Product Development Protocol (PDP) for Class III Approval

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21 USC §360e Premarket Approval

- Pathway to market for Class III devices
  - Pre Market Approval (PMA)
  - Product Development Protocol (PDP)
- Completion of either process will result in a PMA approval
- Same user fee for PMA and PDP

21 USC §360e (f) PDP

PDP Timelines

- Agency has 30 days from receipt of PDP to determine if it is appropriate to apply the requirements of this subsection.
- Agency has 120 days from receipt to approve or disapprove the protocol.
  - Additional time included if agreed on by Agency and Submitter
  - Approval/denial is final (subject to judicial review)
- Notice of completion filed by Submitter any time after approval of protocol
- Agency has 90 days from receipt of notice of completion to declare the protocol completed or not completed.
  - An order declaring not completed only after an informal hearing on the order.

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21 USC §360e (f)(3)(B) PDP Content

(i) a description of the device and the changes which may be made in the device,

(ii) a description of the preclinical trials (if any) of the device and a specification of

(I) the results from such trials to be required before the commencement of clinical trials of the device, and

(II) any permissible variations in preclinical trials and the results therefrom,

(iii) a description of the clinical trials (if any) of the device and a specification of

(I) the results from such trials to be required before the filing of a notice of completion of the requirements of the protocol, and

(II) any permissible variations in such trials and the results therefrom,

(iv) a description of the methods to be used in, and the facilities and controls to be used for, the manufacture, processing, and, when relevant, packing and installation of the device,

(v) an identifying reference to any performance standard under section 360d of this title to be applicable to any aspect of such device,

(vi) If appropriate, specimens of the labeling proposed to be used for such device,

(vii) such other information relevant to the subject matter of the protocol as the Secretary, with the concurrence of the appropriate panel or panels under section 360c of this title, may require, and

(viii) a requirement for submission of progress reports and, when completed, records of the trials conducted under the protocol which records are adequate to show compliance with the protocol.

The next 8 slides will cover each of these content requirements in detail

21 USC §360e (f)(3)(B)(i) PDP

(i) a description of the device and the changes which may be made in the device

Things to discuss:

- Components, material, design of your device
- Principles of operation and surgical technique
- Does the device being tested differ from the device to be submitted for approval?

21 USC §360e (f)(3)(B)(ii) PDP

(ii) a description of the preclinical trials (if any) of the device and a specification of

(I) the results from such trials to be required before the commencement of clinical trials of the device, and

(II) any permissible variations in preclinical trials and the results therefrom

Things to discuss:

- What preclinical testing have you done?
- What was the acceptance criteria?
- What were the results?

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21 USC §360e (f)(3)(B)(iii) PDP

(iii) a description of the clinical trials (if any) of the device and a specification of

(I) the results from such trials to be required before the filing of a notice of completion of the requirements of the protocol, and

(II) any permissible variations in such trials and the results therefrom,

Things to discuss:

- What clinical trials have you done?
- What does success in those trials look like?
- What results have you seen?
- What results would you expect to need in order to justify approval?

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21 USC §360e (f)(3)(B)(iv) PDP

(iv) a description of the methods to be used in, and the facilities and controls to be used for, the manufacture, processing, and, when relevant, packing and installation of the device,

Things to discuss:

- What are your GMP methods and controls?
- Have you considered packing and installation of the device?

21 USC §360e (f)(3)(B)(v) PDP

(v) an identifying reference **to** any performance standard under section 360d of this title to be applicable to any aspect of such device,

Things to discuss:

- What performance standards have the FDA recommended for this type of device?
- What guidance has the FDA provided?
- Are there other sources of authority for your device?

21 USC §360e (f)(3)(B)(vi) PDP

(vi) if appropriate, specimens of the labeling proposed to be used for such device,

Things to discuss:

- What indication for use will you use?
- What is required for labeling for your device?

21 USC §360e (f)(3)(B)(vii) PDP

(vii) such other information relevant to the subject matter of the protocol as the Secretary, with the concurrence of the appropriate panel or panels under section 360c of this title, may require, and

Things to discuss:

- Outcomes of significant discussions regarding your type of device – in the literature, at the FDA
- Data to address previously stated FDA concerns with features of your device

21 USC §360e (f)(3)(B)(viii) PDP

(viii) a requirement for submission of progress reports and, when completed, records of the trials conducted under the protocol which records are adequate to show compliance with the protocol.

Thing to discuss:

- What is an appropriate schedule for progress reports?
- What kind of information will be included in the progress reports?

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PDPs in practice

- Able to locate 3 cases of the use of a PDP in the current PMA database
  - Keramos ceramic total hip system – N980003
  - Guidant pacemaker pulse generator – N970003
  - AMS penile implant – N970012

PDPs in practice

- Keramos ceramic total hip system – N980003
  - Date Rec'd: 3/8/1998
  - Decision Date: 11/26/2003
  - http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=2908
  - Approval Order for N980003 notes the use of PDP to gain approval for this device.

PDPs in practice

- Guidant pacemaker pulse generator – N970003
  - Date Rec'd: 9/8/1997
  - Decsion Date: 6/3/1999
  - http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=17044
  - Subject of state-law tort case – Betterton v Evans, 351 F. Supp. 2d 529 (2004) on the equivalency of PDPs to PMAs
  - Betterton v Evans and the N970003 Approval Order both note use of PDP to gain approval for this device.

PDPs in practice

- AMS penile implant – N970012
  - Date Rec'd: 12/22/1997
  - Decision Date: 11/2/1998
  - http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=4796
  - Subject of (at least 2) state-law tort case that cite info about the PDP
    - Lawsuit notes use of PDP for approval
      - Malbroux v Jancuska, W.D.La. Aug 29, 2011
      - Rodriguez v AMS, S.D.Tx Feb 4, 2014
    - To receive PDP approval, AMS "submitted a summary of the AMS 700's safety and effectiveness, device design and manufacturing information, performance standards, technical data—including testing, a bibliography, labeling and warning information, clinical data supporting the safety and effectiveness of the AMS 700 and any additional information the FDA required." Rodriguez v AMS, S.D.Tx Feb 4, 2014

Benefits/Risks of PDP

- Benefits
  - Gets data in front of the FDA ASAP
  - Gets early FDA **commitment** about how to proceed
- Risks
  - Rarely used
  - Little guidance
  - Opens company up to LOTS of FDA input about testing before approval
  - Approval may have delays due to FDA inexperience with PDP process

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PDP Checklist

CK	#	Description
	1A	Device requires a PMA (typically Class III)
	1B	Device description
	1C	Device changes over time planned/possible during development
	2A	Preclinical Trials Description
	2B	Preclinical trial results acceptance criteria to move on to clinical trials
	2C	Preclinical trial variations allowed and results (including protocol deviations, etc.)
	3A	Clinical trial/s description
	3B	Clinical trial/s results acceptance criteria to successfully complete the PDP ("protocol")
	3C	Clinical trial variations allowed and results (included protocol deviations, etc.)
	4	Manufacturing and processing methods, including facilities, controls, (packing and installation of device, as appropriate)
	5	Performance standard applicable to any aspect of such device (Section 360d)
	6	Labeling (specimens proposed, if appropriate)
	7	Other relevant information for the device (as required by the FDA / Panel)
	8	Progress reports and pre-clinical / clinical trial reports (when completed) to show compliance with the protocol.