Traceability of biopharmaceuticals in spontaneous reporting systems

Credits to

Niels Vermeer (UU/MEB)

Marieke De Bruin (UU/MEB)
Sabine Straus (MEB/ ErasmusmMC)
Aukje Mantel-Teeuwisse (UU)
Toine Egberts (UU)
Bert Leufkens (MEB/UU)
Eugene van Puijenbroek(Lareb)
Francois Domergue (EMA)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Outline of the presentation

- Introduction
- Challenges
- Facts
- Possible solutions
- Conclusions

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Table 1 Top-selling blockbuster biologics in 2007

Biologic	US sales (billions)	Rank[a]
Aranesp (darbepoetin alfa)	$3.2	5
Neulasta (PEG-filgrastim)	$3.1	6
Epogen	$3.1	6
Remicade (infliximab)	$2.8	9
Eprex	$2.4	12
Rituxan (rituximab)	$2.3	14
Avastin	$2.3	14
Lantus (insulin glargine, rDNA origin)	$1.7	23
Avonex (interferon β-1a)	$1.2	33
Humalog (insulin lispro)	$1.0	44

[a]Based on US sales of all drugs (small molecules and biologics); Lipitor is ranked number 1 at $6.2 billion. Source: Ranking, Verispan, VONA; revenues, company literature.

Traceability of medicinal products:

identification during the whole lifecycle of a drug, from manufacturing to patient's bedside (forward/ backward, track/trace)

Traceability also pivotal in other industries

Is it justified to let medicines fly without a black box?

Citation: Leufkens HG. Is it justified to let medicines fly without a black box? Southern Med Review (2010) 3; 2:3-3

smh.com.au
The Sydney Morning Herald

Surgeons fail to track PIP implants

Cosima Marriner

PLASTIC surgeons have been accused of failing women with faulty breast implants, defying a federal government directive to contact patients for a check-up after the PIP scare.

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

MARCH 8, 2012

Here We Go Again — Another Failure of Postmarketing Device Surveillance

Robert G. Hauser, M.D.

BMJ

Additional 7000 UK women may have faul implants

Adrian O'Dowd

The New York Times

Europe

Deadly E. Coli Outbreak Linked to German Sprouts

By JUDY DEMPSEY and WILLIAM NEUMAN
Published: June 5, 2011

What tools are available to assess benefit risk balance post approval

A GUIDE TO DRUG DISCOVERY — OPINION

New approaches to drug safety: a pharmacovigilance tool kit

Lesley Wise, John Parkinson, June Raine and Alasdair Breckenridge

Abstract | The importance of pharmacovigilance — the ongoing assessment of the safety of a marketed medicine — has been increasingly appreciated in recent years, owing in part to high-profile safety issues with widely used drugs. In response, strategies to improve the collection, integration and analysis of data related to post-marketing drug safety are being initiated or enhanced. In this article, we summarize the key tools that are available for pharmacovigilance, discuss which might be the most appropriate to use in different situations and consider the future directions of the field.

- Virtually all countries have some kind of a system of collecting voluntary reports of (possible) ADRs from physicians, pharmacists, industry, patients.
- Voluntary reports can be (random) 'noise' or real signals of a clinically relevant drug-induced problem.
- Determining the signal-noise ratio is key to pharmacovigilance
- Despite the well-acknowledged problems with voluntary reports (underreporting, selective reporting, reporting out of context, etc) they remain the mainstay of pharmacovigilance

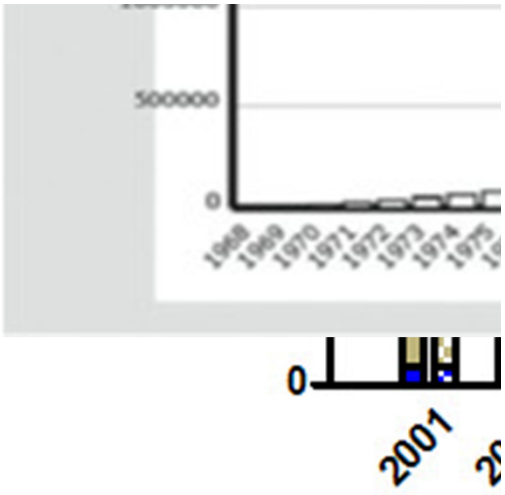
Historically, spontaneous reports have been the corner stone of postmarketing surveillance.

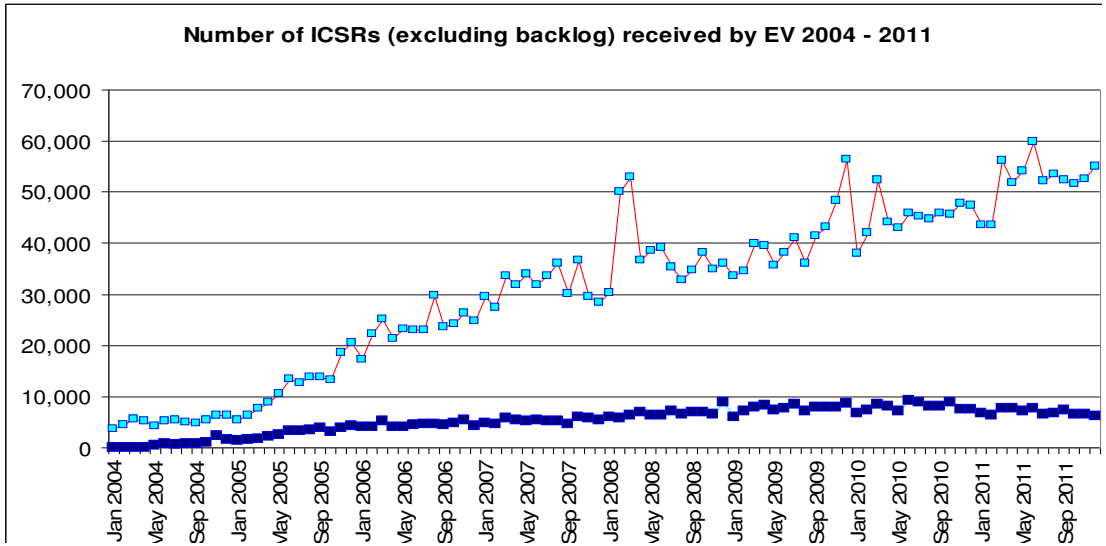
Table III. Presence or absence of evidence (study designs and assessed outcomes) used to support individual product withdrawals from the UK and/or US during 1999–2001

Study design	Outcome type	DRO	CIS	LEV	PHE	PUM	ALO	CER	RAP	GRE	AST	TRO
Animal studies	Surrogate	✓	✓	✓	×	×	×	×	×	×	×	×
Spontaneous reports	Patient relevant	✓	✓	✓	✓	×	✓	✓	✓	✓	×	×
Published case reports		×	×	×	×	×	×	×	×	×	×	×
Published case series		×	×	×	×	×	×	×	×	×	×	×
Cross-sectional study	Surrogate	✓	×	×	×	×	×	×	×	×	×	×
Case-control study	Patient relevant	×	×	×	✓	×	×	×	×	×	×	×
Cohort study		×	×	×	×	×	×	×	×	×	×	×
Non-randomised study	Surrogate	×	✓	✓	×	×	×	×	×	×	×	×
Randomised clinical trials	Surrogate	✓	×	×	×	×	×	×	×	×	×	×
Randomised clinical trials	Patient relevant	×	×	×	×	✓	×	×	×	×	×	×
Other[a]		×	×	×	×	×	✓	×	✓	×	×	×

- EudraVigilance System
  - An average of 72.250 ICSRs are reported on a monthly basis to EudraVigilance
  - Total number of ICSRs now amounts to almost 5 million ICSRs
  - EudraVigilance now ranks within the 3 largest databases on adverse drug reactions in the world

EudraVigilance Reports over time (total)





Spontaneous reporting databases - strengths

- Strengths
  - Inexpensive and simple to operate
  - Large scale
    - Cover all drugs during their whole life cycle
    - Cover the whole patient population, including special subgroups
  - Clinical evaluation of reporting healthcare professional
  - Does not interfere with prescribing habits
  - Can be used for follow-up studies of patients with severe ADRs, to study mechanisms
  - Generation of hypotheses and signals

Brian L. Strom and Stephen E. Kimmel.
Textbook of Pharmacoepidemiology. 2006. Chapters 7 & 8.

Outline of the presentation

- Introduction
- Challenges
- Facts
- Possible solutions
- Conclusions

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Specific challenges in risk management of biologicals

- ✓ Limited predictability pre-clinical.
- ✓ Often used in patients with severe and complex morbidities.
- ✓ Nature of safety issues (often severe e.g. PML, other immune/infection responses, malignancies).
- ✓ Indication dynamics.
- ✓ Difficulties in getting good exposure data.
- ✓ Impact of production/manufacturing
- ✓ Traceability (particularly in the context of immunogenicity, product switching).

Potential risks with biologicals

- Infections

- Dear Healthca

  Centocor, Inc.
  REMICADE®
  arthritis and C

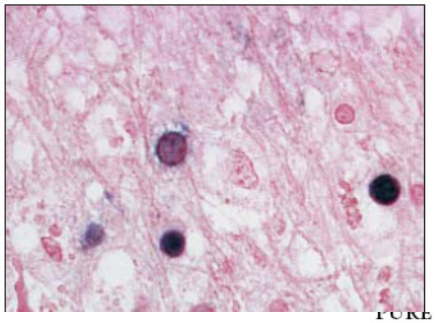
- ## Rare Neurological Condition Linked to Newer Monoclonal Antibody Biologics

  Bridget M. Kuehn

  REPORTS OF A RARE AND DEADLY neurological condition called progressive multifocal leukoencephalopathy (PML) in patients taking certain biologic immunosuppressants for autoimmune or inflammatory conditions are raising concerns about the safety of these drugs.

  In February, the US Food and Drug Administration (FDA) issued a public health advisory alerting physicians and patients to 1 possible and 3 confirmed cases of PML in patients taking efalizumab, a once-weekly injection approved for the treatment of severe plaque psoriasis in adults. The label of this drug ics, which target specific components of the immune system, is forcing physicians and patients to reassess these therapies' risks and benefits.

  PML, a rapidly degenerative neurological condition, is most commonly seen in patients with AIDS; in rare cases,

  rector of infectious disease at Washington Hospital Center and a member of an FDA panel that assessed in 2007 whether to allow the marketing of natalizumab for Crohn disease. Smith explained that even among patients with AIDS, the condition is typically seen only in those who have CD4 T-cell counts below 100/µL.

  Clinical trials of natalizumab identified 2 cases of PML among 1869 patients treated with the drug for multiple sclerosis and 1 case in a trial involving 1043 patients with Crohn disease. Such data suggest the incidence of PML among patients treated with this product may be as high as 1 in 1000. "That's a pretty high risk," she said.

  NUMBER 7

  PURE RED-CELL APLASIA AND ANTIERYTHROPOIETIN ANTIBODIES IN PATIENTS TREATED WITH RECOMBINANT ERYTHROPOIETIN

  NICOLE CASADEVALL, M.D., JOELLE NATAF, M.D., BÉATRICE VIRON, M.D., AMIR KOLTA, M.D., JEAN-JACQUES KILADJIAN, M.D., PHILIPPE MARTIN-DUPONT, M.D., PATRICK MICHAUD, M.D., THOMAS PAPO, M.D., VALÉRIE UGO, M.D., IRÈNE TEYSSANDIER, B.S., BRUNO VARET, M.D., AND PATRICK MAYEUX, PH.D.

- Malignancies

Safety-Related Regulatory Actions for Biologicals Approved in the United States and the European Union

Thijs J. Giezen, PharmD
Aukje K. Mantel-Teeuwisse, PhD
Sabine M. J. M. Straus, MD, PhD
Huub Schellekens, PhD
Hubert G. M. Leufkens, PhD
Antoine C. G. Egberts, PhD

Context Biologicals are a relatively new class of medicines that carry specific risks (eg, immunogenicity). However, limited information is available on the nature and timing of safety problems with their use that were identified after approval.

Objective To determine the nature, frequency, and timing of safety-related regulatory actions for biologicals following approval in the United States and/or the European Union.

Design and Setting Follow-up of a group of biologicals approved in the United States and/or European Union between January 1995 and June 2007. Vaccines, allergenic products, and products for further manufacture and transfusion purposes were excluded.

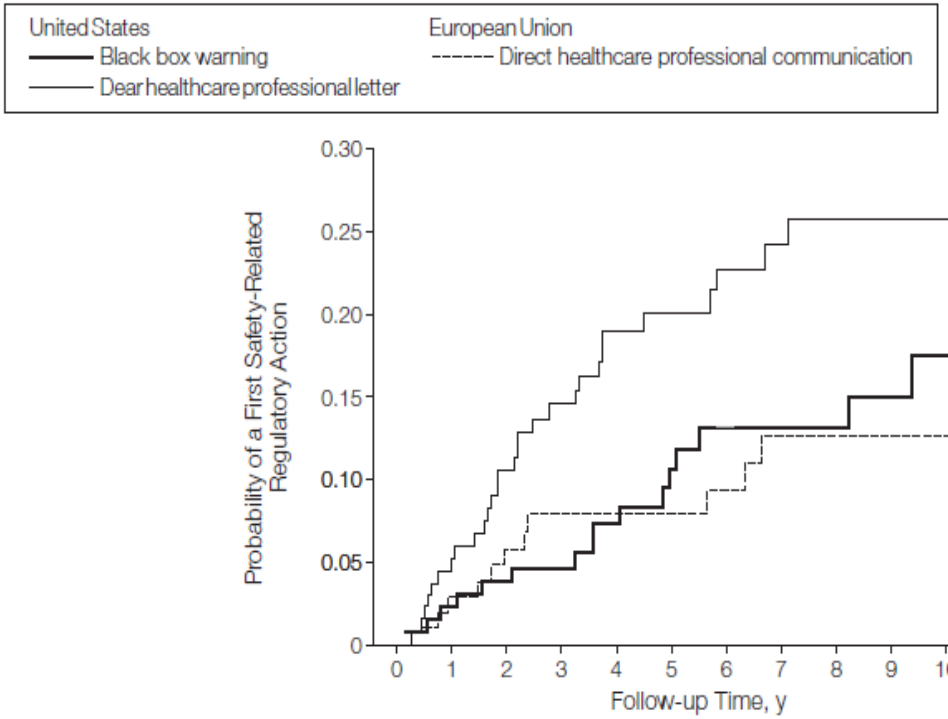
Main Outcome Measures Nature, frequency, and timing of safety-related regulatory actions defined as (1) dear healthcare professional letters (United States) and direct healthcare professional communications (European Union), (2) black box warnings (United States), and (3) safety-related marketing withdrawals (United States and European Union) issued between January 1995 and June 2008.

Results A total of 174 biologicals were approved (136 in the United States and 105 in the European Union, of which 67 were approved in both regions). Eighty-two safety-related regulatory actions (46 dear healthcare professional letters, 17 direct healthcare professional communications, 19 black box warnings, and no withdrawals) were

BIOLOGICALS, DEFINED AS PRODucts of which the active substance is produced by or extracted from a biological source, represent an important and growing part of the therapeutic arsenal.[1] In the United States, the first biological, recombinant insulin, was approved in October 1982.[2] Since then, more than 250 biologicals, including recombinant (blood) products, mono-

COLLEGE TER BEOORDELING VAN GENEESMIDDELEN
CBG MEB
MEDICINES EVALUATION BOARD

Figure. Safety-Related Regulatory Actions for Biologicals



No. of biologicals at risk												
United States												
Dear healthcare professional letter	136	129	115	99	86	70	57	50	42	33	26	16
Black box warning	135	133	124	109	97	76	64	56	50	41	31	19
European Union												
Direct healthcare professional communication	105	102	93	82	78	69	56	47	34	24	13	8

Between January 1995 and June 2008 82 safety-related regulatory actions issued for 41 of 174 biologicals (23.6%)

- 46 dear healthcare professional letters in the United States for 30 different biologicals
- 17 direct healthcare professional communications in the European Union for 11 different biologicals
- 19 black box warnings in the United States for 17 different biologicals
- No marketing withdrawals related to safety

Nature of safety information mostly concerned SOC

- General disorders and administration site conditions
- Infections and infestations
- Immune system disorders
- Neoplasms benign, malignant, and unspecified

ORIGINAL RESEARCH ARTICLE
Drug Saf 2012; 35 (5): 417-427
0114-5916/12/0005-0417/$49.95/0

A Cohort Study Exploring Determinants of Safety-Related Regulatory Actions for Biopharmaceuticals

Hans C. Ebbers,[1] Aukje K. Mantel-Teeuwisse,[1] Ellen H.M. Moors,[2] Fakhredin A. Sayed Tabatabaei,[3] Huub Schellekens[2,4] and Hubert G.M. Leufkens[1,3]

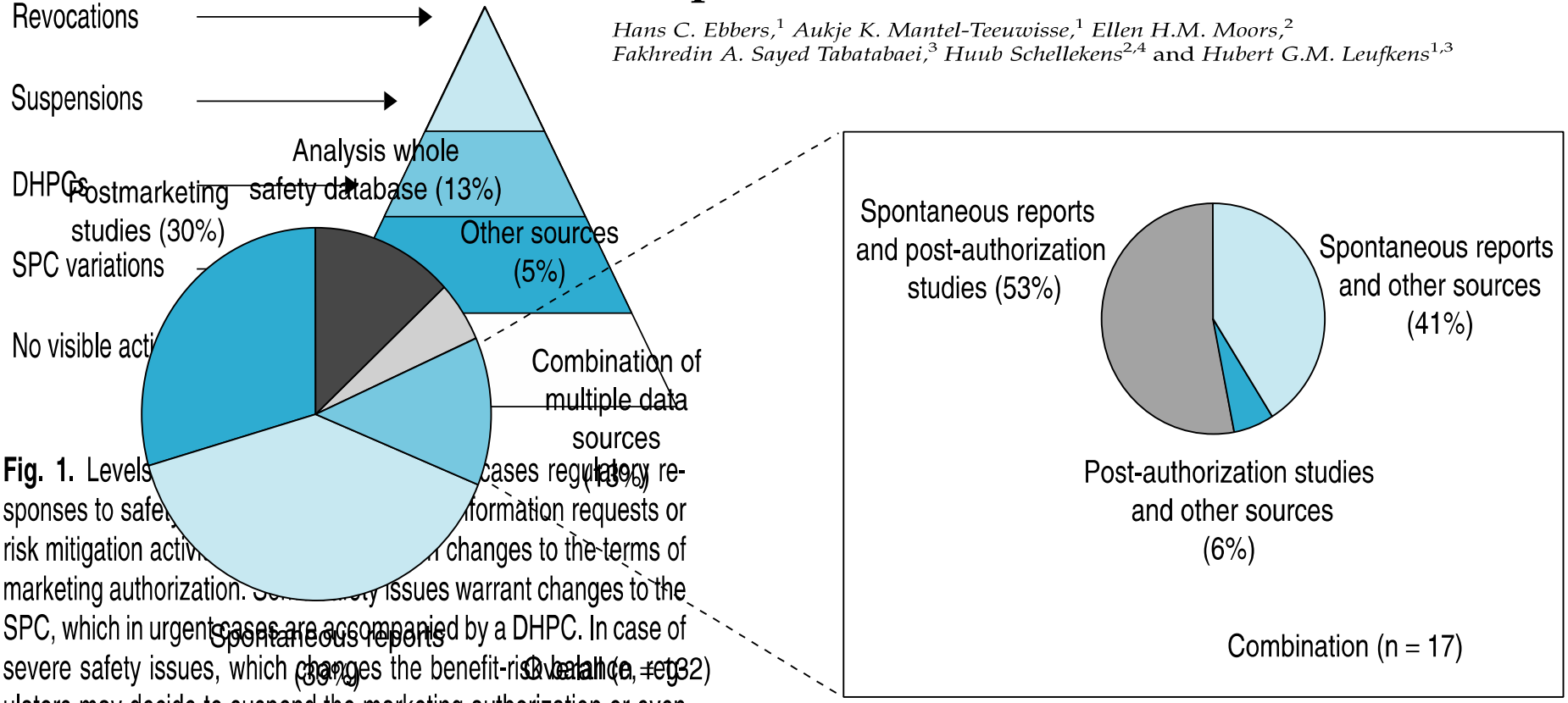


Fig. 1. Levels ... cases regulatory responses to safe... information requests or risk mitigation activi... changes to the terms of marketing authorization. S... issues warrant changes to the SPC, which in urgent cases are accompanied by a DHPC. In case of severe safety issues, which changes the benefit-risk balance, regulators may decide to suspend the marketing authorization or even revoke it. **DHPC** = Direct Healthcare Professional Communication; **SPC** = Summary of Product Characteristics.

Fig. 3. Information source for type II variations included in the study, including the distribution of information sources for variations based on a combination of sources.

A need for rigorous pharmacovigilance programs to monitor all biopharmaceuticals (including innovator products and biosimilars) for safety and efficacy issues during the post-approval period.

Melstedt et al. Annals of Oncology **19**, 411-419 (2008)

This is why clinical experience, through clinical trials and extensive pharmacovigilance programs, remains the most reliable way to assess the immunogenicity and tolerance profile of recombinant therapeutic proteins.

Pavlovic et al. Hormone Research **69**, 14-21 (2008)

Clinical trials and post-authorization pharmacovigilance are essential
to guarantee the product's safety and efficacy over time.
Pharmacovigilance, as part of a comprehensive risk management programme,
will need to include regular testing for consistent manufacturing of the drug.

Locatelli & Roger Nephrology Dialysis Transplantation **21**, v13-16 (2006)

REVIEW ARTICLE

Drug Saf 2011; 34 (4): 273-287
0114-5916/11/0004-0273/$49.95/0

Today's Challenges in Pharmacovigilance

What can we Learn from Epoetins?

metabolites)

- Immunogenicity (large foreign molecules)
  - Clinical consequenc
    threatening advers

- Changes in manufacturing p
  hence clinical efficacy/ safet

  Clinical trial setting:
  - PEGylation thrombopoie
    thrombocytopenia
  - Increased purification g
  - Tungsten in particular b
    red cell aplasia

  Post marketing setting:
  - Eprex®

The New England
Journal of Medicine

VOLUME 346 FEBRUARY 14, 2002 NUMBER 7

PURE RED-CELL APLASIA AND ANTIERYTHROPOIETIN ANTIBODIES
IN PATIENTS TREATED WITH RECOMBINANT ERYTHROPOIETIN

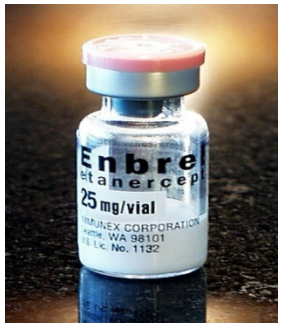
Outline of the presentation

- Introduction
- Challenges
- Facts
- Possible solutions
- Conclusions

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Background
(Regulatory) challenges

- **Biopharmaceuticals subject to manufacturing changes**
  - Might affect in particular immunogenicity→ extensive guidance by EMA/ FDA for demonstrating comparability
  - Some changes in ADR profile might go unnoticed → monitoring benefit risk profile over time
  - Necessary to record detailed exposure information (including batch number)
  - Different formulations:



- **Authorisation of biosimilars**
  - impact on quality attributes: independent development by other manufacturer of generic biopharmaceuticals

<u>→ Usefulness of pharmacovigilance databases depends on the ability to distinguish products and batches within the data</u>

Study to explore the current status of traceability of biopharmaceuticals in the US and the EU in spontaneous reporting systems

period 2004 – 2010,
individual case safety reports (ICSRs) from:

- FDA: **Adverse Event Reporting System** (AERS)
  - Consumers/ health care professionals (voluntary)
  - Manufacturers (mandatory)

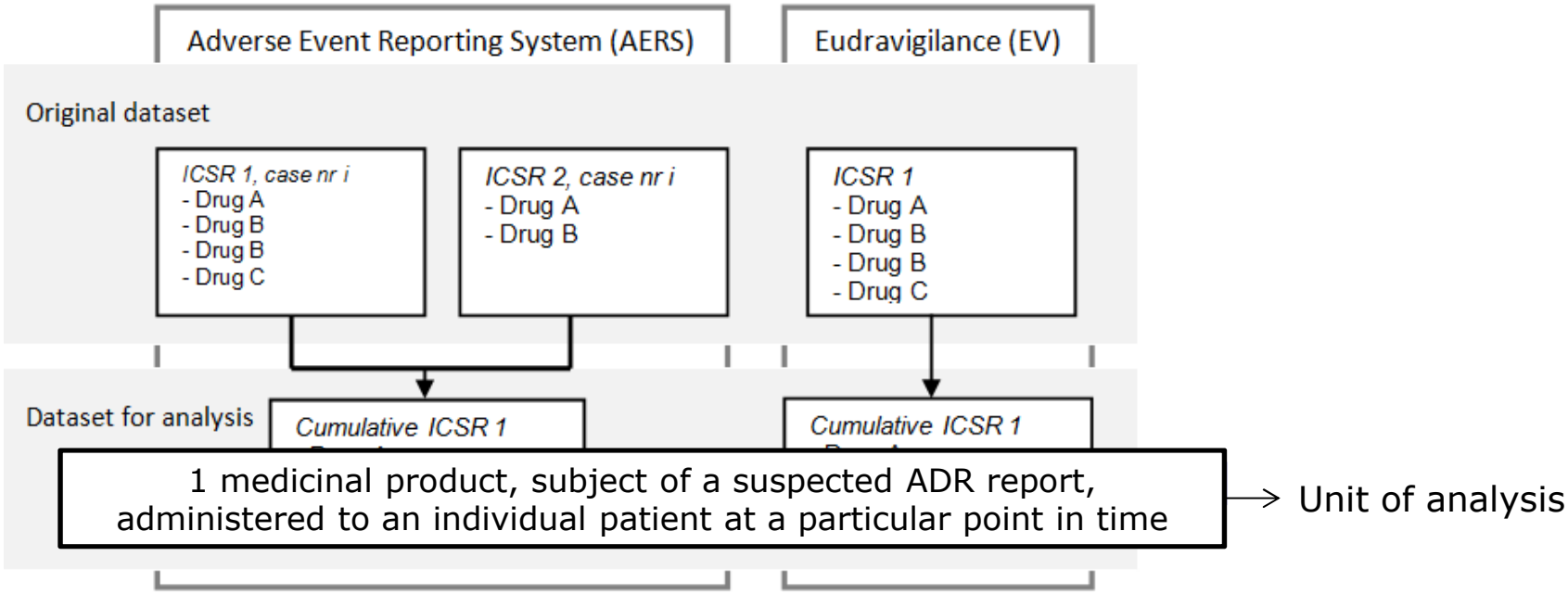
  According to 21CF314.80/21CFR600.80

- EMA: **Eudravigilance** (EV)
  - Consumers/ healthcare professionals
  - National competent authorities (mandatory)
  - Manufacturers (mandatory)

    According to EC 726/2004

- Data extracted from ICSRs:medicinal product, batch number, marketing authorization holder, type of reporter, role code of drug, year of reporting

- Handling of duplicate and follow-up reporting:



Classification of medicinal products and traceability

- **Classification of medicinal products** into (1) biopharmaceuticals and (2) small molecule drugs, on basis of ATC class
  - Role codes into: suspected or non-suspected
  - Exclusion of vaccines (ATC class J07), whole blood or components of whole blood (ATC class B05A), and non-classifiable products

- Verbatim data in **batch number** field → dichotomous variable
  - Aggregating and reviewing data to confirm availability

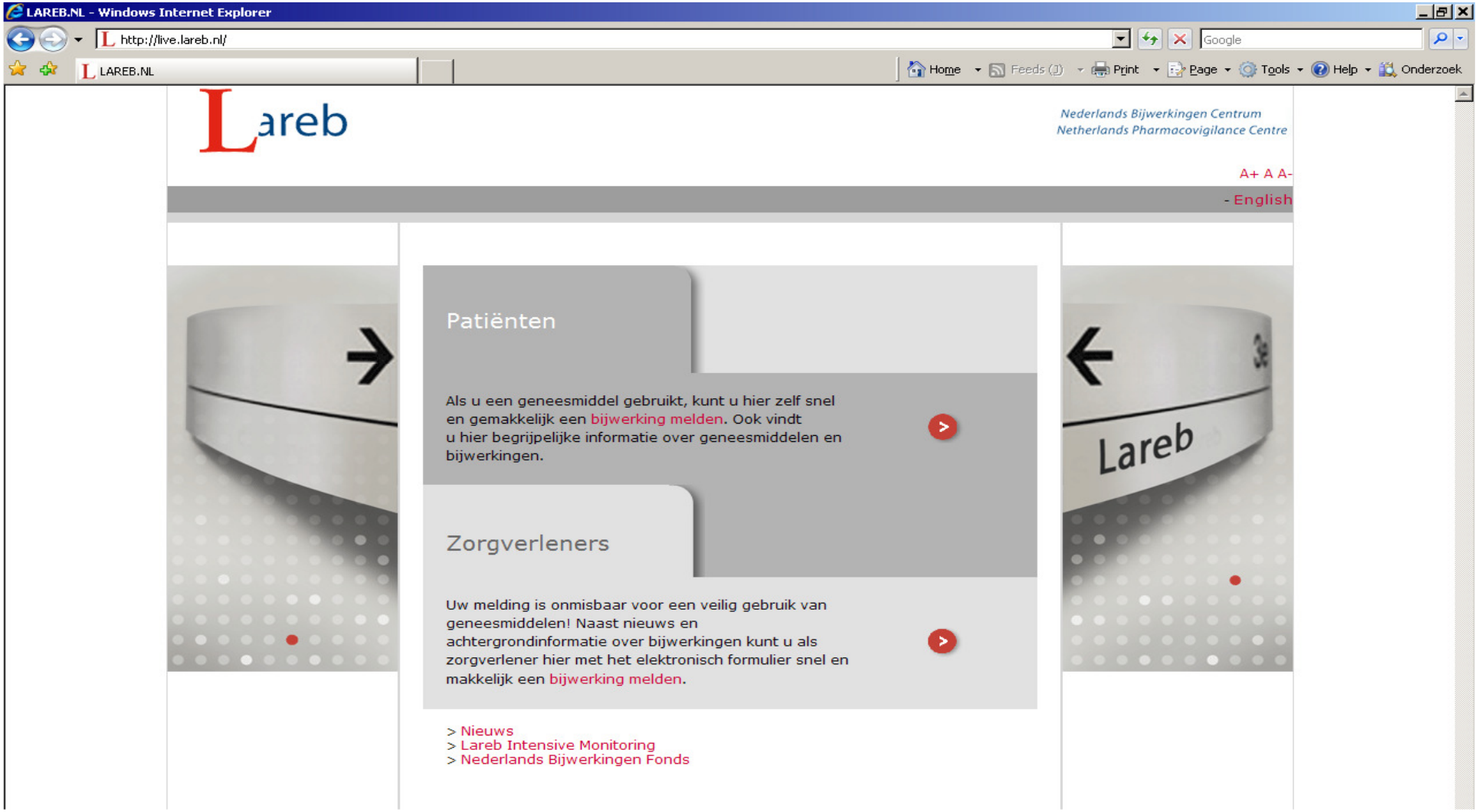
- For biopharmaceuticals for which a biosimilar has been approved for marketing in the EU : **product (traceability) identifiability**
  - Seven biosimilars approved over 3 product classes: epoetin, filgrastim and somatropin
  - Identifiable :
    - Product brand name and/or
    - International non-proprietary name (INN) **+** marketing authorization holder

    (exception: epoetin zeta)

Outline of the presentation

- Introduction
- Challenges
- Facts
- Possible solutions
- Conclusions

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH


LAREB.NL - Windows Internet Explorer
http://live.lareb.nl/
LAREB.NL
Home
Feeds (J)
Print
Page
Tools
Help
Onderzoek
Lareb
Nederlands Bijwerkingen Centrum
Netherlands Pharmacovigilance Centre
A+ A A-
- English
Patiënten
Als u een geneesmiddel gebruikt, kunt u hier zelf snel en gemakkelijk een bijwerking melden. Ook vindt u hier begrijpelijke informatie over geneesmiddelen en bijwerkingen.
Zorgverleners
Uw melding is onmisbaar voor een veilig gebruik van geneesmiddelen! Naast nieuws en achtergrondinformatie over bijwerkingen kunt u als zorgverlener hier met het elektronisch formulier snel en makkelijk een bijwerking melden.
> Nieuws
> Lareb Intensive Monitoring
> Nederlands Bijwerkingen Fonds
Lareb

Lareb

Nederlands Bijwerkingen Centrum
Netherlands Pharmacovigilance Centre

MELDFORMULIER ZORGVERLENERS

Tel (073) 646 9700 fax (073) 6426136 info@lareb.nl

NB: DIT IS HET MELDFORMULIER VOOR ZORGVERLENERS.

Bent u zelf de gebruiker van het geneesmiddel, vul dan het meldformulier voor patienten in.

Wilt u uw melding liever op papier invullen, download dan het meldformulier in PDF formaat

INLEIDING

Zorgverleners kunnen een mogelijke bijwerking van een geneesmiddel melden via het onderstaand formulier.
Wij realiseren ons dat het tijd kost om dit meldformulier volledig in te vullen. Maar meldingen van bijwerkingen zijn onmisbaar voor een veilig gebruik van geneesmiddelen. Alleen met voldoende
informatie over alle omstandigheden die van invloed zijn geweest op de klachten, kunnen wij uw melding goed beoordelen.

Met de help-knop (i) kunt u meer informatie over de vraag bekijken. Commentaar, achtergronden, medicatiehistorie of andere documenten kunt u aan het eind van dit formulier kwijt.
Indien u wilt, kunt u meer over het melden lezen op de Informatiepagina Melden Zorgerverleners.

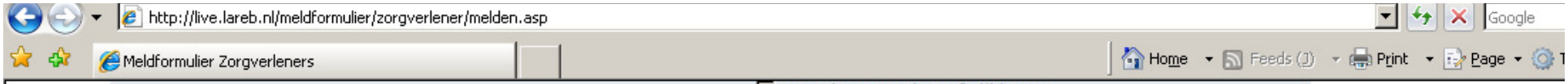
Noodzakelijke velden zijn gemarkeerd met een sterretje (*).

Melddatum: 10-3-2008

A BIJWERKINGEN

Bijwerking [1]

Vermoedelijke bijwerking*	(i)	
Begindatum bijwerking* *(dag en maand zijn niet verplicht, maar graag zo precies mogelijk invullen)*	(i)	-- dag -- -- maand -- -- jaar --
Hoe lang gebruikte uw patient het geneesmiddel voordat de klachten optraden?	(i)	selecteer eenheid
Afloop*	(i)	selecteer afloop...
Waren er nog andere bijwerkingen?		Andere bijwerking +



Overige ernstige afwijkingen

B GENEESMIDDEL

Geneesmiddel [1]

Verdacht geneesmiddel*	INFLU
	HAEMOPHILUS-**INFLU**ENZAE-B-VACC ...
	INFLUENZAVACCIN
RVG code	**INFLU**VAC
Mogelijke interactie	
Startdatum* *(dag en maand zijn niet verplicht, maar graag zo precies mogelijk invullen)*	
Dosering	
Toedieningsweg	selecteer...
Indicatie	
Aanpassing gebruik na optreden bijwerking	selecteer...
Gebruikt andere geneesmiddelen die volgens u ook verdacht zijn?	Ander verdacht geneesmiddel +

Geneesmiddelen die niet verdacht zijn of waarvan u niet weet of ze een rol hebben gespeeld bij de klachten (comedicatie) kunt u hieronder invullen

Comedicatie

Gebruikt uw patiënt daarnaast nog andere - niet verdachte - geneesmiddelen?*

- (•) Nee
- ( ) Onbekend
- ( ) Ja

Heeft de bijwerking geleid tot een van de hieronder genoemde situaties?*

- ○ Nee
- ○ Ja, namelijk:
  - ☐ Overlijden
  - ☐ Levensbedreigend
  - ☐ Ziekenhuisopname
  - ☐ Blijvende arbeidsongeschiktheid
  - ☐ Afwijkingen bij pasgeboren kind
  - ☐ Overige ernstige afwijkingen

B GENEESMIDDEL

Geneesmiddel [1]

Verdacht geneesmiddel*: INFLUVAC

INFLUVAC INJSUSP 2007/2008 WWSP 0,5ML

RVG code

Mogelijke interactie

Startdatum*
(dag en maand zijn niet verplicht, maar graag zo precies mogelijk invullen)

Dosering

Toedieningsweg: selecteer...

Indicatie

Aanpassing gebruik na optreden bijwerking: selecteer...

Gebruikt andere geneesmiddelen die volgens u ook verdacht zijn? Ander verdacht geneesmiddel +

Geneesmiddelen die niet verdacht zijn of waarvan u niet weet of ze een rol hebben gespeeld bij de klachten (comedicatie) kunt u hieronder invullen

Weet niet
Anders, nl.
INFLUVAC INJSUSP 2001/2002 WWSP 0,5ML - Non-Current drug
INFLUVAC INJSUSP 2002/2003 WWSP 0,5ML - Non-Current drug
INFLUVAC INJSUSP 2003/2004 WWSP 0,5ML - Non-Current drug
INFLUVAC INJSUSP 2004/2005 WWSP 0,5ML - Non-Current drug
INFLUVAC INJSUSP 2005/2006 WWSP 0,5ML - Non-Current drug
INFLUVAC INJSUSP 2006/2007 WWSP 0,5ML - Non-Current drug
INFLUVAC INJSUSP 2007/2008 WWSP 0,5ML

Comedicatie

Gebruikt uw patiënt daarnaast nog andere - niet verdachte - geneesmiddelen?*

- ◉ Nee
- ○ Onbekend
- ○ Ja

Heeft de bijwerking geleid tot een van de hieronder genoemde situaties?*

- ○ Nee
- ○ Ja, namelijk:
  - ☐ Overlijden
  - ☐ Levensbedreigend
  - ☐ Ziekenhuisopname
  - ☐ Blijvende arbeidsongeschiktheid
  - ☐ Afwijkingen bij pasgeboren kind
  - ☐ Overige ernstige afwijkingen

B GENEESMIDDEL

Geneesmiddel [1]

Verdacht geneesmiddel*: INFLUVAC

INFLUVAC INJSUSP 2007/2008 WWSP 0,5ML

RVG code:

Mogelijke interactie

Weet niet
Anders, nl.

Startdatum*
(dag en maand zijn niet verplicht, maar graag zo precies mogelijk invullen)
022289 maand -- -- jaar --

Dosering:

Toedieningsweg: selecteer...

Indicatie:

Aanpassing gebruik na optreden bijwerking: selecteer...

Gebruikt andere geneesmiddelen die volgens u ook verdacht zijn? Ander verdacht geneesmiddel +

Geneesmiddelen die niet verdacht zijn of waarvan u niet weet of ze een rol hebben gespeeld bij de klachten (comedicatie) kunt u hieronder invullen

Comedicatie

Gebruikt uw patiënt daarnaast nog andere - niet verdachte
- ○ Nee

- [ ] Levensbedreigend
- [ ] Ziekenhuisopname
- [ ] Blijvende arbeidsongeschiktheid
- [ ] Afwijkingen bij pasgeboren kind
- [ ] Overige ernstige afwijkingen

B GENEESMIDDEL

Geneesmiddel [1]

Verdacht geneesmiddel*: INFLUVAC

INFLUVAC INJSUSP 2007/2008 WWSP 0,5ML

RVG code: 022289

Mogelijke interactie: ☐

Startdatum*
(dag en maand zijn niet verplicht, maar graag zo precies mogelijk invullen)
-- dag -- | -- maand -- | -- jaar --

Dosering:

Toedieningsweg: selecteer...

- selecteer...
- Intra-articulair
- Cutaan
- Intramusculair
- Intraveneus
- Nasaal
- Oog
- Oraal
- Rectaal
- Per inhalatie
- Subcutaan
- Sublinguaal
- Transdermaal
- Vaginaal
- Epiduraal
- Andere toedieningsweg
- Onbekend

Indicatie:

Aanpassing gebruik na optreden bijwerking

Gebruikt andere geneesmiddelen die volgens u ook verdacht zijn?

Geneesmiddelen die niet verdacht zijn of waarvan u niet wee… …eld bij de klachten (comedicatie) kunt u hieronder invullen

Comedicatie

Gebruikt uw patiënt daarnaast nog andere - niet verdachte - geneesmiddelen?*

Outline of the presentation

- Introduction
- Challenges
- Facts
- Possible solutions
- Conclusions

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Alliance for Safe Biologic Medicines Welcomes FDA Biosimilars Draft Guidance, Urges Cautious Approach to Ensure Patient Safety

Monday, April 16th, 2012

Comments to FDA Stress Need for Clinical Trials, Restraint for Interchangeability Designations, and Unique Names for Biosimilar Products

Washington, D.C. — In response to the U.S. Food and Drug Administration's (FDA) draft guidance on the approval of biosimilar medicines, the Alliance for Safe Biologic Medicines (ASBM) submitted comments to the FDA that outlined recommended steps to ensure that patient safety is at the forefront of the biosimilars pathway.

While the FDA's proposed framework demonstrates the agency's thoughtful approach, ASBM stated in its comments that effective implementation of the biosimilars pathway must incorporate prudent measures, including:

- Analytical data and clinical studies to fully characterize the biosimilarity and immunogenicity of a biosimilar product;
- Traceability measures, including unique nonproprietary names for all biologic therapies, transparent product labels and patient/physician notification to enable clinical assessment and adverse event reporting; and
- Before designating a biosimilar 'interchangeable' with its reference product, U.S. regulators must recognize, and address, that the similarity between the reference product and its interchangeable biologic product(s) may change over time as a result of manufacturing or environmental variations.

Conclusions

- Product identification of biosimilars well ensured: 96.2% across 3 product classes
  - Especially epoetin (98.9% of suspected epoetins)
    - Information in SPC: *In order to improve the traceability of erythropoiesis-stimulating agents (ESAs), the trade name of the administered ESA should be clearly recorded (or stated) in the patient file*
  - Expected increase in their usage
    - Patents of top-selling biopharmaceuticals beginning to expire
    - Need for cutting health care spending
- Substitution of biosimilar products in EU (allowed by prescribing doctor)
  - Product has shown comparable efficacy and safety
  - But: concerns on product traceability

CONCLUSIONS

- Current research showed that for approximately 1 in 4 suspected biopharmaceuticals batch information is available
  - Necessary for:
    - Assessing safety profile over time (different pharmaceutical forms)
    - Identification of batch related problems|
    - Relating batch related problems (e.g. pathogen-contaminination, host cell impurities) to adverse drug reactions
  - Less relevant for low-risk products?
    - Risk-based approach
    - New biosimilar guideline: opportunity for smaller biopharmaceuticals to use generic approach
  - Consumers play a pivotal role in maintaining batch-traceability, pharmacists in particular for certain (blood-derived) products
- Improve traceability?
  - New opportunities by two-dimensional barcoding?
  - Encouraging patients/ health professional in product information ?
  - Facilitate reporting of batch numbers
  - Facilitate retrieval of batch numbers?