TABLE 1. Study protocol for paediatric hepatotoxicity

Clinical history number_____
Name/Surname_____
Age (Date of birth)_____
Sex:1. Male 2. Female_____Weight (kg)_____Height (cm)_____Body Surface Area (BSA= $\wp$ weight × height/3600) (m^2)_____Referred from: 1. Hospital 2. Primary health care centre _____City:
Drug(s) suspected of causing the reaction (active ingredient)_____Brand name_____
Total daily dose (mg)_____Interval (h)_____Route of administration: 1. Oral; 2. Intravenous; 3. Intramuscular; 4. Sublingual; 5. Rectal; 6. Aerosol; 7. Topical; 8. Other.
Clinical indications:_____
Duration of treatment: from (day/month/year)_____
to (day/month/year)_____
Duration of treatment (days)_____
Within this period, when did the reaction appear?_____Did it disappear when medication was suspended?
1. Yes; 2. no; 3. N/A_____Did it reappear when medication was resumed?1. Yes; 2. no; 3. N/A_____
Time elapsed until resolution of the reaction (days)_____
Description of the adverse reaction(s)
(including relevant results of physical examination or laboratory analysis) and extra hepatic signs/symptoms
Astenia/Anorexia: 1. Yes; 2. No. Exanthema: 1. Yes; 2. No Pruritis: 1. Yes; 2. No. Jaundice: 1. Yes; 2. No. Eosinofilia: 1. Yes; 2. No
Fever: 1. Yes; 2. No
Concomitant medication

Prescribed or self-medicated, taken by the mother during lactation (excluding the dose taken to treat the adverse reaction)

Drug	Daily dose	Route of administration	Indication	From	To

Relevant clinical background

Allergies. Congenital metabolic disorders. Apgar score. Birth weight. Type of nutrition. Nutritional status. Obstetric background. Coombs test. Medicationtaken by the mother during pregnancy and lactation.
Diagnostic tests
ECG. CT. Cholangiography. Plasma levels of the drug and/or its metabolites, etc.
Liver biopsy
Description and date performed
Plasma levels
Outcome of the reaction (mark as appropriate)
Spontaneous resolution. Treatment required. Persistence of adverse reaction. Need for hospitalisation. Need to prolong previous hospitalisation. Permanent or significant incapacity. Recovery. Patient's life endangered. Death.

	Before treatment (date)	Start of treatment (date)	Evolving (date)	Evolving (date)	At discharge (date)
Biochemical data					
Glucose					
Urea					
Creatinine					
Total proteins					
Albumin					
Alpha-1(g/L)					
Alpha-2					
Beta					
Gamma globulins					
Totalbilirubin(n =)					
Directbilirubin					
AST(range:)					
ALT(range:)					
GGT (range:)					
Alkaline phosphatase (range:)					
Iron					
Transferrin					
Copper					
Ceruloplasmin					
Immunoglobulin M					
Immunoglobulin G					
Immunoglobulin A					
Haemogram					
Erythrocytes					
Haemoglobin					
Haematocrits					
MCV					
ESR					
Platelets					
Prothrombin activity					
Leukocytes					
Polymorphonuclear leukocytes					
Lymphocytes					
Monocytes					
Eosinophils					
Basophils					

	Initial (date)	Evolving (date)	At discharge (date)
Markers			
IgM anti-HAV			
HBsAg			
Anti-HBc			
Anti-HCV: ELISA			
Anti-HCV: RIBA			
Anti-HCV: PCR			
Anti-HEV			
CMV IgM			
VEB IgM			
Others			
Autoantibodies			
ANA			
AML			
AMA			
Anti-LKM-1			
Rheumatoid Factor			
Alpha-1-antitrypsin (n = ...)			
LE cells			

Exclusion of other causes

Congenital malformations
- Biliary atresia
- Congenital choledochal cyst
- Caroli disease
- Malignant choledochal stenosis

Hepatic and biliary tumours

Toxic
- Alcohol
- Industrial intoxicants (glue, varnish, vinyl toys, etc.)
- Illegal drugs

Systemic diseases affecting the liver
- Inflammatory bowel disease
- Rheumatoid arthritis
- Systemic Lupus Erythematosus
- Polyarteritis nodosa
- Cardiac insufficiency
- Hypo/Hyperthyroidism
- Multiple transfusions
- Acute abdominal trauma
- Anoxia / Hypoxia

Vaccinations

Haemolytic anaemias
- Congenital
- Acquired

Post-surgical hepatitis
- Halothane anesthesia
- Bacterial infections / Hypoxia
- Hypotension
- Other drugs

Pregnancy

Tattoos

Physiological hyperbilirubinemia
- Newborn
- Breastfeeding

Viral infections
- Hepatitis A. B. C. D

Virus infections
- Cytomegalovirus
- Toxoplasma
- Epstein-Barr
- AIDS
- Measles
- Herpes simplex
- Varicella zoster virus
- Rubella

Toxins (plants,fungi)

Metabolic disorders
- Gilbert syndrome
- Wilson disease
- Alpha-1 antitrypsin deficiencyCystic fibrosis
- Glycogen storage disease
- Galactosaemia
- Tyrosinemia

Neoplastic diseases

- Coxsackie
- Echovirus

Protozoan infections
- Toxoplasma

Pneumocystis carinii

Bacterial infections
- Sepsis. Salmonellosis. Brucellosis

Intestinal parasistosis