



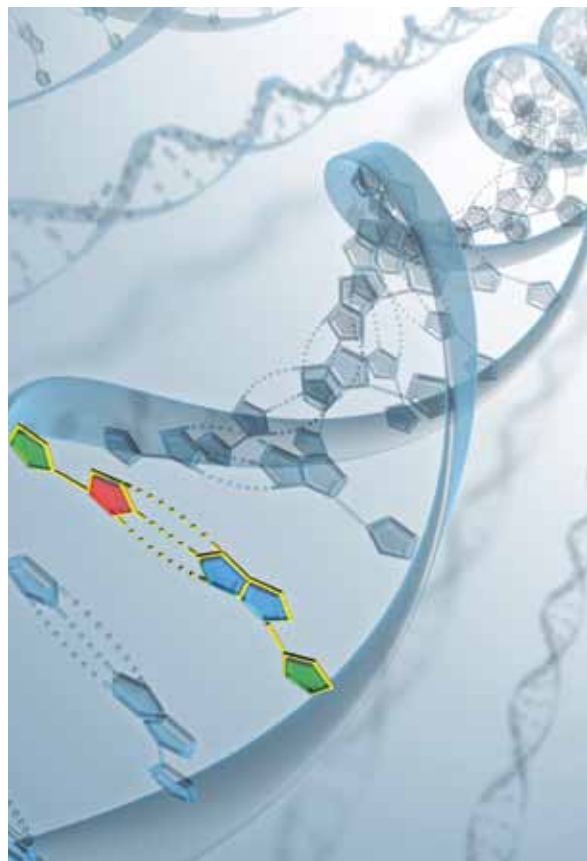
BIOSIMILAR PRODUCTS UPDATE

SUMMER 2011

Therapeutic Proteins, Inc. (TPI) is an independent manufacturer of recombinant therapeutic proteins and antibodies, the first of its kind in the US. The manufacturing facilities of TPI are fully cGMP-compliant and are capable of producing large quantities of proteins and antibodies as API. TPI also assists its clients with finished product formulation and filling on their existing lines as well as regulatory assistance for product registration. Alternately, TPI can assist in providing the finished products through worldwide partners that have cGMP-compliant filling lines.

Biosimilar Products Scene Worldwide

On March 30, 2010, President Barack Obama signed into law a bill ("Biologics Price Competition and Innovation Act" or "BPCIA") that will immediately allow biosimilar product approvals in the US. This is a significant development for pharmaceutical manufacturers worldwide as they now will be able to include the US markets in their marketing plans and projections. Accordingly, a biological product is "biosimilar" to a reference product if it is "highly similar" to the reference product "notwithstanding minor differences in clinically inactive components" and if there are no "clinically meaningful differences" between the products in terms of the safety, purity, and potency. The bill preserves a 12-year period of data exclusivity for reference biological products, during which approval of a biosimilar application relying on that reference product cannot be made effective. The BPCIA describes a showing that may be made to establish the interchangeability of a biosimilar biological product with its reference product. It also provides that the first interchangeable biosimilar is entitled to a period of exclusivity during which no other biosimilar may be deemed interchangeable with the same reference product. The FDA has also been mandated to establish a



user fee for approval of biosimilar products by 2012. FDA draft guidelines are expected by December 2011.

Europeans approvals of biosimilars now count to over 25 products without a single rejection based on comparability; this should be encouraging to new companies entering this fast growing field. However, all of these approvals were granted to companies who manufacture their own API; for all others, the only choice of large-scale cGMP compliant materials remains being supplied by TPI.

Technology of TPI

The breakthrough technology and science of TPI includes many proprietary and patented systems never applied before to the manufacturing of biological drugs, making TPI the most innovative manufacturer of biological drugs in the world.

1. The world's first 100% single-use systems: these include all processes from media and buffer preparation to bioreaction, refolding, mixing, and storage of in-process materials, stainless-steel-free environment, and double RO/EDI water system.
2. The world's first single-use flexible 2D bioreactor:
 - a. For bacterial fermentation.
 - b. Stationary horizontal configuration for every size of batch.
 - c. Scalable without validation to very large commercial sizes.
 - d. Uninterrupted harvesting in a single bag.
3. World's first validated chemical virus-clearing system for a manufacturing environment in downstream processing.
4. Non-infringing pegylation of proteins using an in-situ reaction system providing higher yields.
5. Stabilized Monoclonal Antibodies as NCEs. Backbone strengthening of existing monoclonal antibodies makes them more stable at room temperature and enhances their disposition half-life.

Choose Compliance™

TPI's registered slogan—Choose Compliance™—means many things to us and to our customers. Biological drugs are most difficult to manufacture because of the variations in their quality: often the quality measures are not sufficient to measure this variability. Higher immunogenicity of biological drugs is the most important consideration in choosing a supplier that can provide products manufactured under the most stringent conditions of cGMP requirements. All companies that hold a BLA license must be visited by the

FDA every two years, and thus a client securing its supplies from TPI will always be assured that it has a product in full compliance with the most rigid current standards of cGMP. By choosing TPI, one is choosing compliance.

Locking in Supplies

TPI has begun taking orders for filgrastim (G-CSF) for delivery early 2011 and for erythropoietin in the second quarter of 2011—lock in your orders now as these will be filled on a first come, first served basis.

TPI Products

- **Available Now**
Filgrastim, erythropoietin, and activated PEG
- **Available in 2012**
Etanercept, rituximab
- **Available in 2013**
Infliximab, cetuximab, and trastuzumab

