Challenges and Opportunities in Combination Product Development Industry Perspective

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Combination Products Session

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Optimal State?

Current State?

QUIZ

HOW MANY CONSULTANTS DO YOU NEED TO CONVINCE THE COMPANY THAT THEY HAVE A COMBINATION PRODUCT?

Outline

Challenges:

- Industry Structural and Business Environment Factors
  - Device Perspective
  - Drug Perspective
- Technical Considerations
  - CMC
- Regulatory Scheme/Policy
  - Risk based?

Opportunities:

Notice

Content Based on Experience in Industry and a Recent Informal Survey

Observations expressed here does not necessarily represent broad industry position or my clients.

INDUSTRY STRUCTURE AND ENVIROMENT

Device Manufacturers' Perspective

- Industry Profile
  - Mostly small companies, most fewer than 25 employees
  - Mostly "510(k)" type companies
  - "Faster" product iterations
  - Difficulty in securing pharmaceutical partners - A significant challenge for cross labeled products
  - Significant decrease in investment in medical products
  - Medtech Investors expect fast returns*
    - Expectation of a 3 year return
  - Struggle with the quantity and depth of data required by drug reviewers

* Patient Capital 3.0: NVCA and MedIC, April 25, 2013

Device Manufacturers' Perspective

- Technical Expertise
  - Engineers, material scientists, hardware/software experts, etc.
  - No in house "CMC" competency
    - Significant investment for different talent pool – CMC, biopharmaceutics; pharmacology, toxicology, clinical
    - Challenge of recruiting and retaining technical talent
  - Lack of awareness and know-how to address technical requirements related to drug constituent part –e.g. drug/device compatibility or "intra-operability"
- Company culture and approach
  - Naiveté of complex requirements for combo products
  - Expectation of ability to "negotiate out" requirements

Device Manufacturers' Perspective

- Regulatory/Quality Personnel
  - Most without drug development experience
  - Lack of technical knowledge to manage drug supplier properly
  - Challenge of knowing all the applicable requirements
  - Difficult to keep current

Device Manufacturers' Perspective

- Interactions with FDA
  - CDRH viewed as more "accessible"
  - Cultural shock when dealing with CDER
    - Very limited access to reviewers and CDER management
    - Interactions very regimented and formal
    - Existence of many well established guidances (e.g. ICH Guidances) in drug industry – viewed as "burdensome"

Drug Manufacturers' Perspective

- Industry Profile and Culture
  - Smaller Number of companies, many large multi-nationals
  - Small companies' personnel often come from large pharma
  - Investors have more patience - clinical data is a given
  - Lack of awareness that their product is a "combo product" – e.g. inhalers; transdermal patch, etc.
  - Often view device manufacturer as hostile competitor (i.e. "generic"). This is especially challenging for "cross labeled" combo products.
  - Often view device requirements as "unnecessary"
    - E.g. Human Factor, biocompatibility

Drug Manufacturers' Perspective

- Technical Expertise
  - No device expertise
  - Drug scientist may view device requirements as less "scientific" – e.g. Leachables/extractables vs biocompatibility
  - Often "outsourced" device expertise – e.g. via partnership/supplier
  - Some large pharma company building internal competency

Drug Manufacturers' Perspective

- Regulatory/Quality Personnel
  - Easier transition from drug to device than vice versa
- Interactions with FDA
  - No direct interaction with device reviewers. Some requirements viewed as "unnecessary".
  - Wish the requirements will go away or CDER will "overrule" the requirements

TECHNICAL CONSIDERATIONS

Technical Data Challenges

- Apparent divergent requirements – some confusion from both technical and regulatory personnel
- Examples:
  - Pharmaceutical Development (ICH Q8) vs Design Controls in Q.S. Regulation and Combo Product cGMP
  - Human Factor from CDRH and Medication Errors from CDER
  - Manufacturing process validation guidances (CDER vs GHTF)
  - Biocompatibility guidance/ISO 10993 vs leachables/extractables for container/closure systems

Technical Requirement Challenges

Some examples which may benefit from clarification:

- Device verification/validation vs drug manufacturing process validation
- Batch vs continuous manufacturing
- Application of related CDER guidances, e.g.
  - Analytical method development and validation; In-vitro/In-vivo correlation; OOS investigation

REGULATORY SCHEME AND POLICY

Regulatory Scheme

- Regulatory Scheme for Combo Products
  - Not risk based, from a device perspective
    - No risk “classification” like devices
    - Data requirements the same for “high risk” vs “lower risk” combo products
  - Not “least burdensome”
  - High uncertainty
    - Regulatory path
    - Data Requirement
    - Time frame to approval
    - Unfamiliar with Lead Center “Rules of Engagement”
    - Many “case by case” basis

Regulatory Challenges

- Regulatory Scheme for Combo Products often unclear
  - Few statistics available
  - General lack of knowledge of which products are combo products
  - Status of ICA
  - Applicability of precedents

OPPORTUNITIES

Opportunities

- Increase Transparency: FDA can publish list of approved combo products and link to:
  - CDER Review summaries from drugs@fda
  - PMA SSE
  - 510(k) summaries
  - CBER SBA
- Early communication from Lead Center that the product is being regulated as a combo product
  - Proactive early engagement of consulting Center
- Agency alignment of approaches and clear delineation of final decision authority
  - CDER vs CDRH approach

Opportunities – Education and Outreach Strategy

- "Cross Pollination" of Education and Outreach – CDRH and OCP
  - Trade Associations, e.g.
    - PhRMA
    - AdvaMed
    - BIO
    - GPIA
  - [Drug] Scientific Societies, e.g.
    - DIA
    - AAPS
    - PDA
  - Other Training Venues
    - MedCon
    - MD&M
- "Combination Product" Advice On FDA Web Site?

Opportunities

- Leverage GMP Regulations for Combo Products to educate industry
  - Target technical/R&D staff
  - "Preamble" very helpful – expand training and interpretation
  - Articulate all related FDA guidances that may apply. For example:
    - Stability Guidance
    - ICH Q7, 8, 9, 10, 11?
    - Process Validation?

Opportunities

- Adopt policy for “risk based” approach? For Example:
  - Legacy products which have long history of human use
  - Longer transition period of “new” requirements
  - Active training, partnering with industry
- PMOA
  - Data requirement in line with relative contribution of each constituent part, esp. when PMOA is the device constituent part
  - Focus on safety vs safety and effectiveness of the drug constituent part

Opportunities

- Combo GMP Guidance Development
  - Seek broad input from all stakeholders
  - Host forum for open discussion for requirements (e.g. SUPAC)
- Chemical Action and Classification Guidance
- Companion Diagnostic Guidance
- Interpretation and Application of Cross Label Products
  - “Cross labeled” products are the “exception” – Preamble to 21 CFR Part 3 Final Rule

Rewards and Positives

- Combination Products are Growing double-digit*
- OCP is accessible and quite responsive
- Binding decision - RFD
- Some formal process/policies established by OCP
- Companies that can crack the “code” can enjoy many years of exclusivity
- Companies that have more resources may do a lot better in this arena

* Research and Markets, July 23, 2010

Thank You!

Questions/Comments?

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