WACKER

CREATING TOMORROW`S SOLUTIONS

SynCo Bio Partners B.V. & Wacker Biotech GmbH: THE MICROBIAL CMO

Human Microbiota: Proof of Concept to Production

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SynCo Bio Partners B.V.

SynCo Bio Partners

The Wacker Group – Over 100 Years of Success

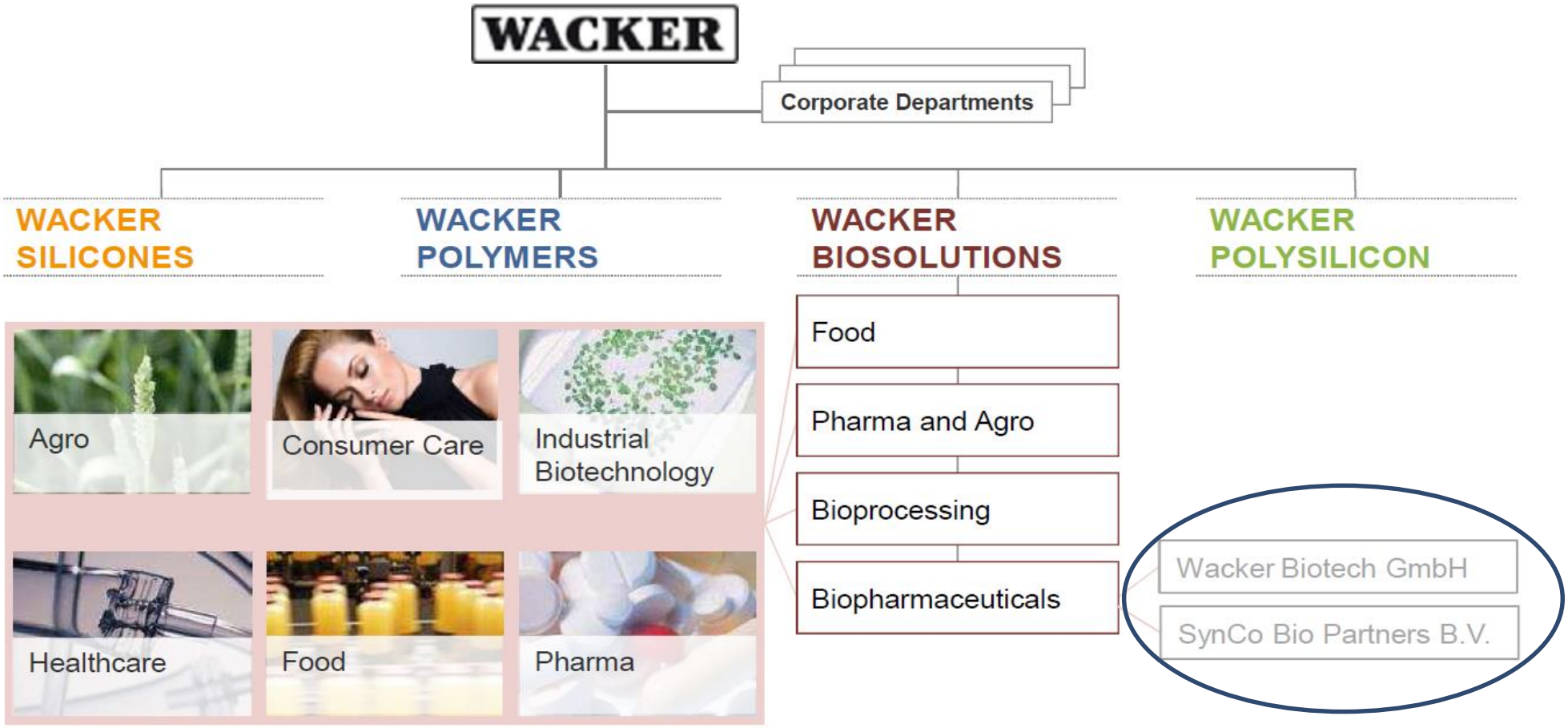
Wacker Chemie AG

- Founded in 1914 by Dr. Alexander Wacker
- Headquartered in Munich

WACKER Group (2017)

Sales:	€4.92 billion
EBITDA:	€1.01 billion
R&D:	€153 million
Investments:	€327 million
Employees:	13,811

Wacker Biosolutions Division



Wacker Biotech & SynCo Bio Partners

Operate 3 State-of-the-art GMP Facilities in Europe

Amsterdam Site

- ~110 FTEs
- 1,500 & 270 L line
- Live bacteria
- Fill & Finish
- EMA approved
- FDA approved
- ANVISA approved

Halle Site

- ~104 FTEs
- 1,500 L line
- EMA approved
- FDA approved

Jena Site

- ~95 FTEs
- 350 L line
- EMA approved

SynCo Bio Partners B.V. Amsterdam

We are **THE MICROBIAL CMO** with a solid track record and strong customer focus

- We are a 100 % subsidiary of Wacker Chemie AG having a high **financial** and **long-term stability**
- Located in Amsterdam, the Netherlands
- GMP licensed for clinical & commercial supply
- Production of **Vaccines, Proteins** and **Live Microbial Products**

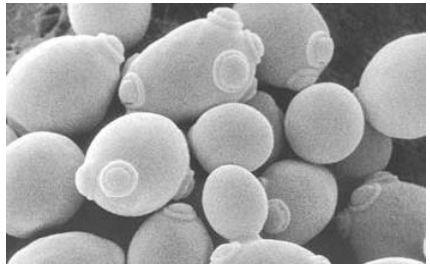
SynCo Bio Partners B.V. Amsterdam

- Licensed cGMP CMO, approved by worldwide regulatory bodies (FDA, EMA, ANVISA, MFDS, Health Canada)
- Production Bulk Drug Substance (20 – 1500L)
  - Live microbial products (LMPs) and microbial derived biopharmaceuticals
  - Oral & parenteral
- Aseptic fill finish & lyophilization
  - Up to 20,000 vials
  - Bulk lyophilization up to 70L
- In house QC testing & QA release, stability studies, regulatory support

Microorganism Experience

Live Microbial Products

- *Bifidobacterium spp.*
- *Lactobacillus spp.*
- *Lactococcus lactis*
- *Oxalobacter formigenes*
  - *Salmonella typhi*
  - *Vibrio cholerae*
  - *Listeria monocytogenes*
  - *Saccharomyces cerevisiae*
- Others (non-disclosed)



Production Organisms

- *Escherichia coli*
- *Pseudomonas fluorescens*
- *Haemophilus influenzae type B*
- *Corynebacterium diphtheriae*
- *Neisseria meningitidis (group A, C)*
- *Bordetella pertussis*
- *Pichia pastoris*
- *Saccharomyces cerevisiae*

- ***Cultured under anaerobic conditions***
  - **Cultured under aerobic conditions**

The Objective

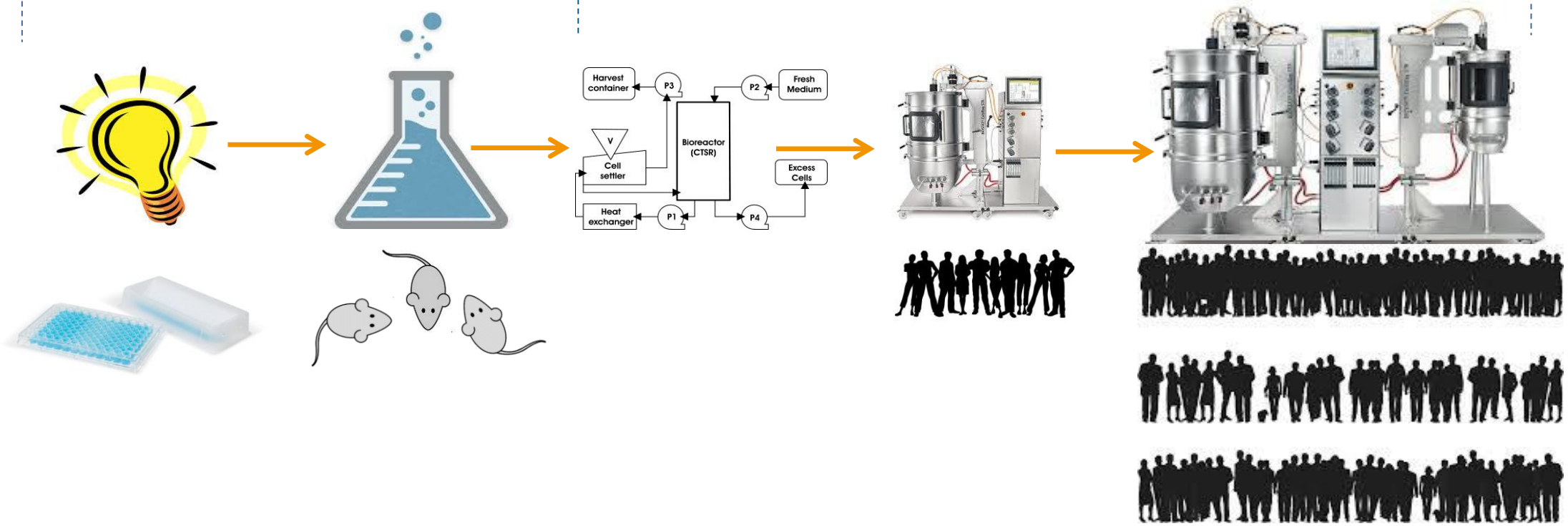
- Share experiences & approaches from various Live Microbial Product cGMP projects

- Early considerations for process development

From Idea to Live Microbial Product

Product Company

Contract Manufacturer



Criteria for GMP Production

Requirements GMP Production

- All equipment calibrated
- All personnel trained for the actions performed
- All raw materials according specifications
- Controlled area
- Execution according to protocol

QA review

Analytical Testing: Content, Chemical and Biological Contamination

Assays qualified/validated

GMP Release of Batch by Qualified Person

The Live Product:
Production Process

- Parenteral/sterile product: Closed, monoseptic process

- Oral/non-sterile product: Aseptic process

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- List of objectionable organisms based on patient population

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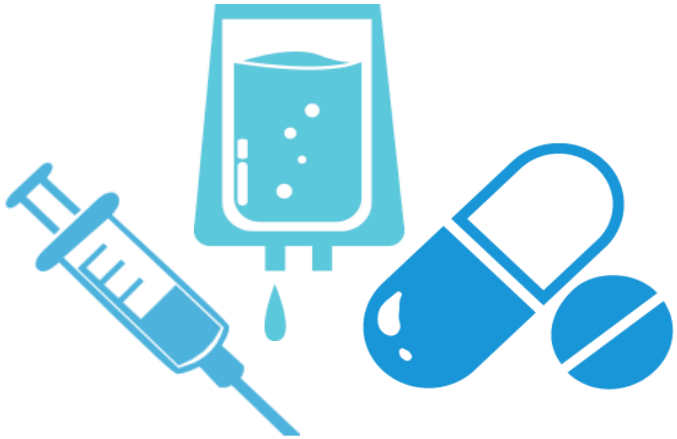
- Closed, monoseptic process desirable



Typical Process Setup for LMPs

- Inoculation
- Precultures
- Fermentation
- Concentrate + wash cells (TFF)
- Formulation

Open, aseptic handling (BHC)

Disposable (sterile) systems

- Filling in vials/trays
- Freeze drying / Liquid formulation

Open, aseptic handling

Class A; Clean Room

Growing the Live Product:
Precultures & Fermentation

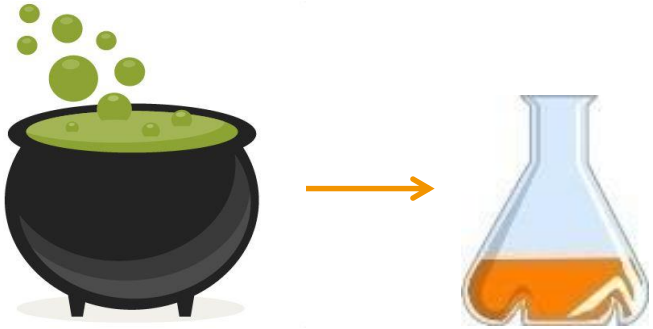
Production Organism

- Potential pathogen (Class I, II, III)
- Genetically modified (GMO, origin of insert)
- Master Cell Bank / Working Cell Bank

GMO License

Growth Medium GMP Compatible

- Free of animal derived components
- All components pharmacopoeia grade
- No antibiotics (definitely no β-lactams)
- Incl. cell bank medium



Growing the Live Product:
Fermentation – Choice of Reactor

Wave Bag

- Ease of use
- Closed system
- Cleaning (validation)

Single-use Bioreactor

- Best of both worlds

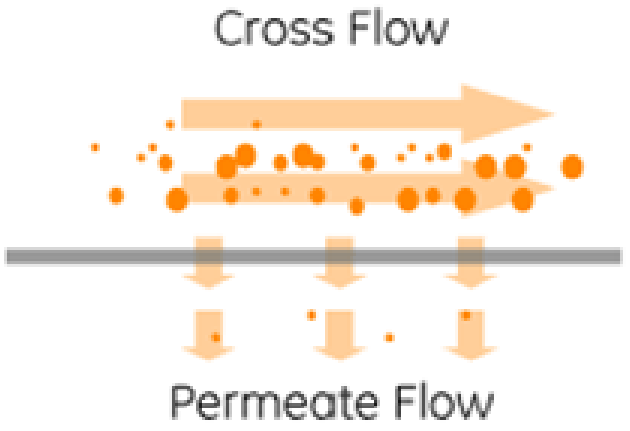
Stainless Steel Reactor

- Aeration
- Mixing
- Volume

Purification and Concentration of the Live Product

Centrifugation

- Open handling / process
- Large product loss



Ultrafiltration / Tangential Flow Filtration (TFF)

- Closed process
- Concentrate cells
- Wash out contaminants

- **Implement TFF at early stage: Change from centrifugation to TFF will affect the impurity profile**

Stabilizing the Live Product:
Viability Will Be Key!

Dilute Product with Cryoprotective Buffer

- Target specific range live cells (e.g. 10^8 – 10^{10} cfu/ml); think of potential loss in viability during freezing / freeze-drying
- Cryoprotectant buffer composition plays vital role in minimizing loss of viability

Fill

- Open handlings with Live Microbes in Cleanroom / Class A
- Aseptic process validation / process simulation for sterile products

Freezing / Freeze-drying

- Viable cell loss 50-95% (depending on organism + cycle)
- Target specific range live cells (e.g. 10^7 – 10^9 cfu/vial) based on clinical requirement

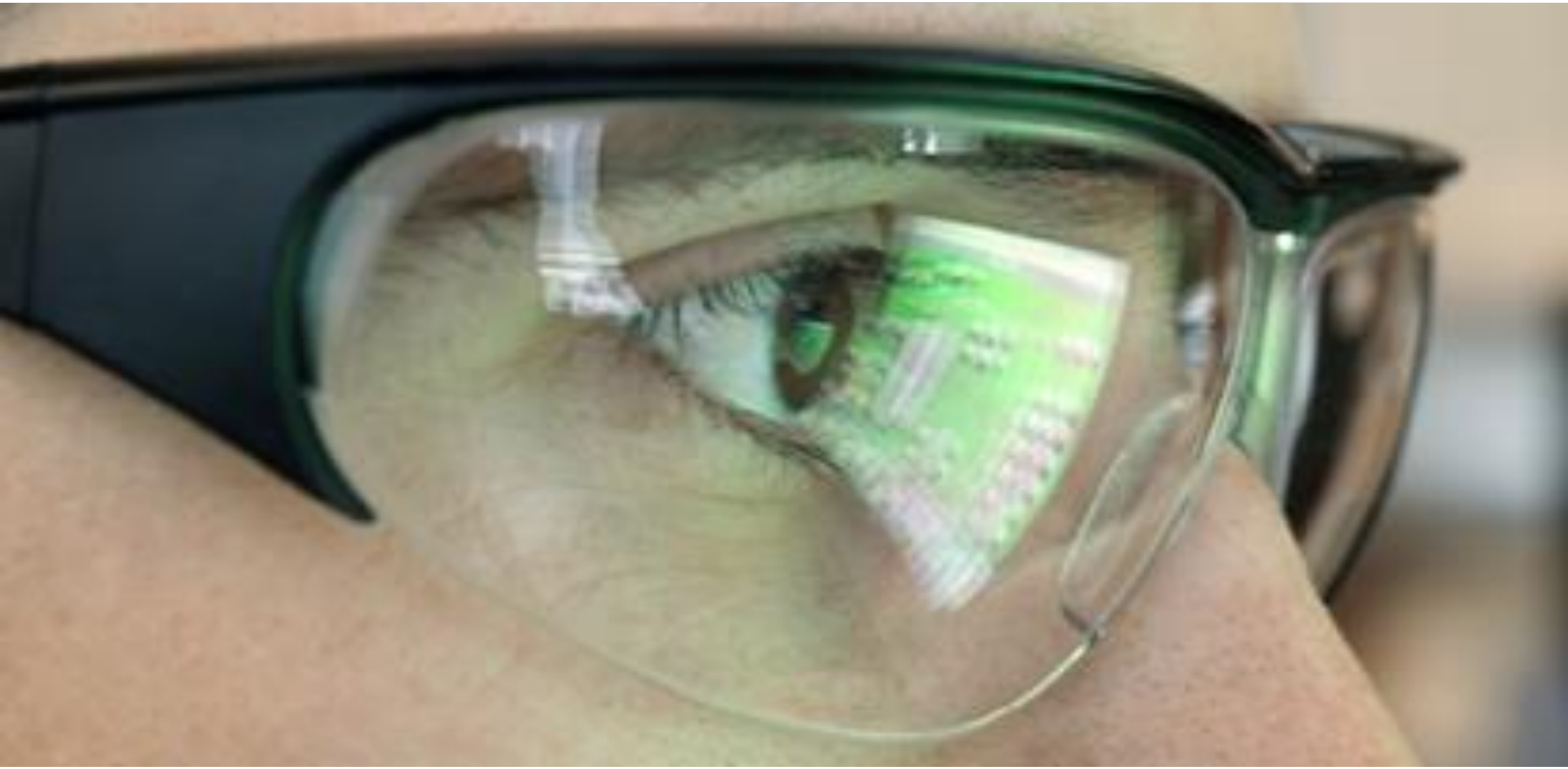
When Preparing for Clinical Trials

Avoid Delays in Clinical Trials!

- Be aware of the requirements
- Think ahead during process development

- If a contract manufacturer is required;
  start looking for suitable partners well in time!

Thank You for Your Attention!



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Your partner in microbial biologics production: **contact@syncobiopartners.com**