Pediatric Advisory Committee
Risk-Based Assessment Proposal
for CDER Products

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Presentation Objectives

- Describe Risk-Based Assessment Proposal for the Center for Drug Evaluation and Research (CDER) Products to the Members of the Pediatric Advisory Committee (PAC)

- Solicit feedback from PAC Members about Risk-Based Assessment Proposal for CDER Products
Presentation Outline

- Brief Overview of Risk-Based Assessment Proposal Process

- Comparison to Current Review Process
  - Factors to consider products low safety risk
  - Abbreviated presentations to web-based reports

- Advantages of Risk-Based Assessment Proposal
Presentation Outline

- Brief Overview of Risk-Based Assessment Proposal Process
  - Comparison to Current Review Process
    - Factors to consider products low safety risk
    - Abbreviated presentations to web-based reports
  - Advantages of Risk-Based Assessment Proposal
Overview of Risk-Based Assessment Proposal

➢ Risk-Based Assessment Proposal is a modification to PAC review for certain CDER products that are designated “low safety risk”

➢ Factors to determine “low safety risk” CDER products built from existing criteria currently used for abbreviated presentations to PAC
Proposed CDER Product Safety Review Timeline

- FDA Adverse Event Reporting System (FAERS) collects adverse events reports
- Office of Surveillance and Epidemiology (OSE) creates Pediatric Post-Marketing Pharmacovigilance review plan
- OSE reviews safety and use data and writes Pediatric Post-Marketing Pharmacovigilance and Drug Utilization Review Draft
Proposed CDER Product Safety Review Timeline

Label Change

Data Collection Phase

Review Plan Phase
1 month

Meeting #1

Data Analysis Phase
3-4 months

Meeting #2

Low Safety Risk Product

Report Edit Phase
1 month

Post report on FDA website

Rehearsal Phase
4-9 months

Present product to PAC

Pediatric Advisory Committee Meeting, April 12, 2016
Proposed Factors Informing Whether CDER Product is a Low Safety Risk

1. No pediatric deaths or pediatric deaths likely attributable to disease progression.
2. No or few serious adverse events (SAEs) attributable to product.
3. No new safety signals identified by FDA through literature review, FAERS case review, drug utilization data review, and ongoing tracked safety issues for product or class of products.
4. Product adequately labeled for pediatric use including dosing information and adverse events included in product label.
5. There is little pediatric use or if the number of adverse events relative to the use is not concerning.
# Proposed CDER Product Safety Review Timeline

## Low Safety Risk Products

<table>
<thead>
<tr>
<th>Phase</th>
<th>Duration</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Collection</td>
<td>1 month</td>
<td>FAERS collects adverse events reports</td>
</tr>
<tr>
<td>Review Plan</td>
<td>3-4 months</td>
<td>OSE creates Pediatric Post-Marketing Pharmacovigilance review plan</td>
</tr>
<tr>
<td>Data Analysis</td>
<td>1 month</td>
<td>OSE reviews safety and use data and writes Pediatric Post-Marketing Pharmacovigilance and Drug Utilization Review Draft</td>
</tr>
<tr>
<td>Report Edit</td>
<td>1 month</td>
<td>Edits and clearance of Pediatric Post-Marketing Pharmacovigilance and Drug Utilization Review Report</td>
</tr>
</tbody>
</table>

- Federal Register notice published
- Open docket
Proposed CDER Product Safety Review Timeline

Low Safety Risk Product

Report Edit Phase
1 month

Post report on FDA website

Not Low Safety Risk Product

Rehearsal Phase
4-9 months

Present product to PAC

Pediatric Advisory Committee Meeting, April 12, 2016
Proposed CDER Product Safety Review Timeline

**Not Low Safety Risk Products**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Duration</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Collection Phase</td>
<td>1 month</td>
<td>OSE creates Pediatric Post-Marketing Pharmacovigilance review plan</td>
</tr>
<tr>
<td>Review Plan Phase</td>
<td>3-4 months</td>
<td>OSE reviews safety and use data and writes Pediatric Post-Marketing Pharmacovigilance and Drug Utilization Review Draft</td>
</tr>
<tr>
<td>Data Analysis Phase</td>
<td>4-9 months</td>
<td>Edits, clearance, and updates (if needed) to safety report</td>
</tr>
<tr>
<td>Rehearsal Phase</td>
<td></td>
<td>Create and rehearse presentation</td>
</tr>
<tr>
<td>Present product to PAC</td>
<td></td>
<td>Presentation in standard or expanded format</td>
</tr>
</tbody>
</table>

- FAERS collects adverse events reports
Presentation Outline

- Brief Overview of Risk-Based Assessment Proposal Process

- Comparison to Current Review Process
  - Factors to consider products low safety risk
  - Abbreviated presentations to web-based reports

- Advantages of Risk-Based Assessment Proposal
## Current CDER Product Safety Review Timeline

<table>
<thead>
<tr>
<th>Phase</th>
<th>Duration</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Collection Phase</td>
<td>5-6 months before PAC meeting</td>
<td>- FAERS collects adverse events reports</td>
</tr>
<tr>
<td>Review Plan Phase</td>
<td>3-4 months before PAC meeting</td>
<td>- OSE creates Pediatric Post-Marketing Pharmacovigilance review plan</td>
</tr>
<tr>
<td>Data Analysis Phase</td>
<td>1-2 months before PAC</td>
<td>- OSE reviews safety and use data and writes Pediatric Post-Marketing Pharmacovigilance and Drug Utilization Review Draft</td>
</tr>
<tr>
<td>Rehearsal Phase</td>
<td></td>
<td>- Edits, clearance, and updates (if needed) to safety report</td>
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<td>Present product to PAC</td>
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- **Meeting #1**: Data Analysis Phase
- **Meeting #2**: Rehearsal Meeting

### Pediatric Advisory Committee Meeting, April 12, 2016
Current Factors for Abbreviated Presentations

**JUSTIFIED ABBREVIATED PRESENTATIONS:**
- for products used to treat certain serious & life-threatening diseases — Rational behind conclusions presented

- Products used to treat serious and life-threatening diseases, such as cancer and HIV

  - YES

  - Deaths and SAEs are labeled appropriately and attributable to the disease.

  - YES

  - Meets all criteria

  - Meets 1, 3 & 4 but has:
    - Greater than 1% use

  - JAR
    - JUSTIFIED ABBREVIATED with RATIONALE Presentation Format

- Meets 2, 3 & 4 but has:
  - More than a few or no pediatric drug related deaths or SAEs

  - DAR
    - Designated Abbreviated Review Presentation Format

- Meets 3 & 4 but has:
  - More than a few pediatric SAEs and high use in pediatric disease

  - Abbreviated
    - (PAC must agree) Presentation Format

**ABBREVIATED PRESENTATIONS:**
- for products used to treat non-serious or non-life-threatening conditions

- Products found to have:
  1. Few or no pediatric drug related deaths or serious adverse events (SAEs)
  2. Low (equal to or less than 1%) use in children; or not to be marketed
  3. No identified new safety signals
  4. Adequately labeled for pediatrics
Current Factors for Abbreviated Presentations

1. Product used to treat certain serious and life-threatening diseases
2. Deaths and SAEs are labeled appropriately and attributable to the disease
3. Product used to treat non-serious or non-life threatening conditions
4. No identified new safety signals
5. Product adequately labeled for pediatrics
6. No or few pediatric drug related deaths or SAEs
7. Low (≤1%) use in children or not to be marketed
Proposed Factors Informing Whether CDER Product is a Low Safety Risk

1. No pediatric deaths or pediatric deaths likely attributable to disease progression.

2. No or few SAEs attributable to product.

3. No new safety signals identified by FDA through literature review, FAERS case review, drug utilization data review, and ongoing tracked safety issues for product or class of products.

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Advantages of Risk-Based Assessment Proposal

- More time for PAC to discuss CDER products that are not designated low safety risk
  - Safety reports of products designated low safety risk will be posted to FDA website and no longer be presented at PAC safety meetings
  - Allows more time for discussion of CDER products presented to PAC during safety meeting

- Future potential to decrease backlog of CDER products awaiting PAC review
  - Use continuous quality improvement process to further increase efficiency and increase number of CDER products the PAC reviews each year
History of PAC Review of CDER Products

Since Adaptation of Current Presentation Format from 2012–2015:

- 99 CDER products were reviewed by PAC
  - 46 in standard presentation format
  - 53 in abbreviated presentation format
History of PAC Review of CDER Products

From 2012–2015:

- 22 CDER products were reviewed by PAC per year
  - Range = 19-24

- 34 CDER products became eligible for PAC review per year
  - Range = 29-39
Advantages of Risk-Based System

- More time for PAC to discuss CDER products that are not designated low safety risk
  - Safety reports of products designated low safety risk will be posted to FDA website and no longer be presented at PAC safety meetings
  - Allows more time for discussion of CDER products presented to PAC during safety meeting

- Future potential to decrease backlog of CDER products awaiting PAC review
  - Use continuous quality improvement process to further increase efficiency and increase number of CDER products the PAC reviews each year
Current Backlog of CDER Products

As of December 31, 2015:

- 37 CDER products await PAC review
  - Median waiting time = 26 months

By December 31, 2016:

- 44 additional CDER products are eligible for PAC review
Projected Backlog of CDER Products Awaiting PAC Review

The estimated backlog increases almost 300% from 2015 to 2020.
Risk-Based Assessment Proposal for CDER Products

- Decrease the number of CDER product presentations during PAC pediatric-focused safety meetings
- As a result, increase the available discussion time of CDER products presented during PAC meetings
- Find further efficiencies in risk-based assessment proposal through continuous quality improvement process
- As further efficiencies are identified, hopefully increase number of CDER products reviewed by FDA per year