

Goals/ Definitions

The development and optimization of the manufacturing process to ensure that the drug substance and product used in the pivotal Phase 3 trial are representative of future commercial product quality.

Manufacturing process developed and scaled up.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
<ul style="list-style-type: none"> Manufacturing process optimization completed 	<ul style="list-style-type: none"> a) Design-of-experiments and quality-by-design (QbD) methodology with consideration given with ICH Q8, Q9 and Q10 guidance b) Drug substance manufacturing process optimization, scale-up, and pilot studies (e.g., modification of synthetic pathways, intermediate selection, selection of unit operations and equipment, purification process refinement, etc.) c) Drug product manufacturing process optimization, scale-up, and pilot studies (e.g., selection of unit operations to support desired formulation, blending process refinement, etc.) d) Packaging line equipment selection, trials, and optimization e) Process flow diagrams and draft operating parameters f) Operating parameter (yield, purity, and form) relationships g) Waste reduction strategy and product/package end-of-life considerations h) Re-packaging considerations (e.g., end-use packaging vs. packaging for re-distribution) 	<ul style="list-style-type: none"> Summary of key data to substantiate conclusions Illustrative data tables or figures may be reported in an appendix
<ul style="list-style-type: none"> Commercial-scale drug manufacturing feasibility assessment completed 	<ul style="list-style-type: none"> a) Evaluation of pilot plant results (product and process) including process economics (e.g. COGs) to make any corrections and a decision on whether or not to proceed with a full-scale plant development b) Safety and ecological assessment of processing and effluents 	<ul style="list-style-type: none"> As above
<ul style="list-style-type: none"> Drug product package characterization completed 	<ul style="list-style-type: none"> a) Leachable/extractable assessment b) Child resistant/senior friendliness testing c) Tamper evidence d) Product compatibility (from package and from environment) 	<ul style="list-style-type: none"> As above
<ul style="list-style-type: none"> GMP Manufacturing 	<ul style="list-style-type: none"> a) GMP Ph 3 DS and DPs released 	<ul style="list-style-type: none"> Summary of key data, e.g. CoA

*Candidate progression is discussed at standing grantee update meetings with the investment team

** If a commercial partner has not been identified by EP2, either the PDP will commercialize the products or, PDP will secure adequate funding to conduct future CMC activities