Sneak Peek

Process Scale-up, Validation and Technology Transfer for Biologics

Dr. Sam Denby
Managing Partner, BioFrey,
United Kingdom

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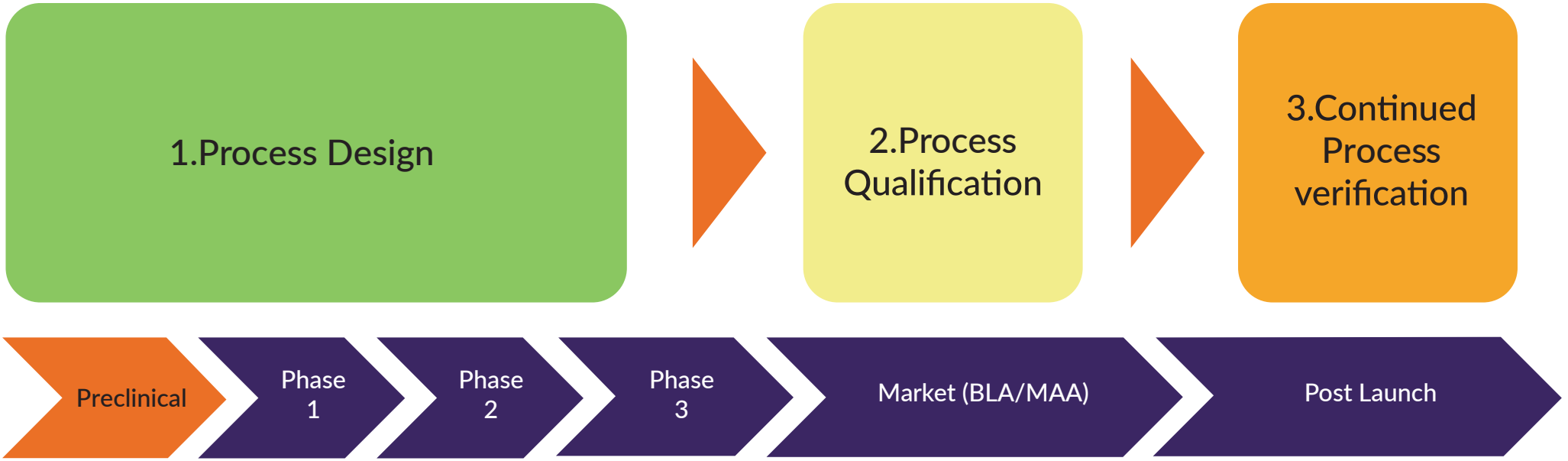
TRAINING

SYMMETRIC

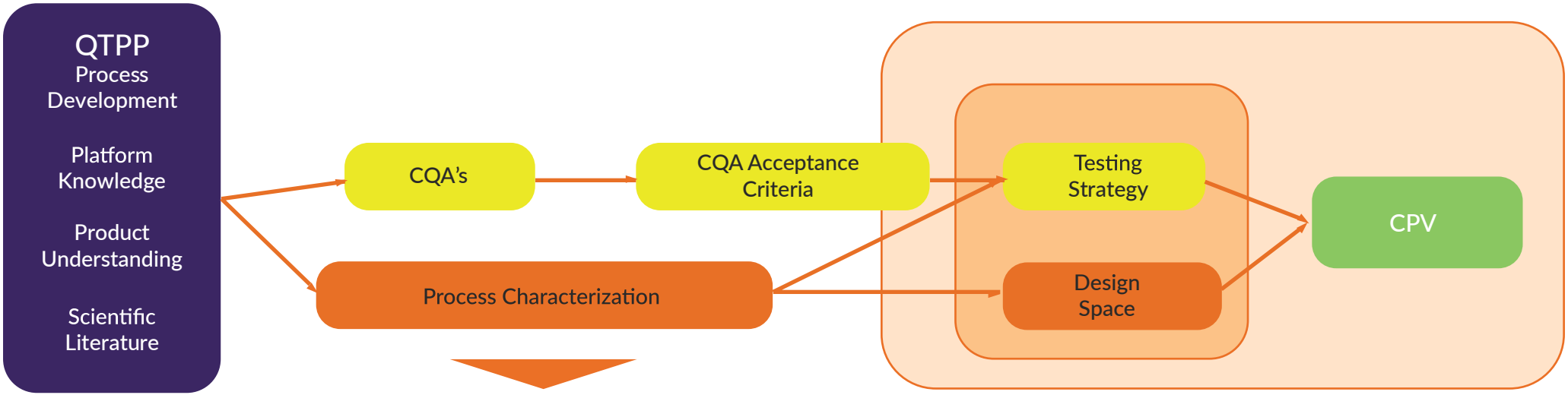
General Principles

The FDA Guidance Process Validation: General Principles and Practices (2011) identifies three stages to process validation



Broadly speaking, this is the model most companies follow

Continually de-risking process



PC Study Design to support confirmation of cPP

Alt et al Biologicals Volume 44, Issue 5, September 2016, Pages 291-305
https://doi.org/10.1016/j.biologicals.2016.06.005

A note on QbD. The above is generally accepted to be QbD. By following these principles you continually increase the likelihood of producting a product of acceptable quality. QbD CAN deliver a design space, but has done so very infrequently (1 filing)

Selecting a manufacturing site

03

Long term relationship

Consider pre-existing relationships – do you have an internal manufacturing site?

Are there CMO's you have worked with previously?

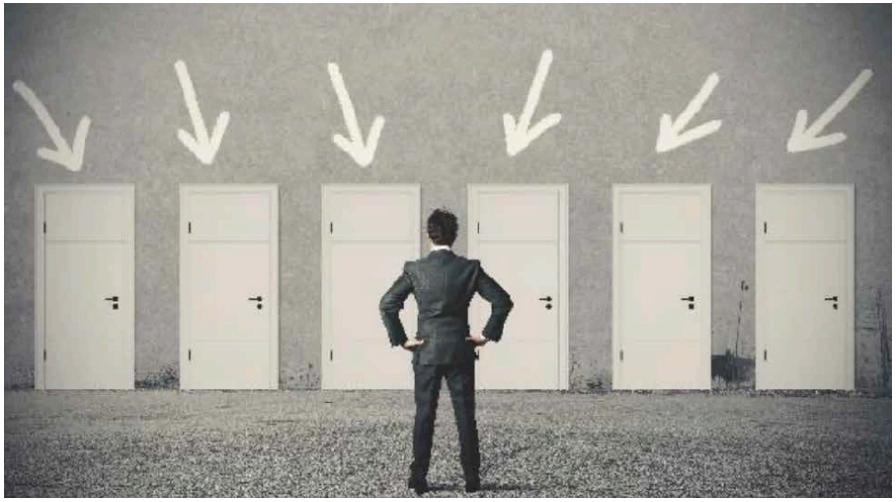
Is development capability critical?

Location?

Prior experience of site?

Audit history/site licenses?

Contract terms



How?

RFP – Ideally involve a procurement professional/consultant. CMC, SME and quality oversight/input

Kepnor Tregoe Matrix

Selecting a manufacturing site

04

What is a Critical Quality attribute (CQA)

3.2.4.2 Critical Quality Attribute (CQA)

A Critical Quality Attribute (CQA), according to ICH Q8(R2), is “a physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality.” To determine a CQA, in principle, is a fairly straightforward three-step process; but, in reality, takes a considerable CMC team resource commitment to carry

How are CQA’s identified

1. List all of the quality attributes (i.e. molecular and functional properties or characteristics) of the biologic
2. Select an ICH Q9 quality risk assessment tool (e.g. RRF or FMEA) and systematically assign a risk score to each and every listed quality attribute
3. Decide what risk score value will be identified as critical

Obligatory CQA's

05

DS and DP

Composition and strength (for a Mab)
- Protein content
- Osmolality
- pH
- Appearance (color, opalescence, clarity)
- Buffer Content
- Excipient Content
- Surfactant Content

Adventitious agent control
- Viruses
- Screening of raw mats esp. cell banks,
- Viral clearance
- Testing of clarified harvest
- Microbiological impurities (Bacteria, Mycoplasma)
- Bacterial Endotoxins

DP Specific

- Subvisible particles
- Visible particles
- Extractbale volume
- Sterility

Validation Master Plan

06

Validation master plan brings all of the work that has been done to date together it's an opportunity to tell the story of the molecule, facility and process. Going forward it's an important document to support key activities such as regulatory filings and inspections. It should be molecule specific.

Many sites (including CDMOs) will have personnel who are highly skilled in designing and executing these protocols. Whoever you are working with, leveraging their expertise is crucial.

Validation master plans typically include:

- Introduction
- Purpose
- Roles and responsibilities
- Overall approach to validation
- Process description
- Process design (History, development, characterization)
- Manufacturing process control strategy
- Process qualification
    - Facility
    - PPQ strategy
    - PPQ Pre-requisites
    - Campaign
    - Specifications and testing
- Supplemental Studies
- Continued process verification

Registration

Sneak Peek

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Mliekarenská 9, 821 09
Bratislava, Slovak Republic
ID: 47 068 124
VAT no: SK2023741973
Office: +421 948 262 346

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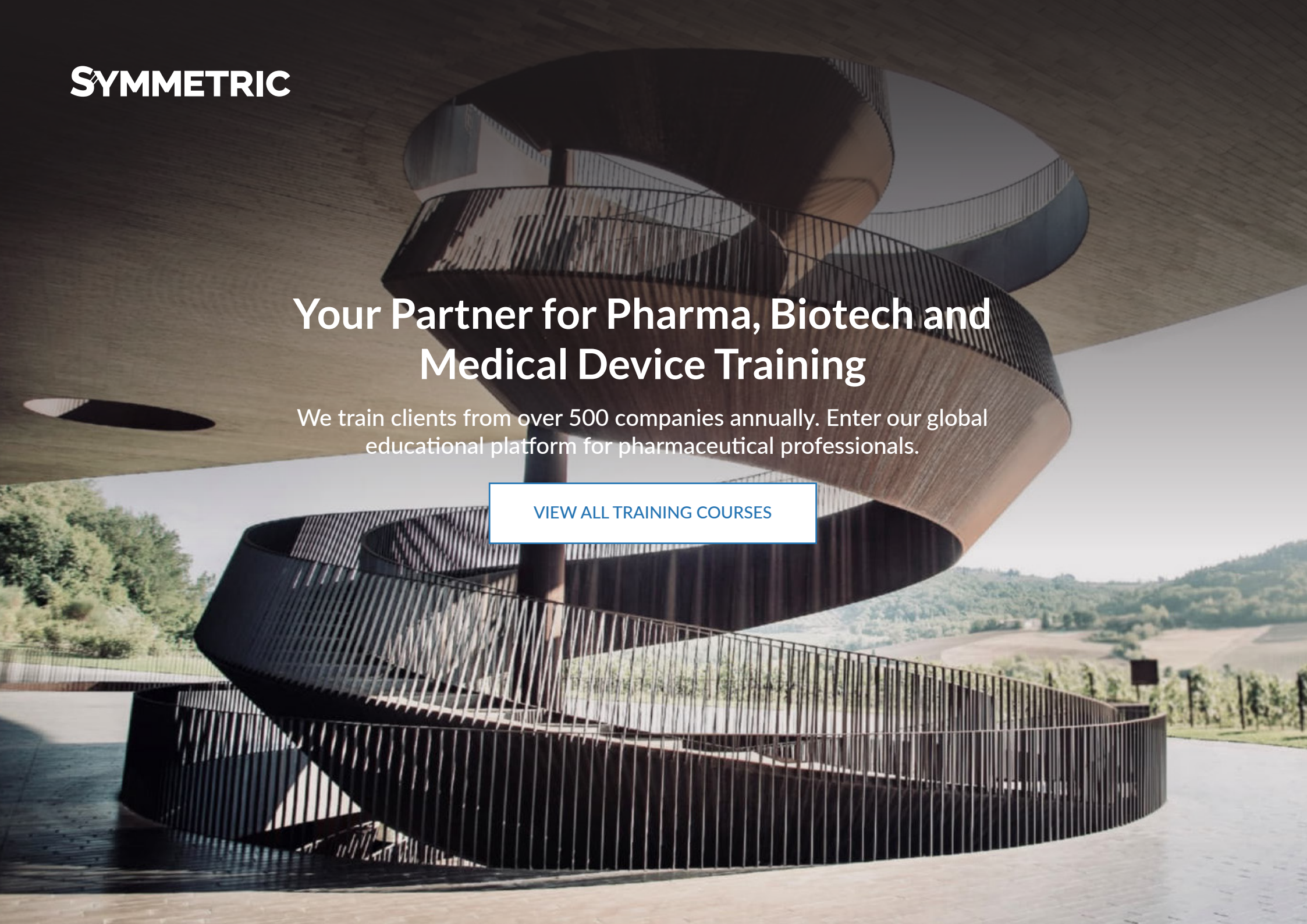
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