Perspectives on Healthcare Issues

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Professional Affairs and Stakeholder Engagement (PASE)
Objectives

- FDA regulatory phrases for new drug approvals.
- Current initiatives in reducing preventable harm from drugs.
- Importance of diversity in clinical trials.
CDER’s mission is to:

• Promote the public health by helping to ensure the availability of **safe and effective drugs**

• Protect public health by promoting the **safe use** of marketed drugs

• Protect public health by helping to ensure the **quality and integrity** of marketed drug products
Drug Discovery Timeline

What role does FDA play in the drug discovery process?

5 Things You Need to Know About New Drug Approval
FDA’s Review Timeline
Approval Tracks

Fast Track

Fast track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need.

Breakthrough Therapy

A process designed to expedite the development and review of drugs which may demonstrate substantial improvement over available therapy.

Accelerated Approval

These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint.

Priority Review

A Priority Review designation means FDA’s goal is to take action on an application within 6 months.
FDA regulatory phrases for new drug approvals.

Current initiatives in reducing preventable harm from drugs.

Importance of diversity in clinical trials.
Safe Use Initiative

• **Goal:** Reduce preventable harm by developing, implementing, and evaluating cross sector interventions with partners committed to safe and appropriate medication use
Conceptual Framework for Non-Preventable Harm

- Indications
- Identified Risks
- Potential Risks
- Missing Information

Unavoidable subset of Identified Risks
Gaps in Current Knowledge
Conceptual Framework for Preventable Harm

- Indications
- Identified Risks
- Potential Risks
- Missing Information

Not incorporating current knowledge when drug is selected
Not taking actions to address the avoidable subset of Identified Risks
Unintended exposures
Intentional misuse
Extramural Research

Safe Use funds projects that “develop innovative methods to create, facilitate, and encourage research in the area of safe medication use that seeks to reduce preventable harm from drugs.”

This is accomplished via the Broad Agency Announcement (BAA), an open and continuous announcement to solicit research proposals.

Details on the BAA can be found at FedBizOpps.gov
Safe Use Partners

• Federal agencies

• Healthcare professionals and professional societies

• Pharmacies, hospitals, and other health care entities

• Patients, caregivers, consumers, and their representative organizations
Drugs with Active Safe Use Projects

Safe Use has 13 current projects. These involve a wide variety of drugs and potential adverse events.

• Opioids
• Antibiotics
• Anti-hyperglycemic agents
• Stimulants
• Appearance and Performance Enhancing Substances
• NSAIDS

https://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/ucm277720.htm
Other Safe Use Projects

Some projects examine safety issues that extend across drug classes.

• A risk reduction tool to assist hospitals assess their level of implementation of best practices regarding high-risk medications

• Educational resource to facilitate provider-patient communication regarding medications which may impair driving

• Studies to assess how providers prefer and digest information from FDA

http://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/ucm277720.htm
FDA regulatory phrases for new drug approvals.

Current initiatives in reducing preventable harm from drugs.

Importance of diversity in clinical trials.
“Variability is the law of life, and as no two faces are the same, so no two bodies are alike, and no two individuals react alike and behave alike under the abnormal conditions which we know as disease.”

- Sir William Osler (1849 – 1919)
Is there a right number?
Enhancing Transparency

• In August 2014, FDA delivered its Action Plan to Enhance the Collection and Availability of Subgroup Data

• The plan includes three overarching priorities for subgroups:
  – Quality of Data
  – Greater Participation
  – Increased Transparency

Part of the 2012 FDA Safety and Innovation Act (FDASIA 907) requires the FDA to report on the inclusion and analysis of demographic subgroups of sex, race, and age in applications for medical products.
Drug Trials Snapshots

- Who were in the clinical trials by **sex, race, and age subgroups**?
- Were there observed differences in **efficacy and safety** among sex, race, and age subgroups?

www.fda.gov/drugtrialssnapshot
Who were in the pivotal trials?

Baseline Demographics (8442 patients)

- Men (6595 patients): 78%
- Women (1847 patients): 22%

Baseline Demographics (8442 patients)

- 18 to 64 years (4299 patients): 51%
- 65 to 74 years (2574 patients): 30%
- 75 and older (1569 patients): 19%
Were there any subgroup differences?

**ENTRESTO (secubitril/valsartan)**

- **Were there any differences in side effects among sex, race and age?**
- **Sex:** The risk of side effects appeared to be similar in men and women.
- **Race:** There was an increased risk of an allergic reaction called angioedema in black patients.
- **Age:** The risk of low blood pressure was higher in patients 65 years and older.
Snapshots Overview

• January 1, 2015: Snapshot written for every New Molecular Entity (NME)
• Permanent program
• Goal to publish 30 days after approval
• Does not apply to previously approved drugs
In 2015, CDER approved 45 novel drugs, either as new molecular entities (NMEs) under New Drug Applications (NDAs) or as new therapeutic biologics under Biologics License Applications (BLAs).

* The percentages of the categories “American Indian or Alaska Native (AI/AN),” “Native Hawaiian or Other Pacific Islander (NH/OPI),” and “Unknown/Unreported” were small enough that we combined them into the “Other” category for the purposes of this review.

**These particular subgroups were calculated as part of a Geriatrics Report and are not a regular feature of the Drug Trial Snapshots.
# Mental Health Drug Approvals (2015)

<table>
<thead>
<tr>
<th>BRAND NAME</th>
<th>INDICATION</th>
<th>WOMEN</th>
<th>AFRICAN AMERICAN</th>
<th>ASIAN</th>
<th>WHITE</th>
<th>OTHER</th>
<th>AGE 65 and OLDER</th>
<th>AGE 75 and OLDER</th>
<th>AGE 80 and OLDER</th>
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<tbody>
<tr>
<td>ARISTADA</td>
<td>Schizophrenia</td>
<td>32%</td>
<td>40%</td>
<td>13%</td>
<td>47%</td>
<td>&lt;1%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>REXULTI</td>
<td>Schizophrenia</td>
<td>37%</td>
<td>24%</td>
<td>7%</td>
<td>63%</td>
<td>6%</td>
<td>&lt;1%</td>
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<tr>
<td>REXULTI</td>
<td>Major Depressive Disorder</td>
<td>69%</td>
<td>12%</td>
<td>&lt;1%</td>
<td>85%</td>
<td>2%</td>
<td>&lt;1%</td>
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<td>0%</td>
</tr>
<tr>
<td>VRAYLAR</td>
<td>Schizophrenia</td>
<td>28%</td>
<td>34%</td>
<td>17%</td>
<td>43%</td>
<td>6%</td>
<td>&lt;1%</td>
<td>0%</td>
<td>0%</td>
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<tr>
<td>VRAYLAR</td>
<td>Bipolar disorder</td>
<td>41%</td>
<td>25%</td>
<td>24%</td>
<td>49%</td>
<td>2%</td>
<td>&lt;1%</td>
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# Oncology Drug Approvals (2015)

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<th>AGE 75 and OLDER</th>
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<tr>
<td>IBRANCE</td>
<td>Breast cancer</td>
<td>100%</td>
<td>1%</td>
<td>6%</td>
<td>90%</td>
<td>3%</td>
<td>46%</td>
<td>9%</td>
<td>3%</td>
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<tr>
<td>YONDELIS</td>
<td>Advanced soft tissue sarcoma</td>
<td>70%</td>
<td>12%</td>
<td>4%</td>
<td>76%</td>
<td>8%</td>
<td>22%</td>
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<td>TAGRISSO</td>
<td>Lung Cancer (T790M+, NSCLC)</td>
<td>68%</td>
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<td>60%</td>
<td>36%</td>
<td>3%</td>
<td>45%</td>
<td>13%</td>
<td>4%</td>
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<td>ALECENSA</td>
<td>Metastatic NSCLC</td>
<td>55%</td>
<td>2%</td>
<td>18%</td>
<td>74%</td>
<td>7%</td>
<td>14%</td>
<td>4%</td>
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<tr>
<td>LENVIMA</td>
<td>Thyroid cancer</td>
<td>49%</td>
<td>2%</td>
<td>18%</td>
<td>79%</td>
<td>&lt;1%</td>
<td>40%</td>
<td>10%</td>
<td>4%</td>
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<tr>
<td>FARYDAK</td>
<td>Multiple Myeloma &amp; other cancers</td>
<td>48%</td>
<td>3%</td>
<td>33%</td>
<td>63%</td>
<td>1%</td>
<td>35%</td>
<td>5%</td>
<td>0%</td>
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<tr>
<td>DARZALEX</td>
<td>Multiple Myeloma</td>
<td>46%</td>
<td>10%</td>
<td>6%</td>
<td>76%</td>
<td>8%</td>
<td>45%</td>
<td>10%</td>
<td>3%</td>
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<tr>
<td>NINLARO</td>
<td>Multiple Myeloma</td>
<td>43%</td>
<td>2%</td>
<td>9%</td>
<td>85%</td>
<td>5%</td>
<td>58%</td>
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<td>&lt;1%</td>
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<tr>
<td>COTELLIC</td>
<td>Melanoma</td>
<td>42%</td>
<td>N/A</td>
<td>N/A</td>
<td>93%</td>
<td>7%</td>
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<td>EMLPLICITI</td>
<td>Multiple Myeloma</td>
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<td>57%</td>
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<td>UNITUXIN</td>
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<td>7%</td>
<td>3%</td>
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<td>8%</td>
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<td>N/A</td>
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<td>LONSURF</td>
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<td>1%</td>
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<td>ODOMZRO</td>
<td>Advanced basal cell carcinoma (BCC)</td>
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<td>94%</td>
<td>6%</td>
<td>54%</td>
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<tr>
<td>PORTRAZZA</td>
<td>Metastatic squamous non-small cell lung cancer (NSCLC)</td>
<td>17%</td>
<td>1%</td>
<td>8%</td>
<td>84%</td>
<td>8%</td>
<td>39%</td>
<td>4%</td>
<td>1%</td>
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<tr>
<td>UPTRAVI</td>
<td>Pulmonary arterial hypertension</td>
<td>80%</td>
<td>2%</td>
<td>21%</td>
<td>75%</td>
<td>2%</td>
<td>18%</td>
<td>1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>REPATHA*</td>
<td>Hypercholesterolemia</td>
<td>50%</td>
<td>5%</td>
<td>9%</td>
<td>84%</td>
<td>2%</td>
<td>28%</td>
<td>3%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>REPATHA**</td>
<td>Hypercholesterolemia</td>
<td>49%</td>
<td>0%</td>
<td>4%</td>
<td>90%</td>
<td>6%</td>
<td>0%</td>
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<tr>
<td>PRAXBIND</td>
<td>Reversal of the anticoagulant effects of Pradaxa during emergency situations or when there is a need to reverse its blood-thinning effects.</td>
<td>47%</td>
<td>&lt;1%</td>
<td>7%</td>
<td>85%</td>
<td>7%</td>
<td>90%</td>
<td>60%</td>
<td>44%</td>
</tr>
<tr>
<td>SAVAYSA</td>
<td>Reduce risk of pulmonary embolism in VTE patients</td>
<td>43%</td>
<td>4%</td>
<td>21%</td>
<td>70%</td>
<td>5%</td>
<td>33%</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>PRALUENT</td>
<td>Hyperlipidemia</td>
<td>40%</td>
<td>4%</td>
<td>3%</td>
<td>90%</td>
<td>3%</td>
<td>32%</td>
<td>6%</td>
<td>&lt;1%</td>
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<tr>
<td>SAVAYSA</td>
<td>Reduce the risk of stroke in a Afib patients</td>
<td>38%</td>
<td>1%</td>
<td>14%</td>
<td>81%</td>
<td>4%</td>
<td>74%</td>
<td>40%</td>
<td>17%</td>
</tr>
<tr>
<td>KENGREAL</td>
<td>Blood thinner following heart procedure</td>
<td>28%</td>
<td>3%</td>
<td>3%</td>
<td>94%</td>
<td>&lt;1%</td>
<td>48%</td>
<td>18%</td>
<td>8%</td>
</tr>
<tr>
<td>CORLANOR</td>
<td>Heart failure</td>
<td>24%</td>
<td>1%</td>
<td>8%</td>
<td>89%</td>
<td>2%</td>
<td>38%</td>
<td>11%</td>
<td>3%</td>
</tr>
<tr>
<td>ENTRESTO</td>
<td>Heart failure</td>
<td>22%</td>
<td>5%</td>
<td>18%</td>
<td>66%</td>
<td>11%</td>
<td>49%</td>
<td>19%</td>
<td>7%</td>
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*Clinical Trial of heterozygous familial hypercholesterolemia (HeFH) Patients
**Clinical Trial of homozygous familial hypercholesterolemia (HoFH) Patients
## 2016 Snapshot Overview

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<th></th>
<th>WOMEN</th>
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</tbody>
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*In 2016, CDER approved 22 novel drugs, either as new molecular entities (NMEs) under New Drug Applications (NDAs) or as new therapeutic biologics under Biologics License Applications (BLAs).
Where do Black or African Americans Live?
Where do Black/AA Participate in Clinical Trials? (Based on NMEs from CY2015-16)
Where do Black/AA Participate in Clinical Trials compared to Non-Black/AA Races? (Based on NMES from CY 2015-16)
Important Questions

• Is there enough data to make conclusions about efficacy and safety for all subgroups?
• How many patients per subgroup are needed?
• When is generalizability ok?
• When differences among subgroups are seen, when are differences clinically meaningful?
Next Steps

• Continuing discussion on variability in response to drugs among subgroups
• Deeper understanding of when subgroup differences are plausible
• Best practices for reporting subgroup differences to the public
• Commitment to continued transparency
FDA regulatory phrases for new drug approvals.

Current initiatives in reducing preventable harm from drugs.

Importance of diversity in clinical trials.
Contact info:

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