Dichiarazione di trasparenza/interessi*

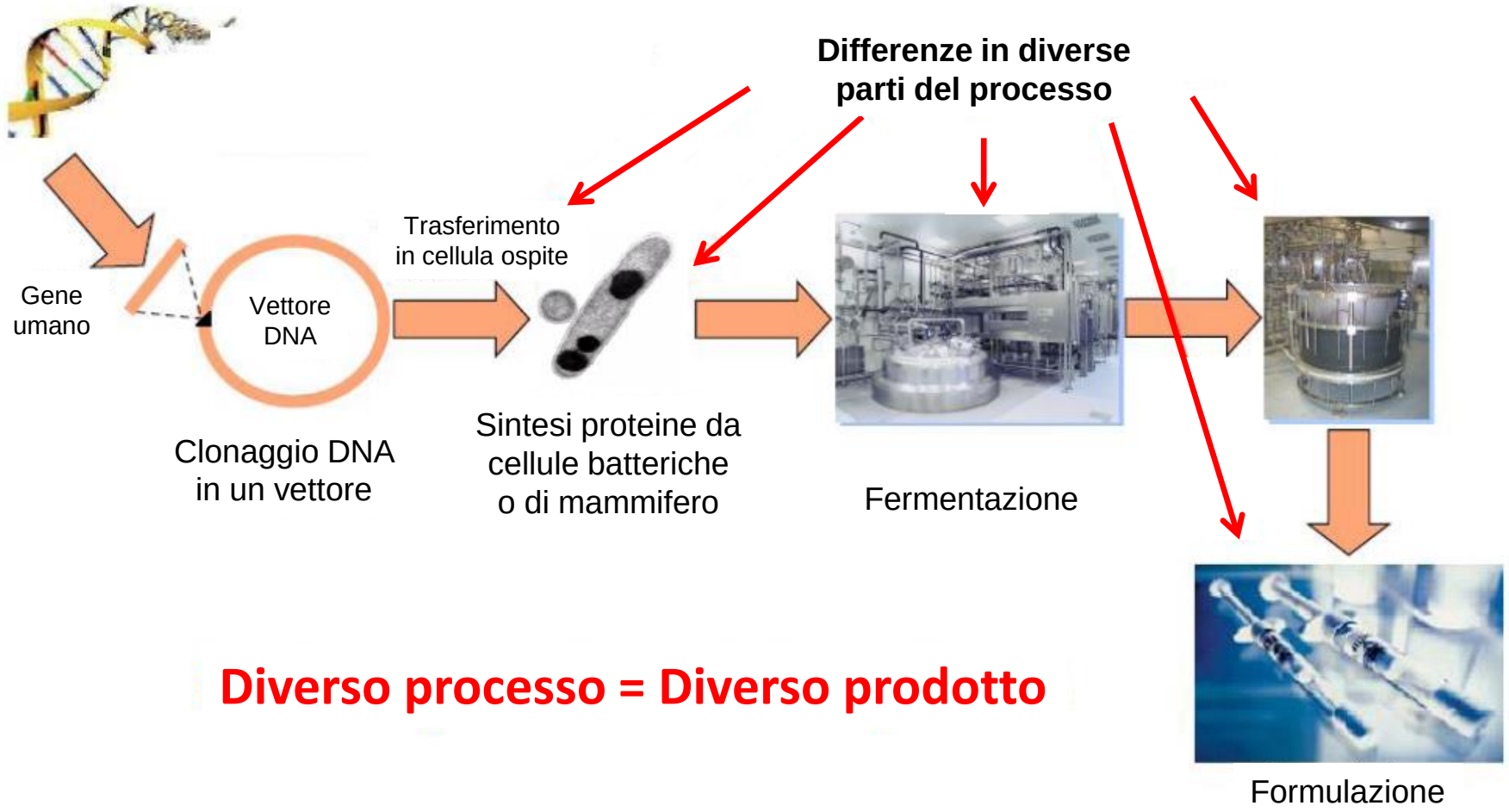
Le opinioni espresse in questa presentazione sono personali e non impegnano in alcun modo l'AIFA

Interessi nell' industria farmaceutica	NO	Attualmente	Precedenti 2 anni	Da oltre 2 a 5 anni precedenti	Oltre 5 anni precedenti (facoltativo)
Interessi diretti:					
Impiego in una società	X				
Consulenza per una società			X	X	X
Consulente strategico per una società	X				
Interessi finanziari	X				
Titolarità di un brevetto	X				
Interessi indiretti:					
Sperimentatore principale	X				
Sperimentatore	X				
Sovvenzioni o altri fondi finanziari			X	X	X

* Armando Genazzani, secondo il regolamento sul Conflitto di Interessi approvato dal CdA AIFA in data 25.03.2015 e pubblicato sulla Gazzetta Ufficiale del 15.05.2015 in accordo con la policy 0044 EMA/513078/2010 sulla gestione del conflitto di interessi dei membri dei Comitati Scientifici e degli esperti.

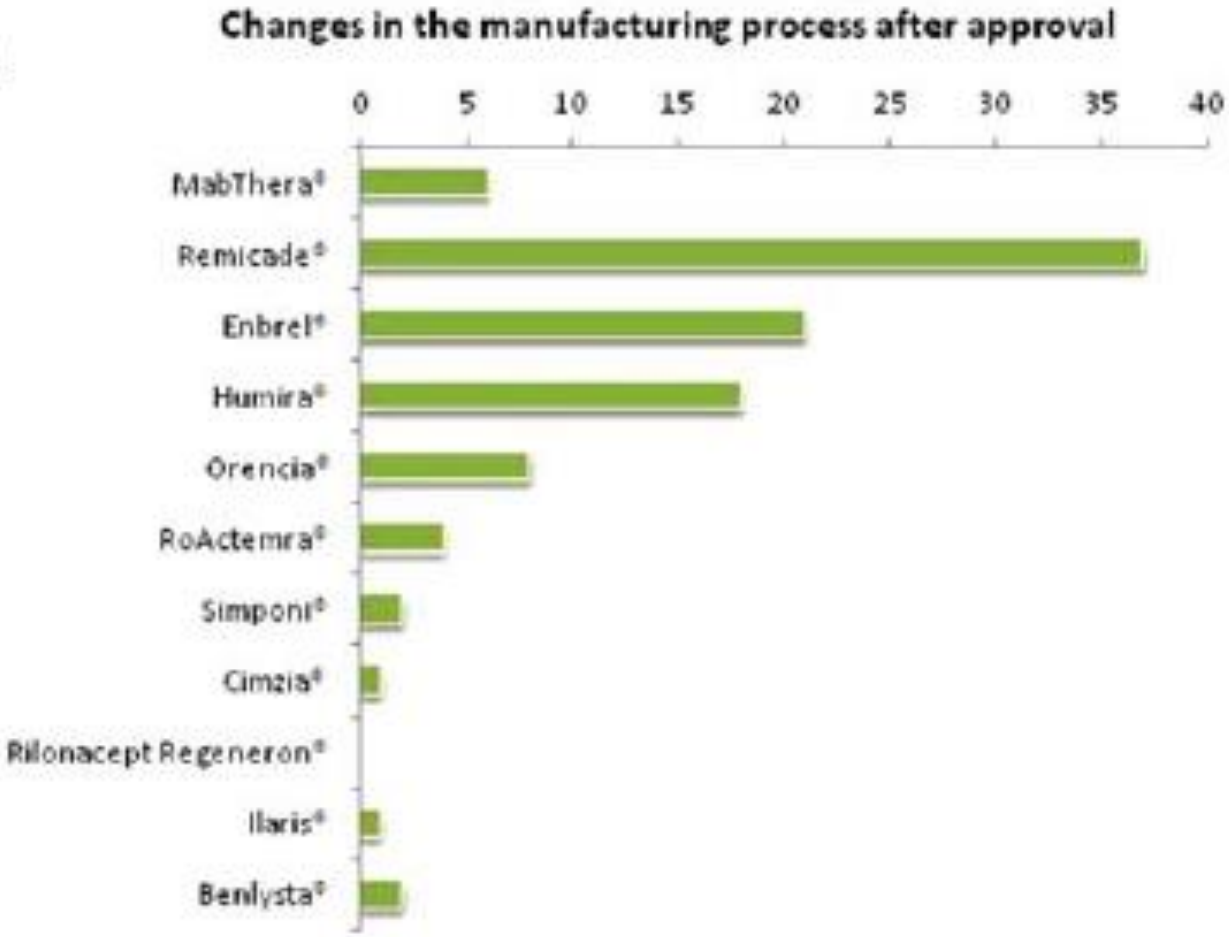
N.B. Per questo intervento non ricevo alcun compenso>.

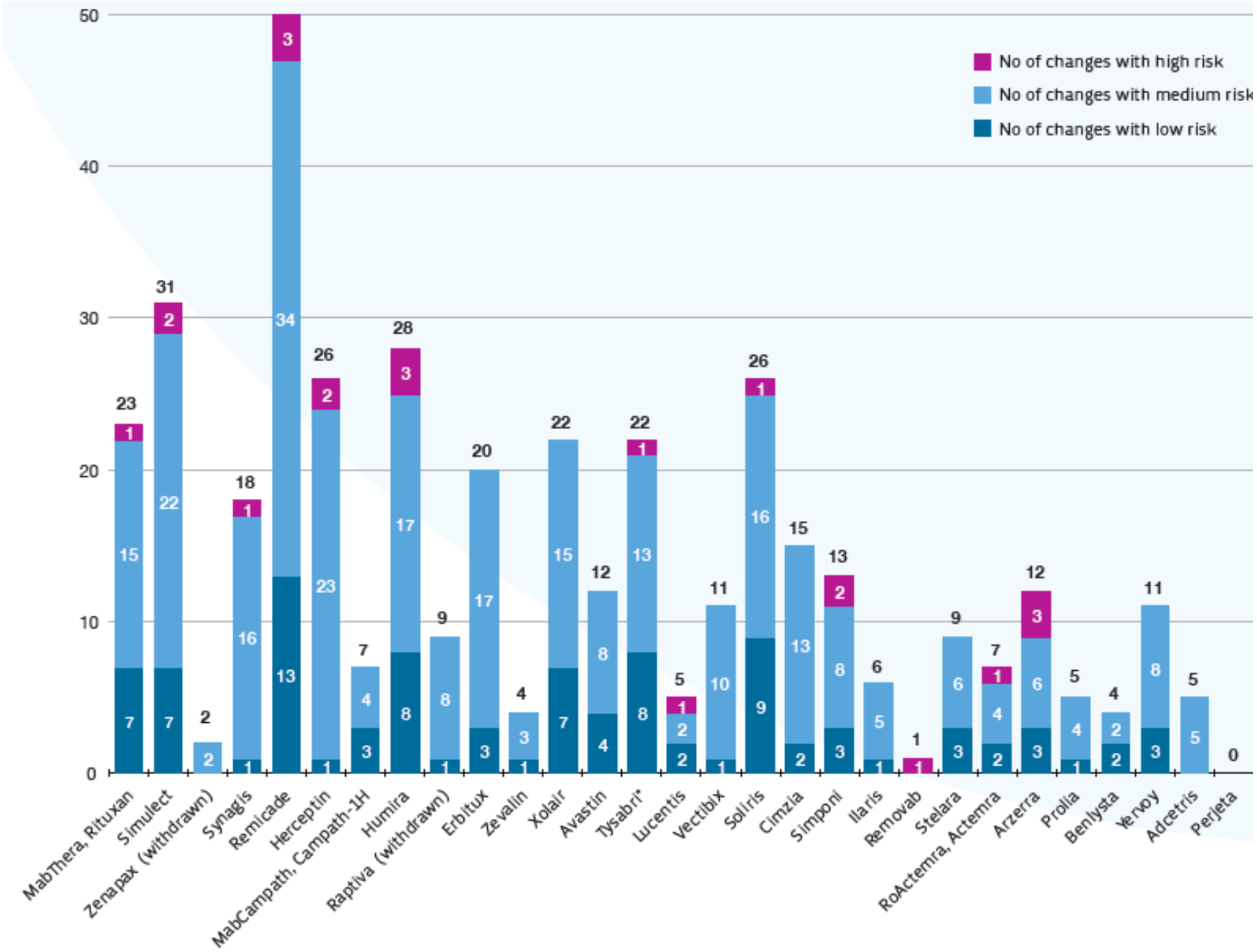
Il processo produttivo di un farmaco biologico è complesso

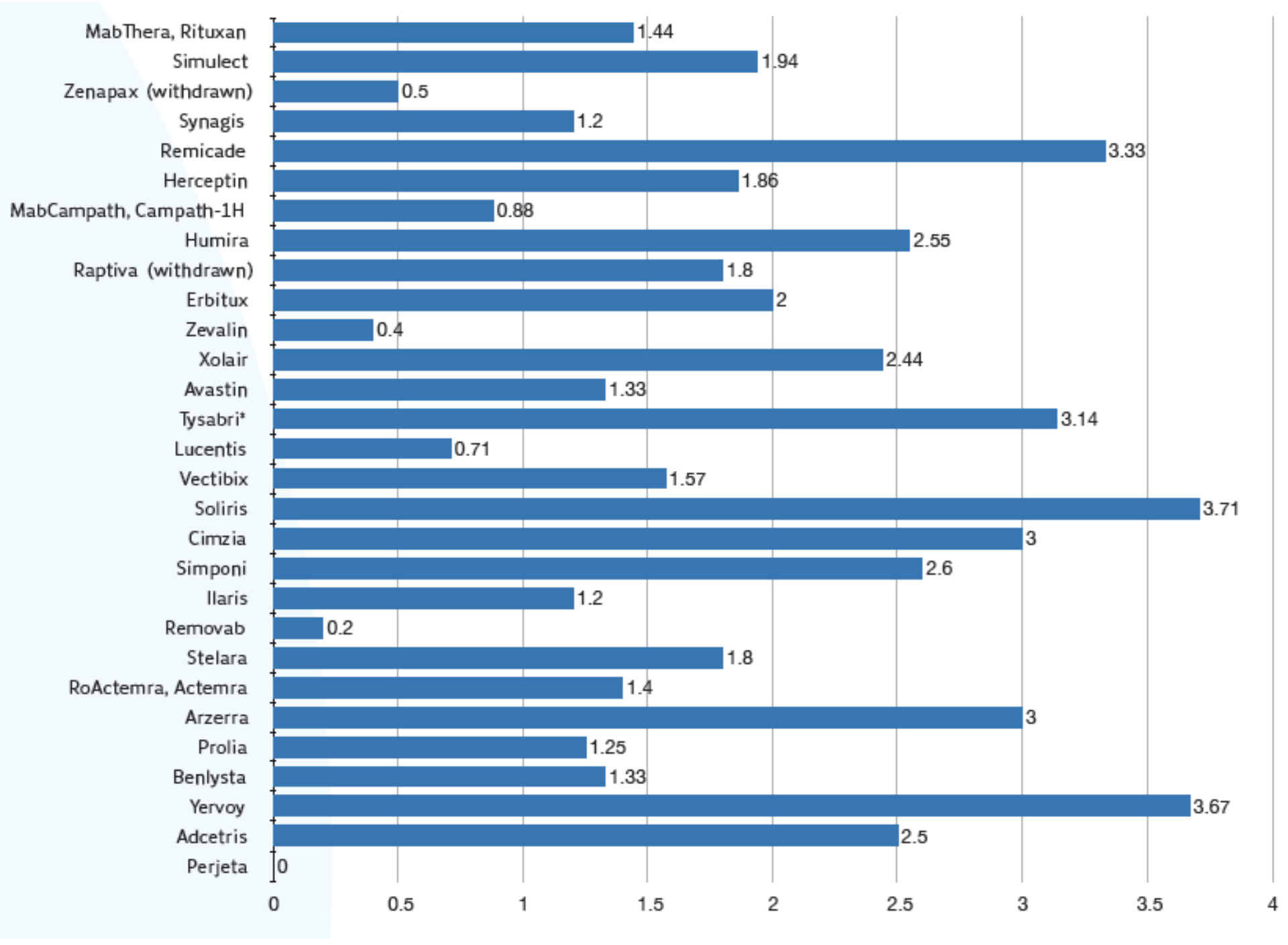


Diverso processo = Diverso prodotto

A

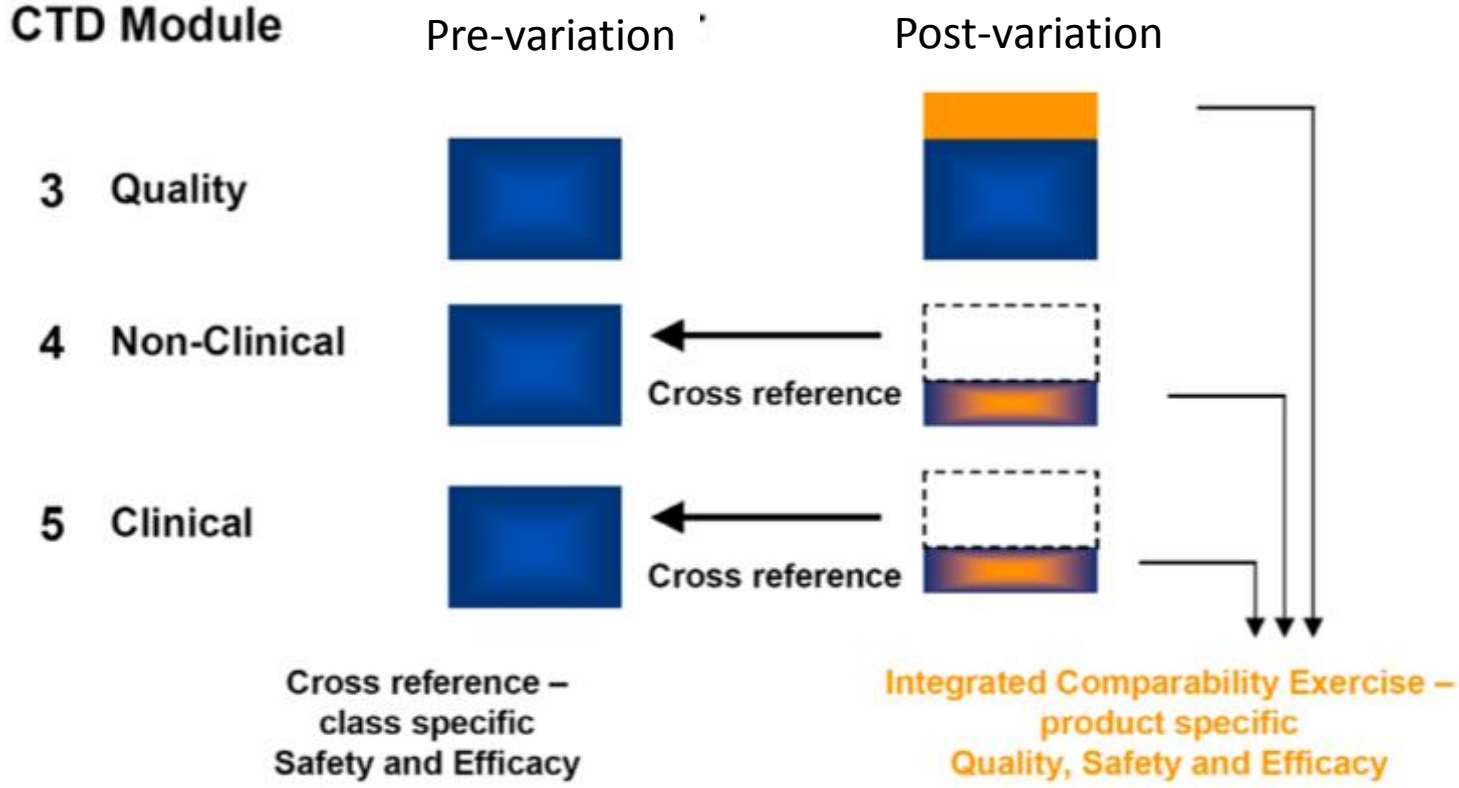

Changes in the manufacturing process after approval
0
5
10
15
20
25
30
35
40
MabThera®
Remicade®
Enbrel®
Humira®
Orencia®
RoActemra®
Simponi®
Cimzia®
Rilonacept Regeneron®
Ilaris®
Benlysta®


No of changes with high risk
No of changes with medium risk
No of changes with low risk
50
40
30
20
10
0
MabThera, Rituxan
Simulect
Zenapax (withdrawn)
Synagis
Remicade
Herceptin
MabCampath, Campath-1H
Humira
Raptiva (withdrawn)
Erbitux
Zevalin
Xolair
Avastin
Tysabri*
Lucentis
Vectibix
Soliris
Cimzia
Simponi
Ilaris
Removab
Stelara
RoActemra, Actemra
Arzerra
Prolia
Benlysta
Yervoy
Adcetris
Perjeta


MabThera, Rituxan
1.44
Simulect
1.94
Zenapax (withdrawn)
0.5
Synagis
1.2
Remicade
3.33
Herceptin
1.86
MabCampath, Campath-1H
0.88
Humira
2.55
Raptiva (withdrawn)
1.8
Erbitux
2
Zevalin
0.4
Xolair
2.44
Avastin
1.33
Tysabri*
3.14
Lucentis
0.71
Vectibix
1.57
Soliris
3.71
Cimzia
3
Simponi
2.6
Ilaris
1.2
Removab
0.2
Stelara
1.8
RoActemra, Actemra
1.4
Arzerra
3
Prolia
1.25
Benlysta
1.33
Yervoy
3.67
Adcetris
2.5
Perjeta
0
0
0.5
1
1.5
2
2.5
3
3.5
4

1) Farmaci biotecnologici prodotti con processi diversi saranno diversi tra loro (*the process is the product and the product is the process*)
2) Piccole differenze in un prodotto biotecnologico possono portare a grandi differenze cliniche e grandi differenze in un prodotto biotecnologico possono portare a nessuna differenza clinica.

Stepwise comparability approach Q → NC → C



European Medicines Agency

June 2005
CPMP/ICH/5721/03

ICH Topic Q 5 E
Comparability of Biotechnological/Biological Products

Step 5

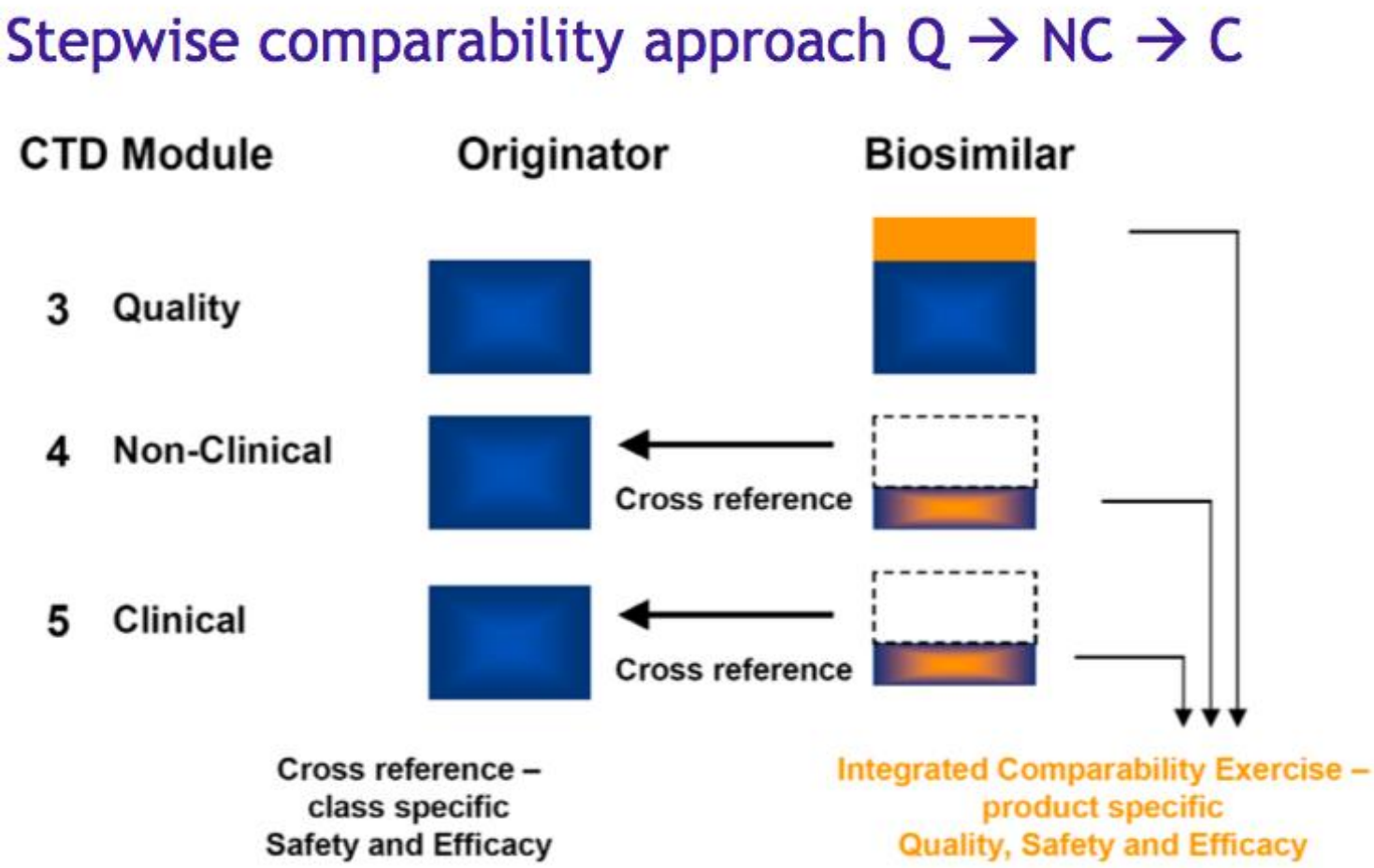
NOTE FOR GUIDANCE ON BIOTECHNOLOGICAL/BIOLOGICAL PRODUCTS SUBJECT TO CHANGES IN THEIR MANUFACTURING PROCESS
(CPMP/ICH/5721/03)

TRANSMISSION TO CHMP	November 2003
TRANSMISSION TO INTERESTED PARTIES	November 2003
DEADLINE FOR COMMENTS	May 2004
FINAL APPROVAL BY CHMP	December 2004
DATE FOR COMING INTO OPERATION	June 2005

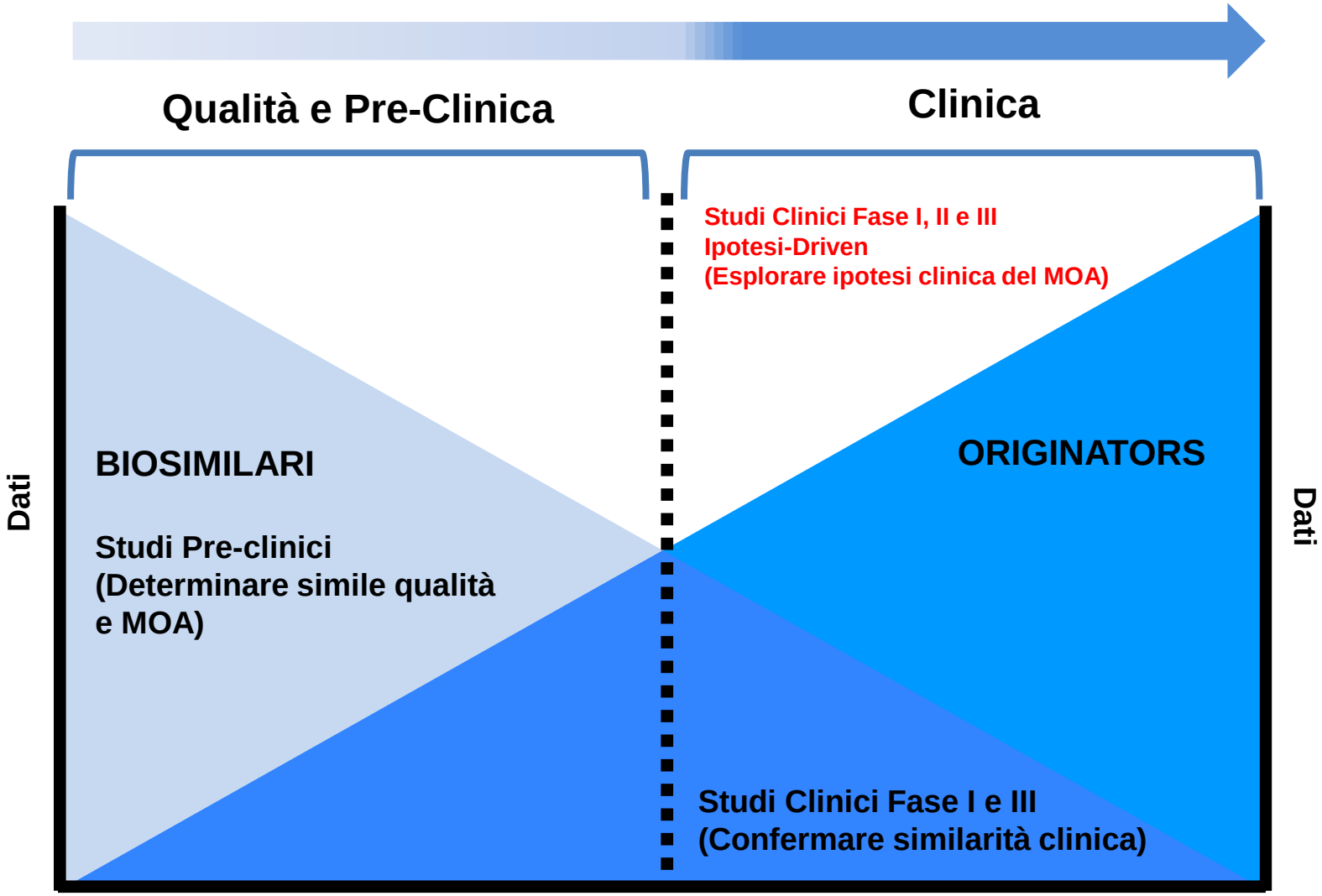
The goal of the comparability exercise is to ensure the quality, safety and efficacy of drug product produced by a changed manufacturing process, through collection and evaluation of the relevant data to determine whether there might be any adverse impact on the drug product due to the manufacturing process changes.

The demonstration of comparability does not necessarily mean that the quality attributes of the pre-change and post-change product are identical, but that they are highly similar and that the existing knowledge is sufficiently predictive to ensure that any differences in quality attributes have no adverse impact upon safety or efficacy of the drug product.

1) Farmaci biotecnologici prodotti con processi diversi saranno diversi tra loro (*the process is the product and the product is the process*)
2) Piccole differenze in un prodotto biotecnologico possono portare a grandi differenze cliniche e grandi differenze in un prodotto biotecnologico possono portare a nessuna differenza clinica.



Biosimilari e Originator: basi scientifiche



Modificata da Schneider CK et al., Nat Biotechnol 30, 2012

My personal perspective

- It is not a question of evaluating single agents, but a question of accepting or not accepting the methodology of comparability and of trusting regulatory authorities;
- Comparability in biological therapies is everywhere.
- Many new compounds have nowadays lower levels of evidence compared to biosimilars (obviously, there are no alternatives in these circumstances);
- At present, the following biosimilars are available: somatropin, epoetin alpha, filgrastim, infliximab, etanercept, insulin glargine.
- From the previous session (only MM): first-line lenalidomide, carfilzomib, daratumumab, panabinostat… are coming. Also. combinations, sequential treatments and significantly longer treatments. Decisions on what <u>we want</u> are warranted.