Agenda

• Introductions
• Presentations
  • Maureen L. Dreher
  • Bertha Torres
  • Chris Cain
• Q&A
  • Q&A box
  • Chat box
• Recording and slides will be available on our website:
  https://mdic.org/mdicx-series/webinar-archive/
Maureen L. Dreher, PhD

Assistant Director for the Policy & Operations Team in the Division of Clinical Science & Quality at CDRH’s Office of Clinical Evidence and Analysis

• Responsible for Investigational Device Exemptions (IDEs) and several CDRH programs including the Expanded Access Program, Breakthrough Devices Program and Early Feasibility Study Program

• Works with CDRH pre-market review teams to interpret FDA statute and regulations pertaining to IDEs, clinical evidence generation, good clinical practice, and human subject protections.
Bertha Torres
Sr. Manager, Clinical Affairs for Transcatheter Mitral & Tricuspid Therapies, Edwards Lifesciences

- Sr. Trial Manager at Edwards Lifesciences
- In the Clinical Research Industry for approximately 20 years
- Experience in starting over 5 Early Feasibility Studies
Chris Cain

Vice President, Clinical and Regulatory Affairs at Conformal Medical, Inc

• Responsible for all aspects of clinical research and regulatory affairs at Conformal.

• Prior to joining Conformal, Chris served as VP, Clinical and Regulatory Affairs for Corindus Vascular Robotics, Inc

• Member of the Association of Clinical Research Professional (ACRP) and the Regulatory Affairs Professionals Society; he holds certifications in both organizations (CCRA, RAC)
CDRH’s Early Feasibility Study Program – History & A Look Ahead

Maureen L. Dreher, PhD
TCEA1A: Policy & Operations Team
Division of Clinical Science & Quality
Office of Clinical Evidence & Analysis
MDIC EFS Webinar September 20, 2019
Patients are at the Heart of What We Do

CDRH Vision: Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world
Supporting Device Innovation

- Pre-Clinical Testing
- Clinical Studies
- Pre-Market Application
- Post-Market

- Real World Evidence
- Breakthrough Devices Program
- Early Feasibility Studies
- Pre-/Post-Market Balance
- Patient Engagement
Motivation for CDRH Early Feasibility Study Program

• Initial clinical testing of novel devices had moved to non-US sites
  – Concern existed that device innovation may follow & improve OUS more quickly
• Devices developed for non-US markets
• There was growing concern regarding the time lag in the availability of beneficial medical devices for US patients

Many clinical study ecosystem factors contributed to these trends, including FDA data requirements for initiating clinical studies in the US
Early Feasibility Study Program

- Designed to bring early human clinical studies of devices back to the US
- Successful first 6 years of the program
What is an EFS IDE?

EFS IDE - A standard IDE application except...

• There may be a greater level of uncertainty about how the device will perform
  o Early in development, or
  o Has a new intended use

• Small number of subjects in the clinical investigation (<15)
  o Initial indication of safety and/or effectiveness
  o Proof of concept

• Often designed to obtain initial insights on device safety & performance, patient population, and to inform design of future studies
Key Policies for EFS Program

• **Doing the “Right Testing at the Right Time”**
  o Comprehensive testing during early phases of device development may add cost without significant return
  o However, informative nonclinical testing should be completed

• **Possible to leverage data from earlier versions of the device**

• **Unknowns and risk can be addressed by...**
  o Using clinical mitigations to provide patients with extra protection
  o The use of more frequent/detailed reporting

• **Provides tools for communicating available data to CDRH → Device Evaluation Strategy**

EFS program is a way to collect early human data that cannot be obtained by non-clinical methods.
EFS Program Benefits

- FDA
- Sponsors
- Innovators

Familiarity with the technology and regulatory considerations

New opportunity to address unmet clinical needs & early experience with innovative technology

Encourages development of high quality medical products

Reminder: Initiating EFS is a collaborative effort that can begin before the IDE application is submitted through effective Pre-Submissions
EFS Program at a Glance

Strong growth in sponsor utilization of the program since inception

- More than a doubling of IDEs submitted over past 6 years
- Over 75% of EFS IDEs get to an approval decision within 2 review cycles
- Over 200 EFS have been approved to treat/diagnose >2500 patients
- FY19 on pace to yield similar submission numbers to FY15-FY17
EFS Distribution Across CDRH

- EFS in wide distribution of clinical specialties
- Highest utilization in cardiovascular and neurological devices

Data reflects FY14-FY18
What Comes After an EFS?

• Interest in learning from the EFS to
  – Improve the device
  – Design and conduct efficient larger studies (e.g., pivotal)

• Approaches to facilitate pivotal transition
  – Start discussion early while the EFS is ongoing
    • E.g., request expansion after EFS patients have been treated but while pivotal study design being developed
  – Address necessary non-clinical testing to support a pivotal study in parallel with EFS progress
    • Continue discussions with your FDA review team
Summary

• EFS Program designed to facilitate early clinical study of devices in the US

• Highly recommend utilizing FDA Pre-Submission process to establish early and ongoing collaboration with FDA to advance the EFS

• Device evaluation strategy based approach key to successful submission
  – Enables appropriate non-clinical testing and use of clinical mitigations to protect human subjects

• EFS Program supports
  – Learning from the study to improve the device design and efficient pivotal studies
  – Utilization by a diverse set of clinical specialties
EFS:
Best Practices in Pursuit of 60/60/60

Bertha Torres
Edwards Lifesciences
## EFS Stakeholder Benefits

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<td>• Access to novel, potentially life-saving technology</td>
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<td>• Mitigation of risks inherent to clinical trials</td>
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<td>• Early exposure to novel technology</td>
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<td>• Better definition of requirements for demonstrating safety &amp; efficacy; reduces development risks.</td>
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<td>• High quality U.S. healthcare data &amp; networks</td>
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<td>• Innovative treatment options</td>
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<td>• Expert Key Opinion Leaders stay involved in innovation</td>
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<td>• Earlier access to high-quality EFS data and outcomes</td>
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<td>• Improved innovation and feedback opportunities</td>
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EFS Site Network Pilot: 60:60:60 GOAL

EFS Metrics: Administrative Baseline

Mean Time from EFS IDE Approval (Days)

- IDE Approval: 68 Days
- IRB Approval: 72 Days
- Contract Approval: 133 Days
- 1st Subject Enrollment: 187 Days

EFS Metric Category:

- EFS Metric Category: Administrative Baseline
  - 60 Days
  - Next 60 Days

60-day IDE approval

- Well-defined patient population
  - Prior early human use experience helpful (e.g., compassionate use or OUS studies) but not required
- Procedural plan established
- Limit number of non-standard of care assessments
- Resist urge to collect data without a known purpose
- Leverage protocols previously approved by FDA
  - Published on clinicaltrials.gov or in major journals after study completion
- Take advantage of FDA’s interactive review process – stay in close contact with reviewer
60-day IRB Approval

- Leverage central IRBs where possible (e.g., WIRB)
  - Central IRBs will review concurrently with FDA
- Ask early/up front for list of required submission items
- Ensure informed consent template covers all necessary items.
  - Frequent dialogue with site research coordinators to understand site-specific requirements
- Educate PI and local study staff on study procedures before IRB meets so that they can attend and provide support where needed
60-day Contract Approval

- Leverage Master Clinical Trial Agreement (MDIC or sponsor-developed)
  - Takes additional time to negotiate but saves time down the line
- Clear alignment between Schedule of Assessments (SoA) in protocol and budget

Sample SoA

Line-item budget worksheet in excel
Helping Patients is Our Life’s Work, and

life is now
EFS Site Best Practices: Implementation Strategies from the sponsor perspective.

Small Company Perspective

Chris Cain
VP, Clinical & Regulatory Affairs
Conformal Medical, Inc.
The EFS Journey
The EFS Journey

- Prep for IDE
- IDE to FPI
- EFS
FDA

- Engage Early
- Frequent Communication
- Interactive Review
- Keep Informed

“Interaction is critical.”
Dr. Andy Farb, CRT2016

101: FDA Meetings
Build the Infrastructure

- Outsource vs. Insource
- Experienced Monitor(s)
- Vendor Selection
  - EDC
  - Core Lab
  - DSMB
  - CEC
Clinical Trial Reimbursement

- CMS: Engage Early
  - Find a contact within CMS...website is a little difficult to navigate
  - Medicare Coverage: Y/N
  - Uncover Surprises
- FDA: Category A/B
The EFS Journey

- Prep for IDE
- IDE to FPI
- Pivotal
Site Selection

- **EFS Experience**
- Patients
- Patience
- Collaborative and Engaged Investigator(s)
  - Procedure may evolve over the course of the trial
  - Device iterations
  - Frequent communication
- Most experienced coordinator(s) assigned to EFS
- Quick IRB Approval
- Quick CTA/Budgeting
CTA / Budgeting

• Contract
  • MCTA (MDIC)
    • Inform Site that you’re using the MCTA
    • Find out if the site had representation at the MDIC roundtable
  • Issues? Get lawyers on the phone

• Budgeting
  • Have CMS/FDA reimbursement identified before creating template
  • Inform sites of reimbursement status
  • If known, provide DRG
  • Establish consistent parameter, e.g. Medicare +20%
  • Get on the phone
  • Experience with procedure costs
Key Learnings

• Engage FDA and CMS **EARLY**
• Frequent Communication
  • Sites
  • Regulators
  • Vendors
• Use the MCTA
• EFS Sites First
• Experienced CRA/CRC
Audience Q&A

Submit your questions through the chat box or Q&A box
Resources available

• MDIC Early Feasibility Studies Initiative page
  https://mdic.org/program/early-feasibility-studies-efs/
  • Subscribe to EFS Express
  • Download tools and templates

• Archived MDICx webinars
  https://mdic.org/mdicx-series/webinar-archive/
Thank You!

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