



Active Pharmaceutical Ingredient (API) Manufacturing Course: Scale-Up, Crystallisation and ICH Q7



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Introduction:

Active pharmaceutical ingredient API manufacturing, from reaction scale-up through crystallisation, isolation and ICH Q7 GMP, is a 5-day course for process engineering, process chemistry, production and drug substance quality staff, ending with an API Process and Control Plan for a case drug substance plant. Plants building local drug substance capacity lose batches when exothermic steps are scaled without heat data, the wrong polymorph crystallises, wet cake dries off-specification and mutagenic impurities are found late. Nominees already run, design or release synthesis steps and inspect case reactor bays, isolation trains and batch data. CoreConcept Training Center delivers this API manufacturing course.

Course Objectives:

- Select and justify a synthetic route and API starting material using step count, hazard, impurity fate and supply criteria
- Scale batch reactions from laboratory to plant using reaction calorimetry, heat removal capacity and controlled reagent dosing
- Design cooling and antisolvent crystallisation with seeding and supersaturation control to deliver the target polymorph and particle size
- Set filtration, cake washing, centrifuge and filter-dryer parameters that meet residual solvent limits without form change or agglomeration
- Build impurity and mutagenic impurity control strategies using purge arguments, solvent recovery rules and in-process testing
- Apply ICH Q7 GMP and potent-compound containment banding to equipment, cleaning, reprocessing and batch release in a drug substance plant

Target Audience:

- Process engineering staff responsible for reactor, crystalliser, filtration and drying equipment in drug substance plants
 - Process chemistry staff responsible for synthetic routes, reaction conditions and impurity investigations at pilot and plant scale
 - Production staff responsible for running synthesis campaigns, charging reagents and executing batch records for intermediates and APIs
 - Drug substance quality staff responsible for ICH Q7 GMP oversight, deviation review and batch disposition of APIs
 - Health, safety and containment staff responsible for operator exposure control when handling potent drug substances
 - Technical project staff responsible for new API plant start-up and drug substance localisation projects
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Course Outline:

Day 1: Drug Substance Supply Chain, Route Selection and Plant Baseline

- API Value Chain From Starting Material to Packed Drug Substance
- ICH Q11 API Starting Material Designation and Justification Criteria
- Synthetic Route Scoring by Step Count, Yield and Hazard
- Multipurpose Batch Plant Layout of Reactor Bays and Isolation Suites
- Current-State Review of Campaign Yields, Cycle Times and Batch Failures

Day 2: Reaction Scale-Up, Thermal Safety and Process Chemistry Controls

- Reaction Calorimetry Data for Heat of Reaction and Adiabatic Rise
- Jacketed Reactor Heat Removal Capacity Versus Reagent Dosing Rate
- Agitation, Mixing Time and Mass Transfer in Glass-Lined Reactors
- Thermal Runaway Scenarios and Basis of Safety Documentation
- In-Process Control Sampling and Reaction Endpoint Criteria by HPLC

Day 3: Crystallisation, Polymorph Control, Filtration and Drying

- Solubility Curves and Metastable Zone Width for Crystalliser Design
- Seeding Strategy, Cooling Profiles and Antisolvent Addition Rates
- Polymorph Identification With XRPD, DSC and Raman Spectroscopy
- Nutsche Filter-Dryer and Centrifuge Cake Washing and Deliquoring
- Vacuum Drying Endpoints, Residual Solvent Testing and Milling of Crystals

Day 4: Impurity Purge, Solvent Recovery, Containment and ICH Q7 GMP

- ICH Q3A Organic Impurity Thresholds and Impurity Fate Mapping
- ICH M7 Mutagenic Impurity Assessment and Purge Factor Arguments
- ICH Q3C Residual Solvent Classes and Recovered Solvent Reuse Rules
- Occupational Exposure Banding and Isolator Containment for Potent APIs
- ICH Q7 Reprocessing, Reworking, Cleaning and Batch Release Requirements

Day 5: Inspection Walkthrough and API Process and Control Plan

- Case Reactor Bay Walkthrough Against Thermal Safety Records
 - Case Crystallisation Batch Data Review for a Polymorph Excursion
 - Case Filter-Dryer and Containment Suite Walkthrough Against ICH Q7
 - Critical Process Parameter and In-Process Control Table Drafting
 - API Process and Control Plan Completion and Peer Challenge
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Skills You Will Gain:

- Synthetic Route Evaluation
- Reaction Calorimetry Interpretation
- Crystallisation Process Design
- Polymorph Characterisation
- Filter-Dryer Operation Control
- Mutagenic Impurity Risk Assessment
- Potent Compound Containment
- Drug Substance GMP Oversight

Why Attend This Course:

- Deliver an API Process and Control Plan for a case drug substance plant to the plant manager, the head of process chemistry and the site quality unit
- Decide whether a reaction can be scaled safely, a crystallisation batch released or a recovered solvent reused, based on heat, form and impurity data
- Avoid thermal incidents, polymorph failures, off-specification drying and late mutagenic impurity findings that stop campaigns and delay supply
- Pass on calorimetry worksheets, crystallisation templates, purge tables and containment checklists to shift engineers and junior chemists

Conclusion:

Back at the plant, the participant hands the API Process and Control Plan to the plant manager, the head of process chemistry and the site quality unit. They use it to approve the basis of safety for scaled reactions, set crystallisation and drying limits, agree the impurity and solvent reuse strategy and assign containment controls for potent steps. After the first campaign run under the plan, the unit should compare yields, polymorph results, residual solvent data and exposure monitoring with the plan and revise the parameter table where limits failed.

Frequently Asked Questions FAQ:

What should participants know before the active pharmaceutical ingredient API manufacturing course?

Participants should already work on synthesis, isolation, engineering or quality tasks in a chemical or drug substance plant and read batch records and analytical results. Basic organic chemistry and heat transfer knowledge is assumed. Anonymised reaction, crystallisation or drying data helps them apply the walkthroughs.

How does active pharmaceutical ingredient API manufacturing differ from finished dosage form manufacturing?

API manufacturing makes the drug substance itself by chemical synthesis, crystallisation, filtration and drying. Finished dosage form courses start from that substance and cover blending, tablet compression, coating and filling, and biologics courses cover cell culture and purification of proteins.

Why does polymorph control matter in active pharmaceutical ingredient API manufacturing?

Different crystal forms of the same molecule can dissolve at different rates and change how the medicine performs. Forms are approved individually, so solvent choice, supersaturation, cooling rate and seeding must be controlled to make the approved form every batch.

What do participants take back from the active pharmaceutical ingredient API manufacturing course?

Participants take back an API Process and Control Plan for a case drug substance plant, with a thermal safety summary, crystallisation and drying parameter table, impurity purge map, solvent reuse rules and containment checklist ready to adapt to their own campaigns.
