Purpose

This document aims to provide guidance to investigators when their study design involves pregnancy and sexual health related testing as per chapter 4.1 of the *National Statement on Ethical Conduct in Human Research (2007, incorporating all updates)* and *ICH Guidance on Non-Clinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorisation for Pharmaceuticals M3 (R2).*

Guidance

When designing and developing a protocol, investigators must refer to the ICH Guidance on Non-Clinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorisation for Pharmaceuticals M3 (R2). This guidance outlines how to conduct reproductive toxicity studies for the population that is to be exposed (men, women not of child-bearing potential or women of child-bearing potential). For each population group, the ICH Guidance provides inclusion criteria as well as essential definitions regarding reproductive terminology (e.g. postmenopausal).

Contraception

Bellberry encourages investigators to only include highly effective, Australian approved contraception methods in communications with participants.

Examples of acceptable forms of highly effective contraception include:

- Established use of oral, injected or implanted hormonal methods of contraception.
- Placement of an intrauterine device (IUD) or intrauterine system (IUS).
- Sterilised male partner (with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate).
- True abstinence: When this is in line with your preferred and usual lifestyle.

Examples of non-acceptable methods of contraception include:

- Condoms alone or double barrier.
- Periodic abstinence (e.g. calendar, ovulation, sympthothermal, post ovulation).
- Withdrawal.
- Spermicide (as it is not approved as a method of contraception in Australia).

Consent Considerations

- Participants need to be clearly informed of potential reproductive risks.
- The participant needs to be provided with opportunities to discuss any concerns with the study doctor.
- Additionally, in the case of participants becoming pregnant during the study, a separate consent form is required to follow up on the progress of the pregnancy and the birth and health of the child. (The Principal Investigator is required to nominate and justify a follow up time, but this is expected to be not less than 12 months following birth.) (See references below.)
- Informed consent should be based on any known pertinent information related to reproduction toxicity, such as a general assessment of potential toxicity of pharmaceuticals with related structures or pharmacological effects. If no relevant reproductive information is available, the potential for unidentified risks to the embryo or fetus should be communicated.
- Fertile men involved with early phase clinical trials where there is an absence of reproductive toxicology studies are required to abstain from unprotected sex and sperm donation for at least 90 days after the last administration of the drug. If the drug has a known mechanism of action that is associated with sperm abnormality, then a different time period may be warranted. For men who are infertile and do not produce sperm (e.g. post-vasectomy), the decision about the period of abstinence from unprotected sex should be made after considering the pharmacological profile of the drug.

The forms listed in the references provide other standard PICF wording that is approved by Bellberry.

References

The National Statement on Ethical Conduct in Human Research (2007, incorporating all updates)
ICH Guidance M3 (R2)
Journal of Clinical Neuroscience 14 (2007) 936–942, The Australian antiepileptic drug in pregnancy register: Aspects of data collection and analysis
The Lancet, published online April 18, 2018 Comparative risk of major congenital malformations with eight different antiepileptic drugs: a prospective cohort study of the EURAP registry
BA F14.1.1 Standard clauses – pregnancy & sexual health
BA F14.1.2 Pregnancy/pregnant partner data release - template