Medicines & Healthcare products Regulatory Agency

MHRA

Falsified Medicines Directive

Key Points for Parallel Traders

This document represents the best information currently available.

This document is not an authoritative reference but is the best advice which we can provide at this time. We will continue to develop this guidance and circulate updates at appropriate times.

The table at the end of each section provides an interpretation of the content of the appropriate article in the Directive or Regulation to help location of the definitive requirement.

Falsified Medicines Directive

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2011_62/dir_2011_62_en.pdf

Delegated Regulation

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2016_161/reg_2016_161_en.pdf

EC page including link to Q & A document

https://ec.europa.eu/health/human-use/falsified_medicines_en

Q & A document

https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/qa_safetyfeature_en.pdf

Why?

The preamble to the Falsified Medicines Directive states:
"There is an alarming increase of medicinal products detected in the Union which are falsified in relation to their identity, history or source. Those products usually contain sub-standard or falsified ingredients, or no ingredients or ingredients, including active substances, in the wrong dosage thus posing an important threat to public health.
Past experience shows that such falsified medicinal products do not reach patients only through illegal means, but via the legal supply chain as well. This poses a particular threat to human health and may lead to a lack of trust of the patient also in the legal supply chain. Directive 2001/83/EC should be amended in order to respond to this increasing threat."

The FMD introduced a series of measures which affect manufacturers, wholesalers, brokers and of particular relevance are two safety features to permit verification of each pack of medicines at the time it is dispensed to the patient.

What?

Verification of the pack is enabled by the introduction of two safety features:
Anti-Tamper Device – to provide assurance that the contents of the pack have not been interfered with since the pack was released by the manufacturer; and
Unique Identifier – to confirm the identity and authenticity of the product.

How?

A Delegated Regulation provided the detail of the implementation for the safety features.

When?

The FMD stipulated a period of three years after the publication of the Delegated Regulation for introduction of the required measures. Member States which had systems in place for verification of packs (Belgium, Italy and Greece) were allowed an additional 6 year period to meet the requirements. Belgium decided to apply the requirements from 9 February 2019 as many of its products are supplied to Luxembourg which must apply the requirements from this date.

The Delegated Regulation was published on 9 February 2016 and therefore all of the requirements must be in place for all stock released after **8 February 2019**.

2001/83 Art 54(o)	Medicinal products of Art 54(a)(1) other than radiopharmaceuticals shall include safety features enabling wholesalers and persons authorised to supply medicinal products to the public to: - verify authenticity of the medicinal product - identify individual packs - device allowing verification of whether the outer packaging has been tampered with
2001/83 Art 54(a)(1)	POM products shall carry the safety features unless on the white list P and GSL products shall not carry the safety features unless on the black list
2001/83 Art 54(a)(2)	DR will set out: (a) characteristics and specifications for cost-effective UI (b) white and black lists considering: (i) price and sales volume (ii) number and frequency of previous falsifications in EU and third countries (iii) characteristics of the medicinal product (iv) severity of the conditions treated (v) other potential risks to public health (c) procedures for changing the lists (d) methods for verification of the safety features (e) provision of repositories, costs to be borne by manufacturing authorisation holders

Products Affected by the FMD

Not all medicinal products are equally vulnerable to falsification. High value and high volume products are at greater risk than products with a lower usage and lower price.

The starting position is that all 'POM' products are required to carry the safety features and 'P' and 'GSL' products are not required to carry them. Not surprisingly, there are exceptions to this simple division and these are included in a 'white list' and a 'black list'.

'POM' products which are not required to carry the ATD and UI (white list) are:

- Radiopharmaceuticals
- Homeopathic products
- Radionuclide generators
- Kits
- Radionuclide precursors
- Advanced therapy products which contain or consist of tissues or cells
- Medicinal gases
- Solutions for parenteral nutrition having an ATC code beginning with B05BA
- Solutions affecting the electrolyte balance having an ATC code beginning with B05BB
- Solutions producing osmotic diuresis having an ATC code beginning with B05BC
- Intravenous solution additives having an ATC code beginning with B05X
- Solvents and diluting agents, including irrigating solutions, having an ATC code beginning with V07AB
- Contrast media having an ATC code beginning with V08
- Tests for allergic diseases having an ATC code beginning with V04CL
- Allergen extracts having an ATC code beginning with V01AA

None of these are likely to be parallel traded products so effectively all parallel traded 'POM' products are required to carry the ATD and UI.

'P/GSL' products required to carry the ATD and UI (black list) are:
Omeprazole 20mg gastro-resistant hard capsules
Omeprazole 40mg gastro-resistant hard capsules

MS may recommend changes to the white and black lists and these will promptly be considered by the Commission and any agreed changes published.

In addition MS may extend the requirement for the UI to any 'POM' product or any product subject to reimbursement for the purposes of reimbursement and pharmacovigilance. MS may extend the requirement for the ATD to any product for patient safety reasons. UK will allow use of the ATD on any medicinal product. The UI can only be applied to products required under the Delegated Regulation.

2001/83 Art 54(o)	Medicinal products of Art 54(a)(1) other than radiopharmaceuticals shall include safety features enabling wholesalers and persons authorised to supply medicinal products to the public to:

	- verify authenticity of the medicinal product - identify individual packs - device allowing verification of whether the outer packaging has been tampered with
2001/83 Art 54(a)(1)	POM products shall carry the safety features unless on the white list P and GSL products shall not carry the safety features unless on the black list
2001/83 Art 54(a)(2)	DR will set out: (b) white and black lists considering: (i) price and sales volume (ii) number and frequency of previous falsifications in EU and third countries (iii) characteristics of the medicinal product (iv) severity of the conditions treated (v) other potential risks to public health (c) procedures for changing the lists
2001/83 Art 54(a)(4)	NCAs may recommend changes to white and black lists
2001/83 Art 54(a)(5)	MS may for reimbursement or PV extend application of UI to any POM or any product subject to reimbursement MS may use information in repositories for reimbursement, PV or pharmacoepidemiology. MS may for patient safety extend ATD to any product.
2016/161 Art 2(1)	DR applies to: (a) POM products unless on white list (b) P and GSL products on black list (c) products to which the MS has extended the application of the UI or ATD

Anti-Tamper Device

Neither the Directive nor Delegated Regulation gives very much information on the ATD. There is no mandatory specification but the ATD “has to allow the verification of whether the packaging of the medicinal product has been tampered with.”

CEN standard EN 16679:2014 “Tamper verification features for medicinal product packaging” is recommended reading!

Tamper verification features which are in accordance with this standard meet the requirements of the FMD.

The ATD should enable a visual check for its presence and any evidence of tampering. It must not compromise the readability of the statutory information on the product packaging.

The standard describes nine ATD technologies and recognises that other technologies are being developed which also meet the requirements.

Folding boxes closed with glue	A glue or combination of glues is applied to close the folding box, which may incorporate perforations to facilitate opening. The box must be cut or torn to access the product and cannot be opened without visual tear-off or ripping of the carton.
Specially constructed folding boxes	The flaps and body of the box are designed that the ATD is activated by inserting the flaps at the time of first closure. First opening of the box produces visible and irreversible damage.
Sealing labels and tape	A paper, film or laminate label or tape is applied to seal the pack. Tampering with the seal should cause visible, irreversible damage or change to the packaging and/or seal.
Film wrapping	The pack is wrapped in a film to provide sealing. The film must be ripped, changed or damaged to access the pack. Mention on the pack that it should be enclosed in a film wrapping.
Shrink wrap sleeve	The sleeve must be ripped, changed or damaged to access the pack. Often used on bottles, etc.

Breakable or tear-away closure	The container is closed with a breakable or tear-away closure (usually plastic or metal) which has a portion which breaks on opening. Often found on bottles, etc.
Display blister pack	The medicine pack is sealed into a display blister pack which must be cut or broken to release the product.
Flexible packaging	The product is sealed in a film or foil pouch or sachet which must be ripped or broken to release the pack.
Blow-fill-seal containers	The container must be opened to access the product. Often used for sterile products.

Some points to consider:

The PI Licence Holder is responsible for ensuring that at appropriate ATD is applied to the pack. MHRA is not intending to review individual solutions for products placed into new cartons. It is the responsibility of the Licence Holder to ensure that the ATD is appropriate.

It is possible to reseal an original pack by applying a new ATD on top of the old, broken ATD in certain circumstances (see Q&A document, paragraph 1.20). Licence Holders wishing to reseal packs must provide MHRA with sufficient information to allow an assessment of the equivalence of the new ATD (description, explanation, pictures, example pack). The new ATD will only be considered equivalent when placed on top of a broken ATD if:

- The new ATD completely seals the pack and covers any visible sign of the original, broken ATD.
- The replacement of the ATD is conducted in accordance with GMP.
- The authenticity of the UI and integrity of the ATD have been verified before the original pack is opened.

Approval will be for the ATD and not a specific application. The Licence Holder remains responsible for ensuring that the ATD is effective (especially adhesion) in each specific application.

Materials for assessment of the ATD should be sent to:

Parallel Import Unit, Licensing Division,
MHRA,
10, South Colonnade,
Canary Wharf,
London, E14 4PU.

The ATD used on originator packs may change in preparation for FMD so it may not be possible to decide how you will repackage any particular product until much closer to February 2019.

Some hot glue sealed packs are currently opened to allow labelling of the blister and replacement of the leaflet and then re-sealed by heating. Such a glue does not provide tamper evident closure. The glue used on such packs may well change to a combination of hot glue which provides an immediate seal and cold glue which provides a permanent closure not susceptible to melting.

2001/83 Art 47(a)(1)	Safety features are equivalent if they: (i) comply with requirements of the DR (ii) are equally effective in enabling verification and evidence of tampering
2016/161 Art 3(2)	(b) ATD is the safety feature allowing verification of whether the packaging of the product has been tampered with

Unique Identifier

The UI consists of 4 mandatory and other optional data pieces of data, encoded into a two-dimensional Data Matrix barcode. The data elements are:

Product code
Serial number
National number (if required by the MS)
Batch number
Expiry data
Other data

Product code:
This is an alphanumeric or numeric sequence of less than 50 characters which allows identification of the product name, common name, pharmaceutical form, strength, pack size and pack type.
The product code must be globally unique – the same code must not be used on any other product from any other company. This requires the use of product codes to be controlled and coordinated.
MHRA does not require a specific standard for product coding.
The European Federation of Pharmaceutical Industries and Associations (EFPIA) has produced guidance on product coding (EFPIA Coding Guideline V3_6.pdf). This recommends use of the GS1 standard with a 2D Data Matrix and this satisfies the requirements of the Delegated Regulation.
Many companies will be familiar with GS1 through use of EAN-13 barcodes on their products. The same 13-digit number, preceded by '0' can be used as the product code in the UI if the GS1 standard is followed.

Serial number:
This is a numeric or alphanumeric sequence of up to 20 characters.
The combination of product code and serial number must not be reused for a period extending to one year after expiry or five years, whichever is longer.
The serial number must be random and the PI licence holder must ensure that an effective randomisation scheme is used.
The chance of guessing a serial number must be less than one in 10,000.
For readability purposes, it is recommended that the characters used are the digits 0-9 and upper case letters but not using I, J, L, O, Q or U.
It may be useful to allocate certain positions in the serial number for a specific purpose such as reducing the chance of the same serial number being generated on two different print lines at the same time. For example, one position could be used to identify the print line generating the UI. This may be particularly important if the repackaging is being done by external contractors. Another position could identify the year (on a 30-year cycle), two positions for the day from 01-Jan and 4 positions the second (from midnight). This would eliminate the possibility of the same random number being generated on a single print line. This duplication risk reduction uses a

total of 8 positions, leaving 12 positions for each of the 30 possible characters giving 53,144,100,000,000 possible serial numbers allowing for the 1/10000 chance!

National number:
Many countries use a unique number for reimbursement purposes (e.g. Spanish CN numbers) or alternatively a different national number identifying the product may be included if required by the MS.
If the national number is included in the product code, it does not need to be repeated in the UI.
UK is not introducing a national number. Instead this field in the EU-hub will contain the Dictionary of Medicines and Devices (dm+d) code which will need to be included in the batch data upload.

Batch number:
This is the batch number as allocated by the repacker. This may be the original batch number with a suffix (e.g. AQJ123 could become AQJ123/1, AQJ123/2, etc.) or a custom batch number (in which case the original manufacturer's batch number must be visible on the packaging).

Expiry date:
This is the original expiry date of the product.

Other data:
Manufacturers may include other data if permitted by the MS in which the pack will be marketed. Including other information may increase the size of the resulting barcode which will impact placement on the pack. UK will allow this under certain conditions. You should contact the PI Unit if you will to make use of this.

UI Barcode
The UI barcode must be a 2D Data Matrix incorporating appropriate error detection and correction. The structure of the Data Matrix must follow an internationally recognised coding scheme which allows for the identification and accurate decoding of each data element using common scanning equipment.
The manufacturer may select any recognised coding scheme(s) though EFPIA recommend the GS1 standard. This uses Application Identifiers (AI) to describe the following data and Group Separators (GS, ASCII code 29) to terminate the data when it is not fixed length. For example:

Product code (AI=01)	01234567890123	fixed length
Serial number (AI=21)	1015A24GXA45DXHWK<GS>	variable length
Batch number (AI=10)	AQGZ35147<GS>	variable length
Expiry date (AI=17)	160900	fixed length

The barcode must be printed on a smooth, uniform, non-reflecting surface.

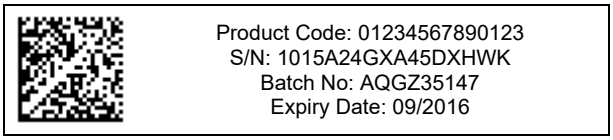
The barcode must be readable one year after the expiry date or five years after release, whichever is the later date. Manufacturers are required to evaluate the quality of printing of the barcode and establish the minimum quality of printing which ensures readability throughout the required period. A lower quality of printing may not be used. The barcode is assumed to be satisfactory if it has a print quality of 1.5 according to ISO/IEC 15415:2011.

The easy solution is to check the quality of your 2D barcode once you have a printing solution in place and ensure it is 1.5 or better.

Parallel traders will need to determine the space required to print a barcode with this quality. The Data Matrix above is approximately 15mm square and this size is likely to be adequate for a thermal transfer printer, but you need to determine for your own printers.

The product code, serial number and national number (if present and not printed elsewhere on the carton) must be printed in human readable format. This does not apply to small cartons where the sum of the two longest dimensions is 10cm or less. If possible the human readable format should be adjacent to the 2D barcode. It may be convenient to include the batch number and expiry date in the human readable block.

The font size used should comply with EC guidelines on readability of labels and leaflet, i.e. 8pt Arial.



The example above is about 17 x 80mm and this space should be sufficient even for a 20 character serial number.

Original manufacturers are likely to print directly onto the (end-flap of the) carton. Printers with this capability are expensive and print up to 300 cartons per minute. This is out of scale with most parallel import products were batches sizes are around 250.

A proportionate approach is to print the barcode onto a label which is then applied to the carton. This is the process used by all parallel importers. The printing process must use an appropriate technology which delivers an acceptable quality barcode. It is important that the label carrying the barcode can not be removed from the carton. The label must use an appropriate adhesive (different carton surface finishes require different permanent adhesives) and a security label should be used which has

features to prevent intact removal (e.g. a frangible structure or micro cuts). Any label carrying the UI must be applied to the carton and not onto another label.

The UI should not be introduced to packs until the corresponding data can be uploaded to the repository system. Packs which have the UI applied now may still be in circulation on 9 February 2019 and will need to be verified before being issued. Packs bearing a UI which has not been uploaded will fail verification and be reported as falsified. Parallel traders will need to work with the UK Medicines Verification Organisation to determine when the system will be ready to accept data and whether a back load is possible.

Actions for updating labels
In the meantime parallel importers may introduce an appropriate blank space on labels and cartons in any new application, in any label update variation or, if the remainder of the label is not affected in any way, in any variation which affects the labels.

The required space can be introduced by:
making a current label bigger by the required space, the additional space may overlap onto a different face of the carton;
introducing an additional label of the required size (and which will fit onto an available face of the carton).

2001/83 Art 54(a)(2)	DR will set out: (a) characteristics and specifications for cost-effective UI
2016/161 Art 3(2)	(a) UI is the safety feature enabling verification of authenticity and identification of an individual pack
2016/161 Art 4	(a) the UI is a sequence of numeric or alphanumeric characters which is unique to a given pack (b) The UI consists of: (i) a ‘product code’ allowing the identification of the name, common name, pharmaceutical form, strength, pack size and pack type (ii) a ‘serial number’ comprising a numeric/alphanumeric sequence of up to 20 characters generated by a deterministic or non-deterministic randomisation algorithm (iii) a national reimbursement number or other national number identifying the product if required by the MS (iv) the batch number (v) the expiry date (c) the probability that the serial number can be guessed is to be less than one in ten thousand (d) the combination of product code and serial number is to be unique until at least one year after expiry or five years after release, whichever is longer.

	(e) where the reimbursement number or other national number is contained in the product code it is not required to be repeated within the UI.
2016/161 Art 5	1. The UI shall be a 2D-barcode. 2. The barcode shall be a machine-readable Data Matrix and have error detection and correction equivalent to or higher than Data Matrix ECC200. Barcode conforming to the International Organization for Standardisation/International Electrotechnical Commission (ISO/IEC) standard 16022:2006 fulfil the requirements. 3. The barcodes will be printed on a smooth, uniform, low-reflecting surface 4. The structure of the UI Data Matrix shall follow an internationally recognised coding scheme which allows the identification and accurate decoding of each data element in the UI using common scanning equipment. The coding scheme will include data identifiers or application identifiers or other character sequences identifying the beginning and end of each data element in the UI. UI having a coding scheme conforming to ISO/IEC 15418:2009 fulfil the requirements. 5. The product code element of the Data Matrix UI must follow a coding scheme and begin with the characters specific to the used coding scheme. It must contain characters or character sequences identifying the product as a medicinal product. The product code must be less than 50 characters and be globally unique. Product codes confirming to ISO/IEC 15459-3:2014 and ISO/IEC 15459-4:2014 fulfil the requirements. 6. Different coding schemes may be used within the same UI providing the decoding is not hindered. The UI must then include standard characters permitting the beginning and end of the UI as well as the beginning and end of each coding scheme. UI which conform to ISO/IEC 15434:2006 fulfil the requirements
2016/161 Art 6(1)	1. Manufacturers must evaluate the quality of the printing of the data matrix, assessing at least: (a) contrast between light and dark parts (b) uniformity of the reflectance of the light and dark parts (c) axial non-uniformity (d) grid non-uniformity (e) unused error correction (f) fixed pattern damage (g) capacity of the reference decode algorithm to decode the data matrix 2. Manufacturer must identify the minimum quality of the printing which ensures the accurate readability of the data matrix throughout the supply chain until at least one year after the expiry date or five years after release, whichever is longer. 3. Manufacturers must not use a data matrix quality of printing lower than the minimum quality identified in Art 6(2) 4. A print quality of at least 1.5 according to ISO/IEC 15415:2011 fulfils the requirement.

2016/161 Art 7	1. Manufacturers must print the product code, serial number and reimbursement or other national number (if not printed elsewhere on the packaging) in human readable-format. 2. This does not apply on small cartons – where the sum of the two longest dimensions is less than or equal to 10cm. 3. Where the dimensions of the packaging allow it, the human-readable data elements should be adjacent to the 2D-barcode.
2016/161 Art 8	Manufacturers may include other data in addition to the UI in the 2D-barcode if this is permitted by the NCA.

Repackaging Operations

The UI and ATD may not be removed or partially or fully covered unless:

1. The MIA holder verifies the ATD and UI and decommissions the UI
2. The MIA holder replaces with an equivalent ATD and UI without opening the immediate packaging
3. Replacement is conducted in compliance with GMP
4. Replacement is subject to supervision by MHRA.

The UI and ATD are equivalent if they comply with the requirements of the DR and are equally effective in enabling verification and evidence of tampering.

MIA holders are regarded as producers and are liable for damages under the conditions of Directive 85/374/EEC.

QPs are responsible for ensuring that the UI and ATD have been affixed to the package.

Parallel traders are responsible for ensuring that the product code, serial number, batch number and expiry date have been uploaded to the repository system before the batch is released and for keeping the information up to date thereafter. The information must be stored in all repositories serving the MS where the product will be marketed and the product code, batch number and expiry date must also be stored in the hub.

Parallel traders must notify the MAH and the NCA in the destination country of their intention of importing a product. If the product is nationally authorised in the source country then the notification must be to the competent authority in the destination country and all required national procedures must be followed (Parallel Import Licence application).

The repackaged product must only carry one 2D barcode for the purpose of identification and verification of the product. Consequently any original UI must be obscured effectively. You may also wish to obscure the original 1D barcode if overlabelling.

Manufacturers applying the UI must ensure that it complies with requirements of the destination state for content and quality, is readable and contains the correct information. Original MA holders are likely to use barcode scanners and vision/character recognition systems to automate the reading and comparison of the 2D barcode and human readable data. MIA holders repacking products for parallel importers will need to investigate appropriate options for this scale of business.

Manufacturers must keep records of all operations affecting the UI until at least one year after expiry or five years after release, whichever is later and must provide the records to MHRA on request.

Batch-to-batch tracking is required. Parallel traders must inform the hub of the batch number and UI of the packs being repacked and batch number and UI of the packs in the resulting batch.

Appropriately authorised manufacturers must verify and decommission the UI of any product before repackaging or re-labelling it for use as an authorised investigational or auxiliary medicinal product.

If the MIA holder has reason to believe on receipt that the packaging of the medicinal product has been tampered with, or the verification of the safety features shows that the product may not be authentic, the MIA holder must not release the product for sale or distribution and must immediately inform the MHRA.

The responsibilities of wholesalers also apply to parallel traders who distribute their products by wholesale.

The Directive and Regulation give no guidance on the decision to over-label or re-carton a particular product. This remains a decision to be taken on the basis of trademark case law, in particular what is necessary to have effective market access. Some articles of the Directive and Regulation do have a major impact on this decision, especially Articles 18, 24 and 30 of the Regulation

> 18. Where a manufacturer has reason to believe that the packaging of the medicinal product has been tampered with, or the verification of the safety features shows that the product may not be authentic, the manufacturer shall not release the product for sale or distribution and shall immediately inform the relevant competent authorities.
> 24. A wholesaler shall not supply or export a medicinal product where he has reason to believe that its packaging has been tampered with, or where the verification of the safety features of the medicinal product indicates that the product may not be authentic. He shall immediately inform the relevant competent authorities.
> 30. Where persons authorised or entitled to supply medicinal products to the public have reason to believe that the packaging of the medicinal product has been tampered with, or the verification of the safety features of the medicinal product indicates that the product may not be authentic, those persons authorised or entitled to supply medicinal products to the public shall not supply the product and shall immediately inform the relevant competent authorities.

Clearly products which have visibly been opened cannot pass through the supply chain.

The situation is complicated by the likelihood of changes to the ATD used on the incoming product. Some glued cartons currently use a temperature sensitive glue which allows opening and re-closing of the pack if the glue is heated. The adhesive used may well change to a mixed adhesive incorporating a thermal glue for

immediate adhesion and a second glue which is not heat sensitive to provide long term closure. Other packs may change the ATD technology completely.

Originator packs may change appearance and/or size in preparation for complying with the FMD. It is impossible to guess how many will change or over what period. MHRA will develop a pragmatic approach but patient safety must remain the priority. Previous experience does not support a general Tell-and-Do solution!

2001/83 Art 47(a)(1)	Safety features shall not be removed or partially or fully covered unless the following conditions are met: (a) MIA verifies the UI and ATD (b) MIA replaces with equivalent UI and ATD without opening the immediate packaging Safety features are equivalent if they: (i) comply with requirements of the DR (ii) are equally effective in enabling verification and evidence of tampering (c) replacement is conducted in compliance with GMP (d) replacement is subject to supervision by NCA
2001/83 Art 47(a)(2)	MIA holders are regarded as producers and are liable for damages in the cases and under the conditions in Directive 85/374/EEC
2001/83 Art 51(1)	QP shall ensure that the UI and ATD have been affixed to the packaging
2001/83 Art 76(3)	Parallel traders must notify the MAH and NCA of the MS of destination of intention to import. If the product is Nationally Authorised notification is to the MS of destination without prejudice to additional procedures (PI licence) and payment of fees.
2001/83 Art 76(4)	For Centrally Authorised Products the parallel trader must notify MAH and EMA, including payment of fee.
2016/161 Art 2(2)	Packaging means outer packaging or immediate packaging where there is no outer packaging
2016/161 Art 9	Products may not carry any other visible 2D-barcodes for the purpose of identification and verification.
2016/161 Art 14	Manufacturers placing the safety features must verify that the 2D-barcode complies with Articles 5 (content) and 6 (quality), is readable and contains the correct information.
2016/161 Art 15	The manufacturer placing the safety features must keep records of every operation affecting the UI for at least one year after expiry or five years after release, whichever is longer and must provide the records to the NCA on request.
2016/161 Art 16	1. Before removing or covering the safety features the manufacturer must verify: (a) the integrity of the ATD (b) the authenticity of the UI and must decommission it if it is being replaced 2. Appropriately authorised manufacturers must verify and decommission the UI of

	any product before repackaging or re-labelling it for use as an authorised investigational or auxiliary medicinal product
2016/161 Art 17	When replacing a UI, the manufacturer must verify that the structure and composition of the new UI complies (product code, national reimbursement or other number) with the requirements of the MS of destination.
2016/161 Art 18	Where a manufacturer has reason to believe that the packaging of the medicinal product has been tampered with, or the verification of the safety features shows that the product may not be authentic, the manufacturer shall not release the product for sale or distribution and shall immediately inform the relevant competent authorities.
2016/161 Art 19	The requirements for wholesalers also apply to manufacturers who distribute their products by wholesale.
2016/161 Art 33(1)	The parallel importer must ensure that the information in paragraph 2 is uploaded to the repository system before the product is released for sale by the manufacturer and that it is kept up to date thereafter. The information must be stored in all repositories serving the MS where the product is intended to be marketed. The information is paragraphs 2(a) to (d) except for the serial number must also be stored in the hub
2016/161 Art 35(4)	For each batch of repackaged or relabelled product carrying the UI the parallel importer must inform the hub of the batch number of the packs being repackaged and of the UI on those packs. The importer must also inform the hub of the batch number of the batch resulting from the repackaging and the equivalent UI in that batch.

Verification and Decommissioning

Parallel Traders must verify each pack of incoming product and decommission the UI before the product is repacked.

Verification requires confirmation of:
(a) the authenticity of the UI (active UI with product code and serial number identical to that being verified);
(b) the integrity of the ATD.

Decommissioning a UI is the act of changing the status of the UI in the repository system from “active” to one which impedes further successful verification.

Wholesalers are required to verify the UI and ATD and decommission the UI prior to supplying to certain types of organisations, referred to as “Article 23” organisations. These organisations are:
(a) persons entitled to supply medicines to the public who do not operate within a healthcare institution or pharmacy;
(b) vets and retailers of vet medicinal products;
(c) dental practitioners;
(d) optometrists and opticians;
(e) paramedics and emergency medical practitioners;
(f) armed forces, police and other governmental institutions maintaining stocks of medicinal products for civil protection and disaster control;
(g) universities and higher education establishments using medicinal products for research and education, except for healthcare institutions;
(h) prisons;
(i) schools;
(j) hospices; and
(k) nursing homes.

When products are recalled, withdrawn or stolen the Parallel Trader must promptly take all the following measures:
(a) ensure the decommissioning of the UI of a recalled or withdrawn product in every repository serving the MS in which the recall or withdrawal is to take place;
(b) ensure the decommissioning of the UI (where known) of a stolen product in all repositiories where the information is stored;
(c) indicate in the repositories that the product is recalled, withdrawn or stolen.

When a product is supplied as a free sample, the Parallel Trader must indicate it as a free sample in the repository system and ensure the decommissioning of the UI before providing the sample.

The status of a decommissioned UI may only be reverted if all of the following conditions are met:

(a) the person reverting the UI is covered by the same authorisation and operates in the same premises as the person who decommissioned it;
(b) reversion takes place no more than 10 days after the UI was decommissioned;
(c) the pack has not expired;
(d) the pack is not recorded in the repository system as recalled, withdrawn, intended for destruction or stolen and the person performing the reversion does not know that the pack is stolen;
(e) the pack has not been supplied to the public.
Products which cannot be reverted because these conditions are not met must not be returned to saleable stock.

A product with a decommissioned UI may only be further distributed or supplied to the public if:
(a) the product is being exported outside the EU;
(b) the product is being supplied by an “Article 23” organisation, is from a part pack which has already been decommissioned, is supplied as a free sample or is supplied within a healthcare institution which obtained the product without “sale” from a wholesaler belonging to the same legal entity and which verified and decommissioned the UI;
(c) the product is a return which cannot be returned to saleable stock, is intended for destruction or is recalled, withdrawn or stolen and is provided to the person responsible for its destruction;
(d) the product is being provided to MHRA.

2001/83 Art 54(a)(2)	DR will set out: (d) methods for verification of the safety features
2016/161 Art 3(2)	(c) decommissioning a UI means changing the active status of the UI to a status impeding any further successful verification (d) active UI is a UI which has not been decommissioned or is no longer decommissioned (e) active status means the status of an active UI (f) healthcare institution is a hospital, in- or out-patient clinic or health centre
2016/161 Art 10	When verifying the safety features, manufacturers, wholesalers and persons authorised to supply medicinal products to the public must verify: (a) the authenticity of the UI (b) the integrity of the ATD
2016/161 Art 11	Verification requires checking the UI against the UI stored in the repository system. A UI is authentic when the repository contains an active UI with product code and serial number identical to that being verified.
2016/161 Art 12	A product with a decommissioned UI may not be further distributed or supplied to the public unless: (a) the product is being exported outside the EU (b) the product is being supplied in accordance with Articles 23, 26, 28 or 41 (c) the product is a return which cannot be returned to saleable stock, the product is

	intended for destruction or the product is recalled, withdrawn or stolen and the product is provided to the person responsible for its destruction (d) the product is being provided to the NCA
2016/161 Art 13	1. The status of a decommissioned UI may only be reverted if all of the following conditions are met: (a) the person reverting the UI is covered by the same authorisation and operates in the same premises as the person who decommissioned the UI (b) the reversion takes place no more than 10 days after the UI was decommissioned (c) the pack has not expired (d) the pack is not recorded in the repository as recalled, withdrawn, intended for destruction or stolen and the person performing the reversion does not know that the pack is stolen (e) the product has not been supplied to the public. 2. Products which cannot be reverted because these conditions are not met must not be returned to saleable stock.
2016/161 Art 16	1. Before removing or covering the safety features the manufacturer must verify: (a) the integrity of the ATD (b) the authenticity of the UI and must decommission it if it is being replaced 2. Appropriately authorised manufacturers must verify and decommission the UI of any product before repackaging or re-labelling it for use as an authorised investigational or auxiliary medicinal product
2016/161 Art 40	When products are recalled, withdrawn or stolen, the parallel importer must promptly take all the following measures: (a) ensure the decommissioning of the UI of a recalled or withdrawn product in every repository serving the MS in which the recall or withdrawal is to take place (b) ensure the decommissioning of the UI (where known) of a stolen product in all repositories where the information is stored (c) indicate in the repositories that the product is recalled, withdrawn or stolen
2016/161 Art 41	When a product is supplied as a free sample, the parallel importer must indicate it as a free sample in the repository system and ensure the decommissioning of the UI before providing the sample.

Aggregated codes

The DR introduced the idea of aggregated codes. These could allow bulk verification and decommissioning of UIs.

Aggregated codes are outside the scope of the delegated regulation and would only be used within a company or between trading partners.

For example, your business software could be set up so that when you scan the barcodes of an incoming batch it checks that the product codes and batch numbers are all the same (confirming batch homogeneity) and stores all of the UIs under an aggregated batch number.

Your software can then verify each UI with the repository system without each pack having to be done individually.

Then when you are about to repackage that batch you can decommission each UI in the same way.

The aggregated code would also be useful in reporting the batch to batch tracking.

2016/161 Preamble (20)	The verification by wholesalers of the authenticity of medicinal products at higher risk of being falsified would be equally effective whether performed by scanning individual unique identifiers or an aggregated code allowing the simultaneous verification of multiple unique identifiers. In addition, the verification could be performed at any time between the reception of the medicinal product by the wholesaler and its further distribution, to equal results. For those reasons, it should be left to the choice of the wholesaler whether to scan individual unique identifiers or aggregated codes, where available, or the timing of the verification, provided that the wholesaler ensures the verification of all unique identifiers of those products at higher risk of falsification in his physical possession, as required by this Regulation.

Repository and Hub

Contact the UK Medicines Verification Organisation – SecurMed (https://www.securmed.org.uk/).

2001/83 Art 54(a)(2)	DR will set out: (d) methods for verification of the safety features (e) provision of repositories, costs to be borne by manufacturing authorisation holders
2001/83 Art 54(a)(3)	Implementation will consider: (a) protection of personal data (b) protection of commercially confidential information (c) ownership and confidentiality of data generated by use of safety features (d) cost effectiveness
2016/161 Art 33(2)	The following information must be uploaded to the repository: (a) the data elements of the UI (b) the coding scheme of the product code (c) the name and the common name of the medicinal product, the pharmaceutical form, the strength, the pack type and the pack size of the medicinal product (d) the MS(s) where the product will be placed on the market (e) where applicable, the code identifying the entry corresponding to the medicinal product in the Article 57 database (f) the name and address of the manufacturer placing the safety features (g) the name and address of the PI licence holder (h) a list of wholesalers who are contracted to store and distribute the product on his behalf
2016/161 Art 33(3)	The information may be uploaded through the hub or a national repository. If it is uploaded via the hub, the hub will store a copy of the data in 2(a) to (d) except the serial number and transfer the complete data to all national hubs serving MS where the product is intended to be marketed. If the upload is through a national repository, the repository will immediately transfer a copy of the data in 2(a) to (d) except the serial number.
2016/161 Art 33(4)	The information in paragraph 2 must be stored in the repositories where it was originally uploaded for at least one year after the expiry date or five years after release, whichever is longer

Glossary

ATD	Anti-Tamper Device
DR	Delegated Regulation
GMP	Good Manufacturing Practice
GSL	General Sale List
MIA	Manufacturer/Importer Authorisation
MS	Member state
NCA	National Competent Authority
P	Pharmacy only sale
POM	Prescription Only Medicine
PV	Pharmacovigilance
QP	Qualified Person
UI	Unique Identifier