# PHARMAVIG-PREGNANCY: A proposal for a common funding route for pharmaceutical companies to fund pharmacovigilance related to medication safety in pregnancy

# Introduction

The ENCePP Code of Conduct for scientific independence and transparency sets out a number of principles which reduce the risk of conflict of interest and its actual or perceived impact on research.

Specifically for the relationship of pharmacovigilance researchers with the pharmaceutical industry, an even stronger assurance of scientific independence would be gained from routing research funding via an independent intermediary, so that there is no direct contract between the research institution and the pharmaceutical company.

A centralised independent funding system may be a “win-win” situation with advantages beyond scientific independence, and for all stakeholders.

# Why focus first on Medicine safety in pregnancy?

- pregnant women are not included in clinical trials
- teratogenic effects are poorly predicted by animal and laboratory studies.
- Pregnant women need to be able to take medicines in pregnancy with evidence as to their relative safety. The fact that most medicines are of unknown safety is not tolerable.
  - Women may not be taking the medication with optimal risk-benefit balance for themselves and their baby
  - Women may not be taking necessary medication at all due to uncertainty regarding safety
- Increasing evidence of neuro-behavioural effects, is increasing anxiety in this area(e.g. valproate).
-

- What is needed?
  - all new medicines marketed should be subject to intensive post-marketing surveillance in relation to their use in pregnancy.
  - there should be a review of all medicines taken in pregnancy to determine gaps in evidence and priorities for pharmacovigilance.
  - The infrequency of pregnancy exposures to specific medications and outcomes such as congenital malformations means we need to take an international collaborative approach.
  - need an overarching framework to make sure that appropriate high quality reproductive pharmacovigilance is conducted in a phased manner.
  - a step change in the quality of reproductive pharmacovigilance, with lasting benefits for women and children.

**The advantages of a single independent funding pot ringfenced for pregnancy-related pharmacovigilance:**

1. To make it easier for pharmaceutical companies to have their reproductive pharmacovigilance research needs addressed, and for research institutes to have priority research areas funded, by having a single point of contact, rather than individual contacts between multiple pharmaceutical companies and multiple research institutions.

2. To enable an integrated approach to reproductive pharmacovigilance funding to be developed for Europe, and clarity in investment in reproductive pharmacovigilance and its infrastructure.

   no funding stream in Horizon2020,

   IMI is limited to large public-private projects, following medium to long term strategic objectives

   need responsive funding streams – responding to signals or new developments (e.g. swine flu related products)

3. Such a system may bring databases into use which are currently not available for access by industry-funded research.
4. Such a system could facilitate the funding of research infrastructures/databases that can address needs across many pharmaceutical companies, regulators and research institutes, or facilitate research on drug classes with products from multiple companies.
5. Such a system can help balance research and pharmacovigilance between new medications and filling the huge gaps in information on medications already in common use for the public benefit.
6. The epidemiological, pharmacovigilance and teratological expertise required to commission and evaluate reproductive pharmacoepidemiological research protocols can be centralised.

7. To enable a single funding contract format to be developed, observing the ENCePP Code of Conduct, and reducing the need for legal input from the pharmaceutical company and research institute for each research contract.

8. To even further reduce the potential for influence of funder on research results or publication.

9. To reduce conflict of interest and increase the perceived credibility of the research.
   - For pharmaceutical company, increasing credibility increases value-for-money, and increases the ultimate impact of the research.
   - For researchers, stating in research papers that funding has, for the current study or past studies, come from a pharmaceutical company can be interpreted by research users as evidence that there may be conscious or unconscious bias, which leads many researchers to avoid pharmaceutical funding sources.

# Potential models

1. Legal obligation or voluntary participation by pharmaceutical industry. There are distinct advantages for industry which could be exploited in a voluntary arrangement while considering further legal obligations.
2. The independent funding agency which administers the funds and coordinates the research programme at EU level can be either a new agency, a department of a medicines regulatory authority, or an existing research council.
3. Unconditional funding could come 100% from pharmaceutical companies as it is a replacement of direct industry funding. There could be redirection of pharmacovigilance fees already paid to EMA or a specific new fee or both. However, a contribution from public funding would have many advantages – to ensure that there is a strong public stake in the process, to meet public expectations, to increase the total amount of funding available in such an important area, and as a further incentive for pharma to take part.

4. The amount contributed by each pharmaceutical company to the central funding pot could be in proportion to sales in Europe, the marketing budget (as previously done in Italy for RD), or in proportion to new products on the market.
5. All funded research should use the ENCePP Code of Conduct.
6. Research projects could be identified by pharmaceutical companies, researchers, regulators or all of the above. Preference is a responsive system (e.g. to allow new signals to be addressed quickly), funding small to large projects.

7. Prioritisation of projects to be funded (i.e. which medications or research needs take priority) could be undertaken by a stakeholder committee, mainly independent of industry and involving patient-public and healthcare professional organisations, regulatory authorities, public health and academic bodies.
8. Research project applications would be selected according to normal processes of peer review and committee selection.
9. Governance model to be determined.

# Proposed deliverables

- Refer to the ENCePP SIG Pregnancy for further support/elaboration (completed);
- Put the proposal to the ENCePP Steering Group for comments (completed);
- Consult the proposal with Agency's Patient Consumer and Healthcare Professionals Working Parties;
- Organise a meeting with industry to discuss;
- Develop the valproate referral as a case study for how such a system might work and its advantages;

# Discussion…..

- The idea of an independent funding pot?
- Voluntary or obligatory on the part of industry? Using which funds? In proportion to what?
- Whether there should be public funding contribution also?
- Appropriate institution to administer?
- Terminology: “Safety” vs “harms” (not merely absence of evidence of harm)