



EVERYTHING MATTERS

# Update on Issues Affecting Personalized Medicine, Biosimilars, and ESC Research in the U.S.

AusBiotech 2010

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Lisa A. Haile, J.D., Ph.D.

**On March 23, 2010, President Obama signed legislation that contains two important provisions that affect healthcare and the life sciences industry in the United States:**

- 1- Abbreviated regulatory approval pathway for generic versions of biological medicines (biosimilars)**
- 2- Patient-Centered Outcomes Research Institute to be created for Personalized Medicine approaches to healthcare**

- **Central to personalized medicine approaches are diagnostic tests**
- **Biomarkers, variant gene sequences, alternative forms of a protein that differ among individuals make up diagnostic tests**
- **Intellectual property protection relating to diagnosing disease or predicting patient response to drugs**
- **Changing legal framework for obtaining patent protection**

- **Bilski v. Kappos (Supreme Court, June 28, 2010)**

- **“Machine-or-transformation test**

**In view of Bilski, other cases are affected:**

**1-Prometheus Laboratories-determine dosage of drug based on metabolite levels**

**2-Classen Immunotherapies-comparing treated versus untreated groups after immunization**

**3-Myriad Genetics-method of diagnosing cancer based on the presence of variant nucleic acid sequences**

- *In re Bilski*, 545 F.3d 943, 88 U.S.P.Q.2d 1385 (Fed. Cir. 2008)
- *Prometheus Labs., Inc. v. Mayo Collaborative Servs., et al.*, 581 F.3d 1336, 1339-40 (Fed. Cir. 2009).
- *Classen Immunotherapies, Inc. v. Biogen IDEC*, Nos. 2006-1634, 2006-1649, 2008 WL 5273107, at \*1 (Fed. Cir. Dec. 19, 2008).
- *Ass'n for Molecular Pathology, et al. v. U.S. Patent and Trademark Office, et al.*, 2010 WL 1233416 (S.D.N.Y. March 29, 2010).

- **Pre-1984, the FDA required full clinical trials before approval of a small molecule drug**
- **In 1984, Hatch-Waxman legislation was passed that introduced incentives to produce low-cost versions of many compounds**
- **Abbreviated approval process (ANDA)**

- **Many companies want to introduce low cost versions of innovative biologics when their patents expire**
- **Global market for biologics estimated at \$50 billion in 2005, \$105 billion in 2010, or >50% of all expenditures, and increasing**
- **Many of the top selling biologics are coming off patent in the next few years**

- **The recently enacted health reform law (March, 2010) includes an approval pathway for generic versions of biopharmaceuticals or biosimilars. The provision:**
  - **Provides original biologic drug makers 12 years of protection before the drug can be subject to competition from biosimilar versions (retroactive to March 1998).**
  - **Provides a year of exclusivity to the first biosimilar drug the FDA declares interchangeable with an original biologic drug.**
  - **Provides an additional six months of exclusivity to the original biologic drug if the manufacturer completes pediatric studies of the drug.**

- **Drugs/Hatch-Waxman – The Orange Book identifies patents covering innovator NDA drug product and methods of use**
- **Biologics – No Orange Book counterpart**
  - **Implications:**
    - **Biologics innovator may have many composition of matter patents, methods of use and methods of manufacture**
    - **Biosimilar companies may have greater Freedom to Operate issues**

- **Hatch Waxman – Bioequivalence**
  - **The absence of a significant difference in the rate and extent of absorption of the active ingredient when a pharmaceutical equivalent is administered to subjects in the same dose under similar conditions (within 80% to 125% of the reference drug)**
  - **Can be differences (e.g., chemical) such as a different salt or ester**

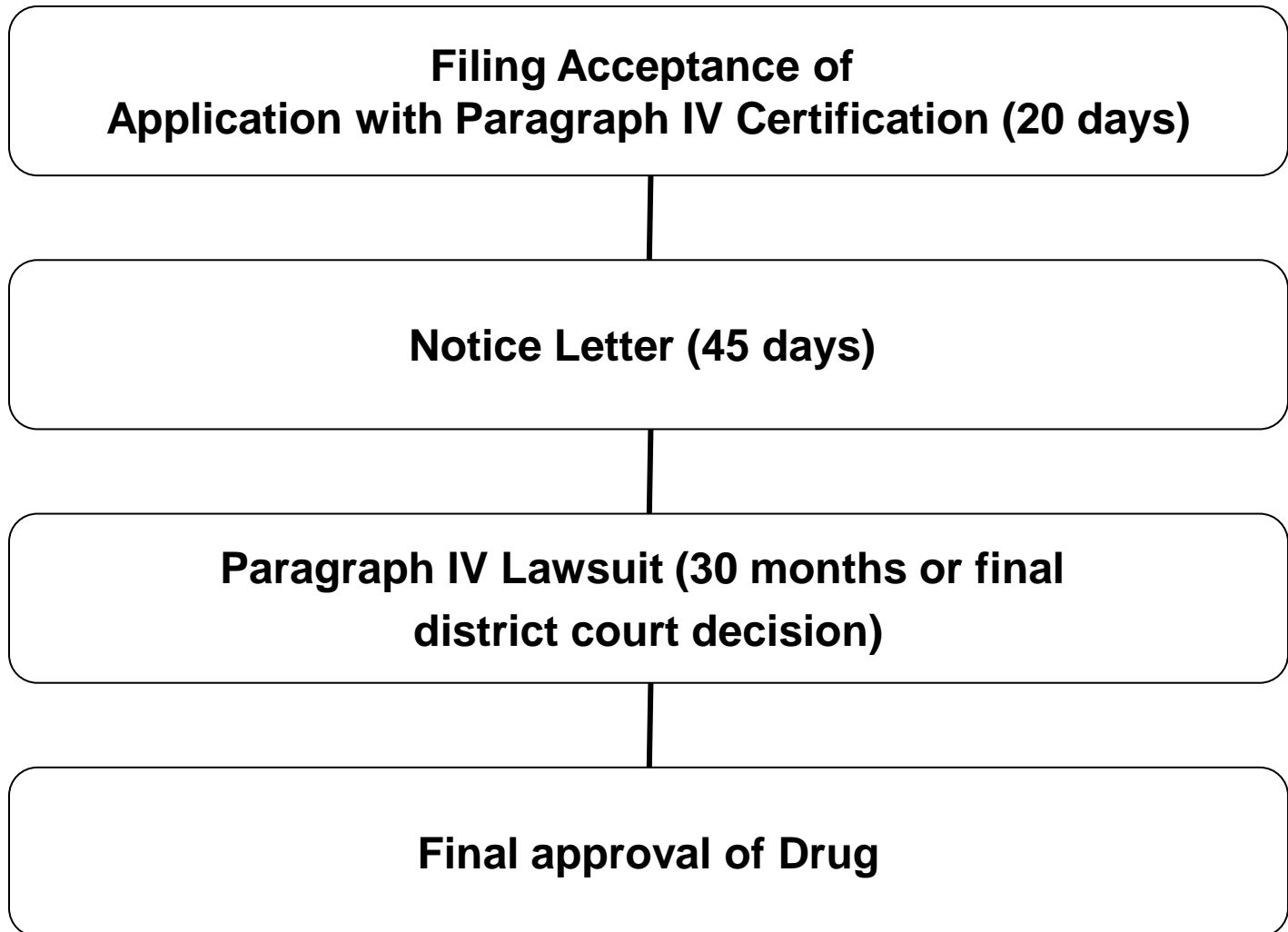
- **Biologics - Biosimilarity and Interchangeability**
- **Biosimilarity**
  - Biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;
  - Provide animal studies (toxicity); and
  - There are no clinically meaningful differences between the biological product and the referenced product in terms of the safety, purity and potency of the product

- **Interchangeability**
  - **Must be Biosimilar to the reference product;**
  - **The biological product produces the same clinical result as the reference product in any patient; and**
  - **The biological product may be substituted for the reference product without the intervention of the health care provider who prescribed (no risk in switching)**

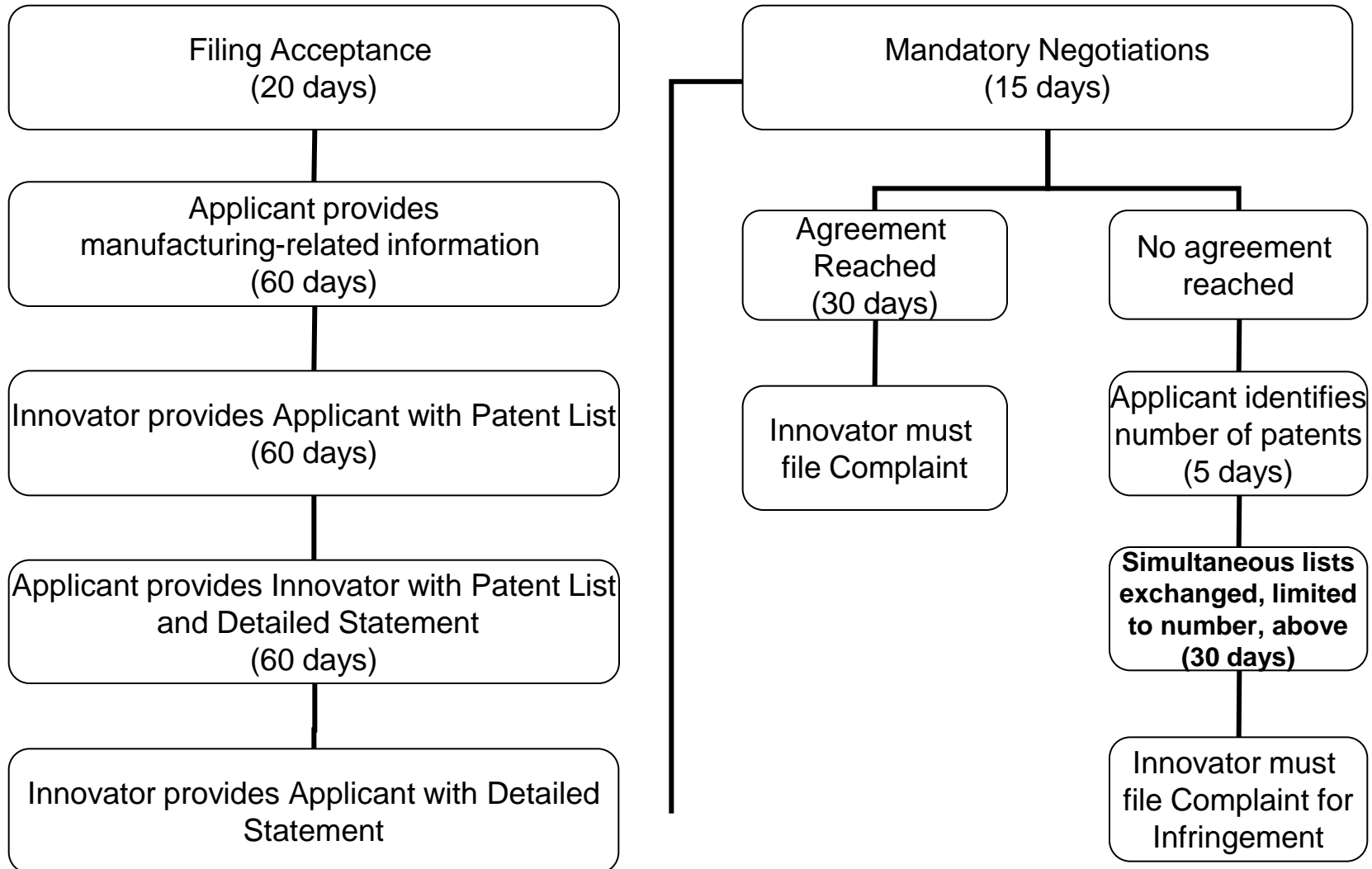
## Additional Requirements:

- **Biosimilar and reference product use the same mechanism of action for the conditions prescribed, if known.**
- **Condition of use previously approved for the reference product**
- **The route of administration, dosage form and strength of the biosimilar are the same as the reference product**
- **The facility in which the biosimilar is manufactured meets standards designed to assure that the biosimilar is safe pure and potent**

# The Hatch-Waxman Timeline



# Proposed Biosimilar/Biologics Timeline



# Update of Federal Funding for Human ESC Research in the U.S.

- **March 2009-President Obama issued an executive order removing restrictions against federal funding of stem cell research**
- **August 2010-Judge Royce C. Lamberth (District Ct-DC) granted an injunction against federally funded embryonic stem cell (ESC) research on the grounds that ESC research "clearly violates" the Dickey-Wicker Amendment**
- **September 2010-Judge Lamberth refused to lift injunction pending conclusion of the case a likely appeal to the U.S. Court of Appeals for the District of Columbia Circuit**
- **September 2010-Justice Department asks the D.C. Appeals Court to lift the injunction via an order pending the appeal of Judge Lamberth's ruling**
- **September 9, 2010-the appeals court granted a temporary override of the injunction until Monday, September 20, 2010**
- **September 20, 2010-D.C. Appeals Court continues the override the injunction more permanently**



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