Paediatric Clinical Research Infrastructure Network

Procedures for the setup of neonatal trials

Enrolment into neonatal trials:
Points to consider during protocol development

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Description
This tool provides a list of points to consider during protocol development for improving the enrolment of neonatal trials

Key words
Neonatal trial, Protocol development, Guidance document, Tool

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

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Improving the enrolment of neonates into trials

Enrolment in neonatal trials is influenced by a variety of factors including protocol design, parental consent and support by health care professionals.\(^1\),\(^2\)

Awareness of how the design of various protocol sections may modify the number of enrolled neonates may help improving recruitment.\(^3\) Effective and repeated communication about the trial in the community may for example support the identification of eligible patients and give future parents time to reflect on the possibility to be approached for the inclusion of their child into a clinical trial.\(^4\)-\(^7\) Research suggests that most parents prefer to have an initial discussion about the trial inclusion prior to birth.\(^7\) Furthermore, understanding the factors that may influence parental decision making may help improving the number of parents consenting.\(^8\) Parent and patient organisations will provide valuable input into the acceptability of the study design, the practicalities of study procedures and the design of the informed consent form.\(^9\) Obtaining endorsement of a study by a local or national patient organisation may further help with recruitment.\(^9\) Finally, HCPs at planned trial sites may be reluctant to identify patients for a variety of reasons and open discussions about the trial may help anticipate and address these challenges.\(^8\),\(^10\) Trial planning should include the provision of sufficient resources to support the conduct of the trial.\(^11\) The Table 1 below lists examples of points to consider during protocol development for improving enrolment in neonatal trials.

Involving parents in neonatal studies has been shown to improve the quality of trial protocols, increase recruitment numbers and reduce costs.\(^12\)-\(^15\) Parents will provide valuable input on a variety of topics such as the protocol, study procedures, trial design, follow up, informed consent and outcome assessment.\(^14\),\(^16\) It is therefore advisable to consult parent organisations during protocol development.\(^17\) Successful collaboration with parent organisations will depend, for example, on careful planning, and effective communication with all stakeholders.\(^14\),\(^16\) For multinational research input should be sought from parents in each participating country. It is important to ensure the expectations of parents with such an initiative are understood, that the role of parents is defined and study results are shared with parents.\(^16\) Table 2 provides examples of parent/patient organisations.

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.
References


### Table 1. PedCRIN Tool: Enrolment into neonatal trials: Points to consider during protocol development

<table>
<thead>
<tr>
<th>Protocol section</th>
<th>Comment</th>
<th>Comment/ rationale</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background</strong></td>
<td>The data presented in this section should support the rationale that the trial is the best way forward to improve the treatment of neonates and that the benefit-risk balance is favourable</td>
<td>Lacking equipoise may reduce the support from health care professionals to include patients</td>
<td>1,2</td>
</tr>
<tr>
<td></td>
<td>All relevant data on risks for all trial interventions (active and control arm) should be presented</td>
<td>Non-disclosure of risks, including those of the comparator arm may reduce the support from health care professionals and the community to include patients</td>
<td>3</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Avoid overlap between risk factors for outcome (as an objective) and exclusion criteria</td>
<td>Recruitment may be reduced, if for example the primary objective is neurodevelopmental outcome in a population of neonates with a high incidence of risk factors for neurodevelopmental impairment and the exclusion criteria require the exclusion of all neonates with such risk factors</td>
<td>4</td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>Broad enough to recruit sufficient patients Specific enough to answer the primary objective(s)</td>
<td>Inclusion criteria which are too broad may not provide sufficient data to answer the primary objectives because the neonatal population is very heterogeneous</td>
<td>5</td>
</tr>
<tr>
<td><strong>Trial procedures</strong></td>
<td>Parents are concerned about pain and distress caused by trial related procedures</td>
<td>Pain and distress related to trial procedures should be kept to an absolute minimum</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>The burden of trial procedures including follow up visits is important for families</td>
<td>Aim to use existing data and procedures where possible and harmonise follow-up with local routine follow-up appointments</td>
<td>7</td>
</tr>
<tr>
<td><strong>Consent</strong></td>
<td>Consider reassessing consent</td>
<td>If it is unclear whether the voluntariness of consent may have been compromised, the quality of consent might be improved by seeking continuous consent</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Consent procedures should be adapted to the disease being studied</td>
<td>Different consent procedures can be used to suit the disease being studied</td>
<td>9,10</td>
</tr>
<tr>
<td></td>
<td>The informed consent form should be written in plain language</td>
<td>Using plain language will facilitate understanding</td>
<td>11,12</td>
</tr>
<tr>
<td></td>
<td>Consent should be sought in the native language of parents</td>
<td>Understanding will be improved using each parent’s native language</td>
<td>13,14</td>
</tr>
</tbody>
</table>


References


### Table 2. PedCRIN Tool: Examples of parent/patient organisations

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLISS for babies born to soon or sick</td>
<td><a href="http://www.bliss.org.uk/">http://www.bliss.org.uk/</a></td>
</tr>
<tr>
<td>ECHDO European Congenital Heart Disease Organisation</td>
<td><a href="http://www.echdo.eu/">http://www.echdo.eu/</a></td>
</tr>
<tr>
<td>ECO European Cleft Association</td>
<td><a href="http://europeancleft.org/">http://europeancleft.org/</a></td>
</tr>
<tr>
<td>EFCNI European Foundation for the care of newborn infants</td>
<td><a href="http://www.efcni.org/">http://www.efcni.org/</a></td>
</tr>
<tr>
<td>EPF European Patients Forum</td>
<td><a href="http://www.eu-patient.eu/">http://www.eu-patient.eu/</a></td>
</tr>
<tr>
<td>IF International Federation for Spina Bifida and Hydrocephalus</td>
<td><a href="https://www.ifglobal.org/">https://www.ifglobal.org/</a></td>
</tr>
<tr>
<td>IPOPI International Patient Organisation for Primary Immunodeficiencies</td>
<td><a href="https://ipopi.org/">https://ipopi.org/</a></td>
</tr>
<tr>
<td>EURORDIS European Organisation for Rare Diseases</td>
<td><a href="https://www.eurordis.org/">https://www.eurordis.org/</a></td>
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