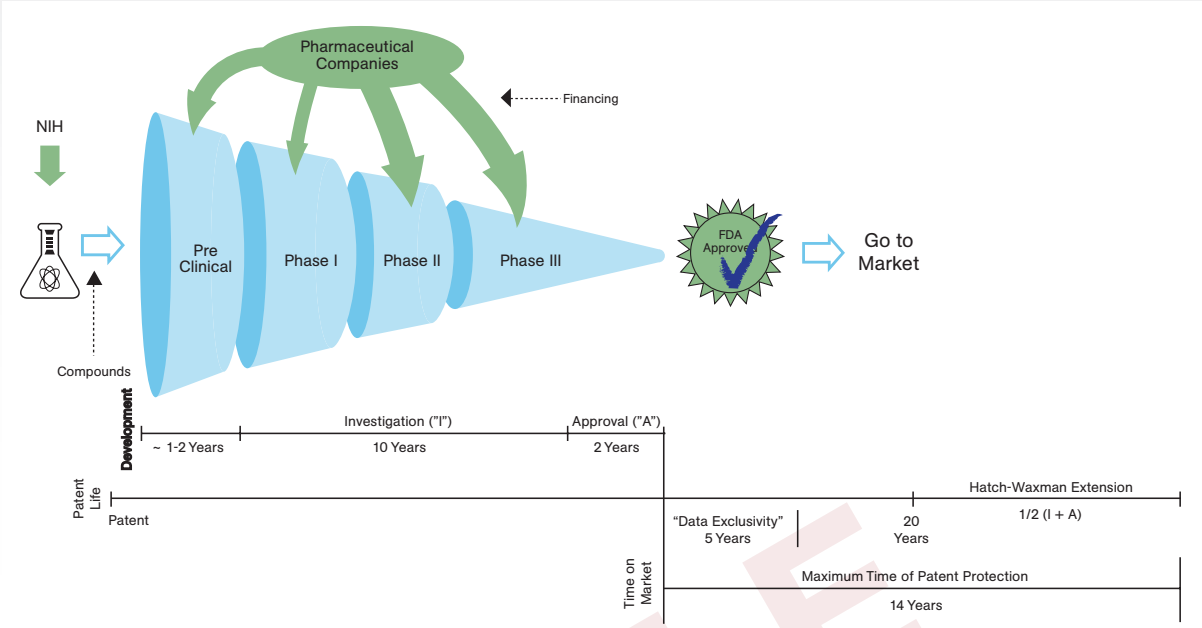
Fig. 3. Hatch Waxman Provisions for Patent Protection



The Hatch-Waxman amendments to the FDCA established (1) the approval standards for generic drugs; (2) non-patent exclusivity incentives for innovative and generic manufacturers; and (3) provisions regarding patent disputes between innovative and generic manufacturers. Legislation was applicable to chemically synthesized and/or small molecule products and did not require generic manufacturers to duplicate safety/efficacy data. Instead, generic manufacturers are permitted to "borrow" safety/efficacy data from the innovator/manufacturer. Given that fact, generic manufacturers do not need to reproduce safety/efficacy data, they must demonstrate that the generic product is similar to the branded product. Demonstration of bioequivalence for a generic is significantly less expensive than the clinical testing that is required to be performed by the innovator. Consequently, this spares the generic manufacturers from conducting their own Phase I-III clinical trials and enables the generic manufacturers to decrease development time and costs, thus selling the generics at a considerably lower price. Distinct from patent protection, reference or innovator product sponsors that receive FDA approval for a new chemical entity are provided with 5 years of exclusivity during which FDA is prohibited from accepting or approving an application for a generic version of the drug. When a reference product sponsor receives approval for a product change, such as a new indication or dosage form, it may receive 3 years of exclusivity for the new indication or dosage form, so long as clinical trials were necessary to support FDA approval of the change. Hatch-Waxman also provides exclusivity to certain generic manufacturers; the first generic applicant who challenges a listed patent of the reference product sponsor, thereby running the risk of having to defend a patent infringement suit, is eligible for 180 days exclusivity against other generics that challenge the patent. In other words, during the first six months of marketing, no other generic version of the same drug may be brought to market.

There are several issues with using the Hatch Waxman Act for Follow-on Biologics. Biologics are more complex than small molecule drugs.,I It is more difficult to devise a process based on bioequivalence, especially due to the fact that they are derived from living organisms. Small differences in structure can significantly impact the effects of a drug in patients. These effects are difficult to identify without conducting clinical trials and could result in significant toxicity not seen with the innovator. Unlike chemically based pharmaceuticals, which are protected by patents based on chemical entities, many of the biologics' patents are based on the production process. Current technology does not allow for

Of the four oncology biologics we compared, with a 25% loss in sales due to biogenerics, it seems that Herbitux would be the most protected, followed by Avastin. Rituxin would have very little growth and Herceptin would have negative growth. Dissimilarly, a 10% loss would have a much smaller effect on the growth of this market segment.

Insulins

Table 10. Total US Sales (in millions) of Selected Top Selling Insulin Products forecasted from 2009 to 2013 Assuming No Competition, total sales with 10% Loss Due to Biogenerics and total sales with 25% Loss Due to Biogenerics.

PRODUCT (Millions in USD)	2009	2013	2013 (10% Loss)	2013 (25% Loss)
Lantus	1452	2008	1807	1355
Novolin	744	650	585	439
Humalog	1008	1395	1255	941
Humulin	381	527	474	356
Total	3585	4580	4122	3091

Fig.10. Expected Growth Rates of Selected Insulins from 2008 to 2013 Assuming No Competition, 10% Loss Due to Biogenerics and 25% Loss Due to Biogenerics