Fast Dynamic Surfactant Reduces Aggregation of Biologics

Joshua Katz

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A note to the reader

These slides were originally intended to be presented at the 2020 ACS Spring National Meeting in Philadelphia, PA. Due to that meeting's cancellation, I am now sharing the slides through SciMeetings. Unpublished data has been removed, and I hope to be able to share that data in another forum soon.

If you have any questions about this presentation or DuPont's work in developing FM1000 for the biopharmaceutical industry, please do not hesitate to reach out to me.

Best regards,

Josh

Joshua.katz@dupont.com

Surfactant Properties

Property	PS80	PS20	PO188	FM1000
Bond Structure	Ester bond	Ester bond	All ether	Amide bond
Chemical Shape	Branched	Branched	Linear	Linear
Average MW (Da) ^a	1300	1200	8300	1400
Polydispersity	Mixture of species	Mixture of species	Narrow	Narrow
HLB ^b	15	16.7	17	12
CMC (ppm) ^c	5.5	6.2	6.0	0.55
γ (0.1 mg/mL) (mN/m)	45	36	50	41

a. Based on the major species. b. Calculated using the equation $HLB = 20 \cdot f_H$ where f_H is the mass fraction of the molecule that is hydrophilic. c. Calculated by intersection of lines of best fit to surface tension vs concentration curves.

FM1000 at 0.05 mg/mL drops to equilibrium >10x faster both with and without IgG compared to PS20 at 0.1 mg/mL.

FM1000 stabilizes IgG at appreciable lower concentration or for longer times

Concentration required to keep aggregates to certain arbitrary size under fixed stress

Time to aggregate with fixed surfactant concentration

FM1000 mitigates agitation stress for Orencia

Orencia reformulated to 5 mg/mL abatacept and 0.1 mg/mL surfactant, pH 5 (citrate buffer)

2 mL added to and sealed into 5 mL vials

Vials shaken on their side at 150 rpm

Aliquots analyzed by SEC:

Percent monomer remaining

FM1000 mitigates agitation stress of Orencia in dilute conditions IV Bags

4 mL formulations of 10 mg/mL abatacept and 2.5 mg/mL surfactant injected into 250 mL IV bags (Baxter) containing 196 mL 0.9% saline

Bags shaken on a rotary shaker at 125 rpm for 24 hrs with samples analyzed by SEC

SEC traces following agitation

Distribution of aggregates at 24 hrs

* Control sample had lost ~50% of its total protein content at 24 hrs. All other samples were within 5% of initial protein content

FM1000 Mitigates Agitation Stresses for Cetuximab (Erbix) at Very Low Level Surfactant

Summary

- New surfactant, FM1000, is cleaner and more stable than incumbent technologies.
- FM1000 is more dynamic and reduces surface tension significantly faster than PS80, PS20 or PO188.
- Formulations with various protein drug models demonstrate 2-3x improvement in protein stability performance compared to next best technology when exposed to agitation stresses.
- Ongoing work focused on process development, toxicology, and continuing to understand surface and protein interactions.

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