Integration of an existing pharmaceutical manufacturing site into Vetter‘s development services

GMP–PHARMA CONGRESS

#sharing challenges and solutions in practice

Martin Schwab, PhD, PMP,
Site Manager Vetter Development Services Rankweil

Part of PharmaCongress – Düsseldorf/Neuss, 31 May–1 June 2022

GMP–PHARMA CONGRESS

CONCEPT HEIDELBERG
Pharmaceutical Quality Training. Conferences. Services.

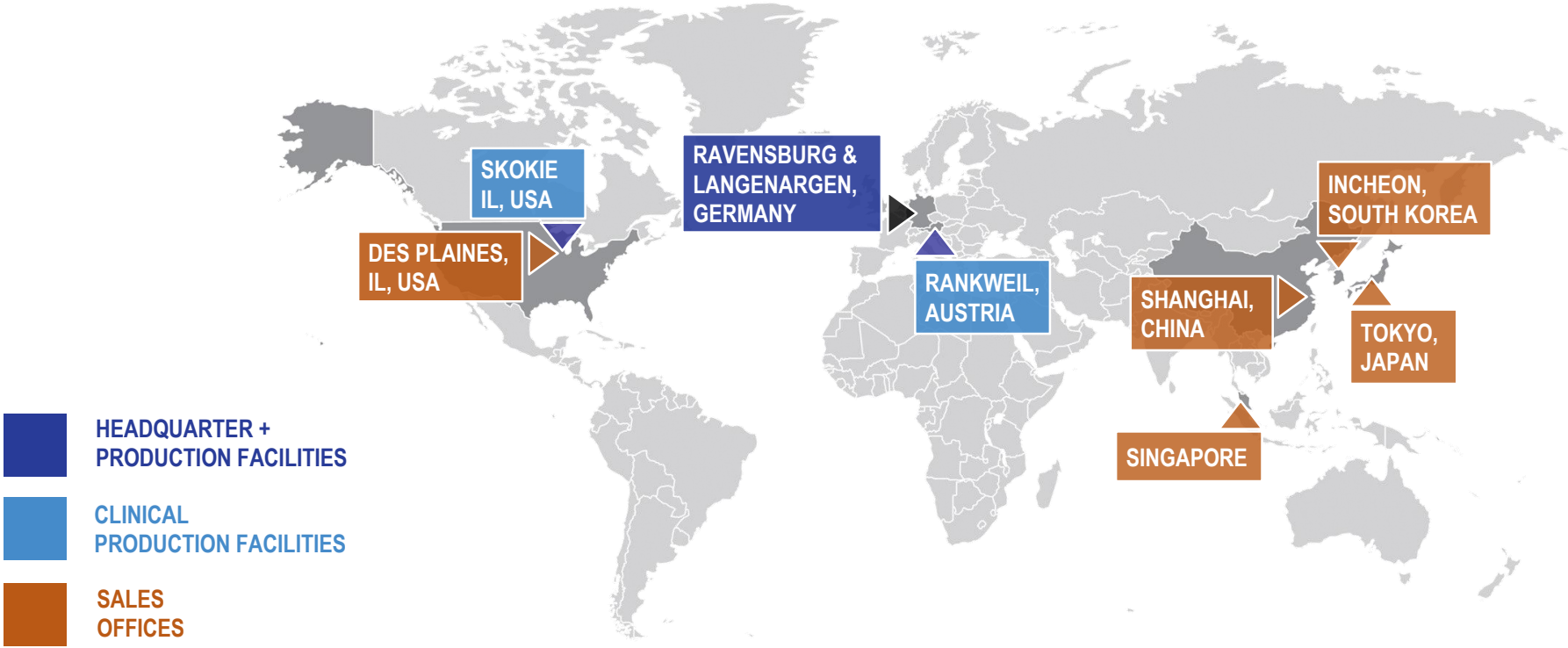
Supported by

ECA Academy
Your GMP/GDP Information Source

Outline

- Vetter Clinical Manufacturing & global clinical trial market
- Backround and features of the site
- The project / structure / timeline
- Work packages, optimization measures, processes & recruiting
- Lessons learned

Vetter – an independent CDMO with a worldwide presence



VDS-C: Clinical manufacturing site

FOCUS

- Optimized processes for preclinical and clinical Phase I and Phase II (including filling and lyophilization)
- Cutting-edge technologies focused on use of disposables to deliver maximized API yields

FILLING LINES

- Vials (liquid and lyophilized)
- Pre-sterilized single-chamber syringes

LABS

- Chemical analysis
- Microbiology

TRANSFER & SCALE-UP

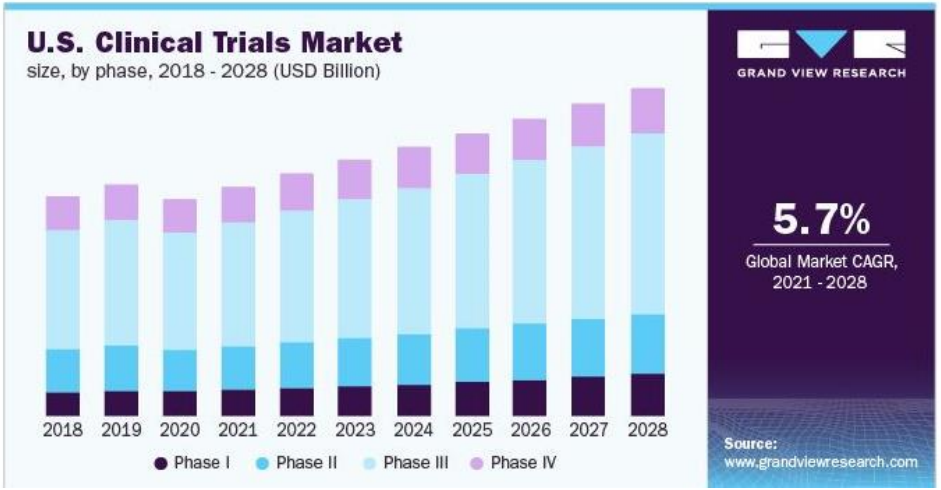
- Critical preparation for Phase III and commercial manufacturing

RABS (Restricted access barrier system)

VISUAL INSPECTION

cGMP STORAGE

Clinical Trials Landscape



Analysts predict significant growth of the global clinical trial market

Drivers:

- increasing prevalence of chronic diseases,
- relatively low costs of trials in developing regions
- Increased RnD expenditure
- Increased number of RnD companies and institutes

Global annual growth rate: ~ 4,5%

1. The site

Site history I

- The facility was built and operated by former owner, start of construction activities was 2016
- Former owner moved into the site September 2017
- Media Fill was performed in April 2018
- Manufacturing licence obtained in August 2018
- First GMP batch was filled August 2018

Site location

Site history II

30. November 2019

stellt den Betrieb ein

Von Andreas Scalet

Schon im Sommer baute die Rankweiler Bio-Techfirma Mitarbeiter ab, nun wurde der Betrieb eingestellt.

RANKWEIL, LAUPHEIM Es war eine Sternstunde für die Vorarlberger Betriebsansiedler, jetzt schaut es danach aus, als ob die An-

- Q2 2019: manufacturing license was resigned and business was shut down
- Utility systems were uninterruptedly kept in operation to avoid contamination of the system
- Nov 2019: contact between owner and Vetter, first discussions regarding a potential take-over of the facility

Site history III

- Early 2020: Vetter Management sends a small team of experts to critically examine the site and its features

Production

Qualification/ Validation

QA & QC experts

QA & QC experts

Engineering

IT

Evaluation of the site, its features and potential gaps/benefits led to the decision to take over the site

Features of Rankweil site

Building consists of 3 parts

- offices, meeting rooms, labs
- Production areas, utilities
- Warehouse, logistics and bays

Room for extension:

- Within the building, i.e. for additional process equipment
- Outside: open space for additional buildings

Lot: ~ 10,000 m2
Building: ~ 5,000 m^2

Located in a mixed zone with close connection to A14 highway

Features of Rankweil site

Filling line:

- RABS-housed automated filling line for vials
- Line speed allows for small to medium sized batches (2R vials ~ 6,000 vials)
- Two heads filling system for two different pump systems
- 100% fill weight control
- Sensor equipped stoppering and capping system
- capping is performed under LF (grade A air supply) within a grade D zone

Features of Rankweil site

Freeze Dryer and loading system:

- Automatic loading / unloading system
- Freeze dryer with 10 shelves
- Vial capacity up to 60,000 2R vials
- Maintenance door in uncontrolled environment

Features of Rankweil site

Material preparation equipment:

- Washing machine
- Autoclave
- Vial washing machine
- Dry heat tunnel
- Various other equipment parts (water baths, freez/thaw-unit etc.)

Features of Rankweil site

Utilities

- Purified Water generation (softening, RO & EDI)
- PW-storage system (6,500l)
- Pure steam & WFI generator
- Hot storage & distribution system
- Pressurized air via compressor,
- Nitrogen via cylinder battery
- Battery system for critical systems

Features of Rankweil site

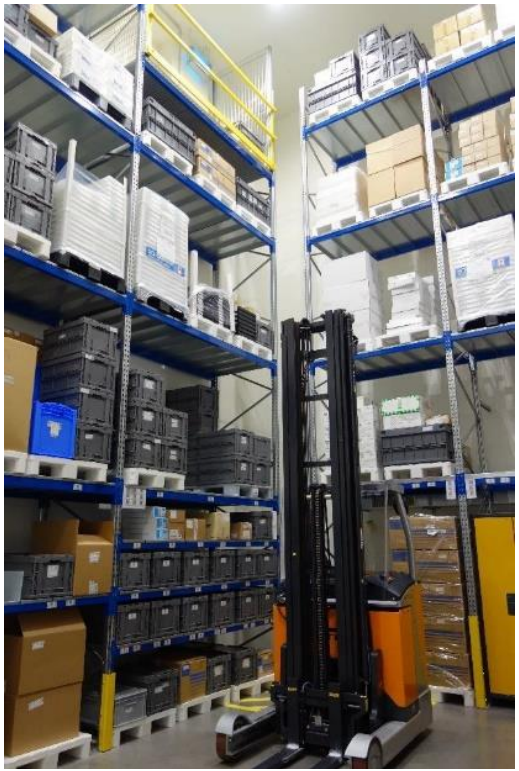
Laboratories

- Dedicated chemical analysis and microbial lab
- Gmp-archive for lab / raw data documentation
- Sample-lock for transfer of samples from production
- Preparation area: washing machine and autoclave
- Storage area for lab supplies
- offices

Features of Rankweil site

Warehouse and logistics

- High bay pallet storage area, RT
- Walk in cold storage
- Walk in freezer
- further RT-storage rooms
- incoming goods bay & outgoing goods bay
- 3 * -80°C freezers
- Offices



2. The decision

Drivers for Vetter to take over the site – the strategic fit

9.7.2020 Schwäbische Zeitung

WIRTSCHAFT SEITE 8 | DONNERSTAG 9. JULI 2020

Vetter will es besser machen

Der Ravensburger Pharmadienstleister übernimmt die ehemalige Abfüllanlage

Vetter-Geschäftsführer Peter Sölkner (links) und Thomas Otto (rechts) mit Mitgesellschafter und Beiratsvorsitzender Udo Vetter am neuen Standort in Rankweil: das Vetter-Logo vor dem neuen Standort in Rankweil. (Foto: Vetter)

- The thriving clinical business in which Vetter already successfully operates
- Possibility to offer an European-based clinical development facility
- Relatively close proximity to Vetter's headquarter / logistic hub
- Vetter's acquisition hinders other potential competitors to take over the site

3. The Project(s)

Strategic approach, scope and aim

- Aim: setup of a new clinical manufacturing site – Vetter Development Services Rankweil (i.e. no commercial production in Rankweil!)

- Scope and workpackages:
  - Roughly defined by outcome of due dilligence
  - Roughly defined by requirements of clinical manufacturing
  - Differentiation of scope, project‘s needs and work packages as team dives deeper into the project

- Strategic approach
  - 2 projects with close cooperation: 2 PMs with close cooperation / reporting structure
    - ⇨ Group of dedicated experts from Vetter Germany
    - ⇨ In parallel building up the future on-site experts

2 projects – one mission & one team: building up VDSR!

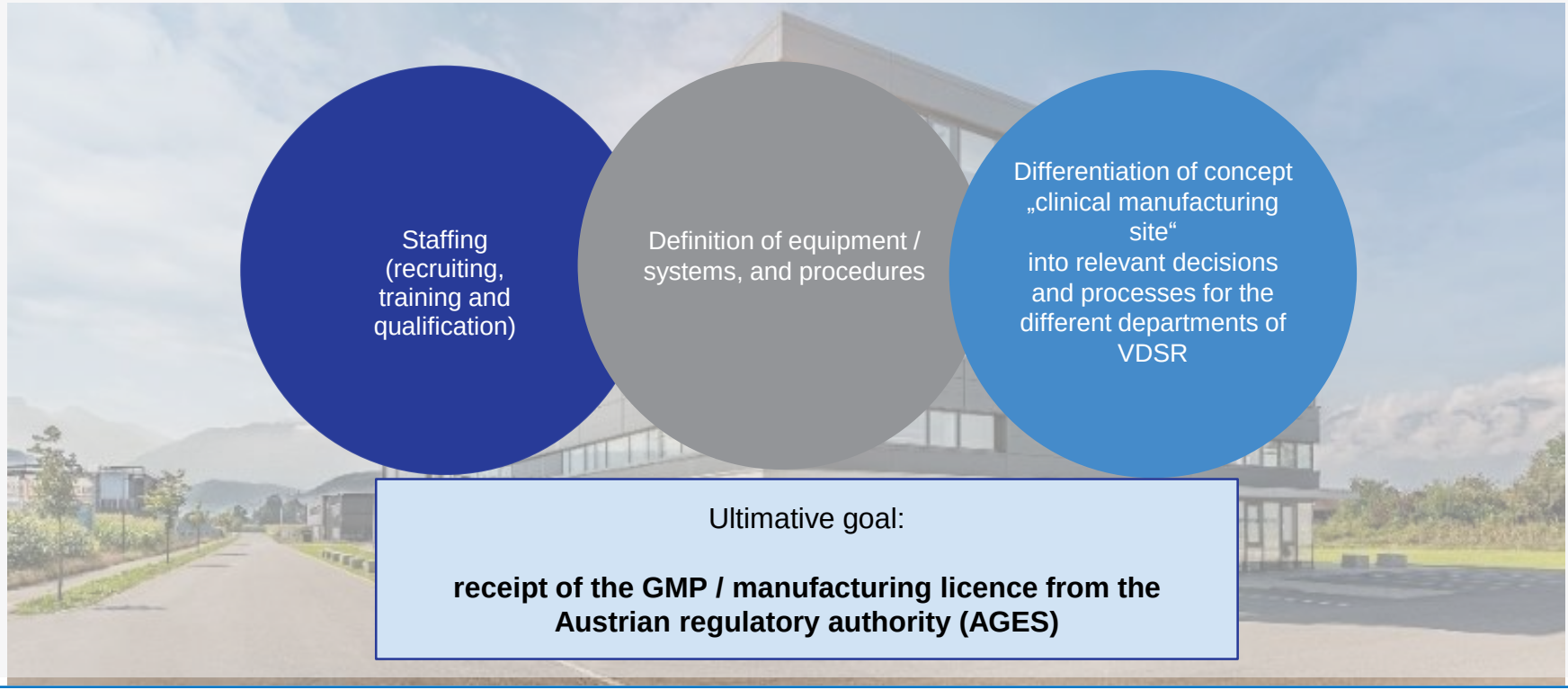
Rankweil project family

Technical Project	Integration Project
D. Neuland / H. Badack	M. Schwab / C. Feußner
▪ Implement technical measures and modifications defined during due dilligence ▪ Qualification of MF-relevant systems and equipment ▪ Target status: site is ready for media fill	▪ Definition of organizational structure and operational principle ▪ Integration into Vetter‘s company structure and processes ▪ Recruiting and training … ▪ Target status: approval from the Austrian authorities

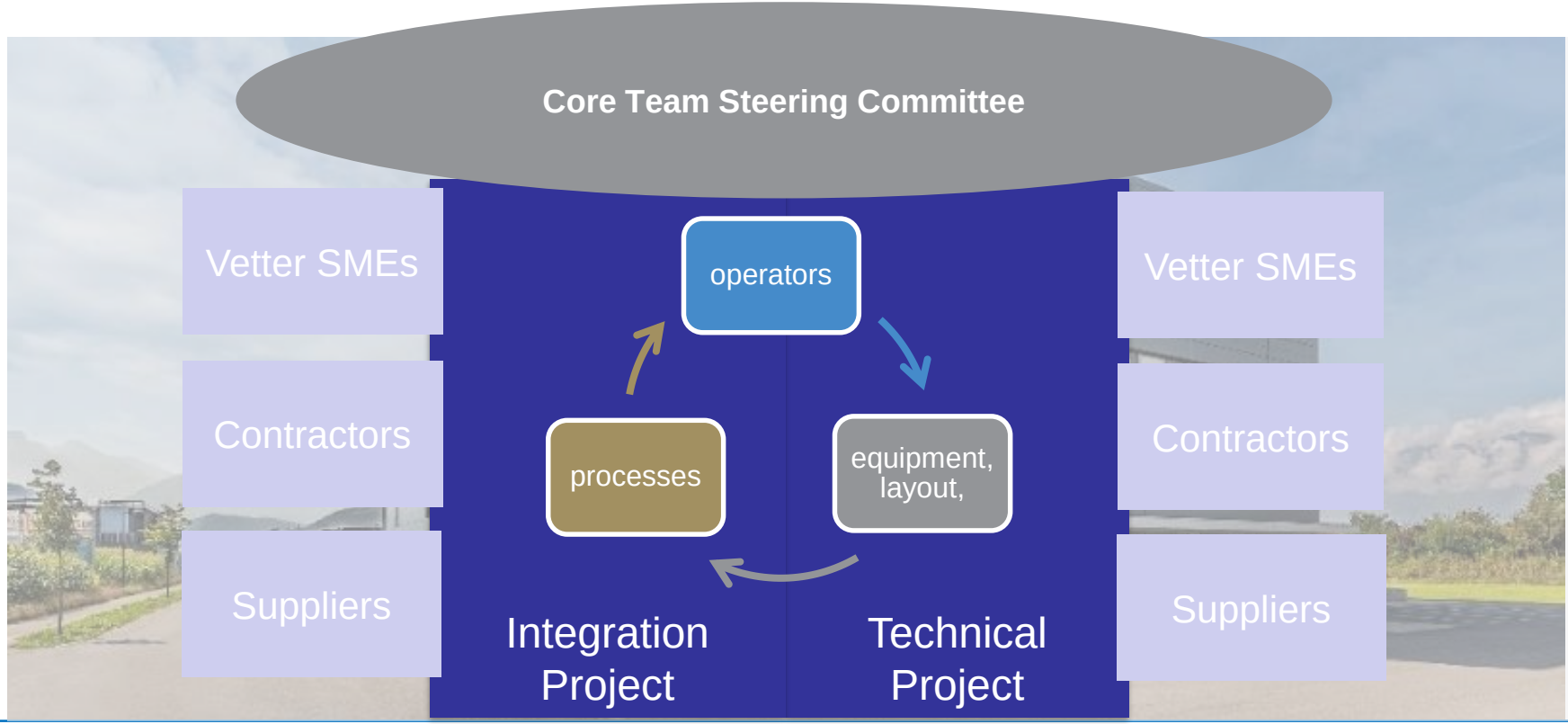
Team Rankweil: kick-off meeting in Rankweil, July 2020

Technical Project: major work packages

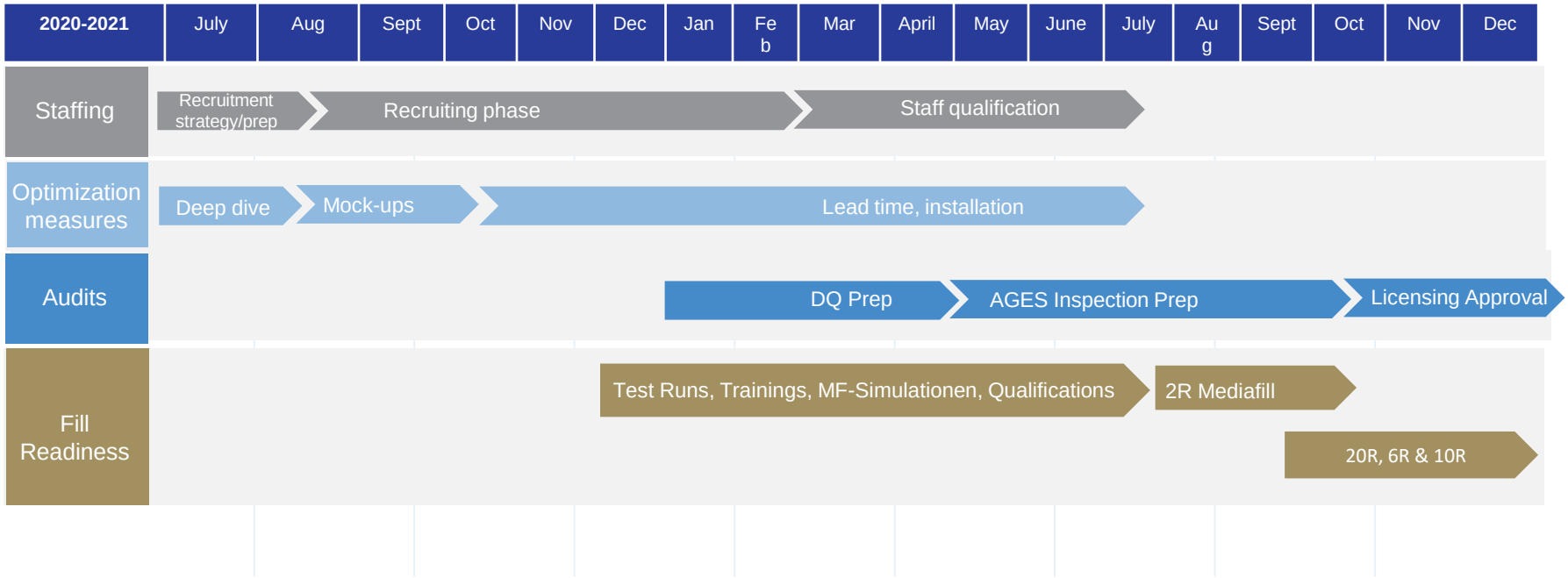
Integration Project: major work packages



Project and Governance Structure

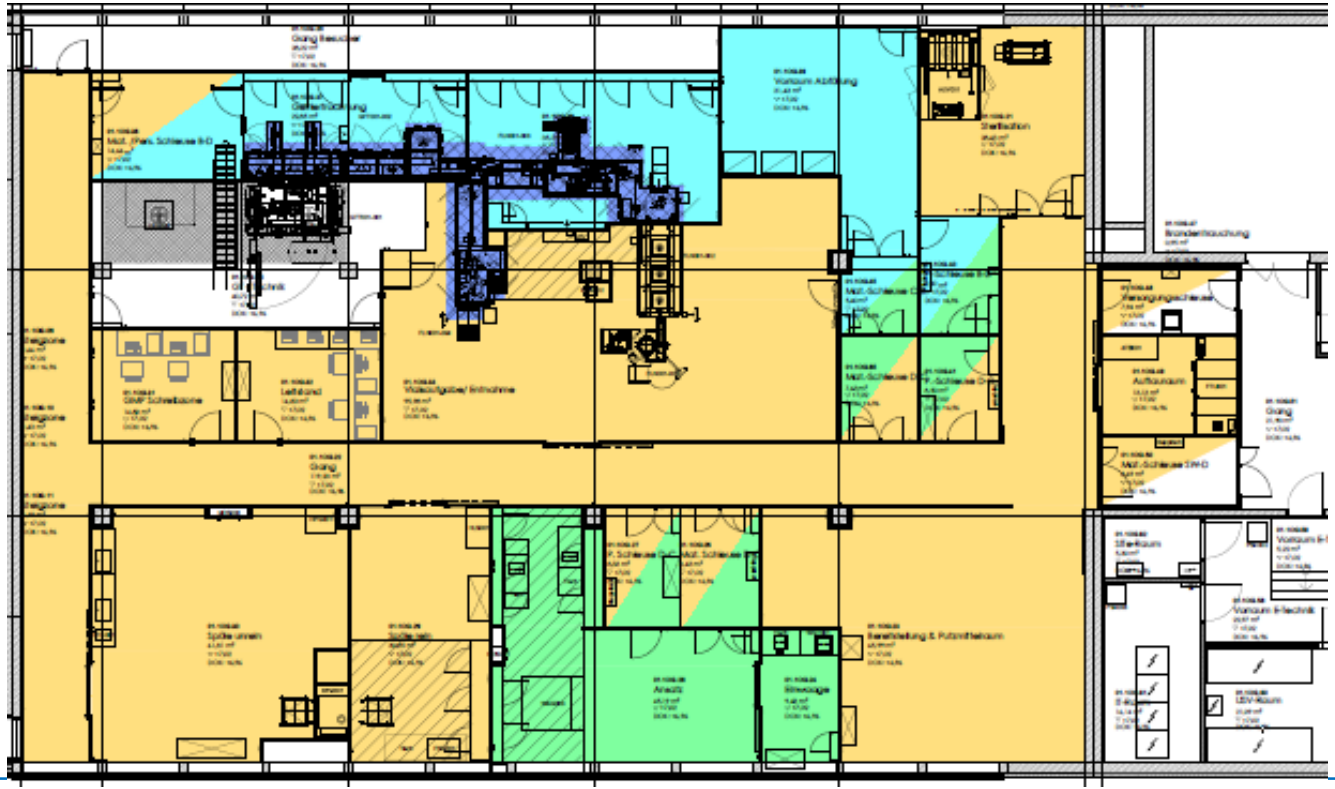


Project Timelines:



4. Work packages and optimizations

Production Layout as taken over



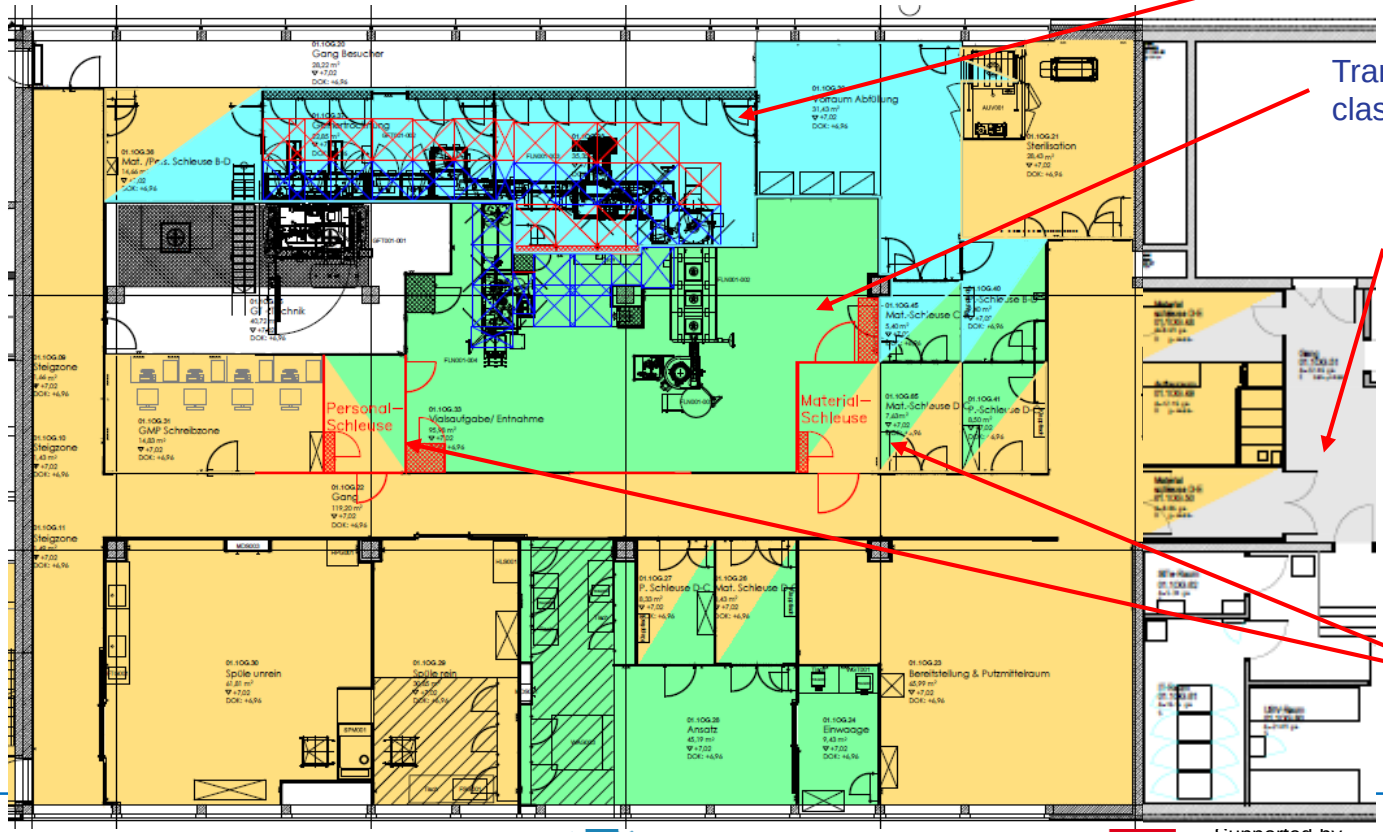
Class color key

D

C

A/B

Planned changes to the layout



Extension of LAF areas filling

Transformation of former class D into a class C environment

Material transfer area:class E (formerly non-controlled area)

Class color key

E

D

C

A/B

New material and personnel locks for transfer from D to C area

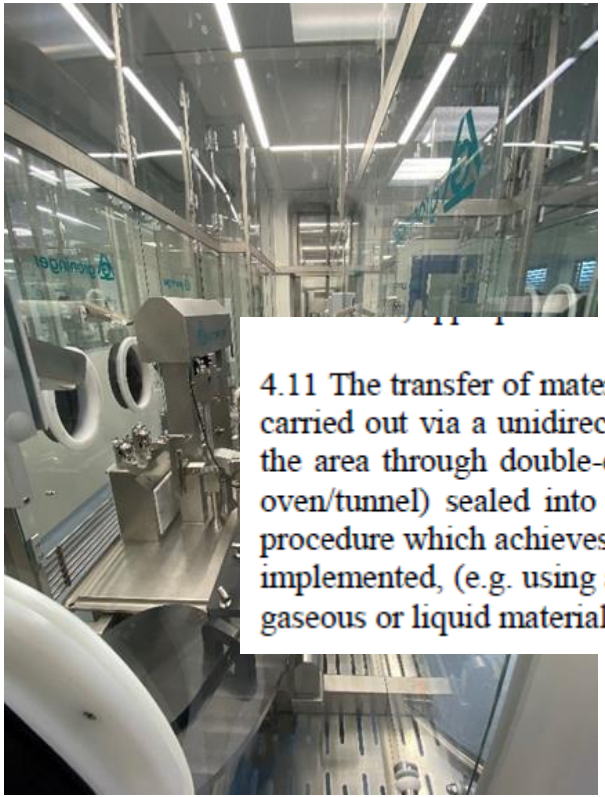
Extension of LAF – areas surrounding the RABS

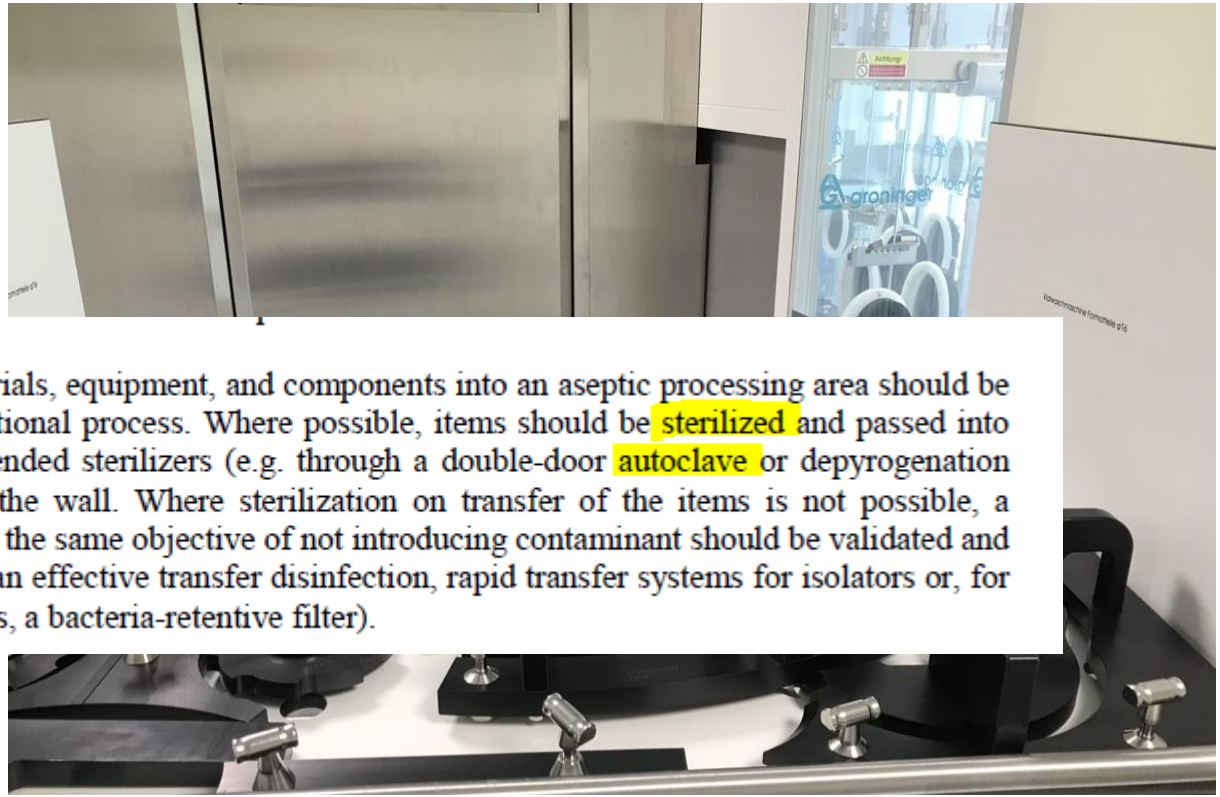
Extension of LAF – areas surrounding the RABS

Extension of LAF – areas surrounding the RABS

Implementation of autoclavable format parts

Implementation of autoclavable format parts



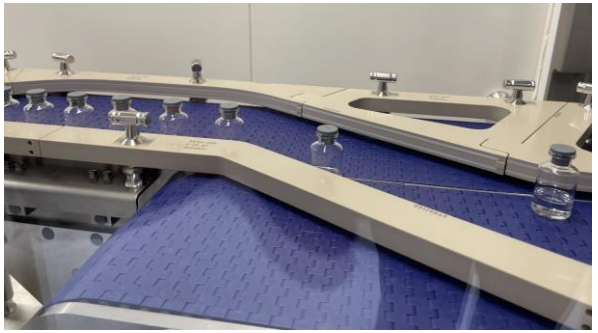


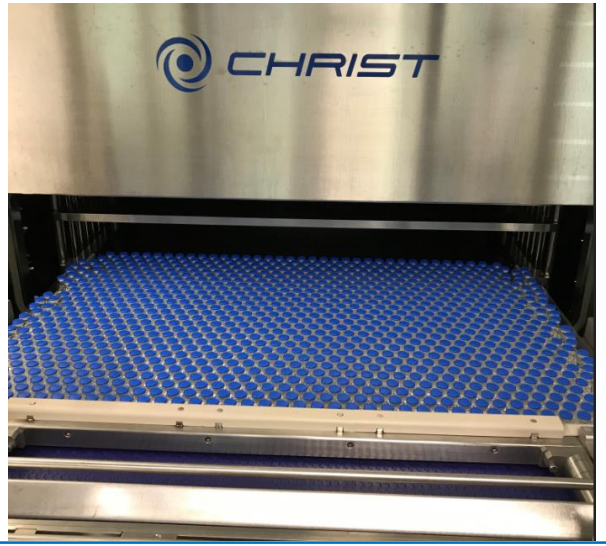
4.11 The transfer of materials, equipment, and components into an aseptic processing area should be carried out via a unidirectional process. Where possible, items should be sterilized and passed into the area through double-ended sterilizers (e.g. through a double-door autoclave or depyrogenation oven/tunnel) sealed into the wall. Where sterilization on transfer of the items is not possible, a procedure which achieves the same objective of not introducing contaminant should be validated and implemented, (e.g. using an effective transfer disinfection, rapid transfer systems for isolators or, for gaseous or liquid materials, a bacteria-retentive filter).

Implementation of autoclavable format parts

Autoclavable format parts

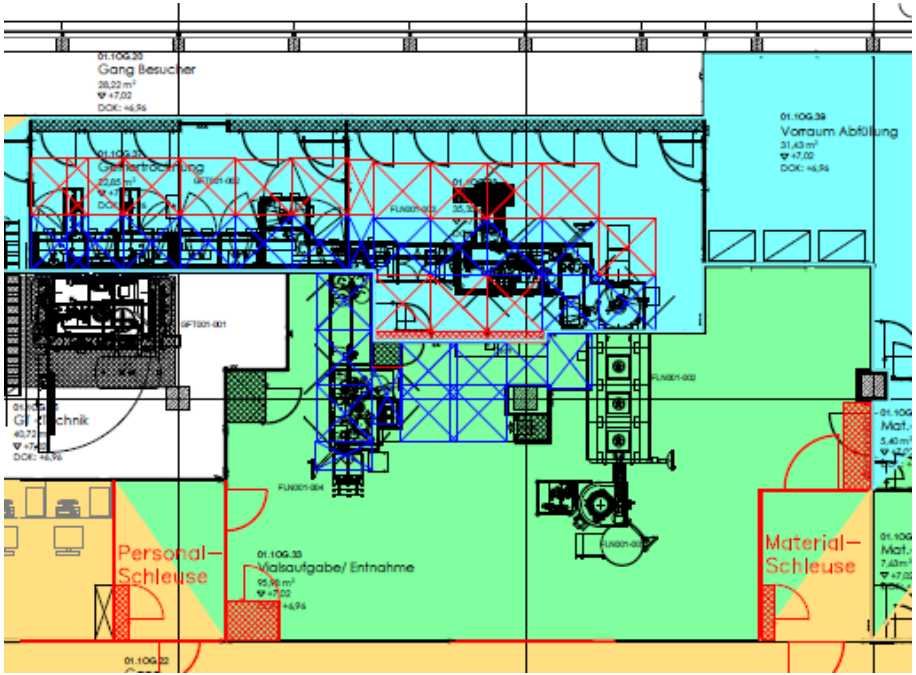
- Evaluation based on quality, effort and costs
- Re-design of format parts, holders and machine bed parts
- Re-design of impacted upstream equipment parts
- development & qualification of cleaning / autoclavation processes of new parts





Autoclavable format parts – upstream activities

Transformation of a class D into a class C environment



- Implementation of locks
- RABS extension
- Changes to Ventilation system
- Structural changes to walls and doors

Transformation of a class D into a class C environment

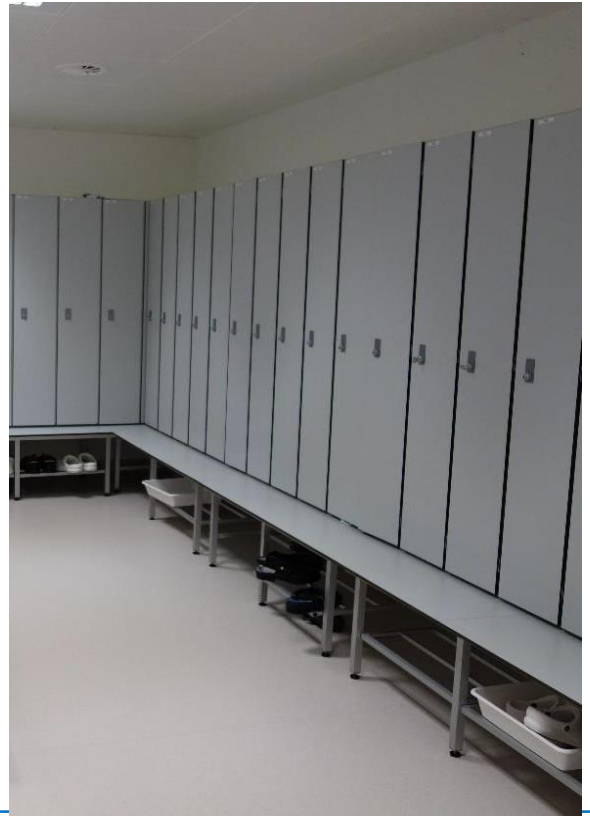
Transformation of a class D into a class C environment

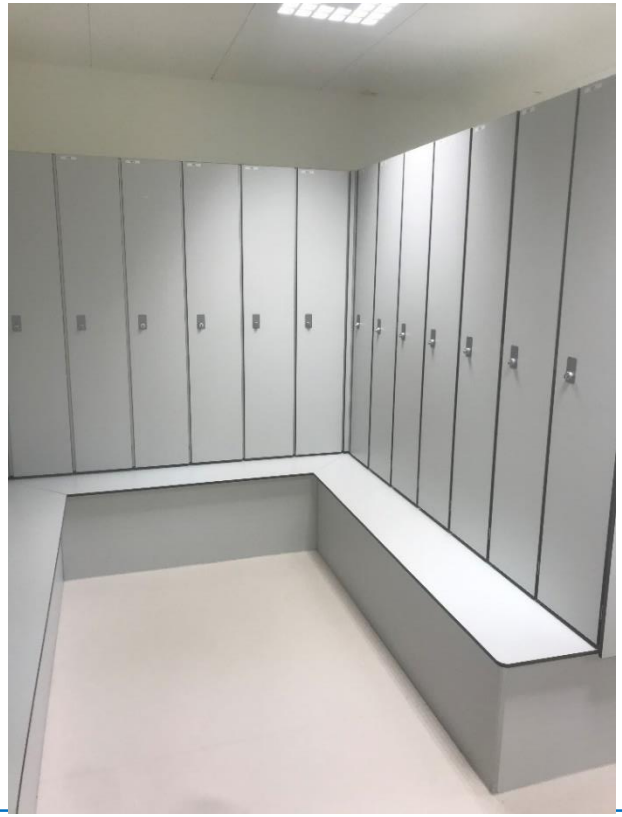
Other optimization measures

Other optimization measures

Other optimization measures

Other optimization measures





5. Finding the right Processes

One fits all? VDSC = VDSR?

Legal Assessment

very different!

Conceptual assessment

no difference between Vetter's clinical sites in Chicago and Rankweil

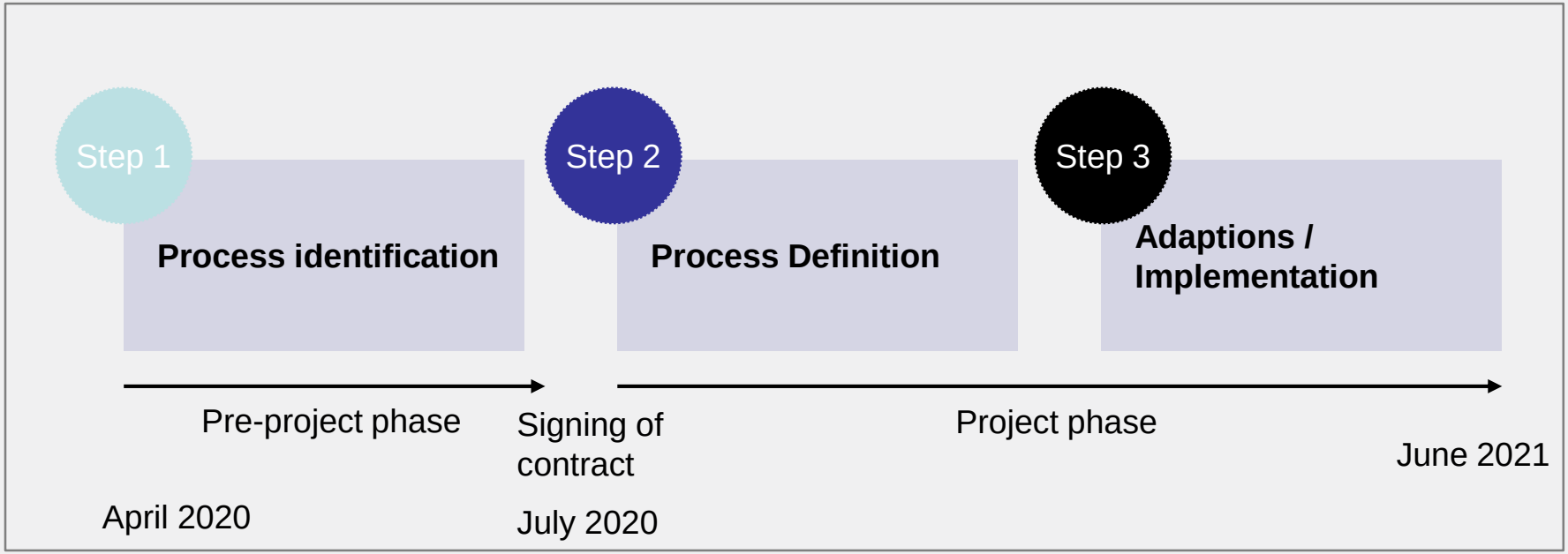
Processes & Systems

VDSR is similar to VDSC

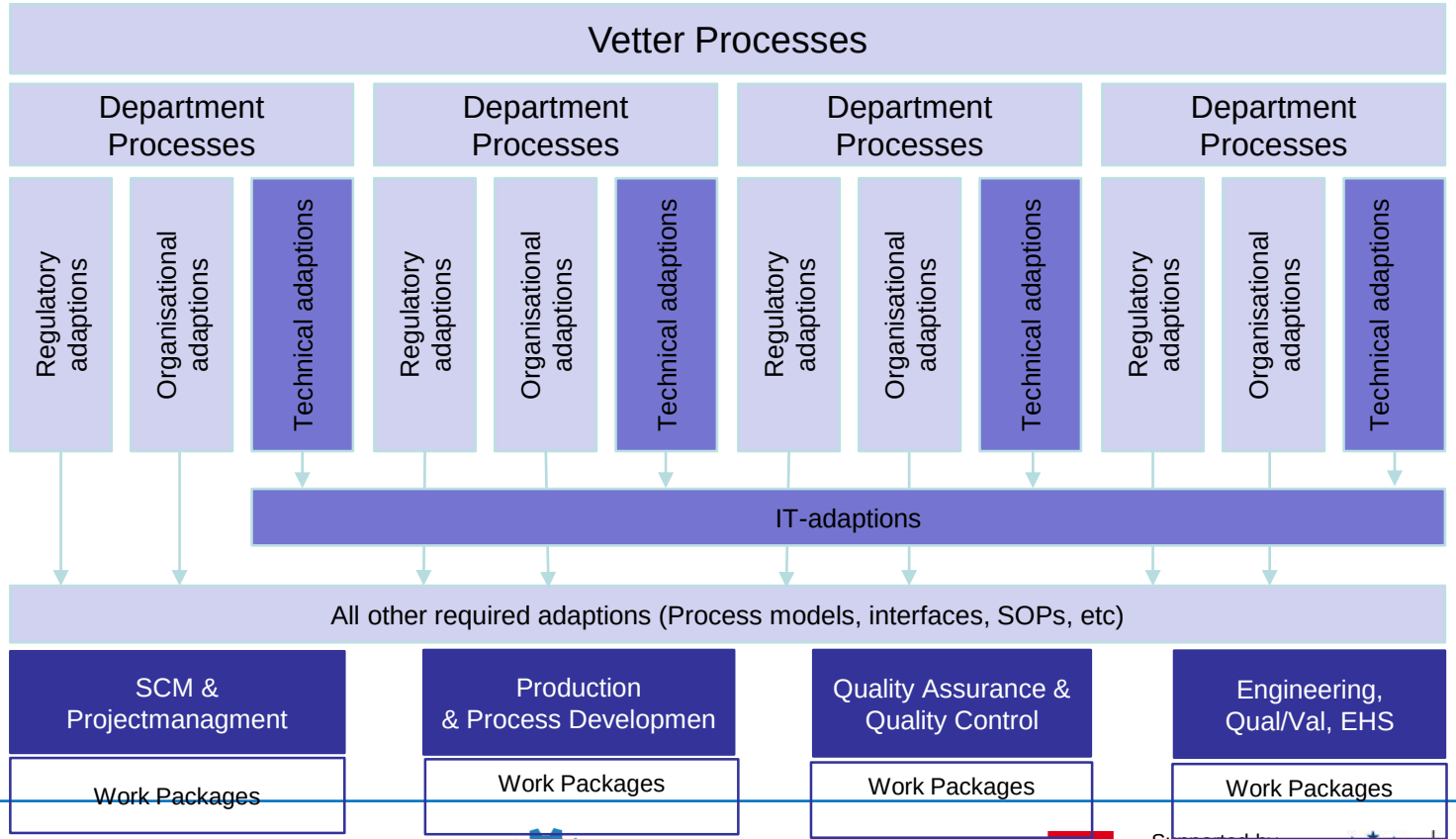
Very different

Inclusion in Vetter Company structure

The route to VDSR-processes



Put the work on many shoulders

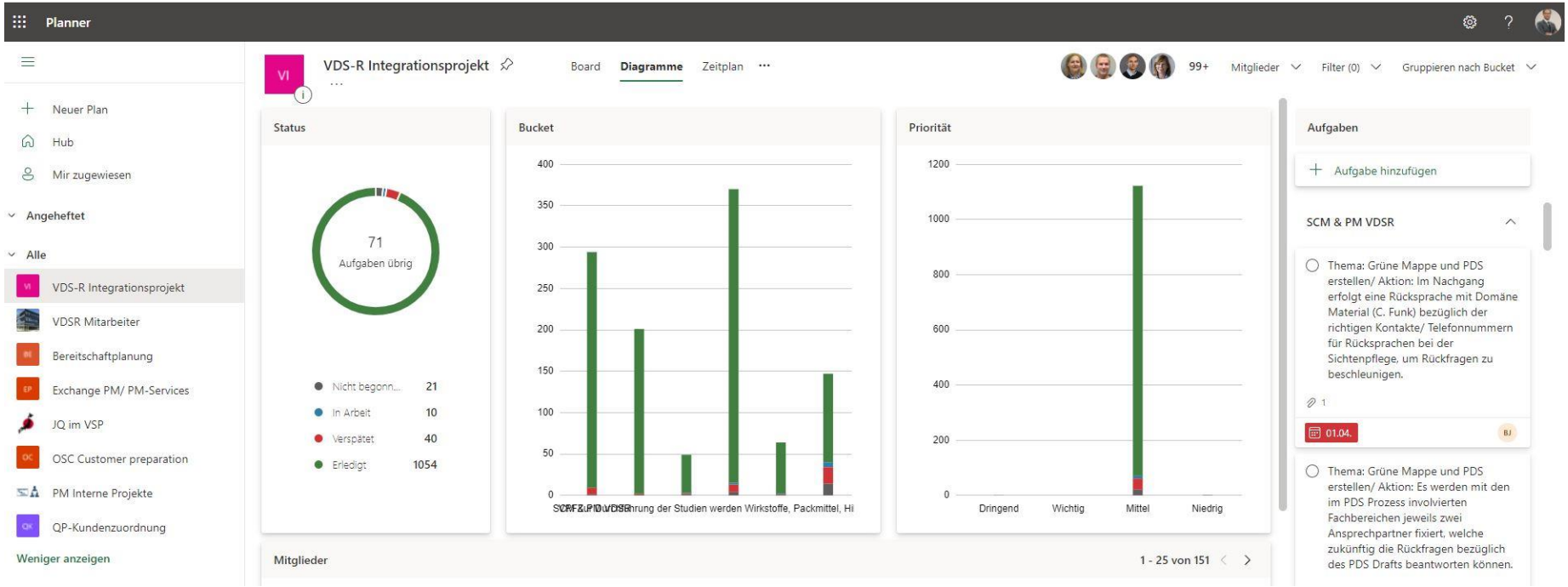


Vetter Process Excellence Department

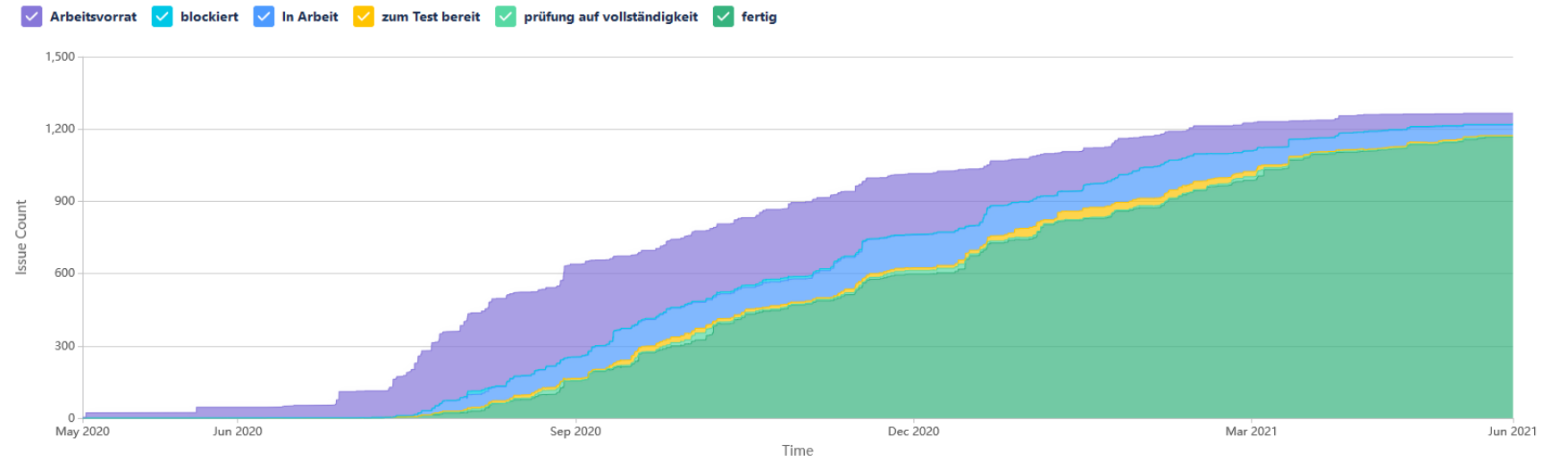
IT-Department

Rankweil & Vetter Germany staff & experts

Use the right tools: allocation, tracking and documentation



IT-work: agile approach and a lot of adaptions

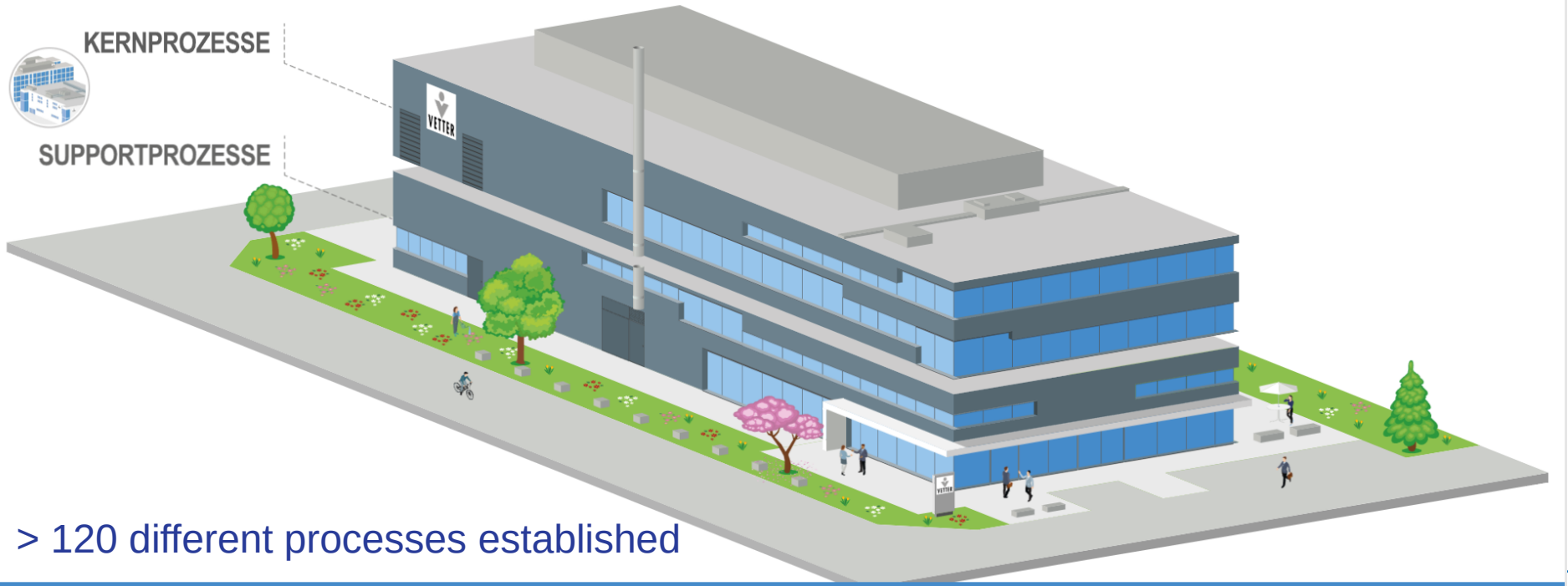


Continuous confirmation of established processe via E2E-Tests

- Department key user utilized as critical successfactors
- Utilize VDSR staff and key user to challenge set up processes
- High quality of established processes was confirmed

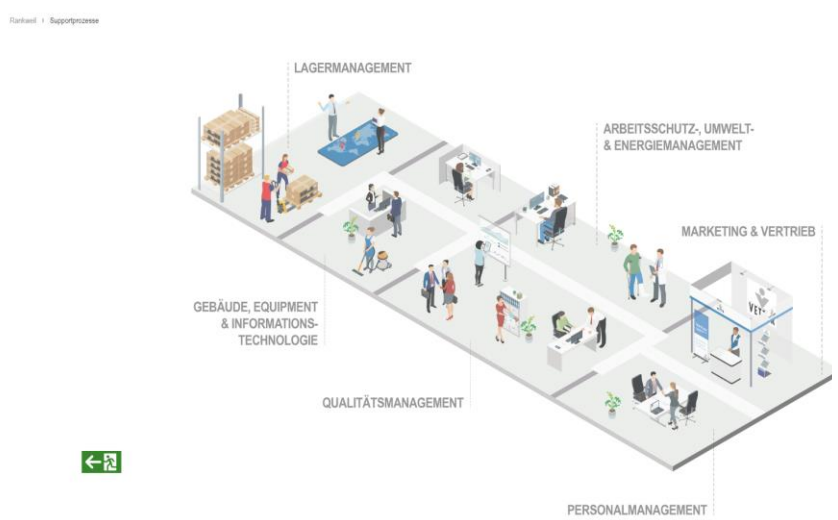
Rankweil processes: defined, implemented and documented

Rankweil



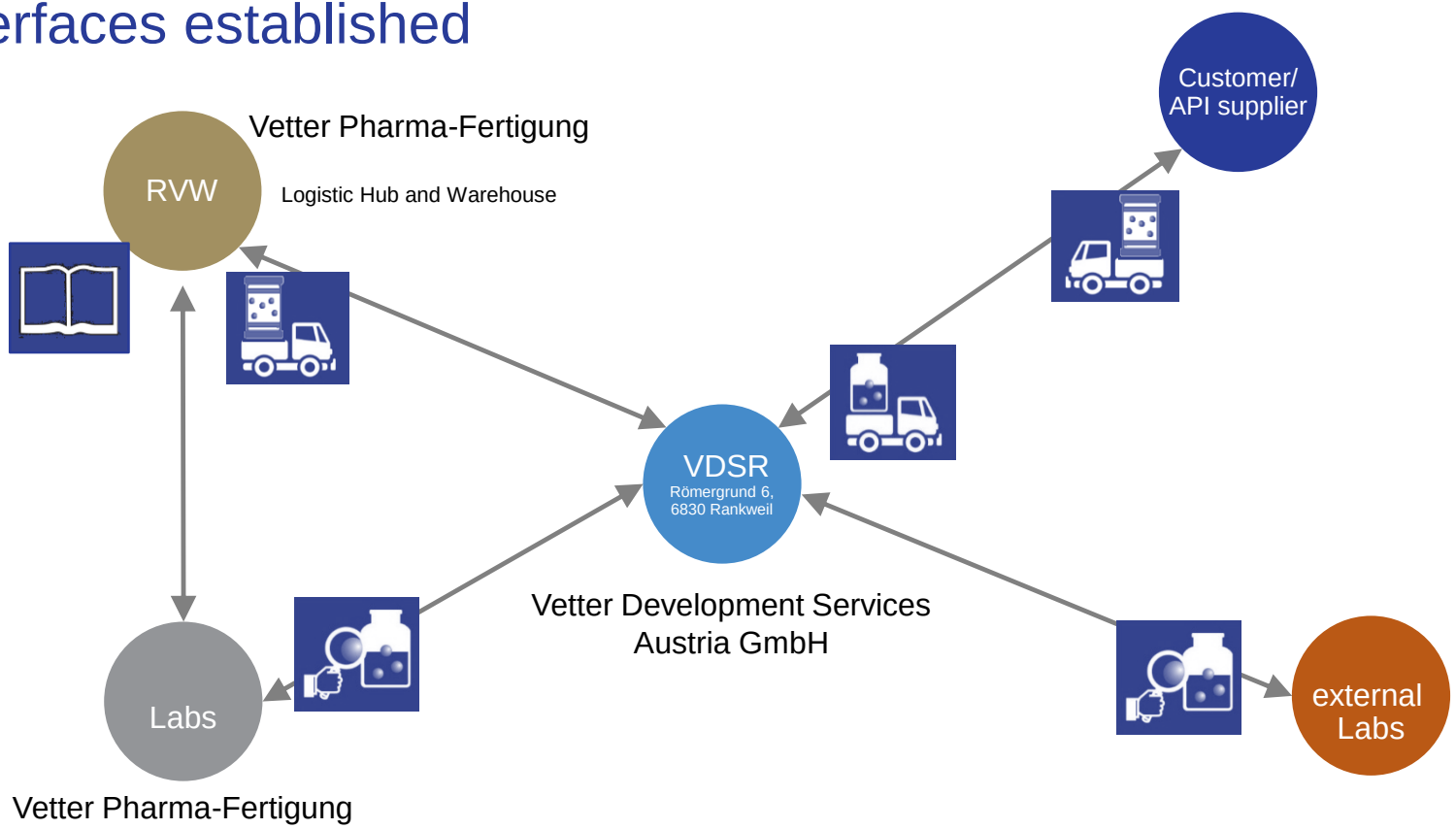
> 120 different processes established

Rankweil processes: defined, implemented and documented



Rankweil processes: defined, implemented and documented

All interfaces established



6. Staff

Successful Recruiting Process

July 2020
preparation and release of job offers

August – December 2020:
Interviews and working contracts signed

September 2020 – June 2021:
Onboarding of staff

~600
applications received

> 110
Interviews held

> 50
trial days organized

1
Motivated team established

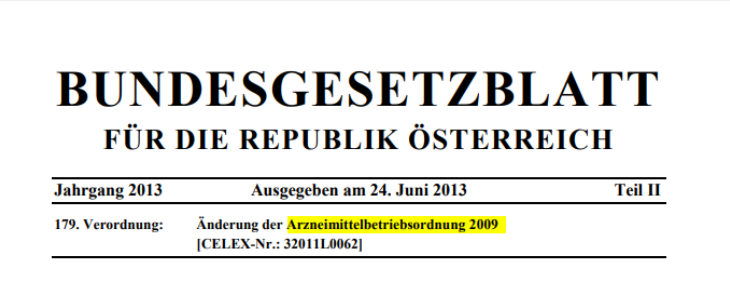
6. Judgement day:

the AGES inspection

Route to inspection-readyness

Start July 2020

Collect information/ requirements, e.g. AMBO review



BUNDESGESETZBLATT

FÜR DIE REPUBLIK ÖSTERREICH

Jahrgang 2013 | Ausgegeben am 24. Juni 2013 | Teil II

179. Verordnung: Änderung der Arzneimittelbetriebsordnung 2009
[CELEX-Nr.: 32011L0062]

Route to inspection-readyness

Start July 2020 – May 2021

Collect information/ requirements, e.g. AMBO review

Contact with AGES/BASG, „Designqualifizierung“

Unser Unternehmen hat Bedarf an Begleitung in der Umsetzung von Gesetzesvorlagen in unsere QM-Landschaft. Kann das Inspektorat hier als Konsulent tätig werden?

Nein.

Das BASG bietet die Inspektion einer Designqualifizierung an, um Pläne /Vorhaben/Änderungen zu prüfen. Die Inspektion einer Designqualifizierung erfolgt "virtuell" anhand der Planungsunterlagen.

Die Designqualifikation wird gemäß Verordnung des BASG über den Gebührenatrif gemäß GESG vergebührt.

Route to inspection-readyness

Start July 2020 – May 2021 – September 2021

Collect information/ requirements, e.g. AMBO review

Contact with AGES/BASG, „Designqualifizierung“

Use of internal / external experience: seminars mock-up audits, self-inspections

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

GMP-PHARMA CONGRESS

CONCEPT HEIDELBERG
Pharmaceutical Quality Training. Conferences. Services.

Supported by

ECA Academy Your GMP/GDP Information Source

AGES on site 5th-8th of October:
Inspection for GMP Licence according to § 63 AMG

Results regarding observations:

- **8 minor („sonstige Mängel“)**
- **0 major („schwere Mängel“)**
- **0 critical („kritische Mängel“)**

➔ **GMP and GDP license approval in December 2021**

Nota bene:
[During initial inspection in May 2018 former owner received:

- *18 minor („sonstige Mängel“)*
- *6 major („schwere Mängel“)*
- *0 critical („kritische Mängel“)]*

6. Lessons learned

Lessons learned

Drivers for the successful project performance:

- Clear Scope:
  - Project objectives & work packages defined by outcome of due dilligence
  - Rough concept for site integration predetermined via successful pioneer project VDS Chicago and subsequently fully differentiated as requirements were further defined

- Clear priorization:
  - Priorization of project‘s needs on all Vetter Management levels and departments
  - Governance structure allowed for quick addressing and escalation of topics
  - Regular update in Management Meetings to keep the momentum high

Lessons learned

Drivers for the successful project performance:

- Strategic approach

  - 2 projects with very close cooperation, both responsible PMs report to the same board
  - Full use of Vetter‘s large potential: project utilized staff with many years experience and specialized in many disciplines
  - Use of learnings, experience and contractors gained and utilized during similar projects
  - No clean slate / total refurbishment in Rankweil - but best use of existing infrastructure and machinery as far as possible

Acknowledgments

Detlev Neuland & Henryk Badack

Vera Polivka, Alexander Ulbrich und Samuel Kunze

Claus Feußner & VDSR staff

...and more than 300 other Vetter colleagues!

Thank you for your attention

QUESTIONS ?