Establishment of a Vibrant U.S. Biosimilars Approval Pathway

Patient and physician confidence in an environment of transparent data, identifiable products and accountable manufacturers

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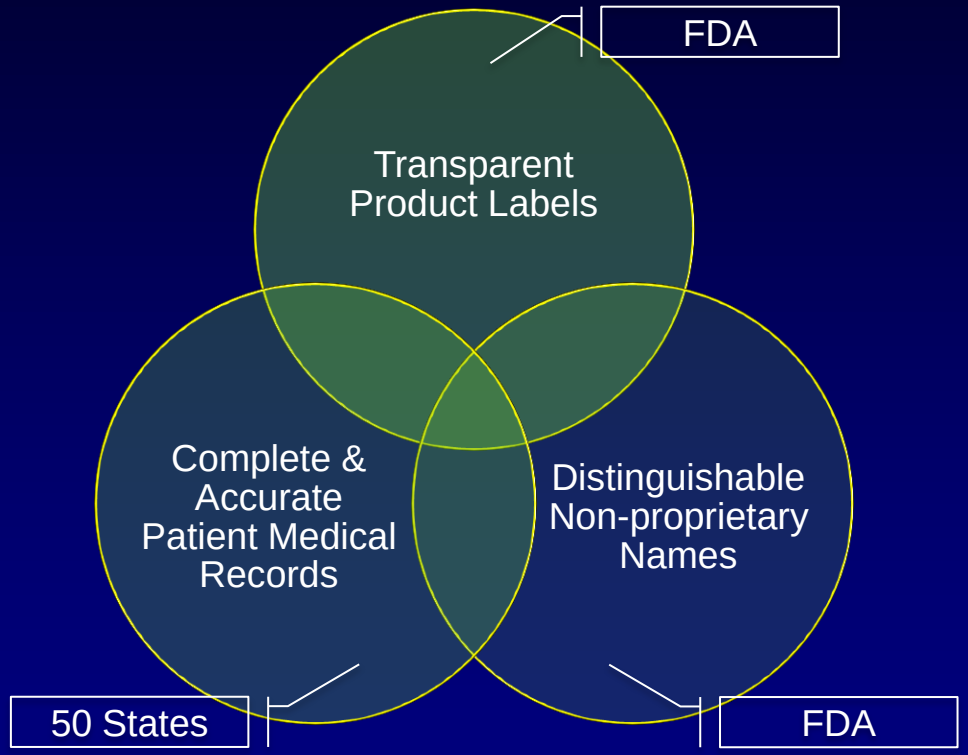
Increased access and robust competition can accompany important patient-focused provisions

- Increased competition ***and / or*** the ability to reliably identify a specific medicine?
- Lower healthcare cost ***and / or*** patients and physicians to know which medicines have been administered?
- Increased access ***and / or*** mechanisms to ensure manufacturers voluntarily stand accountable to patients?



Amgen rejects false choices; we believe in 'and' not 'or'

Physicians and payers support similar but distinguishable names for biologics

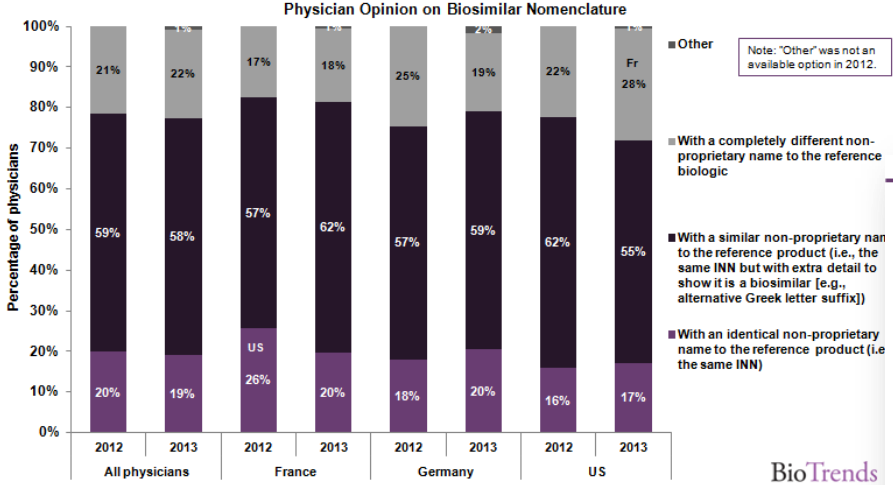
Acceptance of Biosimilars Across Physician Specialties

Biosimilars Advisory Service

Biosimilar Nomenclature

The majority of surveyed physicians in all countries believe that biosimilars should be named with a non-proprietary name similar to the name of the reference product but with extra detail to show it is a biosimilar. There are no significant changes in physician opinion in 2013 versus 2012. Only one-fifth of all physicians believe that a biosimilar should have an identical name to the reference product, likely reflecting concern associated with automatic substitution and traceability for products with identical names.

Physician Opinion on Biosimilar Nomenclature



Note: "Other" was not an available option in 2012.

Q. What is your opinion on how biosimilar molecules should be named (non-proprietary names)?

BioTrends RESEARCH GROUP

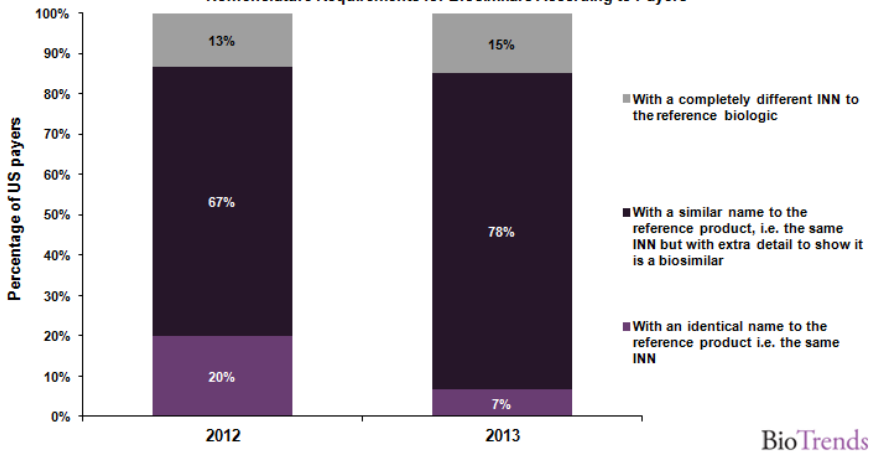
US and EU Payer Perspectives

Biosimilars Advisory Service

Biosimilars Nomenclature

Despite the drop in the proportion of surveyed payers that believe a biosimilar should have an identical INN to the reference product in 2013 compared with 2012, the difference is not statistically significant; overall in 2012 and 2013 the majority (67% and 78%, respectively) believe a biosimilar should have a similar name to the reference product, but with additional nomenclature detail to indicate that it is a biosimilar.

Nomenclature Requirements for Biosimilars According to Payers



Q38. What is your opinion on how biosimilar molecules should be named (non-proprietary names)? (2013: n=60; 2012: n=60)

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Absent proactive policy, the patient medical record will be rendered ambiguous or inaccurate

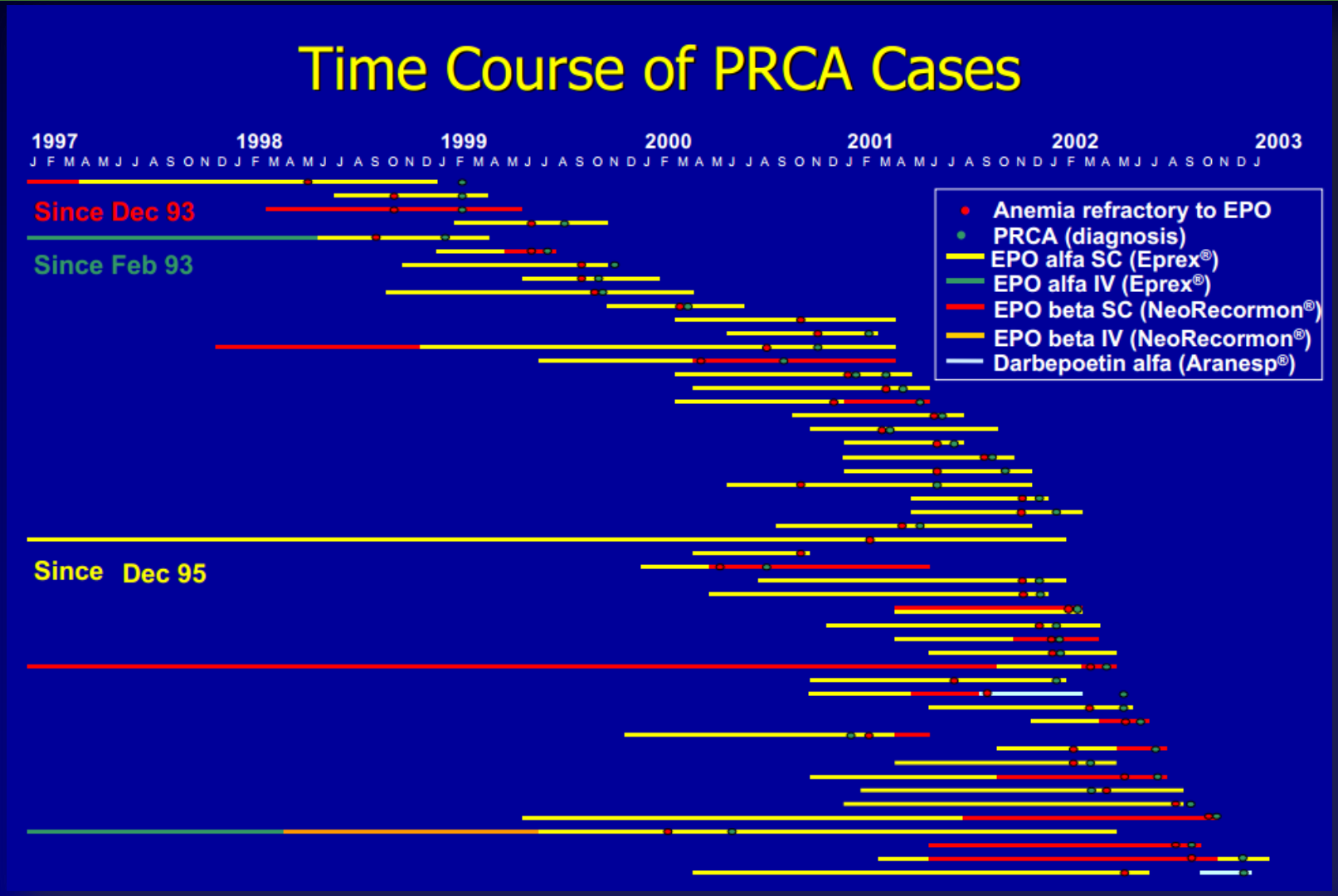
Principle*	Prevailing Generic Requirements	Suggested Biosimilar Requirements
Substitution based on an FDA determination	Yes – Therapeutic Equivalence	Yes – Interchangeable
The prescribing physician should be able to specify 'dispense as written'	Yes	Yes
The patient should be informed of the substitution	Yes	Yes
After-the-fact, the prescribing physician should also be informed of the product dispensed for recording	No	Yes
Pharmacy records should be maintained	Yes	Yes

Substitution policy should be appropriate for <u>biologic medicines</u>:

- *Biologics persist within the body for a much longer period of time than most chemical drugs*
- *Overlap of exposure to circulating biologics from different sources is likely*
- *Latent immune responses (changes in efficacy or tolerance) make attribution to a specific product more challenging*
- *All biologics are sensitive to unintended occurrences during manufacture and handling - postmarket surveillance is an important patient safeguard*

Source: * Based on BIO Principles on Patient Safety in the Substitution of Biologic Products, Jan 24, 2013. Available at http://www.bio.org/advocacy/letters/bio-principles-patient-safety-substitution-biologic-products

Complete and accurate patient medical records are important for <u>all</u> biologic medicines



Source: Casadevall Nicole, Immune-response and adverse reactions: PRCA case example. Presentation to EMA Nov, 2009. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2009/11/WC500011064.pdf

International standards for adverse event reporting rely on patient medical records

E2B(R3) Electronic Transmission of Individual Case Safety Reports (ICSRs) Implementation Guide — Data Elements and Message Specification

B.1.1.1 Patient Medical Record Number(s) and the Source(s) of the Record Number (if allowable)

Record numbers can include the health professional record(s) number(s), hospital record(s) number(s), or patient/subject identification number in a study. The source of the number should be specified to ensure the possibility of retrieval when possible and desirable.

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B.1.8 Relevant Past Drug History (repeat as necessary) (header / entity)

This section concerns relevant drugs previously administered and which have been stopped before the Adverse Event onset. It does not concern drugs taken concomitantly or drugs which might have potentially been involved in the current reaction(s)/event(s). Medical judgment should be exercised in completing this section. Medications that have been stopped might be considered suspect based on the elimina
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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA current thinking on this topic. It does not create or confer any rights for or on any person and operate to bind FDA or the public. You can use an alternative approach if the approach satisfi requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot id the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

For questions regarding this draft document contact (CDER) Krishna Chary 240-487-7377, or (CBER) Deborah Yaplee 301-827-3288.

B.4 DRUG(S) INFORMATION (REPEAT AS NECESSARY)

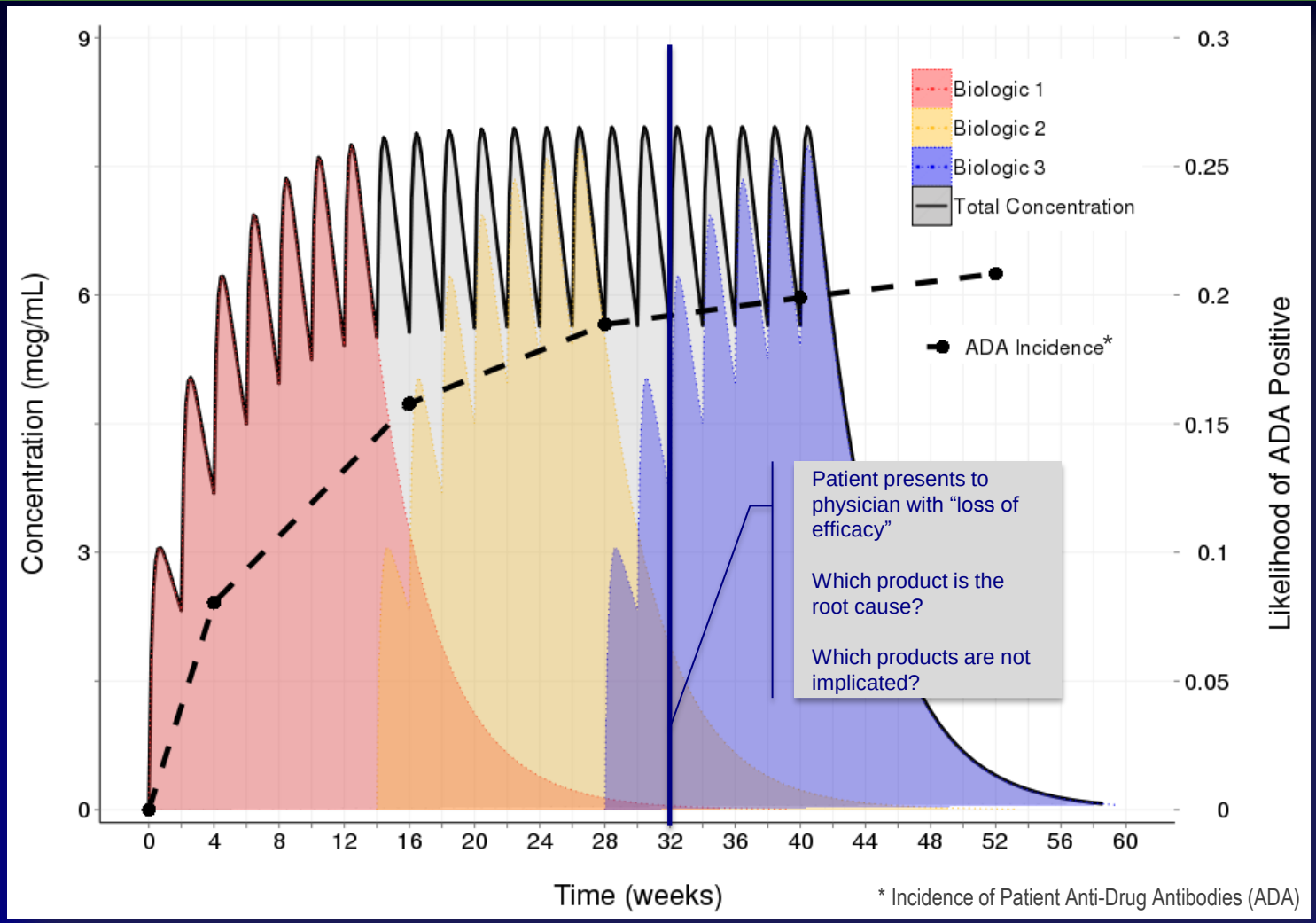
This section covers both suspect and concomitant medications (including biologics). In addition, the section can be used to identify drugs suspected to have an interaction. A minimum of one suspect medication needs to be provided for each valid ICSR. Medications used to treat the reaction/event should not be included here.

For each drug, the characterisation of the drug role (B.4.k.1) is that indicated or implied by the primary reporter, (e.g. the original source of the information). Suspect medications are those health products taken by the patient and suspected by the reporter to have contributed to the adverse reaction described in section B.2. The suspect medication might have been stopped before the reaction is observed, for example, a single dose of an antibiotic could be suspected to cause diarrhoea one week later. However, concomitant medications are only those health products taken by the patient at the time the reaction is observed; other relevant medication history should be recorded in section B.1.8.

As for the designation "i" in section B.2 above, the designation of "k" in this section indicates that each item is repeatable and that it corresponds to the same "k" in all subsections. A separate block (k) should be used for each health product. Within a block (k), subsections can also repeat using the designation "r", and within a subsection (r), further sub-subsections can repeat using the designation "i".

Source: E2B(R3) Electronic Transmission of Individual Case Safety Reports Implementation Guide — Data Elements and Message Specification; and Appendix to the Implementation Guide — Backwards and Forwards Compatibility. Available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm274966.htm

Biologic adverse event attribution will be difficult without complete and accurate patient records



Simulation based on Bartelds, G., et al., Development of Antidrug Antibodies Against Adalimumab and Association With Disease Activity and Treatment Failure During Long-term Follow-up. Journal of the American Medical Association 2011: 305 (14): 1460-1468

Sources: Ben-Horin, S., et al., The decline of anti-drug antibody titres after discontinuation of anti-TNFs: implications for predicting re-induction outcome in IBD. Aliment Pharmacol Ther, 2012. 35(6): p. 714-22. and FDA Humira Clinical Pharmacology Review available at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/ucm080610.htm

Questions