UKGTN Testing Criteria

Test name: **Congenital Generalised Lipodystrophy 5 Gene Panel**	
Approved name and symbol of disorder/condition(s): See website listing	**OMIM number(s):**
Approved name and symbol of gene(s): See website listing	**OMIM number(s):**

Patient name:	**Date of birth:**
Patient postcode:	**NHS number:**
Name of referrer:	
Title/Position:	**Lab ID:**

Referrals will only be accepted from one of the following:	
Referrer	**Tick if this refers to you.**
Consultant Clinical Geneticist	
Consultant Endocrinologist	

Minimum criteria required for testing to be appropriate as stated in the Gene Dossier:	
Criteria	**Tick if this patient meets criteria**
Patient meets 3 major criteria **OR** 2 of the major criteria **AND** 2 or more minor criteria: **Major criteria:** • Lipoatrophy affecting the trunk, limbs, and face. • Acromegaloid features • Hepatomegaly • Elevated serum concentration of triglycerides • Insulin resistance **Minor criteria:** • Hypertrophic cardiomyopathy • Psychomotor retardation or mild to moderate cognitive impairment • Hirsuitism • Precocious puberty in females • Bone cysts • Phlebomegaly • Congenital myopathy Continued over the page…….	

For panel tests:
At risk family members where familial mutation is known do not require a full panel test but should be offered analysis of the known mutation
If the sample does not fulfil the clinical criteria or you are not one of the specified types of referrer and you still feel that testing should be performed please contact the laboratory to discuss testing of the sample.

Additional Information:

Major criteria

•Lipoatrophy affecting the trunk, limbs, and face. Generalized lipodystrophy is apparent at birth. In some individuals, the face may be normal at birth with lipoatrophy becoming apparent during the first months of life. Lipoatrophy gives an athletic appearance, especially because skeletal muscle hypertrophy is also present.

•Acromegaloid features include gigantism, muscular hypertrophy, advanced bone age, prognathism, prominent orbital ridges, enlarged hands and feet, clitoromegaly, and enlarged external genitalia in the male.

•Hepatomegaly. Liver enlargement is secondary to fatty liver early on and to cirrhosis late in the disease course.

•Elevated serum concentration of triglycerides. Serum concentration of triglycerides can be elevated up to 80 g/L, and is sometimes associated with hypercholesterolemia.

•Insulin resistance. Elevated serum concentrations of insulin and C-peptide may occur starting in the first years of life. Overt clinical diabetes mellitus usually develops during the second decade. Its early clinical expression is acanthosis nigricans of the groin, neck, and axillae, which may have, in some cases, a verrucous appearance.

Minor criteria

•Hypertrophic cardiomyopathy may be present in infancy or develop later in life.

•Psychomotor retardation or mild (IQ 50-70) to moderate (IQ 35-50) intellectual impairment. Approximately 80% of individuals with mutations in BSCL2 have mild-to-moderate intellectual impairment, whereas only 10% of individuals with mutations in AGPAT2 have intellectual impairment.

•Hirsutism manifests with low frontal and posterior hairline; hypertrichosis is apparently independent of hormonal stimulation.

•Precocious puberty in females. In a series of 75 individuals with BSCL, three females underwent puberty before age seven years [Van Maldergem et al 2002].

•Bone cysts occur in 8%-20% of affected individuals and have a polycystic appearance on x-ray. Located in the epiphyseal and metaphyseal regions of the long bones, bone cysts are often diagnosed during the second decade and are mostly observed in individuals with mutations in AGPAT2.

•Phlebomegaly. Prominence of the veins of the lower and upper limbs is observed, in part because of the lack of subcutaneous fat