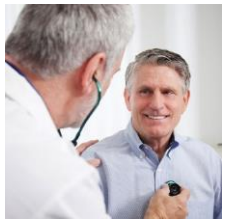
European Federation of Pharmaceutical Industries and Associations

CMC Strategy Forum Europe 2020

Multi-company Survey on the Use and Characterization of Polysorbates in Biotech Products

Klaus Wuchner on behalf of Polysorbate Workstream, 11 May 2020






EFPIA MQEG Biomanufacturing

Satellite Session

Thanks

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Sebastian Peuker, Bayer

Shawn Cao, Amgen

Sonal Saluja, Biogen

Sylvain Huille, Sanofi

Vincent John Corvari, Lilly

Virginie LeBrun, Lonza

To date 16 Companies

23 active team members

Polysorbates (PS) in biopharmaceutical formulations

- Polysorbate 20 and 80 are the most common surfactants in parenteral biopharmaceutical products, alternatives are limited
- PS have a high surface activity at low concentration and are used as excipient to protect protein against interfacial stresses, surface induced aggregation and losses due to adsorption to surfaces
- PS are prone to degradation by oxidation and / or enzymatic hydrolysis due to residual host cell proteins resulting in insoluble degradants like fatty acids (FAs) forming subvisible or visible particles
- FAs are not toxic but presence of resulting particles is unwanted and should be minimized

Purpose and activities of working group

- Started in 2019
- Industry survey to benchmark use of polysorbate, gaps, analytical methods and regulatory expectations, end to end approach
- “Industry for industry” best practices covering entire life-cycle of PS
- Work out common strategies to mitigate risks
- Exchange of scientific information
- Evaluate the benefit/risk profile of all-oleate Polysorbate 80
- Understand better polysorbate quality through technical discussions with main PS manufactures

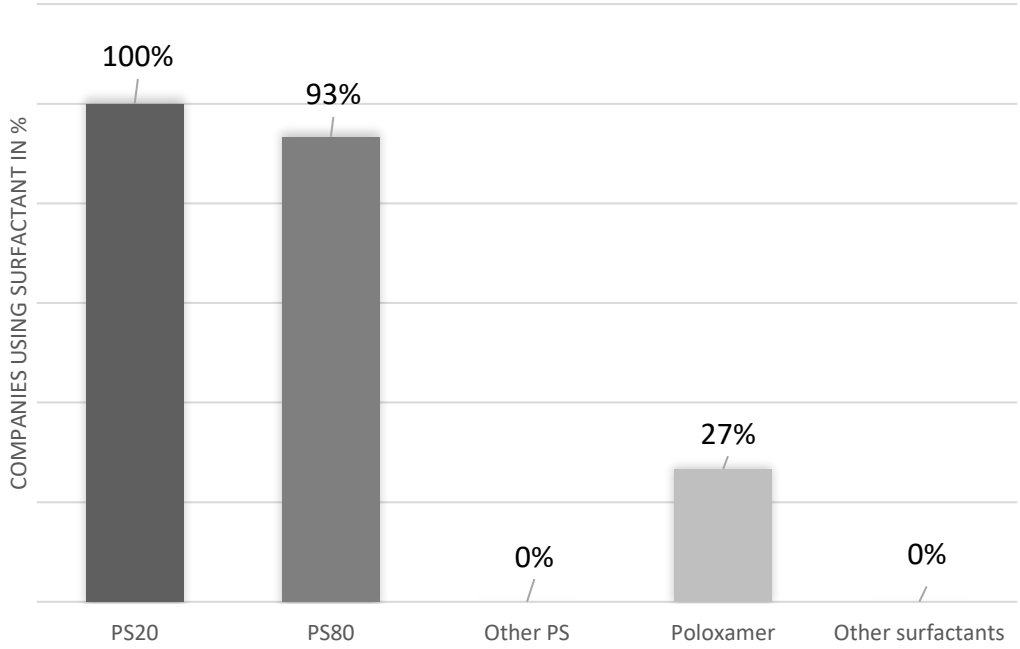
Survey outline

A. Use of surfactants for biological products, incl. new grade PS – general aspects
B. Polysorbate raw material for cGMP use
C. PS handling during cGMP manufacture
D. Degradation of PS in biological products (including proteins and synthetic peptides) and placebos
E. Analytical methods for of PS in products
F. Mechanistic Understanding of PS degradation and detectability
G. Model systems/predictive models
H. Mitigation strategies
I. Safety / toxicology
J. Regulatory interactions related to PS / PS degradation / particle formation / specifications

137 questions, 27-page survey

Survey – preliminary results

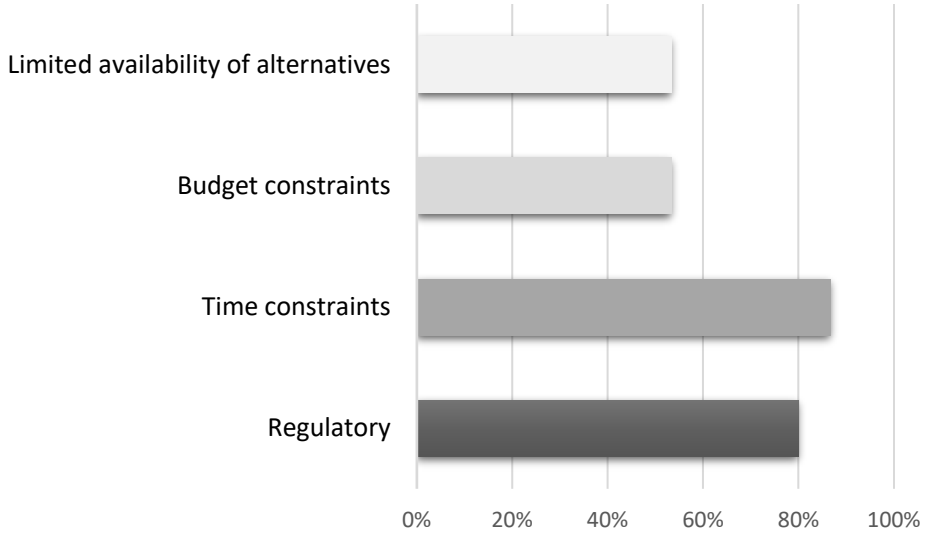
Which surfactants do you use for your products?



- All companies use PS20; 93% of participants PS80; 27% Poloxamers
- PS80 is more often added to products compared to other surfactants
- No other types of surfactants than PS20, PS80 and Poloxamer are currently in clinical development
- However 56% evaluate other surfactants on a research basis to “increase freedom to operate” , “mitigate deficiencies of PS and Poloxamers” , “for improved surfactant stability during shelf life” or “to reduce oxidation and hydrolysis liability”

Survey – preliminary results

Are there hurdles to develop/implement new/alternative surfactants?



- Regulatory hurdles to incorporating novel excipients into clinical stage biotherapeutics
- Safety and experience in the clinic for other surfactants' use is not very well established to date
- Should be considered in an industrial consortium
- Significant efforts need to be given to establish an alternative surfactant that outweighs the benefit polysorbates provide which include well-known capability of stabilization against interfacial stress

Survey – preliminary results

Do you perform an assay for PS content?

- 100% of companies perform an assay for PS content in their product

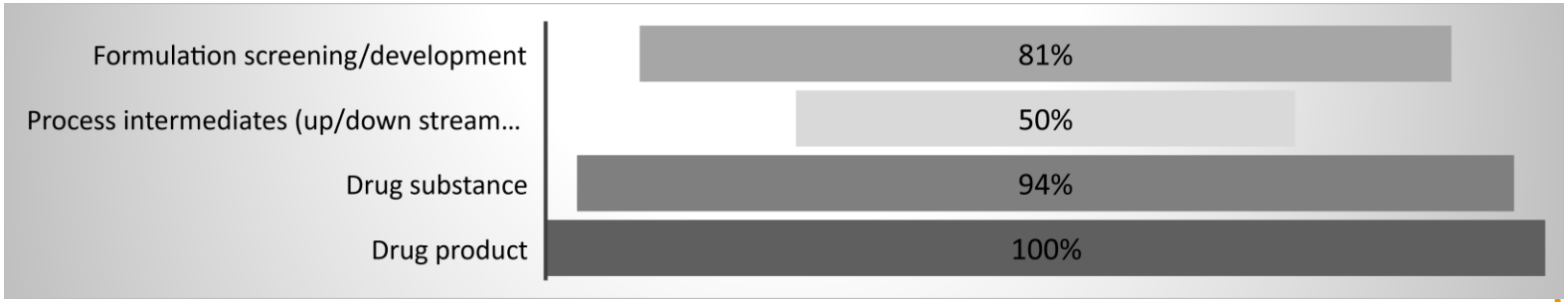
Why do you perform a (routine) assay for PS content?

Internal requirement	Per agency request	Both	Not applicable
63%	75%	50%	13%

Is your PS content assay also stability indicating?

- 75% of companies confirmed stability indicating properties

Do you perform an assay for PS content for...?



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Thank you