

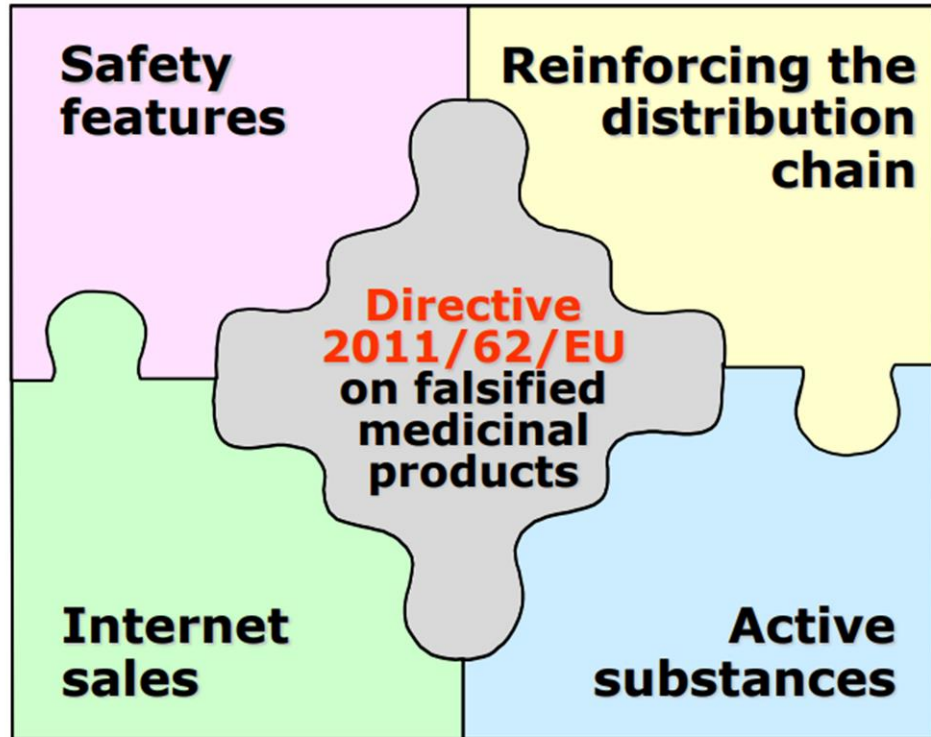
EU TRACK & TRACE SYSTEM - KEYTRUDA CASE

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für Arzneimittel
und Medizinprodukte

EU ACTION AGAINST FALSIFIED MEDICINES



➤ *Directive published 1 July 2011*

➤ *Entered into force 1 January 2013*

Contains measures to increase security of the medicinal supply chain in Europe:

➤ *Strengthen Good Manufacturing and Good Distribution Practices including the sourcing of active ingredients*

➤ *Improve supervision of actors in the distribution chain*

➤ *Ensure product integrity and authentication of medicines (safety features and product serialisation)*

Safety features

Unique identifier (UI)



Code enabling:

- the identification and
- the authentication of a given pack.

Anti-tampering device (ATD)



Device allowing the verification of whether a pack has been opened/tampered with.

Delegated Regulation to the FMD

➤ *Adopted on 2nd October 2015*

➤ *In force since 9th February 2019*





Unique Identifier

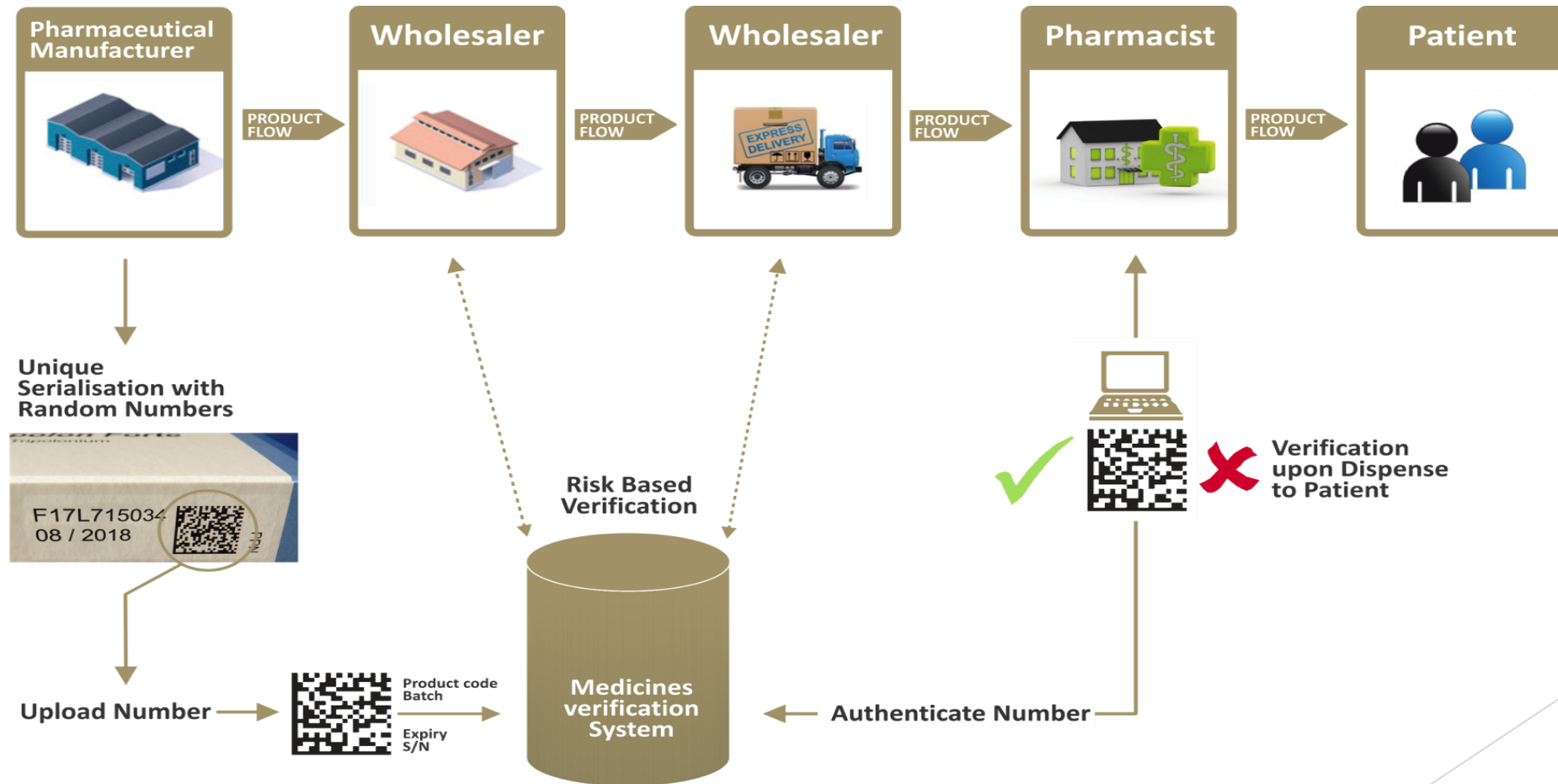
- ▶ Data-Matrix code, developed to ISO-standards
- ▶ Key data elements:
 - Product code (GTIN/PPN)
 - ▶ Batch number
 - ▶ Expiry date
 - Randomised unique serial number
 - National number



Product #: 09876543210982
Batch: A1C2E3G4I5
Expiry: 180500
S/N: 12345AZRQF1234567890



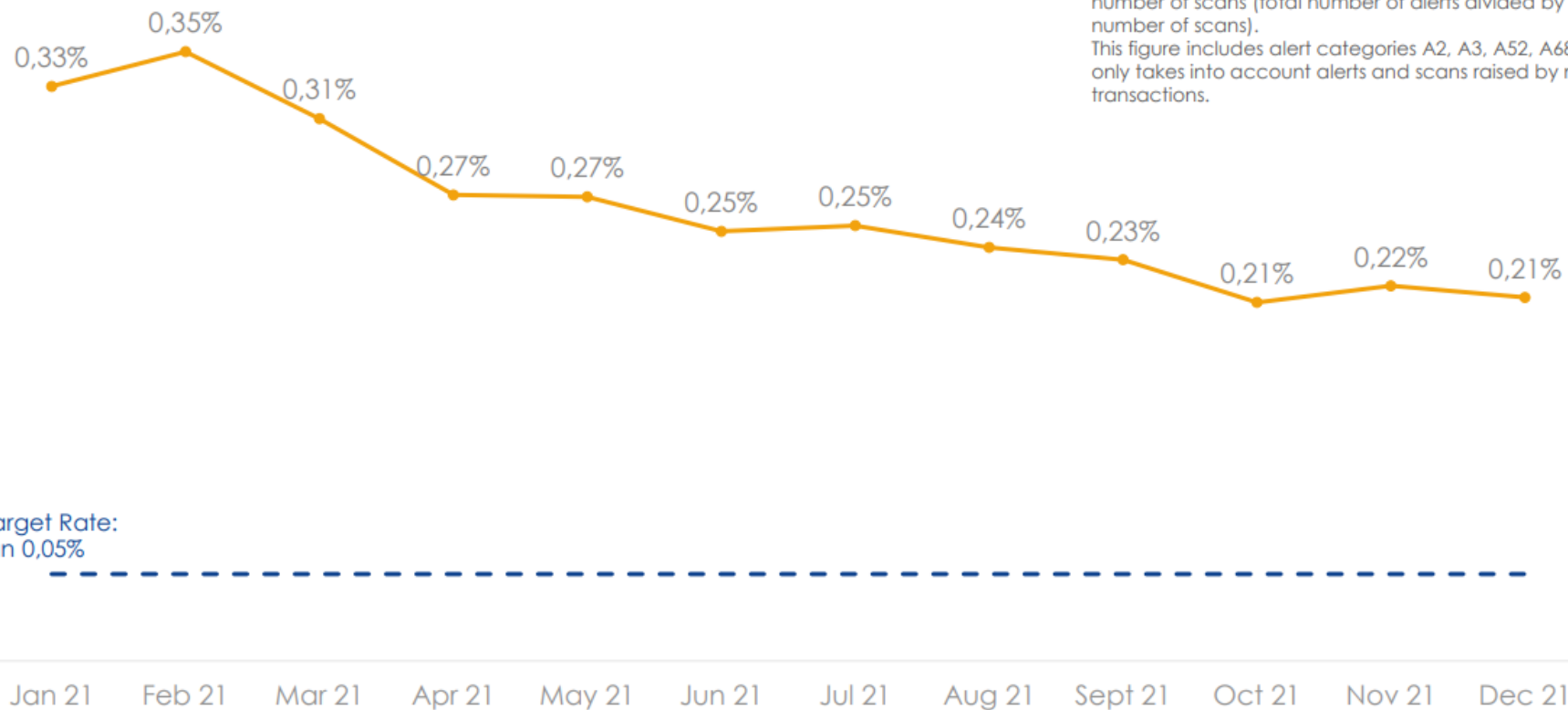
HOW IT WORKS



HOW IT DOESN'T

ALERT REDUCTION: 2021 MONTHLY ALERT RATE

Note: the alert rate is expressed as a percentage of the total number of scans (total number of alerts divided by the total number of scans).
This figure includes alert categories A2, A3, A52, A68, A24, A7 and only takes into account alerts and scans raised by national transactions.



09/02/2022

EMVO'S FMD IMPLEMENTATION WORKSHOP

GAPS IN THE SYSTEM

MONTHLY DECOM RATE FROM JUN. TO AUG. 2022



WHAT IT CAN DO

Report Details				
Operation	Date/Time (UTC)	Entity Location ID	Entity Location Name	Entity Location Address
UPLOAD	25/01/2022 05:46:09	EU:	Merck Sharp & Dohme International Services B.V.: Merck Sharp & Dohme International Services B.V.	Waarderweg , 39, Haarlem, 2031BN, EU, The Netherlands
VERIFY	04/04/2022 07:29:28	BG:	WHOLESALER	бул. Черни връх, София, 1303, BG
VERIFY	04/04/2022 08:29:34	BG:	HOSPITAL	бул. България 104, София, 1618, BG
VERIFY	03/06/2022 06:00:06	BG:	PHARMACY	бул.България 106, гр.София, 1618, BG
VERIFY	03/06/2022 08:16:02	BG:	Фармаджен БГ ООД: гр. София ж.к Красно село. бл.208А-В вх.Г	гр. София ж.к Красно село. бл.208А-В вх.Г склад1, София, 1618, BG
VERIFY	08/06/2022 08:12:32	BG:	Фармаджен БГ ООД: гр. София ж.к Красно село. бл.208А-В вх.Г	гр. София ж.к Красно село. бл.208А-В вх.Г склад1, София, 1618, BG
VERIFY	17/06/2022 14:07:00	EU:	BModesto BV: BModesto BV	Minervaweg, 2, -, Lelystad, 8239DL, EU, The Netherlands
VERIFY	29/06/2022 15:08:35	BG:	Фармаджен БГ ООД: гр. София ж.к Красно село. бл.208А-В вх.Г	гр. София ж.к Красно село. бл.208А-В вх.Г склад1, София, 1618, BG
VERIFY	04/07/2022 11:51:42	BG:	Фармаджен БГ ООД: гр. София ж.к Красно село. бл.208А-В вх.Г	гр. София ж.к Красно село. бл.208А-В вх.Г склад1, София, 1618, BG

Consequences for parallel trade

- ▶ High priority to keep the legal supply chain clean -> FMD
- ▶ Falsification cases in legal supply chain usually in connection with parallel trade
- ▶ Sometimes long supply chains
- ▶ Always international supply chains
- ▶ Bias? Packages are opened and repacked / relabelled -> close control possible
- ▶ Cases detected during incoming goods control at PI
- ▶ Usually serialisation code ok, but classic characteristics (e.g. Enbrel pencils in the package)

Consequences for parallel trade

- ▶ At PI: Code is verified and decommissioned/booked out
- ▶ Tamper-prove device opened
- ▶ Secondary package relabeled (sticker) or reboxing
- ▶ New Tamper-prove device and new code
- ▶ New code of PI booked into the system
- ▶ Problem: There is no connection from first code to second in the system!
- ▶ Only a connection concerning the batches
- ▶ Since the original labelling is known you could check the serialisation system of that MS
- ▶ In DE: Only a few PI have problems with falsifications

Consequences for parallel trade

- ▶ In DE: Only a few PI have problems with falsifications
- ▶ Long supply chains
- ▶ Good-PI-Practice? Only by product from the MS for which the was made.
- ▶ But: One main principle of the EU is the free trade of goods

Case review - Pharmagen

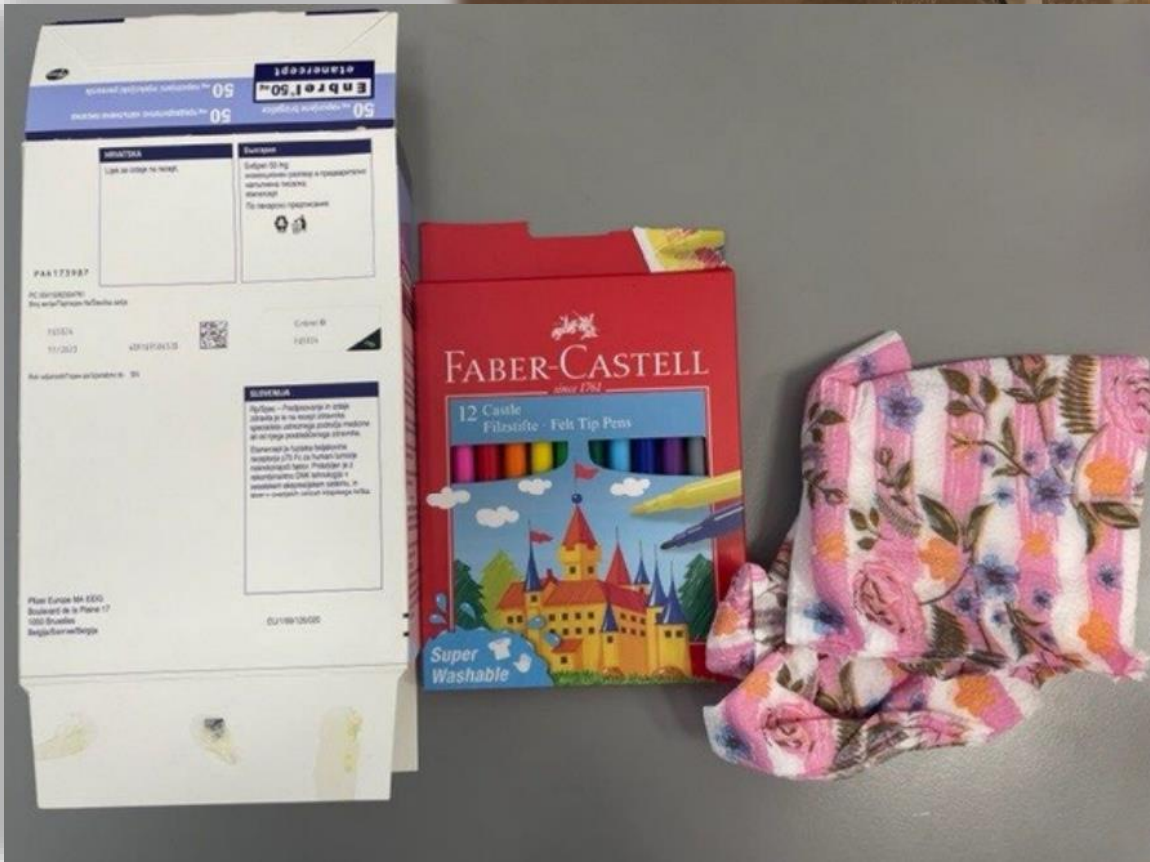
► RAPID ALERTS - KEYTRUDA + ENBREL




Inspectie Gezondheidszorg en Jeugd
Ministerie van Volksgezondheid,
Welzijn en Sport

IMPORTANT – DELIVER IMMEDIATELY Rapid Alert Notification of a Quality Defect / Recall


		Reference Number NLI/38/02
1. To: [updated information in bold] (see list attached, if more than one)		
2. Product Recall Class of Defect: (circle one)		① II 3. Falsification / Fraud (specify)*
4. Product: all products received from Pharmagen (please see attachment for further details): Keytruda, Enbrel, Simponi, Cosentyx, Humira, Roactemra, Trevicta, Xepilion, Xtandi.	5. Marketing Authorisation Number: * For use in humans/animals (delete as required) Keytruda: EU/1/15/1024 Enbrel: EU/1/99/126 Simponi: EU/1/09/546 Cosentyx: EU/1/14/980 Humira: EU/1/03/256 Roactemra: EU/1/08/492 Trevicta: EU/1/14/971 Xepilion: EU/1/11/672 Xtandi: EU/1/13/846	
6. Brand/Trade Name: Keytruda, Enbrel, Simponi, Cosentyx, Humira, Roactemra, Trevicta, Xepilion, Xtandi.	7. INN or Generic Name: Keytruda: pembrolizumab Enbrel: etanercept Simponi: golimumab Cosentyx: secukinumab Humira: adalimumab Roactemra: tocilizumab Trevicta: paliperidonpalmitate Xepilion: paliperidonpalmitate Xtandi: enzalutamide	
8. Dosage Form: Keytruda: concentrate for solution for infusion Enbrel: solution for injection in pre-filled pen Simponi: solution for injection in pre-filled pen, solution for injection in pre-filled syringe Cosentyx: solution for injection in pre-filled pen Humira: oplossing voor injectie in in pre-filled syringe Roactemra: solution for injection in pre-	9. Strength: Keytruda: 25 mg/ml Enbrel: 50 mg/(ml) Simponi: 50 mg (0,5 ml) Cosentyx: 150 mg Humira: 40 mg Roactemra: 162 mg Trevicta: 525 mg Xepilion: 150 mg and 100 mg (1,5 ml)	



Investigation of Pharmagen



РЕПУБЛИКА БЪЛГАРИЯ
Агенция по Вписванията



Търговски регистър и регистър на юридическите лица с нестопанска цел
Единен портал за заявяване на електронни административни услуги

Регистри | Контакти | Помощ | Потребител ▾

Начало > Търговски регистър и регистър на ЮЛНЦ > Справки > Актуално състояние

"ФАРМАДЖЕН БГ" ЕООД
ЕИК 201505694, състояние към дата: 3.11.2022г.Общ статус
Обявени актове
Актуален учредителен акт
Дело
Указания

История

19. Съдружници

17.10.2022 г. 08:28:29 ДАНИЕЛ ЕМИЛОВ ГЕОРГИЕВ, Държава: БЪЛГАРИЯ, Размер на дяловото участие: 70 лв.
Заличено обстоятелство.

МАРТИН ДИМИТРОВ ДИМИТРОВ, Държава: БЪЛГАРИЯ, Размер на дяловото участие: 30 лв.
Заличено обстоятелство.

28.09.2021 г. 14:48:37 ДАНИЕЛ ЕМИЛОВ ГЕОРГИЕВ, Държава: БЪЛГАРИЯ, Размер на дяловото участие: 70 лв.
МАРТИН ДИМИТРОВ ДИМИТРОВ, Държава: БЪЛГАРИЯ, Размер на дяловото участие: 30 лв.

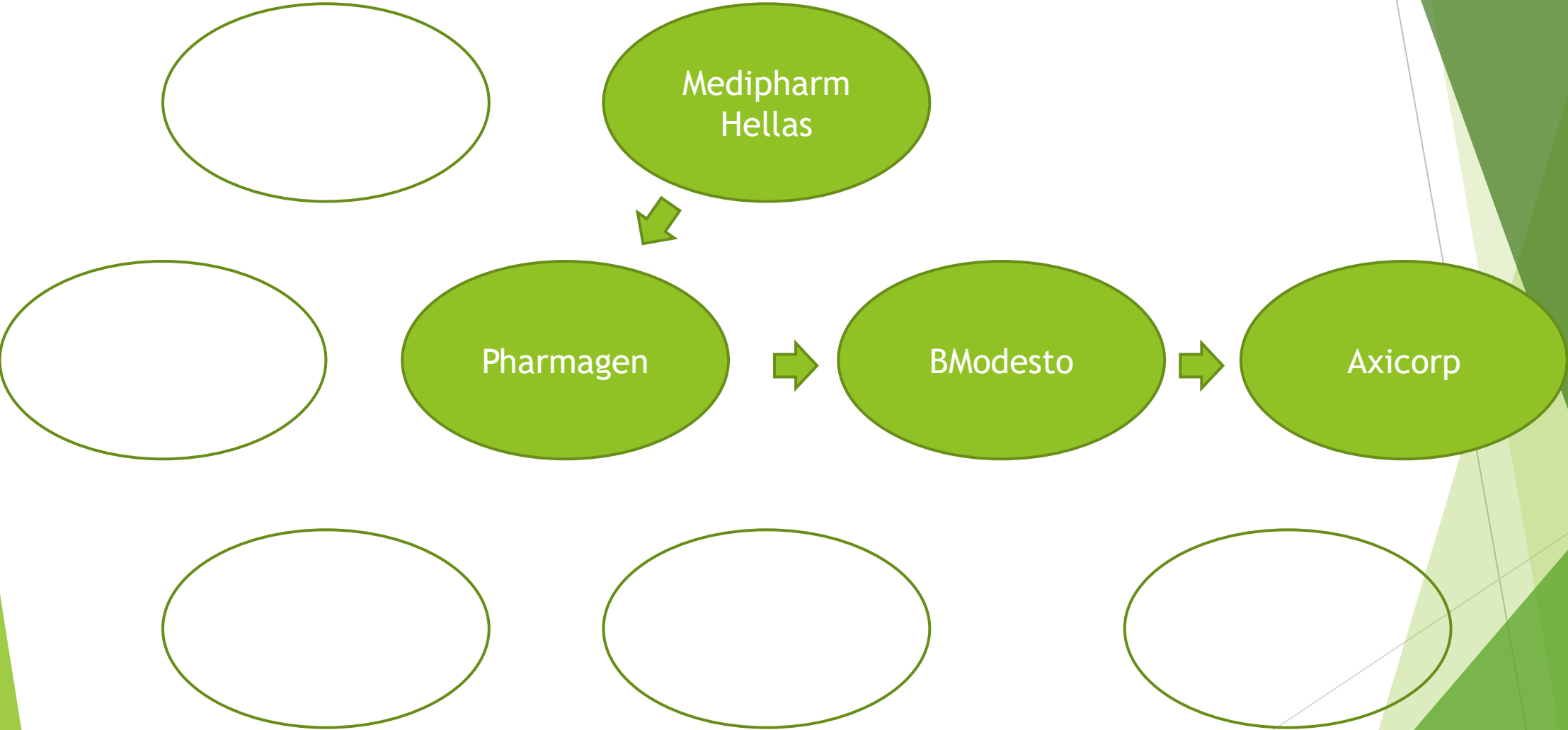
Затвори

Pharmagen Activity

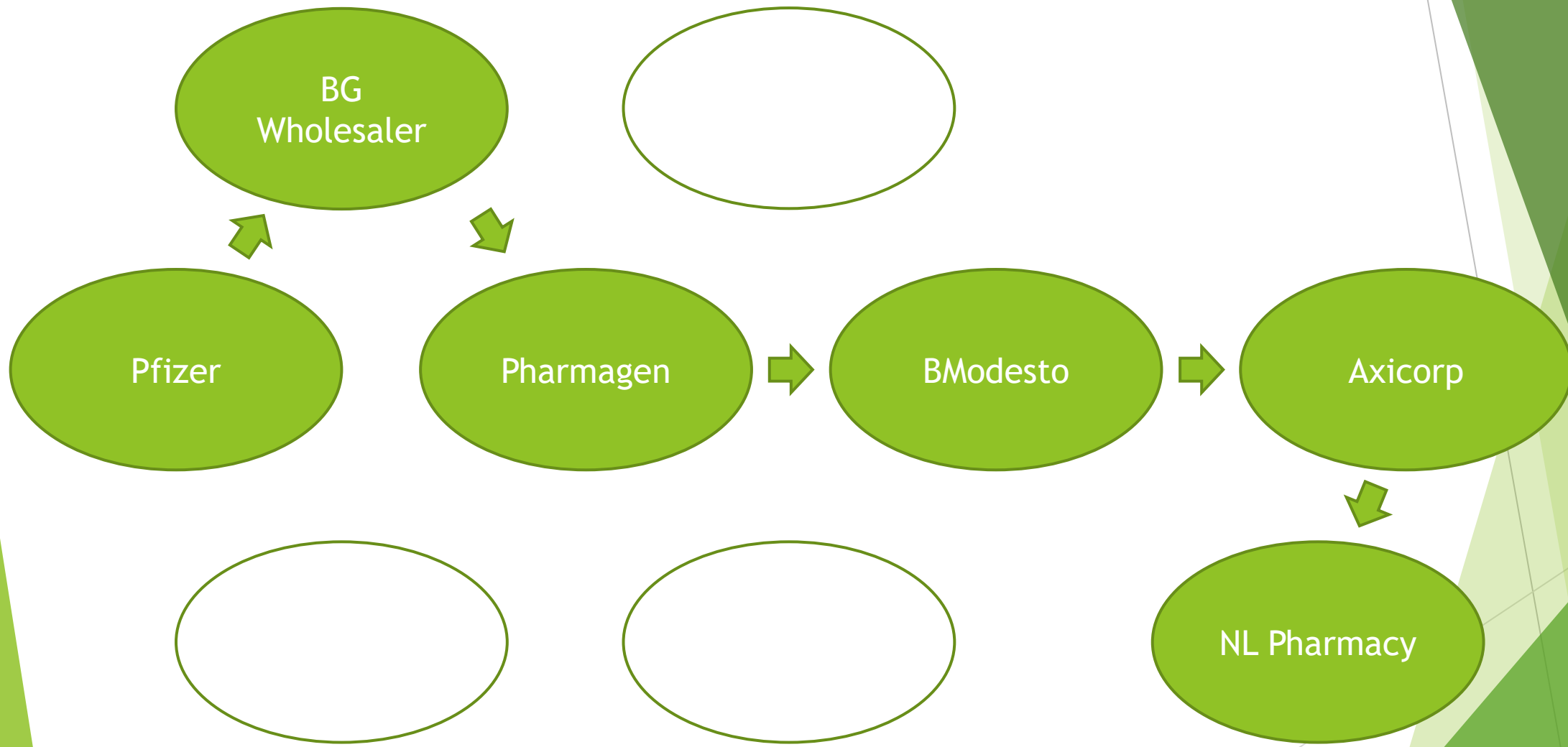
стр. 3

Дата		Отговор	Операция
07.06.22 21:30:45	01080540830195502117843298046017230731101155473	Опаковката може да бъде отпусната.	Провери ЛП
07.06.22 21:30:55	01080540830195502117843298046017230731101155824	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 10:57:14	0108054083011929211591092532611036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 10:57:21	0108054083011929211312247523341036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 10:57:29	0108054083011929211396883631251036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 10:57:41	0108054083011929211785487548711036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 10:57:54	0108054083011929211651837912641036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 10:58:07	0108054083011929211588488836881036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 10:58:20	0108054083011929211591092532611036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 10:58:32	0108054083011929211312247523341036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 11:07:59		Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 11:08:15		Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 11:08:33	010380021151106021100176119880081723123110H0253H12	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 11:09:15	0105948985002433211045297612871723013110W002260	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 11:09:22	0105948985002433211219599664331723013110W002260	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 11:09:33	0105948985002433211383506383821723013110W002260	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 11:12:32		Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:12:33		Опаковката е отписана като отпусната на друго място.	Провери ЛП
08.06.22 19:12:56		Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:13:32		Опаковката е отписана като отпусната на друго място.	Провери ЛП
08.06.22 19:29:50		Опаковката е отписана като отпусната на друго място.	Провери ЛП
08.06.22 19:55:38	0105415062304761217451856597351723123110FM0534	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:55:52	0105415062304761216264206036351723123110FM0534	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:56:02	0105415062304761212560949275001723123110FM0534	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:56:18	0105415062304761215102512535581723123110FM0534	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:56:26	0105415062304761217579265392131723113010FG5024	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:56:42	0105415062304761213157595233291723123110FM0534	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:57:11	0105415062304761214493106872211723113010FG5024	Опаковката може да бъде отпусната.	Провери ЛП
08.06.22 19:57:42	010599530920733172312311021A120421300127856488	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:14:21	0105415062304761218901768110441723113010FG5024	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:14:30	0108054083011929211701686368381036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:14:38	0108054083011929211772579903001036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:14:45	0108054083011929211342440794041036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:14:59	0108054083011929211418407011601036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:15:08	010805408301192921168618895991036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:15:15	0108054083011929211255463444941036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:15:21	0108054083011929211639759338721036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:15:33	0108054083011929211396883799921036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:15:54	0108054083011929211781279761191036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:16:00	0108054083011929211224521391051036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 00:16:06	0108054083011929211141623539431036262XH0417231130	Опаковката може да бъде отпусната.	Провери ЛП
09.06.22 11:15:09	0105413868108309211343903609971723083110LIB1M00	Опаковката е отписана като отпусната на друго място.	Провери ЛП
09.06.22 11:15:19	0105413868108309211101161898421723083110LIB1M00	Опаковката може да бъде отпусната.	Провери ЛП

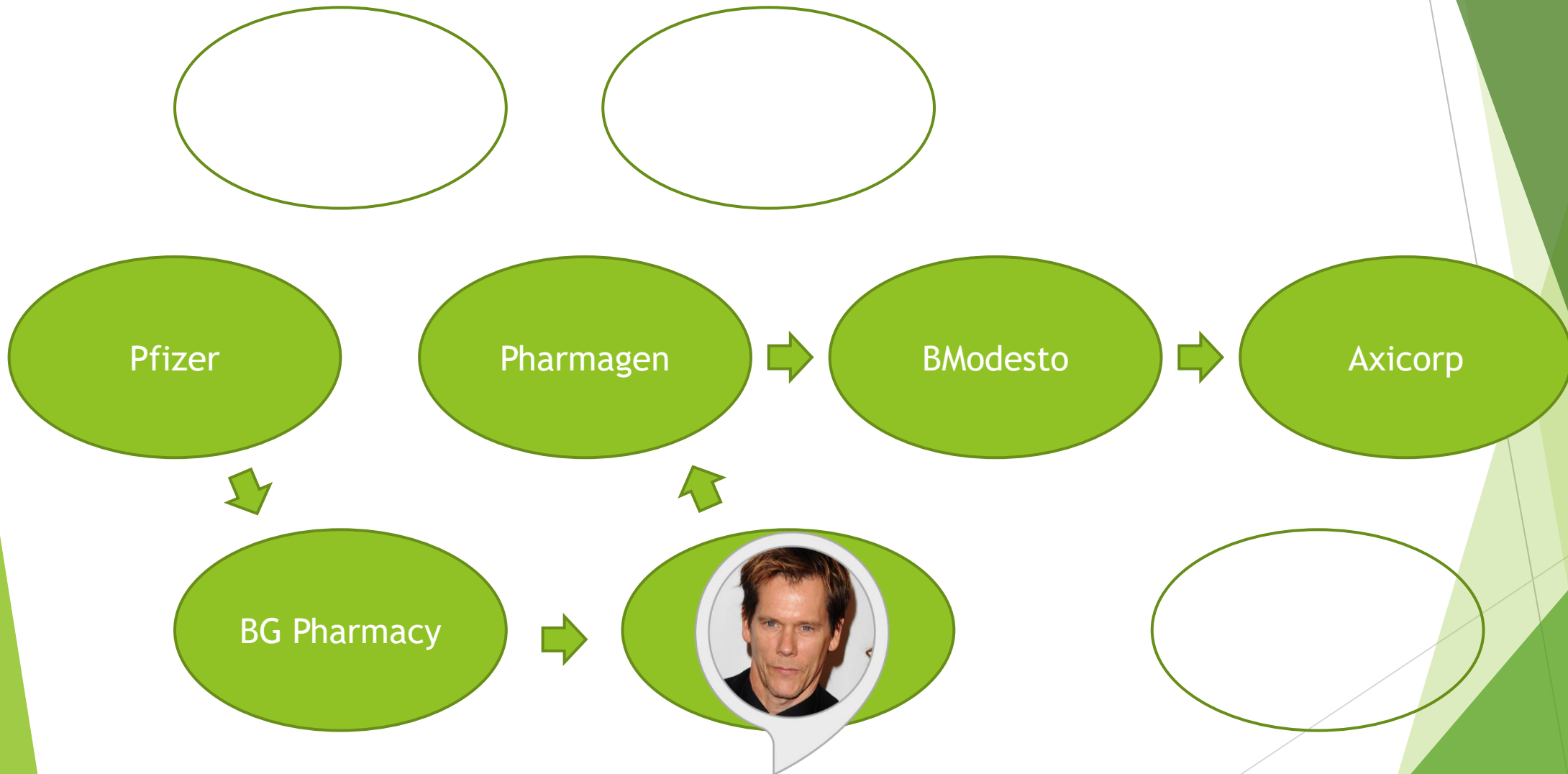
AUDIT TRAIL OF THE ENBREL - INVOICE TRAIL



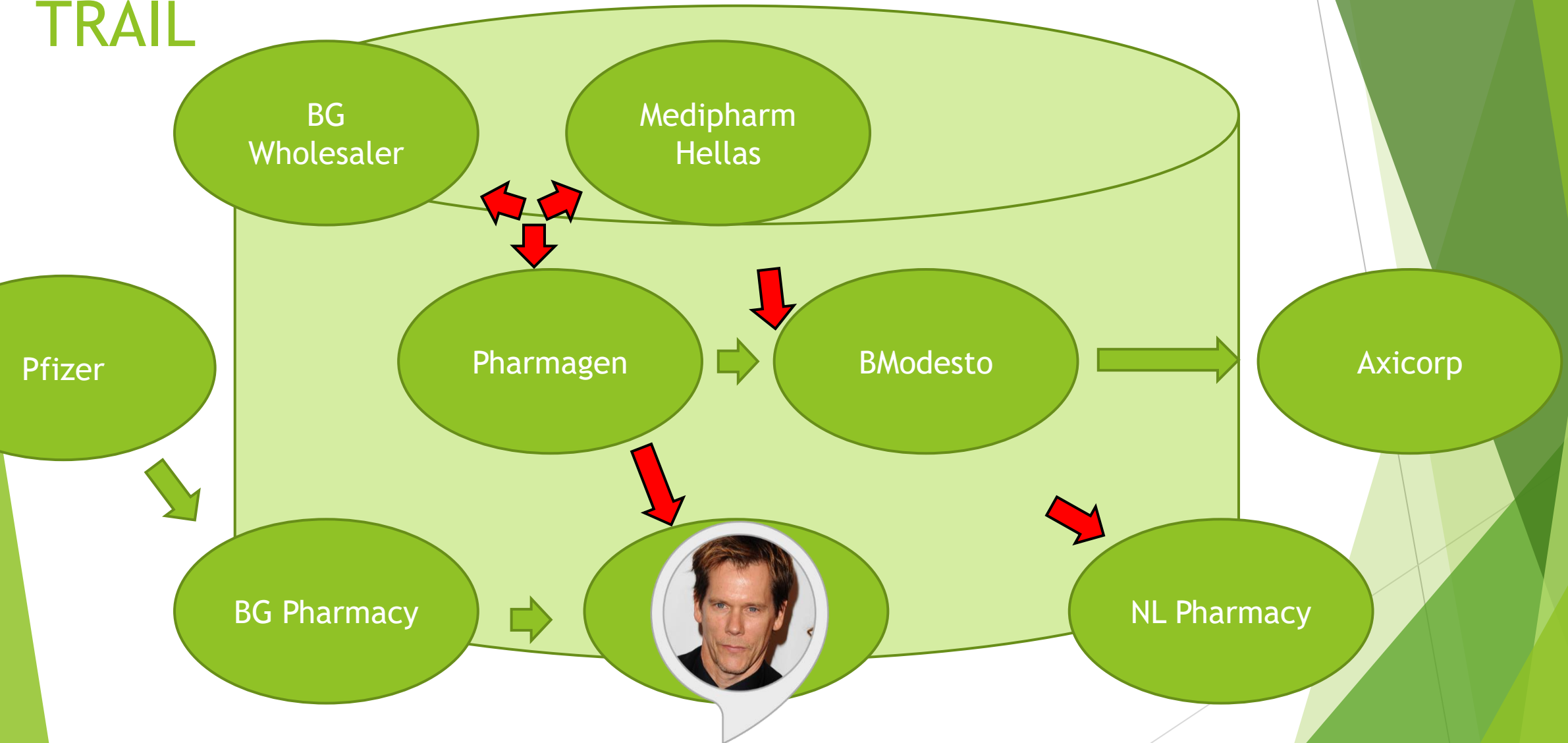
AUDIT TRAIL OF THE ENBREL - EMVS TRAIL



AUDIT TRAIL OF THE ENBREL - TRUE TRAIL



AUDIT TRAIL OF THE ENBREL - BEHIND THE TRAIL



LESSONS LEARNT

- Prevents obvious falsifications.
- The system gives a glimpse into the illegal packs circulation.
- It was still important to circulate the **Rapid Alert** (and its follow-ups) to the Network in a timely manner to warn the other Member States and have communication between the impacted Member States and EMA.
- It was still important to have **GDP inspections/site visits** organised.



- The system is a tool, not a panacea.
- High rate of alerts in the system enables stakeholders to ignore alerts due to various excuses.
- Gaps in the system provide entry points.
- Pack information is available to anyone within the system.
- Audit trail in the system is useful, but may not be entirely accurate.



Problems of the serialisation concerning the German NMVO Securpharm

- ▶ Too many false alerts although error rates are falling
- ▶ Reasons:
 1. handling mistakes (e.g. double dispence),
 2. incorrect printing on of the packs,
 3. missing/incorrect data upload,
 4. bugs in involved systems (EMVS, NMVS, user software),
 5. misconfiguration in the systems involved (software and hardware),
 6. unforeseen system behaviour due to high complexity

Problems of the serialisation concerning the German NMVO Securpharm

- ▶ Reduction of false alerts necessary
- ▶ Clever handling of alerts
- ▶ Providing more reports for authorities
- ▶ So far no falsification detected in DE and in most other MS via the system
- ▶ Interesting alerts include usually international trade
- ▶ Looking for the needle in the haystack: Is the system useful for that?
- ▶ Handling mistakes: Clarification at the pharmacy in retrospect normally not possible

Problems of the serialisation concerning the German NMVO Securpharm

- ▶ Dangerous exceptions on serialization:
- ▶ “Volume problem” in the hospital pharmacy
- ▶ Exceptions for Covid-19 vaccines (some vaccination centres couldn't verify)
- ▶ Exceptions for Donation of medicines to Ukraine (not all UI booked into the system, decommissioning not necessary, risk: packages might come back via illegal channels)

QUESTIONS AND DISCUSSION