Data Protection for Biologics: Balancing Innovation Incentives and Cost Savings

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What is Data Protection?

- Data protection is the period of time after approval before a biosimilar can enter with an abbreviated filing that relies on the innovator's safety and efficacy data
- Under Hatch-Waxman, data protection is 5 years for new chemical entities (plus an additional 2.5 years stay on generic entry for a challenged patent)
- Should it be longer for biologics?

Data Protection Periods for Biologics in US Bills and Europe

- Congressmen Inslee's bill provides for 12 years of data protection for biologics
- Congressman Waxman's bill allows for only 5 years of data protection for biologics
- European Union has 10 year data protection for both new biological and new chemical entities

How Are Biosimilars Different from Generic Drugs?

- Biologics are large complex molecules derived from cell cultures
- Biosimilars are expected to be similar but not identical to the innovator's product:

  "*Because of the variability and complexity of protein molecules, current limitations of analytical methods, and the difficulties in manufacturing a consistent product, it is unlikely that, for most proteins, a manufacturer of a follow-on protein product could demonstrate that its product is identical to an already approved product*."

Dr. Janet Woodcock, Director of the FDA

Biologics: Complex Products Produced From Living Materials

MW = 34,000

Epoetin: A Glycoprotein "Biologic" With 165 Amino Acid Residues Together With Complex Carbohydrate Structures That Determine Both Its Bioactivity And Potential Toxicity (Immunogenicity)

MW = 350

Ranitidine: A "Small Molecule" Drug

For every atom in ranitidine, epoetin has ca. 100 atoms.

Data Protection and Patents Have Complementary Roles

- Data protection recognizes substantial R&D investment is necessary after invention occurs and patents filed
- Effective patent life cannot be assessed until after FDA approval and patent litigation is resolved
- Data protection essentially provides additional market exclusivity under two circumstances
  - When development is particularly long
  - When biosimilars can circumvent innovator's patents
- Effect of patents on market exclusivity are unknown while data exclusivity provides greater certainty

Biosimilars and Patent Protection

- Patents are generally narrower in scope for biologics than for chemical entities
- Given differences in composition and manufacturing process, biosimilars may not infringe innovator's patents
- It is possible that biosimilars may be "different enough" to not infringe on patents, but "similar enough" to qualify for abbreviated approval pathway
- Data protection is a necessary incentive where patents are narrow, uncertain, or short in length

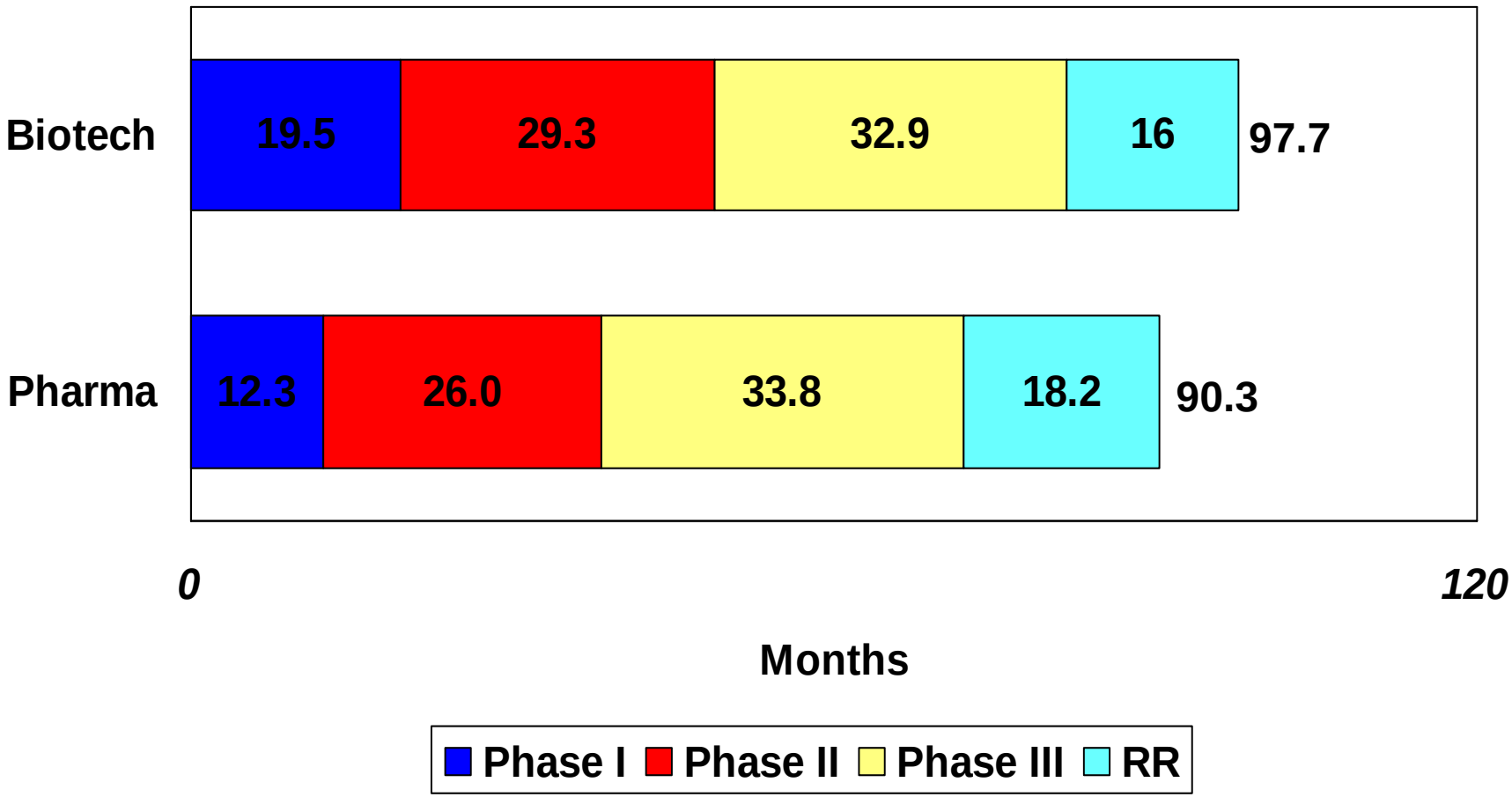
What Industry Characteristics Support a Significant Protection Period?

- When R&D investment is costly, risky, and lengthy in time
- When innovation has important spillover benefits to society
- New biologics satisfy these criteria

Biotech R&D is a Highly Risky Process

- Biologics focus on serious medical conditions like cancer, rheumatoid arthritis and multiple sclerosis
- Few successes must pay for many failures
- Biologics take longer on average to discover and develop than small molecules
- Plant investment costs are significantly higher compared to chemical drugs

Clinical Development and Approval Times



Source: DiMasi and Grabowski, *Managerial and Decision Economics*, 2007

VC Funding and Partnerships are Crucial in Biologics

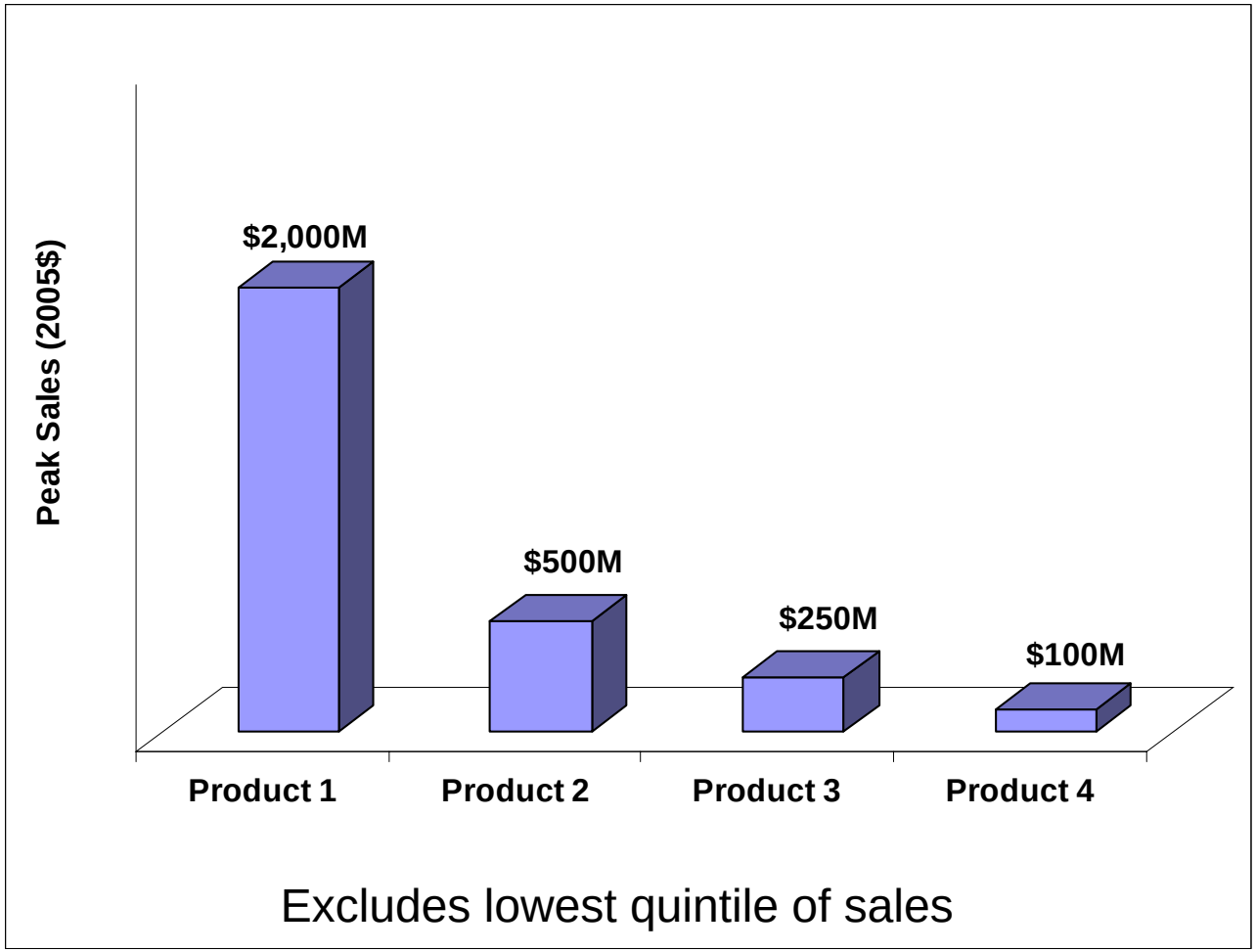
- VC backed firms estimated to have 40 percent of total employment in the biotech sector
- Most ventures are early stage, small, and fewer than 10 percent of companies have marketed products
- The prospects of short protection periods and rapid entry of biosimilars would raise risks to biotech investing in a sector already under pressure

What Is the Breakeven Lifetime for a Portfolio of Biotech Products?

- Representative data utilized on R&D costs and revenues for a portfolio of biotech products
- Original *Nature* article found a breakeven period of 12.9 to 16.2 years for model portfolio
- New analysis considers a range of assumptions on key parameters and data protection periods

Source: Grabowski, HG 2008 *Nature Reviews Drug Discovery* 7.6: 479-488.
Grabowski, Long, and Mortimer 2008 Duke University Working Paper

Model Portfolio Based on Sales Distribution for Established Biological Products



Source: Grabowski (2008)

Comments on Alternative Assumptions

- Innovator's market share erosion expected to be less in case of biosimilars than generic drugs
- Cost of capital and contribution margin vary across firms and products
- Various empirical studies are utilized to get a plausible range on these variables

Cost of Capital Estimates for the Biotechnology Industry

			Cost of Capital	
Source	**Sector/Group**	**Model**	**Nominal**	**Real**
Golec & Vernon (2008)	Biotech industry-wide	Fama-French	16.25%	12.75%
Ibbotson	Median	Fama-French	17.49%	14.07%
Grossman (2003)	Biotech with ≥ 1 drug approved Biotech drugs in phase II or III	CAPM CAPM	18.70% 27.40%	15.24% 23.69%
Myers and Shyam-Sunder (1995)	Medium-sized public firms "Small" biotech firms	CAPM CAPM	19%	14% 16%
Grabowski (2008)	Large biotech firms	CAPM		11.5%-12.5%

Contribution Margins for Public Biotech Firms

Company	Average Margin	Comments
Gilead Sciences, Inc	63.7%	Substantial small-molecule drug sales
Genentech, Inc	63.3%	
Amgen, Inc	60.4%	
Celgene Corp	50.0%	Substantial small-molecule drug sales
Genzyme Corp	44.4%	
Biogen Idec Corp	43.4%	
Chiron Corp	35.8%	Not included in Brill's sample
MedImmune, Inc.	33.6%	Not included in Brill's sample

Biosimilar Assumptions in Several Recent Studies

Source	Peak Biosimilar Penetration Rate	Basis	Biosimilar Price Discount (Relative to Pre-Entry Brand Price)
CBO (2008)	10% (year 1) to 35% (year 4)	Similar market situations	20% (year 1) to 40% (year 4)
Grabowski, et. al. (2007)	10 – 45%	Higher estimates correspond to complex small molecules	10% - 30% (year 1)
Express Scripts (2007)	49%	Therapeutic alternatives	25% (year 1)
Avalere Health (2007)	60% (largest markets)	Average small molecule generic drug penetration rates	20% year 1) to 51% (year 3)

Break-Even Results Under Alternative Data Exclusivity Periods

7-Year Data Exclusivity Period:

CoC	Contribution Margin 60%	50%	40%
11.5%	15.4	>50	>50
12.75%	>50	>50	>50
14.1%	>50	>50	>50

12-Year Data Exclusivity Period:

CoC	Contribution Margin 60%	50%	40%
11.5%	10.4	13.4	>50
12.75%	12.5	>50	>50
14.1%	>50	>50	>50

10-Year Data Exclusivity Period:

CoC	Contribution Margin 60%	50%	40%
11.5%	10.5	18.0	>50
12.75%	14.8	>50	>50
14.1%	>50	>50	>50

14-Year Data Exclusivity Period:

CoC	Contribution Margin 60%	50%	40%
11.5%	10.4	12.9	>50
12.75%	12.4	27.1	>50
14.1%	22.9	>50	>50

Key assumptions:
(1) Biosimilars capture 10% share of molecule in first year, increasing to 35% by the fourth year, per CBO.
(2) Innovator experiences price discount of 10% in first year of biosimilar entry, 20% after four years.
(3) All other assumptions consistent with *Nature* (2008) model.

How Are Saving Estimates Over Next Decade Affected by Data Protection Periods?

- CBO has estimated government savings from biosimilars of $6 billion over a 10 year scoring window
- Bulk of the savings is concentrated in mature, commercially successful biologicals
- Savings estimates are not likely to be substantially increased by shortening data protection to 5 years
- However, the impact on R&D incentives and expenditure commitments is likely to be immediate, especially for early stage R&D

National Academies Have Advocated Longer Data Protection Periods

- In a 2007 report, the National Academies called for a data protection period for large and small molecules at least equal to the 10 - 11 year period that exists for the European Union

> *The current system has been successful in stimulating the creation of new molecules, but the limitations of the patent system sometimes result in denying patients the best that the pharmaceutical industry could offer.*
>
> *The limitations are due largely to the time constraints under which the patent system operates. Patents generally must be filed as quickly as possible after an invention occurs, and the ticking clock creates a tension with other aspects of drug development*

Source: National Academies, Committee on Science, Engineering and Public Policy, 2007. *Rising Above the Gathering Storm: Engaging and Employing America for a Brighter Future*

Unintended Consequences If Data Protection Is Too Short For Biologicals

- Many products with limited or uncertain patent protection are likely to be left on the shelf
- If patent and data protection is inadequate, innovators may turn increasingly to trade secrets protection
- This would have adverse consequences for long term innovation and the ability to build on prior knowledge

Conclusions and Recommendations for Public Policy

- Congress should create an abbreviated process for biologics given their growing importance to health care
- The characteristics of the innovation process for new biologics support a significant data protection period
- Societal gains from a significant data protection period likely far exceed societal losses