

# GCP Discussion

## *Pregnancy of Research Subject's Partner*

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A REGULAR PART OF ICR's popular GCP Forum meetings is the discussion section, where delegates can raise or (preferably) submit in advance questions on the interpretation and application of GCP, other guidelines, legislation and common working practices, often in unusual or challenging scenarios. These are discussed by delegates at the meeting, with supporting citations provided (if possible) by members of the GCP Forum Steering Group. Questions are sometimes discussed by the Steering Group between meetings, and in this case we felt that it would be beneficial to share our thoughts with readers of CRfocus rather than wait until the next Forum meeting on March 17th 2010.



*“The pregnant participant of a clinical trial (or his partner, in this case) should therefore be followed up, at least until they have given birth.”*

### Question

THE QUESTION WE were asked to consider was “What if the partner of a trial subject becomes pregnant: what are the safety reporting procedures? How is consent obtained from the pregnant partner to do this?”

### Steering Group opinion

PART OF THE definition of a Serious Adverse Event (SAE), as defined by ICH GCP 1.50, is a “congenital anomaly/birth defect”. Pregnancy itself is therefore not an SAE. The pregnant participant of a clinical trial (or his partner, in this case) should therefore be followed up, at least until they have given birth. The frequency and length of follow-up should be defined clearly in the study protocol.

Additionally, Volume 9A (Guidelines on Pharmacovigilance for Medicinal Products for Human Use; September 2008) states the Marketing Authorisation Holder (MAH) should follow up all reports of pregnancies where the foetus may have been exposed to one of its medicinal products; this can be a result of maternal exposure or transmission of the medicinal product via semen following paternal exposure.

### Follow-up & reporting

The MAH should gather information relating to both normal and abnormal outcomes. Follow-up should be conducted at suitable intervals. This usually involves follow-up at the time of the initial report and also around/ after the expected delivery date.

The most common inspection finding related to reporting of pregnancies is that there is no mechanism in place to track the expected delivery date; this results in no attempt to follow up to obtain outcome.

Volume 9A clearly defines the requirements for expedited reporting of Individual Case Study Reports (ICSRs) to competent authorities. Expedited reporting is required if a medicinal product has been used during pregnancy which results in an abnormal outcome for the foetus/child. Also, adverse reactions suspected in infants following exposure to breast milk require expedited reporting. By expedited reporting, we mean that the MAH is required to report these incidents in less than 15 days from receipt; this includes both initial and follow-up information. Further follow-up, of course, will be conducted later.

*“... obtaining consent from the pregnant partner is also not so clearly defined in regulations.”*

### US regulations

The US regulations for clinical trial SAE reports (21 CFR 312.32) do not provide specific guidance on what/how to collect. It does state that congenital anomalies/birth defects are serious outcomes (requiring 15 day reports) and that 15-day reports are required for “any finding from tests in laboratory animals that suggests a significant risk for human subjects including reports of mutagenicity, teratogenicity or carcinogenicity”. The best guidance comes from the CIOMS Working Group VI (“Management of Safety Information from Clinical Trials”), page 90, which states: “Pregnancies occurring during clinical trials present a unique situation. Any pregnancy that occurs in a female trial participant during a clinical trial should be followed to termination or term... there may be special situations when it will be necessary to monitor the pregnancy of a woman whose male partner is the trial participant. Partner privacy may become an issue in follow-up for these situations. The protocol should describe in detail the process for monitoring and managing pregnancy occurrences.”

### Obtaining consent

THE ISSUE OF obtaining consent from the pregnant partner is also not so clearly defined in regulations. When some or all of the participants are likely to be in a vulnerable class of participants, ie, women of childbearing age, the protocol and informed consent should describe what additional safeguards are included to protect their rights and welfare, and that the particular treatment or procedure may involve risks to the subject (or to the embryo or foetus, if the subject is or may become pregnant) that are currently unforeseeable (21 CFR 50.25 (b) (2) and ICH GCP 4.8.10 (g)).

If there is a risk of congenital abnormalities arising from a medicinal product by transfer via semen, this needs to be clearly documented in the protocol and consent forms. In this case, a ‘pregnant partner’ consent form can be used. The partner would need to consent as well as the trial subject. In the USA, they would also need to sign a separate authorisation for release of their medical records (in accordance with HIPAA requirements). Sometimes this might be considered as a sub-study. In most cases, the risk to the partner is defined in the trial subject’s consent form with no additional form for the partner to sign.

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## ICR Events



This forum will explore the NHS Research Scotland network and the processes for obtaining R&D approval in Scotland and England, highlighting the similarities and the differences between the two systems.

Scottish Forum  
The R&D approvals process in Scotland – The NRSCC/UK perspective

Thurs 25 February 2010

Glasgow Caledonian University

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