A1. Site/Study ID #:___ ___ / **G**___ ___ ___ ___ A2. Visit Date:___ ___ / ___ ___ / ___ ___ ___ ___ A3. Staff Initials:___ ___ ___
Month Day Year

To DCC ☐

SECTION B: GENERAL INCLUSION/EXCLUSION CRITERIA

B1. Date of Birth: **ELG2B01MM V2(2)/ ELG2B01DD V2(2)/ ELG2B01YY V2(2)/ ELG2B01DT**

Month Day Year

B2. Disease: **ELG2B02 V2(3)**

1. ☐ Bile Acid Synthesis and Metabolism Disorders.
2. ☐ Progressive Familial Intrahepatic Cholestasis (PFIC)
3. ☐ a1-Antitrypsin (a 1-AT) Deficiency
4. ☐ Alagille Syndrome (AGS)

GENERAL INCLUSION CRITERIA:

B3. Less than 25 years at enrollment 1. ☐ Yes 2. ☐ No **ELG2B03 V2(3)**

B4. Currently enrolled in BARC PROBE Study (P003) 1. ☐ Yes 2. ☐ No **ELG2B04 V2(3)**

GENERAL EXCLUSION CRITERIA:

B5. Inability to comply with follow-up 1. ☐ Yes 2. ☐ No **ELG2B05 V2(3)**

B6. Failure to sign consent or HIPAA medical record release form 1. ☐ Yes 2. ☐ No **ELG2B06 V2(3)**

B7. Date consent form signed: **ELG2B07MM V2(2)/V ELG2B07DD V2(2)/ ELG2B07YY V2(4)/ ELG2B07DT**
Month Day Year

SECTION C: BILE ACID SYNTHESIS AND METABOLISM DISORDERS

INCLUSION CRITERIA, Diagnosis of bile acid synthesis confirmed by:

C1. Diagnosis of bile acid synthesis confirmed by:

a. Biochemical evidence of defect by FAB-MS **OR** GC-MS of urine or serum **–OR–** 1. ☐ Yes 2. ☐ No **ELG2C01**

b. Two identified pathological genetic mutations in one enzyme of bile acid synthetic pathway 1. ☐ Yes 2. ☐ No **ELG2C02**

EXCLUSION CRITERIA:

C3. Isolated enzymatic or structural peroxisomal defect producing a recognized syndrome disorder 1. ☐ Yes 2. ☐ No **ELG2C03 V2(3)**

A1. Site/Study ID #:___ ___ / **G**___ ___ ___ ___ A2. Visit Date:___ ___ / ___ ___ / ___ ___ ___ ___
Month Day Year

SECTION D: PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS / BENIGN RECURRENT INTRAHEPATIC CHOLESTASIS

INCLUSION CRITERIA:

D1. Diagnosis of PFIC by (must meet requirements of Section A **or** Sections B **and** C):

a. Documented two mutant alleles in:

i. *ATP8B1* (F1C1) gene **–OR– ELG2D1AI V2(3)** 1. ☐ Yes 2. ☐ No

ii. *ABCB11* (BSEP) gene **–OR– ELG2D1AII V2(3)** 1. ☐ Yes 2. ☐ No

iii. *ABCB4* (MDR3) gene **ELG2D1AIII V2(3)** 1. ☐ Yes 2. ☐ No

–OR–

b. Evidence of chronic liver disease by:

i. Clinical or biochemical hepatic abnormalities of >6 months **–OR– ELG2D1BI V2(3)** 1. ☐ Yes 2. ☐ No

ii. Clinical or histologic stigmata of chronic liver disease **–OR– ELG2D1BII V2(3)** 1. ☐ Yes 2. ☐ No

iii. Sibling of known individual affected by PFIC or BRIC **ELG2D1BIII V2(3)** 1. ☐ Yes 2. ☐ No

iv. Recurrent and episodic cholestatic disease occurring on more than two occasions with episodes separated by at least 3 months and within other known cause. **ELG2D1BIV V2(3)** 1. ☐ Yes 2. ☐ No

–AND–

c. Evidence of cholestatis by:

i. Fasting serum bile acid > 3x ULN for age **–OR– ELGD1CI V2(3)** 1. ☐ Yes 2. ☐ No

ii. Direct bilirubin > 2mg/dL **–OR– ELGD1CII V2(3)** 1. ☐ Yes 2. ☐ No

iii. Fat soluble vitamin deficiency **–OR– ELGD1CIII V2(3)** 1. ☐ Yes 2. ☐ No

iv. GGTP > 3x ULN for age **–OR– ELGD1CIV V2(3)** 1. ☐ Yes 2. ☐ No

v. Intractable pruritus explainable only by liver disease **ELGD1CV V2(3)** 1. ☐ Yes 2. ☐ No

EXCLUSION CRITERIA:

D2. Presence of other known causes of chronic cholestasis **ELG2D02 V2(3)** 1. ☐ Yes 2. ☐ No

A1. Site/Study ID #:___ ___ / **G**___ ___ ___ ___ A2. Visit Date:___ ___ / ___ ___ / ___ ___ ___ ___
Month Day Year

SECTION E: a1-ANTITRYPSIN (a 1-AT) DEFICIENCY

INCLUSION CRITERIA:

E1. Presence of liver disease (check all that apply – must have at least one)

a. Neonatal cholestatis **ELG2E1A V2(3)** 1. ☐ Yes 2. ☐ No

b. AST or ALT > 1.25 x ULN **ELG2E1B V2(3)** 1. ☐ Yes 2. ☐ No

c. Impaired hepatic synthetic function **ELG2E1C V2(3)** 1. ☐ Yes 2. ☐ No

d. Hepatomegaly **ELG2E1D V2(3)** 1. ☐ Yes 2. ☐ No

e. Portal hypertension or cirrhosis **ELG2E1E V2(3)** 1. ☐ Yes 2. ☐ No

f. Abnormal liver biopsy histology **ELG2E1F V2(3)** 1. ☐ Yes 2. ☐ No

–AND–

E2. Diagnosis of α 1-AT deficiency by:

a. Low serum α 1-AT level (_**ELG2E2AMG V2(10)**__mg/dL) **–AND–** **ELG2E2A V2(3)** 1. ☐ Yes 2. ☐ No

b. At least one of the following:

i. PiZZ phenotype **–OR–** **ELG2E2BI V2(3)** 1. ☐ Yes 2. ☐ No

ii. PiSZ phenotype **–OR–** **ELG2E2BII V2(3)** 1. ☐ Yes 2. ☐ No

iii. PiZZ genotype **–OR–** **ELG2E2BIII V2(3)** 1. ☐ Yes 2. ☐ No

iv. PiSZ genotype **ELG2E2BIV V2(3)** 1. ☐ Yes 2. ☐ No

A1. Site/Study ID #:___ ___ / **G**___ ___ ___ ___ A2. Visit Date:___ ___ / ___ ___ / ___ ___ ___ ___
Month Day Year

SECTION F: AGS

INCLUSION CRITERIA:

F1. Presence of liver disease **–AND–** 1. ☐ Yes 2. ☐ No **ELG2F01 V2(3)**

F2. Confirmed diagnosis of AGS 1. ☐ Yes 2. ☐ No **ELG2F02 V2(3)**

a. Diagnostic Characteristics (specify one of the following scenarios): **ELG2F2A V2(23)**

	Family History Of AGS[a]	**Paucity of interlobular bile ducts**	***Jagged1[d] or Notch2* mutations**	**Number of clinical criteria**
1. ☐	Present or absent	Present	Identified[b]	Any or no features
2. ☐	None (proband)	Present	Not identified[c]	3 or >
3. ☐	None (proband)	Absent or unknown	Not identified	4 or >
4. ☐	None (proband)	Absent or unknown	Identified	1 or >
5. ☐	Present	Present	Not identified	1 or >
6. ☐	Present	Absent or unknown	Not identified	2 or >
7. ☐	Present	Absent or unknown	Identified	Any or no features

[a]Family history = AGS present in a first degree relative
[b]Identified = *Jagged1* mutation may have been identified in clinical or research laboratory
[c]Not identified = Not identified on mutation screening, or not screened for
[d]*Jagged1* mutation = mutation, whole gene deletion or deletion of chromosome 20p which includes *Jagged1* locus

Major clinical criteria include cholestasis, consistent cardiac, renal, ocular disease, butterfly vertebrae, or characteristic “Alagille” facies of childhood or adulthood. The specific clinical criteria are:

Cardiac: Heart murmur (with further studies to clarify), Pulmonary stenosis (valvular, pulmonary artery stenosis), pulmonary atresia, tetralogy of Fallot, ASD or VSD.

Ocular: posterior embryotoxon or other anterior chamber defect, retinal pigmentary anomalies

Vertebral: butterfly vertebrae

Characteristic facial features: broad forehead, deep set eyes, pointed chin in child (preteen) or prognathism in adults, triangular face.

Renal: functional defects (such as tubular acidosis), renal insufficiency, renal vascular hypertension, vesicoureteral reflux, structural defects (agenesis, small kidneys, renal cysts, renal artery stenosis, dysplastic kidneys)

Cholestasis: See question F3 for evidence of cholestasis.

A1. Site/Study ID #:___ ___ / **G**___ ___ ___ ___ A2. Visit Date:___ ___ / ___ ___ / ___ ___ ___ ___
Month Day Year

F3. Evidence of cholestasis: (check all that apply)

a. ☐ Fasting total serum bile acid > 3x ULN for age **ELG2F03A V2(2)**

b. ☐ Direct bilirubin > 2 mg/dl **ELG2F03B V2(2)**

c. ☐ Fat soluble vitamin deficiency otherwise unexplainable **ELG2F03C V2(2)**

d. ☐ yGTP > 3x ULN for age **ELG2F03D V2(2)**

e. ☐ Intractable pruritus explainable only by liver disease **ELG2F03E V2(2)**

SECTION G: SUMMARY

G1. Is the subject eligible? 1. ☐ Yes 2. ☐ No 3 ☐ Eligible by exemption **ELG2G1**

ELG2INSIG V2(3) **ELG2SIGMM V2(2)/ ELG2SIGDD V2(2)/ ELG2SIGYY V2(4)/ ELG2SIGDT**

Investigators Signature Date