Survey of the Presentation of Sex Analysis in the FDA Review of Efficacy and Safety Clinical Data of New Molecular Entity Drugs and Biologics Approved From 2007 to 2009
Onyeka Onugu1, Rita Poon1, Vanessa Copeland1, Keshav Khanijow1, Sphoorti Umarjee1, Leslie Chen, Ph.D.2, Emmanuel Fabiran, Ph.D.1, Lei Zhang, Ph.D.1, Amrita Parekh, Ph.D.1
1Office of Women's Health, Office of the Commissioner; 2Office of Clinical Pharmacology, Office Translational Sciences, Center for Drug Evaluation and Research, US Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, MD 20993.

Introduction
Sex differences exist in regards to the pharmacokinetics and pharmacodynamics of drugs and biologics which may affect their overall safety and efficiency outcomes. Adequate performance in clinical trials is not only essential; in assessing sex differences in regards to treatment outcomes and response but also an important step towards personalized medicine. The Food and Drug Administration (FDA) has taken several steps in ensuring that women are adequately represented in clinical trials such as the creation of the FDA Office of Women’s Health and different FDA guidelines as shown below.

Methodology
- Obtained a list of NME drugs and biologics approved between 2007 and 2009 from Drugs@FDA website.
- Excluded NMEs for sex-specific indications, pediatriic indications, or those without clinical data.
- Accessed FDA Medical and Statistical Reviews of approved NMEs on DRUGS@FDA website.
- Sex analysis was tracked using the following coding system similar to the system used in the GAO 2001 report.

Results

**Presentation of Sex Analysis in FDA Reviews of Approved Drugs**

<table>
<thead>
<tr>
<th>NDAs (n=50)</th>
<th>Efficacy</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (0%)</td>
<td>37 (74%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

- Presentation of sex analysis for both efficacy and safety (74%) has slightly increased since GAO 2001’s report of 72% and Yang et al. 2009 report of 71%**.
- *Yang study did not divide sex-based analysis in terms of safety and efficacy.

**Examples**

**Conclusive Safety Analyses**

- NDA21-855 - Femstatin
  - The overall incidence of adverse events during dosing was higher in females than males (33% vs 25%), similarly, the overall incidence of drug-related adverse events was higher in females than males (54% vs 13% respectively. Panelists had higher incidence of hypertension and headache (38% vs 13%, respectively) compared to males (4.5% vs 0%, respectively).

**Conclusion & Future Works**

- After the 1998 regulations on submission of sex analyses was passed, both the 2001 GAO report and the Yang study, sex analysis in FDA reviews from 1998-2002 had increased to more than 70%.
- The current study showed that presentation of sex-based analysis in the FDA reviews of drugs between 2007 and 2009 has remained consistent in the last 10 years at around 74%
  - 26%(efficacy) and 10%(safety) of the sex based analyses were conclusive in the NDA reviews.
  - 55%(efficacy) and 18%(safety) of the sex analyses presented in the reviews of NDAs are exploratory because the clinical studies lacked statistical power.
  - However, 43%(efficacy) and 71%(safety) of the sex based analyses were conclusive in the NDA reviews.
- For the BLA reviews, 72% (efficacy) and 87%(safety) presented conclusive sex-based analysis.
- Further efforts need to be made to design clinical studies that are statistically powered to draw conclusions on safety profiles and efficacy outcomes of therapeutic products by sex.

**References**