Paediatric Clinical Research Infrastructure Network
PedCRIN

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Deliverable D3.7
Procedures for management of neonatal trials

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Abbreviations

CRO	Contract Research Organisation
CTU	Clinical Trial Unit
CVBF	Consorzio per Valutazioni Biologiche e Farmacologiche
ECRIN	European Clinical Research Infrastructure Network
GCP	Good Clinical Practice
PedCRIN	Paediatric Clinical Research Infrastructure Network
SOP	Standard Operating Procedure

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1. Introduction and background

Managing neonatal clinical trials is challenging due to the particularities of the neonatal population which influence for example biosample management, data collection and analysis, pharmacovigilance and trial monitoring.

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 neonatal and paediatric research community in Europe. The gap analysis identified needs related to the procedures for setting up (Deliverable 3.5) and managing (Deliverable 3.7) neonatal clinical trials. PedCRIN deliverables 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.

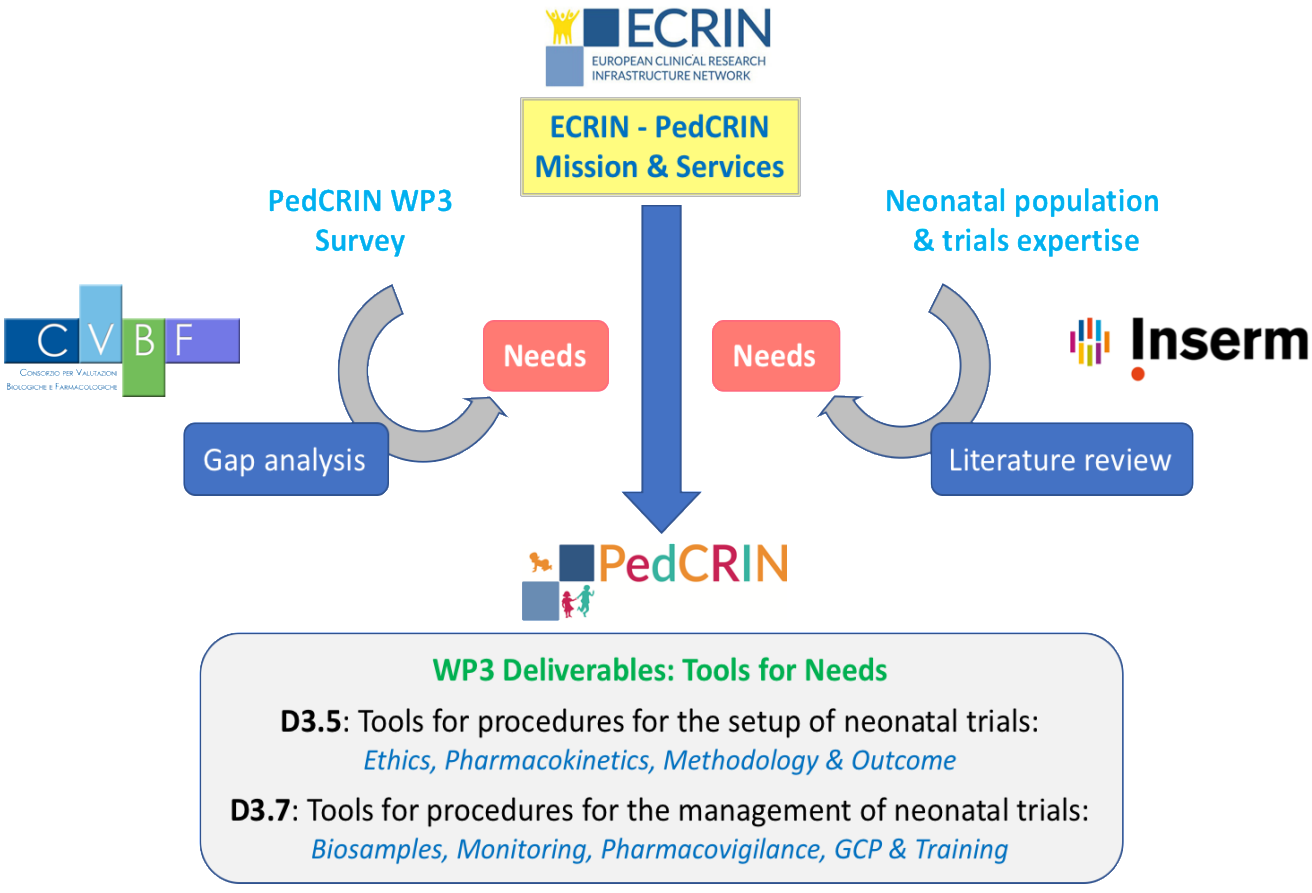

Figure 1. PedCRIN – Process of tool development for neonatal clinical trials

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

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analysis as well as the mission statement and services of European Clinical Research Infrastructure Network (ECRIN).

2. Tools for the management of neonatal clinical trials

Based on the above process more than 40 neonatal tools have been identified to address the needs identified for the setup (D3.5) and management of neonatal clinical trials (D3.7). For D3.7, 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 management

Sponsors, Clinical trial Units (CTUs) and Contract Research organisations (CROs) use Standard Operation Procedures (SOPs) and processes to manage clinical trials. These existing processes and procedures apply to all trials to ensure regulatory compliance. The management of neonatal clinical trials is driven by the relevant clinical trial regulations and the specificities of the neonatal population.

Therefore, the current objective of D3.7 is not to develop a new model/set of management processes for neonatal clinical trials but rather provide "keys" for CTUs 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 management.

2.2. Specific needs in neonatal biosample management, trial monitoring, pharmacovigilance and trial conduct according to Good Clinical Practice and training

The WP3 Gap analysis and literature review revealed specific challenges and identified six main subtopics which need to be addressed in terms of neonatal clinical trial management, i.e. clinical trials from adults to neonates, biosample management, trial monitoring, pharmacovigilance, trial conduct according to Good Clinical Practice (GCP) and training. For D3.7 a total of 25 neonatal tools have been developed in order to respond to the needs identified. The tools for Deliverable 3.7 are listed in Table 1.

3. Conclusions

The neonatal tools developed for PedCRIN Deliverable 3.7 are based on the needs of the paediatric 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 management: clinical trials from adults to neonates, biosamples management, trial monitoring, pharmacovigilance, trial conduct according to GCP and training. These tools will provide guidance to sponsors, CTUs, CROs and investigators unfamiliar with neonatal clinical trials or who have specific questions related to the management of clinical trials in neonates.

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Table 1. PedCRIN Deliverable 3.7 (Procedures for the management of neonatal trials (tools)

Description	D3.7 - Tool number
Clinical trials from adults to neonates	
Clinical trials from adults to neonates – Points to be considered	3.7.1
Biosamples in neonates	
Blood/ biological sample types in the neonatal population	3.7.2
Blood/ biological sample volumes for research in neonates – Guidelines and recommendations	3.7.3
Biosample management in neonatal trials – Collection, storage and shipment	3.7.4
Biobanking of neonatal samples	3.7.5
Trial monitoring plan	
Serious adverse events in neonatal care and implications for clinical trial conduct	3.7.6
Guidelines for clinical trial monitoring in the neonatal population – From theory to application	3.7.7
Patient transfers in neonatal trials: Points to consider for data collection and analysis	3.7.8
Training trial monitors for neonatal studies: Points to consider	3.7.9
Neonatal pharmacovigilance	
Data Safety Monitoring Boards for neonatal trials: Points to consider	3.7.10
Guidelines for pharmacovigilance: Points to consider for the neonatal population	3.7.11
Methods for causality assessment in neonates	3.7.12
Neonatal diseases and complications: Incidence and clinical implications during trial conduct	3.7.13
Serious adverse events in neonatal care and implications for clinical trials	3.7.14
Biological parameters – Reference values for neonates	3.7.15
Pain related to neonatal trial procedures: Points to consider	3.7.16
Severity assessment in neonatal trials	3.7.17
Targeted follow-up forms for serious adverse events in neonatal trials: Points to consider	3.7.18

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Neonatal clinical trial conduct according to Good Clinical Practice and guidelines	
Case report forms for neonatal trials: Points to consider	3.7.19
Points to consider for the data management of safety data in neonatal trials	3.7.20
Explaining benefit-risk to parents/ legal guardians of neonates	3.7.21
Statistical methodology in drug safety data analysis	3.5.15
Training for neonatal clinical trials	
Drug safety in neonatal clinical trials	3.7.22
Drug toxicity stratified by neonatal age group	3.7.23
Drug safety and pharmacovigilance in individual neonatal trials	3.7.24
Neonatal clinical trials and Good Clinical Practice	3.7.25

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