FDA Breakthrough Designation: Will an FDA "Yes" Lead to a CMS "Yes"?

May 22, 2019
Factory-CRO Group: Global Coverage

Local experts in Medical Device merged to form Global Medical Device focused CRO

Supporting Start Up – Strategic Medical Device Companies

Established

In the EU in 1988
In AUS in 1997
In the US in 2000
Discussion

Landscape

FDA/CMS Opportunities

Steps and the Future!
DEVICE/DRUGS/DIGITAL/AI/COMBOS—FAST-Changing....

MEDICAL DEVICE MARKET MAP

GENERAL SURGERY
- ViaSurgical
- Apollo Endosurgery
- OmniGuide
- CMR
- ZipLine
- GECKO
- usbi medical
- EndoGastric Solutions
- SENTREHEART

CARDIOVASCULAR
- Shockwave
- Impulse
- SilRoad Medical
- Arstasis
- Cardiokinetix
- BioVentrax
- Vytronix
- mitralign

OPHTHALMOLOGY
- VIVANTIS
- Freedom Meditech
- Eye Tech Care
- Clarivista
- Retina implant
- TearScience
- AcuFocus

ORTHOPEDICS
- Orthosensor
- Ceterix
- Benvenue
- VertiFlex
- SpineWave
- SBI-BONE

DIAGNOSTICS
- Genalyte
- SomaLogic
- Lineagen
- Biodesix

NEUROLOGY
- NeuroSence
- eNeura
- Neuroscape
- tNeuro

ONCOLOGY
- PRONova
- SENO
- Reflexion Medical
- Medison
gn

IMAGING
- Delphinus
- SonoCine
- Signostics
- VisionGate

PATIENT MONITORING
- Ornim
- OptiScan
- intuity

CB INSIGHTS
Innovator’s Dilemma

Innovator

REGULATORY
- FDA
  - HITECH ACT
  - Medicare
  - Medicaid
- Gov Health Insurance
- Commercial Insurers
- VA/DOD

REIMBURSEMENT
Regulatory and Reimbursement: Distinct Processes and Requirements Blending...

U.S. Regulatory FDA – “safety & efficacy”
- If “safe” no incentive to limit products
- Defined pathways, requirements
- Standards vary by risk
- Competition needs unique approval

Government/Payer - “reasonable and necessary”
- Incentives to limit technology
- Sometimes, ill-defined process, requirements
- Criteria may be more stringent/evidence based
- Burden of proof on innovators increasing
- Comparisons to next best or least expensive alternatives
- Competition uses same pathway
- “real world” evidence required for adoption

Information needs are different. Higher levels of evidence may be required for Medicare coverage than for regulatory approval.
FDA Breakthrough Designation: Why Did it Happen?
20th Century Cures Act established Breakthrough Designation

*December 2016 Congressional Legislation supercedes Expedited Access Pathway*

- Designed to be a more agile process for manufacturers
- Offers “Sprint” discussions with FDA
- More flexibility in study design
- Sponsors can recommend their own experts
- Submit through the Breakthrough Device “Q” Submissions process
Early Feasibility Study IDEs

Finalized EFS Guidance document issued Oct 1, 2013

- Growing interest in US EFS from non-US sponsors
- US EFS used to support CE Mark
- Transition from US EFS to pivotal studies

≈80% of EFS IDE submissions approved in 1 review cycle
A medical device is defined within the Food Drug & Cosmetic Act as "...an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of it's primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."
Why Definitions are so Important

Gene therapy – the next big step in medicine!

...but to be most effective it may need a special device to ensure delivery to target
Some FDA Fundamentals – Device Classification

- Class I
  - Low Risk
  - 55% of devices

- Class II
  - Medium Risk
  - Usually 510k clearance
  - 40% of devices

- Class III
  - High Risk
  - 5% of devices
FDA Designations: Development/ Regulatory Pathways

1: Accelerated approval  2: Fast Track/RMAT  3: ODD and Breakthrough Designation-PD biomarker based
No longer 3 phases....

“Instead of conducting the usual three phases of study, seamless trials encompass one adaptive study where the phases are separated by interim looks. By using one large, continuous trial, it saves time and reduces costs. It also reduces the number of patients that have to be enrolled in a trial.”

-FDA Chief Scott Gottlieb. RAPS. Regulatory Convergence Conference September 2017
Traditional Regulatory Approval Pathway Options

FDA -- considerable discretion to decide whether a product requires a 510(k) or a PMA

The 510(k)...
- Class I devices -- Small number (specifically called out in the regs)
- Most Class II devices -- a few are exempt

The PMA...
Class III Devices -- life saving/high risk
Definition of Breakthrough Designation

Provides more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions;

Has no approved alternatives;

Offers significant advantages over existing approved alternatives; or

Availability is in the best interest of patients.

QUALIFYING FOR FDA DESIGNATION https://www.fda.gov/media/108135/download
FDA Breakthrough Program Stats

Summary data for breakthrough device designation requests.

- **EAP**: 26 (21 Granted, 9 Denied, 9 Withdrawn)
- **Breakthrough Devices Program**: 71 (20 Granted, 9 Denied, 9 Withdrawn)
- **Total**: 97 (41 Granted, 41 Denied, 18 Withdrawn)

Taken from Scott Gottlieb, MD report to Congress. [https://www.fda.gov/media/124747/download](https://www.fda.gov/media/124747/download)
Summary by FDA Division

Distribution of granted breakthrough device designation requests across common clinical specialties and medical device areas.
## Breakthrough Approvals

<table>
<thead>
<tr>
<th>File Number</th>
<th>Applicant/Holder/Submitter</th>
<th>Trade Name</th>
<th>Link to Full Indications for Use</th>
<th>Publicly disclosed as BT Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>P180007</td>
<td>Spiration Inc</td>
<td>Spiration Valve System</td>
<td>PMA database</td>
<td>SSED now available</td>
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<tr>
<td>DEN170045</td>
<td>BANYAN BIOMARKERS, INC.</td>
<td>BANYAN BTI</td>
<td>De Novo Summary</td>
<td>yes</td>
</tr>
<tr>
<td>DEN180001</td>
<td>IDX, LLC</td>
<td>IDX-DR</td>
<td>De Novo Summary</td>
<td>yes</td>
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<tr>
<td>P170019</td>
<td>FOUNDATION MEDICINE, INC.</td>
<td>FOUNDATIONONE CDX</td>
<td>SSED</td>
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<tr>
<td>P170039</td>
<td>CLINICAL RESEARCH CONSULTANTS, INC.</td>
<td>CUSTOMFLEX ARTIFICIAL IRIS</td>
<td>SSED</td>
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<tr>
<td>P160017/S031</td>
<td>MEDTRONIC MINIMED, INC.</td>
<td>MINIMED 670G SYSTEM</td>
<td>SSED</td>
<td>no other info</td>
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<tr>
<td>P180002</td>
<td>PULMONX CORPORATION</td>
<td>ZEPHYR ENDOBRONCHIAL VALVE SYSTEM</td>
<td>SSED</td>
<td>no other info</td>
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<tr>
<td>P180036</td>
<td>IMPULSE DYNAMICS, INC.</td>
<td>OPTIMIZER SMART SYSTEM</td>
<td>SSED</td>
<td>no other info</td>
</tr>
</tbody>
</table>

**Total of 11 Devices Approved:**
- 6 PMA
- 3 De Novo 510(k)
- 2 Traditional 510(k)
CMS Approval and Collaboration with FDA: Breakthrough Designation
Hello, Welcome to the Shells Health Plan. We are here to provide you with a comprehensive explanation of medicare and third party payer reimbursement.

**Coverage**
The criteria under which a product, service or procedure will be paid (NCD, LCD).

**Payment**
The amount paid for a product, service or procedure. (MS-DRG, APC, PFS)

**Coding**
Mechanism by which a product, service or procedure is identified (CPT, ICD10)

*Key components for successful Medicare and third-party payer reimbursement are based upon the three major elements, coverage, coding, and payment.*

How does CMS Cover and Pay?

**COVERAGE** gives Yes to access; **PAYMENT** establishes price....

• **COVERAGE**: *Types of Coverage along the Continuum of Device Development*

  • *Coverage needed to allow Hospitals to Bill for the Trials*: Coverage for Clinical Trials and Devices (IDE Coverage); Coverage of Routine costs of the TRIALS, and can be distinct from coverage of the Device.

  • *Coverage needed at Commercialization* (Coverage with Evidence Development or CED; National Coverage Determinations NCDs), private insurance....
Breakthrough Designation: Coverage Issues

DEFINITION: Coverage of IDE Clinical Trials.

IDE Clinical Trial Coverage: Started in 1995 CMS to give FDA authorization to categorize medical devices to a Category A or B product for purposes of reimbursement. 
https://www.fda.gov/media/98578/download

• **Category A:** Experimental/Investigational. Medicare may cover ONLY the routine care items and services in a FDA-approved Experimental IDE study but NOT the device.
  • Formerly “EFS” studies very small in size, allow for early clinical evaluation.

• **Category B:** Non-experimental/Investigational. Meets definition of Reasonable and Necessary as defined by CMS. CMS May Make Payments for an investigational DEVICE AND ROUTINE Care Items and services for a Category B IDE study.
  • Well-established process includes a “Cross-walk” for Medicare Criteria to approve coverage of routine costs of care and for the device.
CMS Criteria for Coverage of Breakthrough Designated IDE Trials

Medicare Coverage IDE Study Criteria Element Criterion

1. The principal purpose...whether device improves health outcomes
2. The rationale for the study is well supported by available scientific and medical information, or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
3. The study results are not anticipated to unjustifiably duplicate existing knowledge.
4. The study design is methodologically appropriate ....
5. The study is in compliance...
6. The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals....
7. The study is registered with the National Institutes of Health National Library of Medicine's ClinicalTrials.gov.
8. The study protocol describes the method and timing of release of results on all pre-specified outcomes.
9. The study protocol must describe how Medicare beneficiaries may be affected by the device under investigation, and how the study results are or are not expected to be generalizable to the Medicare beneficiary population. Generalizability to populations eligible for Medicare due to age, disability, or other eligibility status must be explicitly described.
FDA/CMS: It starts with Categorization of IDE Studies

How FDA assigns Category A or B

Start

Is the proposed device, or a devices similar to the proposed device, legally marketed?

Y

Does the proposed device have different technological characteristics, a new indication or new intended use compared to the legally marketed device?

N

Category B

Y

Category B

N

Does the available information on the proposed device or similar devices resolve initial questions of S/E*?

N

Category A

Y

Category B

Does the addition of non-clinical and/or clinical data related to the proposed device or similar devices resolve initial questions of S/E*?

N

Category A

Y

Category B

* S/E = Safety and Effectiveness
CMS: What is CMS’s Standard for Coverage?

CMS can easily differ in its views of what is “reasonable and necessary” vs. the FDA’s judgement of “safe and effective.”

New Proposed CMS Rule addresses Payment Only!

How will a new technology or drug be Paid by CMS when it is new?

New Technology Add – On Payments (NTAP) to capture benefits of new technology for a 2-3 year timeframe.

Designed for Inpatient Payment Systems. (DRG-based). (APCs Pass-through for Outpatient products).

3 Criteria: Newness, Cost, and Clinical Equivalence.

“CMS is proposing to modernize payment policies for medical devices that meet FDA’s Breakthrough Devices designation. For devices granted this expedited FDA approval, real-world data regarding outcomes for the devices in different patient populations is often limited. At the time of approval, it can be challenging for innovators to meet the requirement for evidence demonstrating “substantial clinical improvement” in order to qualify for new technology add-on payments. CMS is proposing to waive for two years the requirement for evidence that these devices represent a “substantial clinical improvement.”

Waiving this requirement would provide additional Medicare payment for the technologies for a period of time while real-world evidence is emerging, so Medicare beneficiaries do not have to wait for access to the latest innovations.
NTAP: Impact of proposed change

Established in 2001 with limited use....

• From 2012-2018 only 26 medtech NTAPs were submitted to CMS, compared to 250 cleared submissions at FDA. Only 11 approved for a NTAP.

• New Rule Changes definition of
  • 1. Newness
  • 2. Clinical Substantially Equivalent Criteria.
  • 3. Cost Criteria.

• Will be applied to 17 new NTAP applications for 2020.

***For FY 2020, CMS is proposing to increase the maximum allowed payment amount under NTAP to the lesser of (1) 65 percent of the costs of the new medical service or technology, or (2) 65 percent of the amount by which the cost of the case exceeds the standard DRG payment. Previously, the maximum allowed additional payment was 50 percent.

Breakthrough Designation Issues for Manufacturers

Examples that include a bit of Subjectivity with required negotiation....

• FDA/CMS Complexities for Coverage “YES”....
  • First-in-human trials and first patients treated may not meet CMS criteria. Hospitals and Manufacturers “foot the bill” for usual care.
  • Hospitals won’t start studies unless IDE clinical coverage endorsement obtained from CMS. (IRB approved, hospitals won’t move forward).
  • Difficult to “differentiate between the Procedure and the Device for determination of Coverage.
  • New Indications for currently used technology or drugs present challenges.

CMS and Manufacturers must continue to tailor the process for each product meeting the definition of Breakthrough. All signals point toward collaboration!
Baker and Richner’s Advice: Avoid Costly Mistakes Now or Pay Later

• Join MDMA and Support MICHBIO!
  • Follow MDIC too https://mdic.org/

• Find-out if you meet Breakthrough Designation Definition
  • Use a STRATEGIC Regulatory Partner!

• Understand differences between Category A and Category B.

• Apply for IDE PMA or 510K Clearance (regulatory)

• Understand how to accurately apply for Category B IDE COVERAGE of your trials and/or device depending on Categorization.
  • Use a STRATEGIC Reimbursement Partner! (Hull and Associates)

• Understand how to communicate with CMS and FDA during process.
  • Use a STRATEGIC Reimbursement AND Regulatory Partner!
### Baker and Richner’s Revelations: Where will be in 3 years? What Matters to Manufacturers?

<table>
<thead>
<tr>
<th><strong>CMS:</strong></th>
<th>Will be more transparent and process driven on coverage rules. More flexibility than Private Insurers. Start at first THOUGHT of new product for Coverage negotiations…</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA:</strong></td>
<td>Continuing to improve and drive innovative approaches to study design and adaptive ways to harness available patient records for studying long-term impact of care.</td>
</tr>
<tr>
<td><strong>Hospitals:</strong></td>
<td>Negotiations for trial coverage payments will be hospital-specific and get WORSE as pricing of services becomes more granular.</td>
</tr>
<tr>
<td><strong>Physicians:</strong></td>
<td>Doctors will be part of the new, mini-hospital/insurance systems and will continue to play a predominant role in what will be used or not.</td>
</tr>
<tr>
<td><strong>Manufacturers:</strong></td>
<td>Technology companies will partner with hospitals for conduct of trials, and negotiations with payers. Must accept that long-term data will be required for progressive/continuous coverage and market access unless it is a strictly consumer-based product.</td>
</tr>
</tbody>
</table>
Questions?
Dr. Baker is the President and CEO of Boston Biomedical Associates (BBA). She established BBA in 2000 after an extensive career of nearly 10 years running the corporate clinical research group for Boston Scientific. Prior to BSC, she was employed as a Research Assistant Professor at the University of Massachusetts Medical School where she worked in the Cardiac and Vascular Surgery Departments. She has served as a Professor in Mechanical Engineering at Worcester Polytechnic Institute and has established herself as a leader in clinical research in a variety of medical areas including cardiovascular, neurovascular, orthopedics, GI and GU. Dr. Baker is a licensed professional engineer and holds a BS in Chemical Engineering and a Masters and PhD in Mechanical Engineering with an emphasis in Biomedical Engineering. She has received her degrees from Worcester Polytechnic Institute and her research was performed in the Vascular Surgery Department at UMASS Medical School.

Randel has more than 30 years of experience working in health policy, reimbursement, economics, and data analytics for health service, technology and pharmaceutical companies; her network and influence is well-known. For two years prior to BBA, Randel was a Senior Policy Advisor to Avalere, a health policy and market access firm in Washington DC. Over 9 years, she successfully founded and sold The Neocure Group. Before Neocure, Richner was Vice President, Global Government Affairs, Reimbursement at Boston Scientific Corporation. Randel has been actively engaged in policy initiatives with US Congress and CMS for many years, including appointment as the first industry representative on the Executive Committee (EC) and Medicare Coverage Advisory Committee (MCAC). She serves on several boards, including the Executive Dean’s Advisory Board, University of Michigan’s School of Public Health. She is a lecturer at Dartmouth, University of Michigan School of Engineering and Pharmacy and a Griffith Leadership Fellow at the University of Michigan School of Public Health. Richner started her career in health as a practicing dialysis nurse at U of M and Maclaren Hospital in Petoskey, Michigan.
The Impact of Digital Health

...from Apps, to refined diagnoses to the “digital doctor”
FDA Steps to Regulating the Complexities of AI/Machine Learning

Fundamental Principles:
• Consider SaMD Guidance
• Based on core fundamentals behind Risk-Based Approach
• Total Product Life Cycle

* Issued April 2019