MIBio 2015: Stability of biopharmaceuticals – From molecular interactions to successful products

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21st October 2015, Cripps Court, Magdalene College, Cambridge, UK

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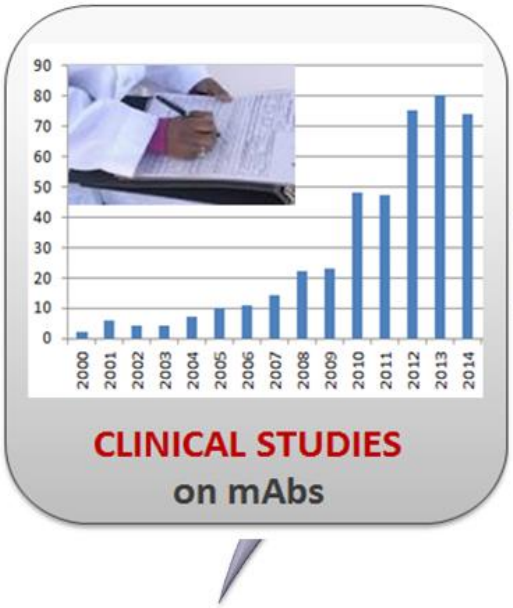
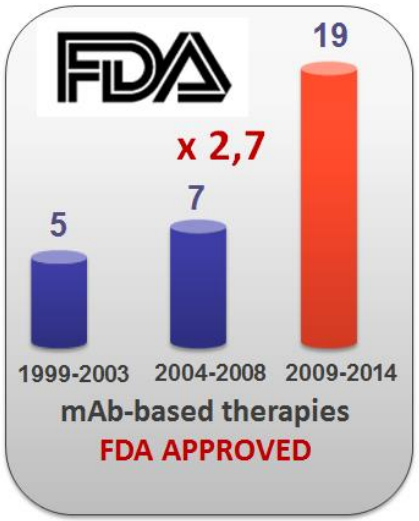
PHARMA. R&D TRANSFORMATION

Significant increase of mAb-based therapies





6 mAbs
Top 20 Drugs
(by 2013 WW Sales)

- **37 mAbs-based therapies approved by FDA**
- **In 2013 US Pharma. companies had 682 biologic products in development of which 50% are mAbs**

https://www.clinicaltrialsregister.eu
http://www.clinicaltrials.gov
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm
PhRMA 2013 report on Biologics Medecines in Development

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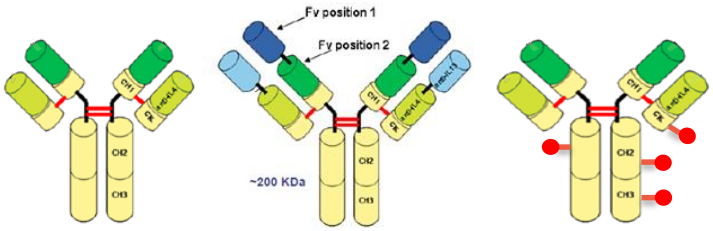
CHALLENGES FACING PROTEIN FORMULATION AND PRODUCT DEVELOPMENT

The formulation development for biologics is constantly changing to reflect the emerging of new antibody scaffolds, the increasing use of subcutaneous injection (as alternative to iv injection) and the growing constraints on development timelines particularly at the early clinical stages.

Intellectual property and freedom to operate: innovators vs. biosimilars

Antibody scaffolds	**Pharmaceutical Form / Drug Device Combination**
Monoclonal antibody (mAb), Bi-specific antibody, antibody drug conjugate (ADC)	Concentrate or Powder for solution for infusion, Solution for injection. PFS, Auto-injector, Large volume device



mAb *bi-spec* *ADC*

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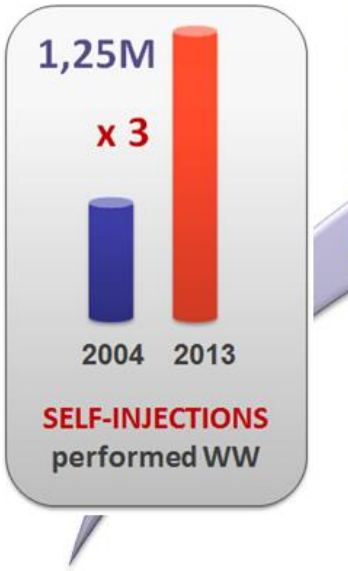
PHARMA. R&D TRANSFORMATION

Growth of self-injectable Combination Products



30 % products in development are Combination Products

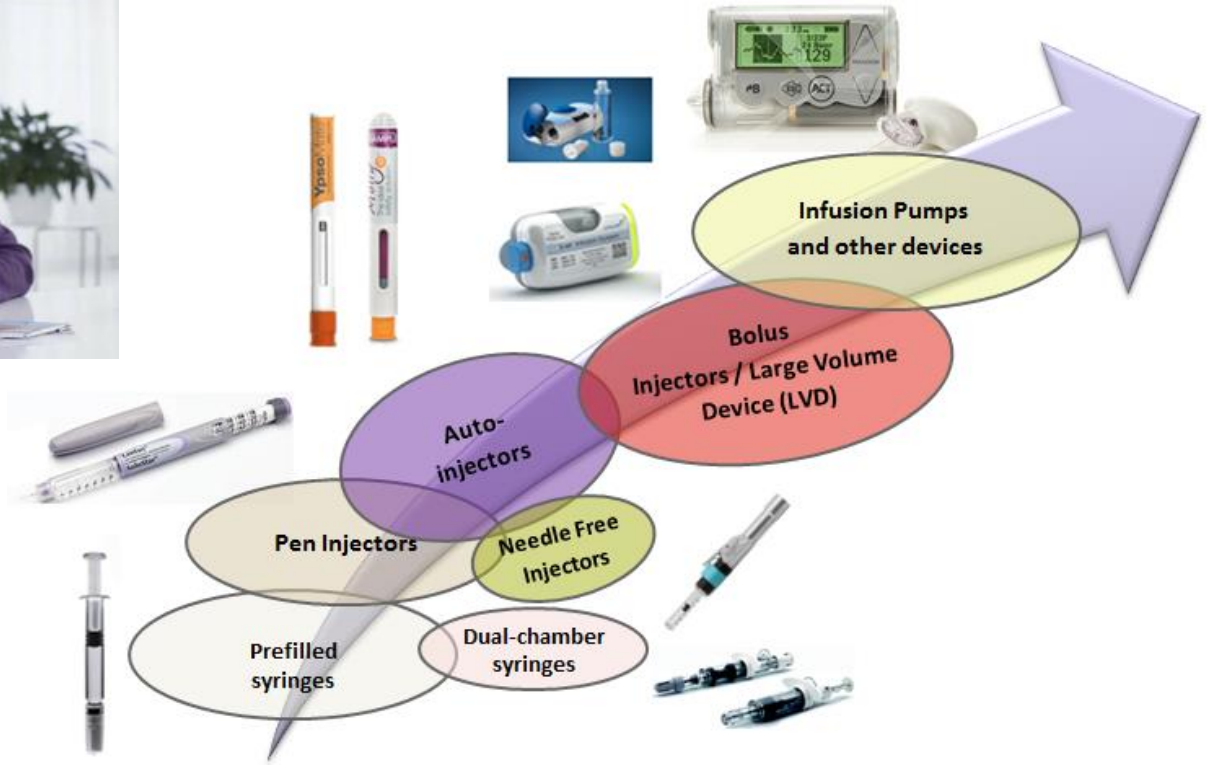
- **Avoid hospitalization, relieve overstretched health systems (staff, expenses)**
- **Patient-centric approach to improve quality of life**
- **Product differentiation enabler**

IMS MIDAS, September 2013

TechnoCatalyst - Next-Generation Self-Administered Drug-Device Combinations Report, October 2012

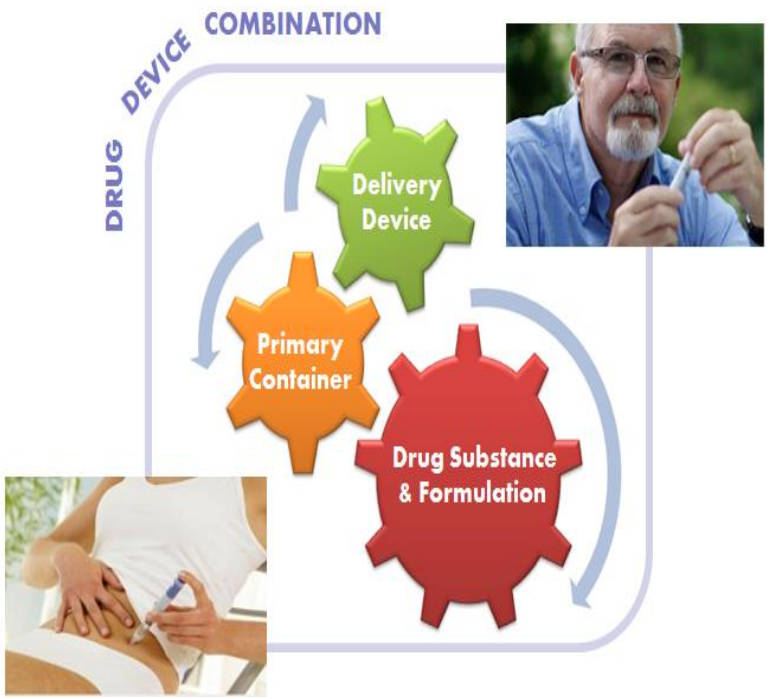
STARTING WITH THE END IN MIND

Development of multiple device-mediated self-injectable delivery technologies



DRUG PRODUCT INTEGRATED DEVELOPMENT: Key Principles

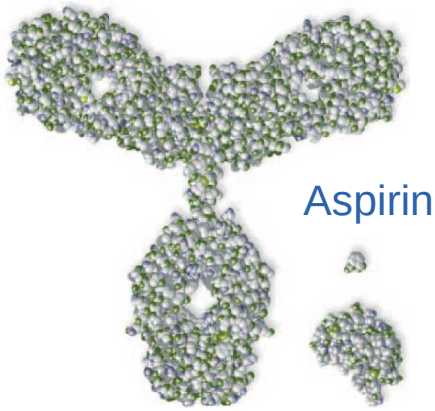
A Combination Product is an integrated system that needs to be considered as a whole



- **This integrated system can be deconstructed into several components**
- **The interactions between each component collectively drive the final product performance and quality in the hands of the patient**
- **Multiple variables could interact between each other and then affect key quality attributes of the final product. Minimize the unexpected : Early characterization is critical**

SMALL MOLECULES vs. THERAPEUTIC PROTEINS: BIOSIMILAR CHALLENGES

Small Chemical Drugs	Recombinant Protein Drugs
Few Degradation pathways	Several degradation pathways
Few analytical tools required to characterize the molecule and degradation products	Large number of analytical tools required to characterize molecules and degradation products
Efficacy (potency) equals to chemical integrity	Potency usually linked to chemical, physical and/ or structural stability
Produced by chemical synthesis	Produced by recombinant technology, cell culture/ fermentation. Process development to maintain structural integrity of molecule
Toxicity	Immunogenicity concerns
	Formulation is integrated as part of the entire development process



Antibody

*~ 150 kDa**
*~ 1200 AA**

Insulin

*~ 50 AA**

**kDa: kilodalton*
**AA: Amino Acid*

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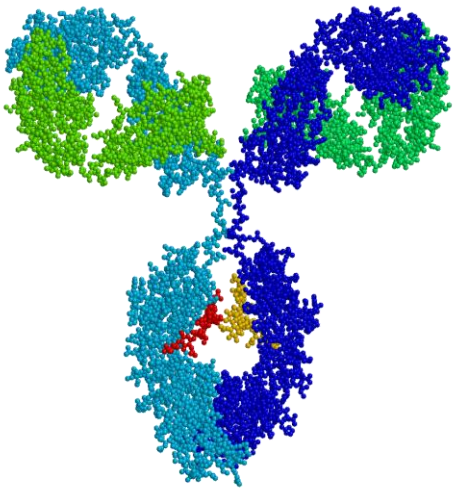
“One process – one product“ paradigm for Bio Formulation development



- Biologics are highly complex molecules whose properties are closely related to their **manufacturing process:**
  - **Fluctuations in the manufacturing process (e.g., pH, temperature, culture media)**
  - **Changes in the manufacturing process (e.g., expression system)**
  - **Batch variability (glycan pattern, oxidation, aggregates)**

- For biotechnology medicinal products, small changes of the drug substance production (upstream processing) and purification (downstream processing) can affect the final drug product.

➔ Changes of the manufacturing process during development should be carefully considered from a formulation perspective.

AGENDA

14:00 Starting with the end in mind. New Approaches to biopharmaceutical development to reduce protein attrition.

Andreas Arnell, (Lonza, UK)

14:30 De devil you know: look early, look hard and minimize the unexpected

Mark Krebs, (Biogen, USA)

15:00 Coffee break. Exhibition Posters

15:30 formulation Patents for Biologics: Challenges and Strategies for innovators and Biosimilar Developers

Tim Shea (Sterne, Kessler, Goldstein & Fox, USA)