APPENDIX Q
SUSPECTED GENETIC METABOLIC DISORDERS: INVESTIGATION AND AUTOPSY PROTOCOL

Peri-mortem investigation by the clinician should include the following

- Prior to death:
  - seek consent from the parents for a metabolic autopsy;
  - consult metabolic physician or histopathologist before collection of samples;
  - blood sample (0.8ml) in a lithium heparin tube and refrigerate;
  - urine sample (5-10 ml);
  - skin biopsy (3 x 2 mm punch biopsies): It is not necessary for the baby to be taken from the nursery for this procedure. The process, which can be undertaken by a registrar, should only take 15-20 minutes, is minimally invasive, with the sites being covered by a small dressing. See Section 4; Appendix 2a Screening for genetic metabolic disorders for futher details of collection.

- Immediately following the death after consultation with the metabolic team and pathologist:
  - Obtain blood sample by cardiac puncture if blood sample not already taken and only if parental consent has been obtained, or establish a fibroblast culture from the baby.
  - Liver and muscle biopsies (for electron microscopy, histopathology and enzymology (for the latter wrap in aluminium foil, snap freeze and store at -70 ºC). These should ideally be taken pror to death, the yield is very low after death.
  - Contact the laboratory to request that all unused portions of blood or urine specimens are retained. If neonatal screening test has been performed, any unused portions of the blood spots can be requested from the state laboratory. Tandem mass spectrometry can identify selected disorders of fatty acid oxidation and amino acid metabolism in dried blood samples.

A recent publication by Christodoulou and Wilcken in Seminars in Neonatology[61] highlighted the need for an increased index of suspicion for genetic metabolic disorders (inborn errors of metabolism) in neonatal care. The authors describe predominant clinical or biochemical presentations of genetic metabolic disorders in the neonatal period and recommend a protocol for screening for these disorders and also for a genetic autopsy. *Please see Section 4; Appendix 2b, Components of the Genetic Autopsy* for details of a genetic autopsy.

The predominant clinical or biochemical presentations of genetic metabolic disorders are as follows: Acute encephalopathy: hypoglycaemia, hyperammonemia, ketosis, disorders of acid-base balance, seizures as an early predominant feature; Acute hepatocellular disease; sudden death; severe hypotonia; non-immune hydrops fetalis; facial dysmorphism, with or without congenital malformations[61].

Appendix K Recommendations

1	To ensure a precise diagnosis, peri-mortem evaluation of infants suspected of having genetic metabolic disorders is required. Parental consent is required for a post-mortem examination and for tissue and blood samples to be taken prior to the death. Clinicians need to counsel parents sensitively about the importance of an accurate diagnosis for future genetic risks in this very distressing time.
2	Due to the complexity and number of different possible diseases, it is strongly recommended that clinicians discuss each individual case with the regional referral Laboratory to identify the optimum tests to request. Should more expert guidance be required a clinical metabolic specialist should be consulted.
3	All tissue samples should be stored and transported to a Specialist Metabolic Laboratory for investigation as convenient. The current development of genetic testing has altered the investigation pathway of metabolic disorders. Antemortem samples are better than post mortem, and post mortem electron microscopy has limited value and low yield. A fibroblast culture which can be established after death, but again is better taken before death can be invaluable.