FiMVO

Suomen Lääkevarmennus

Building a safe medicines supply
Workshop for MAHs 9.1.2019

Agenda for the workshop

9.00 Medicines Verification System – what you still need to do
Maija Gohlke-Kokkonen, General Manager, FiMVO
Tero Vesa, Operations Manager, FiMVO

10.15 Verification processes in the supply chain
Teijo Yrjönen, QA Manager, FiMVO

11.15 New regulations from Fimea
Tarja Kankkunen, Head of Division

11.45 Q&A

12.00 End of workshop

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Where are we - what do you need to do?

Agenda

- Building the system – where are we and what's coming up
- On-boarding of End Users – current situation
- OBPs and MAHs in the system
- Data in system
  - Room for improvement

Building the system

- Release 1.3 on 23.1.2019
  - Alert-changes
  - Bug fixes
  - Reporting with a separate tool and release.
  - Production release for 9.2.2019
- Release 1.4 in June 2019
  - Rest of the NCA reports
  - Arvato’s doublezero in expiration date-implementation changes
  - Fixes for the known issues
- Release 1.5 in November 2019?

General Project Plan

Black=testing not finished
Blue=tested in IQE
Green=In production

Pharmadata, tested
Receptum, tested
CGI, Marela, tested
OneClinic, tested
Abilita, tested
Tricons, tested
Identoi, tested
Mylab, tested

Magnum Medical, on-line
Medapta, created
Medifon, created
Oriola, on-line
Tamro, on-line
Veripalvelu, created

7.1.2019
617 pharmacies created
23 hospital pharmacies
36 dispensaries

29.11.2018
Pre-production started

01.2019
CGI, Vare ready

27.1.2019
Hospital pharmacies + dispensaries installed

9.2.2019
Production mandatory

Apr-Aug 2017	*September 2017 – July 2018*	*August-October 2018*	*Nov 2018- Feb 2019*	*Feb 2019*
Specification and design	Baseline testing	Deployment	Pre-production	Production

June 2018
FiMVS 1.1
- IQE &PRD
- Multi-market packs

20.8.2018
EMVO EU Hub 2.0 Rel. 1.4

29.10.2018
jUAT testing for release 1.2

11.2018
EMVO EU Hub update

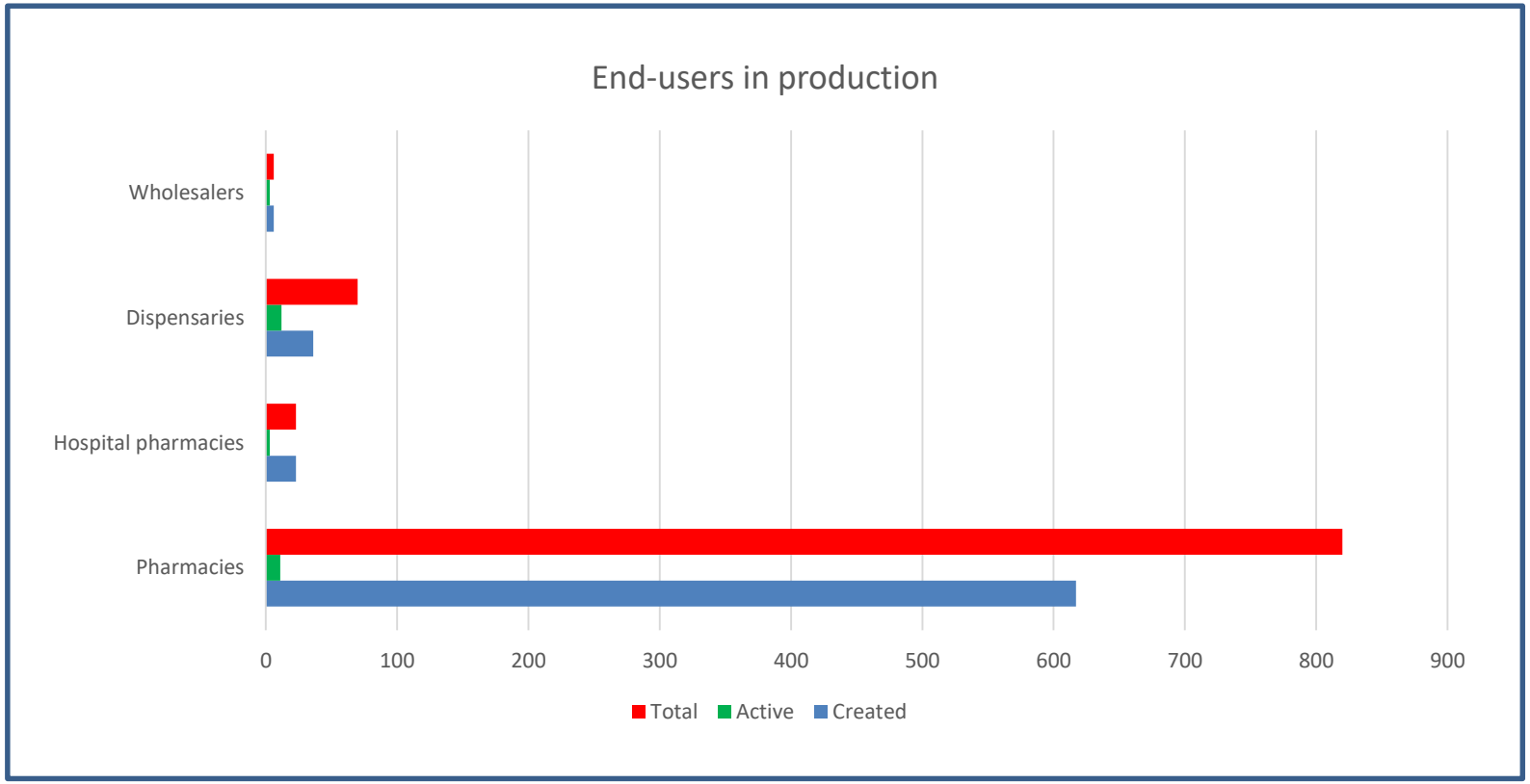
29.11.2018
FiMVS 1.2
- Intermarket transact.
- Withdraw
- Translations
- Alerts

12.2018
EMVO EU Hub update

23.1.2019
FiMVS 1.3
- Alert changes
- Reporting
- Bug fixes

End Users in production 7.1.2019

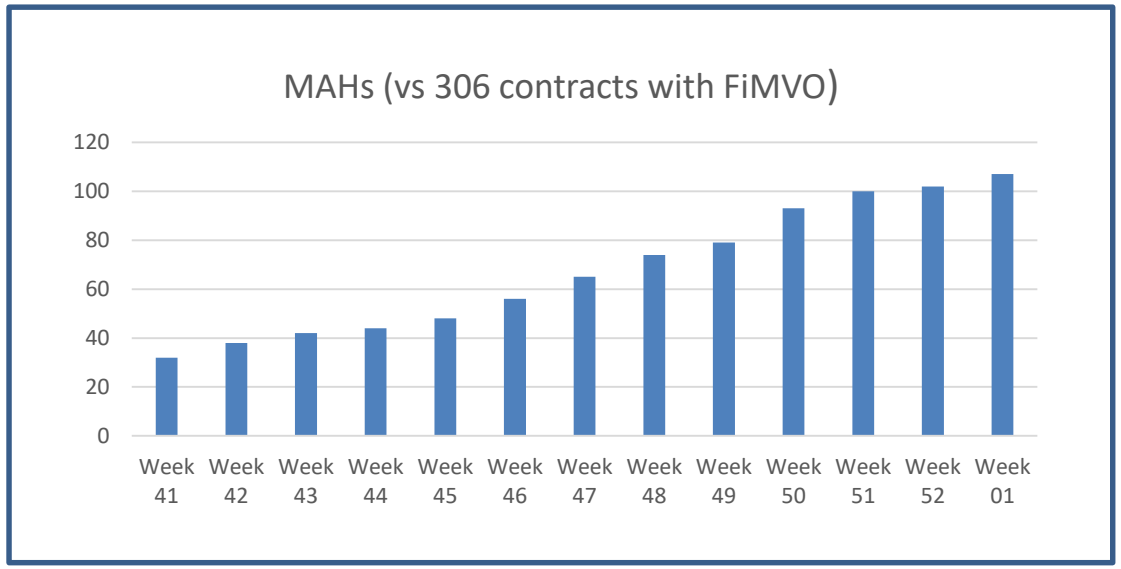
- End Users established by FiMVO (not all have connected to the system)
  - 617 pharmacies/dose dispensers
  - 6 wholesalers (Magnum Medical, Medapta, Medifon, Oriola, Tamro ja Veripalvelu (Blood service))
  - 23 hospital pharmacies
  - 36 dispensaries
- Active users:
  - 11 pharmacies
  - 3 hospital pharmacy
  - 3 wholesalers
  - 12 dispensaries

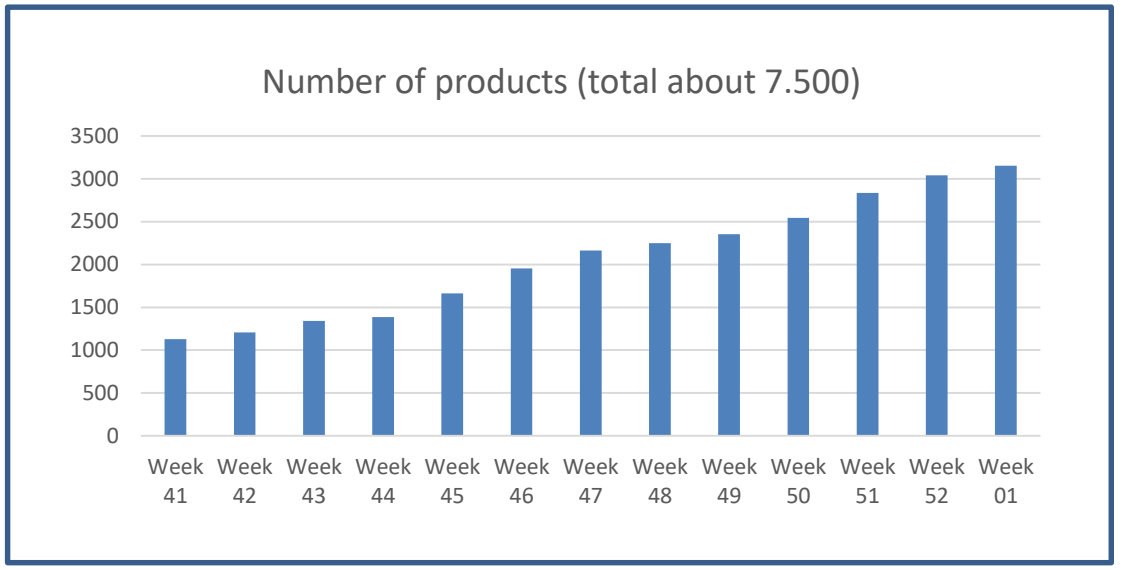


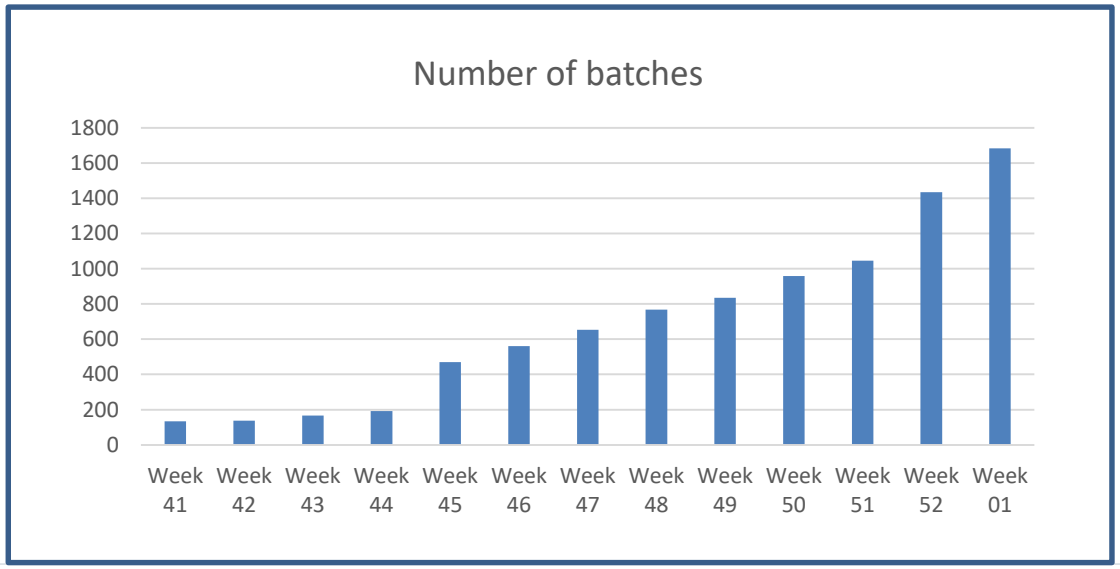
OBPs and MAHs in the system

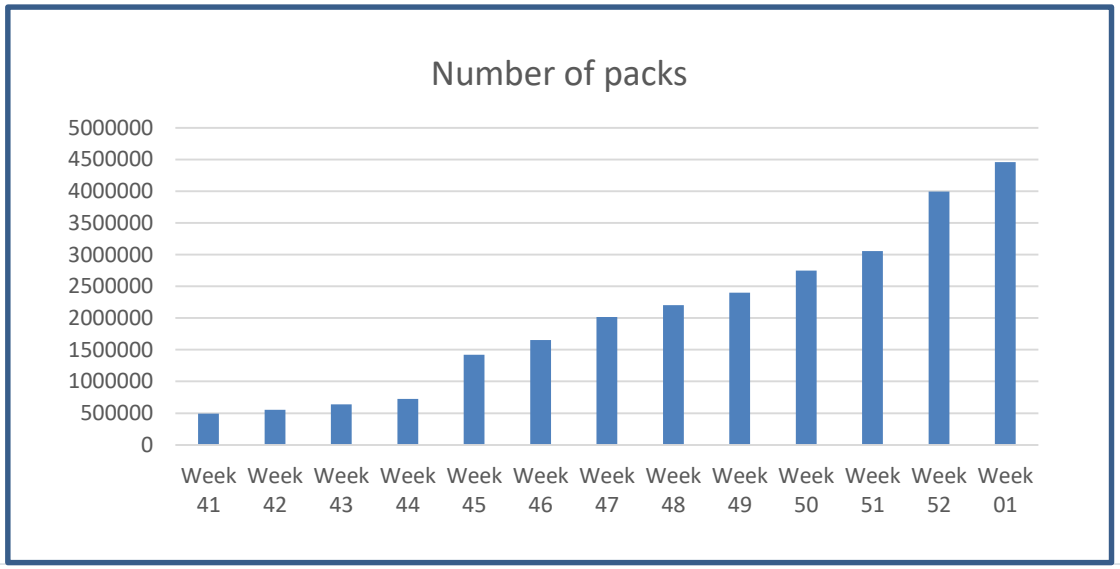
- Just under 500 OBPs in production of the Hub – where are the rest (1700)
  - How many will leave the market after end of shelf live?
- FiMVO has over 300 MAHs contracted – thank you!

Data in FiMVS

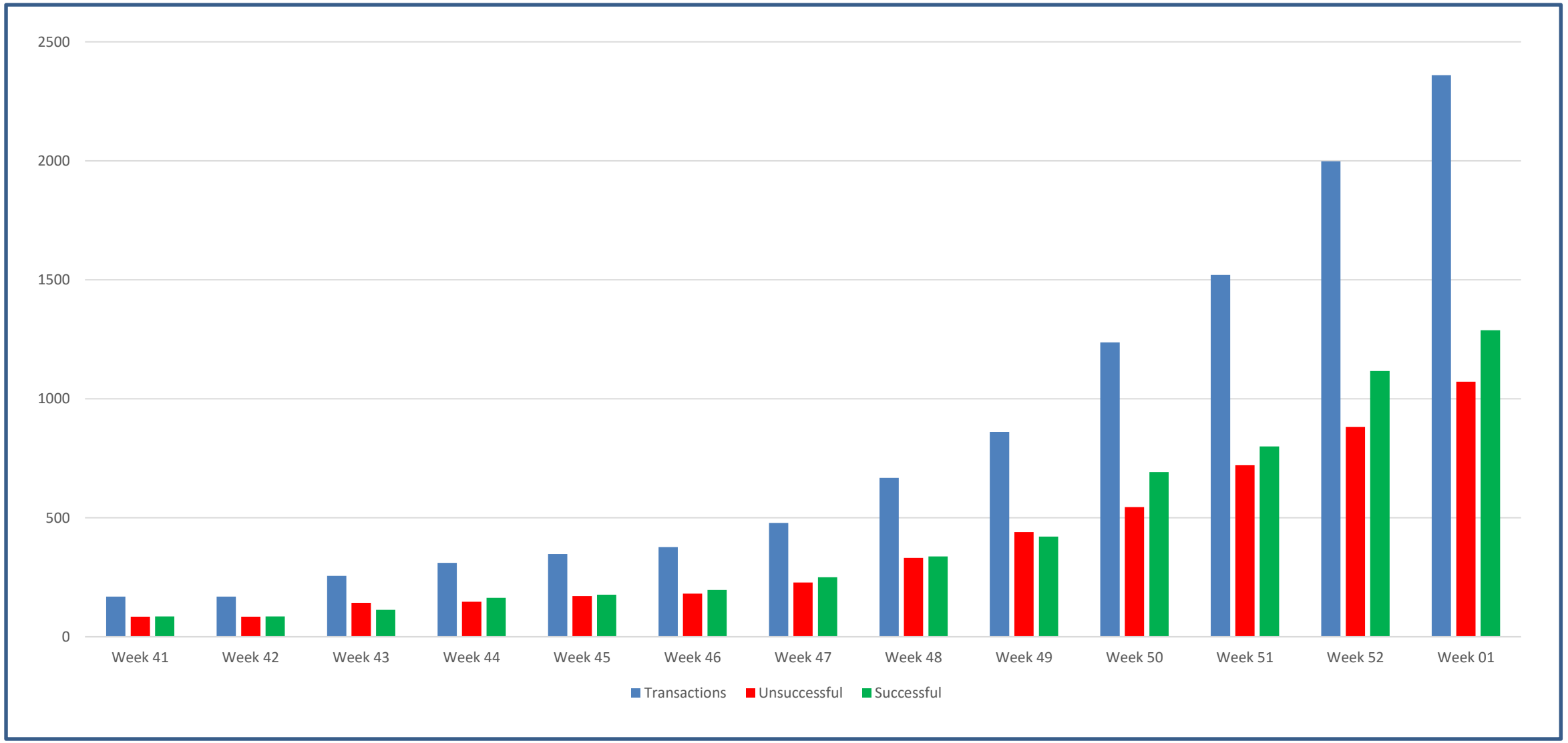




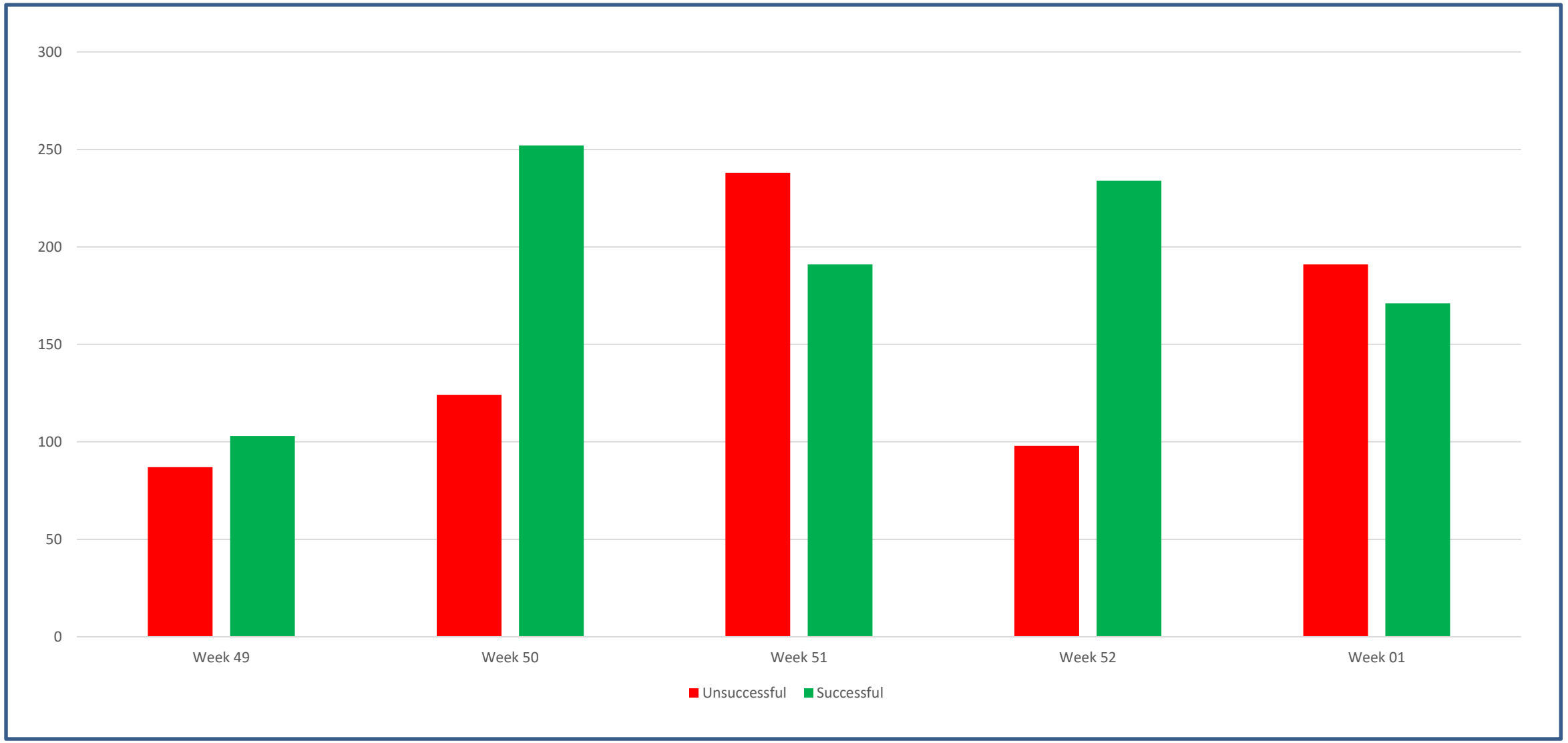




Transactions performed by pharmacies, cumulative



Transactions performed by pharmacies, weekly



Room for improvement

- Upload data
  - Upload Master Data before batches
  - Number of packs in the batch upload has to be exactly the same as produced number of packs, no extra numbers with the upload.
  - You can always test in IQE first if needed – contact us
  - If you want to check your data came through – contact us
- Upload correct data
  - Make sure the data in the code matches the data in system (human readable as well)
    - Especially expiry dates have caused issues
      - Formats MM-YYYY or MM/YYYY or YYYY-MM (00 or last day of month, not exact dates)
- Notify VNR service of GTIN changes
- Make sure you use the VNR service to make the serialisation notification
  - This is crucial for hospital pharmacy resources
  - But please do not make the notification if the data is not in the system – this will cause an alert in hospital pharmacies

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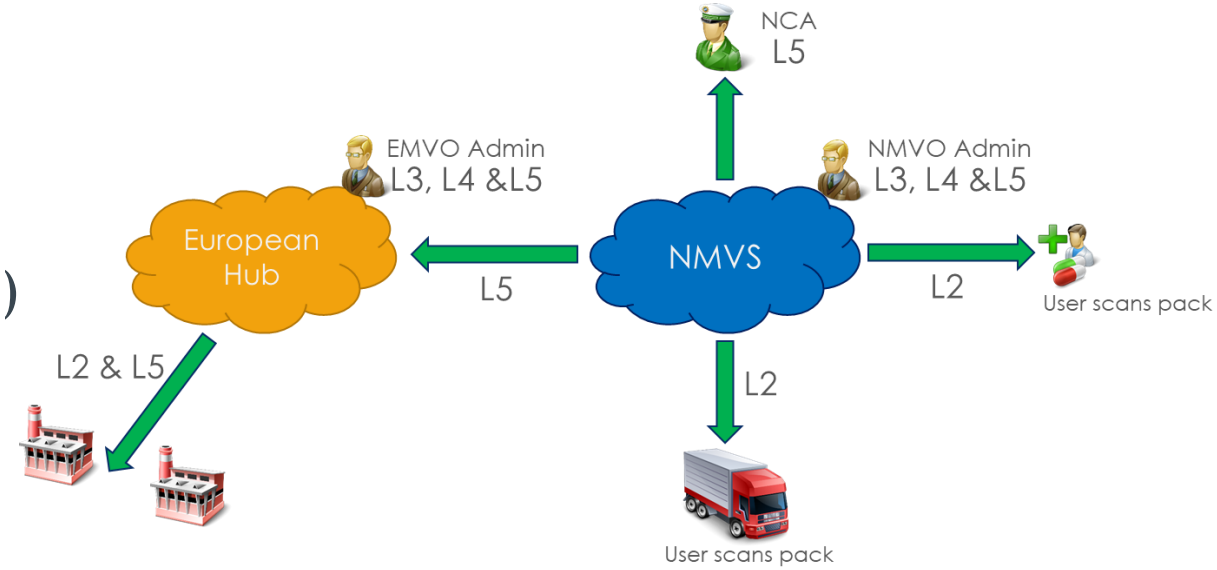
Verification processes in the supply chain

MAH Workshop, Helsinki, 9.1.2019

Teijo Yrjönen, FiMVO

Classification of deviations

- L1: A deviation that the system repairs itself. This deviation does not appear to the user in any way.
- L2: The user receives notice of the deviation.
- L3: The system administrator (EMVO or FiMVO) receives notice of the deviation.
- L4: More than one system administrator receives notice of deviation.
- L5: In addition to the user and system administrators, the OBP and the local competent authority are also notified of the deviation. This may be a falsified pack. L5 level deviations are referred to as alerts.



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Deviations raising a Level 5 (L5) alert

Code	Description	Transaction type
NMVS_NC_PC_01	Unknown product code	V, D, U
NMVS_FE_LOT_03	Failed to find a batch for the given data	V, D, U
NMVS_FE_LOT_12	Expiry date does not match the date held in the NMVS	V, D, U
NMVS-FE_LOT_13	The batch ID does not match the serial number in the NMVS	V, D, U
NMVS_NC_PCK_22	Pack is already inactive	D
NMVS_NC_PCK_19	Property is already set on pack [1]	D
NMVS_NC_PC_02	Unknown serial number	V, D, U
NMVS_NC_PCK_06	Actual pack status doesn't match the undo transaction (set and undo status must be equivalent)	U
NMVS_NC_PCK_20	Defined timeframe between setting this property and the undo was exceeded [1]	U
NMVS_NC_PCK_21	Undo can only be executed by the same user who previously set the attribute [1]	U

[1] Alert generated only as a result of an inter-market transaction. If the pack data is available in the respective NMVS, an alert will not be generated.

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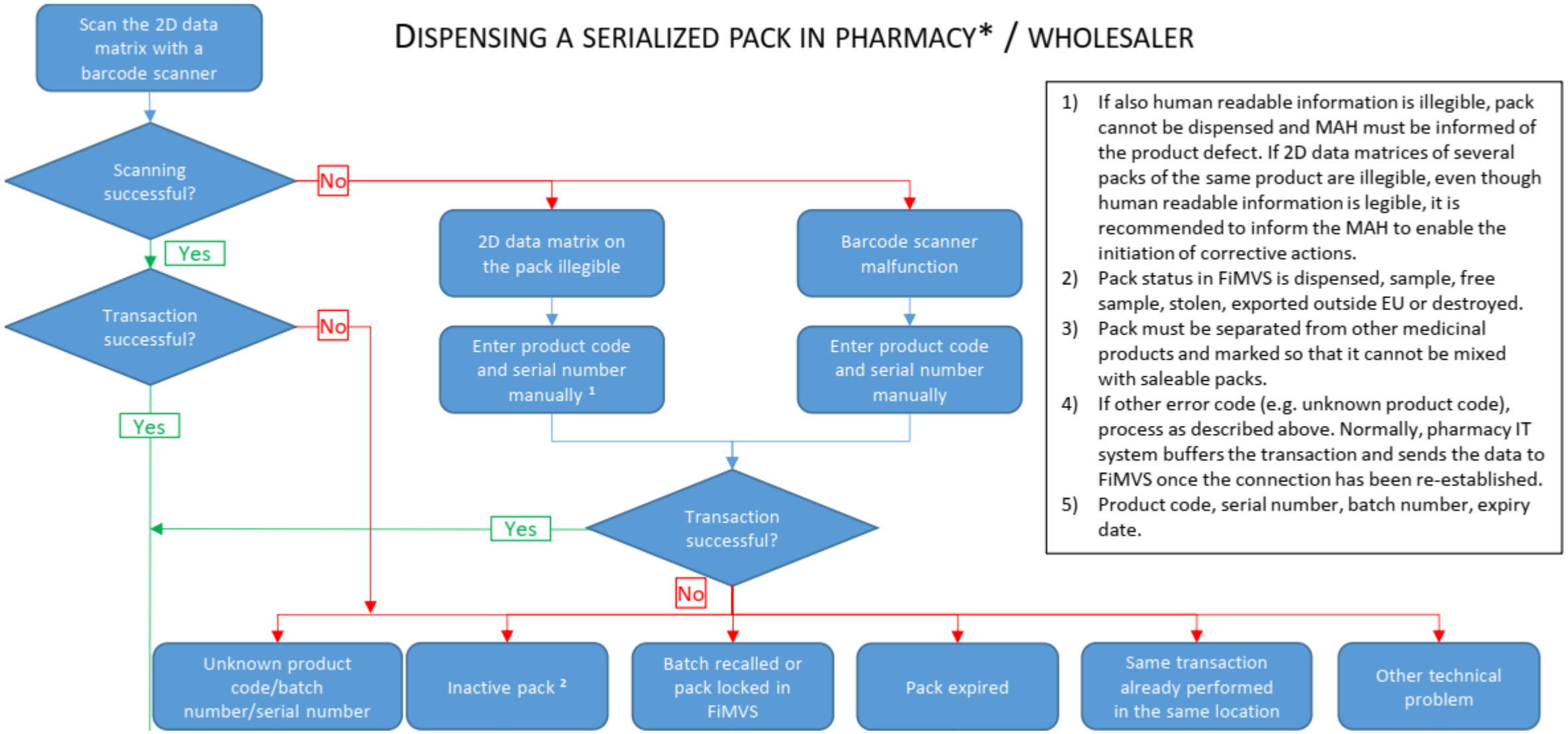
Information content of an L5 alert message

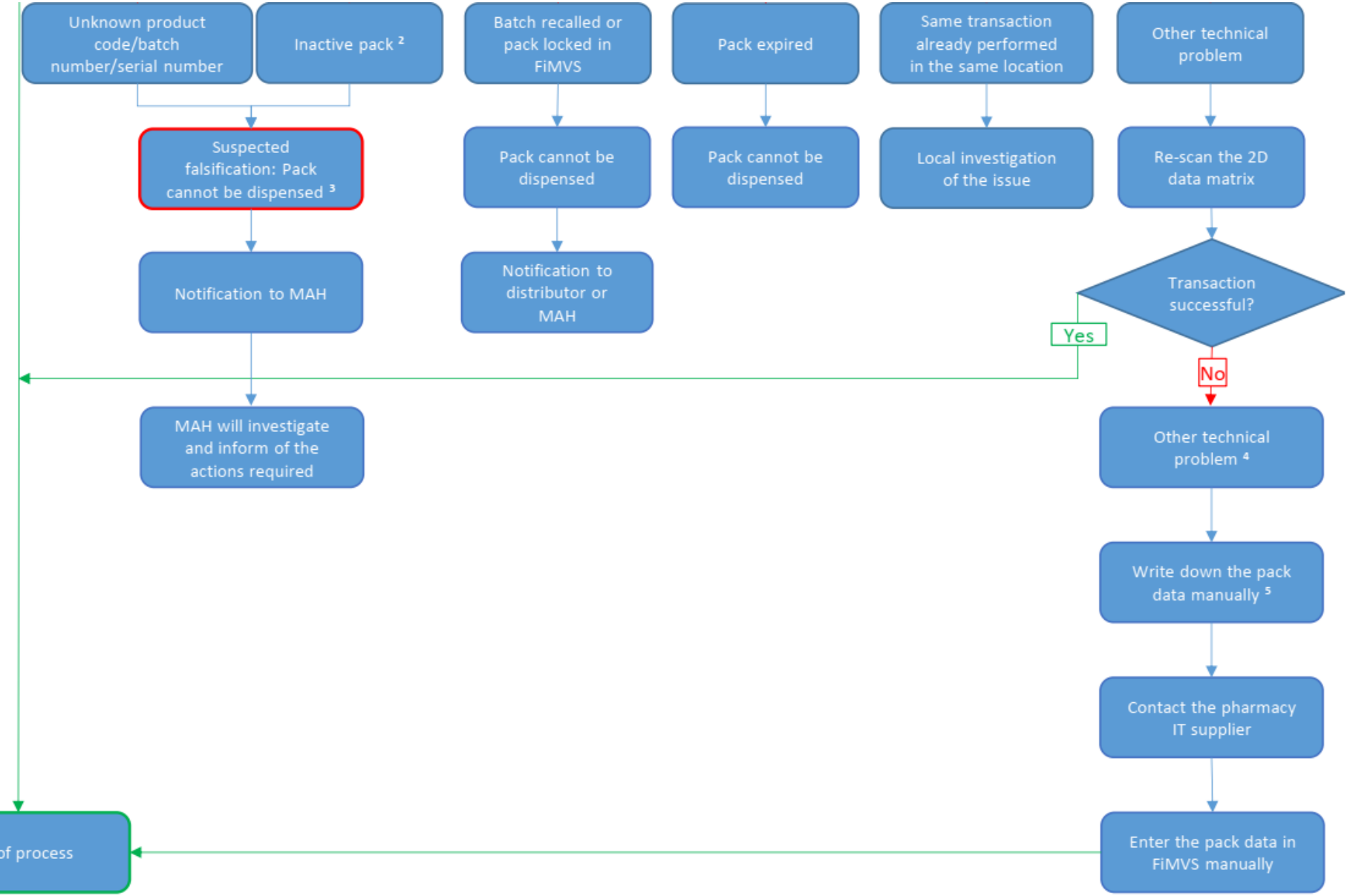
- Time stamp
- Alert ID
- Product code
- Batch number
- Expiry date of the batch
- Serial number
- Return code NMVS
- Return code description NMVS
- Return code Hub
- Client ID
- User ID

Dispensing a serialized pack in pharmacy/wholesaler



1) If also human readable information is illegible, pack cannot be dispensed and MAH must be informed of the product defect. If 2D data matrices of several packs of the same product are illegible, even though human readable information is legible, it is recommended to inform the MAH to enable the initiation of corrective actions.
2) Pack status in FiMVS is dispensed, sample, free sample, stolen, exported outside EU or destroyed.
3) Pack must be separated from other medicinal products and marked so that it cannot be mixed with saleable packs.
4) If other error code (e.g. unknown product code), process as described above. Normally, pharmacy IT system buffers the transaction and sends the data to FiMVS once the connection has been re-established.
5) Product code, serial number, batch number, expiry date.

Dispensing a serialized pack in pharmacy/wholesaler



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Anti-tampering device

- The integrity of the anti-tampering device (ATD) must always be checked before dispensing a pack.
- If the ATD is damaged, this is a product defect. This triggers a normal product defect process.
- N.B. It is possible that there will be serialized packs without ATDs which have been released for sale or distribution before 9.2.2019. In these cases, the pack can be dispensed to the patient despite not having an ATD.

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Exceptions in the dispense process

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The scanner is unable to read the 2D data matrix

- The pack can be dispensed by entering its product code (PC) and serial number (SN) manually using the *G122 Dispense single pack manual entry* function
- If 2D data matrices on multiple packs from the same batch are found to be unreadable it is recommended to inform the Marketing Authorisation Holder (MAH) to enable the initiation of corrective actions
- If the human readable information is illegible the pack cannot be dispensed and the MAH must be informed of the product defect

Unknown product code, batch number or serial number

- If the product code, batch number or serial number is unknown the pack cannot be dispensed to the patient
- The system also alerts if the expiry date encoded in the 2D data matrix differs from the expiry date uploaded into the system or if the serial number does not match the batch number
- Information of the alert is sent automatically from FiMVS to FiMVO and Fimea, and from the EU Hub to the OBP (not to OBP if product code is unknown)
- Suspected pack must be separated from other medicinal products and clearly marked that it cannot be dispensed
- Suspected falsified medicines should be reported to the MAH either through the wholesaler's product defect notification system or directly by email or phone → Fimea receives information directly from FiMVS

Unknown product code, batch number or serial number

- The MAH requests the distributor, if necessary, to place a sales ban on the batch during the investigation
- Together with the OBP, the MAH will investigate the suspected falsification
- The MAH should pay particular attention to keeping pharmacies, wholesalers and Fimea up to date with the situation
- The MAH should plan the information measures and channels in advance
- If the OBP has not uploaded pack or batch information to the FiMVS via the EU Hub or the uploading of the data failed, the information must be submitted to the system without delay → supply chain operators should be informed
- In case of a confirmed falsification, the process for class 1 product defects should be followed

Inactive pack

- If the pack is inactive in the system, i.e. marked as dispensed, a medicinal sample, a free medicinal sample, stolen, exported from the EU or destroyed, the pack may not be dispensed to the customer
- Information of the alert is sent automatically from FiMVS to FiMVO and Fimea, and from the EU Hub to the OBP
- Suspected pack must be separated from other medicinal products and clearly marked that it cannot be dispensed
- Suspected falsified medicines should be reported to the MAH either through the wholesaler's product defect notification system or directly by email or phone → Fimea receives information directly from FiMVS

Inactive pack

- The MAH requests the distributor, if necessary, to place a sales ban on the batch during the investigation
- Together with the OBP, the MAH will investigate the suspected falsification
- The MAH should pay particular attention to keeping pharmacies, wholesalers and Fimea up to date with the situation
- The MAH should plan the information measures and channels in advance
- In case of a confirmed falsification, the process for class 1 product defects should be followed

Batch recalled or pack locked

- If the batch has been recalled from the supply chain or the pack is locked, the pack cannot be dispensed
- The pack must be separated from other medicinal products and clearly marked that it cannot be dispensed
- The supplier or MAH must be contacted for additional information and instructions
- If the MAH has duly informed the supply chain operators of the withdrawal, this is a deviation from the pharmacy/wholesaler processes, which must be investigated in accordance with the pharmacy/wholesaler standard operating procedures

Pack has been expired

- If the expiry date of the pack has been exceeded, the pack cannot be dispensed to the patient
- The expired pack must be disposed of appropriately, and deviation handled according to pharmacy/wholesaler standard operating procedures

Same transaction already performed in the same location

- If a pharmacy/wholesaler tries to dispense a pack which has already been dispensed in the same location, the FiMVS system will notify this, but will not create an alert
- The pharmacy/wholesaler must investigate the cause of this error, (e.g. the pack has been opened and part of the contents dispensed earlier) and try to develop their process to avoid facing a similar situation in the future

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Other technical problem

- If the FiMVS system returns a technical error (e.g. *General exception occurred*), the pack status in the system may be confirmed by using the *G110 Verify single pack* transaction
- If the pack status in the system has not changed and it is still active, the transaction can be performed again
- If the system continues to return an error code, the pharmacy can dispense the pack, but they must write down the pack information (product code, serial number, batch number, expiry date)
- The pharmacy must contact their IT supplier to determine the reason for the error
- Once the error has been fixed, the pack must be registered as dispensed in the FiMVS system by using the *G122 Dispense single pack manual entry* transaction and entering the product code and serial code

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Exceptions in other decommission processes

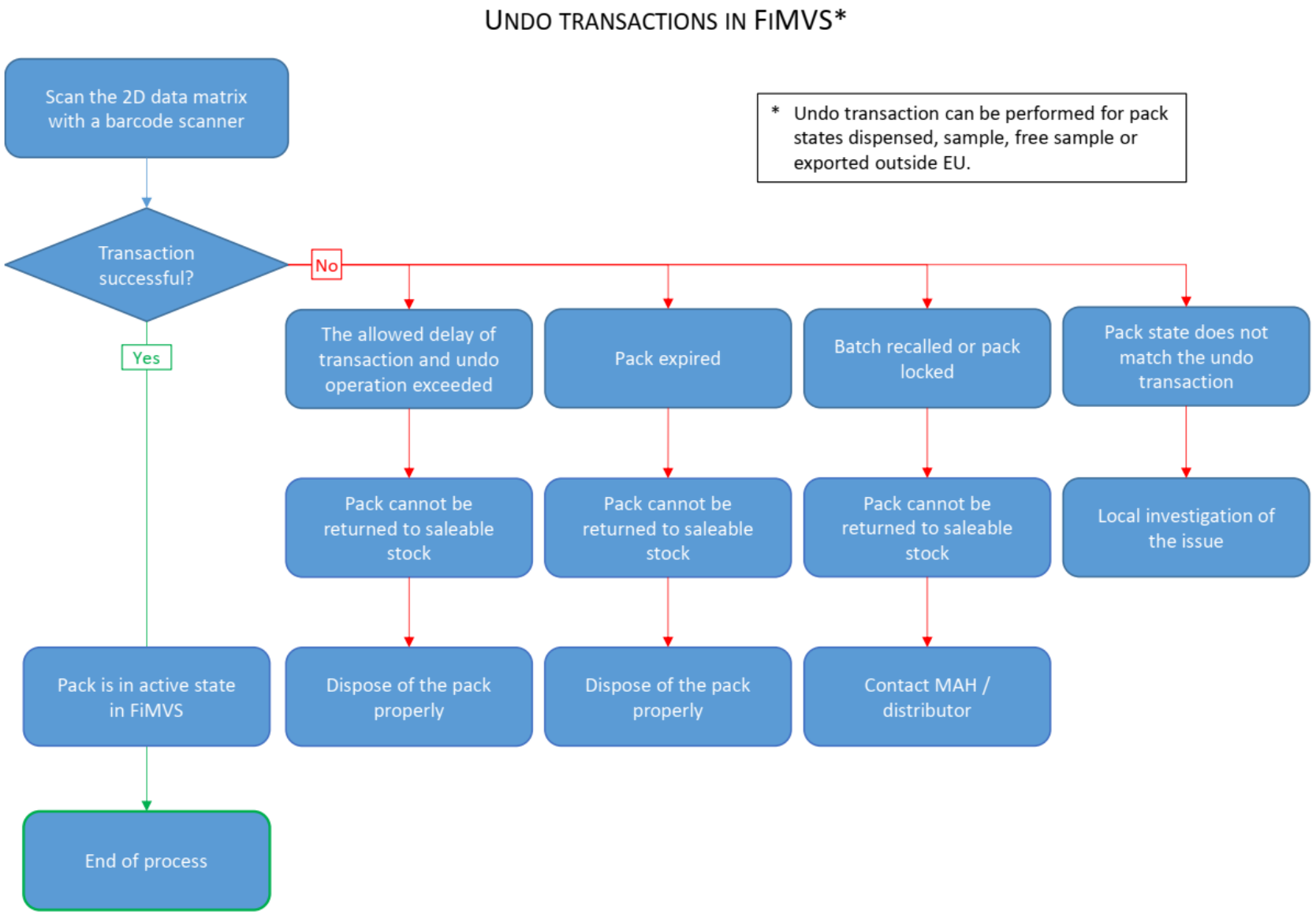
Decommission processes

- Decommission = any transaction changing the status of the pack from active to inactive
  - Dispense
  - Sample
  - Free sample
  - Export
  - Destroy
  - Stolen
- Lock = a transaction preventing any decommission transaction of the pack in the system
  - Locking should only be used when it is justified to ensure patient safety
  - Generally performed only by the OBP through the EU Hub
  - If the pack/batch to be locked is already on the market, this action must be notified to the supply chain operators and Fimea without delay, preferably before the locking is performed
  - Locking can be considered as a supplementary backup measure mainly for class 1 product defects

Exceptions in other decommission processes

- Some transactions can only be performed by the wholesaler or the OBP via the EU Hub, not possible for pharmacies
- The basic process and possible exceptions are the same as for the dispense process

Undo transactions in FiMVS



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Exceptions in the undo transaction processes

The allowed delay of transaction and undo operation has been exceeded

- If more than 10 days (240 hours) has passed since the original transaction (dispense, medicinal sample, free medicinal sample, export outside the EU) was performed, the pack can no longer be returned to the active state in the FiMVS system
- The only exception is locking the pack which has no time limit for undo transaction
- N.B. Packs registered as stolen or destroyed cannot be returned to the active state in the FiMVS system

Pack has been expired

- If the shelf life of the pack has expired after the original transaction was performed but before the undo transaction, the pack can no longer be returned to the active state in the FiMVS system
- The pack should be disposed of properly

The pack state does not match the undo transaction

- If a pack is active in the FiMVS system or the undo transaction does not match the inactive state of the pack, the system indicates that the pack status does not match the undo transaction
- In this case it is necessary to locally investigate and identify the reason for the error message (mix-up of packs, use of an incorrect undo transaction)

Undo successful: Batch recalled or pack locked

- N.B. Even if the batch has been recalled or the pack has been locked after performing the original transaction, the transaction can be undone
- However, in these cases the pack cannot be dispensed because the batch has been recalled or the pack has been locked
- The pharmacy/hospital pharmacy/dispensary/wholesaler must contact the distributor or the MAH to clarify the situation and receive instructions

Lääkealan turvallisuus- ja kehittämiskeskus | Säkerhets- och utvecklingscentret för läkemedelsområdet | Finnish Medicines Agency

Safety Features

Updating of Fimea Regulations

Tarja Kankkunen, Head of Pharmaco-technological section, Fimea

Legislation of Safety Features

- Directive relating to falsified medicinal products (2011/62/EU)
- Comission delegated regulation (2016/161) – binding legislation
- Draft Finnish Governments proposal to the Finnish Parliament to amend the Medicines Act
  - Objective of the amendment:
    - to nationally execute medicinal directives (2001/83/EU) conserning safety features
    - to execute national procedures of the Comission delegates regulation (2016/161)
  - In process on Finnish Parliaments
  - Effective by 9.2.2019

Safety Features

- A unique identifier of individual pack – a two-dimensional barcode and numerical format of the code

And

- Anti-tampering device of the pack

⇒ It is essential to verify both safety features to authenticate the medicine

➢ When the addition of the safety features on the packaging of medicinal products changes the layout of the mock-ups, the marketing authorization holder should notify these changes to Fimea by a 90-day notification. Further information for the cases, when notification is not needed, can be seen on Fimea web-site “Safety features”.

Addition of anti-tampering device on the packaging of OTC products and on the packaging of the medicinal products mentioned in the Annex I of the Commission Delegated Regulation 2016/161

- If the ATD is placed or shall remain on the packaging of the medicinal products other than those required by the Commission Delegated Regulation 2016/161, the marketing authorization holder shall send a notification of them to Fimea by an e-mail to the address mrp@fimea.fi, with a subject "**Anti-tampering device**". The e-mail notification should clearly identify the medicinal product (product name, strength and pharmaceutical dosage form) and the concerned package sizes.

Updating of Fimea's regulations and guidance

- No need for separate regulation conserning safety features identified
- Elaboration and implementation of some necessary details
- Administrative regulations to be updated:
  - 2/2018 Applying for and maintaining a marketing authorisation and registration for a medicinal product
  - 3/2013 Labelling and package leaflets for medicinal products
  - 4/2009 Product defects
  - 5/2012 Good Manufacturing Practices*
  - 5/2013 Good distribution practice of medicinal products*

- Normative guidelines to be updated
  - 1/2013 Labelling and package leaflets for medicinal products
  - Product defects

* No extra requirements directive….

Finnish Medicine Act…

- Legislative proposal including,
  - when the medicinal product should have safety features and when not
  - when the medicinal products safety features can be partly or entirely covered or removed
  - in which national circumtances the wholesaler inspects the safety features and removes the unique identifier from the repository (art 23)

Regulation of reporting suspected falsifications

- Changing Fimea's current regulation of Quality Defects 4/2009
- Commision´s DR 2016/161 determines the requirements of manufacturers, wholesalers, pharmacies and hospital pharmacies as well as requirements of NMVO (Fimvo)
- Fimea's draft regulation for requirements of MAH to report falsifications to Fimea

→It should we clear to all operators in the distribution chain when the case is actually a suspected falsification

→Communication channels from pharmacies to MAHs (via OBPs and wholesalers) should be clarified to be prompt to avoid supply disruptions in pharmacies (if product information is not put in the HUB retrospectively, even though safety features are placed on packaging under the transition period)

Timetable

- Fimea´s Regulation Drafts on hearing by 16.1.2019
- Fimea´s Regulations and Guidelines effective by 9.2.2019
- Medicin Act effective by 9.2.2019

National advice on Fimea´s website

Q & A of Fimea on this webpage (updating on regular basis):
https://www.fimea.fi/myyntiluvat/laakkeiden-turvaominaisuudet

- Q & A for MAHs in English, other Q & A in Finnish in the same document, here:

https://www.fimea.fi/documents/160140/741488/Kysymyksi%C3%A4+ja+vastauksia+turvaominaisuuksista/f1b7a018-4be2-9042-6daa-922d6040711c

Questions of MAHs to:
MRP@fimea.fi
Questions of manufacturers to:
GMP@fimea.fi
Questions of wholesalers to:
GDP@fimea.fi
Questions of pharmacies and hospital pharmacies to:
apteekit@fimea.fi

Links

- European Commission webpage concerning falsified medicines: https://ec.europa.eu/health/human-use/falsified_medicines_en

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

- Fimea´s webpage: https://www.fimea.fi/myyntiluvat/laakkeiden-turvaominaisuudet

- Finnish medicines verification: https://www.laakevarmennus.fi/fimvo-suomen-laakevarmennus