The MDIC Initiative on Early Feasibility Studies in the U.S.

Chip Hance – MDIC-EFS Initiative Board Champion

EFS Budgeting Best Practices Workshop
February 26, 2020
Conflicts

Chip Hance, BS, MBA

I have no relevant financial relationships

Board Member of the Medical Device Innovation Consortium (Unpaid Volunteer)

Board Member of Medical Device companies:
  CroiValve, Maravai, Regatta Medical, Resonetics, Schivo Medical, VivaSure
Many Innovative Cardiovascular Therapies Now Begin Clinical Experience with U.S. EFS

- Earlier access to new medical devices for US patients and investigators
- Geographic proximity of manufacturers to clinical trial sites facilitates interaction
- No language issues
- Familiarizes US regulators with the device earlier
- Familiarizes clinical sites with device/procedure before pivotal trials
MDIC Is Working to Drive Improvements

2013 - FDA Published EFS Guidance

2015 – Blueprint for Early Feasibility Study (EFS) Success

• Commissioned the EFS/FIH Industry Perspectives survey
• Published the Blueprint for EFS Success, supplementing the 2013 FDA Guidance

2017 – Baseline EFS Performance Metrics

• MDIC, Sponsors, and FDA: 1st ever collaboration to share de-identified EFS Administrative and Clinical metrics.
• Baseline represents approximately 25% of EFS trials started FY14 – FY17

2018 – Tools & Processes

On MDIC’s website:
• Master Clinical Trial Agreement
• Patient Informed Consent template
• Education Tools: IRB, Research teams and Patients

2019 – Site Network

• 18 sponsors – 31 sites
• Best Site Practices Workshop
• EFS workstream development
While FDA Processes Are Now Timely, Other Issues Have Arisen

MDIC Baseline Sponsor Metrics (FY14-17)

<table>
<thead>
<tr>
<th>Mean Time (Days)</th>
<th>IDE Approval</th>
<th>IRB Approval</th>
<th>Contract Approval</th>
<th>Completion: Next 60 days (120 days)</th>
<th>Last Subject Enrollment*</th>
</tr>
</thead>
<tbody>
<tr>
<td>68</td>
<td>72</td>
<td>133</td>
<td>187</td>
<td></td>
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Early Feasibility Study (EFS) Metrics Baseline

Target for a U.S. Study:
120 Days to Begin Enrollment
- After IDE Approval
- IRB/Contracting running in parallel

“60/60/60” Site/Sponsor Goal
- 60 Days for IRB Approval
- 60 Days for Contract Execution
- 60 Days for First Patient Enrollment

‡Baseline metrics collected by MDIC from EFS trials conducted FY14 – FY17, compiled from 13 EFS trials and 48 sites
While FDA Processes Are Now Timely, Other Issues Have Arisen

MDIC Baseline Sponsor Metrics (FY14-17)

Baseline metrics collected by MDIC from EFS trials conducted FY14 – FY17, compiled from 13 EFS trials and 48 sites.

2017 Average Time From Site Packet Received to 1st Patient Enrolled = 320 Days!
New Data Shows Some Improvement, But Still Challenges, Especially Contracting

IDE approval to 1st Enrollment: 120 day target

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>New</th>
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<tbody>
<tr>
<td>FY18-19</td>
<td>320 Days</td>
<td>252 Days</td>
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2 Month Reduction

Source:
MDIC Annual Public Forum presentation by Liliana Rincon-Gonzalez, September 2019
FY18-19 data from an additional 9 EFS trials across 60 Sites
Sponsor-Site Contracting: The #1 Challenge to Running a U.S. EFS

- The Median Site takes ~5 months to negotiate a contract with a sponsor
- The Best Sites can take as little as one month
- The Slowest Sites take more than a year

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<tr>
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<th>Baseline: FY14 - FY17</th>
<th>FY18 - FY19</th>
</tr>
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<tbody>
<tr>
<td>Minimum (days)</td>
<td>24</td>
<td>35</td>
</tr>
<tr>
<td>Median (days)</td>
<td>120</td>
<td>149</td>
</tr>
<tr>
<td>Maximum (days)</td>
<td>329</td>
<td>469</td>
</tr>
</tbody>
</table>

Source: MDIC Annual Public Forum presentation by Liliana Rincon-Gonzalez, September 2019
Need for Collective Stakeholder Efforts for Improvement

Overcoming the Challenges of Conducting Early Feasibility Studies of Medical Devices in the United States

David R. Holmes, Jr, MD, \textsuperscript{a} Robert Califf, MD, \textsuperscript{b} Andrew Farb, MD, \textsuperscript{b} Dorothy Abel, BS\textsuperscript{b}BME, \textsuperscript{b} Michael Mack, MD, \textsuperscript{c} Tamara Syrek Jensen, JD, \textsuperscript{d} Bram Zuckerman, MD, \textsuperscript{b} Martin Leon, MD, \textsuperscript{d} Jeff Shuren, MD

\textbf{ABSTRACT}

Initial clinical studies of new medical technologies involve a complex balance of research participant benefits versus risks and costs of uncertainty when novel concepts are tested. The Food and Drug Administration Center for Devices and Radiological Health has recently introduced the Early Feasibility Study (EFS) Program for facilitating the conduct of these studies under the Investigational Device Exemption regulations. However, a systematic approach is needed to successfully implement this program while affording appropriate preservation of the rights and interests of patients. For this to succeed, a holistic reform of the clinical studies ecosystem for performing early-stage clinical research in the United States is necessary. The authors review the current landscape of the U.S. EFS and make recommendations for developing an efficient EFS process to meet the goal of improving access to early-stage, potentially beneficial medical devices in the United States. (J Am Coll Cardiol 2016;68:1908-15) © 2016 by the American College of Cardiology Foundation. All rights reserved.

Executive Committee

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- Bram Zuckerman
- Jeff Shuren

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- Joseph Chin

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- Pamela Goldberg
- Chip Hance
- Jon Hunt

We Work Together Under the MDIC Construct
MDIC Established in 2019 an EFS Pilot Network of Sites Committed to Improvement

- Commit to pursue efficient administrative steps:
  - IRB Approval
  - Contract Execution
  - 1st Subject Enrolled
  - “60/60/60” (Days)

- Track and report EFS Metrics

- Test the utility of EFS specific tools and methods

- Serve as a launching point for a future network of high-performing sites
  - Nationwide coverage
  - Multiple therapeutic areas

Updated: 5/30/2019
Working Together with Supporting Partners
EFS Site Best Practices Workshop

March 6-7, 2019, Arlington, VA

• Over 65 attendees participated from 20 sites, 14 sponsors, FDA, CMS and service providers

• Topics covered:
  • Managing Risk, SAEs & IRB Reporting
  • Timely & Effective Contracting
  • Budgeting between EFS Sites and Sponsors
  • EFS Staffing and Resources
  • Patient Identification, Enrollment & Retention
  • Coverage Determinations & Site Budgets
MDIC / Baylor Developed and Revised an EFS Master Clinical Trial Agreement

18 Lawyers met Feb 2018
To Draft EFS Master Agreement and Standardize Key Contract Language (led by Jaime Walkowiak-Baylor)

EFS MASTER CLINICAL STUDY AGREEMENT

IMPORTANT NOTE: This Early Feasibility Study ("EFS") Master Clinical Trial Agreement template is provided by The Medical Device Innovation Consortium ("MDIC") as an educational tool. It is neither intended, nor should be considered, to be legal advice. Applicable laws may vary in different states. Also, federal and state laws governing clinical studies are subject to change and to varied interpretations by courts in different jurisdictions. Each Institution and Sponsor entering into a clinical study agreement should consult with its own counsel to obtain legal advice on contracts for clinical studies.

This MASTER CLINICAL STUDY AGREEMENT ("Agreement") is made effective as of the [NUMBER] day of [MONTH], [YEAR] (the "Effective Date"), and is by and between [SPONSOR NAME], a [ ] corporation, with offices at [ADDRESS] ("SPONSOR") and [INSTITUTION NAME], a [ ] corporation with offices at [ADDRESS] ("Institution").

WHEREAS, SPONSOR is engaged in the development of medical device technologies, and in connection therewith intends to conduct one or more early feasibility clinical studies (each a "Study" or collectively, "Studies") of such medical device(s) (each a "Study Device"); and

WHEREAS, SPONSOR wishes to engage the Institution to perform one or more Studies involving the Study Device(s), as set forth more fully in various Study-specific statements of work attached to this Agreement; and

Revised July 2019
Posted MDIC Website
http://mdic.org/cts/efs/
New Budgeting Working Group Working on Methods to Speed Site-Sponsor Negotiations

Membership:
Sponsors, Sites, led by MDIC

Goals:
Develop strategies to Speed up Processes
Education/best practices

Target Issues:
FMV assessment
• Difference between small and large company
• EFS novel iterations and completely new technology
Budget template
• How to break up numbers (effort, etc)
Discuss requirements and assumptions
Concluding MDIC Perspectives on EFS

The Early Feasibility IDE pathway in the United States is one increasingly pursued by Sponsors as part of the development pathway for novel technology. FDA has streamlined the approval process of EFS studies to less than 60 days on average.

Unfortunately, now the bottlenecks in conducting these studies now lie between the Sites and Sponsors, especially Contracting and Budget negotiations:

- The median time for 1\textsuperscript{st} Subject Enrollment is almost 9 months; not competitive with international standards.
- The best sites achieve 4 months; fully competitive with expectations.

MDIC is championing a pilot effort with leading sites in cardiovascular research to lift the overall EFS clinical trial ecosystem to Best-in-Class performance:

- Have set a target of “60/60/60” to shave months of study prep time.

Perceptions (and Reality) are changing – the U.S. is increasingly a preferred destination for early study of these novel patient therapies.

Improvement in the clinical trial ecosystem will contribute to FDA’s Vision: “Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world.”
Interested in Working With Us?

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