Agenda

• AbiliLife’s Story
• Where to Start and How to Begin
• FDA Strategies and Opportunities
• FDA Labeling
• The Reimbursement Framework
• The Integrated Regulatory & Reimbursement Strategy
• AbiliLife Pre-submission
• Final Conclusions
The Product

**Intended Use/Indication for Use:**
Back brace designed specifically for Parkinson’s patients.

Rolls shoulders up and back for more natural posture.

Rigid back panel supports from tailbone to the top of the shoulder blades.

**Classification:** I, Exempt  
**Regulation:** 21 CFR 890.3490  
**Description:** Truncal Orthosis  
**Code:** IQE

Reg.& Listed # 3011170501
DME-HCPCS Code L047
The Journey

1989

2009

2013

2014

2015

2016

2016
Medical Device Entrepreneurs Address an Unmet Medical Need Through Novel Technology

CONCEPTUAL FRAMEWORK

• Personal Experiences
  • Product Vision and Design

• Novel Technology
  • Little/No Precedent

• FDA Purview
  • Potentially rate and cost limiting

• Reimbursement (ROI)
  • Separate from FDA strategy

• Investor Relationship
  • Separate from FDA Strategy

END GOAL: ACCESS to Intended Medical Population
Where to Start and How to Begin
YOU THINK THE FDA IS WELL INTENTIONED, BUT WISH IT WOULDN’T HOLD YOU BACK IN YOUR AIM TO SAVE THE WORLD.
ACCESS = PRODUCT SUCCESS = *Integrated* Regulatory + Reimbursement Strategy
FDA MISSION: Protect & Promote Health

For Medical Products (Drugs and Devices)

EFFICACY

SAFETY

QUALITY

...POSTMARKETING SURVEILLANCE (safety, supply, manufacture)
FDA Regulates:
$1 trillion worth of products a year

Key FDA Legislation:
Guided by Public Health Events
(> 100 yrs experience)

Legally marketed toxic elixir killed 107 people, including many children

1938: Federal Food, Drug, and Cosmetic (FD&C) Act - safety, factory inspections, labeling

EU thalidomide tragedy and FDA's vigilance that prevented the drug's marketing in US

1962: Kefauver-Harris Amendments - strengthened safety rules, prove effectiveness

Faulty medical devices (including Dalkon Shield) had caused 10,000 injuries, including 731 deaths

1976: The Medical Device Amendments - safety, effectiveness safeguards for devices
FDA Prioritizes: Innovation to Speed Cures and Treatments

➢ Food and Drug Administration Safety and Innovation Act - FDASIA (2012)

➢ 21st Century Cures Act (2016)

- Expedited programs*: Fast Track, Accelerated Approval, Breakthrough Designation, Priority Review, Humanitarian Device Exemption, Expedited Access Pathway, Regenerative Medicine Advanced Therapy
- De Novo Pathways for New Medical Device Technology
- Strengthening Clinical Trial Enterprise
- National Evaluation System for Health Technology
- Patient Focused Product Development
- Real-World Evidence
- Balance Pre-Post-Approval Requirements
- Drug and Device Development Tools

➢ Alliances
- Academia: CERSI, OSEL (includes CMU)
- Global Health Authorities: ICH, IMDRF

*: without lowering standards
2013-2017: Chronic Fatigue Syndrome and Myalgic Encephalomyelitis, Lung Cancer, HIV, Narcolepsy, Idiopathic Pulmonary Fibrosis, Heritable Bleeding Disorders, Inborn Errors of Metabolism, Pulmonary Arterial Hypertension, Fibromyalgia, Sickle Cell Disease, Alpha-1 Antitrypsin Deficiency, Parkinson’s Disease and Huntington’s Disease, GI Disorders, Chagas Disease, Breast Cancer, Female Sexual Dysfunction, Non-tuberculous Mycobacterial Infections, Psoriasis, Neuropathic pain associated with Peripheral Neuropathy, Organ Transplant, Sarcopenia, Autism, Alopecia Areata, Hereditary Angioedema
FDA Opportunities and Strategies
FDA is an Invaluable Resource

Engage Early and Continuously
Build Lasting Relationship grounded on Collaboration & Integrity

PARTNER
Expedited Product & Label Development for ACCESS

LEARN
FDA Workshops, Webinars, Blogs

VOICE
Comments on draft Guidances/Policies

COMPETE
Access to Competitor/Precedent Label, Data, Strategies

ASSIST
FDA Initiatives, Speaker Forums

Build Relationship with Patients, Healthcare Community AND Investors
FDA Enhances Transparency & Learning

Blogs, eNotifications
CDERLearn
CDRHLearn
FDA Meetings, Conferences and Workshops

Basics
➢ Guidances
➢ White Papers
➢ eCFR
➢ Publications
➢ Blogs
➢ Workshops
➢ Federal Register (Regulations.gov)

Product Specific
➢ Label
➢ Review Summaries
➢ Product Recalls
➢ Safety Alerts
➢ Inspection Findings
➢ Advisory Committee Meetings

Current Information & Opportunity to Comment

Competitive Intelligence for Product Differentiation
3 Fundamentals for Expedited Product Development

FDA Submission Strategy & Product Differentiation

➢ Start with **Labeling Development**
  - What is the product and its claims (i.e. the ‘pitch’)
  - THE document for prescribers, patients, caregivers

➢ Build with **Benefit/Risk Framework**
  - What performance, efficacy, safety, quality studies - to validate the label

➢ Optimize with **FDA Engagement**
  - How to achieve label claims & streamlined development pathway, leverage new initiatives, align on submission strategies
What is Labeling?
What is Labeling

Summary for safe, effective use

For Healthcare Professionals to guide prescription

For Patients, Caregivers for use, decision making

Basis for Advertising, Promotion

Preventing Misbranding

DRUG
Indications
Contraindications, Warnings, Precautions
Dosage
Mechanism of Action
Clinical Pharmacology
Safety
Efficacy
Supply

DEVICE
Intended Use
Indications for Use
Contraindications, Warnings, Precautions
Instructions for Use: Physician, Patient
Device Description
Specifications
Safety
Effectiveness
What is a Drug or a Device?

Per the FD&C Act
DRUG or DEVICE defined by its INTENDED USE

Intended for use in DISEASE

➢ Diagnosis
➢ Cure
➢ Mitigation
➢ Treatment

Intended to AFFECT STRUCTURE or any FUNCTION of the body

Does not achieve any of its primary intended purposes through CHEMICAL ACTION within or on the body
((Device only)
Case Study: Mar 2017
The NY General's office settled with three mobile health apps alleged misleading claims and irresponsible privacy practices

➢ Adidas subsidiary Runtastic

➢ MIT Media Lab spinoff Cardiio

➢ Matis, maker of "My Baby's Beat"

Did not function as advertised

Made misleading claims

Did not protect sensitive user information
Labeling Strategy & Product Differentiation drive Submission Strategy

Identify Least Burdensome Pathway to Achieve Desired Labeling

Figure Source: FDA
De Novo Pathway for Startups

Increasing Trend for New Technology

Devices that aren’t comparable enough to a marketed device

Generates New Classification Regulation, Class I/II

★ FDA eager to engage on New Technology

★ No Submission Fee

★ Reasonable Review timelines (120 d)

★ Directly contribute to New Classification Regulation (guided by Proposed Labeling!)

★ First to Market
What is FDA Engagement (no fees)

**Formal Meetings**

**DRUGS**
- Type A, B, C Meetings
- Pre-IND
- End-of-Phase 1
- End-of-Phase 2 (EOP2)
- Pre-NDA
- During and Post-NDA

**DEVICES**
- Pre-Submission
- Informational
- Study Risk Determination
- Agreement Meeting
- Determination Meeting
- Submission Issue meeting
- Day 100 Meeting

Also available via Phone, Email
Fifteen months after the Boulder, CO-based biotech said that it had the data needed for its first approval of binimetinib for NRAS-positive melanoma, execs are walking back the application and its plans for a launch.

In a statement out Sunday evening, Array $ARRY said that after getting feedback from the FDA, execs “concluded that the clinical benefit demonstrated in the Phase 3 NEMO clinical trial would not be found sufficient to support approval of the NRAS-mutant melanoma NDA.”

Shares of Array dropped 26% in pre-market trading Monday.
Engaging with FDA as a Startup To Ensure ACCESS to Intended Population

➢ Start with Label Development
  - What is the Indication/Use? How is it meaningful to patients? What claims to differentiate, market position, present to Investors?

➢ Build with Benefit/Risk Framework
  - Cost/Timeline/Resources based on Labeling Strategy and FDA Innovation, Guide Fundraising strategy, Highlight strengths to differentiate

➢ Optimize with FDA Engagement
  - Leverage all available resources, identify least burdensome strategy(s), Explore novel approaches to enhance value, Gain visibility by engaging in initiatives
The Reimbursement Framework
...but don't ask me to explain the Medicare drug benefit program...

\[ e = mc^2 \]
Reimbursement: Essential for ACCESS

**LABELING** ➔ **COVERAGE** ➔ **CODING** ➔ **PAYMENT**

**Payers**
Seek information on **EFFECTIVENESS, SAFETY & COST-EFFECTIVENESS**

- Centers for Medicare & Medicaid Services, DHHS
- Formed by the Social Security Act
- Seeks Health Care Economic Information

Similar Criteria; Interagency Agreements, Contracts
CMS’ Evolving Strategies share commonalities with FDA’s Guidances, Innovation Initiatives

Transitioning from a Fee for Service (FFS) system to a payment system based on quality and value

6 Goals to improve the quality of care

1. Make Care Safer
2. Strengthen Person and Family Engagement
3. Promote Effective Communication and Coordination of Care
4. Promote Effective Prevention and Treatment
5. Work with Communities to Promote Best Practices of Healthy Living
6. Make Care Affordable
The Integrated Regulatory & Reimbursement Strategy
FDA vs CMS: Integrate and Engage Early

GENERAL Approach - Fragmented
1. FDA approval/clearance
2. Approval for coverage and payment
3. *May need additional studies to address Payer requirements*

INTEGRATED Approach - Simultaneous
Leverage shared evidence source for both Agencies while addressing criteria for decision making
CMS and FDA’s Regulatory Review & Coverage Coordination

Rochelle Fink, M.D., J.D.—
FDA-CMS Liaison
Center for Devices & Radiological Health
U.S. Food and Drug Administration

Program’s Future

FDA Review Team  Manufacturer  Payer

FDA decision  CMS decision
Concept  Regulatory  Payment  Patients

Regulatory
Concept  FDA decision  Payment  Patients

Payer decision
CDRH Innovation:

Payer Communication Task Force (PCTF)

➢ Opportunities to Obtain Payer Input Simultaneously with FDA
  a. Pre-Submission Participation
  b. Parallel Review Program

➢ Potentially shorten time between FDA approval/clearance and actual coverage decisions

➢ By communicating earlier, design clinical trials for regulatory approval/clearance and positive coverage determination

➢ Participating Payers: CMS, BlueCross BlueShield, Humana, Kaiser Permanente, NICE (UK!)

→ Discuss and Align on Clinical program with FDA + Payer at Pre-Submission Meeting
→ FDA PCTF co-ordinates participation of CMS + Other payers
Parallel Review Program: The Stats

2011: Pilot Program initiated
2013: Pilot Program extended
2016: Program fully implemented
> 60 inquiries, 29 applications
Several Pre-Submission Meetings have likely occurred

2014

FDA News Release

FDA approves first non-invasive DNA screening test for colorectal cancer
Collaboration with CMS contributed to proposed Medicare coverage

2016

FoundationOne® Accepted by FDA and CMS for Parallel Review and FDA Expedited Access Pathway
Engaging with FDA & Payer as a Startup for Expedited ACCESS to Intended Population

➤ Start with Label Development
  ○ Address FDA and Payer needs - focus on the value to patients, caregivers, medical community

➤ Build with Benefit/Risk & Cost-Effectiveness Framework
  ○ Address FDA and Payer needs in pivotal study

➤ Optimize with FDA & Payer Engagement
  ○ Obtain FDA clearance/approval and Local/national coverage in a timely manner
AbiliLife Pre-Submission
Label Development: Differences in wording impacting Evidentiary Requirements and Submission Strategy

Alert for High Fall Risk

Versus

Prevention of Fall

*business decision
Pre-Sub Meeting led to Portfolio Enhancement Opportunities

BEFORE Pre-Submission

- 1 Medical Device pathway - Fee for Subm.
- FDA purview (?) of Non-Device Platform
- FDA assistance (?) for CMS engagement
- Interaction with CDRH Review Branch
Pre-Sub Meeting led to Portfolio Enhancement Opportunities

AFTER Pre-Submission

- 1 Medical Device pathway - No fee
- 3 FDA Designations for Platform - No Fee
- Streamlined Strategies for Studies
- Facilitated Engagement with CMS
- Facilitated Engagement with Private Payer
- Expanded scope of FDA Interactions
Software Development Prototype

![Software Development Prototype Image]

Temp for 2017-04-06

![Temperature Graph]
Continuum of CDRH Engagement to Optimize Regulatory & Reimbursement Strategy

Alignment of Label/Development/Submission Strategies

➢ F2F Pre-Submission Meeting
  ○ Several email/phone calls with Document Control Center, Branch Chief and Lead Reviewer prior to meeting

Additional Product Registration Strategies

➢ Phone/Email with Master File (MAF) Office

➢ Phone/Email with Medical Device Development Tool (MDDT) Program Office

➢ Phone/Email with OSEL

CMS Engagement

➢ Phone/Email with CMS Point of Contact

➢ Phone/Email with PCTF office

Followup on Optimized AbiliLife Portfolio

➢ T/C with Lead Reviewer
FDA Engagement & Learning: Continuous, Multi-Faceted
Impact of FDA Engagement on External Communications

Portfolio Value Enhancement

Integrated processes between FDA strategy and business development

E.g. Manufacturer, Distributor, Investor, Grant Applications

Value Assessment of Portfolio
Summary of Learnings as an Entrepreneur

• Interact with the FDA early and often
• Make sure that your investors understand the FDA process
• View the FDA as a partner and not as a foe
• Understand the value of having an FDA approved product for when you value your company