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In Vitro Stability of a Monoclonal Antibody, Adalimumab, after DosePro Instantaneous Delivery

In vitro characterization of the stability of a therapeutic monoclonal antibody demonstrates equivalence between instantaneous delivery (<1/10th second) by DosePro® needle-free technology and standard pre-filled syringe control.

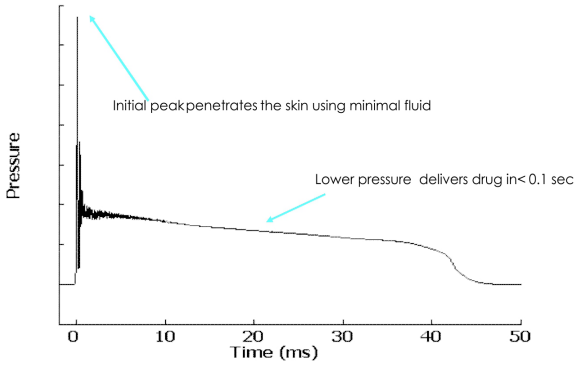
A well-known and characterized monoclonal antibody, Humira® (adalimumab), and accepted assays were selected to characterize protein stability. The therapeutic antibody was used as formulated by the manufacturer (Abbott Laboratories).

Analytical methods selected to characterize stability:

- Dynamic Light Scattering (DLS)
- Size Exclusion Chromatography-High Performance Liquid Chromatography (SEC-HPLC)
- *In vitro* cell-based bioassay: Tumor Necrosis Factor alpha (TNFα) Neutralization.

Adalimumab delivery methods and controls evaluated:

- **DosePro®** – Automatic instantaneous DosePro delivery.
- **Pre-filled Syringe (PFS)** – Manual syringe delivery via standard 30-gauge ½" needle.
- **DosePro Control** – Manual delivery from a DosePro® drug cartridge.
- **PFS Control** – Manual syringe delivery without needle.
- **Pipette Control** – Manual delivery via pipette.



Pressure profile during DosePro® delivery.

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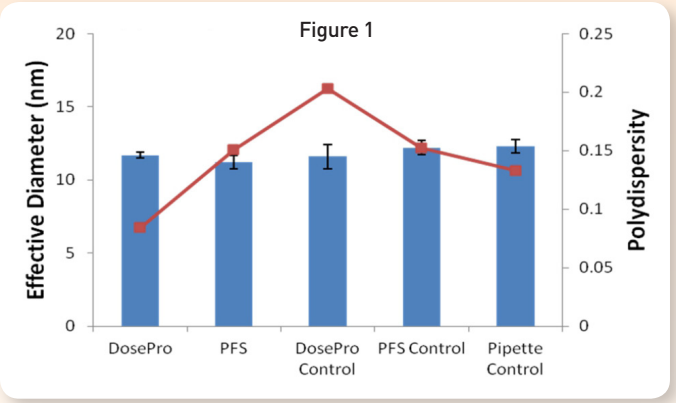

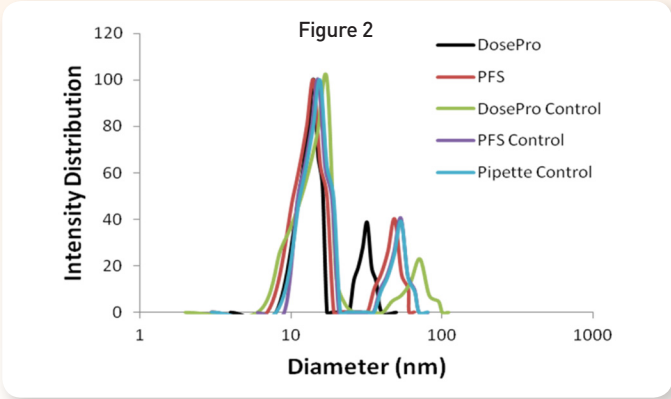

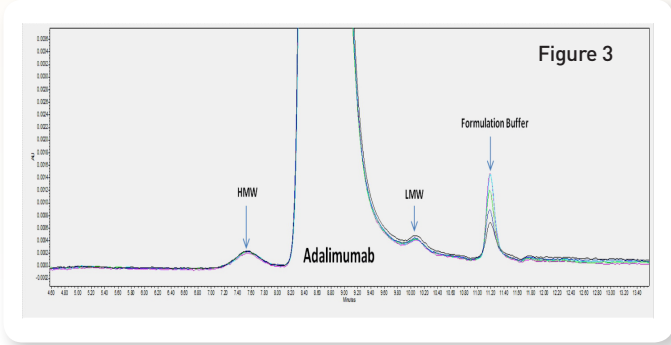

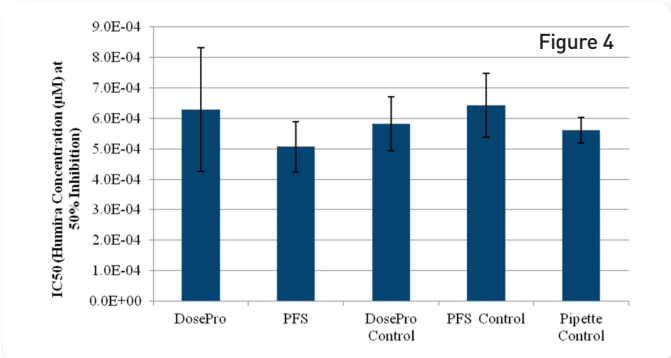

DLS Results

Purpose

- Sensitive light scattering analysis used to detect aggregated protein.

Results

- Figure 1 shows monodispersity of adalimumab with polydispersity ≤0.2 (red) and an effective molecular diameter (blue) at approximately 13 nm for each sample.
- Figure 2 shows intensity distribution for each sample. This is a highly sensitive evaluation that illustrates the presence of aggregates in all samples.

SEC-HPLC Results

Purpose

- Liquid chromatography analysis used to detect adalimumab fragmentation and aggregation.

Results

- Figure 3 shows all sample chromatograms. There was no difference in adalimumab aggregation and fragmentation among samples.

TNFα Neutralization Results

Purpose

- *In vitro* bioassay used to measure adalimumab activity. Activity assay was based on 50% inhibition of TNFα by Humira.

Results

- Figure 4 shows adalimumab activity and standard deviation for each delivery method. There was no statistical difference between delivery methods using an analysis of variance model.

Conclusions

There was no evidence of adalimumab denaturation after delivery by the DosePro® delivery system. Equivalence of adalimumab biological integrity was demonstrated between DosePro® and PFS delivery systems based on statistical comparisons.