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Considerations on WHO's BQ Proposal

Joerg Windisch, PhD, Chair European Biosimilars Group (EBG)
Chief Science Officer, Sandoz Biopharmaceuticals

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Thank you!

The EGA appreciates the WHO INN Office's efforts to counteract the proliferation of divergent naming schemes for biologics around the world.

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Identification is easiest with as few and as simple elements as possible

- Trade name

  or

- INN + company name

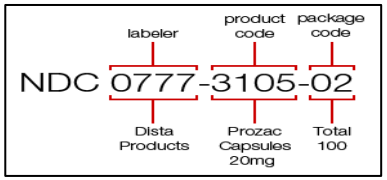
The more elements physicians and pharmacists have to record,
and the more complex these elements are,
the higher the likelihood something will get left out.

Many identifiers are already available today

- Trade name
- INN + company name
- 2D bar code (e.g. EU FMD unique identifier)
- ISO IDMP (identification of medicinal product) standards
- National drug code (NDC)
- Lot number...

INFLECTRA™ INFLIXIMAB

Epoetin alfa HEXAL®
Epoetin alfa



Do we really have a lack of identifiers?

Does another identifier really add value?

Or would it just increase complexity and confusion?

Example of a powerful unique identifier: EU Falsified Medicines Directive (FMD)

- Data-Matrix code, developed to ISO-standards
- Key data elements:

Making each product unique

- Product code (GTIN/NTIN or PPN)
- Randomized unique serial number

Facilitating Pharmacovigilance

- Expiry date
- Lot number
- National health number (where necessary)

Product #:	09876543210982
Lot:	A1C2E3G4I5
Expiry:	140531
S/N:	12345AZRQF1234567890

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Traceability requires strong systems and training rather than additional identifiers

- Strong systems exist today and provide excellent results
- These systems share a number of features:
  - Obligation to keep complete and accurate records
  - Simple and clear forms
  - Simple and clear submission procedures
  - Obligation to report for healthcare providers
  - Easy reporting for patients
  - Possibility to capture information electronically
  - Systematic follow-up if information is incomplete
  - National safety surveillance systems communicate with each other
  - Safety data is pooled and summarized

No system can ever compensate for the failure of health care providers to maintain complete and accurate records

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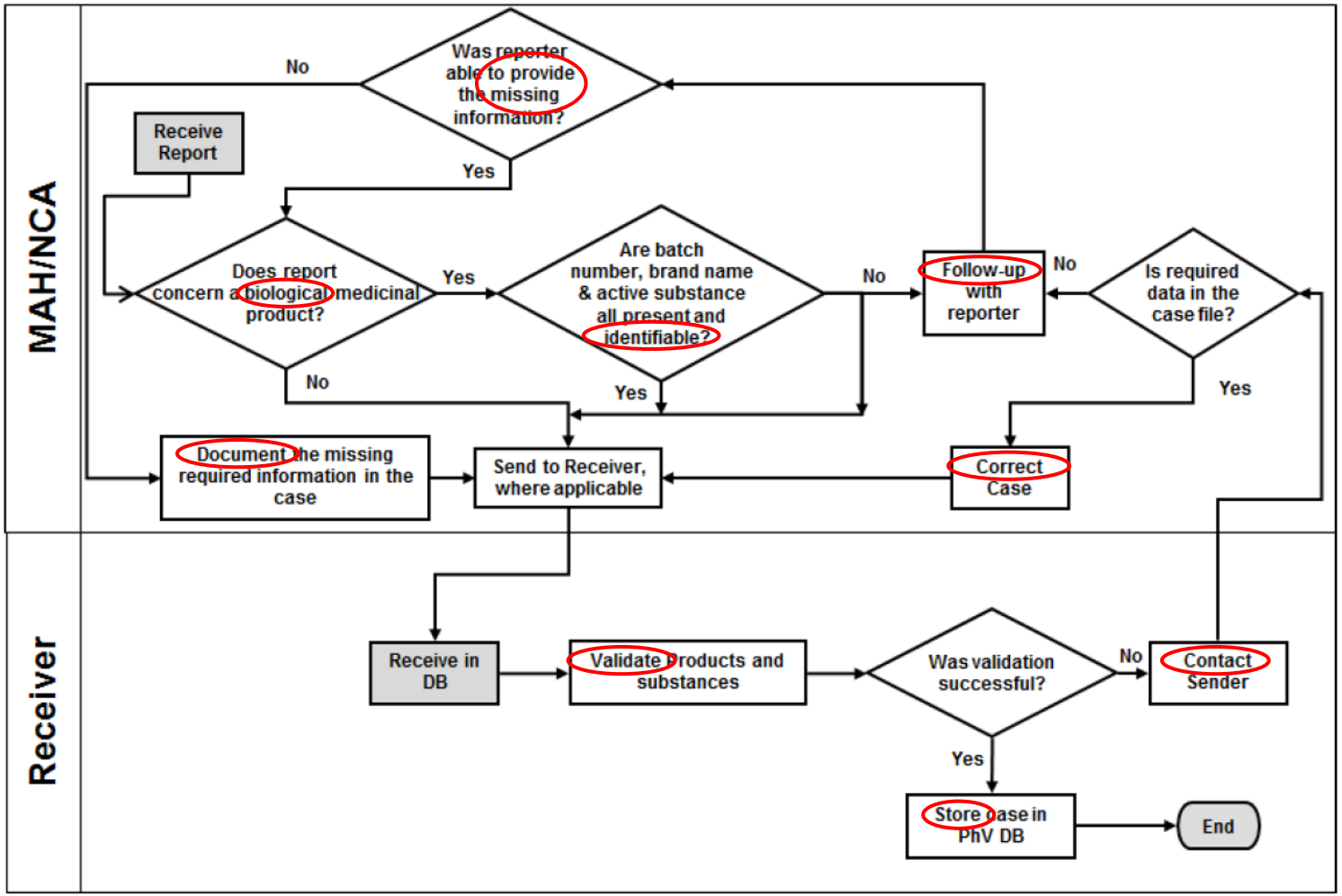
Example EU pharmacovigilance system: Process map: identification of biologicals



Source: EMA Guideline on good pharmacovigilance practices (GVP), Module VI – Management and reporting of adverse reactions to medicinal products (Rev 1), 8 September 2014, EMA/873138/2011 Rev 1*

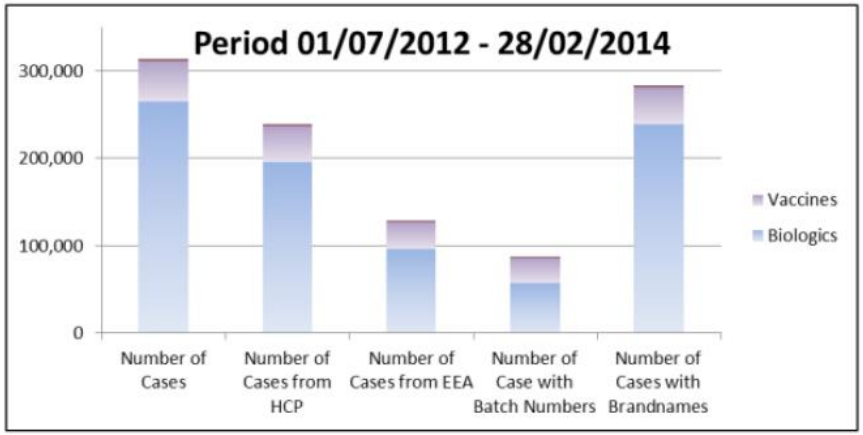
Strong systems have proven to work: EMA data

EUROPEAN MEDICINES AGENCY

Adverse reaction reporting and biologics (2)

Period 01/07/2012 - 28/02/2014

	Number of Cases	% Cases from HCP	% Cases from EEA countries	% Case with Batch Numbers	% Cases with Brandnames
Biologics	264,796	74	36	22	90
Vaccines	48,765	88	67	62	89



2 Session 4 discussion

Source: Presentation Sabine Brosch, EMA, at 12th EGA International Biosimilar Medicines Conference, London, 4 April 2014

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Strong systems have proven to work: Sandoz data

Epoetin alfa: Binocrit®/ Epoetin alfa Hexal®/ Abseamed®/ Novicrit®	Somatropin: Omnitrope®/ Scitropin®	Filgrastim: Zarzio®/ Filgrastim Hexal®
Total Spontaneous (HCP, Non-HCP) AEs/ ADRs reported:	Total Spontaneous (HCP, Non-HCP) AEs/ ADRs reported:	Total Spontaneous (HCP, Non-HCP) AEs/ ADRs reported:
285	**1335**	**279**
Reported as: • Abseamed: 87 • Binocrit: 172 • Epoetin alfa Hexal: 16 • Epoetin alpha Sandoz: 1 • Erythropoietin Sandoz: 1 • Novicrit: 1 • Unknown Erythropoietin alfa/ Epoetin alfa/ Erythropoietin: 7 (2%)	**Reported as:** • Omnitrope®: 1297 • Scitropin®: 8 • Somatropin BS S.C. Injection (Sandoz Japan) : 8 • Unknown somatropin: 22 (2%)	**Reported as:** • Zarzio®: 246 • Filgrastim Hexal®: 15 • Unknown Filgrastim or G-CSF: 18 (6%)
126.780.280 patient days until 31 Aug 2014 (Date of PSUR 22Oct14)	**68.688.036 patient days** until 30 Sep 2014 (Date of PSUR 12Nov14	**7.730.543 patient days** until 31 Jul 2014 (Date of PSUR: 29Aug14)

Source: Sandoz PSURs, sreedhar.sagi@sandoz.com; all trademarks are the property of their respective owners

Any new identifier bears risks

- The current system works well
- The introduction of a special system for a specific class of products disrupts this well working unified system
- Physicians and pharmacists will be confused as to what to do with the new, unknown identifier. This increases the a risk of
  - prescription errors,
  - dispensing errors,
  - medication errors and
  - adverse reaction reporting errors.

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A random identifier is especially challenging

- Any identifier which has no unambiguous meaning can cause confusion
- A random identifier of consonants is much harder to remember:
  - yzxw, dpqb ...
- The likelihood is high a random identifier will be
  - misspelled or, even more likely,
  - not recorded at all.

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Any new identifier system must be tested systematically to ensure it does not do more harm than good

Consequently, any new identifier system must be tested:

- By an independent, renowned institution
- In comparison to the system today (trade name or INN + company)
- To demonstrate it actually does improve identification and reduce safety risks
- With all key stakeholders (physicians, pharmacists, patients, drug safety officers, etc.)

In the interest of patient safety, no decision can be made on implementation prior to systematic testing and discussion with all stakeholders

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It needs to be clear which issues the BQ can address and who will use it

- The following arguments were brought in support of the BQ:
  - Traceability, adverse reaction reporting, prescribing
- All of these needs can be better fulfilled either with a trade name or by the combination of the INN + company name
- Unless it is clear
  - what the need is, and
  - whether or not the proposed change effectively and safely addresses this need

no change should be introduced.

So what need is being addressed with the BQ?

Which countries will use it?

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WHO has supported INN + company since 1993 – a system which has worked well

- The INN has always been the name for the active substance and was never intended to identify products on its own

- Resolution WHA46.19 on nonproprietary names for pharmaceutical substances requests Member States to "enact rules or regulations [...] to encourage manufacturers to **rely on their corporate name and the international nonproprietary names** [...] to promote and market multisource products introduced after the expiry of a patent"

WHO INN guidance:
http://www.who.int/medicines/services/inn/innguidance/en/

This has worked well in many countries for more than 20 years – why change now?

Will "filgrastim dqpb" really work better than "filgrastim TEVA"?

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Summary

- A clear and well working naming system for all drugs is already in place
- Traceability requires strong systems, training and consequent follow-up rather than additional identifiers
- Any new identifier bears safety risks and must be tested with all stakeholders
- We need to be clear which issue the BQ should actually address – and be sure that it does not do more harm than good
- EGA remains supportive of the use of trade names or INN + company name

EGA appreciates the efforts of the WHO INN office to maintain a globally unified naming system and is looking forward to contributing to further discussions!

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Additional information for consideration by the INN Office and Expert Committee

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Even a identifier reminiscent of the company name bears safety risks

- „filgrastim-sndz“ given to Sandoz‘s Zarxio® by the FDA as a placeholder nonproprietary name
- Med-ERRS, a a highly respected and independent organization specializing in the testing of names for the potential for medication errors, tested this name and came to the following conclusions (1=poorest, 5=best):

Proposed name	Score	Vulnerability	Issues
filgrastim-sndz	**2**	**high**	Look-alike name(s) Sound-alike name(s) misinterpretation of suffix

filgrastim-sndz	• Unclear what sndz stands for • Unsure of pronunciation. Do you say the individual letters? • Suffix likely to be left off or missed

- Due to the above information, Med-ERRS believes that the nonproprietary name filgrastim-sndz is **vulnerable to error**. This rating is due to the **potential confusion** with existing filgrastim products as well as potential **misinterpretation of the suffix** “sndz”.“
- → **A four letter suffix or code can never be as clear and powerful as a trade or company name** - Zarxio® (filgrastim) or filgrastim SANDOZ

Source: Med-ERRS report on filgrastim-sndz

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The BQ must not separate the product from the company accountable for its safety

- The current proposal to connect the BQ to the active substance manufacturing site is problematic:
  - Disconnects the product from the company legally responsible for its safety - the market authorization holder
  - Falls short of capturing the finished product manufacturing facilities, distribution, storage etc. and is redundant because the lot number already provides this information
  - Would prevent a global system due to the use of different (combinations of) manufacturing sites for different jurisdictions – this cannot be the intent of a WHO system
  - Is problematic for combination drugs that contain more than one active moiety

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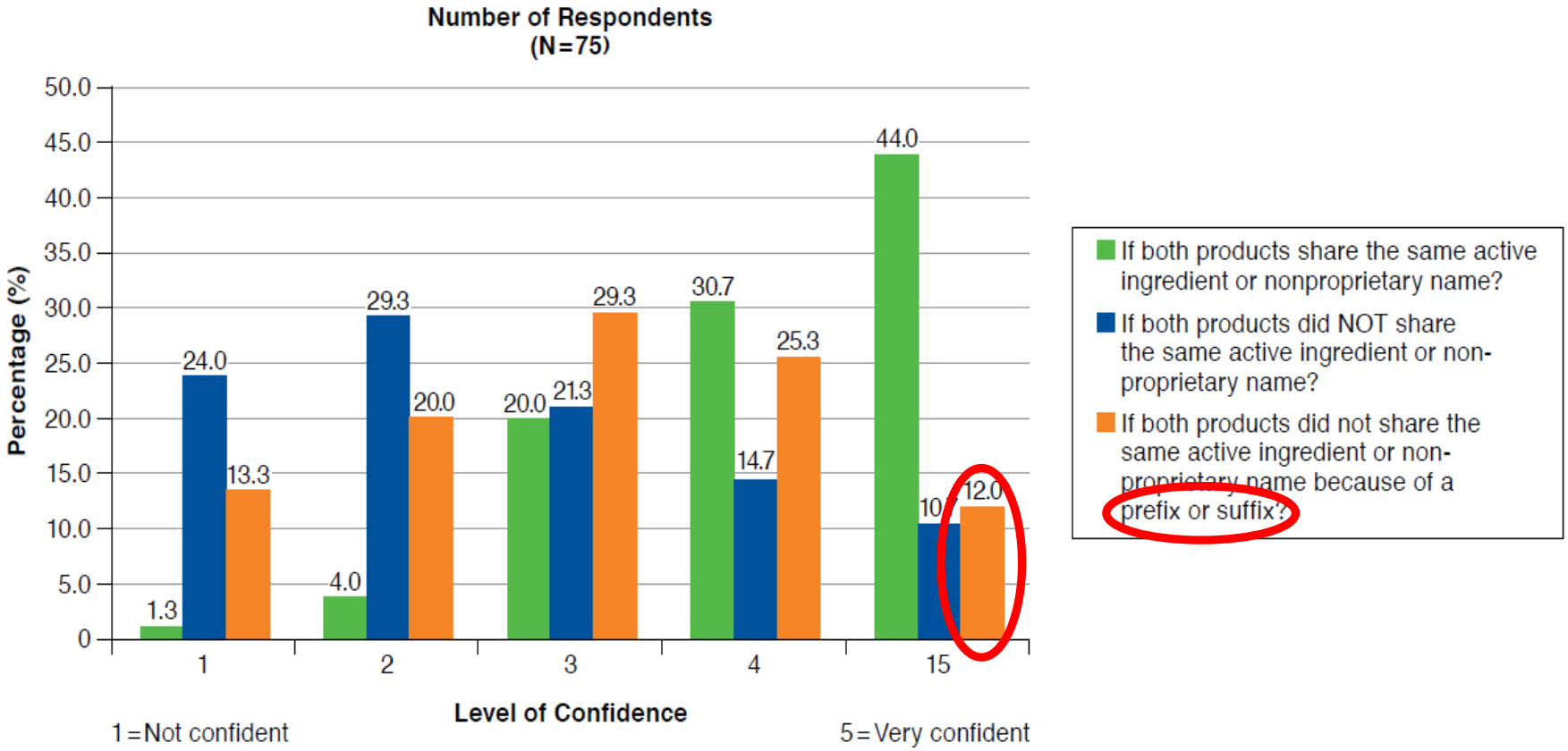
Many practical questions regarding the BQ would still have to be answered

1. How would the random sequences be generated?
2. How would BQs be tested to ensure safety
   - Memorability, look alike, sound alike, decipherability when handwritten, compatibility with all WHO member languages etc.
3. Would same BQ apply to all products from the same site?
4. What would the application process look like?
   - Which information will be required? When?
   - How can delays in approvals be ruled out?
5. How and when would BQs be assigned for products already approved?
   - How could compliance be ensured?
6. How would the BQ database be set up?
   - Which information would it contain?
   - Who would have access to this information? How would it be controlled?
   - How would trade secrets be protected?

Prefixes or suffixes for biosimilars only would negatively influence perception

FIGURE 3 Confidence of Survey Respondents in Substituting Interchangeable Biosimilars



Sara Fernandez-Lopez et al., *J Manag Care Spec Pharm*. 2015;21(3):188-95

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Any identifier must apply to all biologics, not just biosimilars

- It would already be confusing enough to introduce an identifier just for biologics, and not for all other drugs
- It would be even more confusing, and discriminatory, if an identifier were introduced only for products which go through a specific regulatory pathway
  - The premise of regulators is that the approval process for a biosimilar provides just as much reassurance as that for a novel biologic, only using a different, reference-based approach
  - Fundamentally, a biosimilar is just another biologic about which much is already known
- Introducing the BQ for biosimilars only, but not for original biologics, would worsen traceability as it will make the BQ appear optional in reporting
- So if a BQ is to be introduced it must
  - apply to all biologics
  - apply retroactively
  - not be linked to a specific regulatory pathway

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Acronyms

- BQ Biological Qualifier
- EBG European Biosimilars Group
- EGA European Generic medicines Association
- EU European Union
- INN International Nonproprietary Name
- PV Pharmacovigilance
- WHO World Health Organisation