

## **Appendix 1: Wording of questions in surveys to clinicians and women to determine clinically important difference**

### For clinicians:

We are planning to unblind and analyse the PITCH trial (UDCA vs. placebo) as we have not been successful in obtaining HTA funding for the main trial.

We are writing a more detailed statistical analysis plan prior to any unblinding and would like to look at maternal itching score as a main outcome measure for the UDCA (vs. placebo) comparison. We assessed maternal itching using a Visual Analogue Scale where 0mm represented no itching and 100mm the worst itching. You will be aware that UDCA is currently not licensed for use in pregnancy and that there is no definitive evidence of fetal benefits or harms.

We would like to pre-specify a CLINICALLY USEFUL decrease in itching score so that we do not over-interpret or misinterpret our results – which may show some statistically significant, but not clinically meaningful difference. We are also asking the same question to women who have had obstetric cholestasis.

At enrolment prior to randomisation, the mean score for the worst episode of itching in the previous 24 hours was 60mm. What decrease in itching score do you think is clinically meaningful, such that you would recommend UDCA to pregnant women?

- 5mm (a very small decrease in itching)
- 10mm
- 15mm
- 20mm
- 25mm
- 30mm
- 40mm
- 50mm
- 60mm (complete resolution of itching)

### For women (recruited through the OC Support UK patient support group):

Suppose you are pregnant and have obstetric cholestasis (OC). You have been offered a drug that may help reduce your itching. This drug has never been fully tested for use in pregnancy so doctors don't know how safe it is. However, it has been used to treat women with OC and so far there have been no reports of any problems for either the mother or the baby. It is also known to be safe for people who aren't pregnant.

We'd like you to imagine that you agree to take the drug and that every week you will be asked to score your itch on a scale from 0 (no itching) to 100 (the worst itching). Before taking this drug your score is 60. How much of a decrease would you need to have on the scale (next time you score your itching) for you to consider that the drug is worth taking?

- 5mm (a very small decrease in itching)
- 10mm
- 15mm

- 20mm
  - 25mm
  - 30mm
  - 40mm
  - 50mm
- 60mm (complete resolution of itching)