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CLINICAL, METHODOLOGICAL AND PATIENT/PARENT EXPERT ADVICE IN PAEDIATRIC DRUG DEVELOPMENT VIA CONECT4CHILDREN

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Introduction Children have the right to new and improved medicines. conect4children (c4c) aims to promote innovative trial design to optimise paediatric development plans while ensuring the voice of young patients and their families is heard. To address this a multidisciplinary advice service was set up

Methods A network of Experts, divided into Expert Groups, was set-up via an open call for Experts. In parallel a Patient and Public Involvement (PPI) database was formed to include the expert opinion of paediatric patients and their parents. Advice is given according to the following process: (1) Sponsors contact c4c (2) a scoping interview is held (3) formation of ad-hoc Strategic Feasibility Advice Group (5) an advice meeting is held (6) an advice report is provided. To continuously improve this process, feedback from Experts and requestors on the service was collected

Results 24 clinical and innovative methodology Expert Groups, consisting of >300 Experts, diverse in gender, seniority and geographical location were established. The PPI database includes registrations in 4 subgroups. To date (Dec 2021) 30 advice requests were received from academia and industry and 23 have been completed. Clinical, methodology and PPI Experts participated in several of these requests. Sponsors appreciated the diversity of the Expert Groups as well as the quality of the advice which in many cases significantly contributed to shaping the paediatric development strategy. Experts and PPI participants were satisfied with the advice process

Conclusions c4c has shown a successful proof of concept for a European, multidisciplinary, advice service for paediatric drug development, tailored to industry and academia. This service presents a new framework for innovative and feasible paediatric trials

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COLLABORATION IN NEONATAL AND PAEDIATRIC CLINICAL PHARMACOLOGY: CREATING A PEER-BASED MENTORING PLATFORM IN A PAN-EUROPEAN CLINICAL TRIAL NETWORK

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Introduction In recent years, substantial improvements in clinical trial facilitation have been made through a pan-European network conect4children (c4c), funded by the Innovative Medicines Initiative 2. Within c4c, collaboration and experience-based teaching were attainable due to live meetings and structured social interactions. Since the COVID-19 pandemic, meeting platforms were limited and strictly virtual, creating an

artificial communication environment and a gap for young talent to interact and learn.

Methods In light of c4c's main objective to build strong collaborations and connections between different national clinical trial networks, the younger generation was in need of support. In May 2021, the young investigators community (YIC) platform was launched to facilitate an informal teaching and connecting vehicle. However, interaction with the experienced and leading generation was lacking, in order to mentor the 'starters' for a durable network.

Results Within the first year, the YIC created an open platform in which the 32 members could interact on a regular basis. Topics included involving medical students, how to build and prepare sustainable business plans and working and interacting with industry partners. Inspired by Erasmus+ funded Pathway project and McBride et al (2017) Mentorship profiling, a 4-page intake questionnaire for both mentor and mentee has been designed, that focuses on specific skills and a plan-of-action for the mentorship session, maximizing efficiency of the interaction.

Conclusion Within YIC, a questionnaire was designed to approach mentor and mentee selection, to be used to minimize the gap between young talent and the established community. The method could be beneficial to other national and international network

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FEASIBILITY OF THE PRAGMATIC PBPK MODELLING APPROACH – TOWARDS MODEL-INFORMED DOSING IN PAEDIATRIC CLINICAL CARE

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Introduction More than half of all drugs are still prescribed off-label to children. To support off-label dosing, pharmacokinetic (PK) data are needed. Physiologically-based pharmacokinetic (PBPK) models are increasingly used to study PK and guide dosing decisions. We hypothesize that combining existing compound models with a paediatric population model can be used to pragmatically predict paediatric exposure.

Methods Seven drugs, with various pharmacokinetic characteristics, were selected (i.e. meropenem, ceftazidime, azithromycin, propofol, midazolam, lorazepam, and caffeine). Simcyp v20 was used to predict exposure in adults, paediatrics and preterm neonates by combining an existing compound file with various virtual populations. Predictive performance was evaluated by calculating the ratio of predicted-to-observed PK parameter values (0.5 to 2-fold acceptance range) and by a visual predictive check.

Results Overall, model predictions in adults were able to capture clinical observed PK data and confidence in PBPK model performance for predicting PK in this population was therefore considered high. However, predictive performance decreased when predicting PK in the paediatric population, even more so in preterm neonates.

Conclusions Pragmatic PBPK modelling in paediatrics is feasible, though the approach is not straight forward as limitations, such as inadequate parameterization with respect to paediatric-specific ADME properties, have been observed. A thorough understanding of the models assumptions and limitations is