# Issues in PET Drug Manufacturing

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# Topics

- ANDA process for FDG
- User fees
- Contract manufacturing

PETNET's perspective

# Colleagues

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# PETNET's ANDA process for FDG

*Observations—*

- June 2007: Submitted application
- May 2008: Preapproval inspections
- June 2008: Submitted additional copies due to administrative error in OGD
- April 2009: Microbiology questions received
- April 2010: Labeling questions received

# PETNET's ANDA process for FDG

*Concerns—*

- Yet to receive questions on CMC section
- Lengthy review process
- Lack of prioritization against PDUFA drugs
- Lack of PET experience in OGD

*Recommendations—*

- Office of New Drugs should drive the review process
- Inspections of PET manufacturing facilities should consider a centralized approach

# User Fees

*Observations—*

- PDUFA reauthorized in 2007
- Reduced 2008 establishment fees for PET facilities from $392,700 to $65,450
- Fee for applications that require clinical data is same as other NDA drugs ($1,178,000 in 2008)
- User fees do not apply to generic drugs

*Concerns—*

- Reduction in establishment fees is a good start
- Fees remain excessive given size of US market

# User Fees

*For example—*

- Total annual US market for FDG is approximately $300 million
- Assume 100 manufacturing sites are required for a nationwide supply of FDG
- If FDG was approved in 2008 with clinical trial data, the user fees would be:
  - Application: $1,178,000
  - Establishments: $65,400 x 100 = $6,540,000
- Total is about $7,700,000 or 2.6% of market

# User Fees

*By comparison—*

- Many individual therapeutic products have total annual sales more than 4x $300 million
- Number of manufacturing sites is much lower
- If a $1.2 billion "Product X" was approved in 2008 with clinical trial data, user fees would be:
  - Application fee: $1,178,000
  - Establishment: $392,700 x 2 = $785,400
- Total is about $2,000,000 or 0.2% of market

# User Fees

| | FDG | Product X |
|---|---|---|
| ***Market Size*** | 300 | 1,200 |
| ***Application Fee*** | 1.178 | 1.178 |
| ***Establishment Fee*** | 6.54 | 0.785 |
| ***Total User Fee*** | 7.7 | 2.0 |
| ***% of Market*** | 2.6% | 0.2% |

*Values in millions of $*

# User Fees

*Conclusion—*

- Existing user fee structure will create a significant barrier to innovation in the development of new PET biomarkers in the US
- User fees will limit public access to safe and effective PET imaging agents

*Recommendations—*

- Society/industry groups should lead an initiative to spearhead a fair and equitable user fee structure for PET

# Contract Manufacturing

*Observations—*

- Multiple production sites
- Different operators
- Different equipment

*How we ensure product uniformity—*

- Qualify facilities, operators and equipment to execute validated processes & methods
- System suitability to ensure equipment operability
- Clearly defined specifications and release criteria
- Routine QC on each batch prior to administration

# Contract Manufacturing

*Concerns—*

- Tendency to concentrate on chemistry module instead of the formulation and active ingredient
- Manufacturing standards focus on production and testing of a single biomarker at multiple manufacturing sites

*Recommendations—*

- Focus on active ingredient, impurity profile, and formulation
- Chemistry modules are equipment that can be qualified
- Innovators and contractors need to consider standards that enable production and testing of *multiple* biomarkers at *multiple* sites

# Summary

- ANDA process for FDG
  - Office of New Drugs should drive the review process
  - Inspections of PET manufacturing facilities should consider a centralized approach
- User fees
  - Society/industry groups should lead an initiative to spearhead a fair and equitable user fee structure for PET
- Contract manufacturing
  - Focus on the active ingredient, impurity profile and formulation instead of chemistry modules
  - Innovators and contractors need to consider standards that enable *multiple* biomarkers at *multiple* sites