Review: BIOSIMILARS

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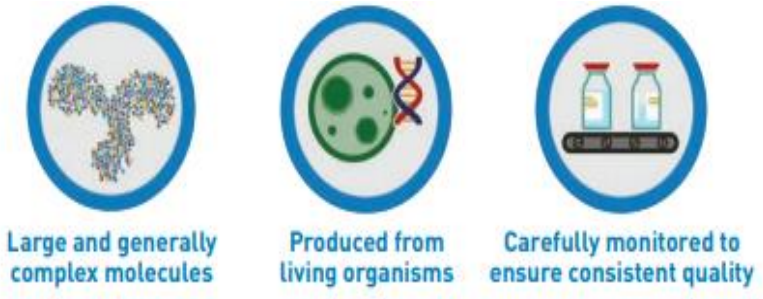
Biologics Price Competition and Innovation Act 2009 (BPCI Act)

- Created an abbreviated licensure pathway
- Defined how a biological product can be called biosimilar
- Set standards for determining interchangeability
- Established 12 year period of exclusivity for the initial reference product
- Established exclusivity period for first biosimilar determined to be interchangeable
- Defined incentives to encourage pediatric studies

Terms to Know

- Biological product
  - Product that is produced in a living system (i.e. microorganism, plant cell or animal cell)
  - Generally are large, complex molecules
  - Types of biological products include therapeutic proteins (e.g. filgrastim); monoclonal antibodies (e.g. Humira); and vaccines



- Reference product
  - Biological product already approved by FDA, against which a proposed biosimilar is compared

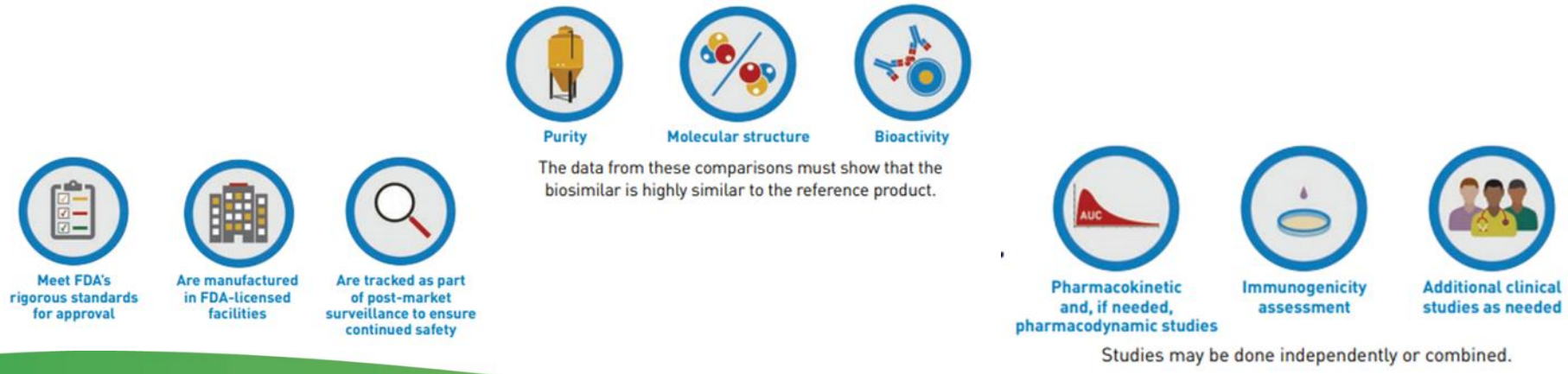
Terms cont.

- Biosimilar product
  - Biological product that is “highly similar” to reference product
    - Determined by extensive analysis of the structure and function of both reference and proposed biosimilar product
  - Has no “clinically meaningful” differences from the reference product
    - Does not differ greatly from the reference product in terms of safety, purity and potency

- Interchangeable product
  - Biosimilar product that produces the same clinical result as the reference product in any given patient
  - Safety and efficacy of switching between the reference and interchangeable product has been evaluated

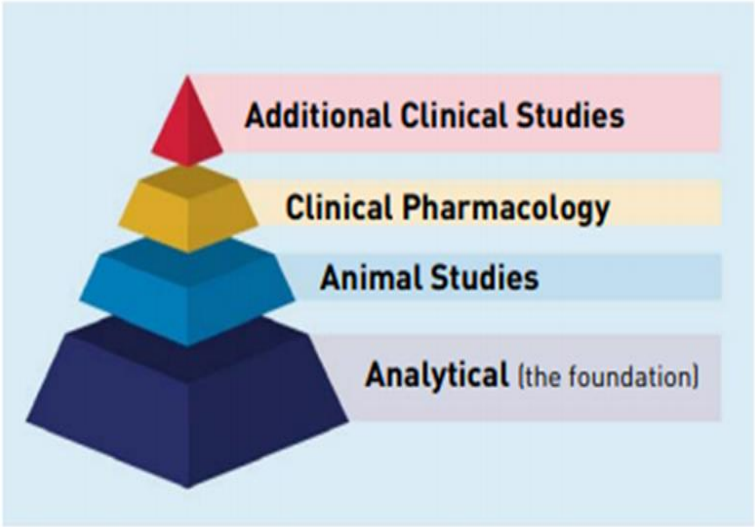
Biosimilar Approval Process

- Manufacturer of proposed biosimilar product gives extensive data comparing the proposed product to the reference product
  - Given data does not show the same full profile of nonclinical and clinical data as the reference product; rather demonstrates that the proposed product is highly similar and does not have clinically significant difference from the reference



Approval Process cont.

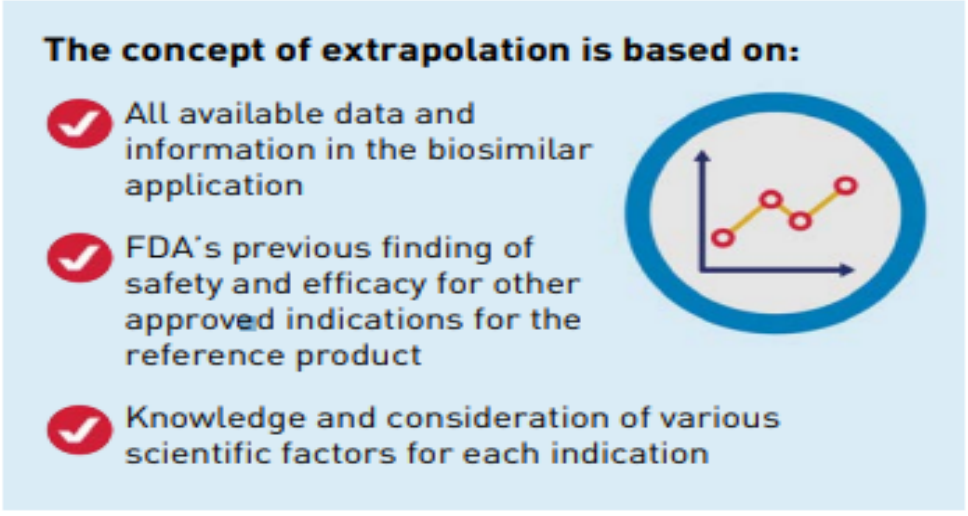
- Includes data from
  - Analytical studies
  - Animal studies
  - Clinical study/studies
- If requesting approval for interchangeable they also have to include data that show
  - Interchangeable product is expected to produce the same clinical result as reference in any given patient
  - If administered more than once, switching between products does not show a change in the safety or efficacy of the treatment



When considering licensure of a biosimilar product, FDA reviews the totality of the data and information, including the foundation of detailed analytical (structural and functional) characterization, animal studies if necessary, then moving on to clinical pharmacology studies and, as needed, other comparative clinical studies.

Extrapolation

- Extrapolation is a critical component of the abbreviated pathway to approval set in motion by the BCIP Act.
- A biosimilar can be used for an indication that the reference product has FDA approval for even though the biosimilar was not necessarily studied for said indication
  - Data needed to support extrapolation are determined with input from FDA to the product manufacturer during the development process



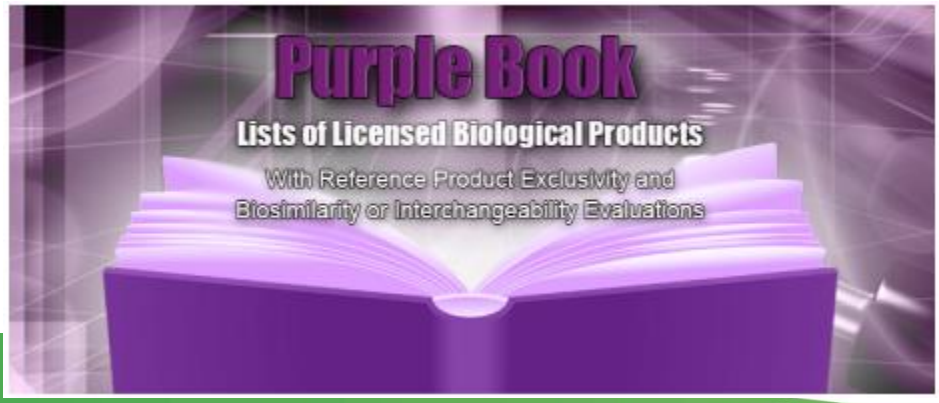
Importance of Abbreviated Approval Pathway

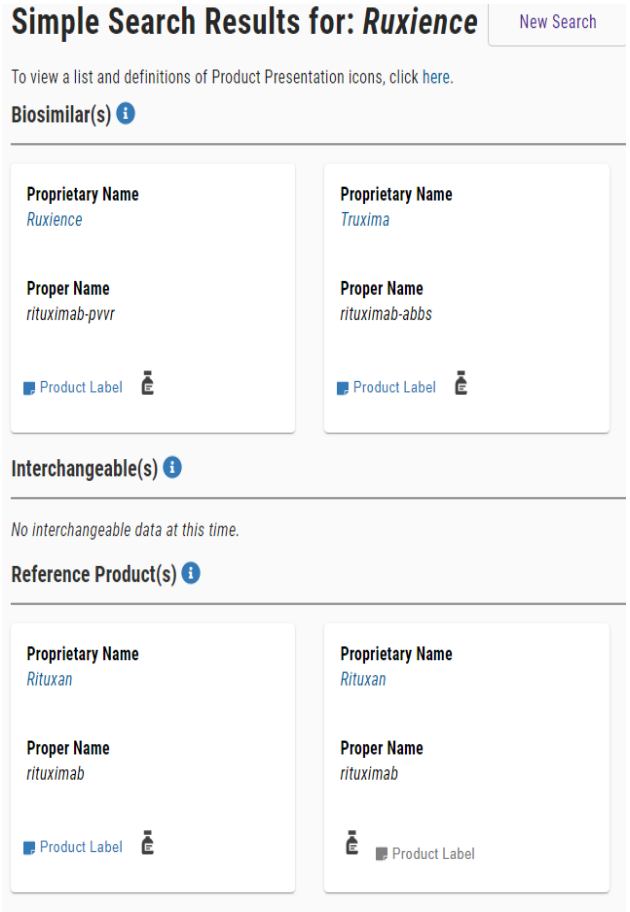
Trillium Community Health Plan®

- Allows public to have greater access to safe and effective biological products
- Allows for more treatment options and potential for cost savings
- Allows for the potential for faster, lower cost drug development
- The abbreviated approval pathway *does not* mean that there are lower approval standards for biosimilar and interchangeable products

The “Purple Book”

- An online database that gives information on whether a biological is a reference product, biosimilar or interchangeable product to assist with prescribing, substitution, and interchangeability.
- https://purplebooksearch.fda.gov/





Biologics, Biosimilar and Interchangeable Products

Trillium Community Health Plan

Reference Product	Biosimilar (s)	Approval date	Interchageable(s)
Avastin (bevacizumab) J9035	Mvasi (bevacizumab-awwb) Q5107	09/2017	None at this time
	Zirabev (bevacizumab-bvzr) Q5118	06/2019	
Enbrel (etanercept) J1438	Erelzi/Erelzi Sensoready (etanercept-szzs)	08/2016	None at this time
	Eticovo (etantercept-ykro)	04/2019	
Epogen (epoetin-alfa) J0885	Retacrit (epoetin alfa-epbx) Q5106	05/2018	None at this time
Herceptin (trastuzumab) J9355	Herzuma (trastuzumab-pkrb) Q5113	12/2018	None at this time
	Kanjinti (trastuzumab-anns) Q5117	06/2019	
	Ogivri (trastuzumab-dkst) Q5114	12/2017	
	Ontruzant (trastuzumab-dttb) Q5112	01/2019	
	Trazimera (trastuzumab-qyyp) Q5116	03/2019	

Reference Product	Biosimilar (s)	Approval date	Interchageable(s)
Humira (adalimumab) J0135	Abrilada (adalimumab-afzb)	11/2019	None at this time
	Amjevita (adalimumab-atto)	09/2016	
	Cyltezo (adalimumab-adbm)	08/2017	
	Hadlima (adalimumab-bwwd)	07/2019	
	Hulio (adalimumab-fkjp)	06/2020	
	Hyrimoz (adalimumab-adaz)	10/2018	
Neulasta (pegfilgrastim) Neulasta Onpro J2505	Fulphila (pegfilgrastim-jmdb) Q5108	06/2018	None at this time
	Nyvepria (pegfilgrastim-apgf)	06/2020	
	Udenyca (pegfilgrastim-cbqv) Q5111	11/2018	
	Ziextenzo (pegfilgrastim-bmez) Q5120	11/2019	

Reference Product	Biosimilar (s)	Approval date	Interchageable(s)
Neupogen (filgrastim) J1442	Nivestym (filgrastim-aafi) Q5110	07/2018	None at this time
	Zarxio (filgrastim-sndz) Q5101	03/2015	
Remicade (infliximab) J1745	Avsola (infliximab-axxq) Q5121	12/2019	None at this time
	Inflectra (infliximab-dyyb) Q5103	04/2016	
	Ixifi (infliximab-qbtx) Q5109	12/2017	
	Renflexis (infliximab-adba) Q5104	05/2017	
Rituxan (rituximab) J9312	Ruxience (rituximab-pvvr) Q5119		None at this time
	Truxima (rituximab-abbs) Q5115		

Pharmacy Claims

- Biosimilar medications are less utilized than the reference biological products.
- Enbrel and Humira biosimilar products are not in use in the US yet however they are FDA-approved.
- Recent changes to criteria are steering toward biosimilar product preference

Medication	Number of Claims (1 year)
Humira (adalimumab)	719
Enbrel (etanercept)	275
Epogen (epoetin alfa)	3
Retacrit (epoetin alfa-epbx)	0
Zarxio (filgrastim-sndz)	8
Neulasta (pegfilgrastim)	3

Medical Claims

Medication	Number of Claims (1 year)
Epogen (epoetin alfa)	56
Retacrit (epoetin alfa –epbx)	36
Neupogen (filgrastim)	1
Zarxio (filgrastim-sndz)	90
Avastin (bevacizumab)	615
Mvasi (bevacizumab-awwb)	8
Neulasta (pegfilgrastim)	65
Remicade (infliximab)	102
Inflectra (infliximab-dyyb)	141
Rituxan (rituximab)	83
Truxima (rituximab-abbs)	3
Herceptin (trastuzumab)	45

Questions, Comments, Concerns ?

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