Paediatric Clinical Research Infrastructure Network

Procedures for the setup of neonatal trials

Feasibility assessment of neonatal studies and study population: Points to consider

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Description	This tool provides points to consider for the feasibility assessment of neonatal study populations
Key words	Neonatal trial, Protocol development, Guidance document, Tool, Feasibility

Authors: Beate Aurich, Valéry Elie, Naura Mahmoudi, Evelyne Jacqz-Aigrain

Disclaimer: **Sponsors and researchers unfamiliar with clinical trials in neonates and/or neonatology are advised to seek expert advice due the complexity of neonatology.**

Correspondence email: pedcrin@ecrin.org

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Feasibility assessment and neonatal study population: Points to consider

Assessing the feasibility of a neonatal trial protocol with regards to the number of eligible patients can be challenging. A combined review of the current literature, electronic healthcare databases and disease registries can be useful in estimating the number of potentially eligible neonates for a planned recruitment period.[1,2] However, neonatal data on such databases may lack sufficient precision with regards to the coding of neonatal diseases, age and information on comedication (including dose, frequency and duration) or confounding and risk factors for adverse drug reactions (ADRs) and outcome.[2,3] Consideration might be given to search for additional information from local hospital records, prescription data, neonatal consultants and focus groups (e.g. parent or patient associations).

The incidence and prevalence of neonatal disease may vary considerably between different trial centres.[4] In the absence of sufficient data to estimate the number of eligible neonates a pilot study might be considered.

Considerable local variations in the diagnosis and management of neonatal diseases may exist which may required negotiations to agree on a common approach to be implemented for the trial.[2] Therefore particular attention should be paid to the procedural aspects of the protocol and whether they are consistent with local clinical practice of the future trial centres.[2]
Information on neonatal pharmacokinetics (PK), pharmacodynamics (PD), age appropriate biomarkers and the availability of an age appropriate formulation, efficacy and serious neonatal ADRs which may lead to study drug discontinuation will further inform the feasibility assessment.[2] Finally procedural limitations e.g. for blood volume and other investigations may impact on the feasibility of a study.[5] Table 1 provides points to consider for the feasibility assessment of neonatal study populations.

Competing interests

All authors consider not having any competing interests for this tool. BA has worked for GlaxoSmithKline between October 2006 and September 2009 and holds company shares. Between October 2009 and May 2015 she has worked for Novartis.

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Table 1. Feasibility assessment and neonatal study population: Points to consider*

Feasibility assessment item	Possible sources of information	Points to consider for neonatal clinical trials
Prevalence/ incidence	Electronic health care records	- Databases may lack precision - Information from several databases may need to be combined
	Literature	Information may be limited
	Investigator survey	- May over- or underestimate the number of eligible patients - May confound number of patients with disease with number of eligible patients
Local practices of diagnosis and management of neonatal diseases	Local investigators and health care professionals	Study procedures should be consistent with local practices in order to avoid protocol violations and to reduce the risk of trial failure
	Literature	Local practices may vary from international, published standards
Study drug: - Neonatal pharmaco-kinetics & pharmacodynamics - Neonatal efficacy - Neonatal ADRs & benefit-risk balance	Summary of Product Characteristics/ Label	- Neonatal data is frequently lacking - Formulation may not be adapted to neonates
	Literature	Information on the drug class should be included
	Investigators	May have experience with the off-label/ unlicensed use of the study drug
	Neonatal pharmacologists	- Can provide advice on dose selection, age appropriate formulation and data to be collected to inform dosing and efficacy - CHMP, PDCO 2009. Guideline on the investigation of medicinal products in the term and pretem neonate. - CHMP 2006. Guideline on the role of pharmacokinetics in the development of medicinal products in the paediatric population.
	Neonatal/ paediatric drug safety physicians	- Can provide advice on the current understanding of the drug safety profile, risk management and data to be collected to inform the benefit-risk balance and thus reduce the risk of trial failure - CHMP, PDCO. Guideline on the investigation of medicinal products in the term and pretem neonate. - EMA. Guideline on GVP - Product- or Population-Specific Considerations IV: Paediatric population.
- Risk factors for adverse outcome (including age and weight groups) - Comedications (incl. dose, frequency, duration)	Electronic health care records	- Databases may lack precision - Information from several databases may need to be combined
	Literature	Information may be limited
	Investigator survey	- May over- or underestimate the number of eligible patients - May confound number of patients with disease with number of eligible patients
Limited blood sampling and investigations	Literature	CHMP, PDCO. Guideline on the investigation of medicinal products in the term and pretem neonate.
	Investigators	Protocol procedures should be consistent with local practice in order to avoid protocol violations and reduce the risk of trial failure

* Not exhaustive

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