AMGEN: Evaluation of Plastic Pre-filled Syringes for Packaging Therapeutic Proteins: Part 2

Amgen is a leading human therapeutics company in the biotechnology industry. Amgen pioneered the development of novel products based on advances in recombinant DNA and molecular biology and launched the biotechnology industry’s first blockbuster medicines.

This project is a continuation of last year’s joint KGI-HMC TMP-Clinic on packaging therapeutic proteins in plastic pre-filled syringes and is currently an important project in Amgen’s product development group. As a repeat project there is no doubt the sponsors were happy with the progress achieved by HMC-KGI students. We do have a significant amount of in-house knowledge on the project. Although a major part of the project is experimental in nature, the project incorporates significant amounts of market and intellectual property research. This project allows the students to be a part of the technology that will possibly be used for packaging most, if not all, therapeutic proteins in the future.

With the advances in COC/COP (cyclic-olefin copolymer/homo-polymer) materials, the medical device industry has begun producing novel plastic syringes that are able to be used with therapeutic products. Amgen is interested in evaluating the use of novel pre-filled plastic syringes for commercial and late stage products. The major challenge in using current plastic syringes for therapeutic protein storage is the inherent oxygen permeability of these materials. During the last academic year, the joint KGI/HMC team had worked with Amgen to identify strategies to minimize oxygen permeation in plastic syringes. This involved the development of computer models to predict oxygen permeation levels inside a syringe; surrogate marker for detection of oxygen levels; and evaluation of the closure integrity and ease of use of these new syringes.

Amgen wishes to extend work on this project in the following ways. The glutathione oxidation method needs refinement, including exploration of reaction rates of non-enzymatic oxidation; further characterization of bi-phasic properties of oxidation within a plastic syringe; and exploration of other methods for oxidation estimation. Further work in unlimited oxygen transmission rate testing is desired, both in various syringes and in secondary pouches/packaging systems.

Amgen is also interested in further refinement of the oxygen permeation mathematical model, and validation of the model predictions using experimental data gathered using the glutathione oxidation method.

Project Charter

Goals of Amgen Syringe are:

1. Design and Evaluation of secondary pouches and oxygen absorber systems:
- Exploration of dessicant/oxygen absorber options and performing validation experiments with packaging systems that include oxygen absorbers.
- Validation of secondary pouches using the glutathione oxidation method.

2. Refinement of oxygen permeation software model:
   - Develop software model using the glutathione oxidation data to determine transport coefficients and develop predictive capabilities.
   - Make appropriate adjustments from experimental data.

1. Incorporate secondary packaging and absorber systems into model
2. Incorporate seals and tip cap into model.

3. Refinement of the glutathione oxidation method:
   - Explore reaction rates of non-enzymatic oxidation of glutathione.
   - Further characterize bi-phasic properties of glutathione oxidation within a plastic syringe.
   - Explore use of other suitable peptidic compounds as well as amino acids for estimation of oxidation (such as methionine).
   - Explore oxidation estimation alternatives to the colorimetric assay such as HPLC, microparallel liquid chromatography, mass spectrometry, etc.

4. Purchase in-house Mocon testing machine or equivalent for unlimited oxygen transmission rate (OTR) testing:
   - Pursue extended OTR testing of glass and plastic syringes.
   - Pursue extended OTR testing of secondary pouches.

5. Market research:
   - More in-depth patent landscape research on plastic syringes.