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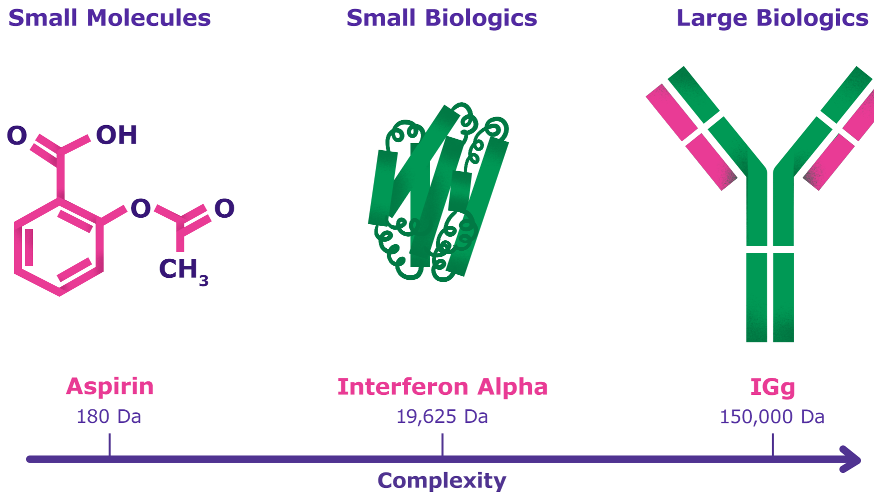
MERCK

HOW TO OVERCOME THE CHALLENGES IN BIOLOGICS DEVELOPMENT & QUALITY CONTROL

The global biologics market is booming. By 2021, it is expected to reach a value of $319B. Though biologics are currently celebrating momentum, their development remains greatly challenging. Even small variations in the highly complex structure of biologics can already have an effect on the biologics’ safety, efficacy, and function. This can cause severe immune reactions in patients and trigger life-threatening conditions. It is therefore essential to address the challenges in biologics development as early as possible.



Small Molecules

Aspirin
180 Da

Small Biologics

Interferon Alpha
19,625 Da

Large Biologics

IGg
150,000 Da

Complexity

TYPES OF BIOLOGICS

Monoclonal antibodies (mAbs)

Fusion proteins

Antibody-drug conjugates (ADCs)

WORKFLOW OF BIOLOGICS DEVELOPMENT

PRODUCT DISCOVERY

- Target Selection & Identification
- Candidate Selection
- Optimization
- Early System Biology Studies
- Biomarker Identification
- Preclinical Testing
- Cell-Based Assays: Early Toxicity, Efficacy, Safety

PROCESS DEVELOPMENT

- Cell Line Development
- Animal Studies: Toxicity, Efficacy, Safety
- Pharmacokinetic (PK) & Pharmacodynamic (PD) Formulation Development
- Stability Studies
- Product Characterization
- Process Characterization

CLINICAL DEVELOPMENT

Proof of Concept

PHASE I

- Safety
- GMP Production
- Stability Studies
- Product Characterization
- PK & PD in Healthy Humans
- Method Validation

PHASE II

- Safety
- Efficacy
- PK
- Scale-up
- Stability Studies
- Dose Titration

IND

PHASE III

- Safety
- Efficacy
- Full GMP Production
- Quality Assurance
- Quality Control
- Stability Studies
- Product Release Testing
- Process Validation & Characterization

PHASE IV

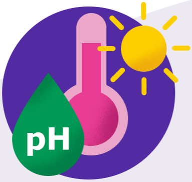
COMMERCIAL

✓ **REGULATORY COMPLIANCE**

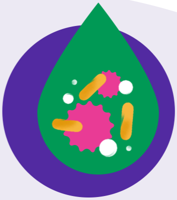
10-12 YEARS

20-25 YEARS

BIOLOGICS DEVELOPMENT & QUALITY CONTROL COME WITH A NUMBER OF CHALLENGES...



Sensitive to environmental factors, e.g. pH, temperature, light



Susceptible to contamination, e.g. of host cell protein, viral or microbial origin

Challenging to find the right reference standards

Difficult to allocate resources to method development

Complex to scale up

Subject to evolving regulations

If anything in the development of biologics goes wrong, it can result in manufacturing failures, severe time delays, regulatory issues, and risks for the patient. One change triggers a cascade of changes!

HOW DOES MERCK SUPPORT BIOLOGICS DEVELOPMENT & QUALITY CONTROL?

To prevent contamination, Merck* has

- 40+ years of sterility testing expertise
- Developed the Monocyte Activation Test (MAT) *in vitro* test kits for pyrogen testing, to move away from animal-based tests
- A complete portfolio for microbiology quality control monitoring of air, surfaces, people, raw materials, in-process samples & the final product

To address reference standard challenges, Merck has

- Developed a comprehensive portfolio of 100+ common impurities often found in extractables & leachables studies

To free more resources for method development, Merck uses

- The SigmaMAb ADC Mimic as a non-toxic drug mimic for mass spectrometry & high-performance liquid chromatography
- The SOLu-Trypsin enzyme for mass spectrometry. SOLu-Trypsin is a convenient, ready-to-use trypsin solution for protein digestion & is stable in solution when refrigerated

To support its customers through the regulatory maze, Merck

- Has decades of regulatory experience
- Complies with numerous global regulatory standards, e.g. ISO, ACS, USP, PhEur, JP, FDA CFR
- Offers products with a range of specifications & accreditations

MEET MERCK'S LIFE SCIENCE BRANDS

> *Merck life science portfolio brands have their own unique way of doing things, but all are connected by a common purpose and ambition: solving the toughest problems in life science by collaborating with the global scientific community and accelerating access to solutions that improve health for people everywhere.*
>
> **Wayne Way, Global Strategy Pharma QC at MilliporeSigma**

Millipore®
Preparation, Separation, Filtration & Monitoring Products

Ecosystem of products & services spanning preparation, separation, filtration & monitoring

Supelco®
Analytical Products

Portfolio of analytical solutions for analytical chemists to ensure accurate, precise & reproducible results

Milli-Q®
Lab Water Solutions

Portfolio of lab water solutions to ensure consistent water quality & full compliance, freeing time for vital work

Sigma-Aldrich®
Lab & Production Materials

Strong & ever-expanding offering of lab & production materials

BioReliance®
Pharma & Biopharma Manufacturing & Testing Services

This offering includes biopharmaceutical characterization, safety testing, process development & clinical & commercial biomanufacturing

Tackle biologics development and quality control now! Benefit from Merck's expertise and check out its latest educational content and products here!

*The life science business of Merck operates as MilliporeSigma in the U.S and Canada

List of Acronyms

ACS - American Chemical Society
ADC - Antibody-Drug Conjugate
ATP - Adensosine Triphosphate
Da - Dalton
FDA CFR - Federal Drug Administration Code of Federal Regulations
GMP - Good Manufacturing Practice
IGg - Immunoglobulin G
IND - Investigational New Drug Application
ISO - International Organization for Standardization
JP - Japanese Pharmacopeia
mAb - Monoclonal Antibody
PD - Pharmacodynamic
PhEur - European Pharmacopeia
PK - Pharmacokinetic
QC - Quality Control
USP - United States Pharmacopeia

SOURCES

- California Manufacturing Technology Consulting
- European Medicines Agency, SME Office
- Pharma Focus Asia
- Merck KGaA, Darmstadt, Germany

Want to work with us?
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