Synergy Satellite Session: Biosimilars in cancer care - the next challenge

Clinician's perspective in prescribing biosimilars

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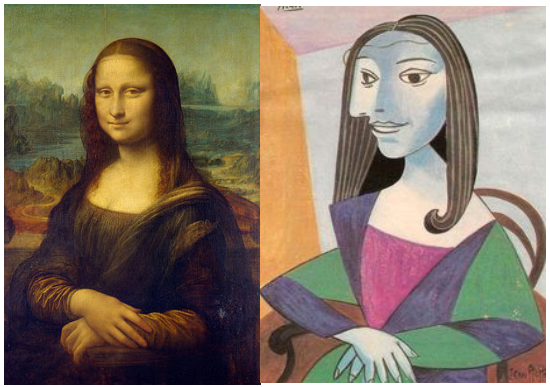
EU Policy Committee, ESMO

the views expressed are the personal views of the presenter and may not be understood or quoted as being made on behalf of or reflecting the position of others

DISCLOSURE

NO FINANCIAL RELATIONSHIPS TO DISCLOSE

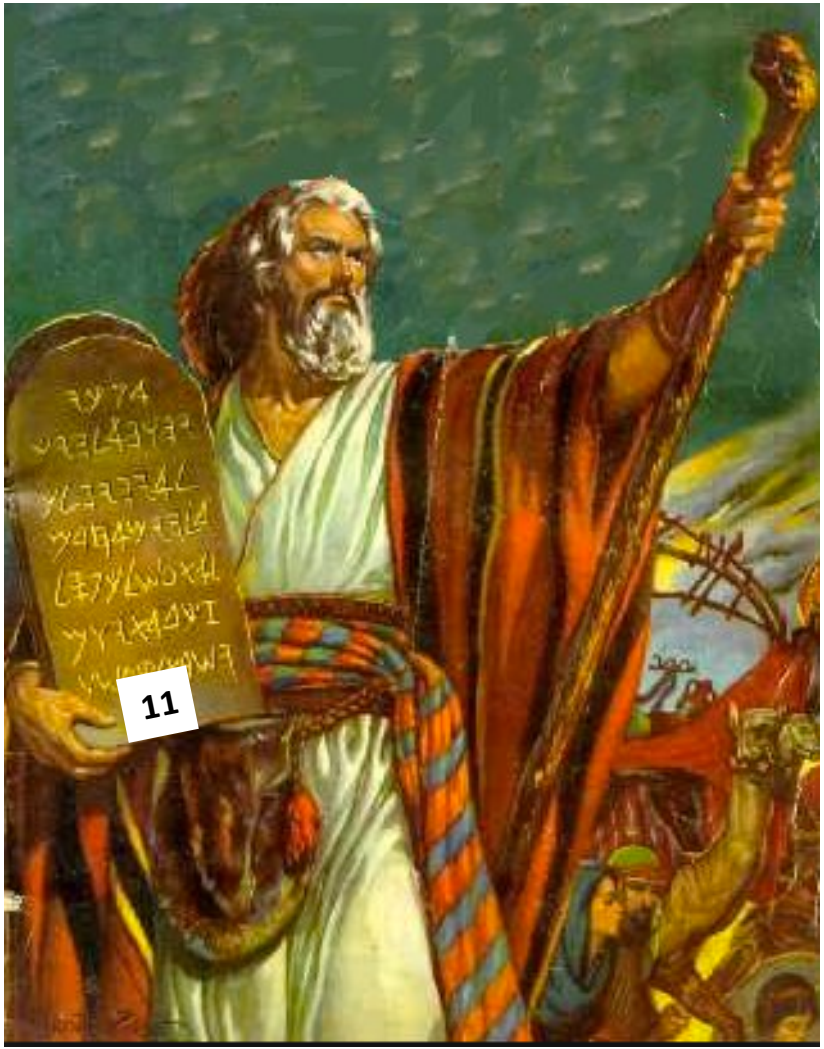
AGENDA



BACKGROUND on clinical perspective on biosimilars and possible reasons/barriers to prescription

The role of learned societies: the ESMO position paper

How to build confidence to prescribe biosimilars



The 11° commandment:

You will prescribe new drugs after they'll have been assessed by the *one and only* scientific methodological pathway:

-Phase I
-Phase II
-Phase III

Thou shalt never move from that

AN UNPRECEDENTED REVOLUTION in ONCOLOGY

Few examples

-Immunotherapy: drugs that WORK despite evidence of (radiological) progression

-The molecular revolution: isn't it time to challenge the 11° commandment, is it?

-Costs and affordability discussions:
how many oncologists have been trained for that?

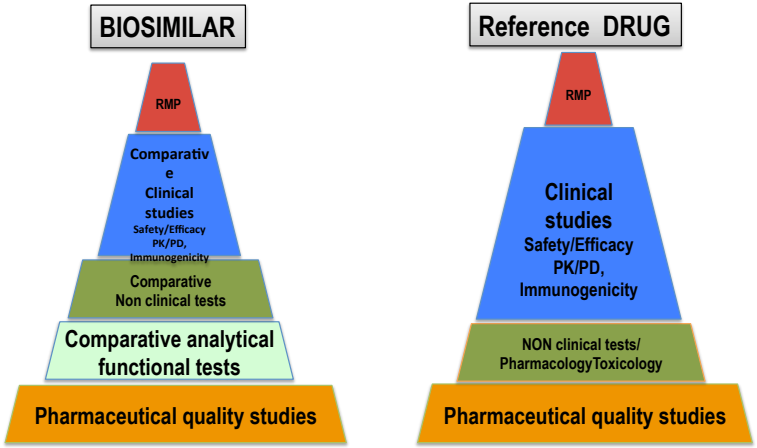
Terra incognita
(another one…)

And along comes a “new” paradigm for drug development

Pivotal trial S&E → **COMPARABILITY Ex**

Phase III trial→ better performance

vs

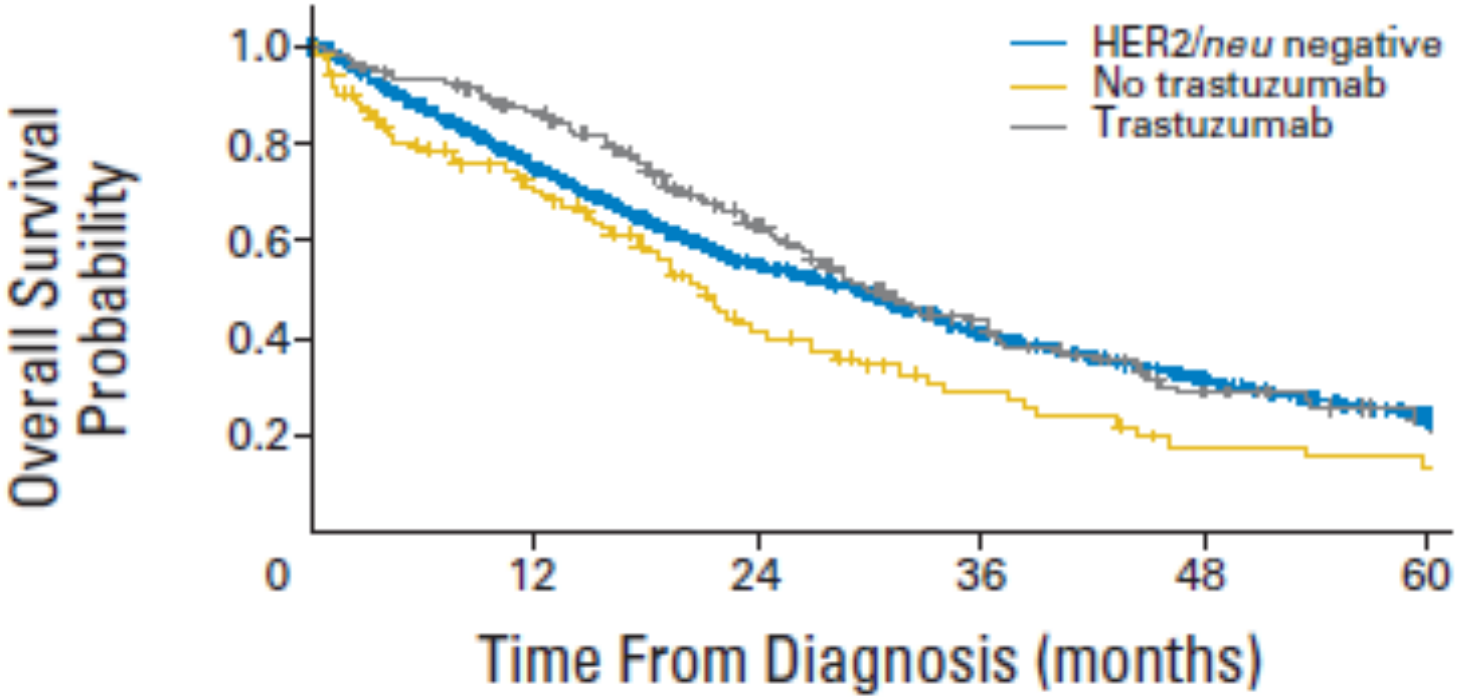


-More efficacy
-Less toxicity/ better tolerability
-Both

New language + new methodology
Learning curve

PROGNOSIS BY HER2 STATUS AND H TREATMENT

Dawood, JCO 2010

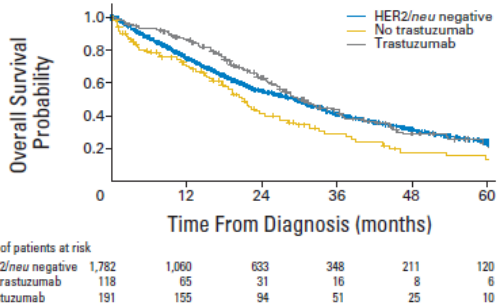


No. of patients at risk

HER2/*neu* negative	1,782	1,060	633	348	211	120
No trastuzumab	118	65	31	16	8	6
Trastuzumab	191	155	94	51	25	10


11


And so..
Dr Giuliani is
Lost In Translation


Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0
HER2/neu negative
No trastuzumab
Trastuzumab
12
24
36
48
60
Time From Diagnosis (months)
No. of patients at risk
HER2/neu negative 1,782 1,060 633 348 211 120
No trastuzumab 118 65 31 16 8 6
Trastuzumab 191 155 94 51 25 10


FROM THE DIRECTOR OF THE LORD OF THE RINGS TRILOGY
AN UNEXPECTED JOURNEY
Terra incongita

ESMO – EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

The leading professional organisation for medical oncology

ESMO is the leading European professional organisation for medical oncology, working across Europe and around the world to erase boundaries in cancer care and to provide medical oncology education within an integrated approach to cancer care.

- A member-based alliance of **18,000 oncology professionals**
- Represents over **150 countries**
- Cooperates in partnership with all stakeholder groups to ensure the **highest level of standards** for medical professionals

ACROSS ONCOLOGY. WORLDWIDE.

ESMO 2020 VISION

3 SUSTAINABLE CANCER CARE

Advocating for equal access to quality treatment and for cancer prevention

1 INTEGRA CANCER

Bridging canc research, earl and treatment patient outcor

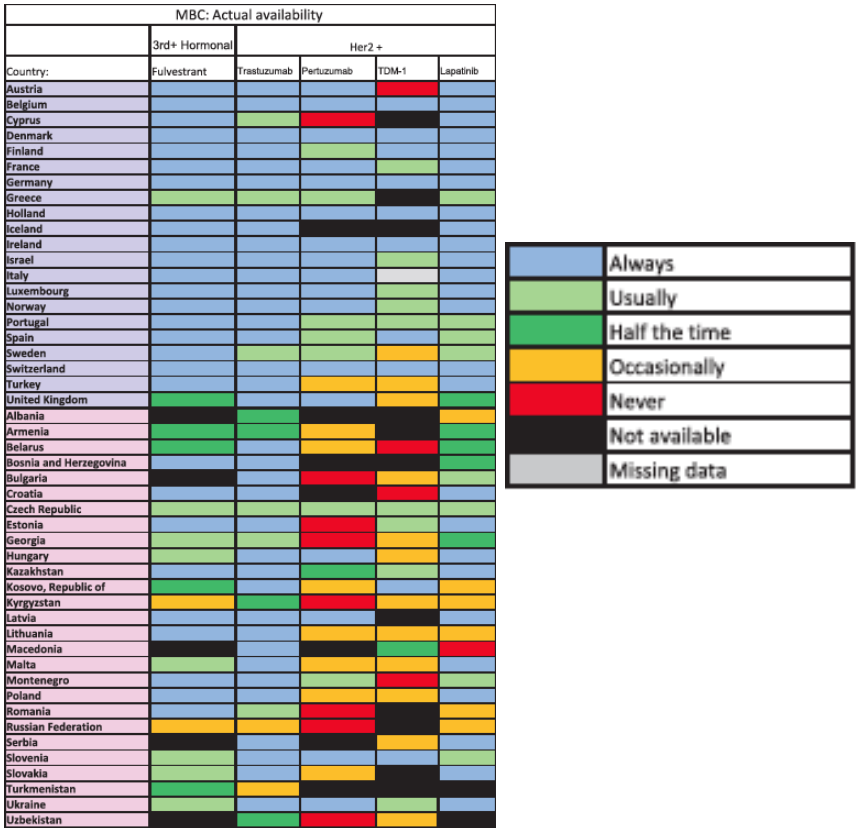
INABLE R CARE

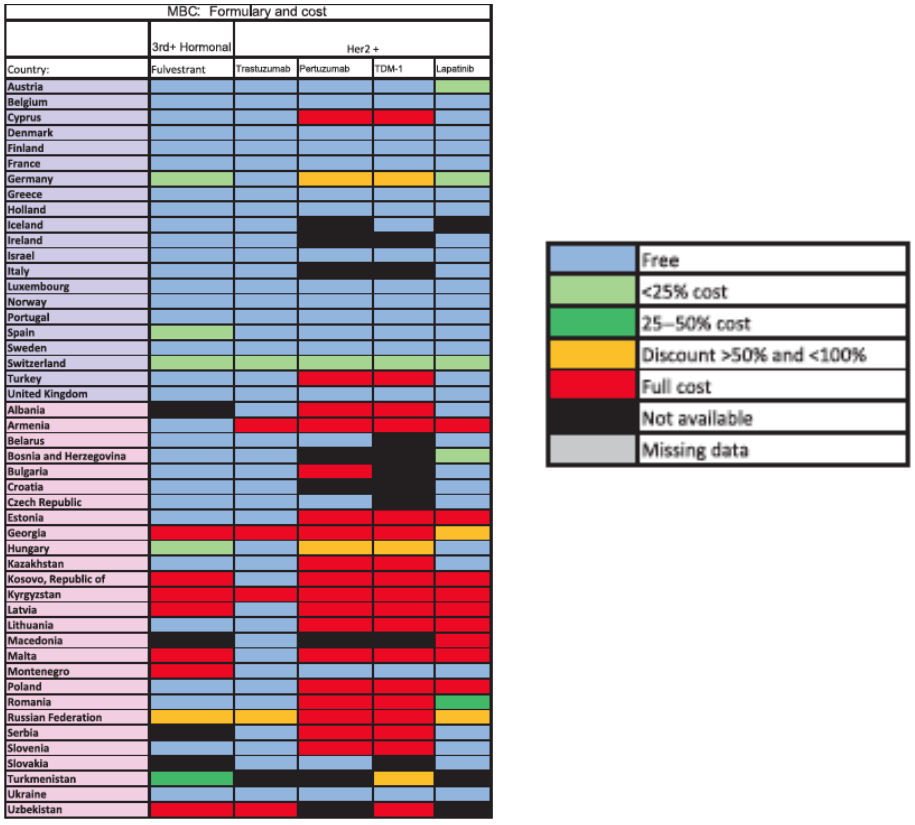
or equal access atment and for ention

ESMO European Consortium Study on the availability, out-of-pocket costs and accessibility of antineoplastic medicines in Europe

Annals of Oncology 27: 1423–1443, 2016

N. Cherny[1*], R. Sullivan[2], J. Torode[3], M. Saar[4] & A. Eniu[5]





Open Access Review

ESMO Open
Cancer Horizons

Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers

Josep Tabernero,[1] Malvika Vyas,[2] Rosa Giuliani,[3] Dirk Arnold,[4] Fatima Cardoso,[5] Paolo G Casali,[6] Andres Cervantes,[7] Alexander MM Eggermont,[8] Alexandru Eniu,[9] Jacek Jassem,[10] George Pentheroudakis,[11] Solange Peters,[12] Stefan Rauh,[13] Christoph C Zielinski,[14] Rolf A Stahel,[15] Emile Voest,[16] Jean-Yves Douillard,[2] Keith McGregor,[2] Fortunato Ciardiello[17]

Open Access Review

ESMO Open Cancer Horizons

CrossMark

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SETTING THE SCENE

- Expenditure for medicinal products will be up to 1.3 trillion EUR by 2020
- In EU biosimilars are approved by a stringent regulatory process

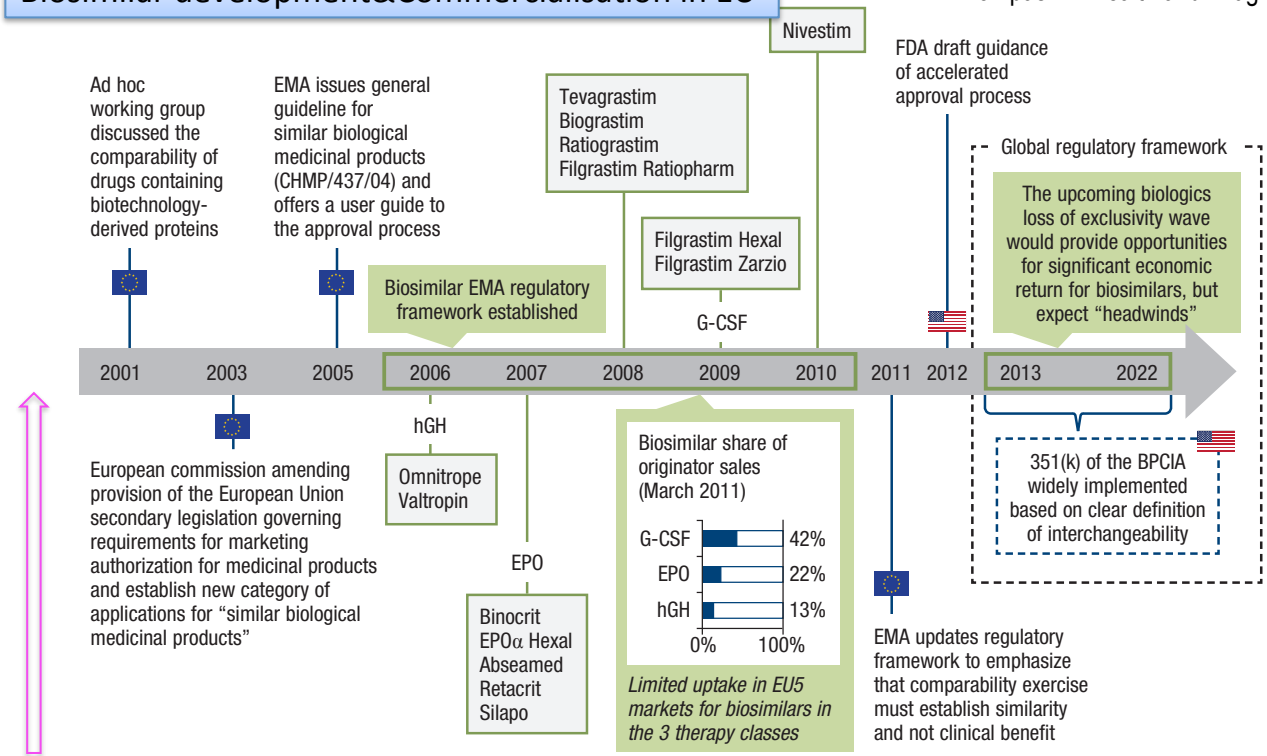
- When properly developed and used, biosimilars, medicinal products which contain a highly similar version of the active substance, represent an

OPPORTUNITY to

-Increase ACCESS to biologic therapies in EU and worldwide
-Lower COSTS
-Contribute to the SUSTAINABILITY of healthcare

Biosimilar development&Commercialisation in EU

Rompas Am health and Drug Benefits, 2015

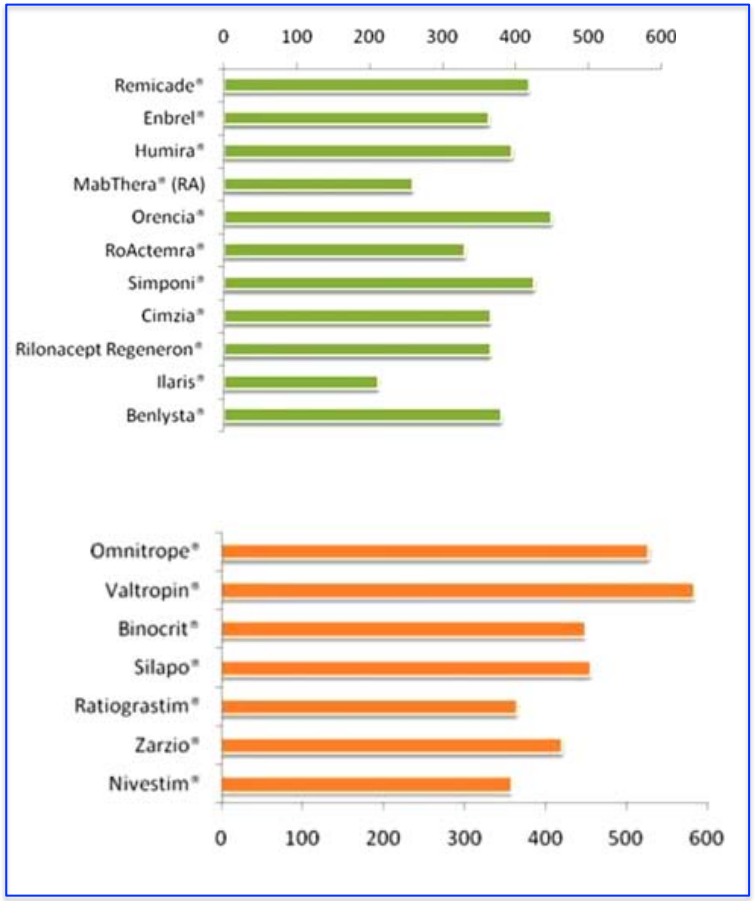


June 1998
CONCEPT paper
On comparability
of biotechnology-
derived products

Comparability in a X product following changes in the production process
Comparability of *recombinant drugs* developed by another manufacturer

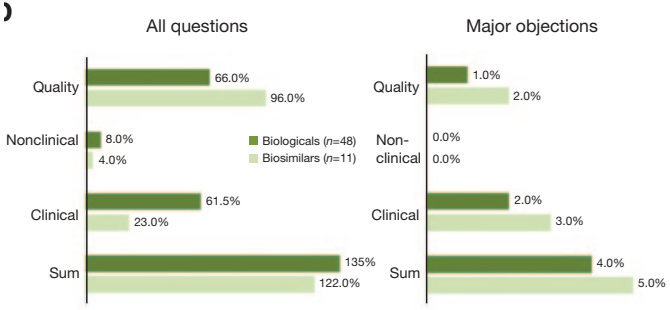
This was the beginning of the biosimilar discussion at EU regulatory level

Time to approval (days)



Schneider, Ann Rheum Dis 2013

Questions during the MA procedure



Schneider, Nature Biotech 2012

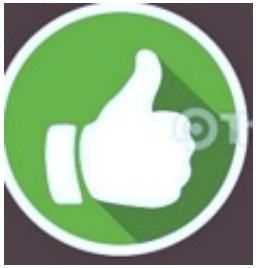
LABELLING

Should

-Include the submitted information from the **clinical studies**: HCPs should be clearly informed about the **sensitive patient population** and the **sensitivity of the endpoints** used;
-**Report the Pharmacovigilance plan**;
-Specify the brand name of the reference product;
-Comprehensively report data on **extrapolation**, **interchangeability**, **switching**, **automatic substitution**, **immunogenicity.**

ADEQUATE INFORMATION/EDUCATION OF HCPs AND PATIENTS IS CRUCIAL

EXTRAPOLATION



Analytical, preclinical, PK, PD and clinical data along with immunogenicity should be collected to be correctly extrapolated to all indications of the reference product

EXTRAPOLATION may be **ACCEPTABLE** IF there are enough **RELEVANT DATA** of Safety and Efficacy of the BIOSIMILAR

EXTRAPOLATION IS A WELL ESTABLISHED SCIENTIFIC PRINCIPLE

SWITCHING

REFERENCE PRODUCT → BIOSIMILAR

BIOSIMILAR → REFERENCE PRODUCT

BIOSIMILAR 1 → BIOSIMILAR N

AUTOMATIC SUBSTITUTION SHOULD BE AVOIDED

-Physicians are responsible for the act of prescribing medicines
-Patients should be thouroughly and continously informed
-Patients should be closely monitored

BIOSIMILARS_ESMO in Action

Position paper published in Jan 2017

European Commission Stakeholder Event on Biosimilar Medicinal Products, Josep Tabernero, ESMO President-elect, chaired a session "Collaborative Approach in the Use of Biosimilar Medicines" in May 2017.

15th Biosimilar Medicines Conference organised by Medicines for Europe in March 2017: ESMO was represented by Rosa Giuliani, ESMO PPSC member, who participated in a panel discussion.

ESMO special session during ESMO 2017 in Madrid: "The incoming wave of biosimilars in oncology". Report in the process of being prepared. (~700 participants)

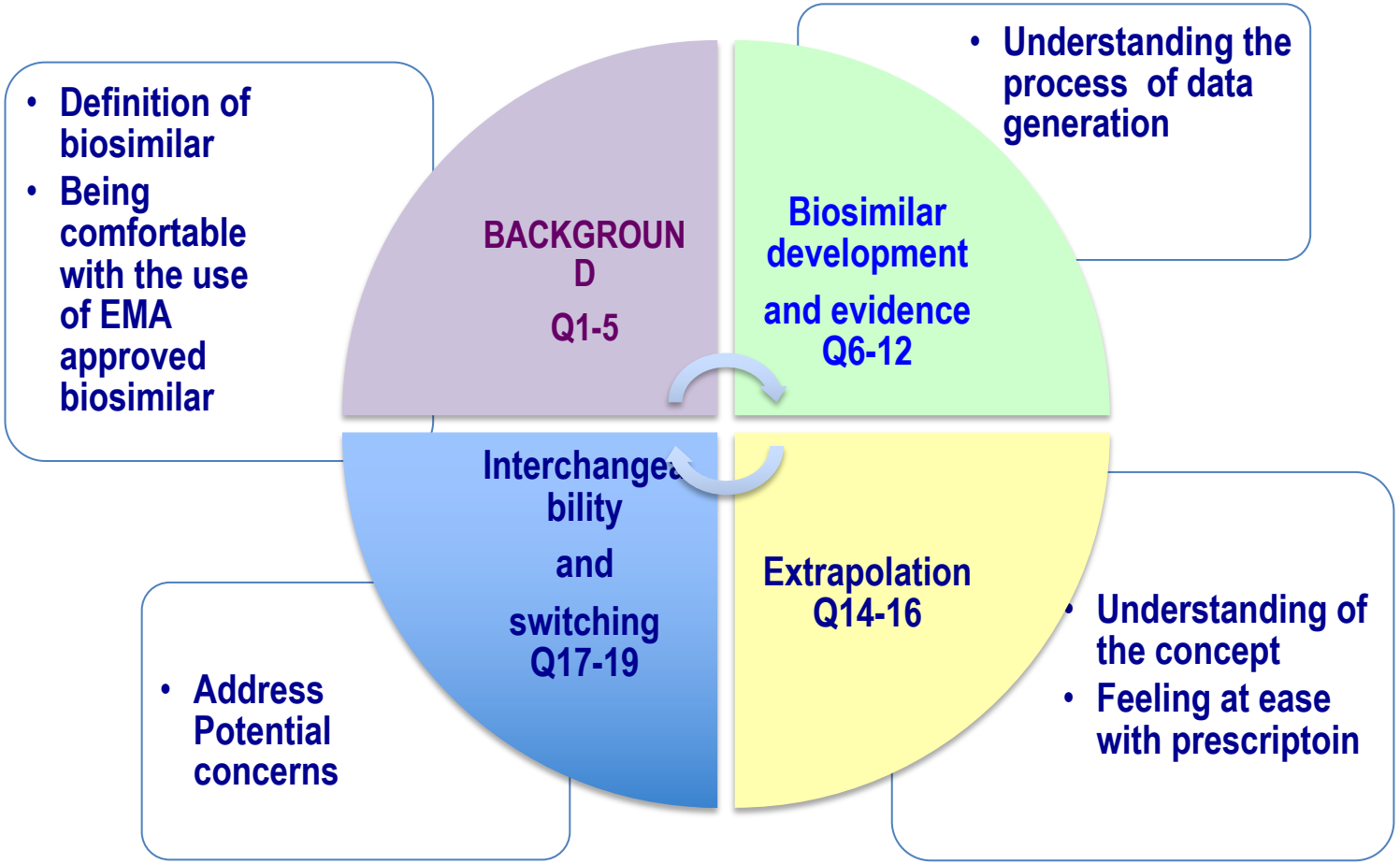
ESMO survey on awareness of biosimilars launched during ESMO 2017 in Madrid. Results in the process of being analysed. Survey also being conducted nationally in select countries.

ESMO meeting with the Biosimilar Medicinal Products Working Party (BMWP) – EMA in London, 21st September

ESMO Colloquium on biosimilars during ESMO Asia 2017 in Singapore (~180 participants)

ESMO special session during ESMO 2017 in Madrid*: "The incoming wave of biosimilars in oncology*
700 participants

ESMO Survey on Biosimilars in Oncology



HOW TO BUILD CONFIDENCE

SCIENCE

GUIDANCE

INTERACTION/ COLLABORATION

DATA COLLECTION

DATA ANALYSIS


Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers

EU COMMISSION

ESMO

Other Societies/ Acaademic bodies

CLINICIANS

EMA

PATIENTS

PHARMACISTS

NURSES

INDUSTRY

WHO

MS/NCA

End users + data generators

Capture Data Systems (registries, PhVig, et cet…)

CHALLENGES of RWE generation

FRAGMENTATION

LACK OF INTEROOPERABILITY

Infrastructures for data sharing

Data linkage across resources

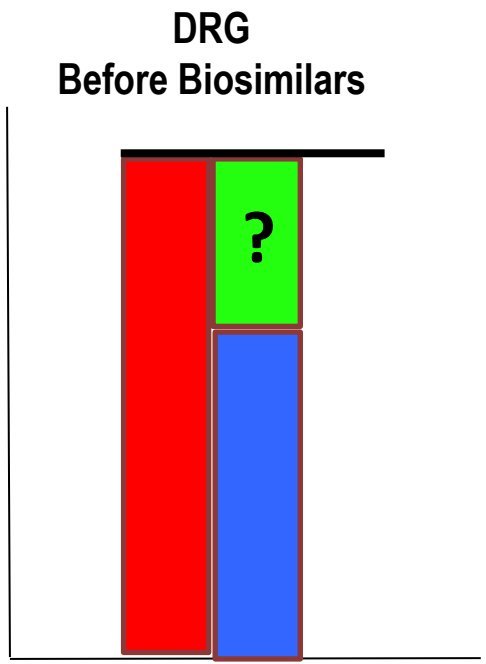
EHR

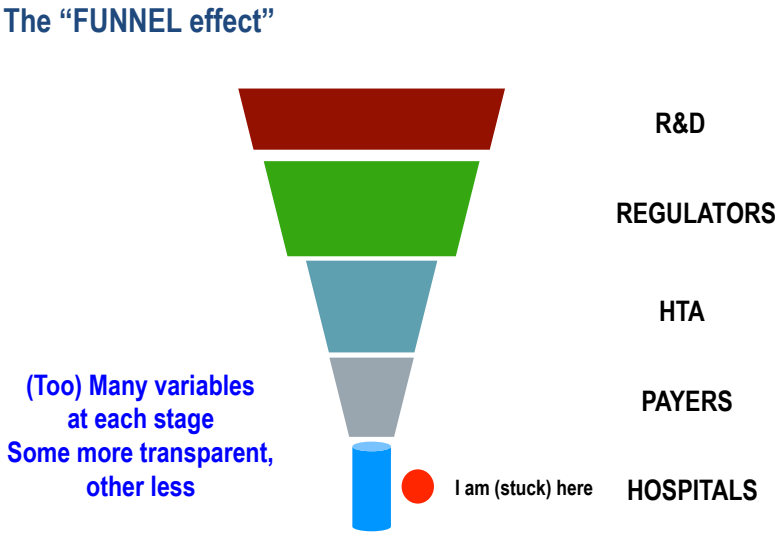
Phase IV trials
Pragmatic trials
Registries
Post-authorization safety/efficacy studies
Observational studies
Expanded access/compassionate use programmes
Data collected by NCA (eg. MEA)

What is RWE?

We need to know that we're doing well, aka MOTIVATION

TRANSPARENCY
in resource (re)allocation at Global (EU, ROW), National and even more importantly at local level (hospitals)





Adapted from Steinar Madsen, Biosimilar Medicines Conference 2017

EVIDENCE

The EU regulatory process for the assessment of biosimilar medicines is rigorous and leads to the approval of safe and effective drugs.

Collection of post-approval Data should be envisioned.

EDUCATION

Concepts (and lexicon!) of comparability exercise, extrapolation and switching "sound" relatively new, though acknowledged.

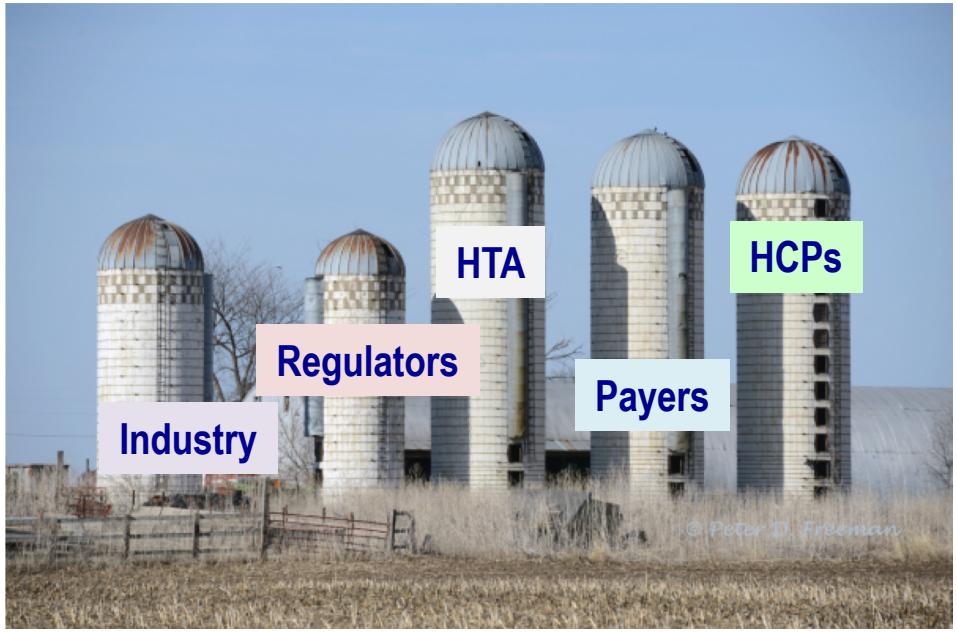
Guidance from regulators, learned societies, NCA, NGO is key

ENGAGEMENT

Interaction and collaboration among HCPs and with "other bodies" is required for the safe and successful implementation of biosimilars.

It's up to us!

SUCCESSFUL IMPLEMENTATION

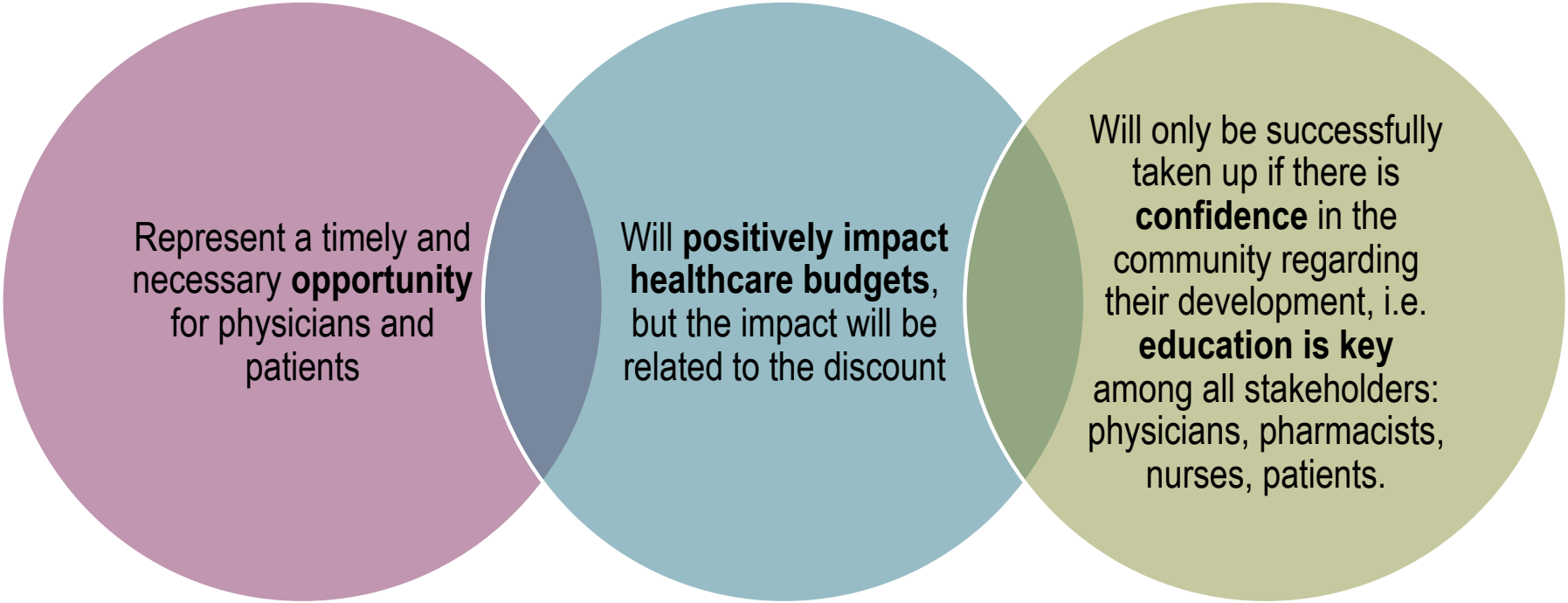


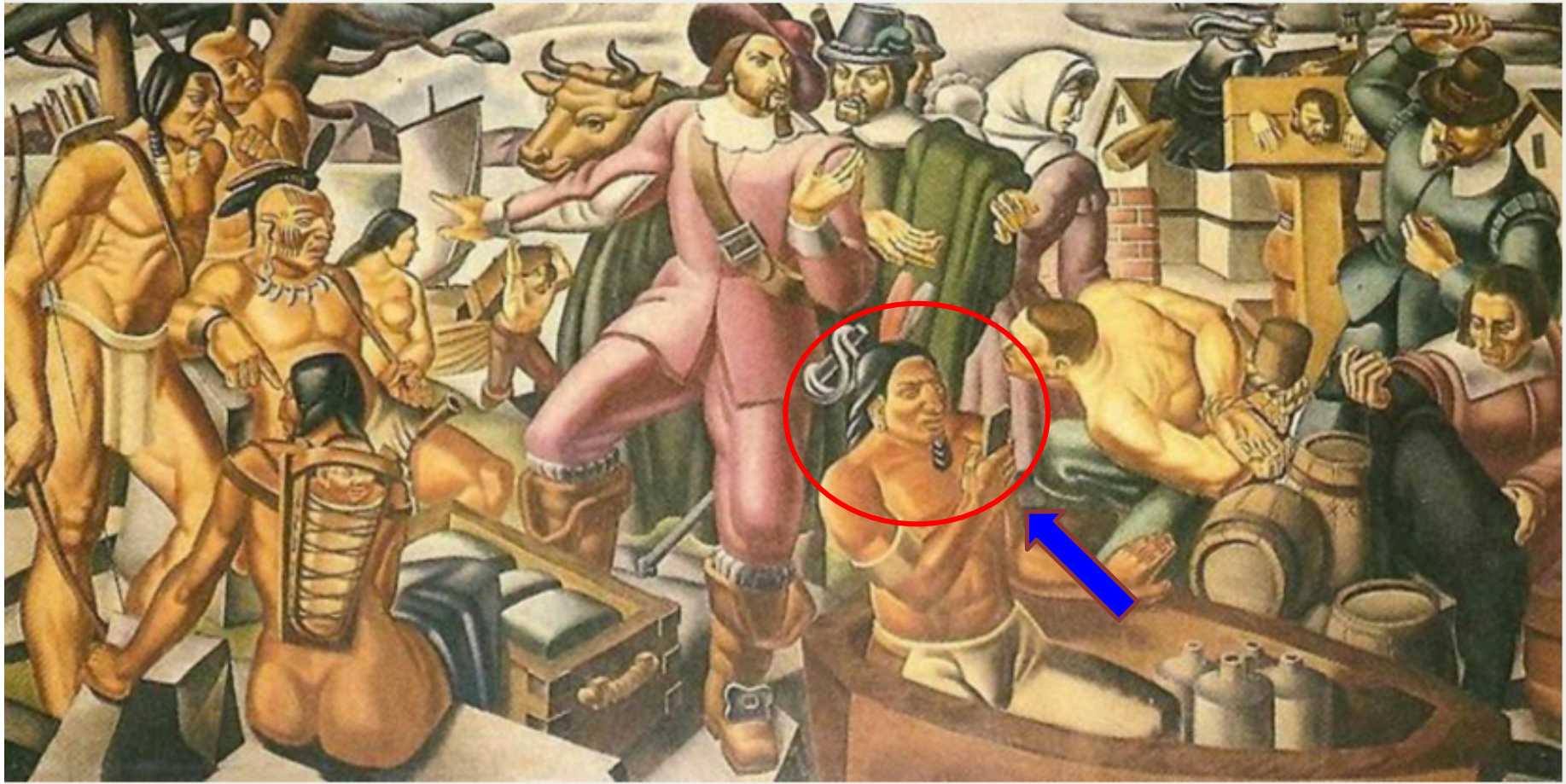
From SILOS to POWER STATION

Comprehensive strategy of evidence generation

Conclusions

Biosimilars for moAbs in oncology…





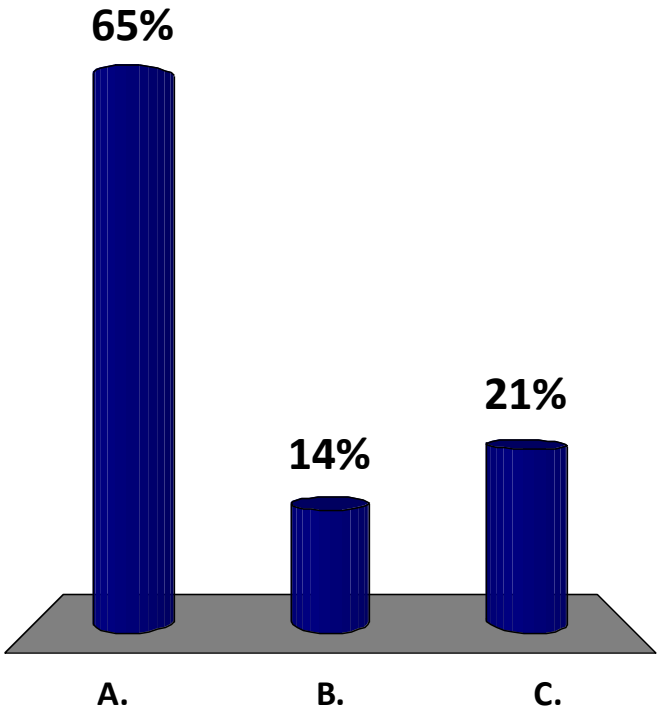
“Mr. Pynchon and the Settling of Springfield”. U. Romano ,1937

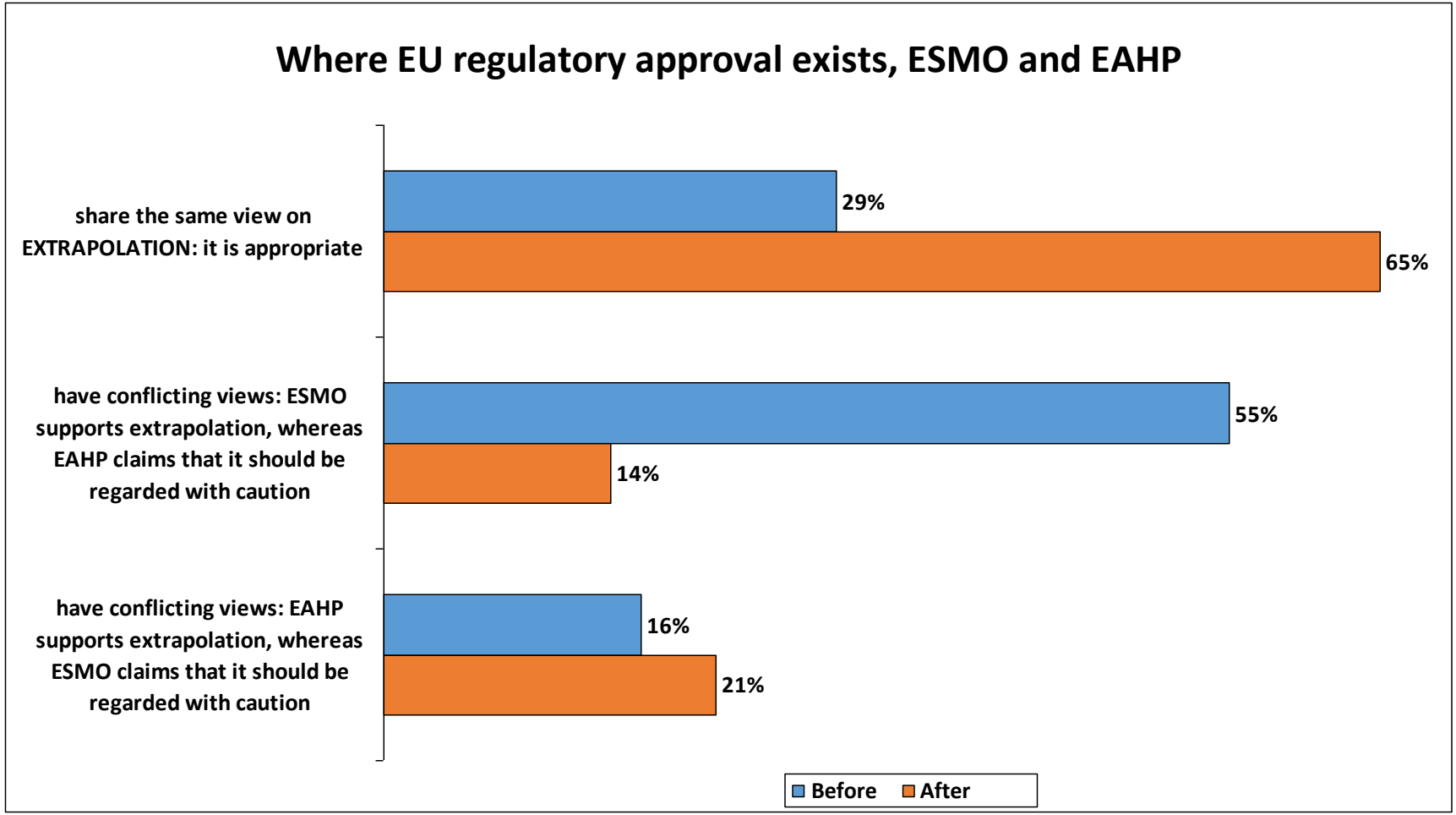
Where EU regulatory approval exists, ESMO and EAHP

A. share the same view on EXTRAPOLATION: it is appropriate

B. have conflicting views: ESMO supports extrapolation, whereas EAHP claims that it should be regarded with caution

C. have conflicting views: EAHP supports extrapolation, whereas ESMO claims that it should be regarded with caution



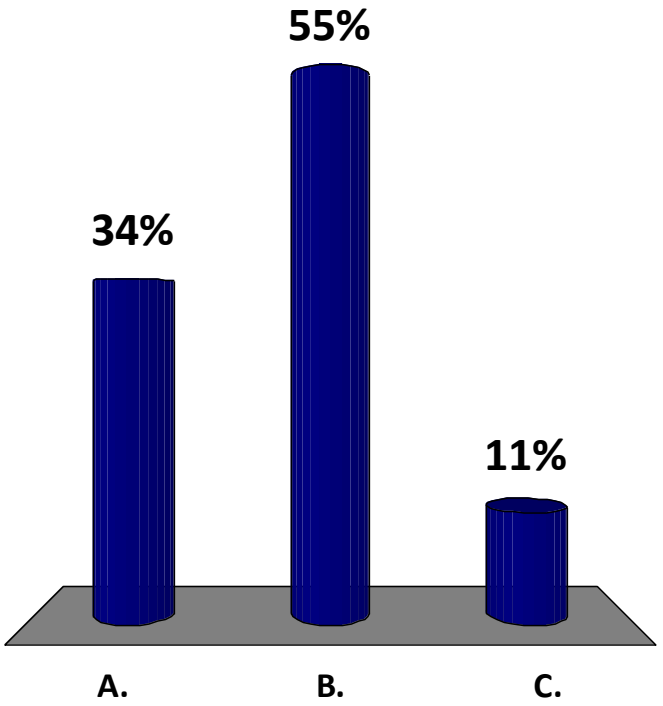

Where EU regulatory approval exists, ESMO and EAHP
share the same view on EXTRAPOLATION: it is appropriate
29%
65%
have conflicting views: ESMO supports extrapolation, whereas EAHP claims that it should be regarded with caution
55%
14%
have conflicting views: EAHP supports extrapolation, whereas ESMO claims that it should be regarded with caution
16%
21%
Before
After

The regulatory processes for the assessment of biosimilars and the time for their regulatory approval at central (EMA) level

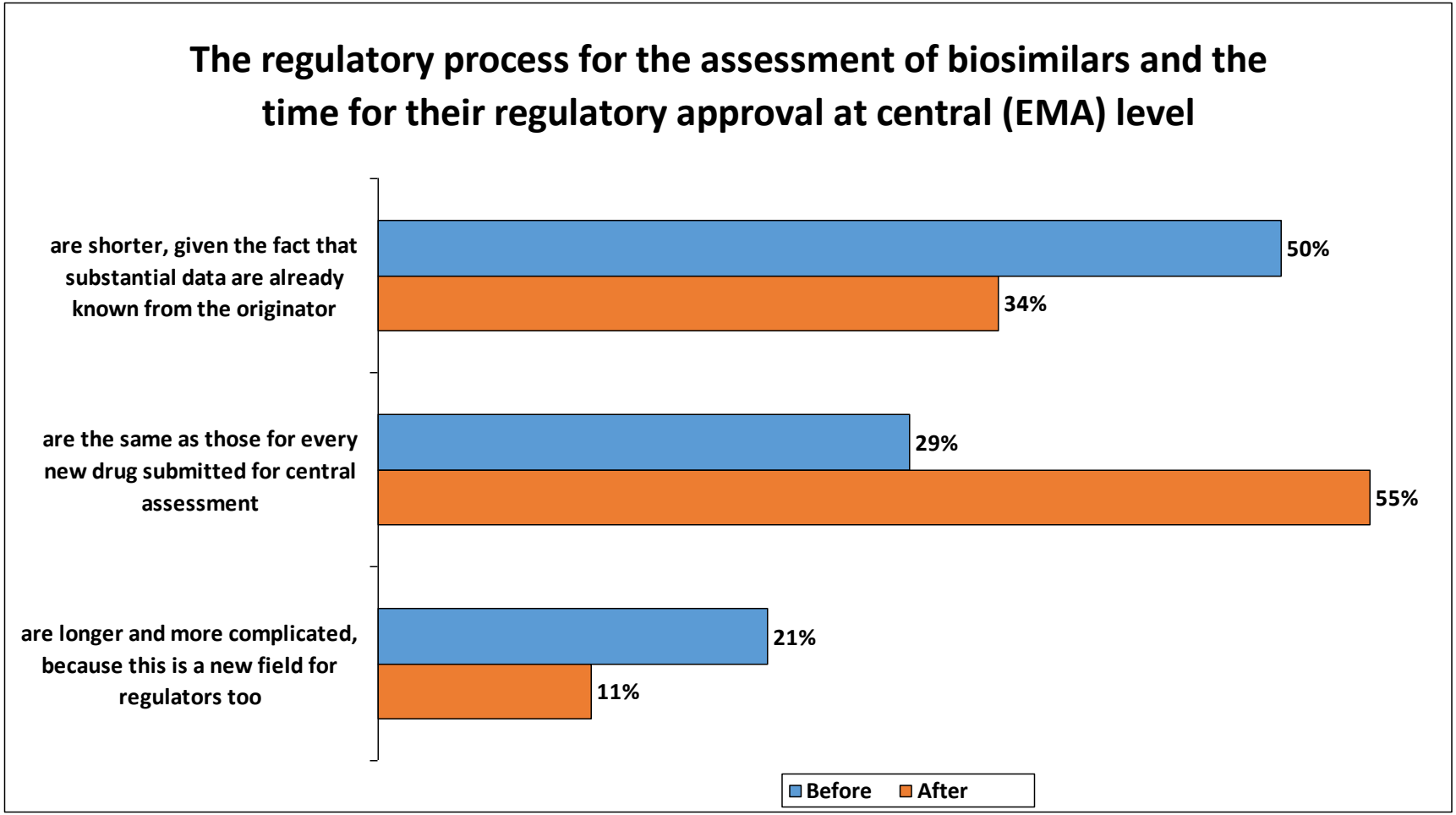
A. are shorter, given the fact that substantial data are already known from the originator

✓ B. are the same as those for every new drug submitted for central assessment

C. are longer and more complicated, because this is a new field for regulators too



The regulatory process for the assessment of biosimilars and the time for their regulatory approval at central (EMA) level

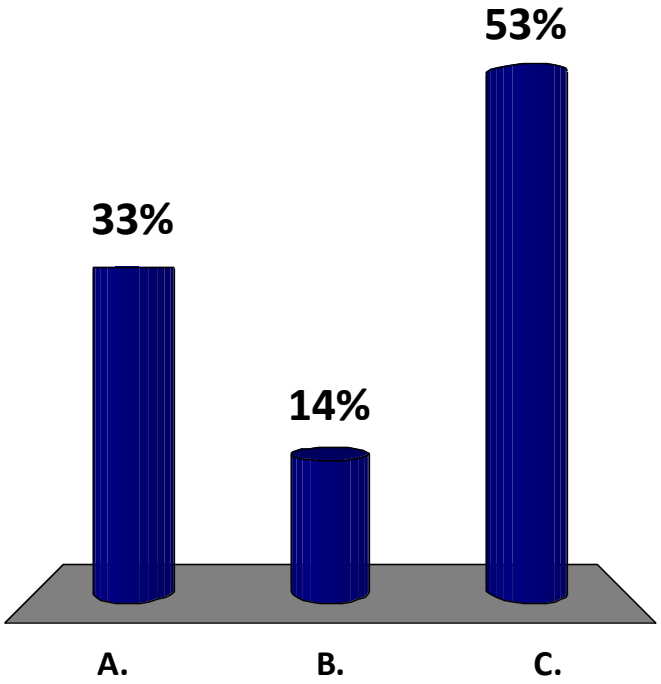


Where EU regulatory approval exists, ESMO and EAHP

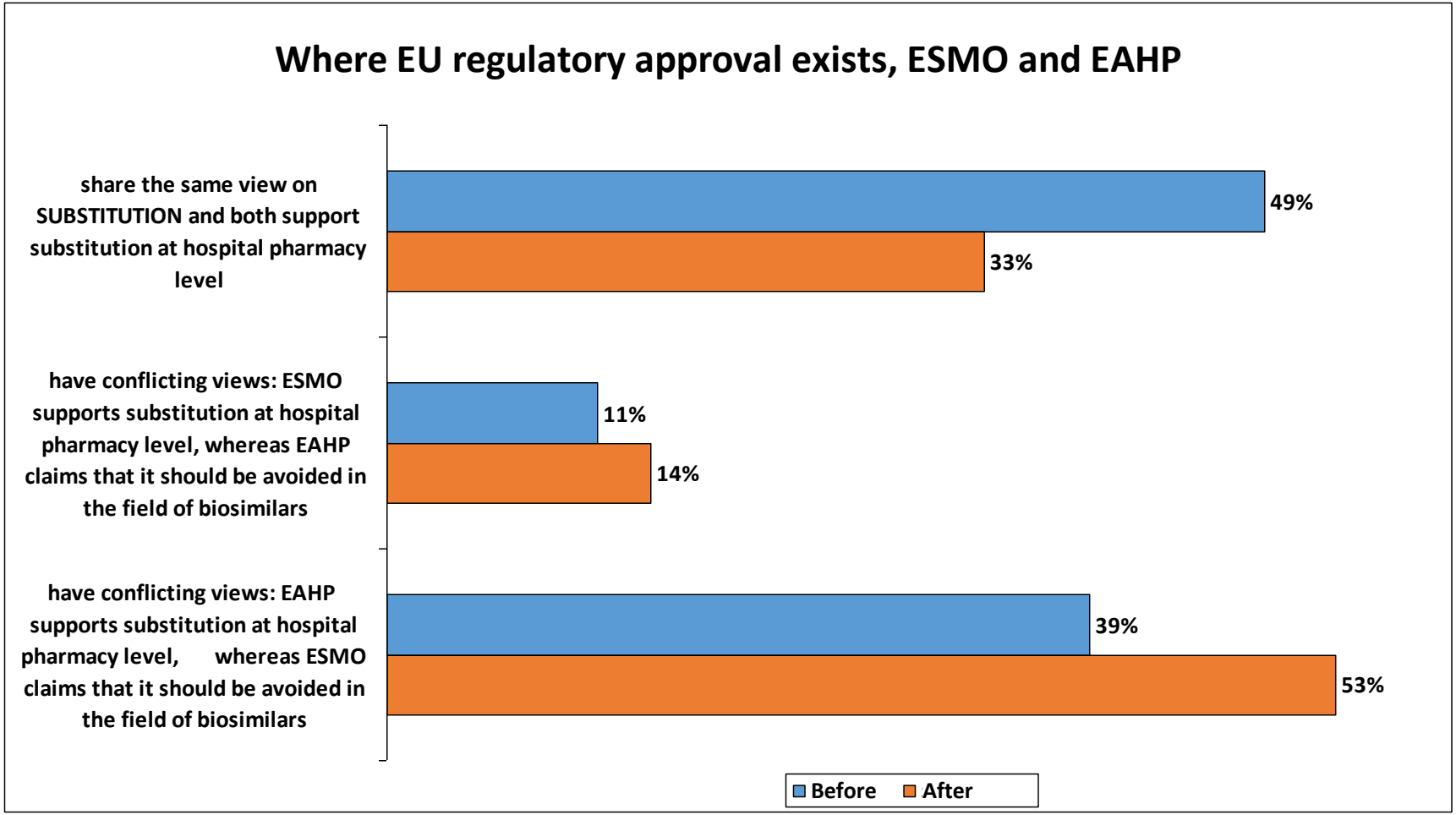
A. share the same view on SUBSTITUTION and both support substitution at hospital pharmacy level

B. have conflicting views: ESMO supports substitution at hospital pharmacy level, whereas EAHP claims that it should be avoided in the field of biosimilars

✓ C. have conflicting views: EAHP supports substitution at hospital pharmacy level, whereas ESMO claims that it should be avoided in the field of biosimilars



Where EU regulatory approval exists, ESMO and EAHP



Sample of questions heard around the hospital aisles

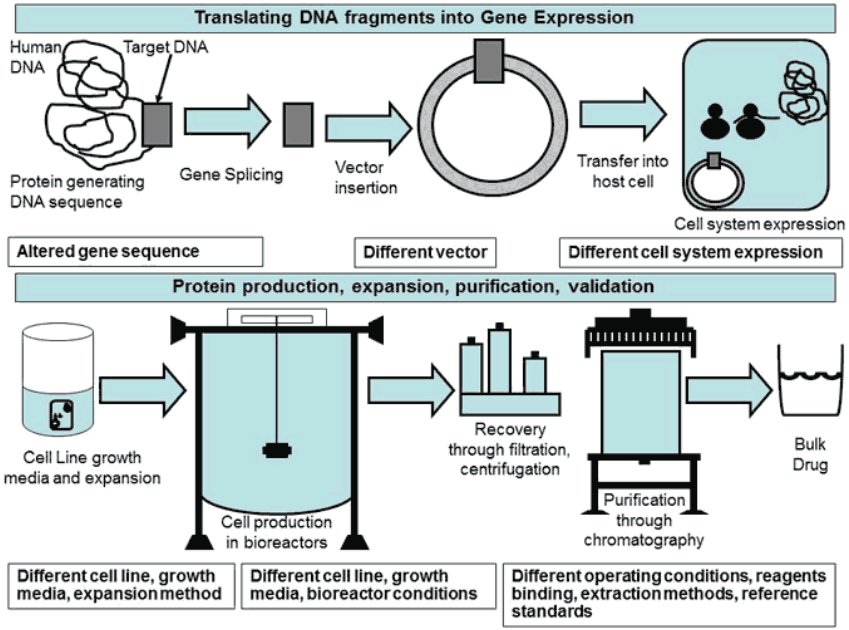
-The drug is the process
Oldie, but goodie….

-How the equivalence margin is chosen?
-How much of variability can we tolerate?
Am I putting my patients at risk?

-Are regulators using the same criteria to assess a biosimilar?
Consistency among regulators

-Concerns about the interaction of biosimilars with other moAb (steric hindrance, binding of the ligand), when co-administered (eg for metastatic breast cancer, the combination of pertuzumab and trastuzumab
This is easily addressed and may offer reassurance

Changes of originator biologicals are well known



Changes in the manufacturing process after approval include

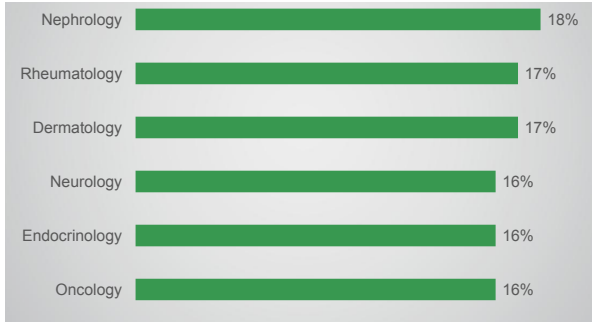
- -Supplier of cell culture media
- -New purification methods
- -New manufacturing sites

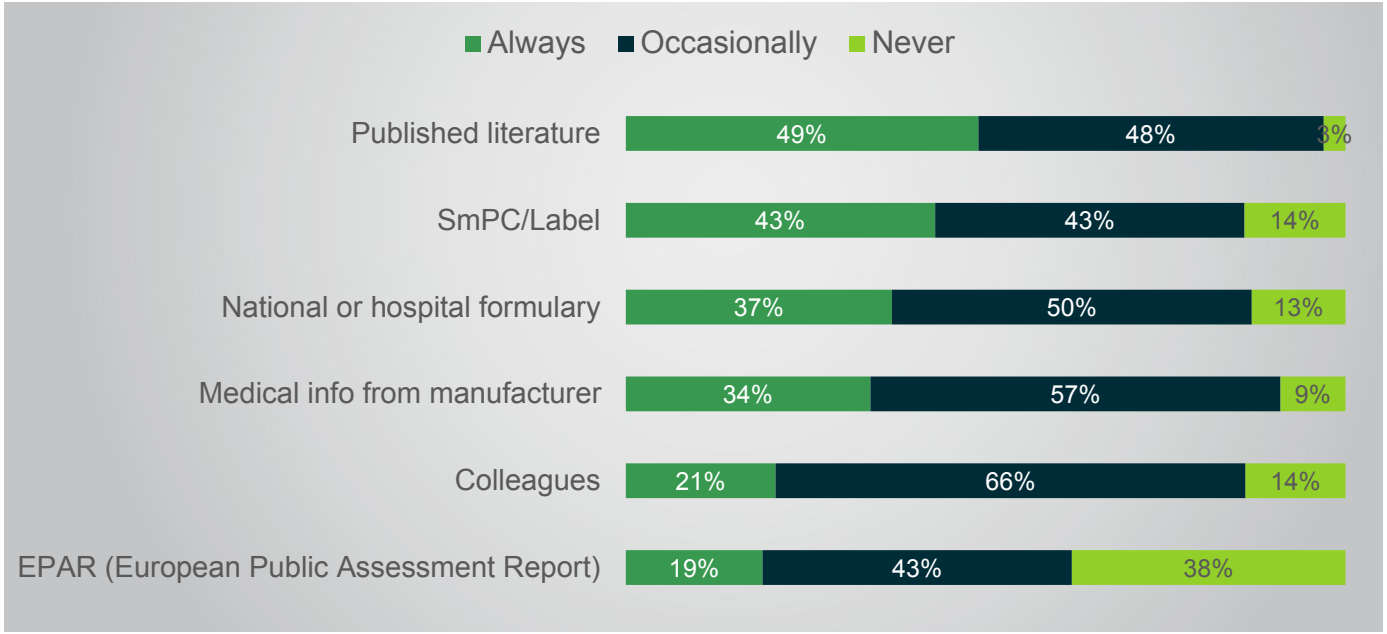
Product changes are closely monitored by regulators

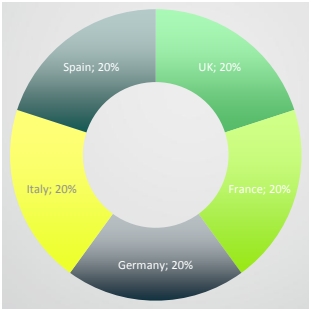
When the manufacturing process of the originator changes (type II variation) new data on safety and efficacy related to the new process are NOT requested

EUROPEAN PHYSICIANS SURVEY ON BIOSIMILARS

Sources used to learn about a medicine







(ASBM, Alliance for Safe Biological Medicines), 2013