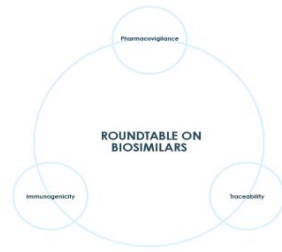


Kevin Klein, MSc, The Netherlands

- Researcher, Escher; Project Officer, Lygature, The Netherlands



Current challenges in traceability of biologicals – a case study from the Netherlands

Kevin Klein, MSc, The Netherlands
15 November 2016

Traceability of Biologics - A Case Study from the Netherlands

Escher, the Lygature platform for Regulatory Innovation

Read our publication in Drug Safety:
DOI [10.1007/s40264-015-0383-8](https://doi.org/10.1007/s40264-015-0383-8) [open access!]



ESCHER

THE LYGATURE PLATFORM
FOR REGULATORY INNOVATION

Escher's mission

- Escher is an initiative of Lygature, the Dutch independent research enabler, and functions independently from other organisations in the pharmaceutical sector.
- Escher promotes scientific research and international debate in the field of policy and regulations for the development, market authorization, reimbursement and use of medicines and medical technology.
- Escher partners with authorities, academic institutions, companies and NGOs.



Areas of interest for Escher

Evidence generation methods and evidence requirements

Examples:

- Use of Biomarkers
- Trial design
- Scientific advice
- Post-marketing safety research

Scientific dialogue and stakeholder interaction

Examples:

- Values & risk preferences
- Ethics in post-authorization studies
- Public trust in the regulatory system

The decision-making process and benefit-risk assessment

Examples:

- Decision support in B-R
- Patient-perspectives
- Appropriateness of new drug prescribing

Health Technology Assessment and evaluating societal impact

Examples:

- Cost-effectiveness assessment of regulations
- Access and reimbursement trajectories
- Medical need in decision-making

www.lygature.org/escher

Background and objective

Background

- Due to the complexity of biologics and the complexity of their manufacturing process a degree of variability may exist between different products and batches of same product
- EU Pharmacovigilance legislation (2012):
“...Member States shall ensure (...) to identify clearly any biological medicinal product (...) which is the subject of a suspected adverse reaction report by the name of the product [brand name] and the batch number”
- Literature: \approx 90% brand name / \approx **20% batch number** traceability for biologics

Objective

- Understanding of the gaps in the traceability of biologics in the EU → pilot in the Netherlands:
 - Identify the underlying reason for missing brand name and batch number information spontaneous ADR reports.
 - Estimate the potential impact of misclassification of (similar) biological products on safety signals detection (modeling experiment) [<http://escher.lygature.org>]

Executed in collaboration with Utrecht University, NVZA, KNMP, Exon Consultancy and with support from the Netherlands Pharmacovigilance Centre Lareb. Part of the activities were funded by EBE through an unrestricted grant.



Approach

Evaluation of the information recording systems and practices in different healthcare settings:

1. Hospital setting evaluation:

- Mapping the processes in the hospital setting
- Quantitative analysis: Hospital pharmacy survey

2. Community setting evaluation:

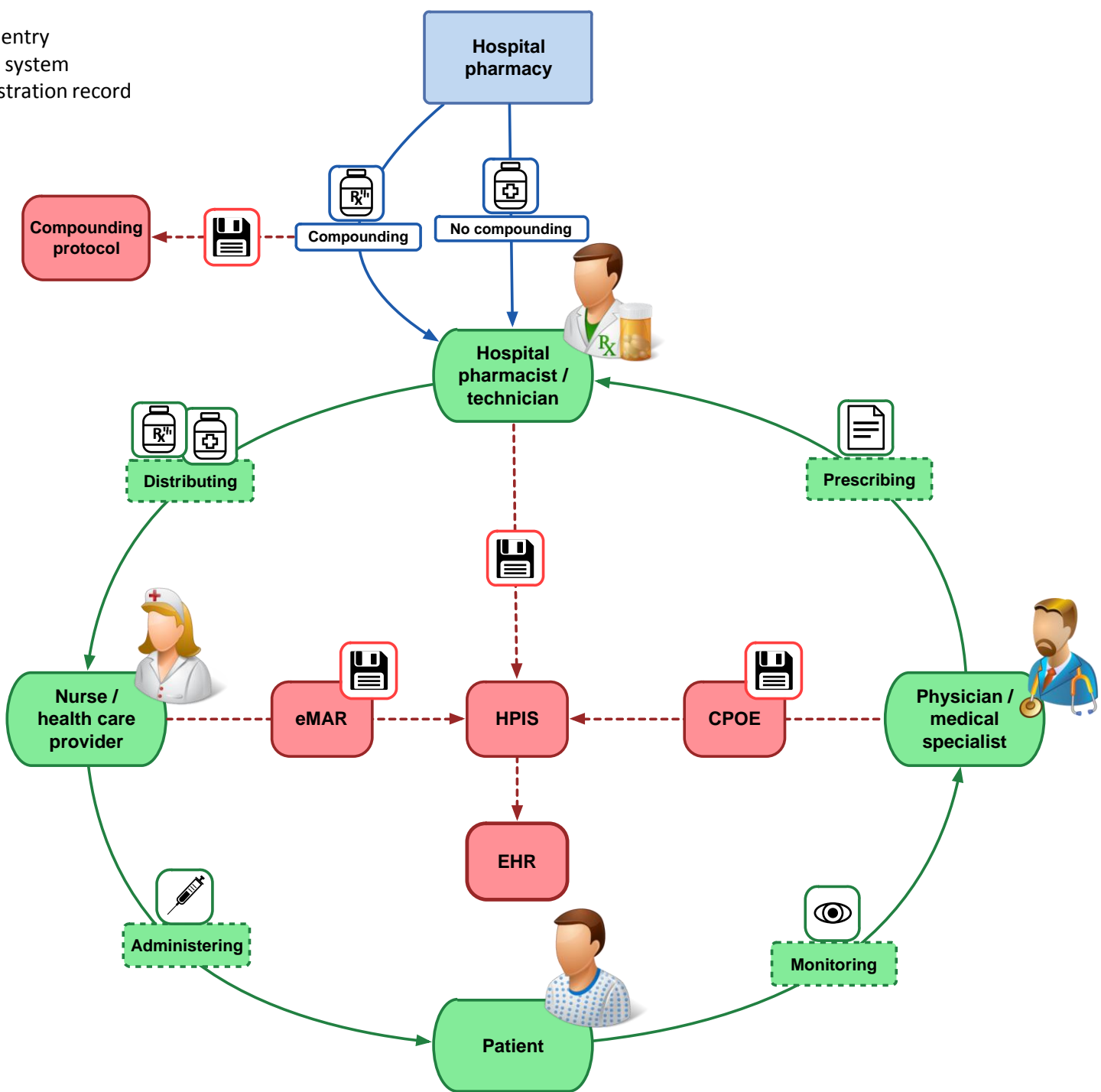
- Assessment of the information recording systems and practices in the community pharmacy with a quantitative analysis: Community pharmacy survey

3. Adverse drug reaction data analysis in the Netherlands (Lareb):

- Analysis of the ADR reporting quality for biologics in the Netherlands

CPOE: computerized physician order entry
HPIS: Hospital pharmacy information system
eMAR: electronic medication administration record
EHR: electronic health record

- “Ideal situation” in which all IT systems *communicate*
- Various different IT suppliers may prevent information sharing within one hospital



Brand name and batch number recording in different information-recording systems in the Dutch hospital setting

Information-recording system	# of respondents indicating system in place in hospital [n] ¹	% Brand name recording [n (%)] ²	% Batch number recording [n (%)] ²
Hospital pharmacy information system (HPIS)	34	27 (79%)	0 (0%)
Electronic medication administration record (eMAR)	25	15 (60%)	0 (0%)
Electronic health record (EHR)	34	22 (65%)	0 (0%)
Additional			
Compounding protocol	34	23 (68%)	34 (100%)

¹ Total number of responses: 34 out of 93 hospitals.

² Recording on a routinely basis.

Approach

Evaluation of the information recording systems and practices in different healthcare settings:

1. Hospital setting evaluation:

- Mapping the processes in the hospital setting
- Quantitative analysis: Hospital pharmacy survey

2. **Community setting evaluation:**

- **Assessment of the information recording systems and practices in the community pharmacy with a quantitative analysis: Community pharmacy survey**

3. Adverse drug reaction data analysis in the Netherlands (Lareb):

- Analysis of the ADR reporting quality for biologics in the Netherlands

Survey among community pharmacists

- Survey among 56 selected community pharmacies to assess brand name and batch nr. recording in the community setting:
 - Pharmacy information system:
 - 91% indicated brand name recording
 - 4% indicated batch number recording
 - Compounding protocol
 - Only two respondents indicated that biologics are compounded in the community pharmacy
 - Compounding plays a minor role in the community setting for biologics (and therefore the opportunity to record/retrieve batch numbers in the compounding protocol...

Approach

Evaluation of the information recording systems and practices in different healthcare settings:

1. Hospital setting evaluation:

- Mapping the processes in the hospital setting
- Quantitative analysis: Hospital pharmacy survey

2. Community setting evaluation:

- Assessment of the information recording systems and practices in the community pharmacy with a quantitative analysis: Community pharmacy survey

3. **Adverse drug reaction data analysis in the Netherlands (Lareb):**

- **Analysis of the ADR reporting quality for biologics in the Netherlands**

Overall ADR reporting analysis

- Lareb received 12,413 ADR reports between 2009 and 2014 for the selection of recombinant biologics:
 - 90% contained a brand name
 - 15% contained a batch number

Overall ADR reporting analysis

- Lareb received 12,413 ADR reports between 2009 and 2014 for the selection of recombinant biologics:
 - 90% contained a brand name
 - 15% contained a batch number
- **1,523 (12%) ADRs reported directly to Lareb:**
 - 76% contained a brand name
 - 5% contained a batch number*
- **10,890 (88%) ADRs reported to the MAH:**
 - 92% contained a brand name
 - 16% contained a batch number**

* 74 ADR reports
** 1,741 ADR reports



Reporter type analysis for ADRs: differences between reporter types for brand name and batch nr. reporting

Reporter type	# Of ADRs reported [n (%)]		% Brand names reported [n (%)]		% Batch numbers reported [n (%)]	
Hospital: Physician/nurse	866	(57%)	587	(68%)	13	(2%)
Hospital: Pharmacist	78	(5%)	54	(69%)	28	(36%)
Community: GP	78	(5%)	67	(86%)	2	(3%)
Community: Pharmacist	239	(16%)	229	(96%)	17	(7%)
Patient	223	(15%)	193	(87%)	11	(5%)
Unclassified	39	(2%)	22	(56%)	3	(8%)
Total	1523	(100%)	1152	(76%)	74	(5%)

Brand name:

- High brand name reporting for community pharmacists
- Low brand name reporting for hospital physicians/specialists/pharmacists

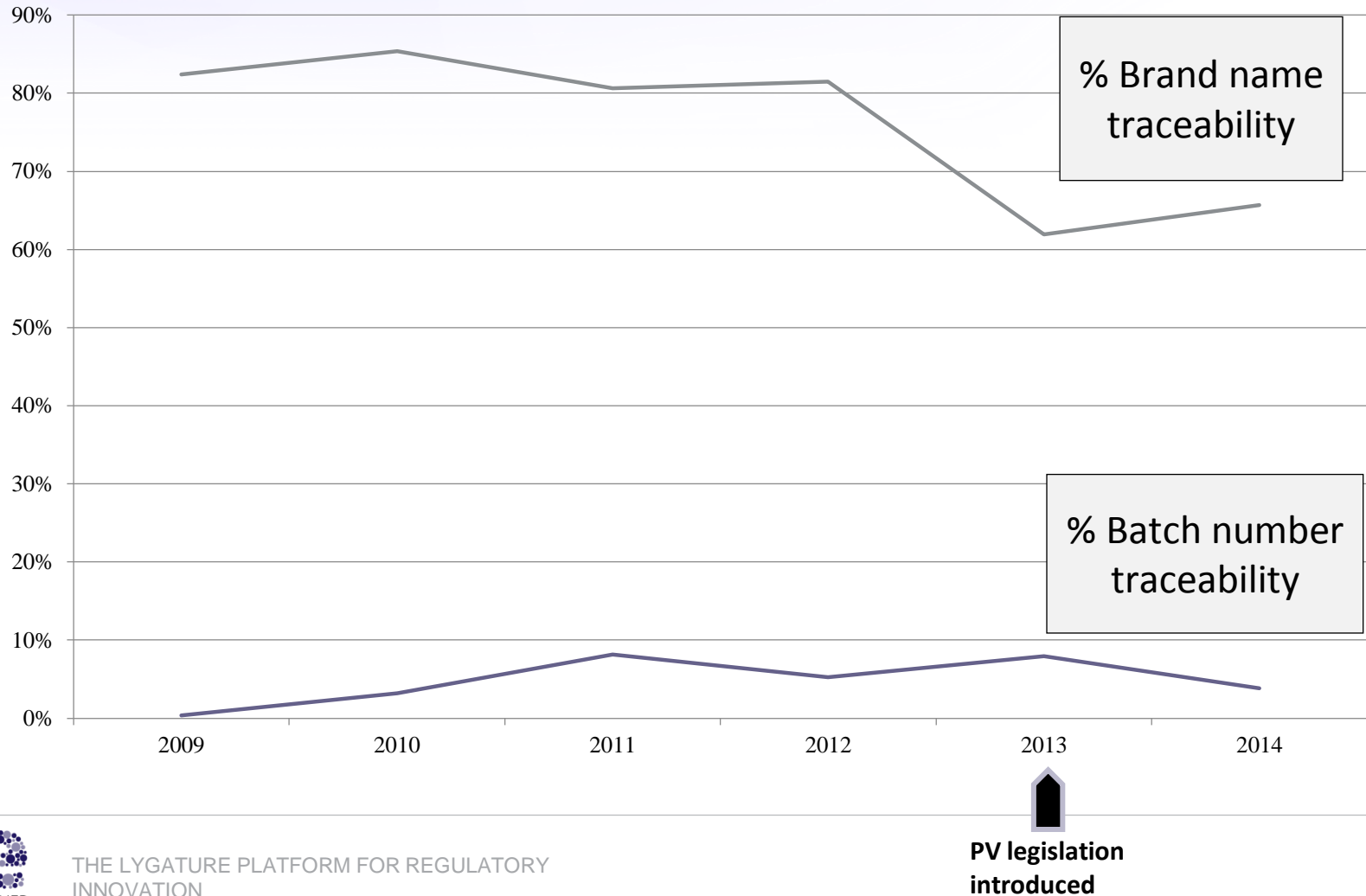
Batch number

- High batch number reporting for hospital pharmacists

Product class analysis for ADRs: differences between product classes for brand name and batch nr. reporting

Product class	# ADR	% Brand names reported		% Batch numbers reported	
Somatropins	4	3	(75%)	0	(0%)
Epoetins	43	40	(93%)	0	(0%)
Filgrastims	19	17	(89%)	1	(5%)
Follitropins	21	21	(100%)	1	(5%)
Monoclonal ABs	797	536	(67%)	45	(6%)
Insulins	180	164	(91%)	18	(10%)
Interferons	51	45	(88%)	3	(6%)
Antihaemoph. factors	52	52	(100%)	1	(2%)
Fusion proteins	232	178	(77%)	5	(2%)
Enzymes	2	1	(50%)	0	(0%)
Other	122	95	(78%)	0	(0%)
Total	1523	1152	(76%)	74	(5%)

No visible increase over time for brand name or batch number reporting was observed



Other survey findings:

- Information recording system often do not allow batch number recording
- Healthcare systems are “waiting” for digital batch number information (2D barcodes) provided on the primary package
- Awareness still needs improvement:
 - 18% of the respondents unaware of requirement to include brand name in ADR reports
 - 41% of the respondents unaware of requirement to include batch number

Summary of findings

- The availability of the brand name and batch number for products in clinical practice corresponds with the (lack of) inclusion of this information in ADR reports (in particular the batch number)
- To align practice with the ambition of the EU pharmacovigilance legislation regarding traceability, brand name and batch number recording needs to be (further) improved
- Additional case studies in different Member States could help to map EU differences, commonalities and potential success factors for activities/interventions to improve traceability.