

# Biotechnology 2007

---

## **NEW DEVELOPMENTS AND THE REALITIES OF DEALING WITH THE FDA IN TODAY'S REGULATORY ENVIRONMENT**

Bruce F. Mackler, Ph.D.,J.D.  
Life Science Management Group  
[bmackler@Lsmgrp.com](mailto:bmackler@Lsmgrp.com)

# A. ATMOSPHERE AT FDA

---

## □ MORALE WITHIN FDA

### ■ Congressional Oversight

- impact of prior drug safety hearings on reviewer attitudes & power
- potential impact of Democratic Congress
  - new legislation and oversight

### ■ Workloads

### ■ Reorganizations

### ■ Implementation of Regulatory Initiatives

## □ LEGACY OF WHITE HOUSE INTERFERENCE

### ■ Abortion Issues

- RU 486
- Plan B Morning After Pill
  - Delay in Senate hearings on FDA Commissioner

### ■ Biogenerics

- Human Growth Hormone precedent

# B. FDA APPROVALS (CDER)

---

## □ **18 NEW DRUGS APPROVED IN 2006**

- 32% NEW INNOVATIVE DRUGS
- 68% CHANGES IN OLD DRUGS

## □ **TIMEFRAMES**

- 15 MONTHS AVERAGE FOR APPROVALS
  - VERY FEW RECEIVED APPROVALS WITHIN 10 MONTHS
  - PREPONDERANCE OF 'APPROVABLE' LETTERS
  - EMEA 52 drugs approved by FDA 11 months before EU
- PRIORITY NDAs – 12 submitted
  - 7 - approved within 6 months
  - 2 - received approvable letters
  - 3 - still in their 6 month review

## □ **MESSAGE FROM THESE NUMBERS**

# C. PRESCRIPTION DRUG USER FEES (PUFA)

---

- **THE ORIGINAL PUDFA BARGAIN**
  - **Fees for more FDA Review Resources**
  
- **2006 - FULL NDA FEE - \$767,400**
  - **Lost revenues to FDA \$13,045,800**
    - **17 less NDAs than in 1999**
    - **Congressional Funding and New Mandates – food safety, bioterrorism, drug safety,....**
  
- **2007 - FULL NDA FEE - \$896,000**
  
- **TUFTS: \$802 million cost for new drug development**

# D. CRITICAL PATH INITIATIVES

---

## □ FDA'S NEW INITIATIVE

- Use current scientific tools to predict whether drug/biologic candidates will be safe & effective (to decrease Phase III failures)

### ■ Tools:

- Exploratory IND (eIND) – Phase 0 with reduced preclinical data requirements to assess PK/PD, biodistribution, micro-dosing, imaging,....
- Use of biomarkers as surrogates to predict efficacy
- Reduced cGMP requirements to facilitate earlier entry in Phase 0 & I clinical studies
- Use of screening IND to study closely related active moieties

# CRITICAL PATH INITIATIVE

conti

---

- **What is Old, Is New Again  
(21 CFR 361.1)**
- **Investment Paradigm Effect**
  - **facilitate an earlier proof of concept**
  - **allow selection of the best candidate from a group**
  - **earlier input from FDA based on eIND discussions**
  - **realities**
    - **reviewer acceptance & training in Initiative**
    - **lack of regulatory precedents to follow**
    - **toxicology (full vs. abbreviated)**
    - **non-cGMP laboratory manufacturing**

# E. PRE-IND MEETINGS

---

## □ REALITIES

- PUDFA Credit (none)
- Do you want to cancel your Pre-IND?
  - FDA gives you the answers to your questions 4-5 days before the scheduled Pre-IND meeting date.
- Technical Package only 50-60 pages
  - What do you focus on?
  - How much information does one provide?
- The Official Minutes
  - The answers are the minutes
  - Add your responses, but not change their answers
- When to schedule a Pre-IND in the development process?

# E. APPROVABLE LETTERS

---

- **Definition: FDA will approve your NDA/BLA if certain conditions are met.**
  - new preclinical and/or clinical data
  - manufacturing/analytical data
- **Need a Strategy & Follow-up with FDA**
- **Press Release must accurately reflect the reality of the requested data**
  - FDA reads your press release
  - SEC investigates/Lewis Hearing

# F. FOREIGN CLINICAL DATA

---

## □ STRATEGY CONSIDERATIONS

### ■ Where Do You Manufacture?

- Export (21 vs non-21 countries)/ QP in EU
- Satisfying Import requirements (EU v non-EU)

### ■ FDA Concerns:

- Comparable Standard Of Medical Practice to US
- Ethnic Factors – burden to convince FDA that then patient population comparable to that found in the US patient population

### ■ Regulatory Documentation

- GCPs
- Access to patient Source Data
- Disease characterization and progression,....

# G. BIOGENERICS

---

- **BIOSIMILAR (FOLLOW-ON BRANDED)**
  - **First Generation – ‘Biosimilar’ a Commodity Product**
    - **Is this a commercially viable product?**
  - **Second Generation – ‘Follow-on’ Branded Product**
    - **old drug plus new technology, value pricing?**
  - **Lesson learned – simultaneous development of 1<sup>st</sup> & 2<sup>nd</sup> generation**
  
- **Draft FDA Guidance (CDER)**
  - **Substitutable we will know it, when we see it**
  - **Non-Substitutable**
    - **Omnitrope (505(b)(2) NDA**
      - **FDA (100 pts) vs EMEA (200 pts)**
  
- **Congressional Legislation Pending**
  - **505 (b)(2) NDA process for drugs**
  - **authorizing biologic biogeneric process**

# H. Product Development Issues to Consider

---

- **Exploratory INDs**
  - Can it facilitate product development?
- **Screening INDs**
  - How to narrow choice where multiple moieties
- **Pharmacogenomics**
  - Use of genetic test to enrich patient responders
- **Clinical Endpoints**
  - QoL, improved physical functioning. improved tumor related symptoms, time to progression,....
- **Biomarkers**
  - Early integration/validation - Phase I & II
  - Salvage of data (71 Fed. Reg., 1429, 1/9/2006)

# I. Perspective on EU Clinical Studies

---

- ❑ **LACK OF HARMONIZATION OF CTA DOSSIER REQUIREMENTS WITHIN EU**
- ❑ **INCREASED NATIONAL BUREAUCRACY / UNCERTAINTY**
- ❑ **DIFFERENT INTERPRETATIONS IN WHAT AN INVESTIGATIONAL MEDICINAL PRODUCT IS**
- ❑ **NON-ACCEPTANCE OF QUALIFIED PERSON DECLARATION FROM THIRD COUNTRIES & SCOPE OF MANUFACTURING LICENSE REQUIREMENTS**

# J. RESOURCES

---

## ▣ LIFE SCIENCES DUE DILIGENCE & REGULATORY ANALYSIS

**Volume 1, Issue 1 October 2006**

**COURTESY COPIES AVAILABLE UPON E-MAIL  
REQUEST TO [bmackler@Lsmgrp.com](mailto:bmackler@Lsmgrp.com)**

### **Contact:**

**[Bruce F. Mackler, Ph.D., J.D.](mailto:bmackler@Lsmgrp.com)**

**Life Science Management Group**

**[bmackler@Lsmgrp.com](mailto:bmackler@Lsmgrp.com)**

**cell: 301-529-6984**

**ofc. 240-314-0450**

