# NDA REVIEW PROCESS OVERVIEW

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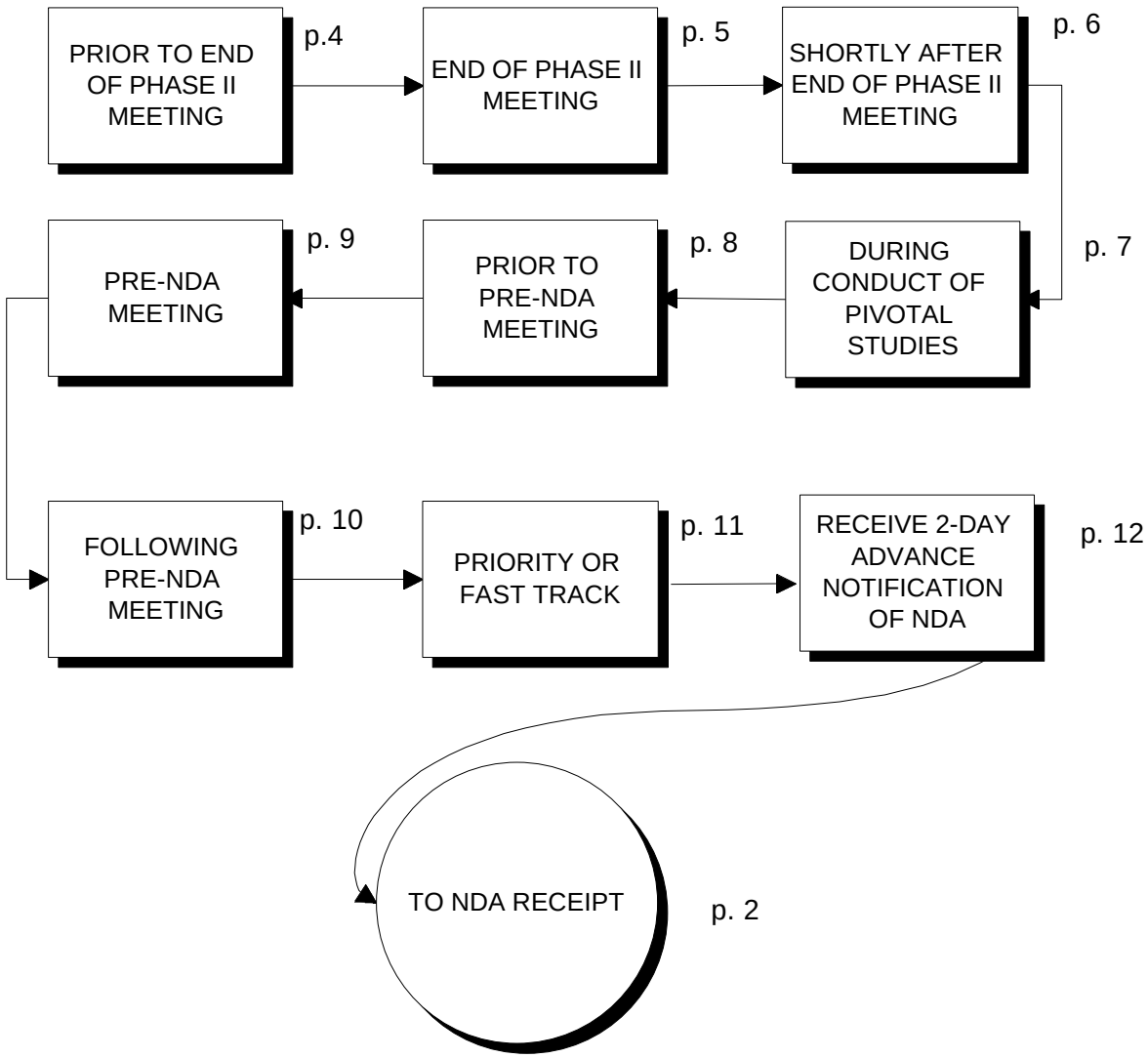
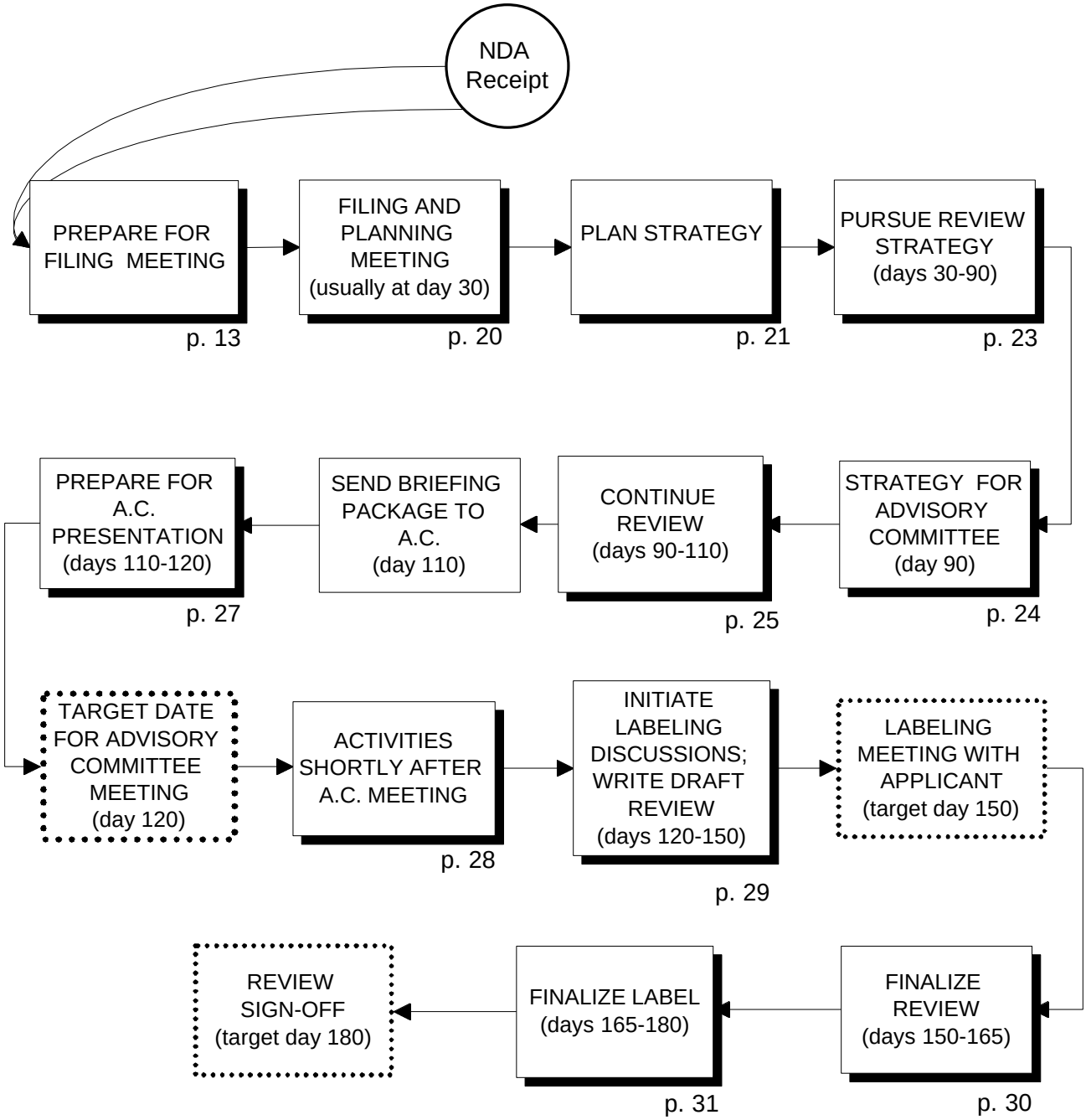
* Edited from a previous version created by David Lepay.

# REVIEW PROCESS BEFORE FORMAL RECEIPT OF NDA



## REVIEW PROCESS AFTER RECEIPT OF NDA



## GUIDING PRINCIPLES IN NDA REVIEW

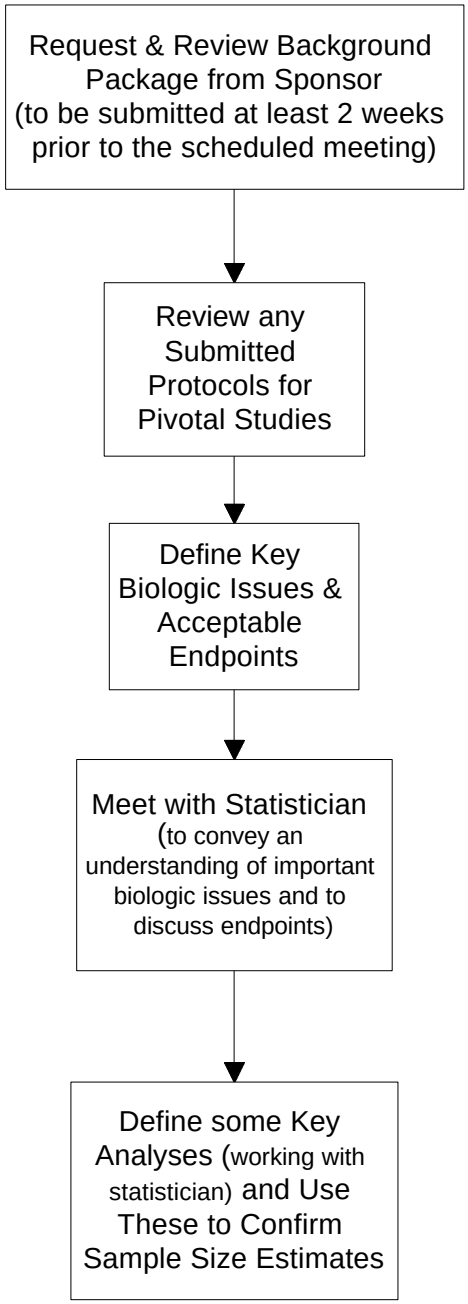
* End-of-Phase 2 and Pre-NDA Meetings are key components of the NDA Review Process.

* Notwithstanding regulatory requirements, all priority reviews should target toward completion in 180 days or less

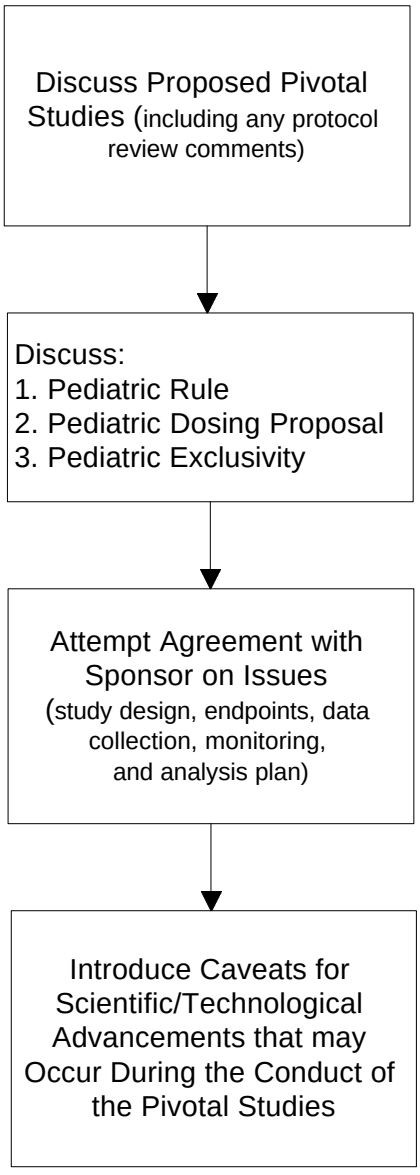
* For Fast Track applications, ROLLING NDA's (i.e., pre-submission of pharm-tox reports, clinical study reports, and even data summaries and listings from the first of two or more pivotal trials) are encouraged. *NOTE: This method requires some available capacity and flexibility in reviewer workload, but has always proved feasible within HFD-530.*

* Review target dates must generally conform to the AC meeting calendar which is pre-established at the beginning of the fiscal year (i.e., prior to precise knowledge of NDA receipt dates).

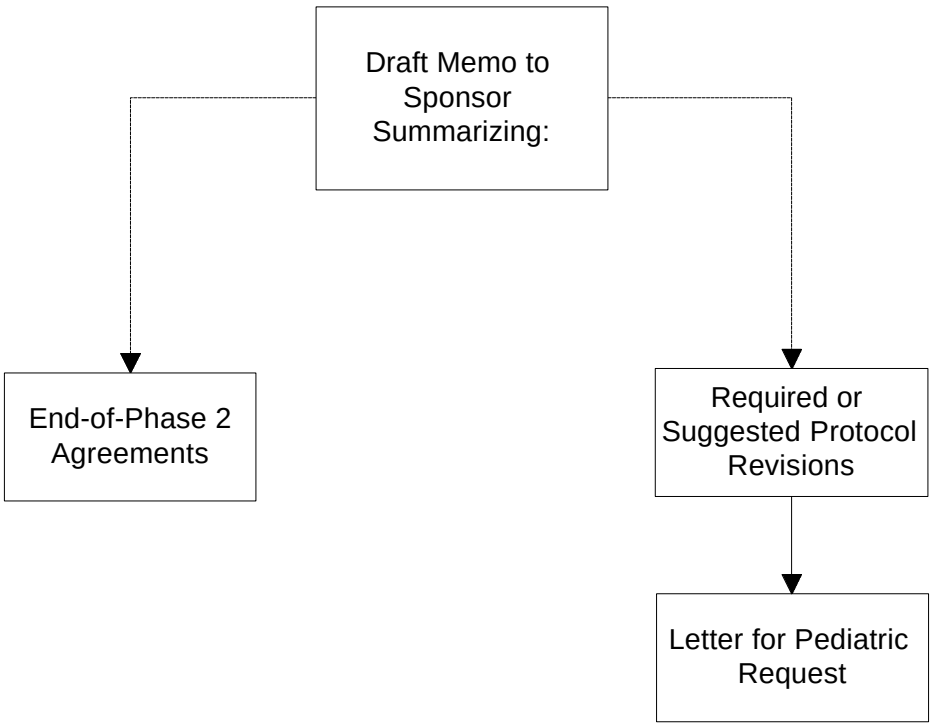
## REVIEW PROCESSES OCCURRING PRIOR TO THE END-OF-PHASE 2 MEETING



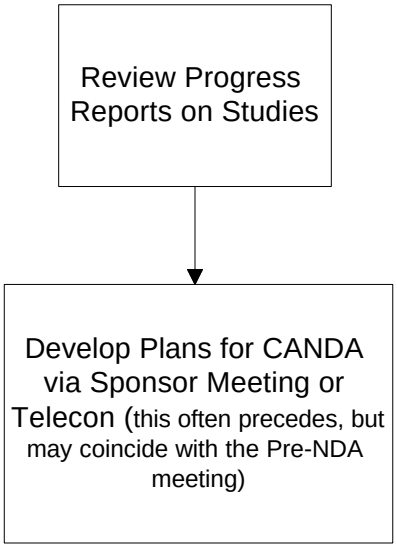
## REVIEW PROCESSES OCCURRING AT END-OF-PHASE 2 MEETING WITH SPONSOR



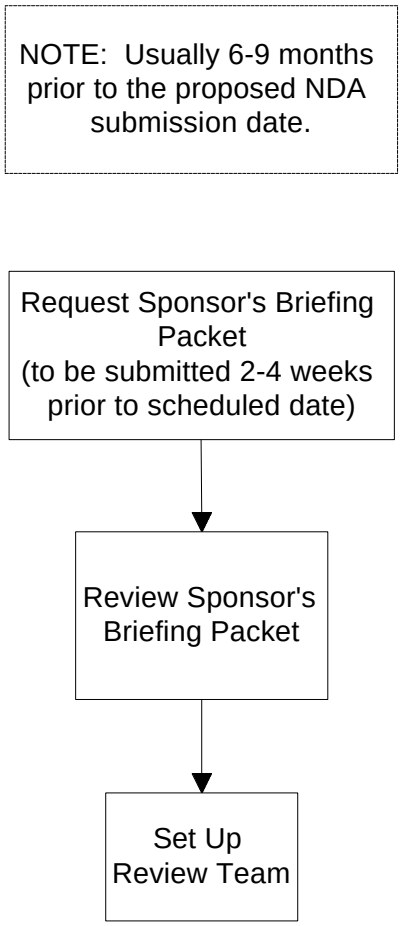
## REVIEW PROCESSES OCCURRING SHORTLY AFTER THE END-OF-PHASE 2 MEETING



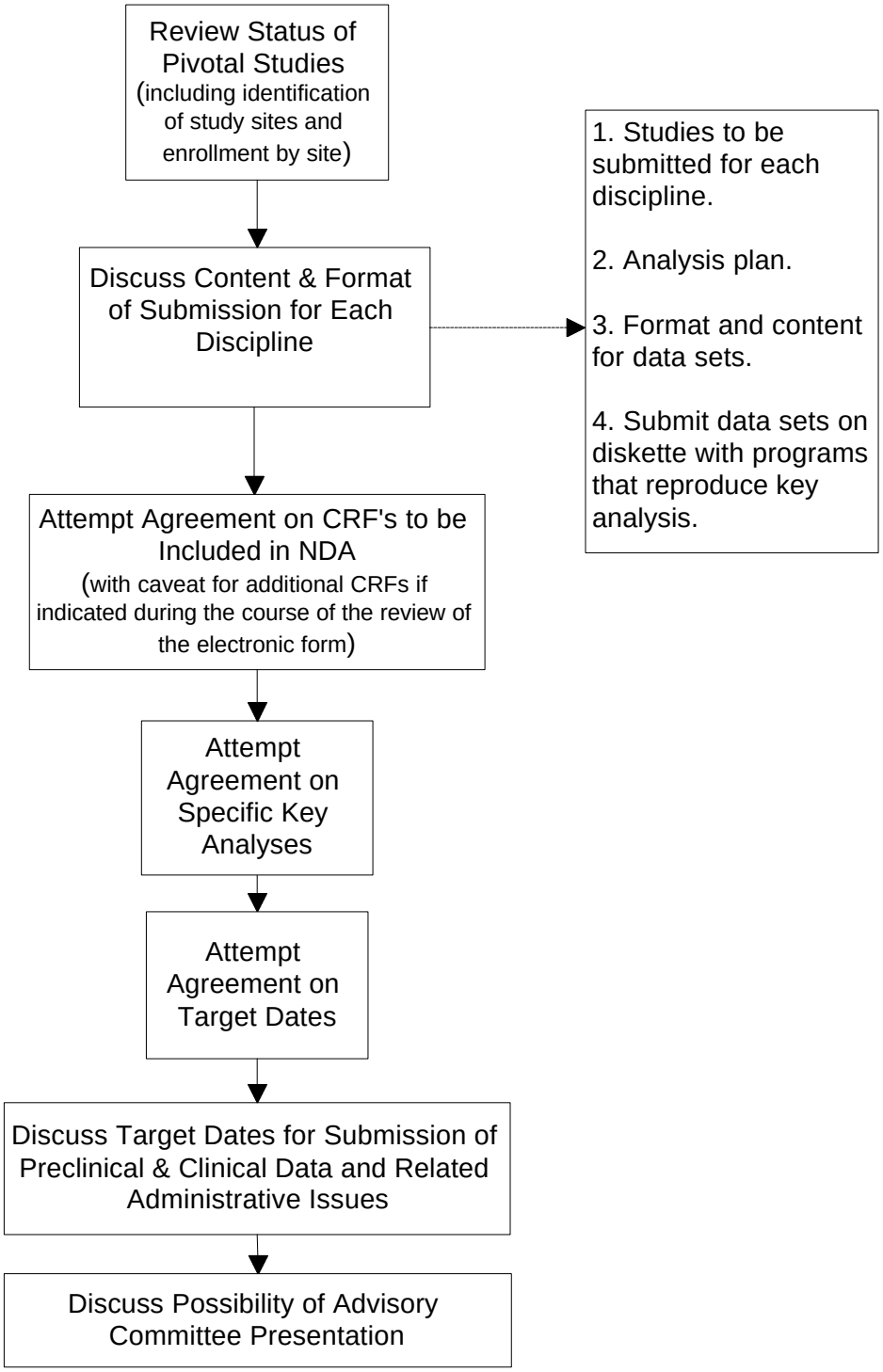
REVIEW PROCESSES OCCURRING DURING
CONDUCT OF PIVOTAL STUDIES



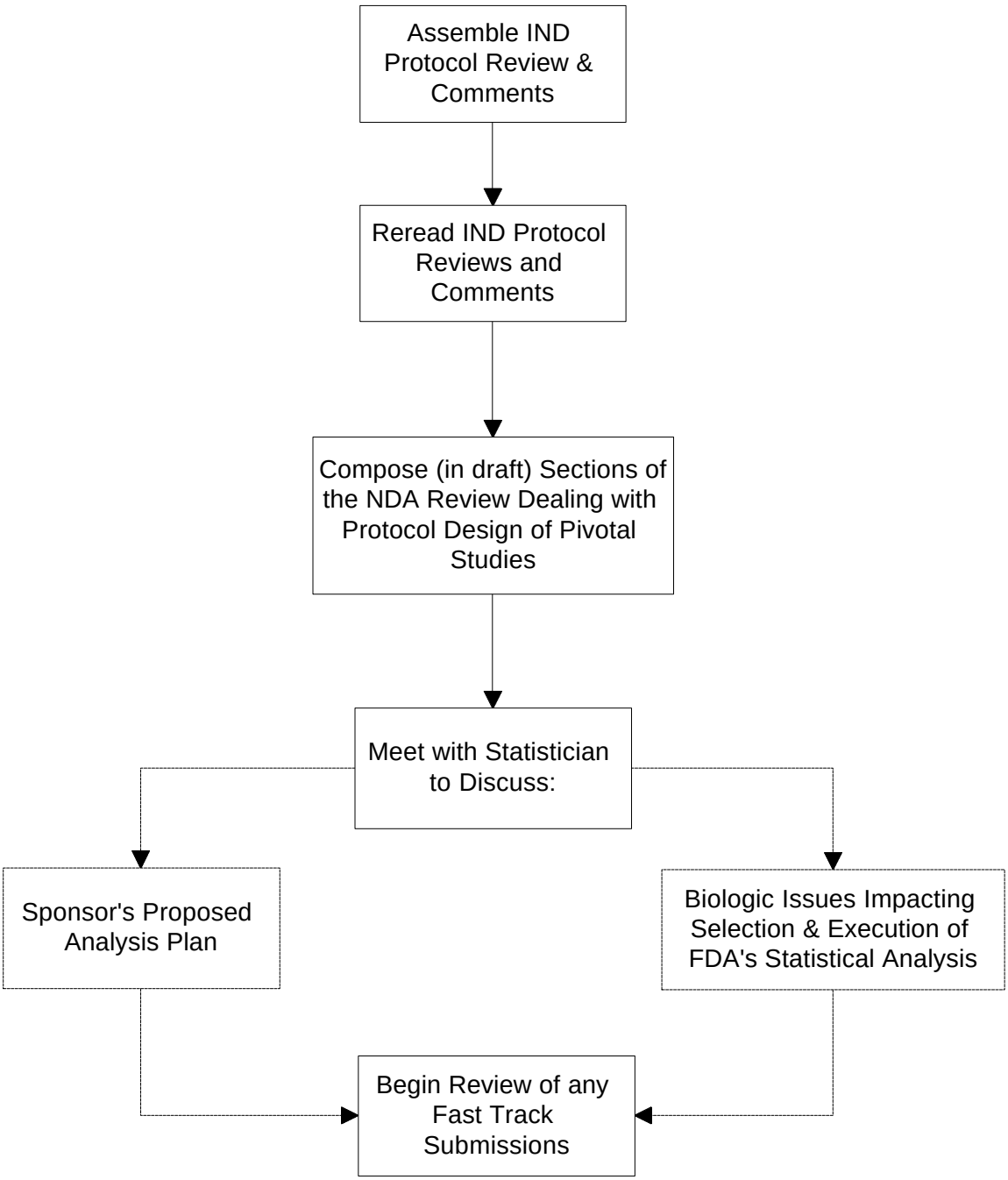
# REVIEW PROCESSES OCCURRING PRIOR TO PRE-NDA MEETING



**REVIEW PROCESSES OCCURRING AT PRE-NDA MEETING**



**REVIEW PROCESSES OCCURRING FOLLOWING PRE-NDA MEETING**

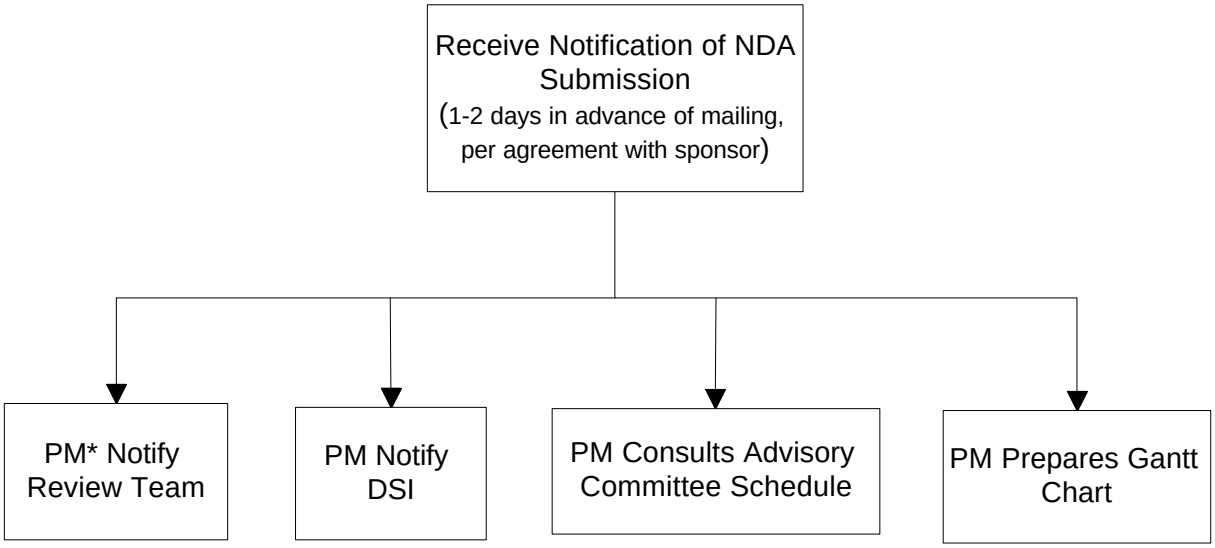


## REVIEW PROCESSES OCCURRING DURING THE Priority (FAST TRACK) NDA

* If possible, approach this review in the same sequence as for an NDA submitted formally as a single unit. (i.e., start with label, then study summary reports, efficacy for each pivotal study, and then safety across studies and by study).

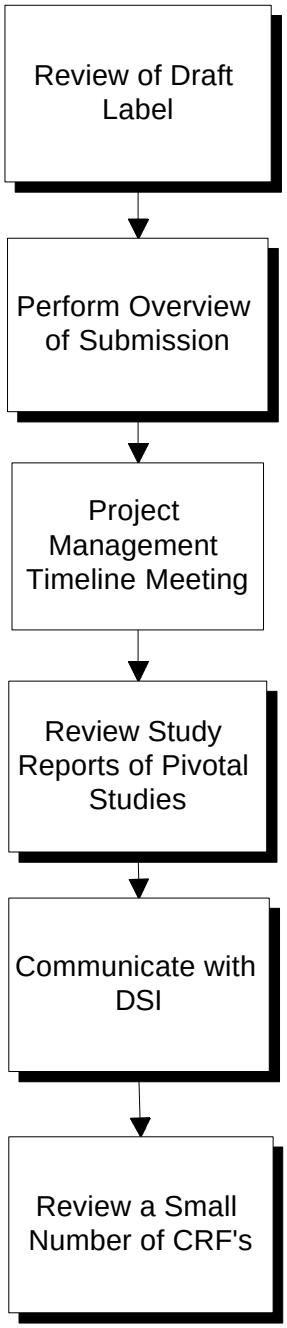
* If the Fast Track ROLLING NDA is submitted out of a conventional sequence, begin the review with the most general efficacy and safety summaries available.

## ADVANCE NOTIFICATION OF NDA SUBMISSION




* Project Manager

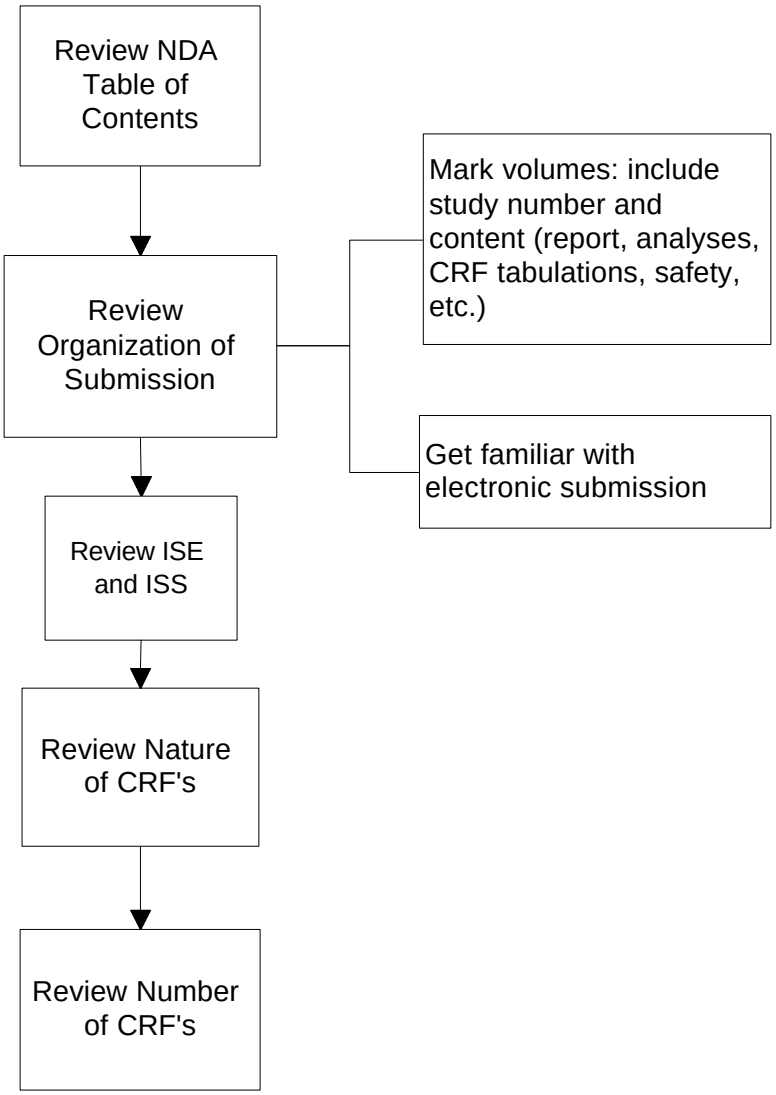
## REVIEW PROCESSES OCCURRING PRIOR TO 45-DAY FILING MEETING



## REVIEW OF DRAFT LABEL

Use the label to outline sponsor's efficacy and safety claims as presumed "best case" scenario.

## PERFORM OVERVIEW OF SUBMISSION



## PROJECT MANAGEMENT TIMELINE MEETING

* The project management timeline meeting occurs approximately one week after formal submission.

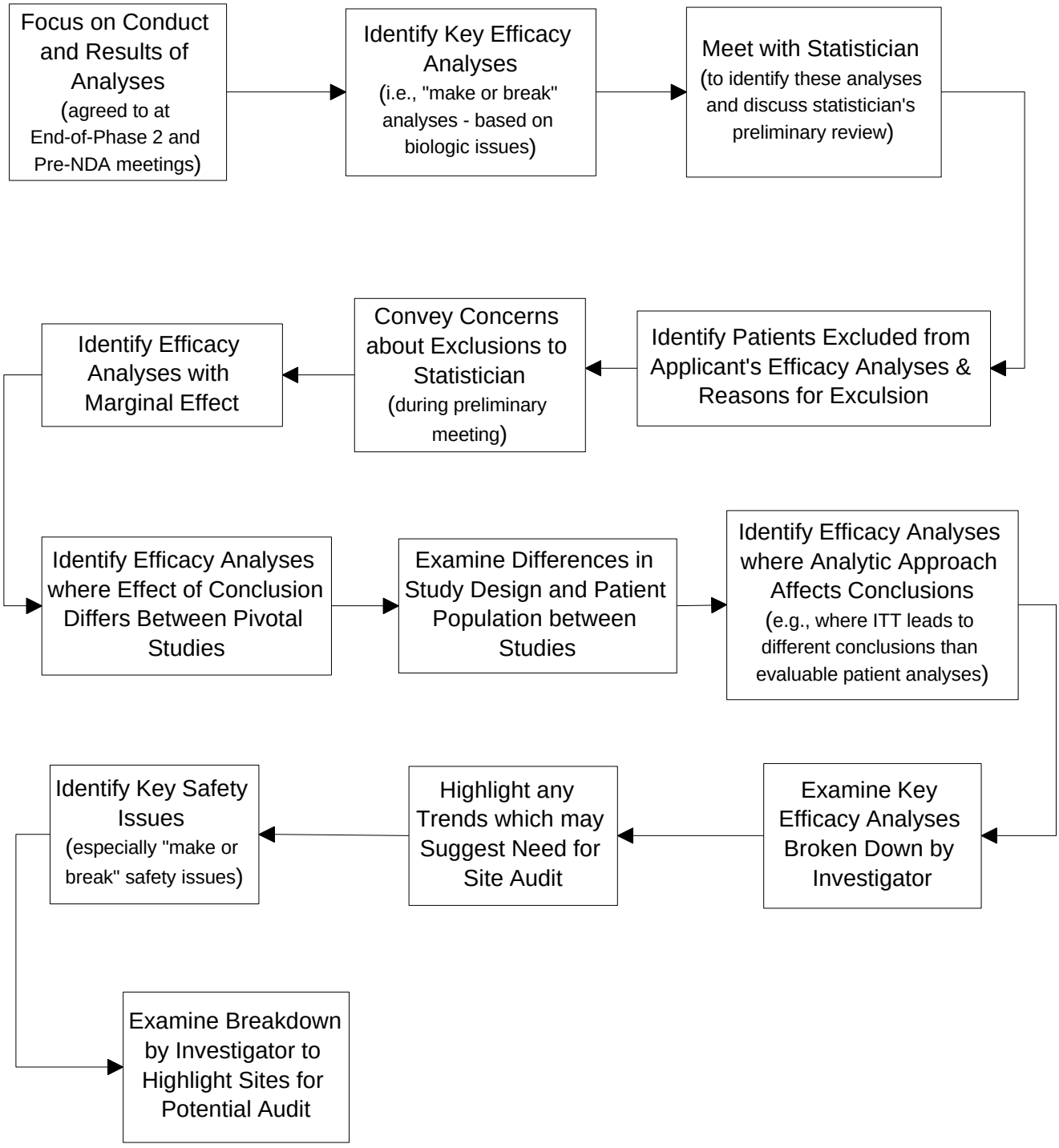
* The meeting is used to discuss draft Gantt charts and target dates (still subject to revision).

* Check if each discipline has received necessary data.

* Check if statistical reviewer has received datasets.

* Check if DSI has been notified.

## REVIEW STUDY REPORTS OF PIVOTAL STUDIES



## COMMUNICATE WITH DSI

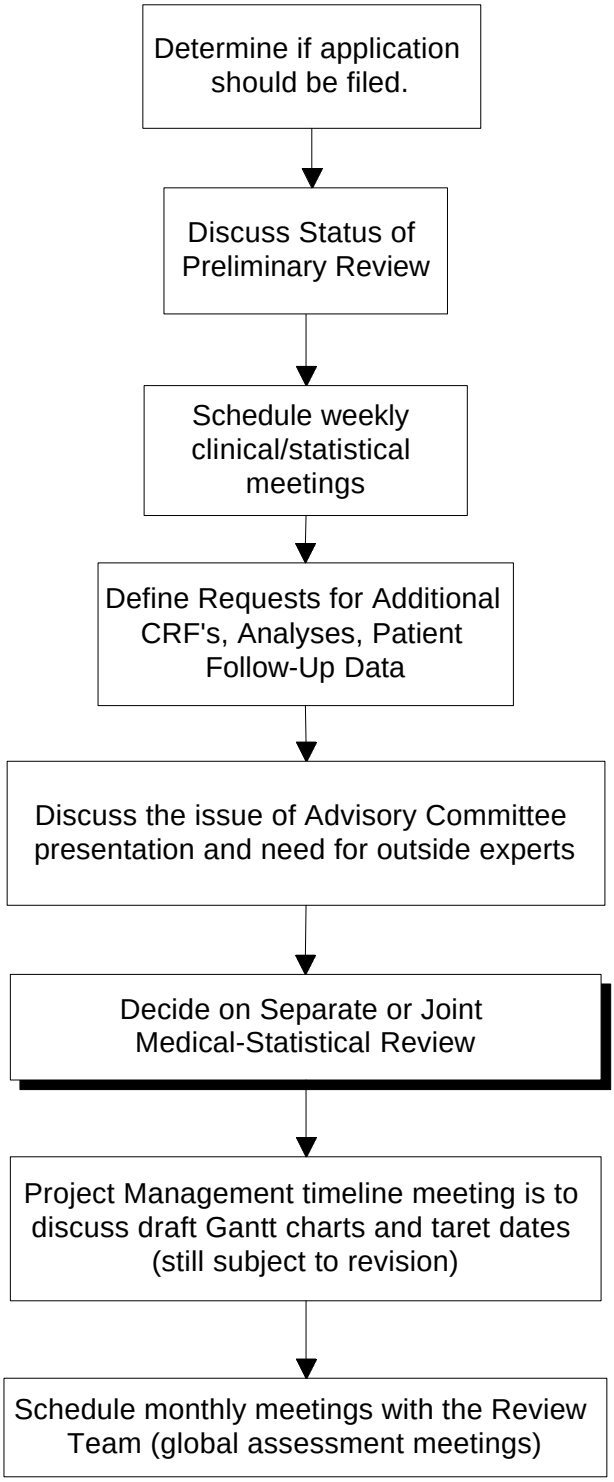
Communicate with DSI to discuss sites for audit based on site enrollment, questionable compliance history of study investigators, and unusual trends in efficacy or safety data examined during review of summary volumes of pivotal studies.

## REVIEW A SMALL NUMBER OF CRF'S

* Review a small number of electronic CRF's (10) to assure legibility, completeness, and consistency with issues identified during review of summary volumes.

* The initial CRF review should focus on some representative patients excluded from the sponsor's analyses, deaths on study, and early discontinuations from study medication.

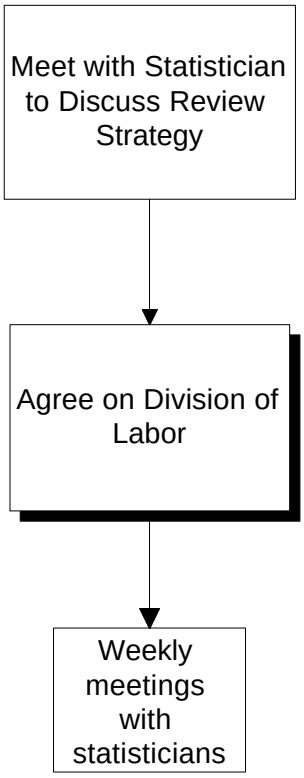
## 45-DAY FILING AND PLANNING MEETING




p. 21

## PLAN STRATEGY



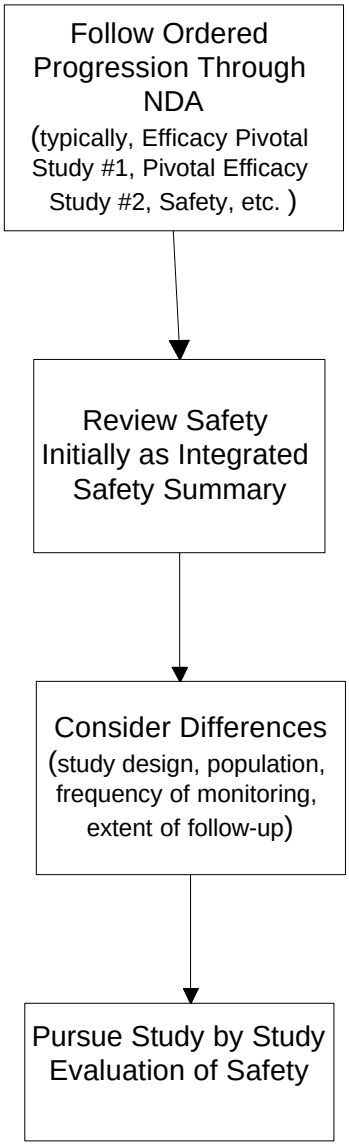



p. 22

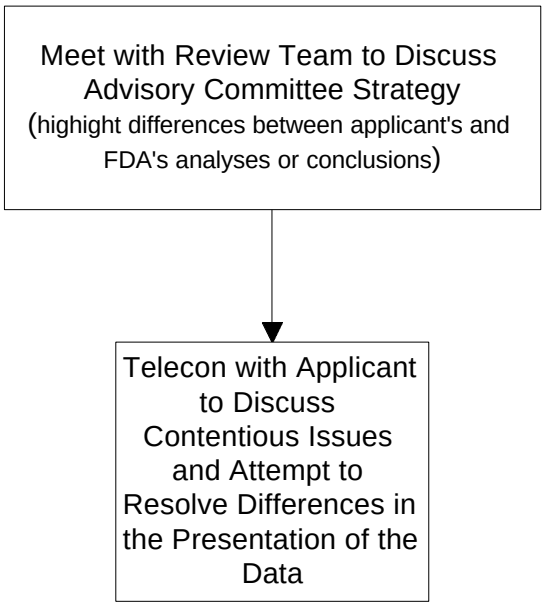
## DIVISION OF LABOR

* Medical Officer:
  * Spot validate data listings from CRF's.
  * Evaluate appropriateness of patient exclusions in applicant's analyses.
  * Select applicant's key analyses to be reperformed by statistician.
  * Specify FDA analyses suggested by primary data and/or biologic relevance. Perform simple analyses.
* Statistician
  * Validate applicant's primary analysis.
  * Perform FDA analyses suggested from discussion with Medical Officer (focus on more sensitive analyses: Kaplan-Meier plots, stratified analyses, regression analyses)
  * Highlight problem analyses or analytic approaches. Discuss biologic relevance with Medical Officer.

**DAYS 45-90**
**PURSUE REVIEW STRATEGY**

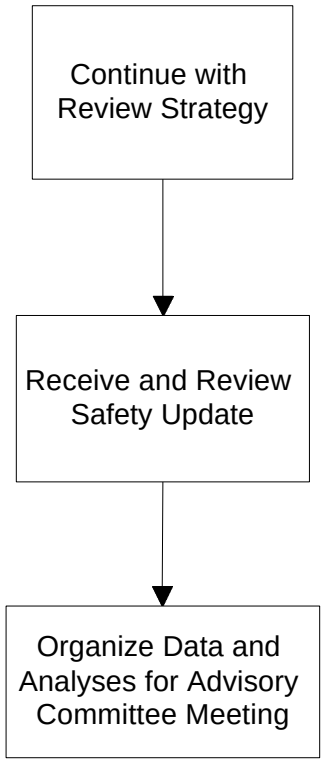


**ADVISORY COMMITTEE STRATEGY**
**(DAY 90)**



**CONTINUE REVIEW**

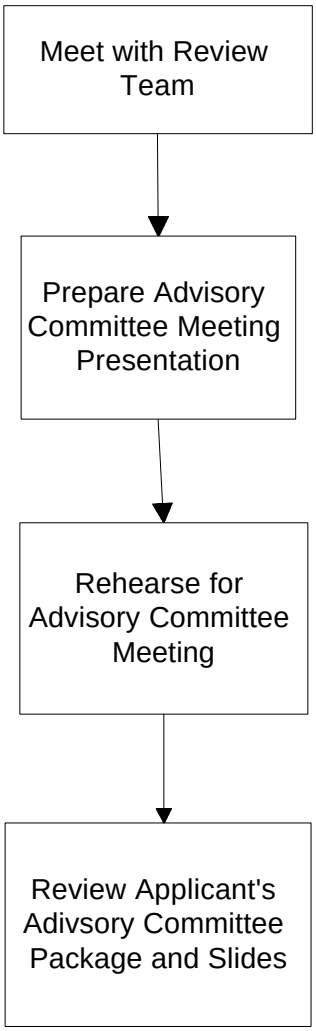
**DAYS 90-110**



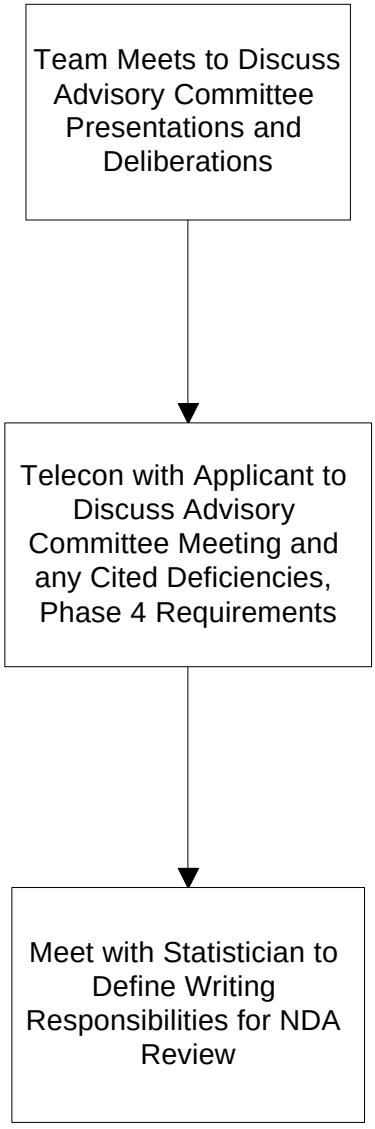
## DAY 110

SEND BRIEFING
PACKAGE TO
A.C.
(day 110)

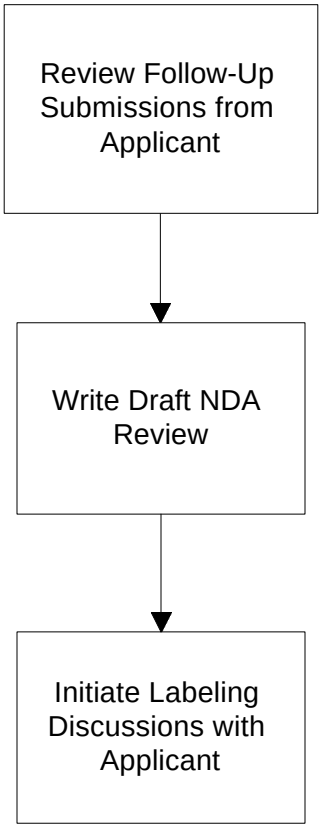
**DAYS 110-120**
**PREPARE FOR A.C. PRESENTATION**



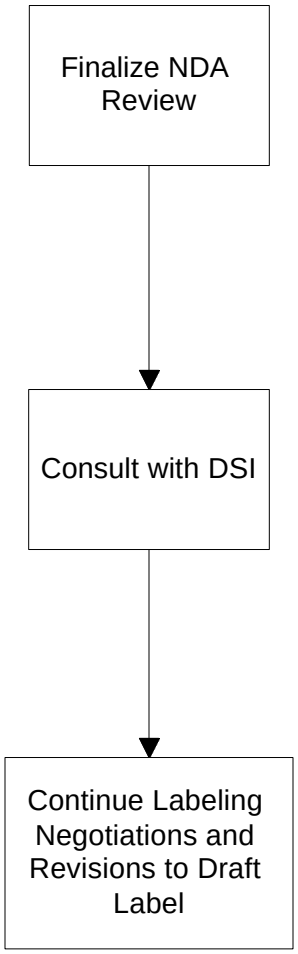
## ACTIVITIES POST-ADVISORY COMMITTEE MEETING



**WRITE REVIEW**
**(DAYS 120-150)**



**FINALIZE REVIEW**
**(DAYS 150-165)**



**FINALIZE LABEL**
**(DAYS 165-180)**