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Premarket Approval Applications (PMA) and Humanitarian Device Exemptions (HDE)

Kristin Zielinski Duggan

Partner, Hogan Lovells US LLP

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Objectives

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- Required elements and FDA review considerations for Premarket Approval (PMA) applications
- Required contents and FDA review considerations for Humanitarian Device Exemption (HDE) applications
- Post-approval and post-marketing considerations for approved PMAs and HDEs

Premarket Approval Applications (PMA)

Premarket Approval

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- Class III devices (those *not substantially equivalent* to preamendments class I or II devices) are subject to premarket approval
  - those devices for which insufficient information exists to assure safety and effectiveness solely through general or special controls
  - usually those devices that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury
  - Not all class III devices require PMAs, but all PMAs are for class III devices

Contents of a PMA Application

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- Table of Contents
- Summary of Safety and Effectiveness Data (SSED)
- Device Description
- Description of Manufacturing
- Results of Nonclinical Studies
- Results of Clinical Studies
- Proposed Draft Labeling
- Miscellaneous Sections (bibliography, etc.)

Device Description

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- Device Components
  - Description of each - physical function
  - Status of each component
  - How they fit together
- Functional description of system
- How the device or system treats the disease or condition for which it is intended

Manufacturing Information

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- General information about device and manufacturer
- Design control section (Dossier)
- Design and development planning summary and methods of control
- Risk analysis
- Manufacturing dossier
- Overview of the quality system and SOPs
- Manufacturing process flow diagram
- Key manufacturing and quality control points with attached SOPs and records demonstrating compliance with procedures

Preclinical Data

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- Mechanical and Biomechanical Testing
- Biocompatibility
- Animal Studies
- Each test should discuss:
  - Study Purpose/Rationale
  - Protocol
  - Results
  - Analysis of Results
  - Conclusion

Clinical Section

- Clinical sites and investigators
- Detailed protocol and results
- Tabular results and discussion of results
- Statistical methods & rationale
- Justification for pooling
- Discussions of risks versus benefits
- Conclusions drawn from study

Foreign Clinical Data

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- New rule February 2018 that data from OUS clinical investigations to support marketing applications must be conducted in accordance with Good Clinical Practice (GCP)
  - Reputable investigators
  - Scientifically sound data
  - Rights, safety and welfare of patients not violated
- Applicable to U.S. Population
- Considerations:
  - Differences in clinical conditions
  - Differences in study populations
  - Differences in regulatory requirements
- See:
  - 21 CFR §814.15
  - FDA Guidance *Acceptance of Clinical Data to Support Medical Device Applications and Submissions Frequently Asked Questions* (February 21, 2018)

Real World Evidence

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- **Real-World Data (RWD)** are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.
- **Real-World Evidence (RWE)** is the clinical evidence regarding the usage, and potential benefits or risks, of a medical product derived from analysis of RWD.
- RWD may be used as evidence to support approval of an HDE or PMA
- In order to determine the suitability of RWD for regulatory decision-making, FDA will assess the relevance and reliability of the source and its specific elements.
  - Relevance refers to whether data adequately addresses the applicable regulatory question or requirement. This includes factors such as the representativeness of the patients and its generalizability to the population being evaluated; location(s) and breadth of the data source; and how well the data reflects patient experience.
  - Data reliability refers principally to "data accrual," or how the data was collected, and whether the collection/analysis processes sufficiently assure quality, integrity, and bias minimization.
- Sponsors should determine how RWD can answer a specific regulatory question (e.g., long-term treatment effects, serious adverse events, etc.).
- Protocols and analysis plans should address the same elements that would be addressed in a traditional clinical trial protocol and statistical analysis plan.
- See *Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices* (August 31, 2017)

Benefit/Risk Determination for PMAs

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- FDA's Guidance: *Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications (August 30, 2019)* explains the principal factors that FDA considers when making benefit-risk determinations in the premarket review of certain medical devices.
- FDA will review the data submitted as part of the PMA application and determine – based on a number of factors – if the data support the claims made by the sponsor concerning clinically significant results from the device, i.e., intended use and indications for use, and if the data analysis demonstrates that the probable benefits of the device outweigh its probable risks.
- **Factors FDA Considers in Making Benefit-Risk Determinations**
  - Assessment of the Benefits: type of benefits, magnitude of the benefits, probability of the patient experiencing one or more benefits; duration of effect(s)
  - Assessment of the Risks: Severity, types, number and rates of harmful events associated with use of the device; probability of a harmful event; duration of harmful events; risk from false-positive or false-negative results for diagnostics
  - Additional Factors: Uncertainty; Patient-centric assessments and patient-reported outcomes (PROs); Characterization of the disease; Patient perspectives; Availability of alternative treatments or diagnostics; Risk mitigation; Postmarket data; Novel technology addressing unmet medical need

Referencing Information in Master Files

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- Pertinent information already in FDA files and specifically referred to by an applicant may be incorporated into a PMA by reference.
- Device Master File System – Created to help preserve the trade secrets of the ancillary medical device industry and at the same time facilitate the sound scientific evaluation of medical devices
- A master file may be considered when several applications may be submitted for different products which may use a common material or process, etc., such as the same sterilization method.
- Information in a master file or other information submitted to FDA by a person other than the applicant will not be considered part of a PMA, unless such reference is authorized in writing by the person who submitted the information or the master file

SSED

- Detailed summary of safety and effectiveness data on which approval (or denial) decision is based
- Includes:
  - Indications for Use
  - Device Description
  - Summary of Preclinical Studies
  - Summary of Clinical Studies
- FDA document
  - But company drafts
- Becomes public following approval

Modular PMAs

Modular PMAs

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- Sponsors make submissions of preclinical or clinical data or manufacturing information when sufficient information available to complete a module
- It is a modular approach to:
  - Submission
  - Review
  - Closure

Definitions

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- "Module" is a unit of elements, tests and information addressing a selected aspect of the device
- "PMA Shell" is an outline of modules required to complete PMA application
  - PMA shells and modules will differ depending on the nature of the particular device for which the shell and modules are developed

FDA-Sponsor Agreement

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- Parties must agree on elements of PMA Shell
- Parties must agree on the contents of each Module
- Once agreement is reached on the content and form of the Shell and Modules, it must be formally submitted to FDA
- Upon receipt of formal submission, FDA issues a letter acknowledging agreement of the shell and Module proposal and assigns a shell number, such as “MXX0001”

Modular PMA Timeframe

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- FDA's objective is to complete the review of each module and issue a deficiency letter or an acceptance letter within 90 days of receipt.
- Each module reviewed and closed -- unless changes are made, module is considered closed to review
- Submit SSED and table of contents each time
- Once final module is submitted, FDA targets decision on approvability of the PMA within 180 days of FDA review time

PMA Module Submission Schedule

Modular PMA Shell

Company:

Device Name:

Module Name	Contents	Date of Submission

Non-clinical Information	• Table of Contents for Non-clinical Information Module
	• Executive Summary – Non-clinical Information Module
	• Device Description and Principles of Operation
	• Declaration of Conformance to Standards for Module
	• Bibliography/References for Module
	• Non-clinical Laboratory Studies
	  ○ Biocompatibility Testing
	  ○ Animal Studies
	  ○ Engineering / Bench Testing
	  ○ Sterilization
	  ○ Stability / Shelf Life
	  ○ Packaging Information
	  ○ Shipping Validation
		Q? 20XX

Module Name	Contents	Date of Submission

Manufacturing Information	• Table of Contents for Manufacturing Module
	• Executive Summary – Manufacturing Module
	• Device Description and Principles of Operation
	• Manufacturing Information
	  ○ Quality management system information
	  ○ Design control dossier
	  ○ Manufacturing dossier
		Q? 20XX

Module Name	Contents	Date of Submission
Clinical	• Full PMA Table of Contents • SSED (i.e., compilation of executive summaries) • Clinical Data (including Protocols, Results and Analyses) • Financial Disclosure Information • Proposed Labeling: Physician Instructions • Pediatric Use Information • Bibliography/References for the Final PMA Module	Q? 20XX

- Sponsors should provide the approximate timing of the submission of each PMA module in the PMA shell
- Applicants should submit modules at intervals that will allow the agency enough time to review the module, provide feedback, and close out the module prior to the arrival of the next module.
  - The one exception is the manufacturing module, which may be submitted without regard to the timing of submission of other module(s).
- Any outstanding deficiencies from previously submitted modules should be addressed when submitting final PMA module
- Example of Proposed Submission Timeline:
  - 3-4 months between submission of Modules 1 and 2
  - 7-8 months between submission of Modules 2 and 3
  - Approximately 9-12 month process to complete submission of entire PMA

The PMA Review Process

PMA Review Timeframe

- Acceptance Review (within 15 days)
- Filing Review (within 45 days)
- Substantive Review (within 90 days)
- Day 100 Meeting
- Advisory Panel Meeting (if needed)
- Preapproval (QSR and BiMo) inspections

Day 100 meeting

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- Purpose is to review the PMA status and any deficiencies identified by the Agency
- Discuss action plan with estimated dates of completion
- Identify need for panel involvement
- Discuss possible premarket versus postmarket requirements
- Sponsor should submit a written request along with the PMA application or separately within 70 days after the application is filed

Breakthrough Devices Program

- The Breakthrough Devices Program is a voluntary program for medical devices that provide for **more effective** treatment or diagnosis of **life-threatening or irreversibly debilitating diseases or conditions**.
- The goal of the Breakthrough Devices Program is to provide patients and health care providers with timely access to these medical devices by speeding up their development, assessment, and review, while preserving the statutory standards for premarket approval, 510(k) clearance, and De Novo marketing authorization
- Breakthrough Designation request can be submitted any time prior to the marketing submission

Criteria	Description
First Criterion	The device provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions
Second Criterion	The device also meets **at least one** of the following:
	a) Represents Breakthrough Technology
	b) No Approved or Cleared Alternatives Exist
	c) Offers Significant Advantages over Existing Approved or Cleared Alternatives
	d) Device Availability is in the Best Interest of Patients

Safer Technologies Program (STeP)

- The Safer Technologies Program (STeP) is a voluntary program for medical devices that are reasonably expected to significantly improve the **safety** of currently available treatments or diagnostics that target an underlying disease or condition associated with **morbidities and mortalities less serious than those eligible for the Breakthrough Devices Program**
- Has similar features to Breakthrough program:
  - Additional interaction mechanisms like sprint discussions and Data Development Plan review
  - Additional resources for IDE, PMA, etc.

Criteria	Description
First Criterion	Not eligible for the Breakthrough Devices Program due to the less serious nature of the disease or condition treated, diagnosed, or prevented by the device
Second Criterion	Should be reasonably expected to significantly improve the benefit-risk profile of a treatment or diagnostic through substantial safety innovations that provide for **at least one** of the following:
	a) a reduction in the occurrence of a known serious adverse event
	b) a reduction in the occurrence of a known device failure mode
	c) a reduction in the occurrence of a known use-related hazard or use error
	d) an improvement in the safety of another device or intervention

PMA Amendments

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- Information generally submitted during review of original PMA (or PMA supplement) prior to approval
  - To respond to FDA deficiencies
  - To respond to not-approvable letter
- Review period may be extended up to 180 days if a major amendment is submitted (significant new or updated data or information, detailed new analyses)

Advisory Committee (Panel) Review

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- FDA may refer PMA to outside panel of experts
  - PMAs for first-of-a-kind device
  - Applications that present an issue best addressed through panel review
- Panel Package provided to panel members
  - Sponsor and FDA Executive Summaries
  - Other information from PMA (e.g., SSE, labeling)
  - FDA questions to panel for their consideration
- Public meeting
- See *Procedures for Meetings of the Medical Devices Advisory Committee* (September 2017)

Panel Recommendations

- Vote on effectiveness, safety, risk-benefit
- Simultaneous electronic voting
- Panel decision is a recommendation to FDA; not binding on the Agency

Preapproval QSR Inspections

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- Required before issuance of approval order
- Generally limited to device subject to PMA
- Prepare as for routine QSR Inspection
- Sometimes “approvable” letter issued by FDA prior to satisfactory manufacturing inspections

Preapproval BiMo Inspections

- Bioresearch monitoring inspections of clinical data
- Required before issuance of approval order for original PMAs with clinical data
- Inspections of Sponsor and selected clinical investigators

FDA Review Considerations

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- Safety and Effectiveness Evaluation:
  - Valid Scientific Evidence
  - Probable Benefit to Health Weighed Against Probable Injury or Illness From Such Use
  - Clinically Significant Results For A Significant Portion of Target Population
  - Persons for Whose Use Device is Intended
  - Reliability of the Device
  - Adequate Directions for Use
  - Clinical Data Supports Intended Use

Recommendations for Successful Submission

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- Testing guidance
- Clinical protocol review
- PMA statistical guidance
- FDA guidance documents (*e.g.*, PMA modular submissions)
- Pre-Submission (Pre-PMA) meeting with FDA
- Perform detailed risk-benefit analysis

Steps to a PMA Approval

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1. Perform preclinical testing
2. Develop clinical study protocol
3. Pre-Submission (Pre-IDE) meeting with FDA
4. Submit IDE application
5. Respond to FDA questions, requests
6. IDE Approval
7. Conduct pilot studies, if necessary
8. Conduct pivotal study
9. Analyze clinical results

Steps to PMA Approval

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10. Full compliance with QSRs
11. Pre-Submission (Pre-PMA) meeting
12. Submit PMA
13. FDA review of PMA
14. Day-100 meeting with FDA
15. Respond to deficiencies
16. Panel meeting (if required)
17. Preapproval inspections (QSR, BiMo)
18. Post panel issues; negotiate labeling, post-approval study
19. Approval Decision

FDA Decisions on PMA

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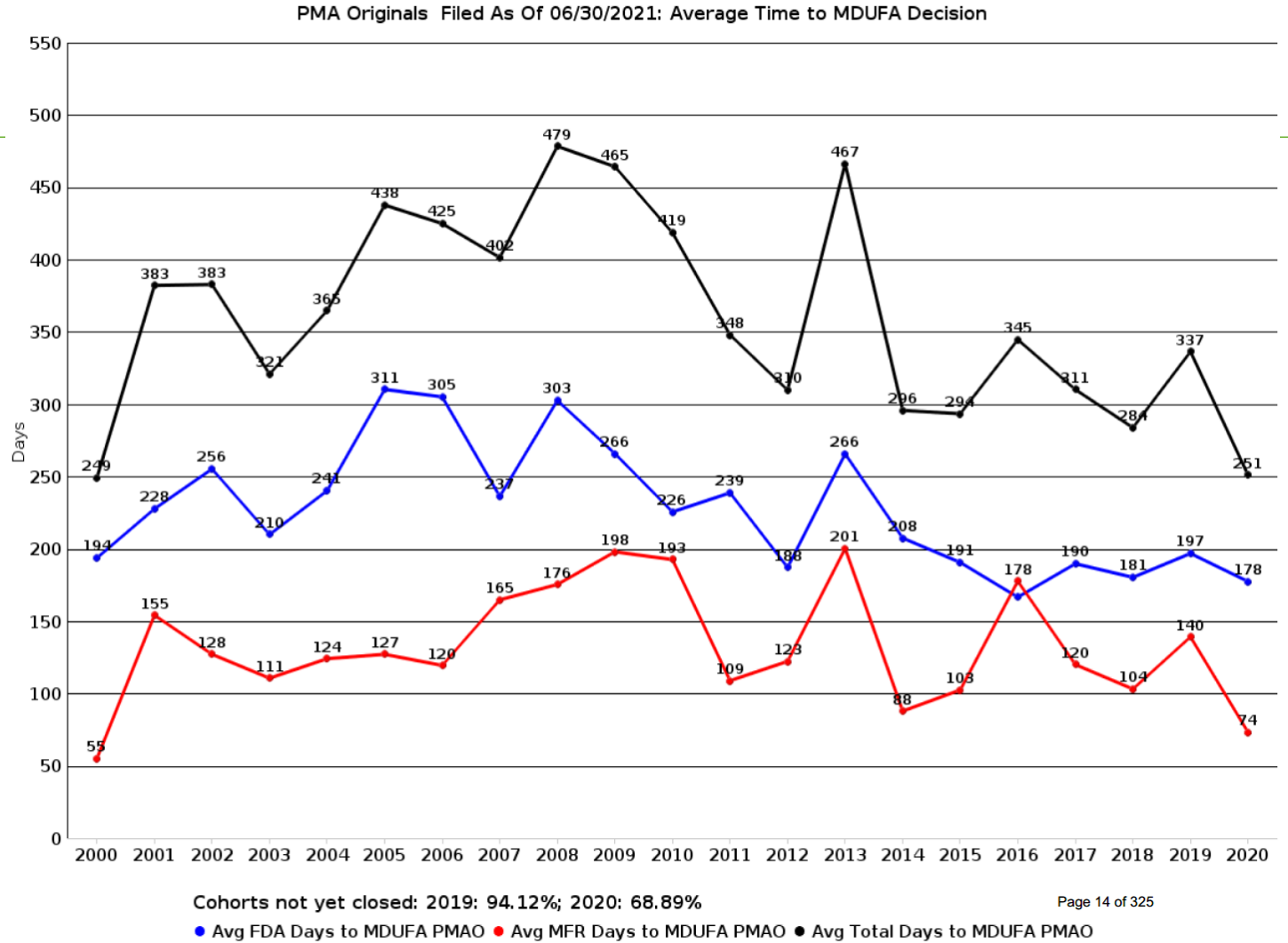
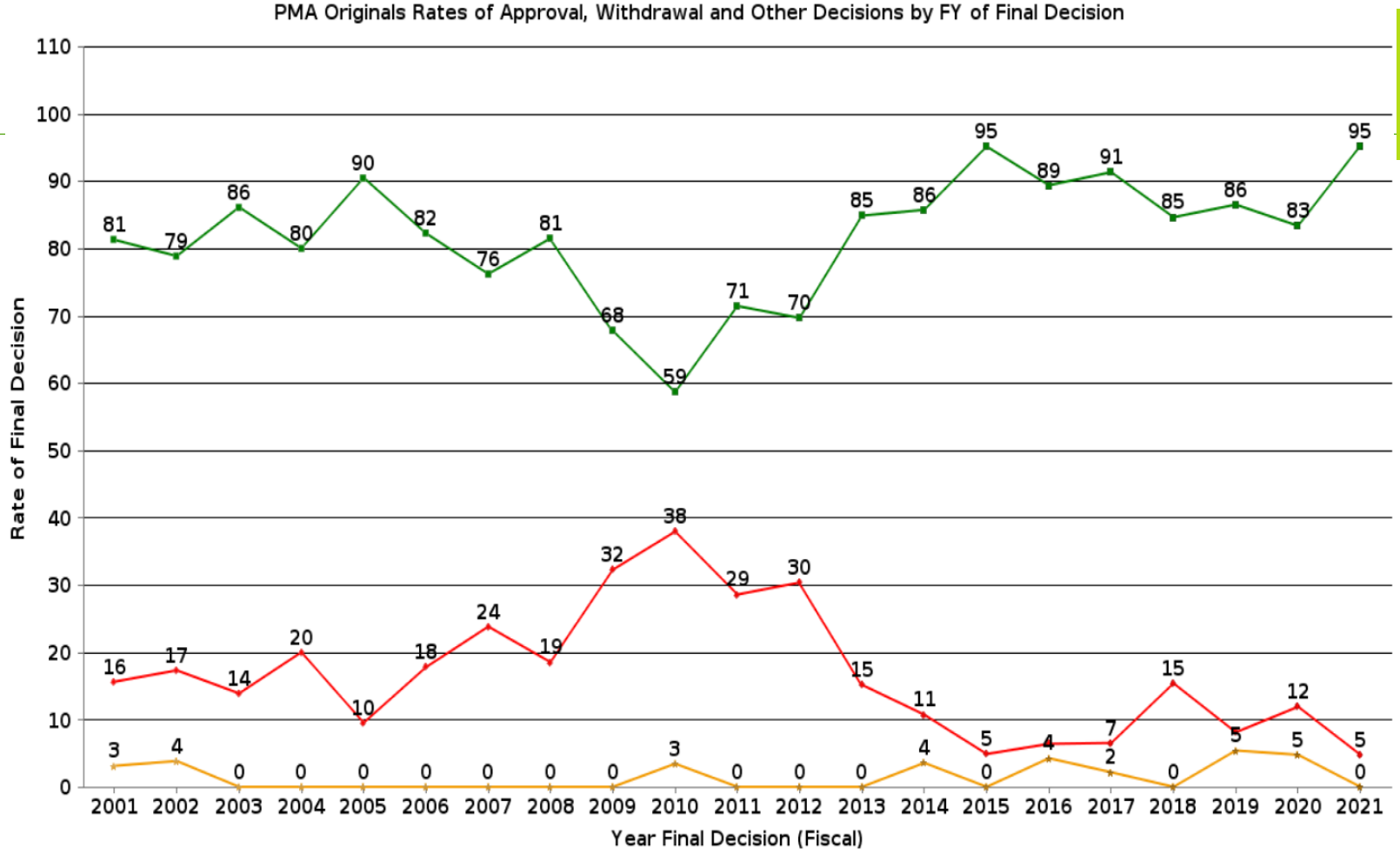
- Approval with conditions
- Approval pending
  - QSR Inspection
  - Agreement to approval conditions
- Not approvable
  - Major Deficiencies
- Denial of Approval


PMA Originals Filed As Of 06/30/2021: Average Time to MDUFA Decision
Days
550
500
450
400
350
300
250
200
150
100
50
0
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020
249 383 383 321 365 438 425 402 479 465 419 348 310 467 296 294 345 311 284 337 251
194 228 256 210 241 311 305 237 303 266 226 239 188 266 208 191 178 190 181 197 178
55 155 128 111 124 127 120 165 176 198 193 109 123 201 88 103 178 120 104 140 74
Cohorts not yet closed: 2019: 94.12%; 2020: 68.89%
Avg FDA Days to MDUFA PMAO
Avg MFR Days to MDUFA PMAO
Avg Total Days to MDUFA PMAO



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Post Approval Considerations

Post-Approval Considerations

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- Mandatory conditions
  - PMA supplements for certain changes
  - Periodic (annual) reports
  - MDR reporting
- Other postmarket controls
  - Post-approval studies (PAS)
  - Device tracking
  - Postmarket surveillance

Conditions of Approval: Post Marketing Requirements

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- PMA Supplements - Required
  - Required before making a change affecting the safety or effectiveness of the device
  - When unanticipated adverse effects increase in incidence or device failures necessitate a labeling, manufacturing or device modification
  - If the device is to be modified and animal or clinical testing is necessary to demonstrate safety and efficacy
  - If requirements are met, 30-Day Notices or PMA Supplements-Changes being Effected may be used
  - Contents of PMA Supplement are limited to information needed to support the change

Types of Changes that May Require a PMA Supplement

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- New Indications for Use
- Labeling Changes
- Different Manufacturing or Sterilization Facility
- Changes in Manufacturing Methods or Quality Control Procedures
- Changes in Sterilization Procedures
- Changes in Packaging
- Changes in Design or Performance Specifications, Components, Principle of Operation, or Physical Layout
- Extension of Expiration Date (no approved protocol)

Types of PMA Supplements

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- Types of PMA Supplements
  - 180-Day PMA Supplement (814.39(a))
  - Special PMA Supplement – Changes Being Effected (814.39(d))
  - 30-Day Notice and 135-Day PMA Supplement (814.39(f))
  - PMA Manufacturing Site Change Supplement (180 days)
  - Real Time Review
  - Annual Report or 30-Day Supplement (814.39(e))
    - For certain types of changes specified by FDA
- Other mechanisms to handle changes
  - Annual report - for changes that do not affect the safety or effectiveness of the device
  - Document to file - for "trivial" changes (e.g., editorial change to SOP)
  - New PMA – for major changes (new indications, patient population)

Post Marketing Requirements

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- Postapproval (Annual) Reports
  - Required at one (1) year increments from approval date
  - Submission must identify changes made to the device that do not affect safety or efficacy
  - Submissions must provide a bibliography and summary of research involving the device or a similar device
  - Submissions also must summarize reports in scientific literature concerning the device

Post Marketing Requirements

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- Medical Device Reporting ("MDR")
  - Required within 30 days (or 5 days) of when manufacturer becomes aware of information that reasonably suggests that the device
    - May have caused or contributed to a death or serious injury or
    - Has malfunctioned and such or a similar device marketed by the manufacturer would be likely to cause a death or serious injury if the malfunction were to recur

Post Approval Studies

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- May be required under 21 CFR § 814.82(a)(2)
  - Post-approval requirements may include as a condition to approval of the device: continuing evaluation and periodic reporting on the safety, effectiveness, and reliability of the device for its intended use
  - FDA will state in the PMA approval order the reason or purpose for such requirement and the number of patients to be evaluated and the reports required to be submitted
- See draft guidance *Procedures for Handling Post-Approval Studies Imposed by Premarket Approval Application Order* (May 27, 2021)

How do Marketing Submissions Differ?

How Do Marketing Submissions Differ?

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Attribute	PMA	*De Novo*	510(k)
Regulatory standard	Safety and effectiveness	General and special controls provide reasonable assurance of safety and effectiveness	Substantial equivalence
Permission to market	Must be “approved”	Must be “granted”	Must be “cleared”
Data standard	Valid scientific evidence	Probable benefits > probable risks	Comparison to existing (predicate) device
Data requirements	Almost always accompanied by clinical data	Most *de novo* petitions contain clinical data	10-15% contain clinical data
Application	Detailed, lengthy application	Medium	Shorter, even if hybrid

How Do Marketing Submissions Differ?

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Attribute	PMA	*De Novo*	510(k)
Confidentiality	Pending PMA is confidential, Summary of Safety and Effectiveness released after approval	Pending *de novo* is confidential; approval letter and decision summary publicly posted	Pending 510(k) is confidential, entire 510(k) (with proprietary information redacted) available post-clearance; 510(k) summary posted after clearance
Exclusivity	Like a product license or regulatory patent	No exclusivity	No exclusivity
Inspections	Manufacturing (QSR) and clinical (BiMo) inspections required before approval	Typically not required pre-clearance	None required pre-clearance
Manufacturing Information	Must be provided	Not required	Not required

How Do Marketing Submissions Differ?

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Attribute	PMA	*De Novo*	510(k)
Labeling	Extensive labeling review	Less extensive	Less extensive
Advisory Panel Review	Often	Rare	Extremely rare
Statutory FDA Review Time	180 days	120 days	90 days
Actual time to decision	Longer (~1 year)	Medium (~7-9 months)	Shorter (~4 months)
Post-approval study	Typically required	Can be ordered in some cases	N/A
User Fee (FY 2021)	$365,657 or $91,414 (small business) (eligible for first PMA waiver if gross recipes/sales <$30 million)	$109,697 or $27,424 (small business)	$12,432 or $3,108 (small business)

Humanitarian Device Exemption

HDE Requirements

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- A humanitarian use device (HUD) is a device that is intended to benefit patients in the treatment and diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year
- No comparable device, other than another HUD approved under the HDE regulation or a device being studied under an approved IDE, may be available to treat or diagnose the disease or condition
- Before submitting an HDE application, the applicant should submit a request for a HUD designation to the Office of Orphan Products Development (OOPD)

HDE Contents

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- OOPD's HUD Designation Letter;
- Explanation of need for HDE;
- Summary of safety and probable benefit
- Indications for use
- Device Description
- Preclinical data
- Clinical data (valid scientific evidence)
- Labeling
- Manufacturing
- Postmarket study proposal

HDE Procedures

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- Submission format similar to PMA
- Key difference is standard of evidence
  - Safety and probable benefit vs. Safety and effectiveness
  - Devices subject to the HDE process are exempt from the effectiveness requirements of a PMA
  - Typically results in smaller supporting clinical study
- FDA has 75 days from the date of receipt to review an HDE application
  - Similarly, the review timeframe for HDE supplements is also 75 days
- The QSR applies to HDEs but FDA states that the agency will focus on the manufacturing practices most relevant to the safety of the device
- The FDC Act and implementing regulations require IRB review and approval before an HUD is used

FDA Review Considerations

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- HDE Approval is based on
  - Reasonable assurance of device safety
  - Probable benefit to health
  - Good manufacturing practices
  - Truthful and accurate labeling

HDE Postmarket Considerations

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- Restrictions on HDE Approved Device
  - Profitability was previously not allowed but has been amended over time, first to allow profit for pediatric HDEs but now also for HDEs used in adults
  - IRB approval and monitoring
  - Not exceeding Annual Distribution Number (ADN)
    - Number of devices per year reasonably needed for each individual in the HDE application or HDE supplement
    - The number of HDE devices that may be sold for profit is limited to the ADN quantity

COVID-19 Guidance

New COVID-19 Guidance

- *Supplements for Approved Premarket Approval (PMA) or Humanitarian Device Exemption (HDE) Submissions During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency* (May 2020)
  - FDA does not intend to object to limited modifications to the design and manufacturing of devices approved through either a PMA or HDE without prior submission of a PMA or HDE supplement or 30-day notice for the duration of the public health emergency.
  - Examples of modifications may include, but are not limited to:
    - Design and manufacturing changes to address component unavailability due to supply chain disruptions
    - Manufacturing changes to allow the establishment to maintain operations and accommodate social distancing practices
    - Changes in manufacturing facility or establishment
    - Changes to packaging procedures

Recent FDA Guidance

New HDE Guidance

- *Humanitarian Device Exemption (HDE) Program (September 6, 2019)*
  - Reflect changes in the HDE Program resulting from statutory amendments made by the 21st Century Cures Act (Cures Act)
  - Explains the criteria FDA considers to determine if "probable benefit" has been demonstrated as part of the Agency's decision-making process regarding marketing authorization for a HUD

Resources

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- *Acceptance and Filing Reviews for Premarket Approval Applications (PMAs) (December 16, 2019)*
  - Separated the criteria for *PMA* filing into
    - 1. Acceptance criteria
      - Review involves the assessment of the completeness of the application
    - 2. Filing Criteria
      - Determine the basic adequacy of the technical elements of the PMA

Conclusions

PMA Conclusions

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- PMA process is a lengthy one (for applicant and FDA)
  - Study design issues still a major hurdle
  - Serial reviews of clinical data and labeling are the rule, not the exception
  - Post approval studies are typical and may be lengthy
  - Recent developments emphasize real-world considerations (patient preference, real world evidence, postmarket evidence)

PMA Conclusions

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- Submit thorough, well analyzed, persuasively presented clinical section and SSE within complete PMA application
- Use modular approach, if appropriate
- Meet with FDA (via pre-submission)
- Prepare for QSR and BiMO audits
- Promptly address all deficiencies
- If Advisory Panel review is required, Panel preparation is critical

HDE Conclusions

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- Two-step process can be lengthy, with review times for HDE as long or longer than PMA, on average
- Product will remain under quasi-investigational status permanently
- Eligibility increase to 8,000 and changes to profitability rules may make this process more attractive for limited populations where large clinical study is infeasible

Polling Questions

Questions

1. PMAs are required for (select all that apply):
   a) Devices that are substantially equivalent to class I or class II devices
   b) Devices that support or sustain human life, are of substantial importance in preventing impairment of human health, or present a potential, unreasonable risk of illness or injury
   c) Devices for which insufficient information exists to assure safety and effectiveness solely through general or special controls
   d) Devices for which general controls, or general and special controls, provide reasonable assurance of safety and effectiveness

2. After the final PMA module is submitted, FDA targets a decision on approvability within how many days:
   a) 60 days
   b) 90 days
   c) 120 days
   d) 180 days

3. A humanitarian use device (HUD) is intended to benefit patients in the treatment and diagnosis of disease or condition that affects or is manifested in not more than _____ in the United States per year.
   a) 5,000 individuals
   b) 6,500 individuals
   c) 8,000 individuals
   d) 8,500 individuals

Useful Resources

Resources

- *FDA Advice on PMAs: https://www.fda.gov/medical-devices/premarket-submissions/premarket-approval-pma*
- *FDA Advice on HDEs: https://www.fda.gov/medical-devices/premarket-submissions/humanitarian-device-exemption*
- *Humanitarian Device Exemption (HDE) Program (September 6, 2019)*
- *Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions (August 30, 2019)*
- *Acceptance and Filing Reviews for Premarket Approval Applications (PMAs) (December 16, 2019)*
- *Premarket Approval Application Modular Review (November 3, 2003)*
- *Breakthrough Devices Program (December 18, 2018)*
- *Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices (August 31, 2017)*

Questions?

Kristin Zielinski Duggan

+1 202-637-8894
kristin.duggan@hoganlovells.com

www.hoganlovells.com