Single-Use Systems
A new Age of Drug Making

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May 2023

PDA
Parenteral Drug Association

CONNECTING PEOPLE SCIENCE AND REGULATION®

Guidelines

all questions are welcome!

please share your knowledge and experiences

Agenda

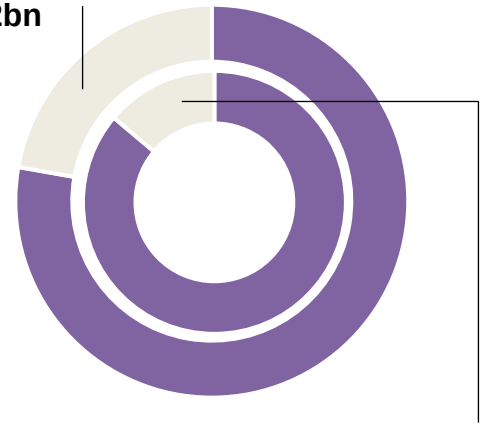
- A new Age of Drug Making
  - Current Market Trends
  - Manufacture in Biopharma Industry
  - an Example: ADCs
- Single-Use Systems
  - Advantages
  - Challenges
- Outlook: Today & Tomorrow

A new Age of Drug Making

Trends in the Target Markets

Growing and aging population[1]
9 billion people by 2050

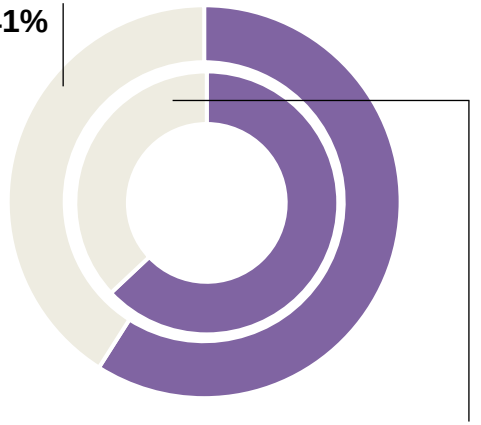
World population over age 60 in 2050
>2bn



World population over 60 in 2022
~1bn

Biologics are gaining importance[2]

Sales share of biologics in 2028
~41%



Sales share of biologics in 2022
~37%

~10%
CAGR[3] for the biopharma market in 2022–2026

[1] United Nations: World Population Prospects, 2019 [2] Evaluate Pharma: World Preview 2022, Outlook to 2028, August 2022 [3] Compound Annual Growth Rate

What are Biopharmaceuticals?

	Active agent	Manufacturing	Administration
Chemical drugs	 Small molecules	 Chemical synthesis	 Mainly oral
Biopharmaceuticals	 Large molecules > 20,000 atoms	 Cell culture processes with living cells	 Mainly intravenous

What are Biopharmaceuticals?

Advantages

- First-time or improved treatment of serious illnesses, such as cancer, multiple sclerosis, rheumatism
- Targets only diseased cells
  - fewer side effects
  - High efficiency
- New vaccines

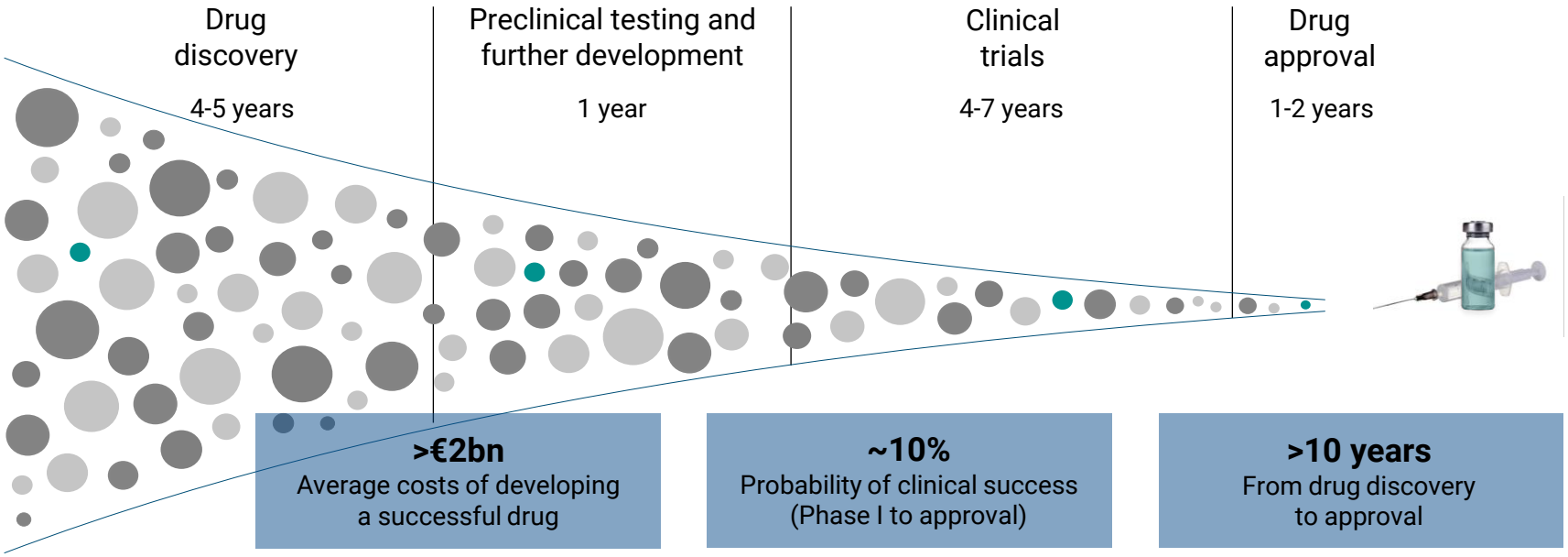
	Active agent	Manufacturing	Administration
Chemical drugs	Small molecules	Chemical synthesis	Mainly oral
Biopharmaceuticals	 Large molecules > 20,000 atoms	 Cell culture processes with living cells	 Mainly intravenous

Challenges

- Difficult and complex analyses
- Expensive R&D and production
- High in-production contamination risks
- Potentially harmful when released (*e.g.* toxin)
- Treatment costs can be extremely high

Why do we encounter these challenges?

Only one out of 10,000 New Drug Candidates reaches the Market

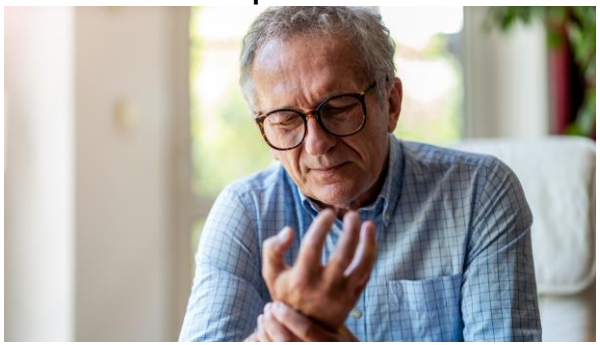


Schematic example of biologic drug discovery with data from the Association of the British Pharmaceutical Industry

Biopharmaceutical Development and Manufacture are complex

As a Consequence, Biotech Medications Are Very Expensive

HUMIRA® | Abbvie



€ ~12,000

Annual cost of treatment in GER

Monoclonal Antibodies

against inflammatory immune diseases such as rheumatism, Crohn's disease, or psoriasis

Approval 2003, first biosimilars available

YESCARTA® | Gilead

€ ~280,000

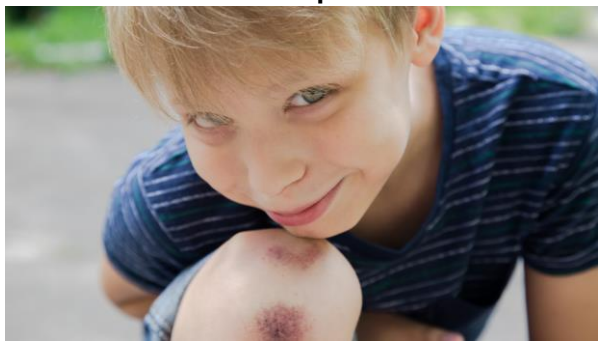
Cost per treatment in Europe

CAR-T Cell Therapy

combating certain types of blood cancer, for example Non-Hodgkin lymphoma

EMA-Approval 2018

HEMGENIX® | CSL



$ ~3.5 Mio.

Cost per treatment in the USA

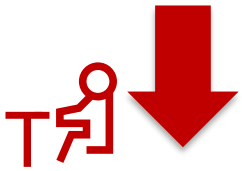
Gene Therapy

against hemophilia, a disorder of blood coagulation

FDA-Approval 2022

Antibody Drug Conjugates (ADCs)

Do you know the answer? Please stand up



Is your answer „no“? Please sit.

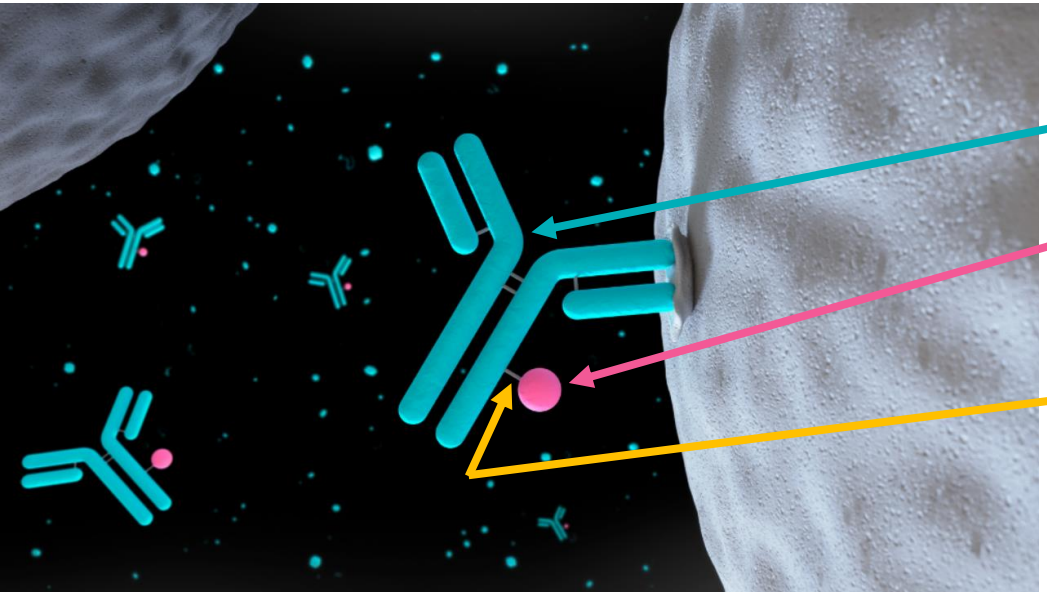
Who has heard of ADCs? (No need to give details)

Who knows what ADCs are? (No details)

Who would like to explain what ADCs are?

Antibody Drug Conjugates (ADCs)

ADCs are new class of highly potent biopharmaceutical drugs composed of a cytotoxic drug conjugated covalently to a monoclonal antibody (mAb) by a linker.



An ADC consists of three components:

- a **monoclonal antibody** (targeting a specific tumor-associated antigen),
- a highly potent **toxic chemical payload** (which enters the cell via the mAb to deliver its toxic effects)
- a chemical **linker** (which connects, via conjunction, the payload to the mAb).

Watch 1st min of "what are ADCs?"

ADC Process Development

Considerations

- Safety
- Processing time
- Costs of goods
- Process control
- Batch size
- Volume limitations
- Purification strategies
- Equipment chemical compatibility
- Cleaning validation
- Contaminated waste
- Cross contaminations

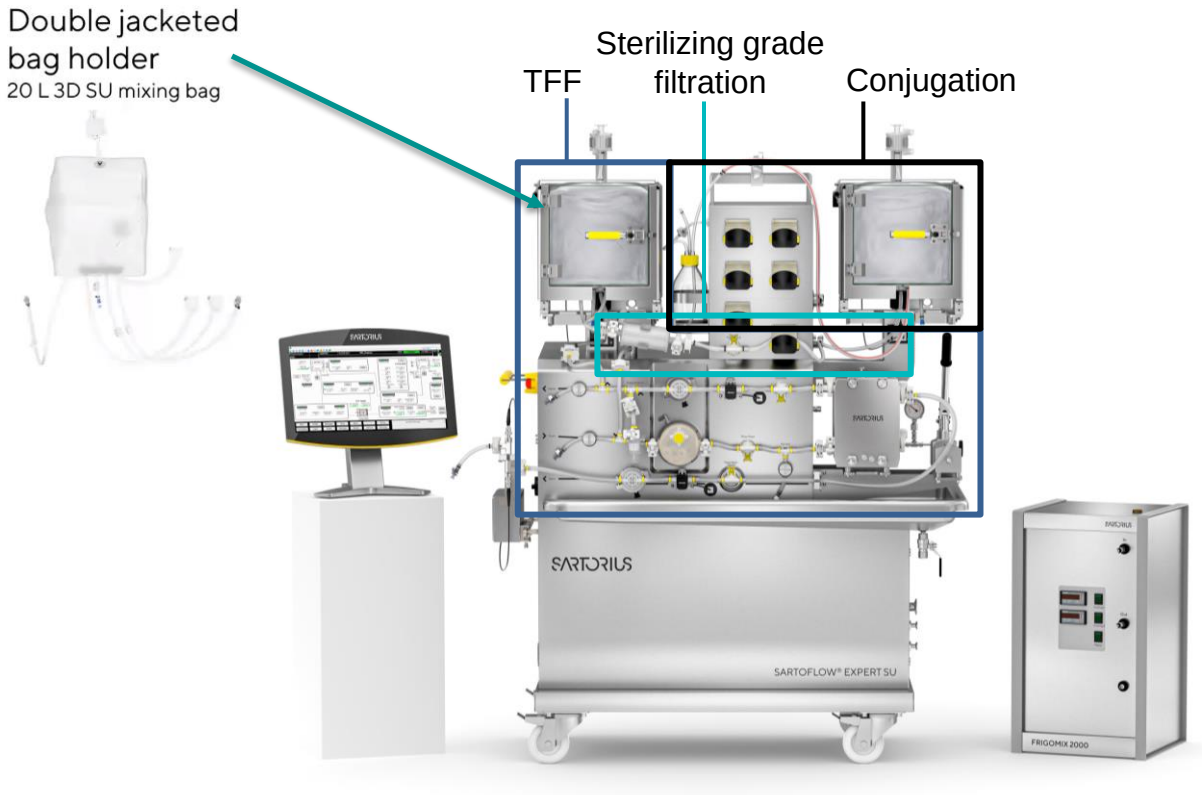
Solution = Single-Use (SU) Manufacturing?

Current Approaches Not Always Sustainable for ADC Development

Current approaches	What does it mean for you?	The new way forward
		
Extensive use of multiuse systems, e.g. glass and stainless steel	Potential risks for operators (breakage/non-closed system) and environment (CIP)	Use chemically compatible SU ‘closed’ solutions and automated systems for lower risk of contamination and greater process flexibility
Using old, complex methods to develop current processes	Delayed time to market and lost market share	Keep an innovative mindset to look for solutions to simplify

CIP – Clean in Place | SU – single use

Example: New Approaches for ADC Development



The new way forward

Use chemically compatible SU ‘closed’ solutions and automated systems for lower risk of contamination and greater process flexibility

Keep an innovative mindset to look for solutions to simplify

Watch remainder of "what are ADCs?"

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Let‘s get to know each other!

Single-Use

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Single-Use

Have you ever used…?

What dis/advantages come to mind?

Single-Use in Bioprocessing

Single-use technology has gained great significance all over the world for biopharmaceutical production.

The global single-use bioprocessing market is expected to witness a compound annual growth rate of **16.24% from 2023 to 2030** to reach USD 80,129 million by 2030*

SU equipment ranges from simple, single-material items (tubing) through to complex controlled systems incorporating many components and materials (bioreactors). Many of the more complicated SU systems contain reusable non-product-contact elements.

*https://www.grandviewresearch.com/industry-analysis/single-use-bioprocessing-market

Single-Use

From the coffee **seller**‘s point of view:
What dis/advantages come to mind?

VS.

Single-Use

Benefits

Challenges

Costs

***Low costs of labor and materials**: Reduction of initial investments and R&D costs. Reduced costs associated with validation, sterilization, cleaning, & maintenance → reduced energy and water demand*

Productivity

***High productivity** follows from reductions in cost, from eliminating the need for changeover cleaning/validation between operations, as well as from high flexibility with different designs (quick to configure)*

How to comply with laws and regulations, such as the demands of **GMP**?

Time Savings

Faster set-up, shorter turn-around time, and reduced space requirements**. This reduces the amount of time the staff spends on preparation, set-up, validation, and documentation along with related costs. → **Reduction of time to market

Risks

Cross-contamination risks are extremely low.

***Film-related**: Particles, extractables & leachables, film integrity, physical strength/ durability (also during transport, mixing, heating/cooling, high pressures, and contact with solvents), labels, secure connectors*
***Operation-related**: Installation, integrity testing, waste handling, training, material robustness, safety, sensors*
***Supply chain-related**: delivery assurance, quality agreements, change control, supplier's suppliers*

Disposal

*Waste can be **thermodynamically recycled** (on site)*

Waste generation and treatment

SUS – A new Age of Drug Making Course Content

SUS + GMP = SOS?

How to comply with laws and regulations, such as the demands of **GMP**?

Single-Use Systems

- Manufacturing of consumables
- Smart wetware design
- General applications (mixing, filtration, storage, dis/connections)
- Integrity tests
- Handling of consumables
- Working under GMP regulation

Good Manufacturing Practice

- Regulative situation: rules & recommendations
- External Requirements
- Data monitoring and evaluation
- Data integrity
- Data analysis
- Fault handling

Agenda – Today (May 10th, 2023)

Start	Duration	Trainers	Topics
8:30 AM	30 mins	ALL	Introduction and Safety briefing
9:00 AM	45 mins	Lina Klein	Introduction to SU bioprocessing
9:45 AM	45 mins	Dominic Parry	GMP Update on SUS (part 1)
10:30 AM	15 mins		Coffee Break
10:45 AM	30 mins	Dominic Parry, Mathias Siebner	GMP Update on SUS (part 2)
11:15 AM	60 mins	Dominic Parry	Hands-on exercise 1: Gowning & Experiment on advantages of SUS
12:15 PM	60 mins		Lunch
1:15 PM	45 mins	Tanja Sedlacek, Ghada ben Amor	Basics of single-use bioprocessing
2:15 PM	15 mins		Coffee Break
2:30 PM	120 mins	Tanja Sedlacek, Ulrike Stollberg, Ghada ben Amor	Hands-on exercise 2: Connection/Disconnection
4:30 PM	30 mins	ALL	Wrap-up
7:00 PM			Dinner

Agenda – Tomorrow (May 11th, 2023)

Start	Duration	Trainers	Topics
8:30 AM	45	Andreas Prediger, Henry Weichert	Sensors and Automation in single-use systems: Overview and demonstration
9:15 AM	60	Tanja Sedlacek, Ulrike Stollberg, Ghada ben Amor, Andreas Prediger	Hands-on exercise 3 (bag types and sensors)
10:15 AM	15		Coffee Break
10:30 AM	60	Dominic Parry	Data Integrity, Data Analysis, and Monitoring
11:30 AM	45		Lunch
12:15 PM	45	Mathias Siebner, Sonja Klaunzler, Claudia Hogekamp	Filtration & CCT
1:15 PM	45	Mathias Siebner, Sonja Klaunzler, Claudia Hogekamp	Hands-on exercise 4 (Filter Integrity testing)
2:00 PM	15		Coffee Break
2:15 PM	30	Dominic Parry, Mathias Siebner	Filter Integrity Testing fault handling – GMP view
2:45 PM	45	Dominic Parry, Mathias Siebner	Hands-on exercise 5 (GMP practical session, failed filter IT)
3:30 PM	30	Maina Kerbrat	Data Recording & Evaluation
4:00 PM	30	ALL	Wrap-up

Conclusions

- Target Markets: Growing and Aging Population

- Biologics are Gaining Importance,
  but are Expensive and Tricky to Develop and Manufacture

- Strategic Implementation of Single-Use Technologies
  can help companies to remain competitive in a global market by
  - increasing flexibility and overall output,
  - decreasing manufacturing costs,
  - reducing facility footprint and
  - reducing inventory

The proliferation, diversification, and uptake of SU technologies will play a vital role in enabling the **manufacturing of affordable biologics** as the industry adapts to the rise of biologic drug development

We hope you enjoy these days with us ☺