Parenteral Biologics Delivery: Key Challenges and Perspectives

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Drug Delivery Technologies & Formulation
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Outline of the Presentation

- **Background**
  - Challenges and Trends in Parenteral Biologics Delivery
  - Expectations for New Parenteral Biologics Delivery Systems and Processes

- **Therapeutic Protein Delivery: Long Acting Formulations**
  - Protein Engineering and Post-Translational Modifications
    - Successful Technologies
    - Perspectives
  - Depot SR Protein Formulations
    - Successful Technologies and Processes
    - Perspectives

- **Conclusions & Perspectives**
Biological Products: a $100 B Market

Development Trends

- Approximately **95 protein drug products are approved**
  - Various final dosage forms
  - Some products exist in both freeze-dried and liquid dosage forms
  - ~ 25+% are mAbs

- **Breakdown of protein dosage forms**
  - Freeze-dried single dose: 33 %
  - Freeze-dried multiple dose: 12 %
  - Liquid single dose: 29 %
  - Liquid multiple dose: 9 %
  - Suspension multiple dose (e.g. insulin): 10 %
  - Others: 7%
    - Including powder inhalation (Exubera): 1 (withdrawn from the market)

- **Development trends**
  - ~ 600 development projects in clinical Phase I-III - ~ 50% are mAbs projects
  - Liquid ready-to-use formulations
  - Multi-dose formulations, i.e. containing preservatives
  - Pre-filled syringes or cartridges for pen (auto-) injector
  - High concentration formulations to reduce volume of injection
    - E.g. mAbs, fusion proteins
What is So Specific About Biologics?

- The High Degree of Complexity of Biologics – Numerous Factors Affecting their Quality

- Process-related impurities
- Aggregation (monom. purity)
- Conformation
- Clipping, Truncation
- Glycosylation
- Oxidation
- Isoform profile
- Deamidation

- Bioactivity depends on 3D structure
- Stability has an Impact on Efficacy, Toxicology Profile and Manufacturability
Key Challenges for Biologics Delivery – Product Improvement & Differentiation (I)

**Antibody design & manufacturing**
- From full mAb to Ab fragments for patent reasons and to avoid Fc-related effects
- Cell lines for higher titer and productivity

**Dose**
- Currently high dose (>> 100 mg up to ~1 g)
- Long i.v. infusion (for 70% mAbs on the market)
- Patient compliance and acceptability issues
- High treatment cost (in hospitals)
- Limited opportunities for s.c. injection

**Stress stability**
- Poor stability under shear stress, exposure to interfaces and surfaces during production, purification and use
- Poor stability under shaking during storage and shipping

**Therapeutic mAbs (Mw ~ 150 kDa)**
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