FDA Vision for Novel Technologies
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Agenda
AbiliLife’s Story
Understanding the FDA
Beyond First FDA Marketing Authorization
AbiliLife FDA Engagement and Product Roadmap
Conclusions
The Product

Intended Use/Indication for Use:
Back brace designed specifically for neuromuscular patients (i.e. Parkinson’s disease, ALS, MS).

Rolls shoulders up and back for more natural and healthy 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

Carnegie Mellon University

2009

Biomedical Engineering

2013

alphalab gear

2014

CMS

2015

NSF

2016

FDA

2016
Post-Marketing: 2016 - Today

- Originally designed for PD patients
- 600 pre-existing codes didn’t include PD
- Sole-providership helped with payment
- Plans to submit for a PD specific claim
The Web:
FDA Strategy Interlinked with Innovation And Business Needs

Meet Patient, Caregiver, Business Needs

Advance Science

FDA Strategy

Personal Experiences

Novel Technology

Investors

Grant Applications

Pricing, Market Share

Payer, Reimbursement

Patent Claims

Patient, Provider feedback
Understanding the FDA
FDA Regulates: $1 trillion worth of products a year
FDA Mission: Protect & Promote Health
FDA Modernization: Streamline, Expedite, Incentivize, Least Burdensome Approach*

*: Minimum amount of necessary information, most efficient manner, right time
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, thousands of babies with malformed limbs - 1962: Kefauver-Harris Amendments safety rules, prove effectiveness

Faulty medical devices (Dalkon Shield) - caused 10,000 injuries, 731 deaths 1976: The Medical Device Amendments safety, effectiveness safeguards for devices

2017-2018 Flu Season- many deaths including > 100 children; vaccine not fully effective. 2018: FDA plan of Action including updating vaccine requirements
Is it a Drug or a Device?
Per the FD&C Act

Intended for use in DISEASE

➢ Diagnosis (disease, conditions)
➢ Cure
➢ Mitigation
➢ Treatment
➢ Prevention

AFFECT STRUCTURE or any FUNCTION of body

CHEMICAL ACTION within or on body (Drug only)
Medical Products

&

FDA Submission Pathways

**DRUGS:** Small Molecule, Biologics
NDA, BLA...and Supplements
ANDA, 505B(2)

**DEVICES:** Hardware, Hardware+Software, Software only
Exempt, 510(k), De Novo, PMA, HDE

**COMBINATION PRODUCT**
Jurisdiction, Request for Designation
Highlight: De Novo Pathway

NOVEL TECHNOLOGY, not comparable to a marketed product

- Promote New Technology
- Reasonable Review timelines (150 d)
- Create New Classification Regulation

Trailblazing...unique device showcasing new technology
- First to Market
- Delay competition

DATA SOURCE: FDA
**FDA Drug/Device Development Overview**

Drug and Device Development

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>DISCOVERY/CONCEPT</td>
<td>Research for a new drug or device begins in the laboratory...maker space....garage</td>
</tr>
<tr>
<td>RECLINICAL</td>
<td>Laboratory and animal testing to answer basic questions about safety, prototyping</td>
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<tr>
<td>CLINICAL</td>
<td>Human testing for safety and effectiveness</td>
</tr>
<tr>
<td>FDA REVIEW</td>
<td><em>Thorough</em> examination of all submitted data; approval or non approval</td>
</tr>
<tr>
<td>POST-MARKET MONITORING</td>
<td>Monitoring safety once products available for use by public</td>
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Key Review Elements

Based on:
 Valid Scientific Evidence
 &
 Totality of Evidence

EFFICACY

SAFETY

QUALITY

Benefit > Risk
Evidentiary & Manufacturing Standards
Risk Management

Benefit > Risk
Product Label
Market Authorization

Manufacture
Safety
Real World Use
New Research

SURVEILLANCE

Product Label Update
Product Optimization
## Product Label

**Primary source for differentiation, patient access, commercial success**

Basis of FDA review, approval

Guide:
- Effective use
- Prescription
- Patient decision

Source:
- 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
FDA Prioritizes: INNOVATION

‘...to Speed Cures and Treatments without Lowering Standards..’

Streamlining and Modernizing

New Technology
3D Printing, Model informed development, Software as Medical Device, Clinical Decision Support, Patient Decision Support........

Small Business Incentives
User Fee Reductions, Grants (SBIR), SBIA, DICE, Small Business Investments, Licensing and Collaboration.......

Other Incentives
Rare Disease programs, Expedited/Priority Reviews, Fast Track, Breakthrough, Priority Review Vouchers..........

Alliances
CMS and Private Payors, Academia (includes CMU), Small Business, Global Health Authorities........
FDA Prioritizes: INNOVATION

Digital Health / AI

2017: Software Precertification Program
Digital health technology with focus on software developer or digital health technology developer
- Apple
- Fitbit
- Johnson & Johnson
- Pear Therapeutics
- Phosphorus
- Roche
- Samsung
- Tidepool
- Verily

2018: AI/Machine Learning Guidances
- Clinical Decision Support Software
- Patient Decision Support Software
STARTUP IS TOUGH
Novel Products
Competition
Budget
Resources
Funding
Investors
Timelines
ROI
Evolving Landscape
Information Overload
Unclear Pathway

REG STRATEGY HELPS
START EARLY
Grounded in Science, Data, Evidence, Quality
Novel Product Development Approaches
Adapt to pivots, unexpected data, resource constraints
Optimize design to support desired label

ENGAGE WITH FDA
Opportunities, Incentives Expedite
Competitive Differentiation Business Strategies

GET DESIRED LABEL
3 FUNDAMENTALS
Of Regulatory Strategy

‘...begin with the end in mind..’

1. Labeling Development
   What is the Indication and desired claims (pitch, patent, differentiation, reg intell.)

2. Benefit/Risk Framework
   What performance, efficacy, safety, studies - to substantiate label (roadmap, funding, investor plans, timelines)
   What Quality measures to ensure continued safety and efficacy (culture of excellence)

3. FDA Engagement (long-term partnership)
   How to achieve label claims
   Opportunities, Incentives to streamline
   Leverage new initiatives
   Lower cost and time
   Align on submission strategies
FDA Engagement

From Discovery to Post-marketing
Several Meeting Types; no cost

Public Events and Workshops

Social Media

Review and Submit comments
Guidances, Legislation, Proposals

Patient Engagement
Public-Private Consortia

Formal FDA Meetings:
e.g. Pre-Submission, Pre-IND, EOP2, Pre-NDA.
Regulatory Intelligence

Continual evolution of landscape

Continual learning is a must

FDA Tutorials
CDER Learn
CDRH Learn

Basics
Code of Federal Regulations
Guidances
White Papers
Publications
Blogs
Priorities
Workshops
Federal Register (Regulations.gov)

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

Current and Emerging Regs
Expedite, Streamline
Incentives
Comment

Precedents
Competition
Differentiation
Small Business Case Study

FDA Partnership

Health + Ancestry Service

Get an even more comprehensive understanding of your genetics. Receive 75+ online reports on your ancestry, traits and health - and more. learn more
2009
FDA Interactions and feedback on reg requirements

Aug 2013
Launch Personal Genome Service (PGS)
No FDA review

Nov-Dec 2013
FDA Warning
Product Suspension

2014......
FDA Engagement on Reg Pathway

2015
De Novo Granted
PGS
Bloom Syndrome

2017
De Novo Granted
PGS
BRCA1
BRCA2

Mar 2018
De Novo Granted
PGS
Hereditary Thrombophilia, Alpha-1 Antitrypsin Deficiency,
Alzheimer’s Disease, Parkinson’s Disease, Gaucher Disease T1,
Factor XI Deficiency, Celiac Disease, G6PD Deficiency,
Hereditary Hemochromatosis Early-Onset Primary Dystonia

Participation in FDA Initiatives
Collaboration with Academia, Industry, Foundations (eg MJFF)
FDA allows marketing of first direct-to-consumer tests that provide genetic risk information for certain conditions

FDA authorizes, with special controls, direct-to-consumer test that reports three mutations in the BRCA breast cancer genes

Test only reports 3 out of more than 1,000 known BRCA mutations and negative result doesn’t rule out increased cancer risk
Small Business Case Study

Lack of FDA Engagement
2016
FDA Formal Meeting

- Office of Compliance
- Office of Device Evaluation
- Requirement of premarket submission to evaluate safety and effectiveness

2017
FDA Warning
FDA review of website Violations

Continued Marketing Eye Exam Mobile Medical App

- No FDA Submission
- No FDA Registration and Listing

ADULTERATION: No approved application

MISBRANDING: No FDA notification of intent to commercialize

FDA ACTIONS: Seizure, injunction, civil money penalties.....
FDA Letter Release, March 2018
Small Business Case Study

FDA Engagement...but… Uncompetitive Product Profile/Labeling
Analysts project blockbuster market

2014 FDA Approval

LABEL Limitations
- Require reduced-calorie diet + increased physical activity
- Only 5-10% weight loss
- Boxed Warning: Suicidal Thoughts; access limitations
- Adverse effects (nausea); poor compliance

Poor uptake by patients, physicians, payers

Mar 2018 Orexigen files for bankruptcy

High % US population obese or overweight

Poor uptake by patients, physicians, payers

Mar 2018 Orexigen files for bankruptcy

Orexigen Therapeutics, Inc. plans for near-term sale using Chapter 11 of U.S. Bankruptcy Code

Orexigen
Beyond First FDA Marketing Authorization
Patient Access

Reimbursement

(Revenue, Return on Investment)

FDA approved PRODUCT LABEL

Safe and Effective

Cost-Effective? Reasonable and Necessary?

Quality of Care and Value?

COVERAGE CODING PAYMENT

Quality of Care and Value?
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**
Obtain Payer Input on Development Program/Proposed Label simultaneously with FDA
Post-Marketing Experience

Safety profile
- Intended population
- Potentially other populations/Indications
- Safety issues
- Manufacturing issues

Real-World Evidence Patient, Physician, Caregiver
- New Tx approaches
- Regulatory decisions
- Coverage decisions
- Clinical practice decisions

Big Data Access and Analytics
- Advance benefit-risk assessment

Utilize for Product Optimization
AbiliLife
FDA Engagement
and
Product Roadmap
Label Development: Differences in wording impacting Evidentiary Requirements and Submission Strategy

Alert for High Fall Risk $$$

Versus

Prevention of Fall $$$$$$$$$$
Continuous FDA Engagement

**2016**
- FDA Pre-Submission Meeting: Full portfolio
- CMS Contact
- Comment on draft FDA Guidance
- Member, Coalition for Software guidances

**2017**
- Pre-Submission Supplement: Software Platform
- Followup FDA T/Cs
- Battelle/CMS contact on Quality Payment Strategies
- FDA MDDT designation Submission

**2018**
- Pre-Submission Supplement: Portfolio, Life Cycle Optimization, Rare disease development
- Parallel FDA-CMS feedback
- Private Payer, VA engagement
• Medical Device Pathway: Traditional
• Options for off-the-shelf software platform
• FDA assistance for CMS Engagement
2016: AbiliLife Portfolio- AFTER FDA Pre-Submission Meeting

- Optimized Portfolio Strategy
- Novel Medical Device pathway
- Potential FDA Designations for Platform
- Streamlined Strategies for Studies
- Facilitated Engagement with CMS
- Support for Grant Application
2017: FDA Pre-Submission Supplement Meeting on Software Platform

- Research Tool strategy
- Software Regulatory Needs and Strategic Options
- Support for Grant Application
2017-2018: Calibrace+ Post-Marketing Experience

CORE COMPETENCIES

Calibrace+

Orthotic Back Brace for Spinal Disorders

- Certified durable medical equipment company (Board of Certification/Accreditation)
- HCPCS codes L1310; L0650; L0651; L0648; L04574

PAST PERFORMANCE

- Hospital Providers:
  - VA Denver Healthcare System
  - VA Philadelphia Healthcare System
  - VA Pittsburgh Healthcare System
- Insurance Providers:
  - TriNet
  - Medicare
  - Blue Cross Blue Shield
  - Cigna

DIFERENTIATORS

- Utility Patent - Pending
- Clinical Trial - Pending
- National Science Foundation STTR grant Phase I

Calibrace+

- Extension of population: Neuromuscular diseases
- Extension of indication: Lower back pain

Smart Calibrace

- Extension of population and subgroups
- Patient Reported Outcome endpoints meaningful to both FDA and CMS

PORTFOLIO OPTIMIZATION

ICD-10 code, L0457; eligible for use for over 600 diagnosis codes

Real-World Evidence
Additional Device Description

Claim:

Only back brace that improves posture and balance by lifting the shoulders up and back and giving entire back support
2018: AbiliLife Optimized Portfolio based on Post-Marketing Experience - FDA Pre-Submission Supplement Meeting

● Briefing Document in progress
Conclusions
Impact of FDA Engagement on External Communications

Portfolio Value Enhancement

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
FDA is an Invaluable Resource

LEARN
FDA Workshops, Webinars, Blogs

PARTNER
Expedited Product & Label Development

COMPETE
Access to Competitor/Precedent Label, Data, Strategies

VOICE
Comments on draft Guidances/Policies

ASSIST
FDA Initiatives, Speaker Forums
What is Benefit-Risk Framework

Benefit > Risk

Valid Scientific Evidence
Well-Controlled, Well Designed, Well Conducted, Well Documented, Qualified Experts

Totality of Evidence
Clinical, Non-clinical, Performance, Patient Perspectives, Post-Marketing, Novel Technology etc.

DRUG

Ensure that the Benefits outweigh its Risks

➢ Analysis of Condition
➢ Current Treatment Options
➢ Benefit: Evidence, Uncertainties, Conclusions, Reasons
➢ Risk: Evidence, Uncertainties, Conclusions, Reasons
➢ Risk Management

DEVICE

Reasonable Assurance of Safety and Effectiveness (RASE)

➢ Benefit: Type, Magnitude, Probability, Duration
➢ Risks: Severity, Types, Number, Rates, Probability, Duration
➢ Other: Uncertainty, Patient Perspectives, Alternative Treatments, Risk mitigation, Post-market data, Novel Technology