPC of 2D code quality, content & readability
- 100% OCR* or IPC presence control for HRI text and print quality

In Lot re-packing
- Decommission serial numbers
- Apply new serial numbers
- Note: A portable scanner or mobile workstation might be an option to be able to remove the part to be repacked from the lot

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* HRI = Human Readable Information
** GTIN = Global Trade Item Number
*** NHRN = National Healthcare Reimbursement Number
* CMO = Contract Manufacturing Organization
* IPC = In Process Controls
* OCR = Optical Character Recognition

Ref
- DR Art. 5, 6, 7
- DR Art. 4
- DR Art. 8
- DR Art. 5, 6, 14
- Directive 2001/83/EC Article 47a
### Quality aspects of coding & serialisation - following the code end to end

**Assumptions:** Codes are printed online, there’s no aggregation

<table>
<thead>
<tr>
<th>Process Step</th>
<th>Data Flow</th>
<th>Points to Consider</th>
<th>Data Upload</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order Complete</td>
<td>Upload serial numbers from packing line to company database</td>
<td>Ensure at least as many codes as packs</td>
<td>Data upload to EU Hub*</td>
</tr>
<tr>
<td>Quality Released</td>
<td>QA review &amp; release</td>
<td>Establish a threshold for the positive difference with justification based on capability and trends</td>
<td>Confirmation of data upload to EU / national Hub</td>
</tr>
<tr>
<td>Quality Certified</td>
<td>QP certification</td>
<td>QA check or IPC if this has been taken place properly, e.g. data consistency and integrity and manage any deviations</td>
<td>Decommission codes for special reasons</td>
</tr>
<tr>
<td></td>
<td>Define who is responsible for upload</td>
<td>Batch document check. Print quality ok? Reconciliation ok? Tamper evidence ok? Production order serial number data set uploaded to company database? Any damages or in-lot re-work must include actions for code / data handling</td>
<td>Free Samples per Art. 41</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Goods for special customers per Art. 23</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Export: EU labelled goods for non-EU markets (Packing orders originally intended for non-EU markets do not need upload of codes) per Art. 12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Investigational products intended for clinical trials per Art. 16</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Note: Any repacking activity after Quality certification must still comply with the regulation (keep or replace code)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Art 33.1 states that “the person responsible for placing medicinal products on the market shall ensure... that the repositories is kept up to date thereafter”</td>
</tr>
</tbody>
</table>

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**Ref:**
- EudraLex Volume 4, EU GMP Guidelines Annex 16: Certification by a Qualified Person and Batch Release of 12 October 2015
- DR Art. 33, 38
- DR Art. 10, 11, 12, 16, 19, 20, 21, 22, 23, 33, 41

Where a manufacturer distributes his products by wholesale, Article 20(q), and Articles 22, 23 and 24 shall apply to him in addition to Articles 14 to 18.
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Assumptions: Codes are printed online, there’s no aggregation

Recalled, withdrawn or stolen product

Ensure decommissioning of unique identifiers

Ensure decommissioning of the unique identifier of recalled / withdrawn product

Ensure decommissioning of unique identifier of recalled / withdrawn / stolen product where known (not always the case)

Note: Suggested principle is that the supply chain actor that initiate an action ensures updates to the hub

In case of tampering or suspected falsification immediately inform the relevant competent authorities

Recalled, withdrawn or stolen product

Returned product

Verify authenticity and integrity

Authenticity must be verified by checking the serial number status against the EU HUB

Products which cannot be reverted to an active status shall not be returned to saleable stock

Verify authenticity of and decommission code

For products intended for destruction authenticity must be verified and the UI* must be decommissioned

General points to consider

Any damages or sampling post QA release must include actions for code / data handling

At end of shelf-life system will automatically change status to unavailable

Ensure harmonization of common data elements for IDMP and EMVS – look for efficiency opportunities

Ensure harmonization of prefixes / expiry date format (per GS1 standard YYMMDD)

Reconciliation and reporting requirements are unclear (at which point in the process?)

Impact of alerts / flags from the EU hub and any enquiries from data transactions

Handling of customer complaints e.g. from pharmacies if issues with reading of codes

Handling of customer complaints e.g. from pharmacies if issues with tampering

Timelines for transition from linear bar codes (OK with different product identifiers during transition?)

Ensure that the information is uploaded to the repositories system before the medicinal product is released for sale or distribution by the manufacturer (see comment on previous slide), and that it is kept up to date thereafter

Ref

DR Art. 18, 40

DR Art. 20, 22(b)

DR Art. 12, 22(c), 40
Complexity Drivers

- The use of a 2D barcode and International Standards has helped to simplify FMD deployment.

- However, there are other topics which will drive unnecessary complexity and cause issues with FMD implementation if not addressed, these are:
  - Human readable text order
  - Prefix (heading) location
  - Use of labels to apply coding
  - Barcode transition requirements post Feb 2019
  - Encoded data order within the 2D barcode
  - Application identifier use
  - Printed format of the 2D Data Matrix

- EFPIA, Medicines For Europe and the EAEPC are working on a set of advocacy documents on these topics and calling for clarification within version 8 of the Q&A document and harmonisation of requirements across the EU.
Harmonisation has increased, but . . .

- To date there have been a number of important decisions made which help harmonise the FMD implementation across Europe:
  - Choice of data carrier (2D DataMatrix)
  - Choice of coding scheme (ability to use International standards such as GS1)

**GS1 - GTIN**

Austria*, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark**, Estonia, Finland**, Germany*, Hungary, Iceland**, Ireland, Latvia, Lithuania, Malta, Netherlands, Norway**, Poland**, Portugal, Romania, Slovakia, Slovenia, Spain**, Sweden, Switzerland, UK

* GTIN for multi country - shared packs
** Some countries will allow GTIN or NTIN

**GS1 - NTIN**

Austria*, France, Germany*

* For market specific packs

**TBC**

Italy and Greece (coding requirements under discussion)

Some countries (outlined in red) also require a national number in the 2D Barcode when using GTIN
Next Steps

• It is vital we resolve the coding and labelling issues

• To do this we URGENTLY need:
  • National Competent Authorities formally and unambiguously clarify the coding requirements which are applicable in their country
  • Alignment across countries (due to issues such as shared packs & movement of good, etc)

• Without formal confirmation companies cannot kick off the serialisation activities and continue to prepare to meet the FMD deadlines

• EMVO stakeholders would welcome a joint response from Commission and National Competent Authorities on the various coding and labelling issues identified

Further clarification could be addressed in Version 8 of the Commission Q&As
Background Slides

Not for presentation purposes but can circulated
Human readable text order and Prefix (heading) location

- Complying with a specific order and layout for the data elements is not achievable due to physical, technical and other regulated requirements.
- We also cannot comply with a specific order where the data is split over several faces of the pack, which is allowed by the DR, art 7(3).
- The order of these data elements does not impact on patient safety or usability of the product as long as the information is clearly laid out and legible.
- It may not always be possible to locate the headers for the human readable data elements beside the elements themselves but instead follow current common practice of locating these near to the data elements.
- Recommend that the answer to question 2.10 of the Commission Q&A document (version 7) is updated and no specific order recommended.
- Clarification added to the Q&A that the headers can be located beside or near to the data elements.

The layout of the elements should not follow a specific order and header location should follow current common practice.
Use of stickers/labels to apply coding

- Stickers/labels are permitted today and are currently used on many types of product packaging
- Examples include:
  - Stickers/Labels on bundles
  - Stickers/Labels on large format packs
  - Stickers/Labels on bottles where there is no outer carton/box
  - Stickers/Labels on plastic packs
  - Stickers/Labels used during repackaging operations
- They also offer a cost effective method of applying the Unique Identifier where repackaging or re-boxing are the only other alternative

Manufacturers should have the choice to use labels/stickers to apply the Unique Identifier and human readable text if they wish.
Barcode transition requirements

- Until Feb 2019 there is no obligation for the 2D DataMatrix to be scanned. For this reason the old linear barcodes need to be kept.

- After Feb 2019,
  - MAHs may want to remove the linear barcode for some products and remove unnecessary information.
  - For other products, there might be a need to keep the linear barcode for packs which are shared e.g. Cyprus/Greece, Romania/ Macedonia.

- Country specific or EU-wide obligations to have the linear barcode removed by 9-Feb-2019 or thereafter should be avoided.
  - Decision to keep or remove the linear barcode should be at the discretion of the MAH.
  - If MAH decides to remove linear barcode, it should not require a regulatory procedure.
  - EMA and CMDh to provide corresponding guidance (similar to DR Implementation Plan).
  - EU Commission to amend answer to Question 2.3 in the EU Commission’s Q&A document accordingly.

Removal of the linear barcode should be at the MAHs discretion.
Encoded data order

- International standards define how data in the 2D barcode should be encoded.
- Scanning and IT systems do not identify the content e.g. Product Code, based on its position in the encoded data. They use the Application Identifiers which "signpost" the data e.g. 01 = product code, 17 = Expiry date, etc.
- Mandating a specific order to encode the data serves no purpose as fields such as batch and serial number vary in length.
- Failing to encode data using these standards will lead to scanning systems not being able to read the codes.

Mandating a specific order violates International Standards – therefore no specific order should be mandated.
Application identifier use

• Application Identifiers are encoded in the 2D barcode to signpost the data for the IT and scanning systems

• International Standards and good practice recommend they also appear on the human readable text to help if the barcode fails to scan, perhaps due to damage.

• Space and technical constraints can mean that these Application Identifiers can not always be included (which is also considered and allowed by International Standards)

• It should therefore be left to the MAH to determine whether to include the Application Identifiers following International Standards

Application Identifiers in the human readable text should be at the discretion of the MAH, in accordance with International Standards
Printed format of the 2D Data Matrix

- Article 5 of DR states that International Standards can be used for the 2D barcode format.
- International standards allow for the 2D barcodes to be produced in several different formats e.g. square and rectangular.
- International Standards also allow the 2D barcodes to be produced in a positive version (black on white) or a negative version (white on black*).
- Different technologies produce either a positive or negative image and this will vary across MAHs.
- Scanning equipment must be able to read all these variations according to International Standards.

* other dark colours may also be used as long as there is a high contrast.
Thank you!