Das Beste herausholen – innovative Lösungen in der biopharmazeutischen Produktion

26. September 2019

Michael Dekner
Head of PS FFF

Takeda

Better Health, Brighter Future

Takeda Austria

Top employer in the Austrian biopharmaceutical industry



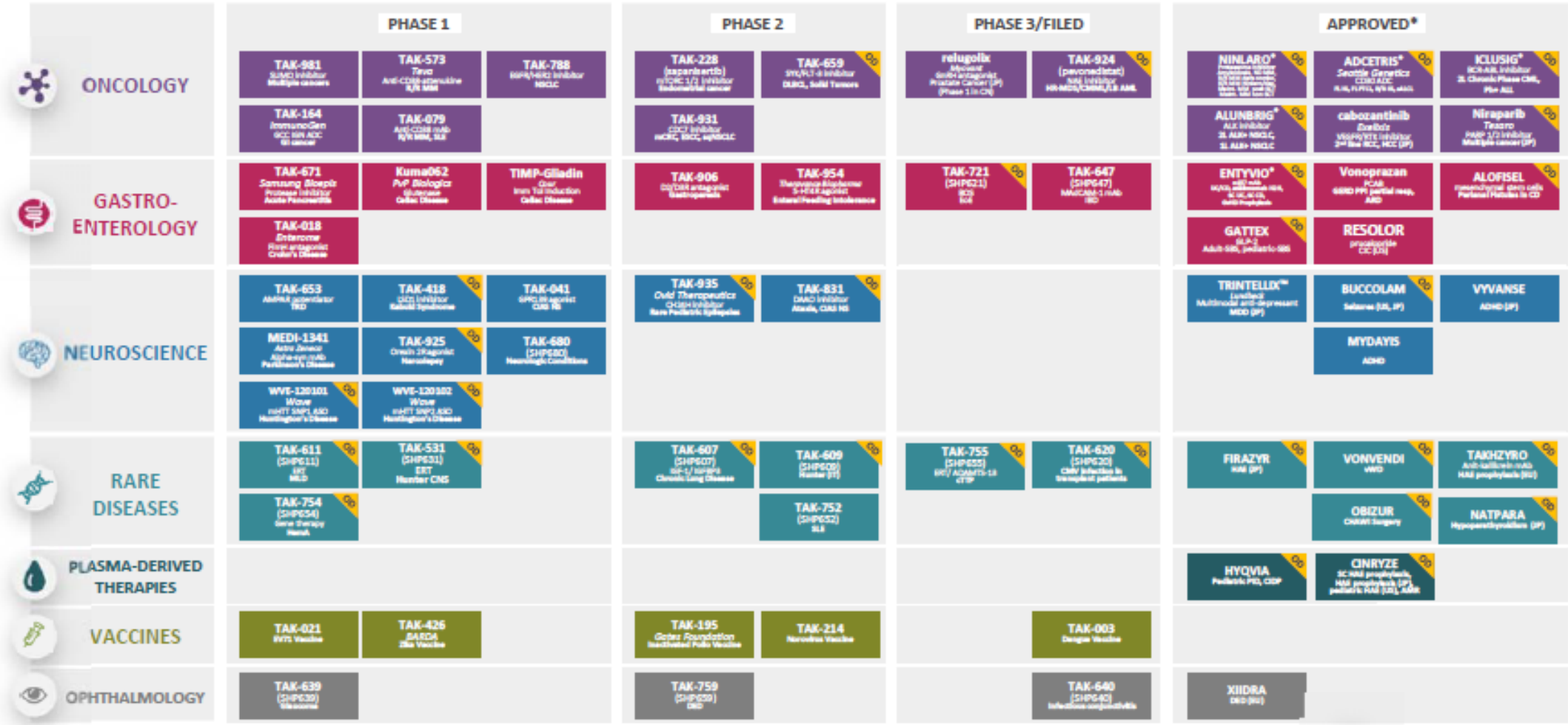







R&D ENGINE

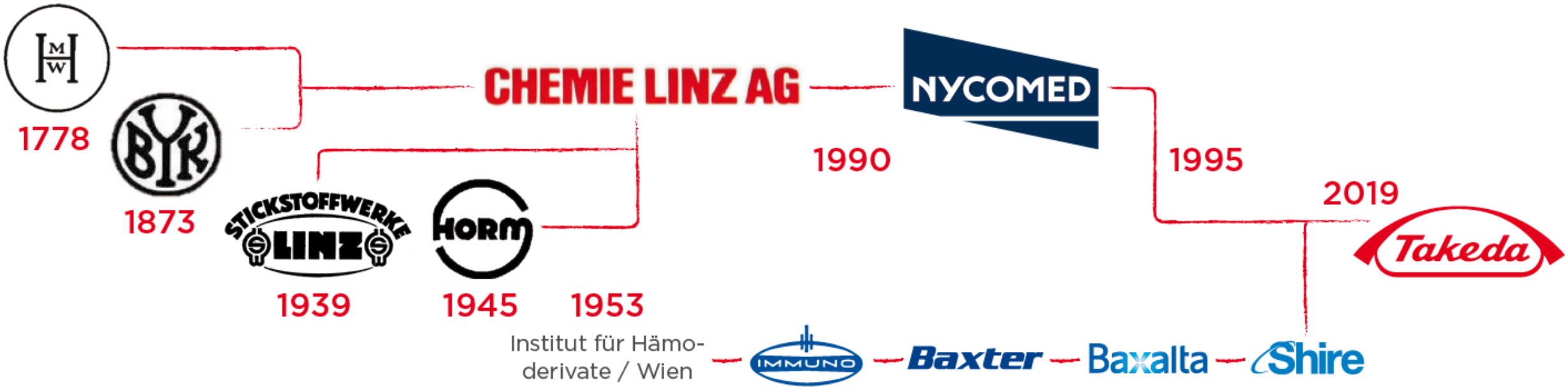
We have an innovative and maturing pipeline



*With ongoing significant clinical development activities. Pipeline as of January 4, 2019 for Takeda and September 30, 2018 for Shire
As announced on October 27, 2018, Takeda has proposed a remedy to the European Commission of a potential divestment of SHP647 and certain associated rights

Orphan Drug Designation

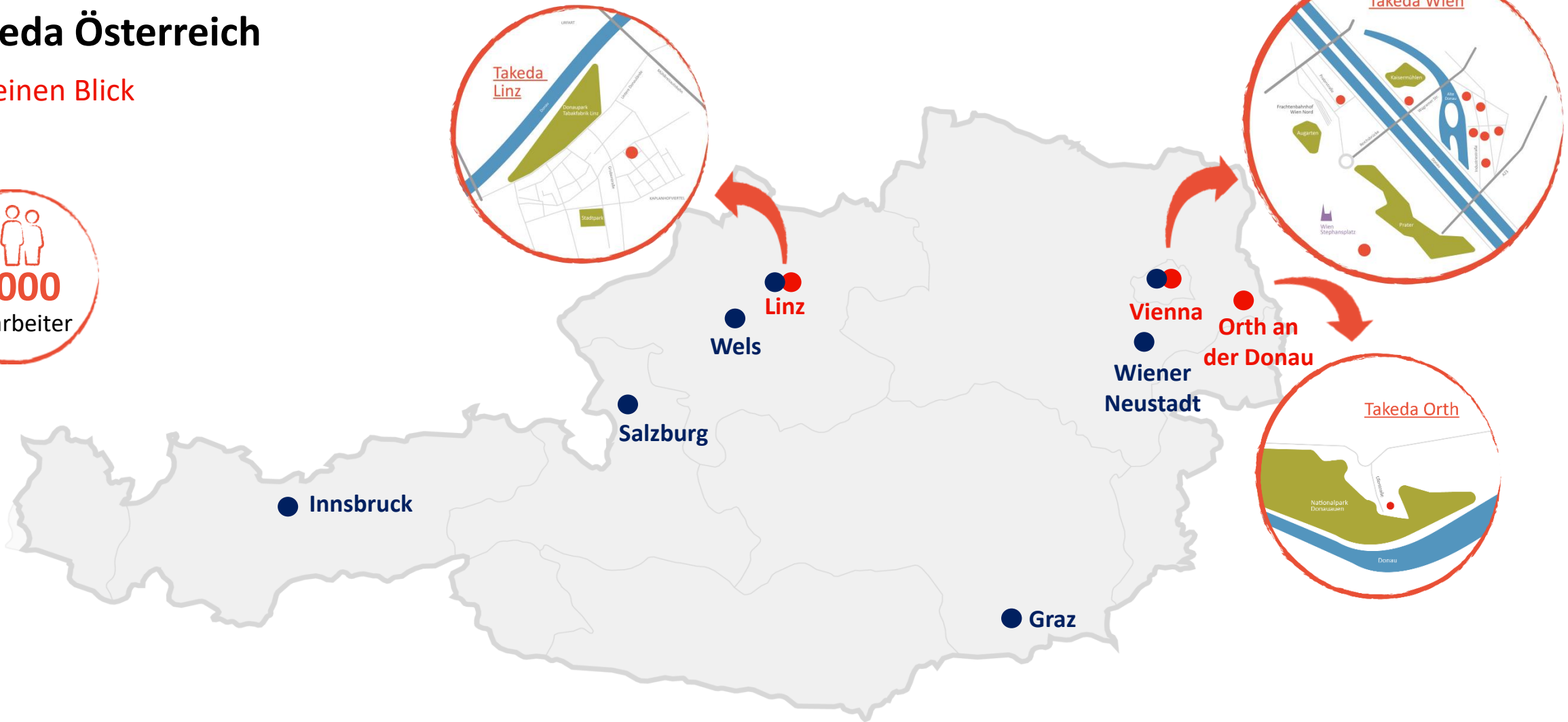
Today‘s integration continues a legacy of great companies coming together in Austria to deliver the highest quality patient care



Takeda Österreich

Auf einen Blick

+4.000
Mitarbeiter



Takeda Österreich

Ein bedeutender Standort mit langer Tradition

TOP

Pharmaarbeitgeber in Österreich

Lange Tradition in Österreich

Heilmittelwerke, Chemie Linz, Immuno, Baxter, Nycomed, Shire

Verarbeitung von 3 Mio. Liter Plasma p.a.

Wien ist eines der größten Fraktionierungs-werke weltweit

Pathogen Safety

Globales Center für Excellence für Pathogensicherheit

Zentrum für Gentherapie

in Orth an der Donau

238 Jahre

Geschichte Takeda international

10 eigene Plasmaspendezentren in Österreich

Gesamte Wertschöpfungskette in Österreich

Forschung – Plasmaaufbringung – Plasmaverarbeitung – Verpackung – Versand in 100 Länder – Vertrieb in Österreich

Heimisches Forschungsteam

mit Weltruf in den Bereichen Hämatologie, Immunologie und Gentherapie

Multi-Product Site Wien

17 Plasmaprodukte aus Wien

	TAKEDA PLASMA-DERIVED PRODUCTS	PRODUCED IN VIENNA
ALBUMIN	Flexbumin	
	Human Albumin	X
α1-GLOBULIN PULMONOLOGY	Aralast	X
	Glassia	
α2-GLOBULIN COAGULATION FACTORS	Hemofil M	
	Immunate	X
	Immunine	X
	Feiba	X
	Prothromplex, Bebulin	X
	Prothromplex T	X
	Factor VII	X
α2-GLOBULIN COAGULATION INHIBITORS/INACTIVATORS	Cinryze	X
	ATIII Antithrombin	X
	Ceprotin	X
β-GLOBULIN BIOLOGICAL TISSUE SEALANT	Artiss	X
	Tisseel	X
	Thrombin	X
γ-GLOBULIN ANTIBODY CONCENTRATES	BabyBIG	
	Hyqvia	X
	Cuvitru	X
	Gammagard Liquid/Kiovig	X
	Gammagard SD	

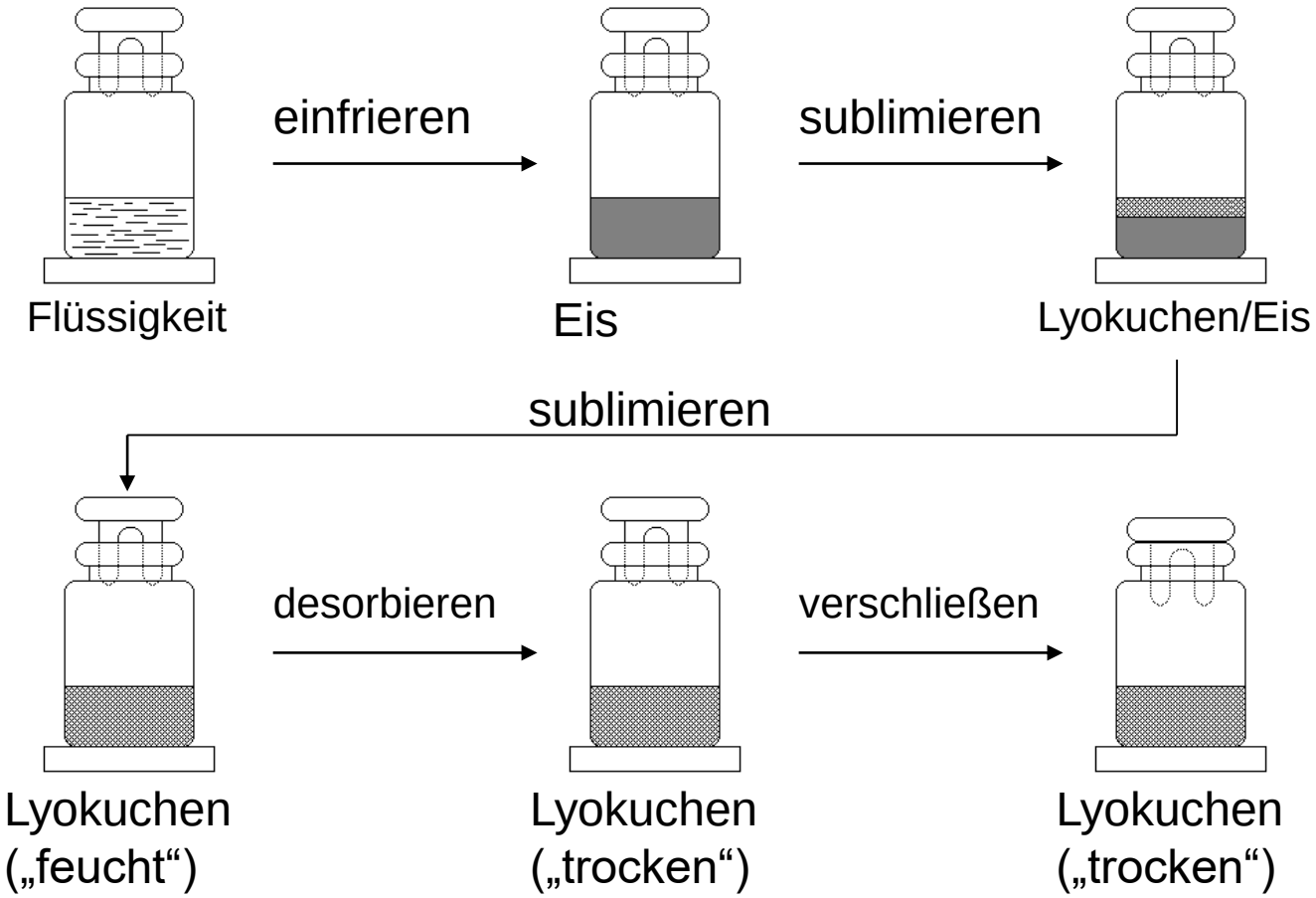
17 products made in Vienna and shipped in over 100 countries.

Gefriertrockung

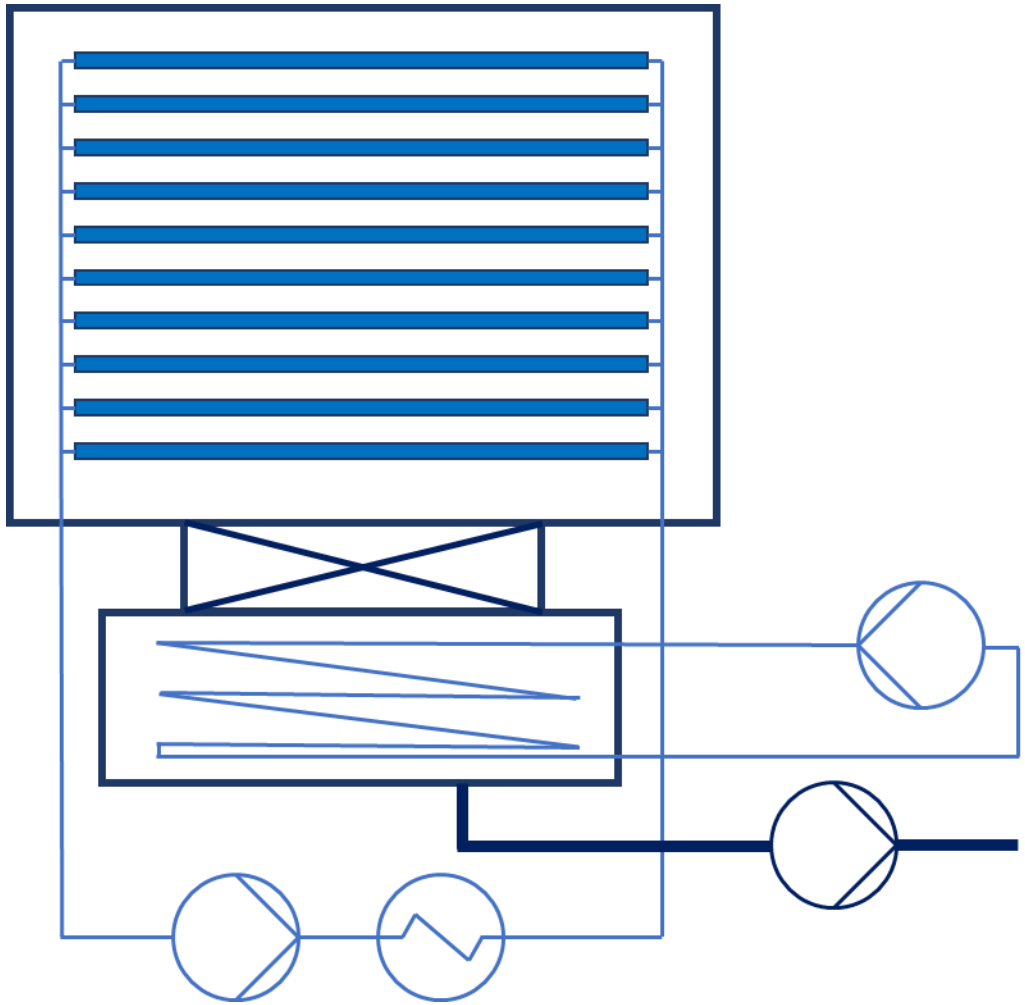
„**Lyophilization** is defined as a **stabilizing process** in which the **substance** is first **frozen** and then the quantity of the **solvent** is **reduced** first by sublimation (primary drying) and then by desorption (secondary drying) to values that will **no** longer support **biological growth** or **chemical reactions**.“

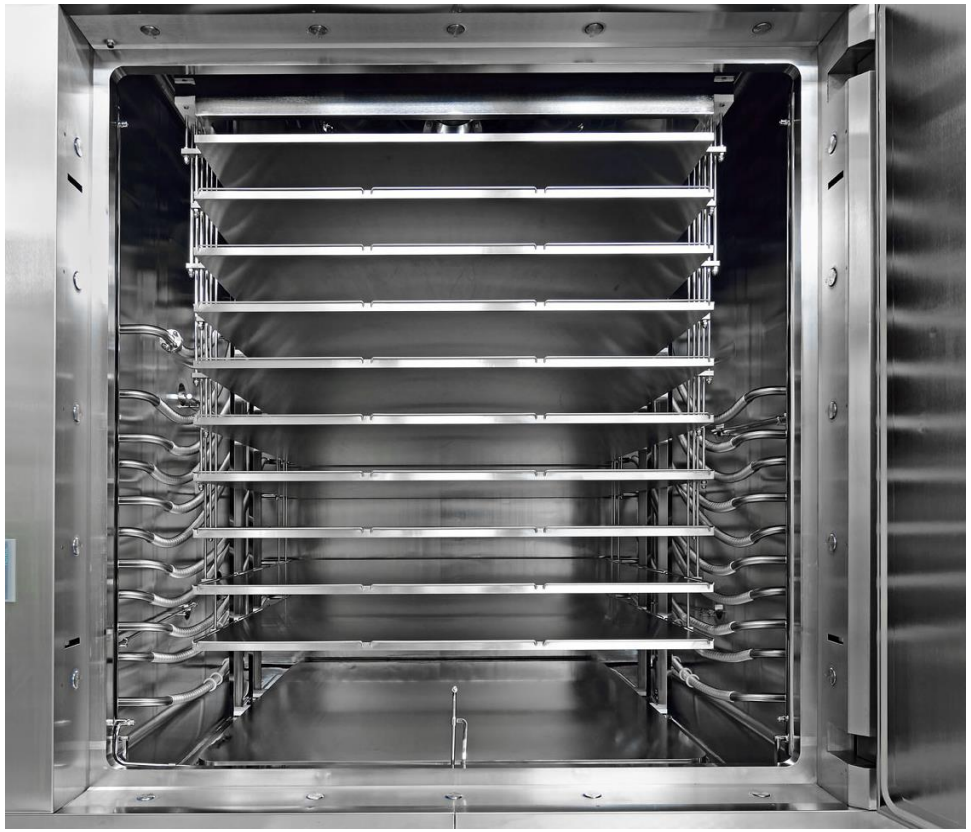
Thomas A. Jennings, Lyophilization

Vorgänge im Produkt



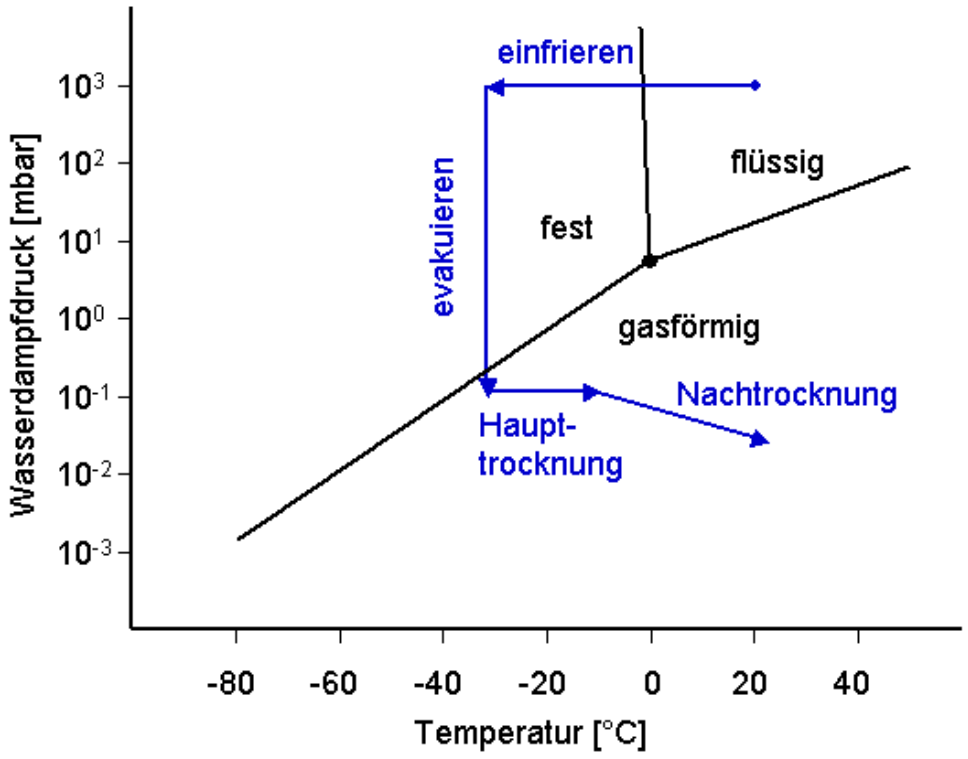
Gefriertrocknung konventionell

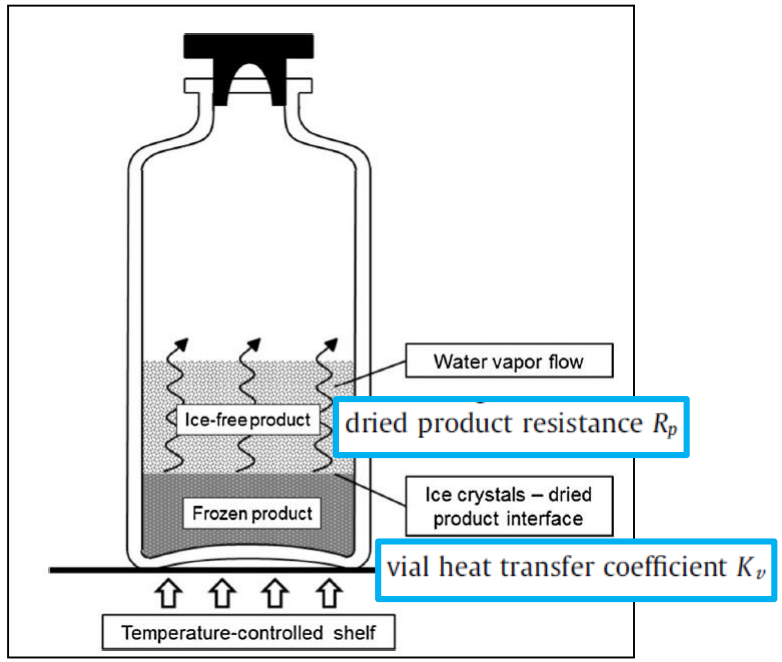




http://www.hof-pruefsysteme.de/en/communication/important-downloads/news-archive/article/hof-sonderanlagenbau-gehoert-zu-den-top-100.html

Physik der Gefriertrocknung





T_c collapse temperature (maximum allowable product temperature during primary drying

Uncertainty analysis as essential step in the establishment of the dynamic Design Space of primary drying during freeze-drying

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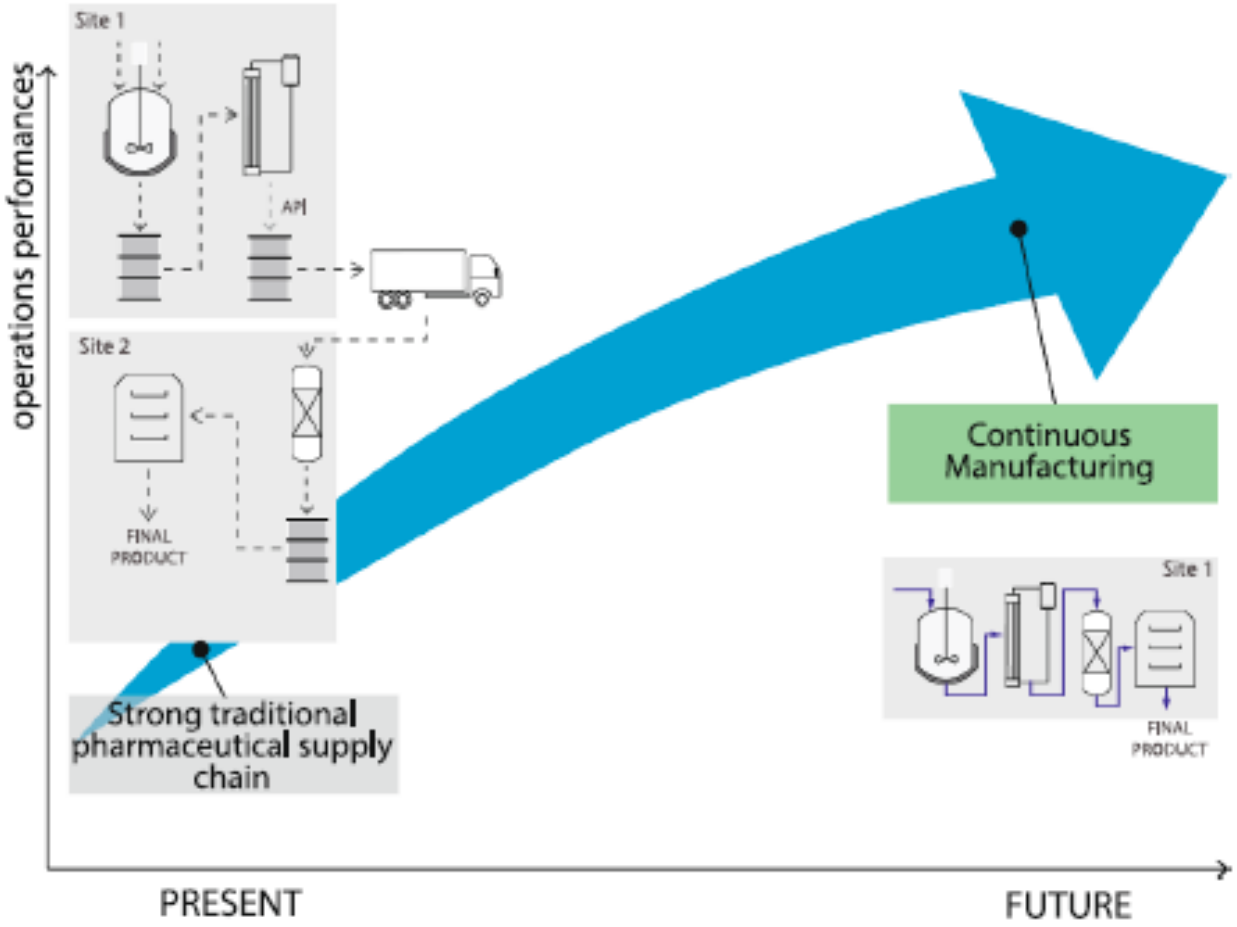
[c] CAPEC-PROCESS Research Center, Department of Chemical and Biochemical Engineering, Technical University of Denmark, Building 229, 2800 Kgs. Lyngby, Denmark

Warum kontinuierlich



- Flexibilität
- Scale-up weniger komplex
- Real-time Analyse
- Geringerer Platzbedarf

Achieving continuous manufacturing in lyophilization: Technologies and approaches

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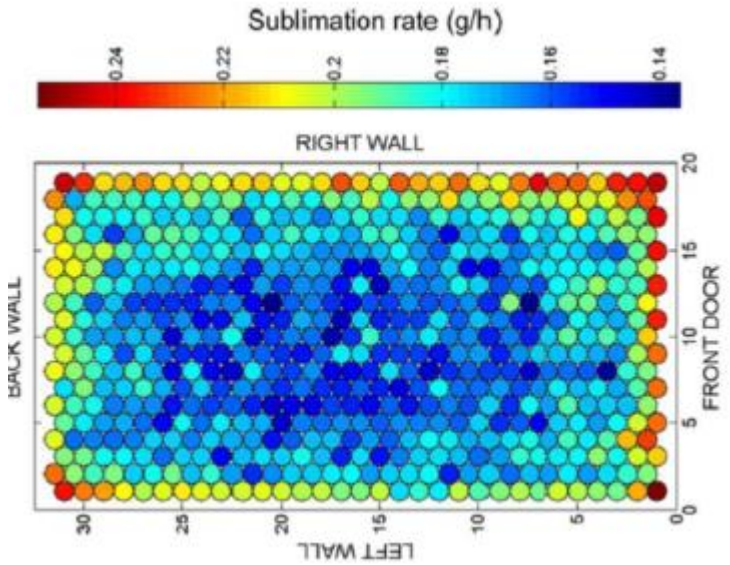
Von Batchprozessen zu kontinuierlichen Prozessen

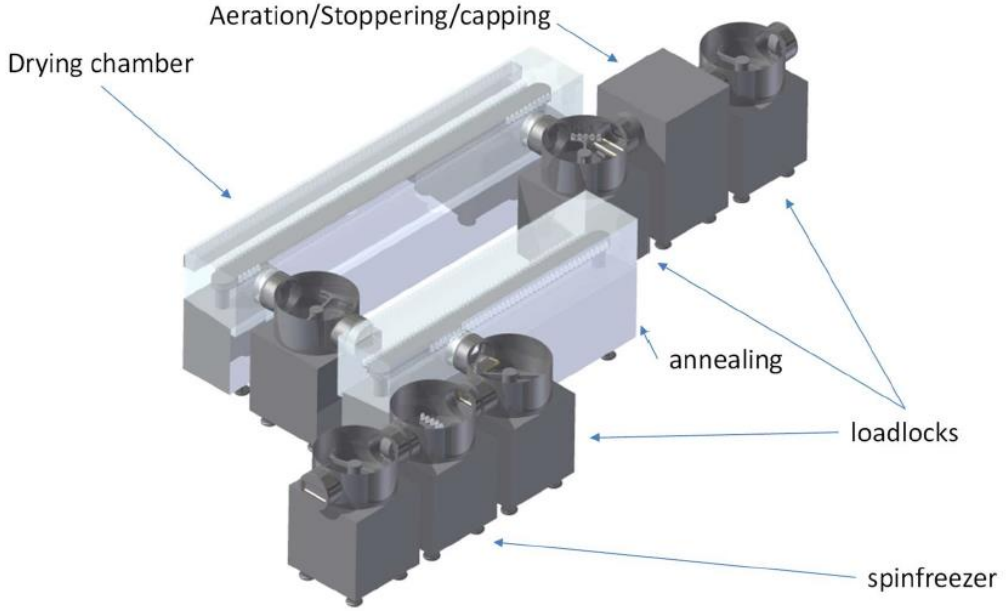


Gefriertrocknung im Batchverfahren

- Inhomogene Eisnukleation
- Inhomogenes Trocknungsverhalten
- Transfer und Scale-Up herausfordernd
- Lange Prozesszeiten

Kontinuierliche Gefriertrocknung

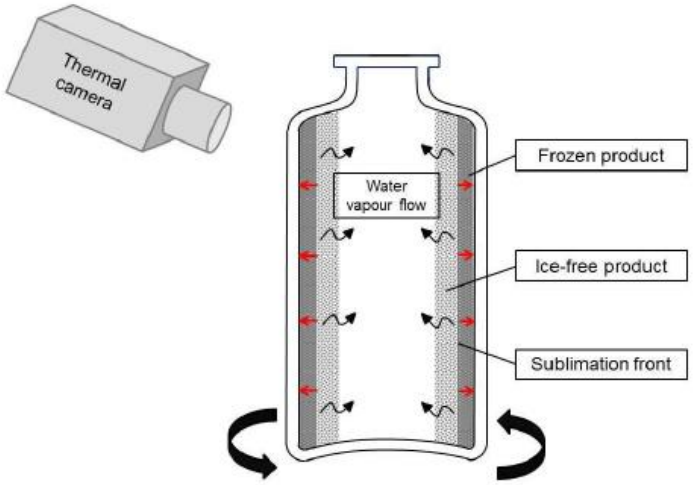
- Homogene Eisnukleation
- 100% Kontrolle über JEDES Vial
- Einfacher Transfer und Scale-Up (Out)
- Kurze Prozesszeiten

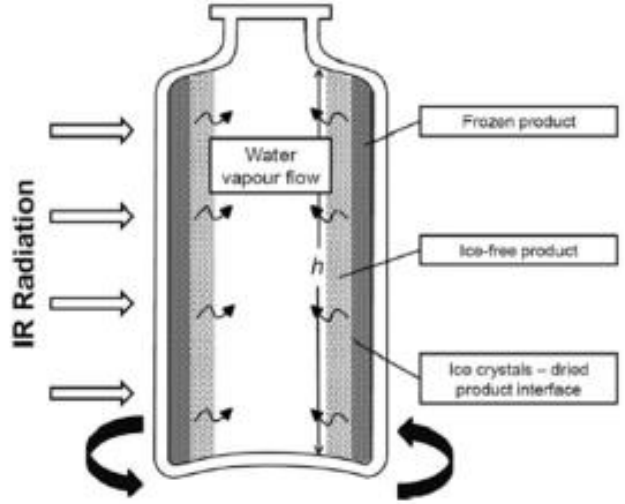


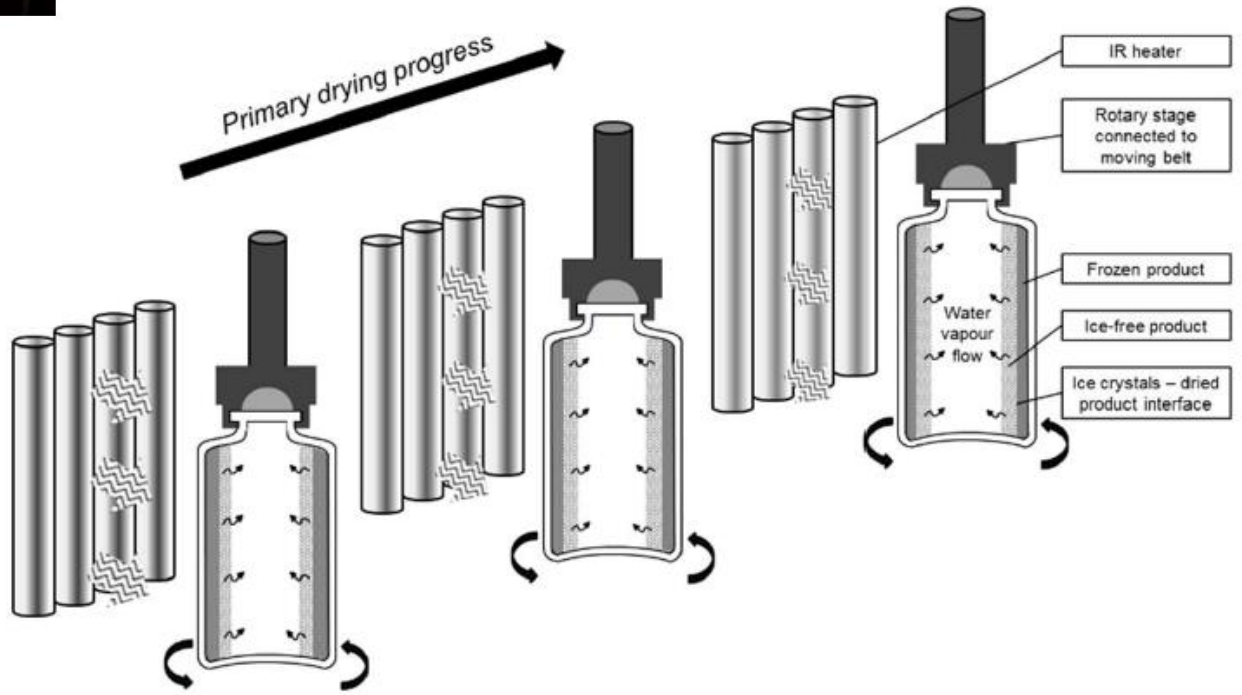
Gefriertrocknung kontinuierlich

Spin-freezing

Drying







Der Plasma Fraktionierungsprozess

The plasma fractionation process is based on the method of Cohn *et al.* 1940´s

Plasma

Edwin Joseph Cohn, Ph. D.

5 Parameter system

- pH
- Temperature
- Ethanol concentration
- Conductivity
- Protein concentration

Separation methods

- Centrifugation
- Filtration

Das 5 Parameter System der Ethanol Fraktionierung

EtOH Konzentration:
Im Cohn Fraktionierungsschema zwischen 0 und 40%.
Durch Dehydratisierung werden Proteine unlöslich und präzipitieren in der EtOH – Wasser – Mischung.

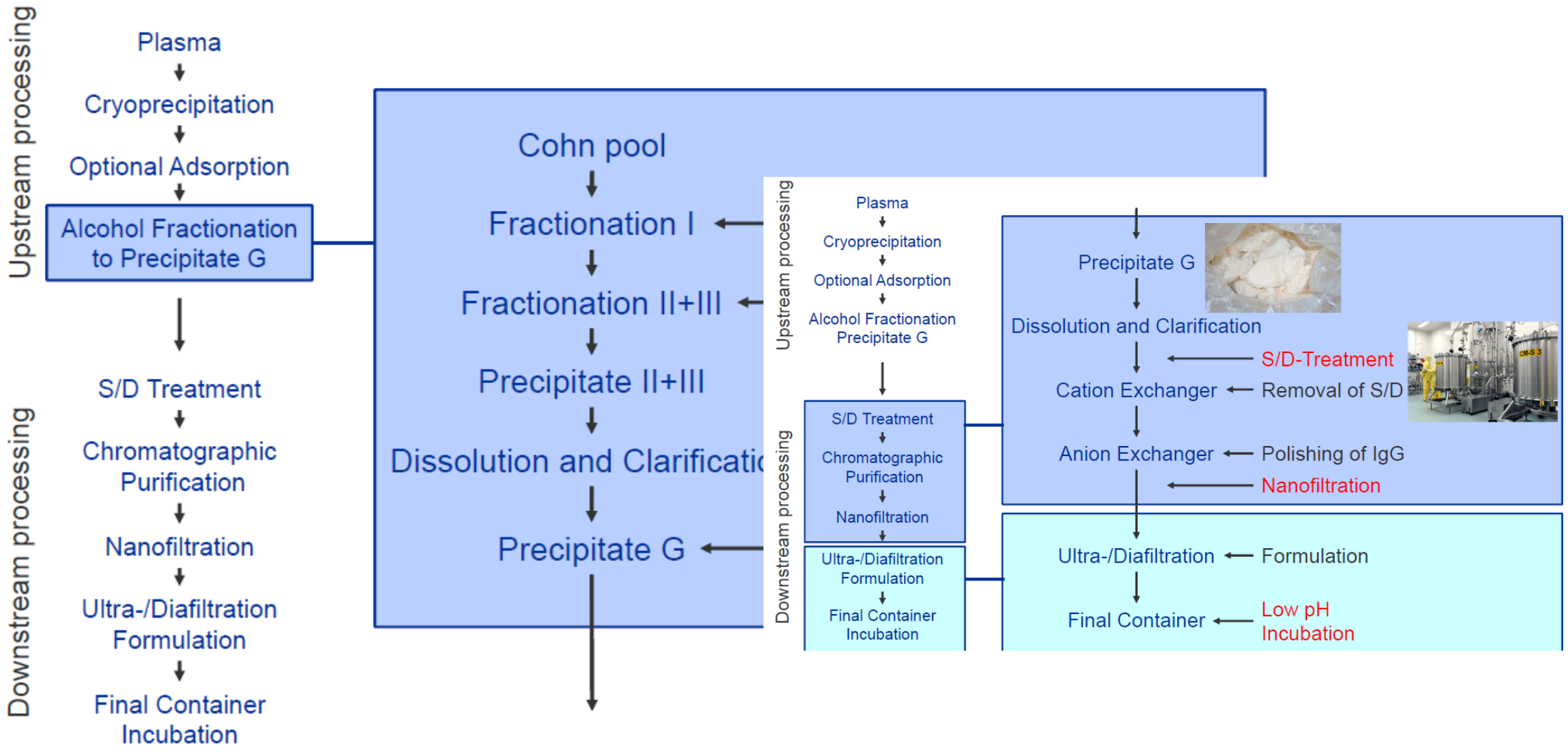
pH:
Proteine präzipitieren leichter am Isoelektrischen Punkt, jenem pH Wert einer Lösung an dem die Primärladung eines Proteins Null ist.

Temperatur:
Muss zwischen 0 und -10°C gehalten werden, um Denaturierung zu verhindern.

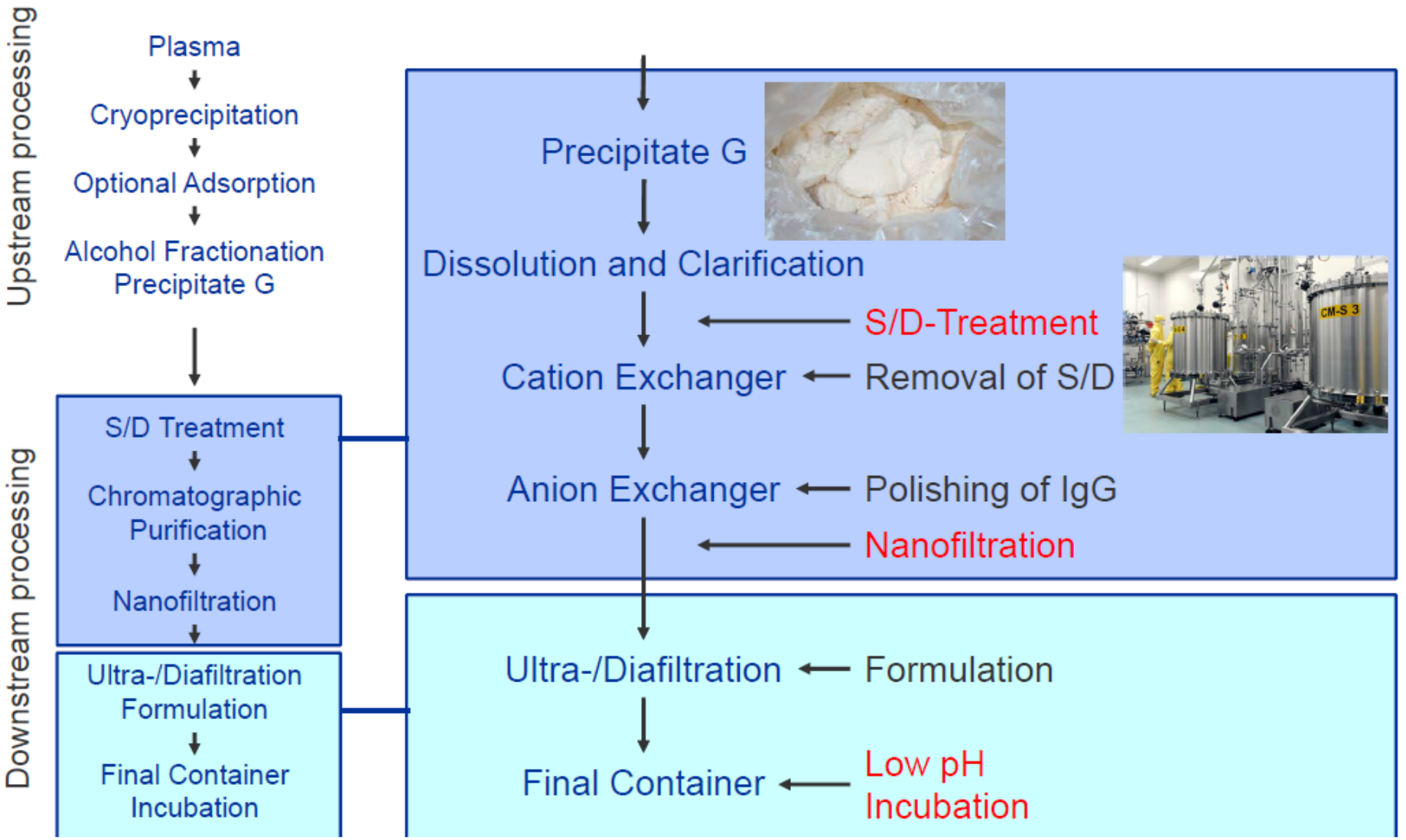
Protein Konzentration:
Je höher die Konzentration desto besser die Präzipitation.

Leitfähigkeit:
Beinflusst die Löslichkeit der Proteine

Ethanol Fraktionierung



Downstream - Purification



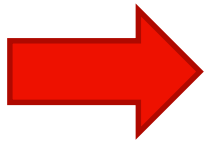
Wirkstoff aus Plasma ohne Ethanol Fraktionierung durch Direct Capture

Approach

- Capture IgG out of Plasma, Cryo Poor Plasma or Cohn Pool
- Utilize commercially available affinity resins
- Major challenge: column load, impurities, conditions

Results

- 80% footprint reduction with Direct Capture
- Direct Capture IgG subclass distribution comparable to standard distribution
- Process intensification to optimize performance and to reduce process steps
- Equipment investment and run costs significantly lower due to downsizing



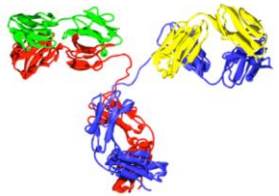
process based on direct capture promising for emerging market and fast to clinic scenarios

Beispiel: Direct Capture für e.g. IgG

Process Development → PoC → Scale Up (Piloting) → Ready for GMP

Approach Prozessentwicklung:

- Auswahl des geeignetsten Ausgangsmaterials
- Feasibility study
- Proof of concept study
- Scale up / Piloting
- Industrialization



Plasma intermediate Starting Material

↓

Affinity Chroma

↓

Polishing

↓

Nanofiltration

↓

Ultrafiltration

↓

Drug Substance

Vielen Dank!

Michael Dekner

Head of PS FFF

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