

Limitations of working with human embryonic/fetal tissue

Collection

- **The frequency and age of tissues collected cannot be guaranteed**

The HDBR have no input or influence on the working practice of the clinics from which material is collected. The material collected from consenting women may be from any stage of pregnancy that the HDBR has ethical approval to approach. In addition, the women attending clinic are under no obligation to consent, and are free to withdraw their consent at any time up until the time of the termination. As the HDBR are completely independent and separated from any material collection centre, the developmental stage or the frequency of the material being collected cannot be predicted.

Staging

- **Difference between gestation and post conception weeks**

Clinicians usually refer to a pregnancy in terms of gestation weeks: day one commences with the start of the women's menstrual period and ovulation and fertilisation occurring during the end of second week/beginning of the third week. Up until this time the woman is not pregnant, and therefore the age of developing embryo or fetus is often described in terms of post conception weeks (PCW) starting from the point at which fertilisation took place. This means there is an approximate 2-week difference between the number of gestation weeks and the post conception weeks of an embryo/fetus. It should be noted however, that both of these terms are not used universally and when referring to PCW sometimes the term gestational weeks will be used interchangeably by different authors. All fetal samples in the HDBR collection are staged as PCW.

- **Staging guides**

HDBR samples are staged according to their external physical appearance and measurements and not to the estimated last menstrual period. All embryonic samples (8 PCW and younger) are classified as belonging to a particular Carnegie stage using the staging guide that can be viewed here:

http://hdb.org/downloads/embryo_staging_guidelines.doc and fetal samples using these criteria

http://hdb.org/downloads/fetal_staging_guidelines.doc.

- **Differences between the age of samples of the same stage**

Developmental variability may be observed between samples that have been staged to the same Carnegie stage or to a particular fetal week. Both of these classifications cover a time range during development, not a specific time point. This may be

especially apparent if two samples are at the two extremes of a particular stage or week.

Sample variation

- **Natural sample variation**

For the majority of the HDBR samples the exact genotype is not determined. However, most samples are karyotyped and samples both with and without chromosomal anomalies are available for request.

Some anonymous donor information is available to accompany some of the samples - age, BMI, previous pregnancy outcomes, alcohol and tobacco consumption and drug use.

- **Tissue processing times**

There is an unavoidable delay between the material becoming available at clinic and it being processed in the laboratory. The time taken between these two events will vary for each sample, this and the nature of the clinical procedure itself means there can be significant sample to sample variation in the time of tissue processing.

- **Archived fixed samples (wax blocks or slides) will suffer nucleic acid and protein degradation over time**

Whilst every effort is made to minimise the time prior to fixation and to eliminate RNase, DNase and protease contamination of the HDBR material, regrettably, the samples will suffer some degradation over time. All slides sectioned by the HDBR are verified by either in situ hybridisation or immunohistochemistry, depending on their intended use, with our quality control probes or antibodies prior to leaving the tissue bank. However, samples that are sent as wax blocks to be sectioned by users are not QC tested.

Governance considerations

- **The consent, use and disposal of HDBR samples is regulated by the UK Human Tissue Authority (HTA)**

The HDBR is a Research Ethics Committee (REC) approved and HTA licenced tissue bank. This means that most research projects based within the UK do not need to obtain their own REC approval.

Users outside of the UK may also apply to use material from the HDBR; however, a letter from an ethics committee of equal standing to a UK REC committee must be obtained prior to any material being released from the tissue bank.

A Material Transfer Agreement (MTA) is required between the receiving Institute and the HDBR collecting centre for both UK and international research groups. In addition,

HDBR contact details

Institute of Genetic Medicine, International Centre for Life, Newcastle upon Tyne, NE1 3BZ · email hdbn.ncl.ac.uk
UCL Institute of Child Health, 30 Guilford Street, London WC1N 1EH · email hdbn@ucl.ac.uk

the tissue must be used, stored and disposed in accordance with the HDBR conditions of their REC approval, which can be downloaded here <http://hdbr.org/registration/ethics.html>.

Potential pathogens

- **HDBR samples are not screened**

None of the samples are tested for the presence of pathogens and therefore all samples should be handled as potentially pathogenic. In addition, all material will be couriered to the receiving institute as a Biological Substance, Category B, UN3373 sample.

HTA guidance on handling human tissue can be found at https://www.hta.gov.uk/sites/default/files/Code_of_practice_9_-_Research.pdf

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