Paediatric Clinical Research Infrastructure Network
PedCRIN

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Deliverable D3.5
Procedures for setup of neonatal trials

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Working Package: WP3 (Tools for neonatal trials)-INSERM

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Abbreviations

CTU	Clinical Trial Unit
CRO	Contract Research Organisation
CVBF	Consorzio per Valutazioni Biologiche e Farmacologiche
ECRIN	European Clinical Research Infrastructure Network
PedCRIN	Paediatric Clinical Research Infrastructure Network
PK	Pharmacokinetics

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1. Introduction and background

Setting up neonatal clinical trials is challenging due to the particularities of the neonatal population which influence for example research ethics, feasibility, protocol development, data collection and data analysis.

In the context of the PedCRIN project (Paediatric Clinical Research Infrastructure Network) a survey and gap analysis were conducted by Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF) in order to identify the needs of the research community in Europe. The gap analysis identified needs related to the procedures of setting up (Deliverable 3.5) and management (Deliverable 3.7) of neonatal clinical trials. PedCRIN Work packages D3.5 and D3.7 have been set up to address these needs by either adapting existing tools or by developing new ones where necessary. The process of tool development is illustrated in Figure 1.

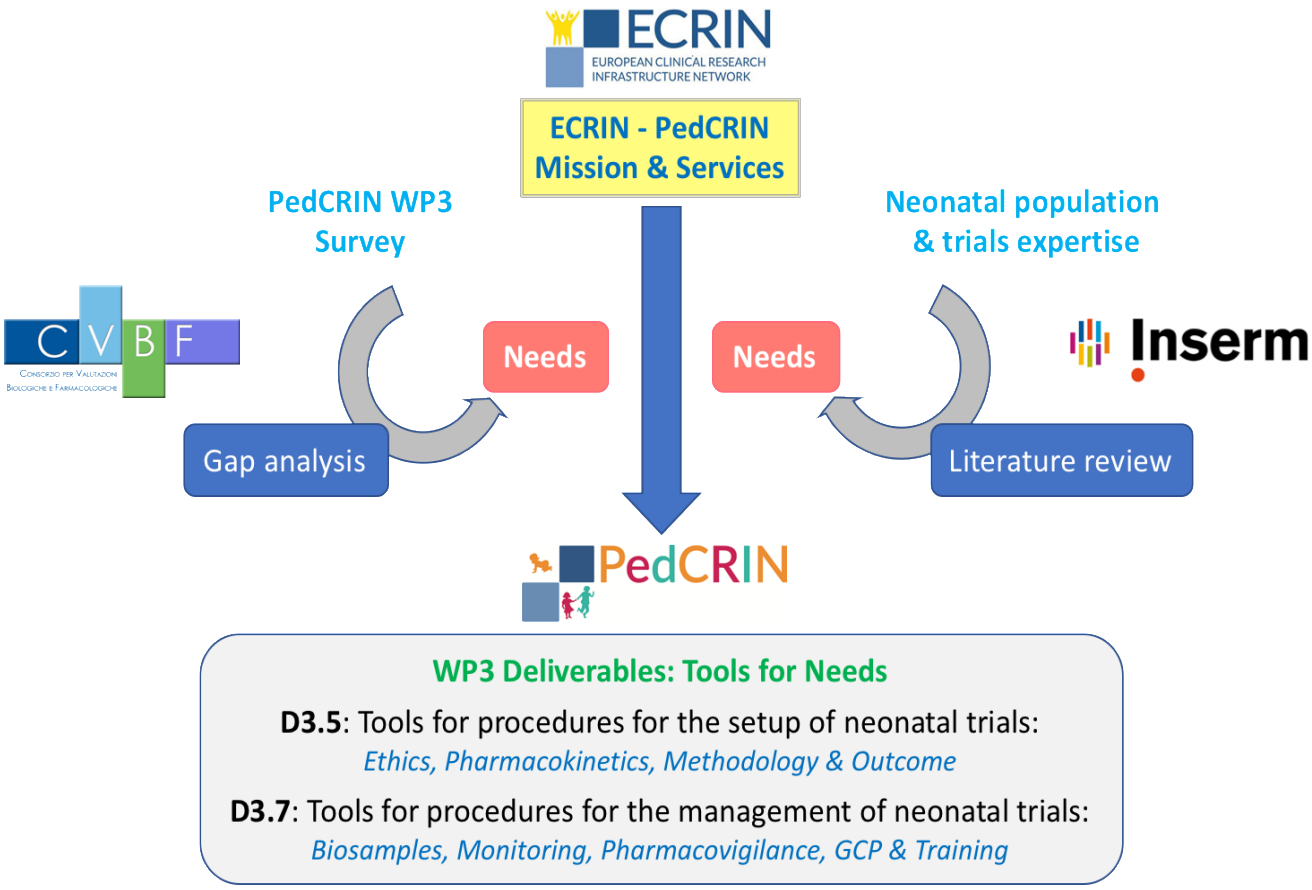

Figure 1. PedCRIN – Process of Tool development for neonatal clinical trials

As illustrated in Figure 1, in addition to neonatal expertise and literature reviews, the process of developing the neonatal tools took into consideration the results of the survey and its gap analysis as well as the mission statement and services of European Clinical Research Infrastructure Network (ECRIN).

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2. Tools for procedures for setting up neonatal clinical trials

Based on the above process more than 50 neonatal tools have been identified to address the needs identified in the setup (D3.5) and the management of neonatal clinical trials (D3.7). Presently D3.5, the following methodology was applied for the development of each tool: the relevant literature was reviewed and summarised. Where needed existing tools were adapted for the neonatal population and where necessary new tools were developed.

2.1. Objective of tools developed for neonatal trial procedures

Many clinical trial procedures already exist and are created in accordance with the templates developed by the Sponsors, Clinical Trial Units (CTUs) or Contract Research Organisations (CROs). Clinical trial regulations and processes apply independent of study age-groups. Nevertheless, procedures are adapted and specific to each individual clinical trial.

Hence, neonatal clinical trials are different from those conducted in older age groups, as they have specific methodological and regulatory requirements but existing procedures can be adapted to fit the neonatal trial population.

Therefore, the present objective of D3.5 is not to develop a new model/set of procedures for neonatal clinical trials but rather provide "keys" for Clinical Trial Units or any other entity involved in clinical trial development to understand and adapt their existing practices to the specificities of neonatal population.

These "keys" are translated into specific tools complementing the various aspects of neonatal clinical trial setup.

2.2. Specific needs in ethics, pharmacokinetics, design, methodology, and neonatal outcome measures

The WP3 Gap analysis and literature review revealed specific challenges and identified five main subtopics which need to be addressed in terms of neonatal clinical trial setup: ethics, pharmacokinetics, design, methodology and neonatal outcome measures.

For D3.5 a total of 25 neonatal tools have been developed in order to respond to the needs identified. The tools for Deliverable 3.5 are listed in Table 1.

3. Conclusions

The neonatal tools developed for PedCRIN Deliverable 3.5 are based on the needs of the research community and the mission statement and the services provided by ECRIN. Twenty five neonatal tools have been developed to address the needs identified complementing various aspects of neonatal clinical trial setup: ethics, pharmacokinetics, design, methodology, and neonatal trial outcome measures. These tools will provide guidance to Sponsors, Clinical Trial Units, Contract Research Organisations and investigators unfamiliar with neonatal clinical trials or who have specific questions related to the setup of clinical trials in neonates.

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Table 1. PedCRIN Deliverable 3.5 – Procedures for setup of neonatal trials (tools)

Description	D3.5 - Tool number
Ethics during the setup of neonatal trials	
Information of parents: discussion process & enrolment improvement	3.5.1
Involvement of parents in neonatal studies	3.5.2
Pharmacokinetics in the setup of neonatal trials	
Study procedures	3.5.3
Innovative population pharmacokinetic studies: scavenged samples	3.5.4
Population pharmacokinetic studies and extrapolation	3.5.5
Neonatal pharmacokinetic studies: Point to consider	3.5.6
Design in the setup of neonatal trials	
Design of neonatal clinical studies: classical and innovative designs	3.5.7
Methodology in the setup of neonatal trials	
Feasibility assessment and selection of neonatal centres: Points to consider	3.5.8
Feasibility assessment and neonatal study population: Points to consider	3.5.9
Defining the target population: Standardising neonatal age groups	3.5.10
Defining the target population - Data collection in neonatal trials: Points to consider	3.5.11
Defining the target population - Data analysis: Points to consider	3.5.12
Controls in neonatal trials: patients and drugs (comparator/reference): Points to consider	3.5.13
IMPs - GMP: Points to consider for neonatal formulation development	3.5.14
IMP- GMP: Points to consider for excipients used in neonatal formulations	3.5.15
IMP - GMP: Formulations and excipients in neonates: Examples of documents published by regulatory authorities and institutional bodies	3.5.16
Drug safety and protocol development: Points to consider	3.5.17
Statistical methodology in neonatal drug safety data analysis: Examples of potential confounders and risk factors for adverse events/outcome	3.5.18
Statistical methodology in neonatal drug safety data analysis: Points to consider	3.5.19
Inclusion and exclusion criteria and patient safety: Points to consider	3.5.20

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Methodology for small sample size in neonatal efficacy studies: Points to consider	3.5.21
Statistical methodology in neonatal trials & challenge of small sample size: Points to consider	3.5.22
Outcome measures in the setup of neonatal trials	
Neonatal Patient-centred outcome measures - What data should be collected	3.5.23
Neonatal Patient-centred outcome measures - Short-term outcome: Points to consider	3.5.24
Neonatal Patient-centred outcome measures - Long-term outcome and follow-up: Points to consider	3.5.25

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