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COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

Le project Européen c4c

Johan Vande Walle –

F Schaefer, J. Vande Walle

E. Gasthuys, L. Nuytinck

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777389.
The Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

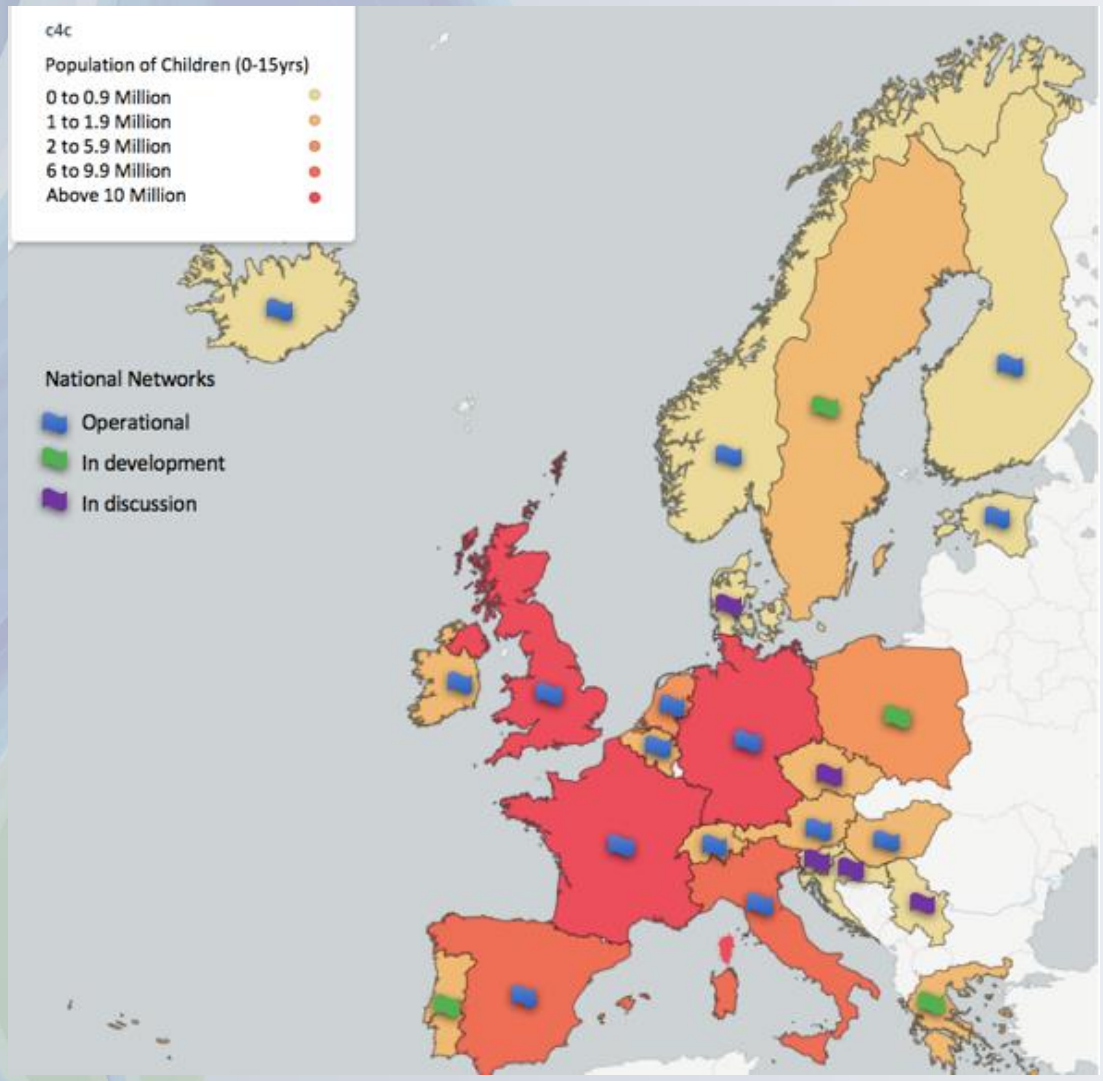
c4c vision

Better medicines for neonates, children and young people through a pan-European clinical trial network

c4c will use a **coordinated approach** to deliver high quality "regulatory grade" pediatric clinical trials in:

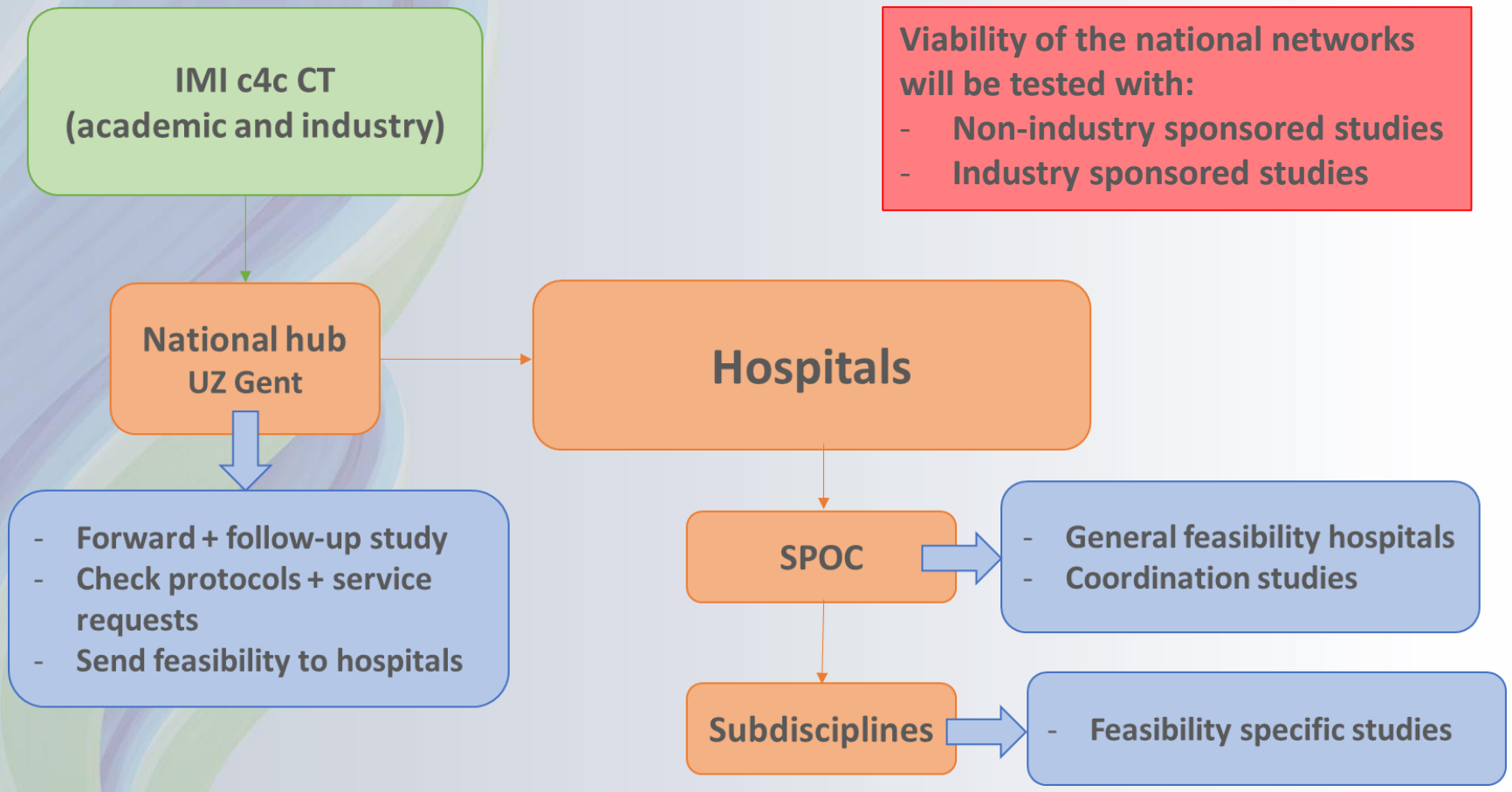
- Multiple countries (development Belgian national network)
- Multiple sites
- All pediatric age groups

The c4c consortium members



- 10 EFPIA companies
- 18 pediatric national networks
- 2 large patient advocacy groups
- 8 EU Multinational sub-specialty Networks
- 2 large children's hospitals

Start-up Belgian pediatric clinical research network (in the context of c4c)(2018-2024)



DON'T MISS THE DEADLINE!

Viability c4c network

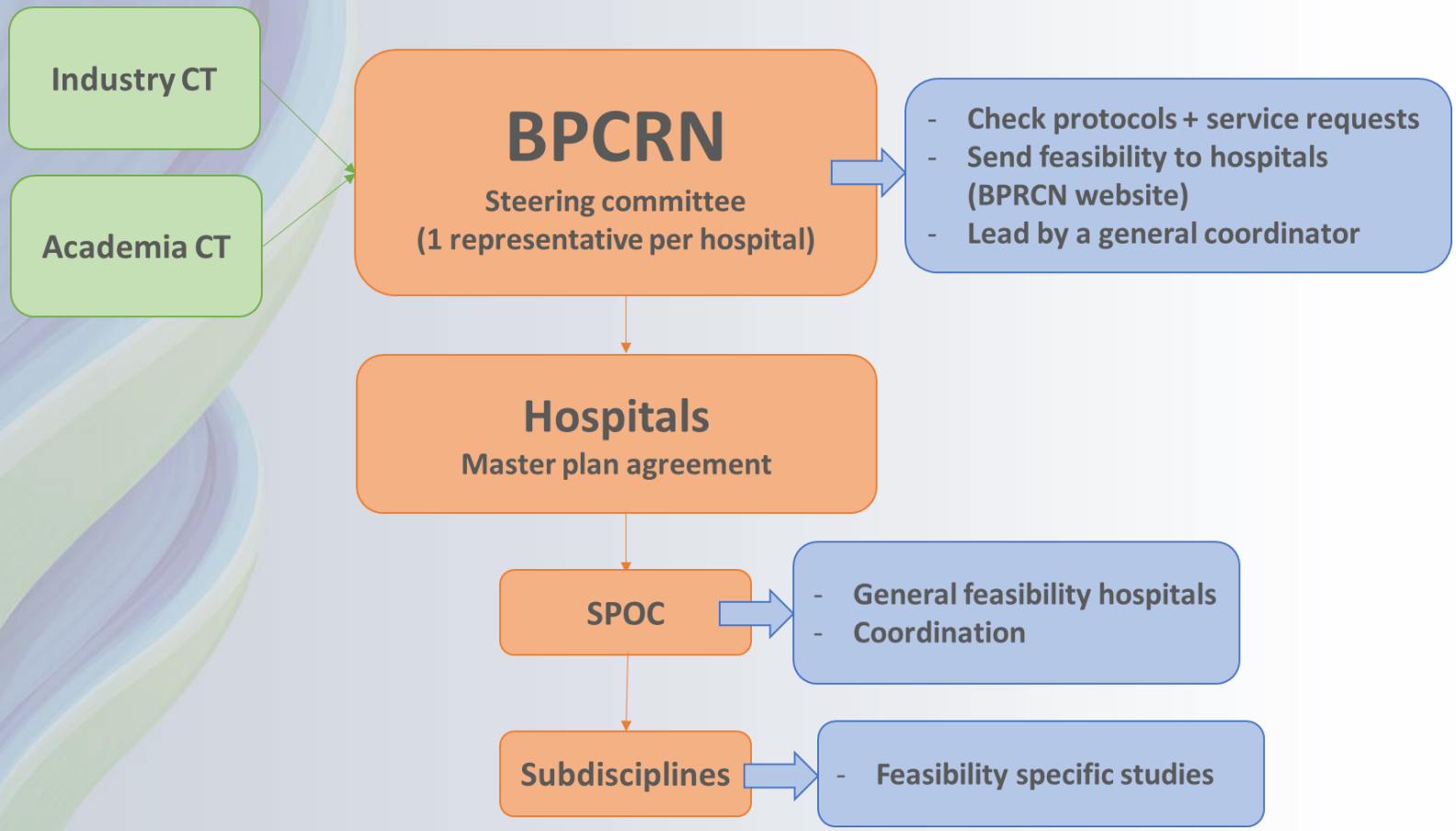
Non-industry sponsored studies (2019-2023)

- 57 letters of interest submitted to c4c (multidisciplinary)
- Feasibility of different studies was send to subdisciplines VUB
- 4 of the 57 studies will be selected
- Belgium will take part in at least one study

Industry sponsored studies (2019-2023)

- Feasibility will be send by the c4c (requested by industry)
- At the moment: 1 survey J&J (IBD, feasibility completed)
- 4 studies will be selected
- Belgium will take part in at least one study via the national hub

Implementation Belgian pediatric clinical research network (2024-)



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COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

The Telemonitoring and ACE Inhibition in Children with Hypertension (TELEMACH) Trial

F Schaefer

E Wuhl

G. Montini

J. Vande Walle

imi innovative medicines initiative

efpia

Arterial hypertension (HTN) + ACE-i

- ACE-inhibitors are the prototype of the FDA and EU-regulations on pediatric drug CT
  - Adult blockbusters.. With adult incentive
  - PIP mandatory
  - Previous regulatory trials largely excluded the pediatric populations in greatest need of antihypertensive drugs, i.e. patients with advanced CKD and/or severe hypertension , comorbidities
  - failed to receive drug approval..
- Pediatric blood pressure (BP) management faces various practical challenges, which include infrequent doctor visits of otherwise healthy children, common white-coat HTN, and poor adherence of adolescents.

Arterial hypertension (HTN) + ACE-i

- A previous trial (Wühl, NEJM 2009) demonstrated a substantial nephroprotective benefit of intensified BP control using ACE inhibition, which lead to international recommendations for BP targets in the low-normal range for children with CKD (Lurbe, J Hypertens 2016).
- However, a recent 'real-world' study revealed that current BP management fails to achie
- ve recommended targets in a large proportion of European children (Schaefer, cJASN 2017). The recent ESH pediatric HTN guideline lists personalized antihypertensive dosing and innovative BP monitoring technologies as research priorities.

c4c offers a unique opportunity to perform a practice-changing clinical trial by

- (1) using the transnational network combining general pediatric and pediatric nephrology expertise to assemble a large cohort of children with essential and renal HTN,
- (2) exploiting the unique pediatric clinical pharmacology expertise available in the network, and
- (3) involving patients and families in designing a trial meeting their needs both in terms of study feasibility and facilitation of day-to-day BP management.
- While BP telemonitoring was demonstrated to facilitate BP control in hypertensive adults (Franssen, Lancet 2018), the feasibility and efficacy of this innovative technology awaits exploration in children.
- Furthermore, we hypothesize that the efficacy and safety of ACE inhibition can be optimized by rational utilization of pharmacokinetic (PK) and endocrine biomarker information.

Aim of the trial

- The planned trial will
- develop and demonstrate efficacious use of the emerging pan-European network infrastructure along with expert and young patient advisory support during trial planning and execution;
- to test the potential of PK data, renin/angiotensin blood levels and other biochemical markers to predict the antihypertensive and antiproteinuric efficacy and safety of the ACE inhibitor lisinopril, aiming to develop an individualized dosing concept to avoid both overtreatment and treatment resistance

Methods :

- Hypertensive patients aged 2-17 years will be started on lisinopril monotherapy dosed according to GFR
- PK profiles and plasma renin/aldosterone will be measured after treatment start.
- Patients will be stratified by age, GFR and HTN type and randomized to standard-of-care management or BP telemonitoring.
- While all families will receive telemetric BP monitors and central surveillance to maximize treatment safety,
- only In the intervention arm telemonitoring access will be provided also to local investigators, enabling them to frequently adapt medications to achieve the BP target

C4C: national coordinator : Régis Hancard

- Olivia Boyer-Gillion France Paris,Hopital Necker Enfants Malades Study site
- Justine Bacchetta France Lyon, UCH Study site
- Robert Novo France Lille, UCH Study site
- Ariane Zalozyc France Strasbourg, UCH de Hautepierre Study site
- Jerome Harambat France Bordeaux, UCH Study site
- Others ? Johan.Vandewalle@uzgent.be