Regulatory Roundtable on advancing women's health and precision medicine
17th September 2020

Introduction

On 17 September 2020, the Women's Brain Project (WBP) held a landmark regulatory roundtable on advancing sex and gender precision medicine.

The regulatory roundtable brought together key regulators and other stakeholders to learn from the experience of the U.S. Food and Drug Administration (FDA), which has a dedicated Office of Women's Health (OWH) and to see how we can further prioritise women's health / sex and gender medicine / diversity issues in other regulatory agencies.

The roundtable was an invitation only event and was held under the Chatham House Rule. In the spirit of the rule, we cannot disclose who said what, but we have put together the key takeaways of the meeting here in this document.

WBP – in a snapshot

The WBP is an international non-profit organisation studying sex and gender determinants of brain and mental health to achieve precision medicine. WBP is a global leading player in the field of brain research, supporting innovative science, precision medicine, unbiased artificial intelligence (AI) and promoting gender health equity to make healthcare systems more sustainable. The vision of WBP is to create a sex and gender precision medicine research institute.

The Food and Drug Administration Office of Women's Health (OWH)

The starting point was reminding everyone of the historical background: the thalidomide tragedy of the late 1950s and early 1960s, which led to the exclusion of women of childbearing age in clinical trials (CT), then in the 1990s the demographic rule (regulations that mandated the sponsors to include gender, age and race into analysis of CT data) and the creation of the Office for Women's Health (OWH) to promote the inclusion of women in CT.

The OWH was established by Congressional mandate in 1994, as part of the Office of the FDA Commissioner.

The OWH promotes and conducts research initiatives that facilitate FDA regulatory decision-making and advances the understanding of sex differences across health conditions, including health conditions unique to women, as well as those conditions that disproportionately impact women.

The OWH is an Office that reports to the Office of the Commissioner of the FDA and collaborates and works across different FDA Centers. Its main program areas are **outreach, science and education.**

Outreach

An example of a successful outreach campaign led by OWH in partnership with the National Institutes of Health Office of Research on Women's Health (NIH ORWH) is the Diverse Women in Clinical Trials Initiative which raises awareness of CT participation and also works to share best practices.

The OWH has a variety of consumer resources including fact sheets and brochures for patients and caregivers. Such resources are printed and published electronically and many have been translated in different languages. In addition to a dedicated newsletter, OWH publishes a blog entitled Knowledge and News On Women and has an active social media presence on Twitter, Pinterest and YouTube.

Science

The OWH supports several research projects each year to advance our understanding of sex differences and advance the health of women and support FDA's regulatory mission to protect and promote public health. OWH funds research through intramural and extramural research programs. One mechanism to fund extramurally is through collaborations with the Centers of Excellence in Regulatory Science and Innovation (CERSI) programs.

A number of OWH led scientific publications looking at women's representation in CT were highlighted. Two examples are below:

- *Participation of Women in Clinical Trials Supporting FDA Approval of Cardiovascular Drugs* - An examination of women's participation and the reported safety and efficacy by gender for pivotal cardiovascular disease (CVD) trials submitted to the FDA supporting marketing applications.
- *Evaluation of worldwide clinical trials by gender: An FDA perspective.*

Education

The OWH organizes an 'expert speaker' series to educate FDA reviewers and other federal partners on cutting edge novel science related to sex and gender differences. Recent lectures focused on sex differences and vaccines and COVID-19 and pregnancy. Furthermore, OWH hosts scientific workshops, the most recent of which focused on the influences of sex and gender on opioid and nicotine use, dependence, and recovery.

The course entitled *Bench to Bedside: Integrating Sex and Gender to Improve Human Health* was developed in partnership with OWH and the National Institutes of Health

Office of Research on Women's Health (NIH ORWH) to explore sex- and gender-related differences in key disease areas.

OWH developed the Women's Health Research Roadmap to outline priority areas where new or enhanced research is needed. OWH also acts as the lead FDA representative to the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC), which has produced 15 recommendations to advise the Secretary of Health and Human Services (HHS) regarding gaps in knowledge and research on safe and effective therapies for pregnant women and lactating women.

Health Canada

Both sex and gender as determinants of health and how they influence the safe development of therapeutic products is an area of great interest of Health Canada.

The Federal Plan for Gender Equality of 1995 and the original Guidance Document on the Inclusion of Women in Clinical Trials of 1997 were highlighted.

In 2019 Health Canada convened a scientific expert advisory committee on health products for women to provide timely patient-centered, scientific, technical, medical and clinical advice on current and emerging issues regarding women's health and the regulation of medical devices and drugs.

European stakeholders

Innovative Medicines Initiative (IMI)

The Innovative Medicines Initiative (IMI) is a public-private partnership aiming to speed up the development of better and safer medicines for patients.

IMI already has the issue of sex and gender precision medicine on its radar.

All proposals for IMI funding have an obligation to aim for gender equality.

Examples of projects:

- ConcePTION - Building an ecosystem for better monitoring and communicating of medication safety in pregnancy and breastfeeding: validated and regulatory endorsed workflows for fast, optimised evidence generation (2019-2024)
- TRiPP - Translational Research in Pelvic Pain (this project is ongoing)

European Medicines Agency (EMA)[1]

The *Workshop on benefit-risk of medicines used during pregnancy and breastfeeding, 22 September 2020* was highlighted.

The EMA representative found the FDA example 'enlightening and inspiring'.

EMA demands that the CT population is representative of the real world population.

There is a project that will collect data on the impact of COVID-19 in pregnancy in order to guide decision-making about vaccine indications, vaccination policies and treatment options for COVID-19 in pregnant women.

The EMA representative highlighted the importance of transparency and education. EMA holds workshops and expert talks.

In 2017 the EMA held a public hearing on valproate in pregnancy. There was agreement among the participants on the undeniable risks of valproate (a medicine that treats epilepsy, bipolar disorder and migraine) to unborn babies, if used during pregnancy.

Other key points mentioned during the discussions

- The National Institute for Health and Care Excellence (NICE) mentioned Multiple Sclerosis and migraine as examples of diseases that affect more women than men.
- The European Federation of Pharmaceutical Industries and Associations (EFPIA) emphasised the importance of public-private partnerships and academic collaborations in gathering health data.
- WBP highlighted that two thirds of Alzheimer's patients worldwide are women. WBP also referenced that there are two critical issues at play: the participation of women in clinical trials, and the actual sex differences – in terms of safety / efficacy – from a biological standpoint and what this means in terms of precision medicine, biomarkers and research. Further data is needed. Hence, the objective of WBP to create a sex and gender precision medicine research institute.
- WBP summarised with its own call to action:
    - **Analysis of sex differences** in baseline patient characteristics, progression of the disease, clinical outcomes even when using digital or fluid biomarkers etc.

[1] Please note that the views expressed in this meeting are the personal views of the EMA representative and may not be understood or quoted as being made on behalf of or reflecting the position of the EMA or one of its committees or working parties.

- **Awareness of sex and gender differences** among the scientific community, pharmaceutical and technology industries, policymakers and the general public
- **Implement solutions**, such as explainable algorithms in data analysis and drug development to detect bias in the system and implement mitigation strategies
- **Incorporate key ethical considerations** during every stage of technological development, ensuring that the systems maximize well-being and health of the global population

Next steps

WBP hopes that this will be the first of many global stakeholder interactions to advance women's health in the research, development, evaluation and approval of medicines. All marches start with a first step and we think that the world should come together to advance women's health and precision medicine. This will involve all relevant stakeholders coming together, in a multi-stakeholder and multi-disciplinary approach.

The following next steps are proposed:

- A follow-up meeting to be held in Q1 2021.
- In the meantime, we would like to further stakeholder engagement on the issue through a series of bilateral meetings. Global stakeholders, including, the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), the World Health Organization (WHO), the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) should be reached out to, as well as additional National Medicines Regulatory Authorities (MRAs).
- Take the concept of the FDA's Women's Health Research Roadmap globally.
- Focus on educational outreach – hold expert talks for regulatory reviewers.
- WBP to continue in its mission to create a sex and gender precision medicine research institute.

From an EU policy perspective, we believe that there is no better time to advance women's health and precision medicine.

In her State of the Union address on 16 September 2020, President of the European Commission Ursula von der Leyen presented her vision for a Europe that emerges stronger from the pandemic and leads the way towards a new vitality. She called for a stronger European Health Union, and announced the goal to build a European BARDA – an agency for biomedical advanced research and development, and the convening of a Global Health Summit next year in Italy.

Emer Cooke has been nominated the new Executive Director of EMA. Following her hearing at the European Parliament's Committee on Environment, Public Health and Food Safety (ENVI) that took place on 13 July 2020, her appointment was confirmed.

She will be the first woman to lead the agency. She will take over from the current Executive Director Guido Rasi, whose term ends on 15 November 2020.

Horizon Europe, the EU's next funding programme for research and innovation, will launch on 1 January 2021.

EU4Health 2021-2027 – a vision for a healthier European Union, EU4Health is the EU's response to COVID-19, which has had a major impact on medical and healthcare staff, patients and health systems in Europe.

Women's Brain Project