Pfizer CentreOne

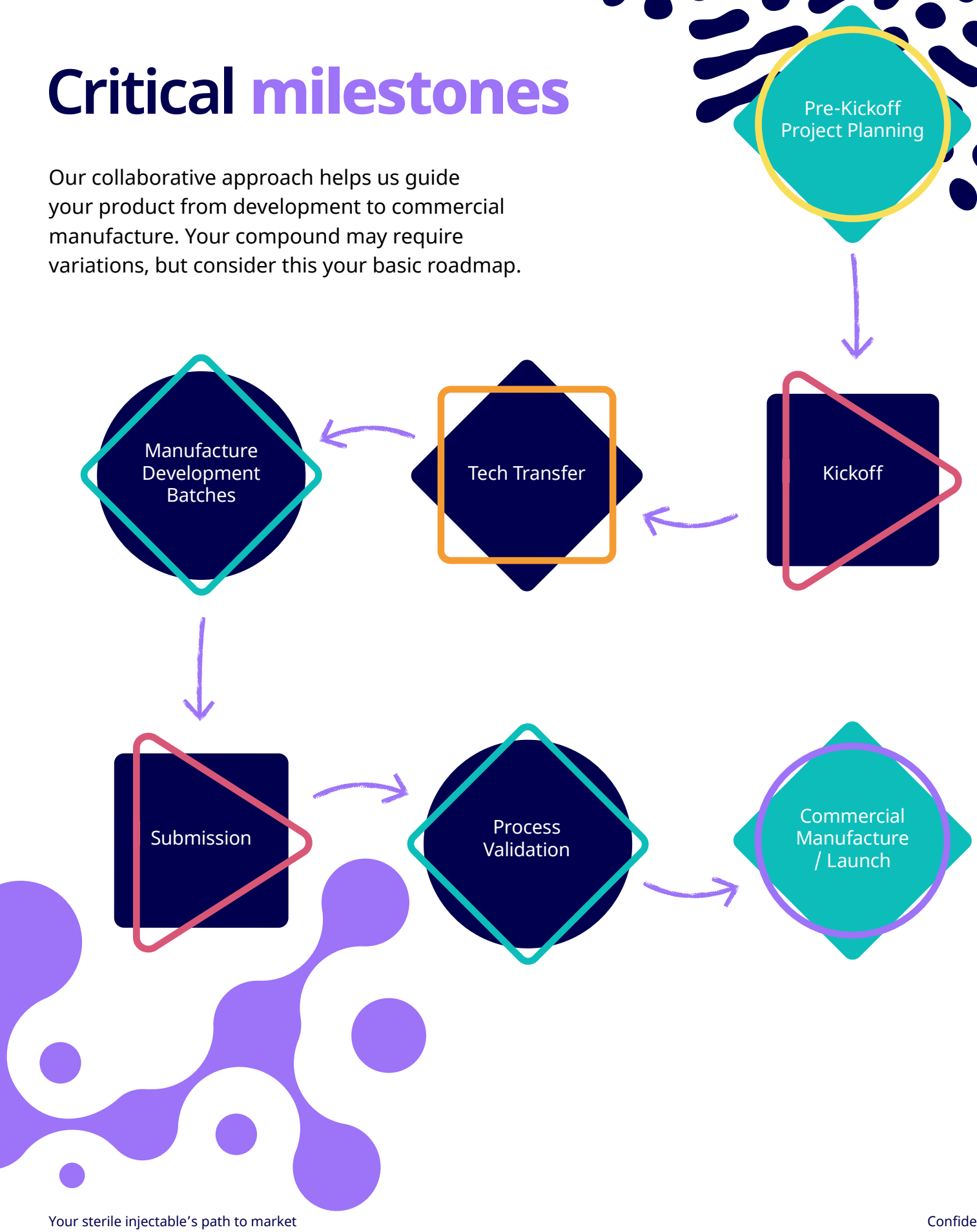
Confidential

Your sterile injectable's path to market

A step-by-step guide to how we help you reach your critical milestones

Critical milestones

Our collaborative approach helps us guide your product from development to commercial manufacture. Your compound may require variations, but consider this your basic roadmap.



1. Pre-Kick Project Planning Purpose

Prepare for an effective kickoff meeting by providing all necessary information to Pfizer CentreOne experts for advance review.

What we'll need from you

- EHS questionnaire
- TSE/BSE and AMC/BET surveys
- Residual solvent survey
- Tech transfer questionnaire:
  - SDS (Safety Data Sheet)
  - Dosing information for cleaning limits
  - Commodity and filter information
- Batch records, development reports and stability data (if available)
- Other information as needed and requested by Pfizer CentreOne Development Services Team

Alignment activities

- Internal Pfizer CentreOne meetings to discuss:
  - High-level manufacturing plan
  - Suggested commodities
  - Environmental Health and Safety (EHS) site assessment
  - Filter information
  - Commodity processing information
  - Container/closure integrity (CCI) evaluation
  - Analytical and microbiological requirements
  - High-level timeline
- Pre-kickoff teleconference or meeting with you to discuss:
  - Secure document-sharing method
  - Additional documentation needed from you
  - Kickoff meeting date

Deliverables

- Kickoff meeting date and time
- Timeframe for establishing document-sharing repository or other secure sharing method
- Timeframe for providing us with additional information/ documents, as needed/requested

2. Kickoff Purpose

Initiate the project by establishing our mutual team and finalizing project scope and expectations.

Alignment activities

- Kickoff meeting to align:
  - Scope of project
  - Mutual project expectations
  - Key timeline requirements
  - Communication expectations
  - Key project risks
  - Core team roles and responsibilities
  - Process validation and regulatory strategy
- Finalize equipment requirements
- Commodity identification

Deliverables

- Statement of project objective and scope
- Core team contact information
- Minutes and action items from the kickoff meeting (list of issues, agreements and action items)
- Project timeline and major-milestone target dates (initial drafts)
- Routine meetings scheduled
- Gap assessments from partner-supplied information
- Commodity samples for assessments or pre-development work

3. Tech Transfer Purpose

Perform the technical transfer activities necessary to complete your development runs and prepare for your first GMP (clinical/registration) batch.

Alignment activities

- Project status meetings
- Meetings/calls to develop and manage:
  - Project schedule
  - Change control expectations
  - Document approval process
  - Cleaning methods and limits
  - Analytical and microbiological method qualifications and transfers to quality and/or stability services groups
  - Visual inspection process, elemental impurities and serialization compliance initiatives
  - Tech transfer/development plan and risk assessment

Deliverables

- Initiation of change control
- New commodity specifications
- Quality technical agreement
- Risk management plan
- Raw material:
  - ID method validation
  - Qualification of new excipients (as necessary)
  - Raw material specifications
  - Qualification of new analytical methods (as necessary)
  - AMC/BET evaluation-validation (as required)
  - API equivalency study (as required for alternate suppliers)
- Analytical – bulk/in-process:
  - Analytical method development/validation/transfer
  - Bioburden method development/validation/transfer
- Analytical – drug product:
  - Reference standard qualification
  - Simple methods evaluation/transfer
  - Complex analytical method development/validation/transfer
  - BET method development/validation/transfer
  - Sterility method development/validation/transfer
  - Preparation of test methods
  - Preparation of drug product specifications
  - Stability protocol
- Filter:
  - Bubble point and/or forward flow
  - Microbial retention
  - Summary filter validation report
  - Chemical compatibility [1]
  - Extractables/leachables [1]
  - Filter flush study
- Cleaning:
  - Confirmation of cleaning limits
  - Development and validation of analytical methods for cleaning
  - Material contact study
  - Material cleanability study
  - Material compatibility study
  - Cleaning recovery study (as necessary)
- Sterilization cycle development/validation (if necessary)
- Engineering, development and clinical run(s):
  - In-plant small-scale batch for trials (if necessary)
  - Protocol and batch records to execute the trials
  - Batch summary reports
- Batch record development
- Product evaluations (as required):
  - Freeze-thaw study
  - Admix study – chemistry and micro
  - D-value and viscosity for terminal sterilization evaluation
  - CCI and/or syringe air transit study
  - Fill volume study
  - AMPET (preservative efficacy) study
  - Photo stability
  - Automated visual inspection (AVI) evaluation (in conjunction with stability samples)
  - Extractables/leachables
  - Tubing study
  - Formulation development
  - Rubber extractables [1]
  - Elemental impurities risk assessment and testing [1]
  - Cold chain study
- Tech transfer protocol and process risk assessment

4. Manufacture Development Batches

Purpose

Manufacture your clinical and/or registration batches, initiate stability studies and deliver your clinical supplies as needed to support IND and other regulatory submissions.

Alignment activities

- Project status meetings
- Meetings/calls to manage:
  - Project schedule
  - Sampling requirements including stability protocol (CCI testing and AVI study as necessary)
  - Deviation/exception reporting and lab investigation process
  - Batch disposition process including CoA format
  - Shipping of samples/finished product

Deliverables

- Batch records for development batches
- Formulation/filling/capping of batches
- Labeling of samples for stability and/or supply to clinical packaging site
- Preparation of samples for AVI evaluation
- Shipping of stability and AVI samples to stability storage and testing site
- Testing and disposition of batch
- Batch shipment
- Stability interim and final reports (if using Pfizer CentreOne stability services)
- Batch summary report
- Update of technical transfer plan and risk assessment [2]

5. Submission

Purpose

Ensure items required for your regulatory filing are complete and accurately represent Pfizer's manufacturing processes and procedures.

Alignment activities

- Project status meetings
- Review of submission schedule

Deliverables

- Elastomeric closures physiochemical, biochemical, and functionality testing report [1]
- Elemental impurities risk assessment and report [1]
- Filter reports:
  - Absorption [1]
  - Chemical compatibility [1]
  - Extractables/leachables [1]
  - Microbial retention [1]
- Stability final reports
- CMC submission compilation (as required)
- Peer review of submission
- Readiness assessment prior to preapproval inspection
- Support for regulatory agency inspection(s)

5. Process Validation

Purpose

Ensure a smooth transition to commercial manufacture by validating the appropriate processes and equipment.

Alignment activities

- Project status meetings
- Update and monitor project schedule
- Review of validation master plans, critical process parameters and critical quality attributes
- Equipment list review and approval

Deliverables

- Initiation of change control
- Process validation:
  - Validation project plan
  - Mix/fill uniformity validation
  - Hold time validation
  - Lyophilization validation (if necessary)
  - Nitrogen headspace validation (if necessary)
  - Validation project plan report
  - Continuous process validation strategy
- Cleaning validation (as necessary):
  - Tank cleaning validation
  - Line cleaning validation
- Equipment validation (if necessary): [3]
  - Tank validation
  - Ancillary equipment validation
  - Freezer validation
  - Media fill validation
- Sterilization validations (if necessary): [3]
  - Wash/depyrogenation validation
  - Container/closure sterilization validation
  - Container/closure integrity validation
  - Product terminal sterilization validation

6. Commercial Manufacture/ Launch

Purpose

While your drug is under regulatory review, perform the activities necessary to prepare it for a successful market introduction. Then upon regulatory approval – launch!

Alignment activities

- Project status meetings
- Update and monitor project schedule
- Confirmation of launch strategy
- Confirmation of labeling and packaging requirements
- Discuss expectations for commercial stability program

Deliverables

- Serialization development
- Label development
- Packaging specification sheet and drawing development
- Packaging engineering trial
- Packaging batch record development
- Commercial readiness review
- Updated tech transfer report and risk assessment [2]
- First lot to stock release and shipment (and/or quarantine ship prior to regulatory approval and then release once approved)
- Change control closure

References

1. Activity initiated at tech transfer milestone to support completion required for submission
2. Deliverables originated in tech transfer phase and revised after engineering batch, clinical/registration batches, and process validation batches, with the final report completed during commercial manufacture
3. Validation activities will be completed prior to process validation lots

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