Agenda

THE FORUM For Collaborative Research℠

12:00 PM ET	Begin	
12:00 PM	**Welcome and Meeting Goals**	Veronica Miller, *Forum for Collaborative Research* Jessica Weber, *Forum for Collaborative Research* Saul Karpen, *Emory University School of Medicine/ Children's Healthcare of Atlanta* Henkjan Verkade, *University of Groningen* Pam Vig, *Mirum Pharma*
12:20 PM	**Stakeholder Perspectives on Demonstrating Efficacy and Safety in Clinical Trials** • Patient Representative • FDA • EMA • Industry	Roberta Smith, *Alagille Syndrome Alliance* Ruby Mehta, *U.S. Food and Drug Administration* Chrissi Pallidis, *European Medicines Agency* Pam Vig, *Mirum Pharma*
1:00 PM	**Next Steps** • Logistics • Subgroups • Outputs	Jessica Weber, *Forum for Collaborative Research*
1:10 PM	**Discussion**	*All*
1:30 PM ET	**Adjourn**	

Goals of this WG

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Overall: to improve the lives of children with rare liver diseases (by development of novel efficacious treatments)

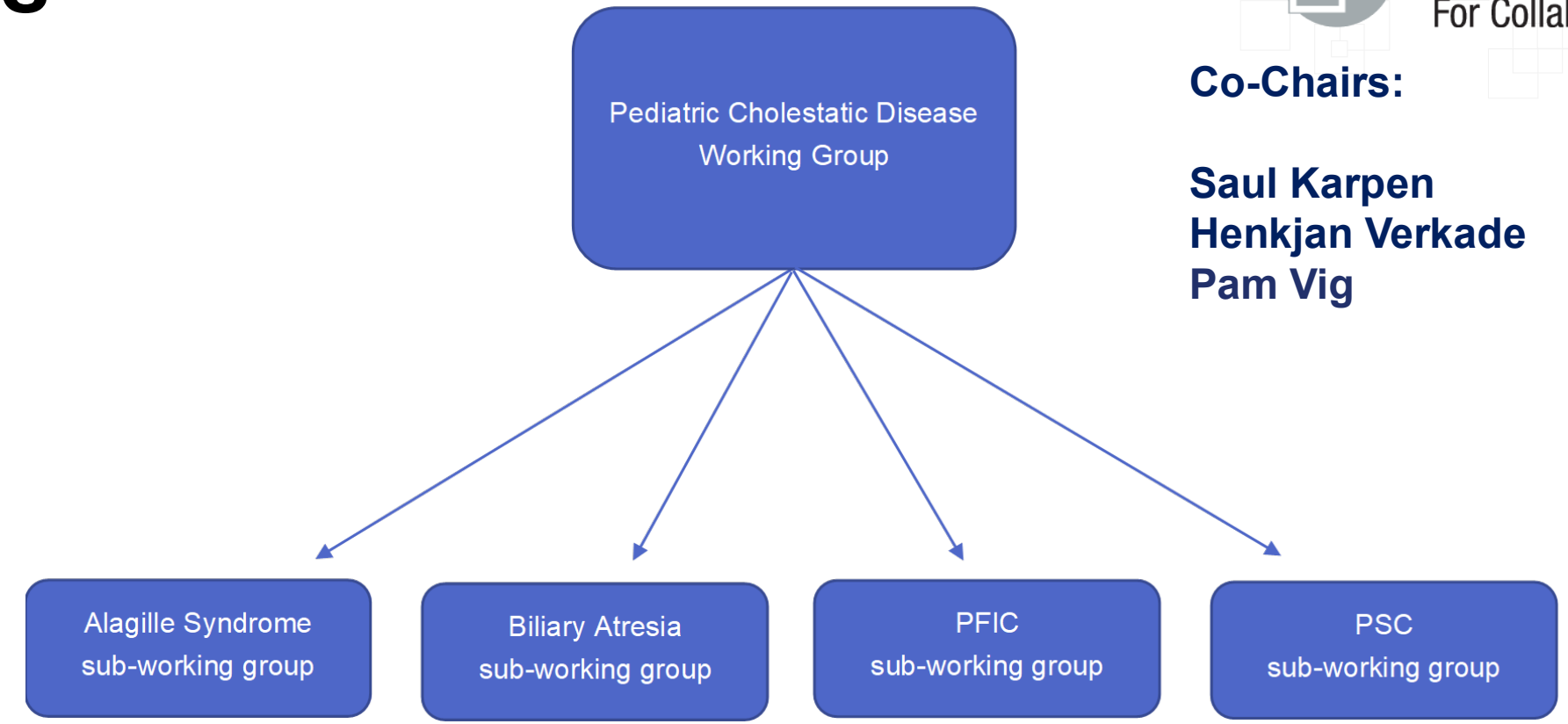
Sub-goals

- Develop, for 4 diseases, agreed-upon outcome measures for trials
- Identify gaps in our understanding of needs and natural history for each disease
- *Define the minimal and reachable needs for regulatory approval*
  Inclusive "round table" approach to incorporate input from stakeholders → academia, families, regulators, industry
- Global, short-term and long-term mindsets

Rationale for this WG

- **Now is the time, with available registry data and new drugs in this space, to help outline outcome measures for clinical trials addressing Pediatric Cholestasis.**

Groups



Co-Chairs:

Saul Karpen
Henkjan Verkade
Pam Vig

Sub-WG's

Co-Chairs (2)

Members Mixed stakeholders

Not expected to be addressed

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- Plans to initiate trials or inform trial design
- A current review of the literature
- DILI classification

Output from each WG

- **Outcome measures: (multiple suggestions expected)**
  - **Primary**
  - **Secondary**
  - **Experimental**
- **Crucial clinical issues**
- **Crucial gaps that can be filled by Registries**
- **Natural history highlights**

Draft Discussion Document

Disease	Working Group Members	Definition	Is there a registry?	Define the natural history that inform outcomes	Other
Alagille Syndrome		Must have pathogenic JAG-1 or Notch-2 variant that experts agree on	- GALA		
Biliary Atresia		Developmental cholangiopathy with obstruction of the biliary tract	- NIDDK-supported ChiLDReN consortium - Canadian Biliary Atresia Registry - European Biliary Atresia Registry - Japanese Biliary Atresia Registry - Netherlands Study group for Biliary Atresia Registry		
PFIC		PFIC1 and PFIC2 caused by impaired bile salt secretion due to defects in ATP8B1 encoding the FIC1 protein and in ABCB11 encoding bile salt export pump (BSEP) protein.	- NAPPED		
PSC		Diagnosis of chronic cholestasis of more than six months duration with either a MRCP/ ERCP showing sclerosing cholangitis, or a liver biopsy taken at any time consistent with PSC in the absence of a documented alternative etiology for sclerosing cholangitis. If diagnosis of PSC was made by histology alone, it must require the presence of fibro-obliterative lesions.	- PSC Partners Patient Registry - IPSCSG - PROGRESS - North American PSC Registry - UK-PSC - Pediatric PSC - Dutch PSC - European Reference Network - Canadian PSC Registry		