



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

REPORT

Workshop on benefit-risk of medicines used during pregnancy and breastfeeding

22 September 2020



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Why a workshop on medicine safety in pregnant and breastfeeding women?

“In our view, we need a paradigm shift in the way marketing authorisation holders develop, and regulators approve, medicines that may be used by pregnant and breastfeeding women. We need to generate more data on medicine safety during pregnancy and breastfeeding in clinical studies, as well as integrate evidence from the real world into decision making in a faster way. Each of us has a role to help create this change for the benefit of women and their children.”

Guido Rasi, EMA’s Executive Director

EMA has drafted a strategy for better research into the benefits and risks of medicines in pregnancy and breastfeeding. The aim of the strategy is to obtain evidence on medicines’ use and safety for pregnant and breastfeeding women and enable better decision-making on medical treatment for women who are planning to have a baby, are pregnant or wish to breastfeed their baby. Change can only be accomplished through collaboration with all parties involved: regulators, medicine developers, marketing authorisation holders, healthcare professionals, academics, patients and women. This is why this workshop was organised.

The need for information in this population is illustrated by the ongoing pandemic: as new treatments and vaccines will soon be available to fight the COVID-19 pandemic, pregnant and breastfeeding women can legitimately ask whether or not these medicines will be safe for their babies. EMA has launched initiatives during the pandemic to accelerate our understanding of the benefits and risks of medicines to prevent and treat COVID-19 in pregnant women, with the ambition to further develop this for other disease areas.

Steps to improve the generation of data on medicine safety in pregnant and breastfeeding women have already been taken globally, with innovative research methods being developed in non-clinical as well as clinical and post-authorisation settings. These must be taken to the next level for a real change to happen.

Videos and presentations from the workshop are available on [EMA’s website](#).

“As more and more people live with a chronic condition, women, their partners and their doctors constantly have to make decisions about their ongoing treatment in a context of uncertainty. Collecting the right data, including real world evidence, will be key to fill the knowledge gaps and help women make better informed decisions.”

Kaisa Immonen, Co-Chair of EMA’s Patients’ and Consumers’ Working Party (PCWP)

“As a clinician working in haemato-oncology, I prescribe aggressive cancer treatments and I am constantly confronted with the problem of having to advise women on their treatment while existing data are insufficient. We need more guidance and exchange of information so that the best possible decision can be made for and with our patients.”

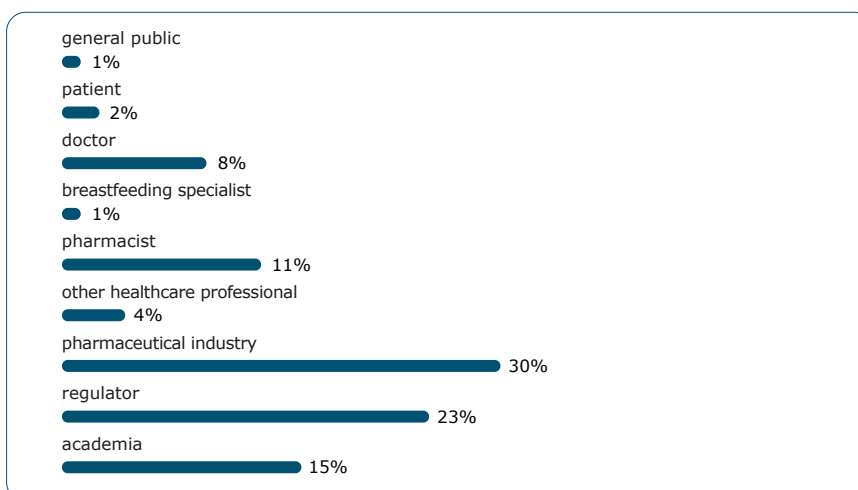
Ulrich Jäger, Co-Chair of Healthcare Professionals’ Working Party (HCPWP)

A global issue: close to 500 people from across the world followed the workshop live



Feedback collected in real time from workshop attendants using an audience polling tool (Slido).

Medicine developers, regulators, patients, healthcare professionals, academics: a wide range of stakeholders attended the event, as everybody has a role in addressing the issues at stake





Session 1 – What changes are needed

Chaired by Kaisa Immonen, Co-Chair of EMA’s Patients’ and Consumers’ Working Party (PCWP)

PROBLEM STATEMENT AND STRATEGY OUTLINE

In high income countries, 90% of pregnant women take medications during their pregnancy, 25% of whom for a chronic disease, such as asthma, depression, diabetes, epilepsy, HIV/AIDS or hypertension. Other reasons for using medicines during pregnancy include the need to treat infections or pregnancy complications. In addition, many women use medicines while they do not yet know that they are pregnant. The situation is similar in breastfeeding women, who often use medicines for chronic diseases as well as for postnatal health issues such as depression.

While there is a clear need for using medicines during pregnancy and breastfeeding, information is not routinely available on how safe and effective medicines are in these women and on whether dose adjustments are required. In Europe, very few medicines are authorised explicitly for use in pregnancy and breastfeeding. This is due to the limited knowledge and understanding of the risks that medicines may pose to the baby. Moreover, the uncertainty about how to balance potential risks to the baby against the - mostly known

- benefits to the mother can be challenging. In addition, questions can arise as to whether pregnancy should lead to changes in the dosage of medicines. To date, little research has been done in this area.

As a consequence, some medicines may unnecessarily be withheld from pregnant and breastfeeding women, or a suboptimal treatment option may be chosen. This leads to anxiety among women because of the uncertainty and heightened risk perception about the impact of their medicine use (or non-use) on their babies.

There is a shared view that effective treatment should not be withheld from pregnant women because of potential safety concerns for the baby, which may only be theoretical concerns. Only very few medicines have been proven to be teratogenic in humans. On the other hand, we also only have robust information about safe use during pregnancy without negative impact on the baby for very few medicines. While the information on benefit-risk for the mother can often be extrapolated from information on women who are not pregnant, for most medicines this approach leaves considerable uncertainty regarding safety for the baby.

“Medicines are generally contra-indicated or considered unsafe during pregnancy; yet stopping some medications can lead to worse outcomes for both the mother and the baby. Successful management of asthma during pregnancy for instance outweighs any potential risks associated with use of asthma medicines.”

Paul Ryan, GP and pharmacist, ICGP/ UEMO

Women have clearly expressed the need to have access to more information on the safety of medicines during pregnancy and breastfeeding.

A survey carried out in the context of the [IMI ConcePTION](#) project showed that:

Out of almost 2,000 women across 74 countries:

- 85% of the women reported a need for information about medications during pregnancy/lactation
- 1 in 2 women had experienced discrepancies between different medication information sources
- 1 in 5 had difficulties understanding information given, the most common reason being that the information was not precise enough

“The thalidomide tragedy resulted in pregnant women’s exclusion from clinical trials and research. Sixty years on, no meaningful progress has been made. We need a regulatory strategy that better protects pregnant and breastfeeding women as well as their children and addresses this unacceptable societal neglect.”

Hildrun Sundseth, past President of European Institute of Women’s Health

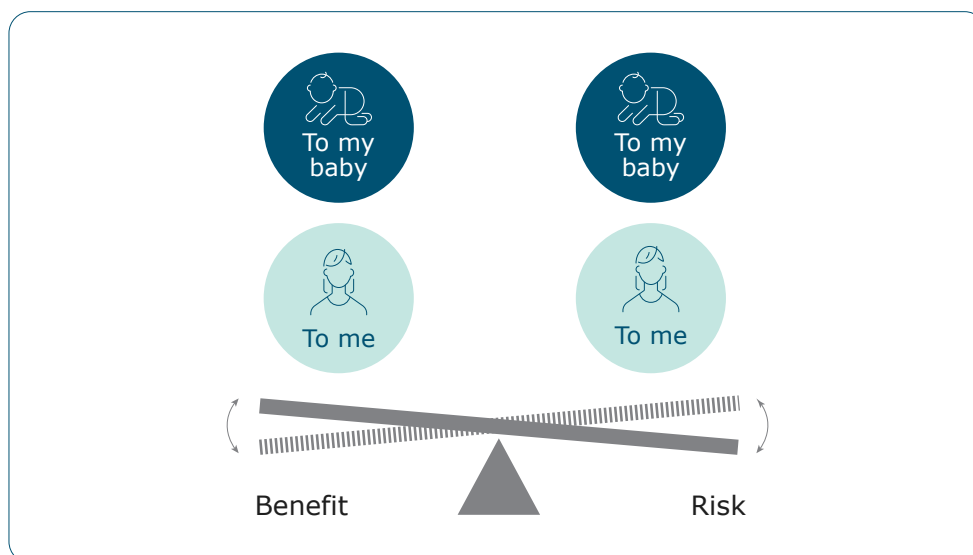
Medicines regulators already collect, assess and communicate evidence on medicine safety in pregnancy based on data from non-clinical reproductive toxicity studies, knowledge from the medicine’s mechanism of action and class, as well additional information from pharmacovigilance activities. Although there are methodological and ethical challenges, increasingly there are also opportunities for building up evidence, by creating infrastructure for research on the topic, and through cross-disciplinary collaboration, for example between researchers in epigenetics, pharmacoepidemiology and neurodevelopment. These opportunities will support generating more data on medicines safety for the unborn and breastfed baby.

PANEL DISCUSSION AND FEEDBACK FROM THE AUDIENCE

The panel:
Hildrun Sundseth, European Institute of Women’s Health (EIWH); Paul Ryan, Irish College of General Practitioners/ European Union of General Practitioners (ICGP/UEMO), Agnès Saint-Raymond (EMA’s Head of the International Affairs Division); Ulla Wändel Liminga, EMA’s Safety Pharmacovigilance Risk Assessment Committee (PRAC), Swedish Medicines Agency; Miriam Sturkenboom, Utrecht University Medical Centre, Netherlands; Helen Dolk, EUROmedICAT, Ulster University, UK.

“A change in mindset is needed when it comes to benefit-risk considerations. We should stop focusing solely on the risks to the unborn baby, and also consider the benefits to the mother of being treated, as well as the consequences to both the mother and baby of not being treated.”

Agnès Saint-Raymond, EMA, qualified paediatrician



Available data should support evaluating the benefits of using a medicine for the mother and the baby on the one hand, against the risks for the mother and the baby on the other hand, with an assessment for each patient.

The benefits and risks should also be considered in the context of disease severity of the mother. The possible impact on the mother, and possibly her baby, of not being treated needs to be carefully assessed. More research is needed to better understand the natural course of certain diseases during pregnancy, as well as the potential impact of a disease on the pregnancy outcome.

During the panel discussion, the workshop participants were polled about their need for further information: of the 156 respondents, 62% said they would like more information on the benefits for the mother and baby of using a medicine compared with not using it, emphasising the need to better understand the consequences of not being treated.

In terms of data generation, more can be done throughout the medicine's lifecycle. International guidelines refer to animal studies to investigate the harmful effects of medicines during pregnancy and breastfeeding; however, these models have limitations, and therefore uncertainties about their predictive value remain.

Innovative methods to better predict any potential harmful effect a medicine may have on an unborn baby should be further developed and applied. The more predictive data can be generated during the early stage of medicine development, the better it is for planning of later development phases and post-authorisation evaluation. Examples of such innovative methods include building on learnings from epigenetics, data-sharing of non-clinical data and applying artificial intelligence methods, as well as novel methodologies for developing non-clinical models of medicines and breastfeeding, as is currently being developed in the CONCEPTION project.

Clinical studies aim to show efficacy and safety of medicines in the patient population for which an authorisation is being sought; pregnant women are usually excluded from these studies for ethical and feasibility reasons. In the pre-authorisation phase, the clinical trial setting is geared towards evaluating the benefits and risks in a relatively homogenous population; therefore, including pregnant women, particularly in the early development of the medicine, is often not justified as there is limited knowledge about the potential benefits and risks of the substance. The panel agreed however that systematic exclusion of pregnant women from all stages of clinical studies is not the right approach. This view was shared by workshop participants who emphasised the need to involve pregnant women in decision-making about their participation.

The nature of the disease and the medicine being tested (e.g. whether it is new or belongs to a known class of medicines, or whether it is likely to be used during pregnancy) and existing knowledge about the potential risks or benefits from other studies should be taken into account. The panel also highlighted that opportunities to gather more knowledge during clinical research should be seized, for instance from women who become pregnant unexpectedly while taking part in a clinical trial. While it is required to monitor the health of these women, and their babies if applicable, in practice, challenges often prevent effective follow up; these issues need to be explored and addressed.

Once a medicine is on the market, information may become available in clinical practice about its use in pregnant and breastfeeding women, and this should be collected systematically and used efficiently so that women have the latest information.

“Pregnancy is a unique time in life when all women see a healthcare professional regularly. We need to take full advantage of these opportunities to collect information.”

Helen Dolk, Professor of Epidemiology and Health Services Research at Ulster University, UK

Although healthcare data are routinely recorded post authorisation, several issues prevent their effective use, limiting the ability to turn these data into evidence that can help inform decision making.

These issues include the lack of standardisation in how data are recorded and gaps in the data that need to be collected. In addition, systems for collecting data are not always fit for the purpose of post-authorisation evidence generation and, while it is acceptable to keep the data locally, i.e. at regional or national level, the various pregnancy registries and databases should be better interconnected to allow meaningful analysis.



Did you know?

EMA and the heads of EU medicines agencies have set up a [big data steering group](#) whose work plan aims to increase the utility of big data in regulation, from data quality through study methods to assessment and decision-making. Stakeholders will have the opportunity to discuss the [workplan](#) and its implementation at a virtual multi-stakeholder forum in late 2020.

All panel members also highlighted the need for a sustainable model of post-authorisation data collection and analysis that will generate strong and reliable evidence for decisions on medicine use during pregnancy and breastfeeding.

“There is a lot of capacity to analyse the vast amount of healthcare data that is collected every day, but we need a sustainable model so that these data can be used fully and optimally. We have the means to realise the change, but we need political willingness.”

Miriam Sturkenboom, pharmacoepidemiologist, Professor in Observational Data Analysis, UMC Utrecht, the Netherlands

When it comes to communicating on the benefits and risks of using a medicine during pregnancy or breastfeeding, healthcare professionals and patients shared the view that recommendations included in the summary of product characteristics (SmPC) and package leaflet (product information) are too conservative and risk averse, and do not provide meaningful information on which they can base their decisions. The suggestion was made to add links to other sources of information; however, this would need to be considered in the broader perspective of overall improvement of the product information.

In one or two words, what do you see as the biggest challenge for achieving improvements in the area of medicine use in pregnancy and breastfeeding?

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Workshop participants emphasised the necessity to also look at the needs of breastfeeding women specifically, as they are different to those of pregnant women. More research is necessary to better understand the transfer of medicines into breast milk, subsequent uptake of the medicine by the baby, and the potential risks such exposure may cause. Ways to encourage women who are breastfeeding and using medicines to contribute to medical research in this area were suggested. These included: encouraging physicians, gynaecologists and midwives to talk about the benefits of collecting information and the importance of research; establishing financial incentives for providing milk samples; explaining how the milk will be used; sharing the outcomes of research to promote engagement; collaborating with breastfeeding support organisations; and setting up easy sample collection systems.

CONCLUSION OF SESSION 1

- Although only very few medicines have been proven to be teratogenic in humans, there remains considerable uncertainty for most medicines regarding their safety for the baby. Because withholding treatment may also be harmful to the mother and baby, there is a clinical need and an ethical imperative to generate the right efficacy and safety data to better inform decision making on the use of medicines during pregnancy and breastfeeding.
- A change in mindset across all stakeholders is needed when it comes to considering the benefits and risks of medicines for pregnant and breastfeeding women. It is already recognised that the potential risks of a medicine to the unborn baby should be seen in the context of its benefits to the mother, the severity of the disease and the consequences of not treating a condition, both for the mother and the unborn baby. However, the lack of information on the safety of the medicine to the unborn or breastfed child makes decision making in clinical practice challenging and this uncertainty needs to be addressed.
- The current approach of almost systematically excluding pregnant and breastfeeding women from clinical trials is too rigid; a different approach is required when it comes to generating and obtaining data on the benefits and risks of medicines in those women. Their participation in clinical trials should be considered more routinely.
- Healthcare data are routinely recorded post-marketing. During pregnancy and breastfeeding, virtually every woman in Europe is in contact with a healthcare professional, and this provides us with unique opportunities for collecting such data. However, currently the data are not used optimally. A sustainable process and funding model are necessary to help ensure the data can better inform evidence-based decisions on treatment options during pregnancy and breastfeeding.



Session 2 – What is currently being done

Chaired by Sabine Straus, Chair of EMA’s Pharmacovigilance Risk Assessment Committee (PRAC)

THE EU REGULATORY FRAMEWORK

In the EU, the medicine’s regulatory framework requires a product-specific evaluation of the benefits and risks of a medicine in order to grant marketing authorisation, without a mandatory head-to-head comparison of products. At the time of marketing authorisation, regulators will have assessed non-clinical data on the effects of a medicine at all stages of reproduction, as well as any clinical data related to reproduction if available, also taking into account knowledge about similar medicines, the medicine’s characteristics and the disease itself.

Based on this pre-authorisation knowledge, each medicine needs a risk management plan (RMP). This may include plans for collecting information on potential risks for pregnant and breastfeeding women, as well as other missing information as applicable. It also contains any additional risk minimisation measures that need to be put in place, such as the requirement for the company to produce educational materials, or the need for patients to use effective contraception while using the medicine, and any requirement for additional studies to be conducted post-authorisation.

If concerns have been identified either from non-clinical studies or from similar medicines, strict recommendations (such as avoiding use in pregnancy) may be included in the product information.

Once medicines have been authorised, they may be used in a broader population than that included in clinical trials, including pregnant and breastfeeding women. In addition, medicines can be used in populations or for disorders that are not covered by the approved indication (off-label use). Post-authorisation, several regulatory tools are therefore in place to further characterise the medicine’s benefit-risk profile by gathering information from clinical practice. They include:

- routine regular reviews of the benefits and risks in so-called periodic safety update reports (PSURs);
- routine signal detection of suspected adverse reactions reported in databases and in the literature;

- post-approval safety studies addressing, for example, pregnancy outcomes and effectiveness of risk minimisation activities.

EMA is currently developing a [good pharmacovigilance practice](#) (GVP) chapter to specifically address medicines' safety monitoring in pregnant and breastfeeding women.

“The aim is to minimise adverse outcomes from medicine use during pregnancy, without unnecessarily withholding useful treatment options from pregnant women.”

Ulla Wändel Liminga, Scientific director pharmacovigilance, PRAC and Swedish Medical Products Agency

Safety monitoring will focus, for instance, on detecting any cases of adverse outcome after pregnancy exposure classified as serious reports and any signals of possible teratogenic effect (e.g. a cluster of similar abnormal outcomes) to be notified immediately to authorities (see in GVP Module IX).

These activities can lead to new risk minimisation measures being put in place post authorisation, with the objective of reducing risk to the baby as much as possible while considering the benefits and need for treatment of the mother.

COVID-19: A CONCRETE EXAMPLE OF WHAT CAN BE DONE – THE CONSIGN STUDY

A high number of small and large-scale studies are taking place across the world to test therapeutics and vaccines for COVID-19. To date most of these clinical trials have excluded, or included very few, pregnant or breastfeeding women, making it impossible to formulate evidence-based recommendations on the use of COVID-19 treatment options for them.

In early 2020, EMA launched an invitation to tenders to develop evidence-based decision-making about COVID-19 vaccines, vaccination policies, and treatment options for pregnant women.

Mid-July EMA signed a contract with Utrecht University and the University Medical Center Utrecht as coordinators of the CONSIGN project ('COVID-19 infectiOn aNd medicineS In preGNancy'). This project will collect data on the impact of COVID-19 in pregnancy in order to inform risk management planning for future COVID-19 vaccines and treatments. It is being carried out in collaboration with the [ConcePTION consortium](#), which was established under the EU's [Innovative Medicines Initiative](#), the [COVI-PREG project](#) and the [International Network of Obstetric Survey Systems \(INOSS\)](#).

CONSIGN will analyse existing data sources (e.g. electronic health records, hospital data) and cohorts of pregnant women to provide information on the effect of SARS-CoV2 infection and its treatments in different trimesters of pregnancy and in neonates.

The project will include primary data collection throughout pregnancy and up to birth using standardised formats, as well as secondary use of healthcare data to allow for retrospective analysis of recorded data.

“We know from surveys that women are willing to share their data with doctors and academics to help other women, as long as compliance with data protection rules is guaranteed. However, pregnancy is also a time in life when women tend to be too busy to actively participate in such projects. We need therefore to support them and facilitate data collection for them.”

Miriam Sturkenboom, pharmacoepidemiologist, Professor in Observational Data Analysis, UMC Utrecht, the Netherlands

Through collaboration with other international initiatives, coordinated together with EMA and through the International Coalition of Medicines Regulatory Authorities (ICMRA), all clinical, epidemiological and analytical expertise available within the international community will be used to generate high quality evidence in a transparent manner.

One of the objectives of the project will be to test whether the real-world evidence collected and analysed in this way will be sufficient and of sufficient quality to support regulatory decision making. It is envisaged that in the future, the infrastructure and network built through the CONSIGN project, as well as the international collaboration through ICMRA, will provide opportunities for evidence generation on medicine use in pregnancy beyond COVID-19.

PANEL DISCUSSION AND FEEDBACK FROM THE AUDIENCE

According to a poll carried out during the workshop, collaboration between the various stakeholders' groups, access to quality data and increased funding were highlighted as the main drivers for achieving meaningful improvements.

It is one thing to collect and analyse data on medicines; communicating on the benefits and risks is another. The case of valproate, where the high risk of developmental problems was not known to many women being treated with the medicine despite this information being included in the product information, is a good example of the key role of communication in ensuring that information reaches the right audience and is understandable.

Healthcare professionals observe that once patients know the harmful effects of a medicine, they understand that restrictions are for their own good and why regulators are being prescriptive. When safety concerns have been identified, a common risk minimisation measure is to recommend use of effective contraceptives. According to a poll carried out during the workshop, 2 out of 3 respondents consider that regulators should be relatively forceful when it comes to recommending using effective contraception. However, this should not go so far as to, for example, require two effective forms of contraception if one of those includes sterilisation. Overall, the aspiration should be to find an appropriate balance.

“Recommendation to use contraception should only be envisaged when teratogenicity is known and established for a medicine. We would not like such recommendations to be included commonly in package leaflets.”

Hildrun Sundseth, past President of European Institute of Women's Health

CONCLUSION OF SESSION 2

- The EU regulatory framework, and especially the pharmacovigilance system, provides a number of tools to monitor the benefits and risks of medicines once they are used in clinical practice, from the detection of new signals to the conduct of post-authorisation studies.
- Structured ways of collecting pregnancy data in clinical practice are being explored in the context of COVID-19 and will benefit other disease areas.
- Communication is of utmost importance to ensure that patients and their healthcare professionals make informed decisions about their treatment during pregnancy and breastfeeding. This needs to include different situations of planned and accidental exposure (e.g. in unplanned pregnancies, which are not uncommon). High quality information sources are key to enable such decision making and to support trust between patients and their healthcare professionals.



Session 3 – How to move towards a paradigm shift in clinical research and medical practice

Chaired by Ulrich Jäger, Co-Chair of Healthcare Professionals' Working Party (HCPWP)

There are many sources of healthcare data on medicine use and outcomes in pregnancy and breastfeeding, from primary care to hospital data, prescription data, maternity data/medical birth registries, child development data, disease registries, pregnancy exposure registries and birth cohorts.

Medicine developers, regulators, patients, healthcare professionals, academics: everybody has a role in the route to collecting, processing, validating, analysing and ultimately turning these data into evidence that will support well-informed decision making.

However, many issues prevent full use being made of healthcare data. These include suboptimal or no recording of:

- hospital prescriptions at the level of individual patients
- non-prescription medicines
- drug-drug interactions and treatment switching

- actual use (i.e. adherence to treatment), dose and timing of treatment
- confounding factors, such as the disease itself, any comorbidity, socioeconomic factors, lifestyle factors, etc.

In addition, the delay between exposure (*in utero*) and outcome (e.g. birth defects, developmental delay, other disorders that are not detected until several years later during child development) throws up challenges when it comes to evaluating the benefit-risk of medicine use in pregnancy and, to a lesser extent, during breastfeeding.

A post-marketing surveillance system where evidence generation would include both primary data collection (with real-time collection of information as exposures occur) and secondary use of routinely recorded data, as well as hybrid approaches (i.e. linking primary data to secondary data), is needed.

“Making reporting of new or rare pregnancy exposures to national pregnancy registries mandatory, as well as improving the data available for secondary use of healthcare data, would greatly facilitate evidence generation.”

Helen Dolk, Professor of Epidemiology and Health Services Research at Ulster University, UK

The [IMI ConcePTION project](#), which will run for 5 years until March 2024, is an opportunity to achieve a leap forwards in terms of generating evidence that meets regulatory acceptance and, as such, could lead to changes in the medicine label and SmPC. The project aims to develop an infrastructure, including a prototype for a single European knowledge bank and human breastmilk biobank, to facilitate evidence generation and dissemination. The project builds on existing initiatives such as [EUROmedICAT](#), a network and database comprising data from population-based congenital anomaly registries and pharmacy dispensing data, as well as other sources, which support both systematic signal detection and signal evaluation.

A paradigm shift is needed around evidence generation and secondary use of healthcare data¹. The ambition is to create a regulatory-healthcare bridge that would allow a move from single-product evaluation to disease-based benefit-risk evidence. This requires an efficient system for collection and analysis of diverse sources of data, supported by new technologies and digital tools such as mobile apps and increased and sustained funding. It was suggested that marketing authorisation holders’ fees to fund pregnancy pharmacovigilance activities might be considered.

“To improve knowledge and understanding and achieve well-informed decision making on benefit-risk, a multipronged, global approach will be required. There is momentum globally for initiatives in this area, in the context of COVID-19 and the recent EU review of [valproate](#). In designing the EMA strategy, we will build on experience gained with these various initiatives.”

Corinne de Vries, EMA, Head of Translational Sciences Office



¹ See [workshop](#) report on the application of the General Data Protection Regulation (GDPR) in the area of health and Secondary Use of Data for Medicines and Public Health Purposes.

CONCLUSION OF SESSION 3

- Increased and sustained investment is needed to ensure a high-quality infrastructure is developed and maintained for routine and de novo data collection and analysis methods in pregnancy and breastfeeding. A multinational approach is necessary in view of the rarity of certain adverse events.
- We are not starting from scratch: a number of ongoing initiatives (EUROmediCAT, ConcePTION, CONSIGN, as well as additional population-based cohorts) can be built on to achieve such infrastructure.
- Collaboration between the various stakeholders' groups, access to quality data and increased funding were highlighted as the main drivers for achieving meaningful improvements.
- A constructive way forward would be a coordinated approach between the different stakeholders, harnessing their respective knowledge, tools and input, when it comes to both data collection and evaluation and joint communication on the benefit-risk balance.
- There was a call from participants to organise a follow-up workshop with two separate streams: one for pregnancy and one for breastfeeding.



Conclusion and next steps

The use of medicines in pregnant and breastfeeding women is a reality. A large majority of pregnant women take medications while information about the medicine's safety to the unborn child or the extent to which it is transferred to milk at levels that may affect the breastfed infant is not available.

Change is needed on multiple levels so that these women have the evidence they need to make well-informed decisions about their medicine use.

First, there is a need for awareness of the challenges surrounding the benefit-risk evaluation across all stakeholders. There is a general consensus that any potential risks to the baby should be seen in the context of maternal disease and the benefits a medicine will bring to the mother. Not treating a condition or stopping treatment can also have serious consequences for the mother and baby that need to be carefully considered. Despite this consensus, uncertainties regarding safety to the unborn or breastfed child, combined with emotive aspects, can make it very challenging to make the optimal treatment decision. This is not something regulators, researchers, medicines developers, clinicians or patients can solve in isolation. It is EMA's ambition to work collaboratively with our

stakeholders to find innovative solutions to better tackle these long-standing challenges and help alleviate these uncertainties.

There is a call to use all relevant tools to generate more data on the benefits and risks of medicines in pregnant and breastfeeding women throughout a medicine's lifecycle. In addition, there is consensus that change is required from the almost routine exclusion of pregnant and breastfeeding women from clinical trials. While it is justified to exclude pregnant and breastfeeding women in the early stages of medicine development when little is known about the effects of the medicine, their participation should however be considered in the later stages.

During pregnancy and breastfeeding, there tend to be multiple interactions between women and their healthcare professionals, and a vast amount of data is routinely recorded in clinical practice. Although this represents a unique opportunity to collect relevant data, there is a shared view that these data are not being used efficiently and optimally. A sustainable model and infrastructure are needed so that these data can be systematically tapped into, recorded, collected, processed, analysed and turned into evidence that can support better informed decision-making, before being communicated

in an effective manner. Such an approach is currently being tested globally in the context of COVID-19 and should provide helpful learnings, and possibly infrastructure, for other disease areas.

EMA and its safety Committee PRAC have been working on dedicated guidance for medicines' post-authorisation monitoring in pregnant and breastfeeding women, as part of a new GVP module which is currently being finalised following a public consultation.

EMA is also developing a strategy for generating better information on the benefits and risks of medicines in pregnancy and breastfeeding. The feedback and suggestions received from stakeholders during the workshop will inform this strategy.

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