

## The Critical Steps of Pharmaceutical Development

In a business steeped in risk, it makes a lot of sense to focus on the basics, what De Young & Hayden call the “**S E C**” of biopharmaceutical development. To ensure that the target product label supports the competitive **Safety, Efficacy**, and/or **Convenience** to make a product successful requires careful tracking of details. Hence, the following table lists the elemental steps required to develop a pharmaceutical product and bring it successfully to market.

The table provides a convenient means to track a step-by-step approach to the science and marketing needed to bring a pharmaceutical product from development into the market. Using the table is one part of the successful management of risk.

Each step listed in the table is critical in the successful development of pharmaceutical product from Start of Development, through IND, then Phases I-III to NDA and, ultimately, the commercialization of the product.

The steps are listed here in a checklist format broken down by relevant category to enable development teams and their managers to mark their progress and track their success. While De Young & Hayden, LLC, provides support for development teams in a number of areas and ways, we have **emphasized** the ones in which we are most commonly engaged in adding value to the process.

We hope that the table will be a useful addition to the drug development armamentarium. Please contact us if we can be of assistance.

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**Start of Development**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

		Not Done	Pending	Done	NA (explanation)
<b>Start-up Health Economics</b>					
1.	The disease state(s) or procedures involved/to be treated have been evaluated.				
2.	We understand the disease and the outcomes of standard therapy, as well as current procedures, drugs, and devices used to manage the disease.				
3.	There is a significant unmet clinical need.				
4.	Any significant epidemiological considerations that affect the projected size of the market have been evaluated.				
5.	The projected clinical outcomes have been characterized.				
6.	We will know at launch the standard therapy in the major markets.				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
7. We have determined our projected economic advantage compared with comparator therapies, including value of incremental benefit.				
<b>Start-up Commercialization</b>				
8. The magnitude of the market for the projected clinical indication is well characterized.				
9. The projected size of the patient population has been researched and quantified.				
10. Whether the population be expanded by marketing activities has been evaluated.				
11. How improvements over current therapy can represent significant improvements has been researched and documented.				
12. The competitive landscape is well understood,				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
including products that are currently in the market, as well as products that are in the pipeline.				
13. The treatment paradigm at the time of launch been evaluated.				
14. We are in a position to prepare preliminary forecasts.				
15. The patent status of the development candidate is suitable.				
16. Competitors' experience with molecules in this class has been evaluated.				
17. The rationale to propose the new candidate is well characterized; e.g., the proposed mechanism of action is important in the target disease.				
18. The most likely reasons why the candidate might				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
not be successful have been studied.				
19. The advantages and disadvantages of the candidate compared with other lead compounds have been quantified.				
20. Problems with current therapy for the target disease is well documented.				
21. Need for a new therapy has been thoroughly documented..				
22. All other competitive products/technologies currently in development have been evaluated.				
23. We have determined our “drop dead” price based on cost of goods.				
24. We know whether health economics supports the “drop dead” or a higher price.				
25. We know who will “pay” for this therapy.				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
26. We understand how this therapy will be reimbursed.				
<b>Start-up CMC</b>				
27. The chemical purity on a batch-to-batch basis is measurable, reproducible, and satisfactory.				
28. The enantiomeric purity is measurable, reproducible, and satisfactory.				
29. In the of case polymorphism, all polymorphs to date have been characterized.				
30. The rationale for selecting a polymorph has been established.				
31. The synthesis is capable of being scaled-up for the manufacture of drug substance required for development up to the freezing of specifications in preparation for pivotal study.				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
32. Qualified assays are available that can measure low levels of impurities.				
33. The drug substance has been characterized physiochemically.				
34. Based on the physiochemical characteristics, a dosage form has been developed that has sufficient bioavailability for the desired routes of administration.				
35. Specifications have been established for raw materials, drug substance, and preclinical dosage forms.				
36. Stability of the drug substance and the preclinical dosage form will be acceptable over the intended length of the planned toxicology studies.				
37. The degradation profile has been determined.				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
38. The appropriate environmental, safety, and health issues have been identified.				
<b>Start-up Toxicology</b>				
39. The candidate or its metabolites are not potentially mutagenic, based on similar chemical structures and in-vitro testing.				
40. Findings from initial studies with appropriate repeat dosing in an appropriate animal model (with blood concentration measurements) suggest that the candidate is safe at the expected exposure in humans.				
41. The therapeutic index for the candidate based on blood concentration measurements and dose-limiting toxicity has been determined in an appropriate animal model.				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
42. The toxicological profiles have been determined for impurities and decomposition products.				
43. Organ systems of toxicity have been identified.				
<b>Start-up Preclinical/Safety Pharmacology</b>				
44. The drug substance produces the desired pharmacological effect(s) in vitro and in vivo.				
45. The candidate is active in an animal model when desired routes of administration are used.				
46. The pharmacological effect is related to systemic blood concentration.				
47. The candidate produces acceptable effects on vital function in animals and these effects relate to the blood concentration needed to produce the desired pharmacological effect.				

Startup of Development

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Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
48. In anti-infective drugs and chemotherapeutic drugs, it has been evaluated whether there is a potential that the candidate produces drug resistance or cross-resistance to other drugs in current use.				
<b>Start-up Pharmacokinetics &amp; Drug Metabolism</b>				
49. Validated drug assays are available.				
50. The drug is stable in biological matrices under normal sample handling and storage conditions.				
51. The half-life, bioavailability, and volume of distribution of the candidate are understood in the pharmacology efficacy model and in animal species proposed for toxicology studies.				
52. The metabolic profile of the candidate in relevant tissues has been determined.				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
53. The in vitro metabolic profile in animal and human preparations is understood.				
54. The mass balance of the drug in rodents has been determined.				
55. Any potential drug-drug interactions (e.g., for drugs likely to be administered in combinations with the candidate) have been studied.				
56. It is known whether there will be significant new human metabolites found that were not seen in the animal species used for toxicology testing.				
<b>Start-up Clinical Pharmacology</b>				
57. The pharmacodynamic endpoints for predicting clinical efficacy have been determined.				
58. The relationship between dose and plasma				

Startup of Development

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
concentrations is understood.				
59. The relationship between dose and key pharmacodynamic markers has been characterized.				
60. The dose range most likely to produce an effective therapeutic effect has been determined.				
61. It is understood how the parent drug is cleared.				
62. The time course of onset and offset of pharmacodynamic effect is understood.				
<b>Start-up Clinical Therapeutics</b>				
63. The projected clinical indication has been determined.				
64. The medical need for the projected indication has been evaluated.				

**Entry into Human (EIH)**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

		Not Done	Pending	Done	NA (explanation)
<b>EIH Health Economics</b>					
65.	We have defined the major factors that drive cost.				
66.	We understand our health economic hypothesis: Where and to whom can we demonstrate value.				
67.	We have defined the relevant data to collect in the Phase II/III program.				
68.	We have determined whether quality of life will be an important endpoint.				
69.	We understand our geographic scope.				
70.	We know if there are going to be reimbursement hurdles.				

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Entry into Human

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

		Not Done	Pending	Done	NA (explanation)
<b>EIH Commercialization</b>					
71.	We understand what endpoints in clinical studies would most credibly establish the candidate's advantages to clinicians.				
72.	A suitable formulation has been developed. (CMC 69)				
73.	The product is focused on a single therapeutic area.				
74.	If the product is targeted at multiple therapeutic areas, then market priorities have been established.				
75.	For multiple therapeutic areas, balance of speed to market versus size of indication has been resolved.				
76.	The time frame to market has been determined.				

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**Entry into Human**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

					Not Done	Pending	Done	NA (explanation)
<b>EIH CMC</b>								
77.	Scale-up is feasible.							
78.	A qualified analytical procedure is available to characterize the desired dosage forms.							
79.	Reference standards are available for major drug substance impurities and degradation products.							
80.	The stability data support the use of the dosage form in clinical studies.							
81.	An appropriate Phase I formulation been developed.							
82.	For a parenteral formulation, appropriate methods of sterilization have been developed and qualified.							
83.	The impurity profile is consistent and all major impurities have been qualified at the doses to be							

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**Entry into Human**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
used.				
84. Contract manufacturers have been selected for drug substance (DS) and drug product (DP) that will be able to scale up and produce commercial materials.				
85. Materials intended for human use meet the required quality standards for early phase clinical supplies in the territories for which they are intended to be tested.				
<b>EIH Toxicology</b>				
86. The duration of toxicology studies is sufficient to conduct clinical studies that answer the critical therapeutic questions.				
87. The therapeutic index of the compound based on the "free fraction" plasma concentration is known.				
88. We understand which clinical signs should be				

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**Entry into Human**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
monitored in human studies based on the findings in the subchronic studies.				
89. Toxicology data at this stage provide an adequate evaluation that can support safe entry into humans for the assessment of kinetics and tolerance.				
90. The maximal no adverse effect dose in the appropriate animal model has been determined.				
<b>EIH Preclinical/Safety Pharmacology</b>				
91. The major metabolites observed in drug metabolism and toxicological studies have been evaluated for pharmacological activity.				
92. Any undesirable effects (CNS, pulmonary, cardiovascular etc.) observed in safety pharmacology studies have been noted.				
93. The predicted pharmacological dose (systemic				

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**Entry into Human**

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Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
exposure) in human has been determined.				
<b>EIH Pharmacokinetics &amp; Drug Metabolism</b>				
94. The pharmacokinetics of the drug during toxicology studies (toxicokinetics) has been characterized.				
95. It is known whether the pharmacokinetic profile changes over time.				
96. It is known whether there is evidence of liver enzyme induction.				
97. Enzymes responsible for the metabolism of the drug in humans and animals have been determined.				
98. It is known whether the drug/metabolite(s) inhibit any of the major human drug metabolizing enzymes.				
99. It is known whether there is evidence of drug accumulation.				

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**Entry into Human**

**Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.**

	Not Done	Pending	Done	NA (explanation)
100. The predicted pharmacokinetic and metabolic profile in humans (allometric scaling) is known.				
101. We understand how the pharmacokinetic information compares between the toxicology species and the pharmacology efficacy model.				
102. We understand whether there is a pharmacokinetic/ pharmacodynamic relationship.				
103. We have evaluated any relationship established between plasma concentrations and activity and toxicity.				
104. We understand the nature of the plasma protein binding of the drug in test species and humans.				

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**Entry into Human**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
<b>EIH Clinical Pharmacology</b>				
105. We understand what should be the starting single dose based on preclinical data and human experience with similar drugs.				
106. We have evaluated whether the starting dose should be a “no effect” dose.				
107. We know whether the first studies should be conducted in healthy volunteers or patients.				
108. We know at what rate the dose should be escalated.				
109. We know whether dose escalation can be predetermined or whether it should be based on subject response.				
110. We understand what the endpoint will be for the highest dose (toxicity, pharmacodynamic response,				

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Entry into Human

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
or other parameters).				
111. Apart from standard safety parameters, we understand what other parameters should be monitored for safety, based on toxicology findings and/or experience with similar agents in humans.				
112. There is suitable pharmacodynamic measurement that will provide information to establish a dose or concentration-effect relationship and allow prediction of a therapeutic dosing regimen.				
113. The pharmacodynamic parameter is suitable for a “go/no go” decision.				
<b>EIH Clinical Therapeutics</b>				
114. The pharmacodynamic parameter is an accepted surrogate endpoint for predicting clinical efficacy.				

**Preparing for NDA**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
<b>NDA Prep Health Economics</b>				
115. The financial analysis (health economic strategy) evaluation supports further development.				
116. Based on the Phase II results, the health economic hypothesis is viable.				
117. We have done a review to evaluate if the pharmacoeconomics environment has changed.				
<b>NDA Prep Commercialization</b>				
118. We understand the relative importance of the distinguishing product attributes as regards the commercial potential of the compound.				
119. Studies to support these attributes have been				

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**NDA Prep**

**Keep in mind any potential impact on Safety, Efficacy, and/or Convenience.**

	Not Done	Pending	Done	NA (explanation)
planned as part of the NDA; if not, then it will be acceptable to perform these studies and publish the results in Phase IIIB or IV.				
<b>120. We have determined what price is a reasonable trade-off for the product advantage.</b>				
<b>121. We understand how the price will vary with differing levels of efficacy and safety.</b>				
<b>122. We have determined whether the product will continue under development or be better licensed out.</b>				
<b>123. We have a strategy for ex-U. S. sales.</b>				
<b>124. The market research is complete, including knowledge of the market, its attitudes and practices.</b>				

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NDA Prep

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
125. The Target Product Profile (TPP) is complete and are all go/no-go decisions points have been clearly identified.				
126. The trademark has been registered.				
127. The branding strategy has been established.				
128. The publication plan been developed.				
129. Key Opinion Leaders have been identified, approached, and considered for sites in the clinical trials program.				
130. The major conventions and medical meetings relevant to the product have been identified, and we are making key presentations.				
131. The key scientific and product messages for the				

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NDA Prep

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
product been agreed upon.				
132. The strategic launch plan is complete (such as tactics for pricing, reimbursement, sales force mapping, <b>positioning, SWOT, and MIRS</b> ).				
<b>NDA Prep CMC</b>				
133. Suitable in-process controls have been established.				
134. The synthesis meets standards of quality (impurities profile, stability, efficiency, safety, and environmental acceptability).				
135. The contract manufacturers are in place to scale-up the process for marketing.				
136. We know whether the synthesis can be scaled-up or whether further development work is required.				

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NDA Prep

Keep in mind any potential impact on Safety,  
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	Not Done	Pending	Done	NA (explanation)
137. We have documented any changes in the synthesis since toxicology studies.				
138. The impurity profile has been updated along with any changes in synthesis.				
139. We have determined whether toxicology studies need to be repeated or additional studies initiated.				
140. The formulation is acceptable in the primary markets.				
141. The formulation is internationally acceptable.				
142. The formulation has been optimized.				
143. We know if additional development work is necessary to optimize the formulations.				
144. The stability of the "optimal" formulation is adequate.				

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**NDA Prep**

**Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.**

	Not Done	Pending	Done	NA (explanation)
145. Scaling-up and the development of the final formulation allows for bioequivalence studies without delaying NDA submission.				
146. The formulation can be produced on a large scale at the current contract manufacturer.				
147. The final synthesis and the manufacturing process for the drug substance are at the selected contract manufacturer.				
148. Specifications exist for excipients and they meet international pharmacopoeia requirements.				
149. Contract manufacturers able to manufacture to meet cGMP requirements for Phase III and commercial products.				
150. Appropriate chemical and physical drug interaction studies been conducted.				

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**NDA Prep**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
<b>NDA Prep Toxicology</b>				
151. We have done the appropriate animal carcinogenicity studies				
152. We know whether toxicology studies will be required for metabolites.				
153. We have defined the toxicology profile of impurities.				
154. The duration of the chronic toxicology studies supports the planned Phase III studies.				
155. The appropriate toxicology studies have been planned to support the patient population (e.g., women, children) that will be studied in Phase III.				
156. We understand what blood concentration levels are expected to be observed in Phase III studies.				

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**NDA Prep**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
157. We have defined whether special toxicology studies will be required to explain the mechanism of toxicities in humans.				
<b>NDA Prep Pharmacokinetics &amp; Drug Metabolism</b>				
158. We have evaluated whether drug-drug interaction studies in animals suggest unexpected pharmacological effects in humans.				
159. We know how the pharmacokinetic profile in humans compares with that in the species studied in toxicological and pharmacological studies.				
160. We understand similarities in the metabolic profile in the toxicology species compared with that in humans.				
161. The routes of elimination, metabolic profile, and activity/toxicity of parent drug and major metabolites				

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**NDA Prep**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
have been determined.				
<b>NDA Prep Clinical Pharmacology</b>				
162. We understand the relationship among dose, drug plasma concentrations, toxicity, and efficacy.				
163. The pharmacokinetic characteristics are adequate to meet the target profile.				
164. We have defined the appropriate pharmacokinetic and pharmacodynamic models for applying population-based analysis in subsequent clinical trials.				
165. We have determined whether there are any problematic drug-age, drug-disease (e.g., hepatic or renal impairment), drug-gender, or drug-drug interactions.				
166. We understand which interactions need to be				

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**NDA Prep**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
investigated prior to enrollment of patients into Phase II/III studies.				
167. We have evaluated the pharmacokinetics during single- and multiple-dose clinical studies.				
168. We have evaluated dose proportionality.				
169. The pharmacokinetics is consistent from single- to multiple-dose studies is understood.				
170. We have evaluated whether there is evidence for enzyme induction or unexpected drug accumulation.				
171. Appropriate bioequivalence studies have been planned to demonstrate equivalence of the investigational dosage forms and the marketed dosage forms.				
172. We have evaluated how the human pharmacokinetics compares with that of the species				

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NDA Prep

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
used in the toxicokinetic studies.				
173. We have evaluated how the anticipated exposure of patients in Phase II (steady state plasma concentrations and area under the curve) compares with that observed in the toxicokinetic studies (i.e., a safety margin).				
174. We have defined the likely optimal dose range in patients (that should be tested in Phase II) based on the pharmacodynamic and tolerability observed.				
<b>NDA Prep Clinical Therapeutics</b>				
175. We have documented evidence of efficacy.				
176. There are appropriate clinical endpoints to demonstrate efficacy; e.g., surrogate clinical endpoints will still be considered a valid				



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NDA Prep

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
demonstration of efficacy when the NDA is reviewed.				
177. If the primary endpoint differs from that used in earlier studies, we have evaluated the risk of a negative result associated with this change, and we have defined alternatives.				
178. We have defined the magnitude of the clinical effect we expect and for which endpoint(s).				
179. We have an appropriate overall sample size required to show efficacy or safety.				
180. The cost of the clinical program, and when combined with other pre-and post-launch costs, offers an acceptable return.				
181. The length of the program is acceptable to the business case.				
182. We have correctly defined the key safety endpoints.				

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NDA Prep

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	Not Done	Pending	Done	NA (explanation)
183. We have a strategy in place to convince people that the benefit outweighs the risk (dependent on the relationship between efficacy endpoints, effect size and safety).				
184. We have a strategy in place to convince people that the benefit is worth the price. We have the right indication, efficacy and safety endpoints, effect expectations, and comparators.				
185. We know which dose or plasma concentration has a minimal efficacy compared with the plateau effect.				
186. We have defined the maximum effective dose or plasma concentration.				
187. We know the dosing interval, and how it will be determined.				
188. We understand the safety profile dose or concentration/response relationship.				

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**NDA Prep**

**Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.**

	Not Done	Pending	Done	NA (explanation)
189. The recommended doses have been identified.				
190. We have evaluated whether there are any predicted special safety concerns (e.g., drug-age, drug-disease, or drug-drug interactions) in patients that will be studied in Phase II/III studies.				
191. We have evaluated what modifications will probably have to be made in the dosing regimen for these patients.				
192. Based on the preclinical pharmacokinetic evaluation and food effect studies, we have determined whether the drug will be administered fasting or with food.				

**Filing the (NDA)**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
<b>NDA Filing Health Economics</b>				
193. How the value will be communicated has been determined.				
194. The Health Economic information required for this submission is available.				
<b>NDA Filing Commercialization</b>				
195. The marketing strategy is being implemented as planned. Any problems can be successfully resolved without affecting the product launch.				
196. The launch materials are ready.				
197. The sales training program is ready.				
198. The Package Insert negotiations with FDA are				

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NDA Filing

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
complete, and a Core Data Sheet (CDS) has been completed.				
199. The post NDA marketing plan and Phase IV trials program are ready.				
200. The life cycle management plan is under developed, including filing for other indications.				
<b>NDA Filing CMC</b>				
201. The manufacturing process is validated, or will it be validated prior to approval.				
202. All processes are operable under Good Manufacturing Practice (GMP) conditions in a full-scale manufacturing plant.				
203. Analytical standards of product and process impurities are available for internal and regulatory needs.				

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**NDA Filing**

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
204. Registration lots are planned or already produced.				
205. Analytical procedures have been defined and validated.				
206. Shelf-life and expiration dating have been projected and storage conditions defined.				
207. The method of shipment of bulk drug substance or finished product to contractor sites has been validated.				
208. Appropriate stability and comparability studies have been carried out for reconstituted drug product in standard hospital equipment.				
209. Secondary and tertiary packaging have been designed and mockups produced.				
210. Manufacturing agreements and technical agreements exist with commercial Drug Product (DP) and Drug Substance (DS) manufacturers, and				

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NDA Filing

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
packaging and distribution partners have been identified.				
<b>NDA Filing Pharmacokinetics &amp; Drug Metabolism</b>				
211. The primary metabolites have been identified in humans.				
212. How the primary metabolites compare with those in the toxicology species has been evaluated.				
213. The activity and toxicity of the major metabolites is characterized and understood.				
<b>NDA Filing Clinical Pharmacology</b>				
214. The pharmacokinetics of the drug in the target patient population is well understood.				
215. The pharmacokinetics of the drug in the elderly and				

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NDA Filing

Keep in mind any potential impact on Safety,  
Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
in children is understood.				
216. The pharmacokinetics in target and other common disease states is well characterized.				
217. The pharmacokinetics in renal and hepatic impairment is understood.				
218. How the dosage form used in clinical trials compares with the one intended for marketing has been evaluated in terms of maximum concentration in plasma (Cmax), time passed since administration at which Cmax occurs (Tmax), and area under the curve (AUC).				
219. Any relationship between pharmacokinetics and efficacy and toxicity has been explained.				
220. How the pharmacokinetics in the patient population compares with the pharmacokinetics in the toxicology species has been evaluated.				

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Efficacy, and/or Convenience.

	Not Done	Pending	Done	NA (explanation)
<b>NDA Filing Clinical Therapeutics</b>				
221. The safety of the drug compared with standard therapy has been evaluated.				
222. The efficacy of the drug compared with standard therapy has been evaluated.				
223. Any drug-drug interactions with other therapies has been evaluated.				
224. The safety of the drug in elderly individuals has been characterized.				
225. The efficacy of the drug in elderly individuals has been characterized.				
226. Any drug interaction with concurrent diseases or medications has been evaluated.				
227. The safety of the drug in pediatric patients has been				

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	Not Done	Pending	Done	NA (explanation)
characterized.				
228. The efficacy of the drug in pediatric patients has been characterized.				
229. The safety of the drug in women of child-bearing potential has been characterized.				
230. The safety of the drug during pregnancy has been characterized.				
231. The experience of this drug in the proposed patient population has been thoroughly characterized in terms of its therapeutic rationale, dose range, and use in combination with other medications.				
<b>232. The efficacy of the drug has been shown to be clinically relevant.</b>				
<b>233. The risk/benefit ratio has been explained.</b>				

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	Not Done	Pending	Done	NA (explanation)
234. Any relationships between efficacy or safety and various demographic or patient factors have been explained.				