CDER’s Office of New Drugs Rare Diseases Program

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Disclosures

• No Conflicts of Interest
• Nothing to Report
• Opinions expressed are personal and do not reflect those of the FDA
Rare Diseases Program

• The current team
  • Lucas Kempf
    • Associate Director (Acting)
  • Larry Bauer
    • Regulatory Scientist
  • Althea Cuff
    • Science Policy Analyst
  • Tracy Cutler
    • Science Policy Analyst
    • EMA cluster coordinator
Rare Diseases Program

• Rare disease have less that 200,000 people
• There are 7,000 known rare disease
• 1 in 10 people are affected by a rare disease
Challenges for Rare Disease Drug Development

- Rare diseases **natural history** is often poorly understood/characterized
- Diseases tend to be progressive, **serious**, life-limiting and life-threatening and lack **approved therapy**
- **Small populations** often restrict study design and replication
- **Phenotypic** diversity within a disorder adds to complexity, as do **genetic subsets**
- Well defined and validated **endpoints, outcome measures/tools**, and **biomarkers** are often lacking
- Lack of **precedent** for drug development
- **Ethical** considerations for children in clinical trials
CDER Rare Diseases Program

Mission Statement:

• Facilitate
• Support
• Accelerate

…the development of drug and biologic products for the treatment of patients with rare disorders
Rare Diseases Program Responsibilities

**Coordinate development of CDER Policies and Procedures**

- Guidance development
- Continuing involvement with Senior FDA staff re: Rare Diseases Program and its role

**Assist in development of good science**

- Database adjudication committee for NMEs
- Specific projects/peer reviewed publications
- Workshop development
  - Rare disease trial designs
Rare Diseases Program Responsibilities

**Coordinate internal training in rare diseases**
- 101 course for new reviewers
- 102 advanced training day for review staff

**Assist in external training for the rare disease community**
- Presentations at national and international meetings
- Workshop development
  - Rare disease trial designs workshop
- Panel Participant/ Speaker at Patient Focused Drug Development Workshops
  - FDA
  - Externally Led
Rare Diseases Program
Responsibilities

• Review Rare Pediatric PRV requests and Developed procedures for management
• FDA Rare Disease Council member
• NORD Registries Cooperative Agreement with FDA
Rare Diseases Program Projects

Work collaboratively with stakeholders

• NIH Collaborations
  – NIH/FDA Joint Task Force
  – Rare Disease Day Annual Meeting
  – CDER/TRND Drug Development Meetings
  – NCATS Natural History Studies Initiative
Rare Diseases Program Projects

Work collaboratively with stakeholders

- Patient/Patient Organizations Meetings
  - Face to Face meetings with patient advocacy groups often in collaboration with PAS, PASE, and/or OHCA
  - Presentations to stakeholder groups
  - Planning Committee members for NORD Annual Summit
In 2017, CDER approved 46 novel drugs. The ten-year graph below shows that from 2008 through 2016, CDER has averaged about 31 novel drug approvals per year.
CDER Novel Orphan New Drug Approvals
First Approvals in the US – CY 2015 -2017

<table>
<thead>
<tr>
<th>Year</th>
<th>Total NME</th>
<th>Rare NME</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>45</td>
<td>20</td>
</tr>
<tr>
<td>2016</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>40</td>
<td>20</td>
</tr>
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Expediting Rare Diseases
Drug Development

• Programs have been developed to target serious diseases with unmet medical needs when a new treatment could provide meaningful clinical benefit

Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics, May 2014
## 2017 Rare NME approvals

<table>
<thead>
<tr>
<th></th>
<th>Rare (#18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First in class</td>
<td>56%</td>
</tr>
<tr>
<td>Fast track</td>
<td>44%</td>
</tr>
<tr>
<td>Breakthrough</td>
<td>44%</td>
</tr>
<tr>
<td>Priority</td>
<td>78%</td>
</tr>
<tr>
<td>Accelerated</td>
<td>22%</td>
</tr>
<tr>
<td>First in the US</td>
<td>72%</td>
</tr>
</tbody>
</table>
Statistics: Orphan Drug Designations

Orphan Drug Designations Requested/Granted by Calendar Year

No. Original Requests Received
No. Designated


527
478
Rare Pediatric Disease (RPD) Priority Review Voucher Program: Background

- 2012 FDA Safety and Innovation Act (FDASIA) [Section 908]
  - Provides an incentive to encourage the development of drugs and biologics for rare pediatric diseases

- Upon approval, the sponsor may be issued a voucher redeemable for a priority review for a subsequent application that may not have otherwise qualified for a priority review

- The incentive offers a shorter review clock for marketing applications, 6 months compared with the 10 months standard review time

Rare Pediatric Disease Priority Review Vouchers, Guidance for Industry
RPD Requests and Determinations

Data as of September 15, 2016

(Includes Designations and Consults)
Rare Pediatric Disease Priority Review Voucher Program

• The OOPD reviews requests for Rare Pediatric Disease designation
  • 41 Designated/6 Denied/7 Under Review

• Voucher requests are managed by the OND RDP
  • 11 Voucher requests were submitted with an NDA or BLA
    • 6 Vouchers awarded, 3 denied and 2 pending review
  • Two PRV’s have been redeemed

• Future (?)
  • Sunsets - 30 September 2016 although pending legislation may be extended to 31 December 2022 (for designation)/31 December 2027 (for redemption)
International Regulatory Communications: Development of an EMA/FDA Rare Disease Cluster

- Regularly scheduled teleconferences to exchange information and experiences
- Alternating Chairpersonship EMA/FDA
- Agendas circulated in advance of the teleconferences
- Core Members are joined by expert Reviewers
International Regulatory Communications

Development of an EMA/FDA Rare Disease Cluster

• To share scientific evaluation of various aspects of rare disease drug development
  • Identification of trial end points
  • Potential trial designs in small populations
  • Regulatory flexibility
  • Determination of the size of safety populations
EMA/FDA Rare Disease Cluster

• To share scientific evaluation of various aspects of rare disease drug development
  • Evaluation of pre-clinical data to support human trials
  • Design/conduct of post-marketing studies especially in the cases of breakthrough designation and accelerated approval (FDA) or PRIME designation and conditional/exceptional approval (EMA)
Overall, a total of fifty-three (53) agenda items were discussed between September 2016 – December 2017.
TOTAL DISCUSSIONS SINCE INCEPTION

Percent of protocol assistance discussions 67%

Percent of product discussions 33%

Total number of discussions

EMA/FDA Rare Disease Cluster
Overall Impact of the Rare Diseases Cluster

Percent of discussions led to alignment of understanding: [VALUE]
Percent of discussions led to alignment of actions: [VALUE]
Percent of discussions led to change in regulatory action: [VALUE]
Thank you very much for your attention

Send us a Question at:
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Rare Diseases Program/OND/CDER/FDA