ChiLDReNLink: PROBE

Form 10 Pathology PROBE					
A: REVIEW					
A1	Date of Central Review	___ ___ / ___ ___ / ___ ___ ___ ___			
A2	Participant age when specimen was obtained (days):	___ ___ ___ days			
A3	First slide:	_____ Slide number	_____ Box number	_____ Slot number	
A4	Second slide:	_____ Slide number	_____ Box number	_____ Slot number	
A5	Is this a reread?	O No	O Yes		

B: PATHOLOGY RESULTS					
B1	Type of specimen:	O Needle biopsy → **skip B4** O Wedge biopsy → **go to B4** O Explant → **go to B5**			
Specimen size (measured from slide)					
B2	If needle biopsy, composite length:	___ ___ ___	O cm	O Not palpable	O Not Done
B3	If needle biopsy, average width of core(s):	___ ___ ___	O cm	O Not palpable	O Not Done
B4	If wedge biopsy, two largest dimensions of wedge:	___ ___ ___	O cm	O Not palpable	O Not Done
		___ ___ ___	O cm	O Not palpable	O Not Done
General instructions: This form should be filled out using H&E and Trichrome					
Quality of slides					
Slide 1					
B5	Barcode:	_____			
B6	Quality:	O Acceptable	O Unacceptable		
B7	Stain:	O H&E	O Trichrome		
B8	If unacceptable, reason (check all that apply):	□ Stain quality □ Size or fragmentation of biopsy □ Poor tissue preservation			

B: PATHOLOGY RESULTS		
Slide 2		
B9	Barcode:	_____
B10	Quality:	O Acceptable O Unacceptable
B11	Stain:	O H&E O Trichrome
B12	If unacceptable, reason (check all that apply):	□ Stain quality □ Size or fragmentation of biopsy □ Poor tissue preservation
B13	Number of portal tracts (requires at least two structures [portal vein, hepatic artery, interlobular duct] in a portal tract):	O Number of portal tracts (specify): _____ O Unable to determine because of advanced fibrosis
B14	Number of portal tracts with at least one interlobular duct:	_____
B15	Staging of portal fibrosis (Ishak):	O Stage 0: No fibrosis O Stage 1: Fibrous expansion of some (less than half) portal areas, with or without short fibrous septa O Stage 2: Fibrous expansion of most (half or more) portal areas, with or without short fibrous septa O Stage 3: Fibrous expansion of most portal areas with occasional portal-portal bridging O Stage 4: Fibrous expansion of most portal areas with marked bridging (portal-portal and portal-central) O Stage 5: Marked bridging (portal-portal and/or portal-central) with occasional nodules (incomplete cirrhosis) O Stage 6: Cirrhosis, probable or definite
B16	Staging of portal fibrosis (modified Scheuer):	O Stage 0: No fibrosis O Stage 1: Enlarged, fibrotic portal tracts O Stage 2: Periportal or portal-portal septa but intact architecture O Stage 3: Fibrosis with distorted structure but no obvious cirrhosis O Stage 4: Probable or definite cirrhosis
B17a	Ductal plate configuration (defined as circular orientation of interrupted or continuous duct segments around a central fibrovascular axis):	O Absent → **go to B18** O Present
B17b	If Present, specify:	O Number of portal tracts showing feature (specify): _____ O Number cannot be determined
B18	Interface ductular reaction (defined as those structures at the limiting plate or interface with or without a round or oval lumen, see illustrative microphotograph in front of binder) Scoring should be done according to area of greatest severity. Does not need to be on perfect sections. Trichrome may be helpful. Assess extent first - absent vs. generalized, then assess severity - mild or moderate/marked.	□ Absent □ Focal (< 50% of portal areas): Mild □ Focal (< 50% of portal areas): Moderate/Marked □ Generalized (>= 50% of portal areas): Mild □ Generalized (>= 50% of portal areas): Moderate/Marked

B: PATHOLOGY RESULTS		
B19	Bile duct proliferation (defined as those centrally placed structures with a lumen and a cuboidal epithelial lining, see illustrative microphotograph in front of binder). Scoring should be done according to area of greatest severity. Does not need to be on perfect sections. Trichrome may be helpful. Assess extent first - absent vs. generalized, then assess severity - mild or moderate/marked.	□ Absent □ Focal (< 50% of portal areas): Mild □ Focal (< 50% of portal areas): Moderate/Marked □ Generalized (>= 50% of portal areas): Mild □ Generalized (>= 50% of portal areas): Moderate/Marked
B20a	Periductal fibrosis (defined as concentric fibrosis rimming ducts, onion - skinning)	O Absent → **go to B21** O Present
B20b	If Present, estimate the percent of portal tracts involved:	O 25% or less O 26% to 50% O 51% to 75% O 76% to 100% O Unable to determine due to advanced fibrosis
B21	Portal tract edema:	O Not detected O Present O Not assessable
B22a	Lobular sinusoidal fibrosis (evaluated using trichrome, assessing only zone 3, exclude periportal area):	O Absent → **go to B23** O Present, focal (<50% of lobules) → **skip B22c** O Prominent (50% of lobules or greater) → **go toB22c** O Not evaluable/assessable because no central veins or poor trichrome stain → **go to B23**
B22b	If Present, does it extend beyond zone 3?	O No O Yes O Unable to discern
B22c	If Prominent, does it extend beyond zone 3?	O No O Yes O Unable to discern
B23	Hepatocellular swelling. Swelling is enlargement of the cell with rarefaction of the cytoplasm, in the absence of distinct vacuoles (e.g. in the realm of cholestasis). Often accompanied by sinusoidal compression/obscured sinusoids. Multinucleated cells may or may not be enlarged or swollen. Percents below refer to the percent of hepatocytes with swelling.	O Absent O Rare (<5%) O 5% to less than 50% O ≥ 50%
B24a	Macrosteatosis (defined as one or several vacuoles that displace the nucleus). Percent refers to area of lobule occupied by fat. Macrosteatosis should be assessed under low power.	O Absent → **go to B25a** O Rare (<5%) → **go to B25a** O 5% to less than 50% → **skip B24c** O ≥ 50% → **go to B24c**
B24b	If 5% to less than 50%, what is the predominant distribution of the macrosteatosis?	O Zone 1 O Panlobular O Zone 3 O Non-zonal
B24c	If ≥ 50%, what is the predominant distribution of the macrosteatosis?	O Zone 1 O Panlobular O Zone 3 O Non-zonal
B25a	Microsteatosis (defined as multiple vacuoles with a preserved central nucleus; to include small droplets to fill cytoplasm). Percent refers to number of hepatocytes involved. Microsteatosis should be assessed under high power.	O Absent → **go to B26a** O Rare (<5%) → **go to B26a** O 5% to less than 50% → **skip B25c** O ≥ 50% → **go to B25c**

B: PATHOLOGY RESULTS		
B25b	If 5% to less than 50%, what is the predominant distribution of the microsteatosis?	O Zone 1 O Panlobular O Zone 3 O Non-zonal
B25c	If ≥ 50%, what is the predominant distribution of the microsteatosis?	O Zone 1 O Panlobular O Zone 3 O Non-zonal
B26a	Hepatocellular iron:	O Not assessed (no iron stain available at central review)→ **go to B27** O Limited to zone 1 (with iron stain) → **go to skip B26c** O Diffuse (with iron stain) → **go to B26c**
B26b	If limited to zone 1, specify grading (only to be done with special stain for iron):	O Grade 0: Granules absent or barely discernable x400 O Grade 1+: Barely discernable x250, easily confirmed x400 O Grade 2+: Discrete granules resolved x100 O Grade 3+: Discrete granules resolved x25 O Grade 4+: Masses visible x10 or naked eye
B26c	If diffuse, specify grading (only to be done with special stain for iron):	O Grade 0: Granules absent or barely discernable x400 O Grade 1+: Barely discernable x250, easily confirmed x400 O Grade 2+: Discrete granules resolved x100 O Grade 3+: Discrete granules resolved x25 O Grade 4+: Masses visible x10 or naked eye
B27	Pseudorosette formations (defined as dilated canaliculus lined by more than two hepatocytes).	O Absent O Present (<1/lobule) O Prominent (at least 1 in every lobule)
B28	Giant cell transformation (defined as multinucleated (3 or more nuclei) hepatocytes independent of cell size). Cell swelling is scored separately (see item B23, Hepatocellular swelling).	O Absent O Rare (1-2 per section) O Present (giant cells occupy up to 10% of lobular area) O Common (giant cells occupy 10-49% of lobular area) O Prominent (giant cells occupy >50% of lobular area)
B29	Clusters (defined as 3 or more cells) of coarsely granular red hepatocytes ("oncocytes") with normal to increased cytoplasmic volume and viable nuclei.	O Absent O Rare (1-2 foci per section) O Present (>2 foci per section but <1 focus per lobule) O Common (at least 1 focus per lobule)
B30	Regional non-zonal variability in cytoplasmic volume of hepatocytes resulting in large groups (involving > 50% of the lobule) of apparently small hepatocytes.	O Absent O Present
B31	Lobular extramedullary hematopoiesis (EMH).	O Absent O Rare (average of <1 focus/lobule) O Prevalent (average of few clusters per lobule) O Extensive (multiple clusters in each lobule; sinusoids may or may not be expanded)
B32	Lobular mononuclear inflammation.	O Absent O Rare (<1 focus/lobule) O Focal (> or = 1 focus/lobule) O Diffuse (generalized, present in most lobules)

B: PATHOLOGY RESULTS		
B33	Intensity of portal tract (including EMH) cellular infiltrate (excluding neutrophils). This should be assessed under high power.	□ Absent □ Focal (< 50% of portal areas): Mild □ Focal (< 50% of portal areas): Moderate/Marked □ Generalized (>= 50% of portal areas): Mild □ Generalized (>= 50% of portal areas): Moderate/Marked
B34	Hepatocellular necrosis (evaluate number of necrotic hepatocytes in one section of biopsy).	□ Absent/rare (< or = 2 necrotic hepatocytes per section) □ Few scattered necrotic hepatocytes (> 2 per biopsy but < or = 2 per lobule) □ Many necrotic hepatocytes (>2 per lobule): Scattered □ Many necrotic hepatocytes (>2 per lobule): Confluent
B35	Visible bile plugs (check all that apply). Any bile seen counts as "present". Bile staining in hepatocytes, Kupffer cells or portal macrophages should not be counted. To determine "absent" must extensively examine specimen.	□ Absent □ Canalicular □ Ducts/Ductular (bile plugs in the lumen)
B36	Interlobular bile duct injury (injury is characterized by nuclear size variation, vacuolated cytoplasm, and/or apoptosis).	O Absent O Mild (<50% of bile ducts) O Moderate/marked (> or = 50% of bile ducts)
B37	Acute cholangitis (defined as presence of neutrophils in duct, or infiltrating ductal epithelium. Ducts defined as having a lumen and cuboidal epithelium.)	O Absent O Rare (present in <5% of ducts) O Mild (present in 5 to 50% of ducts) O Moderate/marked (greater than 50% of ducts involved)
B38	Average intensity of neutrophils around ducts/ductules [Mild (1-2 neutrophils around ducts/ductules) or Moderate/marked (3 or more neutrophils around ducts/ductules)].	□ Absent □ Focal (< 50% of portal areas): Mild □ Focal (< 50% of portal areas): Moderate/Marked □ Generalized (>= 50% of portal areas): Mild □ Generalized (>= 50% of portal areas): Moderate/Marked
B39	Mononuclear inflammatory cells present in ducts, ductules, or infiltrating biliary epithelium.	O Absent O Rare (present in <10% of duct/ductular profiles) O Common (present in ≥10% of duct/ductular profiles)
B40	Compact aggregates (3 or more) of bile stained macrophages within portal spaces.	O Absent O Rare (in up to 1 portal tract per section) O Present (in 2 or more portal tracts per section)
B41	Compact aggregates (3 or more) of bile stained Kupffer cells in zone 1, within 2 hepatocytes of portal tract limiting plate.	O Absent O Rare (no more than 1 aggregate per section) O Present (2 or more aggregates per section)
B42a	Overall impression regarding large duct obstruction. One should not try to avoid being wrong, i.e. have an opinion rather than opting for indeterminate.	O Consistent with large duct obstruction → **go to B43** O Not consistent with large duct obstruction O Indeterminate (for large duct obstruction) → **go to B43** O Biopsy insufficient to render impression regarding obstruction → **go to B43**

B: PATHOLOGY RESULTS		
B42b	If not consistent with large duct obstruction, specify other diagnosable condition (i.e. paucity, glycogen storage disease, CMV):	_____
B43	Comment (please add words to lexicon):	_____

C: PATHOLOGIST SIGNATURE		
C1	Did pathologist Signed?	O No → **Done** O Yes _____
C2	Date investigator signed	___ ___ / ___ ___ / ___ ___ ___ ___