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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

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Process Step	Master Data & Artwork management	Process Order Created	Start-up of packing line	Pack Produced	In Lot re-packing
					
Data flow	Verify correct master data available	Create randomised number series	Download data elements to the line	Verify 2D barcode and human readable text Commission (associate pack & serial number)	Decommission serial numbers Apply new serial numbers
Points to consider	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?) * HRI = Human Readable Information ** GTIN = Global Trade Item Number *** NHRN = National Healthcare Reimbursement Number	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…) *** CMO = Contract Manufacturing Organization**	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 * IPC = In Process Controls	100% check or IPC of 2D code quality, content & readability 100% OCR* or IPC presence control for HRI text and print quality * OCR =Optical Character Recognition	Note: A portable scanner or mobile workstation might be an option to be able to remove the part to be repacked from the lot
Ref	DR Art. 5, 6, 7	DR Art. 4	DR Art. 8	DR Art. 5, 6, 14	DR Art. 16, 17 Directive 2001/83/EC Article 47a

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Process Step	Order Complete	Quality Released	Quality Certified	Picked, packed, shipped and free samples
				
Data flow	Upload serial numbers from packing line to company database Reconcile codes, report as part of batch record	QA review & release	QP certification Data upload to EU Hub* Confirmation of data upload to EU / national Hub	Decommission codes for special reasons
Points to consider	Ensure at least as many codes as packs Establish a threshold for the positive difference with justification based on capability and trends QA check or IPC if this has been taken place properly, e.g. data consistency and integrity and manage any deviations	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	Define who is responsible for upload *Article 33, 1st paragraph states "the information is uploaded in the repositories system *before* the medicinal product is released for sale or distribution". Note: The optimal point of data upload might be later in the process to avoid different processes for aggregated and non aggregated goods	Free Samples per Art. 41 Goods for special customers per Art. 23 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 Investigational products intended for clinical trials per Art. 16 Note: Any repacking activity after Quality certification must still comply with the regulation (keep or replace code) 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"
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(a), and Articles 22, 23 and 24 shall apply to him in addition to Articles 14 to 18.*

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Process Step	Recalled, withdrawn or stolen product	Returned product	Destroyed product
			
Data flow	Ensure decommissioning of unique identifiers	Verify authenticity and integrity	Verify authenticity of and decommission code
Points to consider	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	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	For products intended for destruction authenticity must be verified and the UI* must be decommissioned * UI = Unique Identifier
Ref	DR Art. 18, 40	DR Art. 20, 22(b)	DR Art. 12, 22(c), 40

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*

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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.

Some examples of complexity drivers

Human readable text order

Use of Stickers/ labels

2D Data Matrix Format

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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

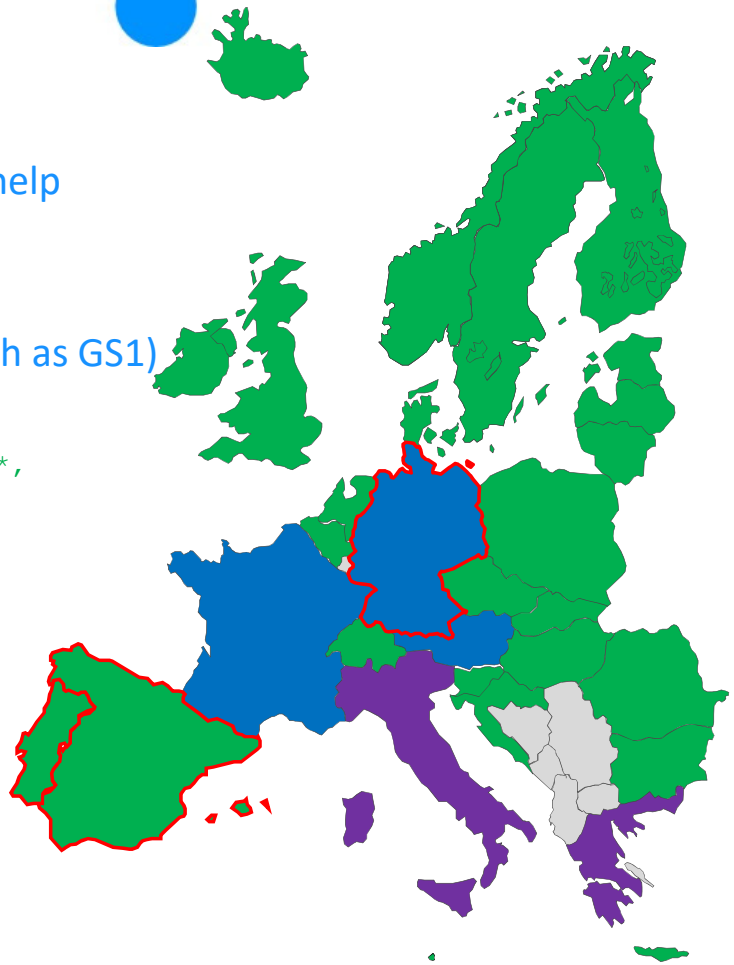
Austria*, France, Germany*

** 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



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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

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Background Slides

Not for presentation purposes but can circulated

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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 can not 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

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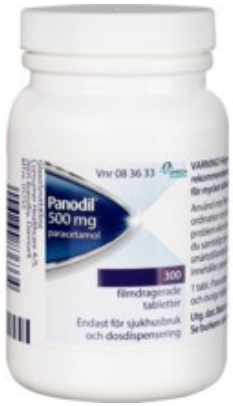

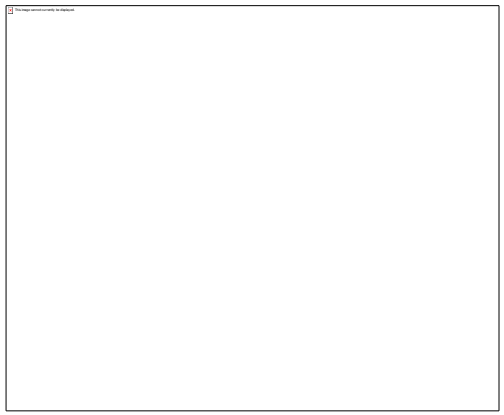

Use of stickers/ labels to apply coding

- 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 re-packaging operations
- They also offer a cost effective method of applying the Unique Identifier where re-packaging 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

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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 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

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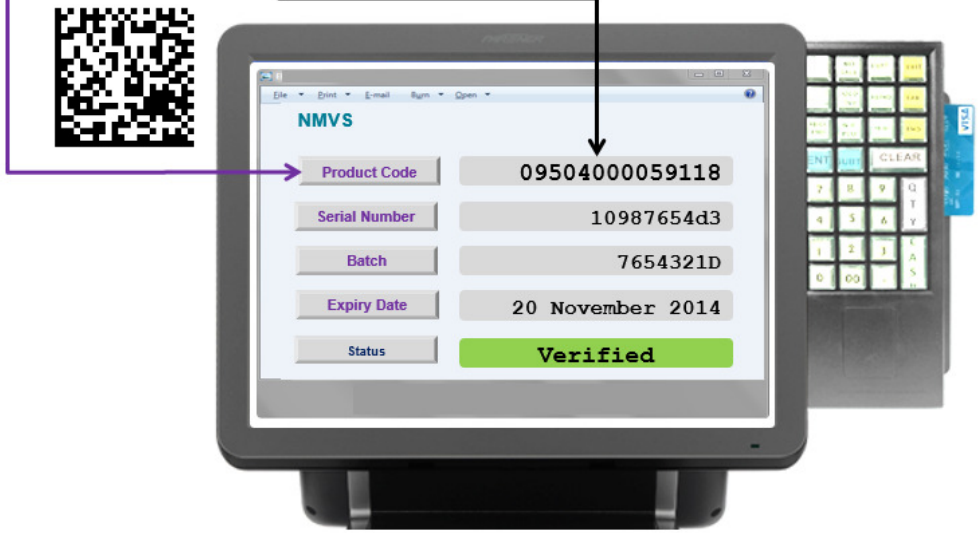

Green = Encoding type used e.g. GS1

Purple = Application Identifiers

Blue = Group Separators

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

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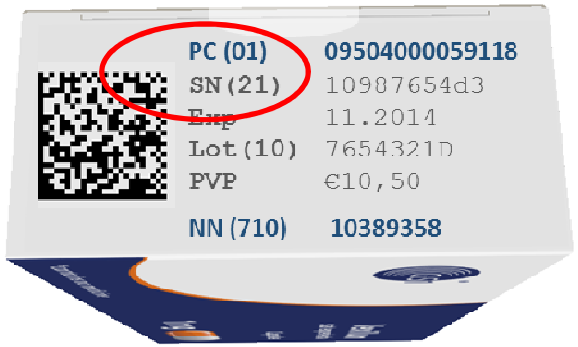

Application identifier use

- 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

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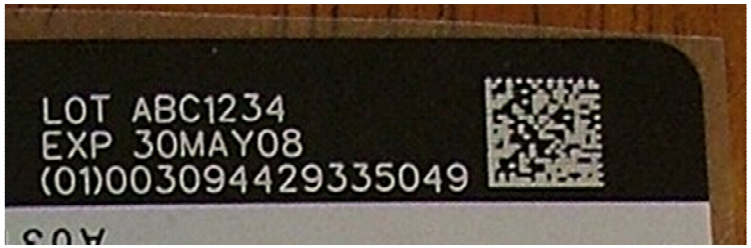

Printed format of the 2D Data Matrix

- 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*

Square, Rectangular, White & Black 2D barcodes must be accommodated

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