INTERNATIONAL NIEMANN-PICK DISEASE REGISTRY (INPDR)

Challenges of regulatory requirements for patient registries in different countries

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BACKGROUND

The INPDR is a disease-specific registry collating the global data of patients diagnosed with Acid Sphingomyelinase Deficiency (ASMD) and Niemann-Pick Disease Type-C (NP-C):

- **Aims to improve standards of diagnosis, care and treatment for Niemann-Pick patients everywhere**
- **Created with the support of an EU grant, by a collaboration of 11 partners in 7 EU countries and 17 associate partners from the rest of the world, including patient groups, clinical and research experts**
- **Now a non-profit, charitable company, with a robust governance structure, an independent Board of Directors and Scientific Advisory Committee**

INPDR – Our Vision:

The creation and ongoing development of a comprehensive, international data resource, specific to Niemann-Pick diseases which benefits patients by increasing understanding of these rare conditions, encourages efficient and timely diagnosis, provides access to expert care and treatment and facilitates progress in research and clinical trials. The INPDR will serve as a valuable resource to patients and their families, healthcare professionals, industry stakeholders and marketing regulatory authorities.

Research Regulatory Approval - our experience:

The delivery of an international disease registry is challenging as the registry sponsor faces multiple barriers. One issue the INPDR has faced is compliance with local, regional, national and supranational research regulatory requirements due to poor or non-alignment between regulatory authorities. Here we explicitly discuss the INPDR's experiences within the United Kingdom (UK) and the United States of America (USA) and the research regulatory requirements of centres who have successfully completed or are currently undergoing approval processes:

United Kingdom:

- All registries are classified as a research study and are required to undertake Health Research Authority (HRA) approval (2) and local clinical site Research and Development (R+D) approval.
- HRA reviews studies at a national level and provides approval which is applicable to all participating clinical sites within the HRA's jurisdiction. HRA review
- R+D approval is undertaken at each participating clinical site, therefore each centre within a registry study is required to undergo local R+D approval.
- **Advantages:** The HRA approval applies to all centres, meaning the initial application process is only undertaken once. Additionally, any amendments to the registry are reviewed by the HRA, reducing the burden of participating sites to undertake a comprehensive amendment review.
- **Disadvantages:** participating sites will undertake local R+D approvals individually. This may lead to a duplication of efforts on each site's behalf. Additionally, the local R+D approval processes can differ significantly between sites, potentially requiring the sponsor to undertake additionally work to support the differing sites processes.

United States of America:

- Registry Sponsors are required to approach the participating site's Institutional Review Board (IRB) (3). The IRB review is applicable to its host centre.
- Studies with multiple participating centres are required to seek IRB approval at each centre.
- It is possible for Registry Sponsors to apply for Cooperative Research, whereby multiple IRB's involved in the same clinical study may jointly review the study and issue approval applicable to all IRB host centres.
- **Advantages:** IRBs are able to review registries with an understanding of any issues or barriers that may exists at the centre.
- **Disadvantages:** there is a duplication of work for the sponsor to produce review documentation for each site.

Common Challenges

Regulation

- Differing centres, regions, countries and also supranational organisations are held to differing regulations.
- Challenge to develop a registry that is robust enough to comply with multiple, and possibility conflicting, regulations.
- For example, research undertaken in the USA must be 45 CRF 46 compliant, whereas research conducted in the EU is required to comply with General Data Protection Regulation (GDPR).
- There can be ocerlap and differences between regulations, so the Registry Sponsors must carefully design their documents to ensure compliance.

Inter-review body variability

- In addition to the variation in regulations between independent bodies, the approval process itself may differ.
- The implementation of multiple review bodies involved with differing requirements, may result in repeated rounds of approval submissions.
- For example, the NHS research review process for registry studies requires two review bodies to be approached.
- This variability between review bodies can contribute to the increased workload of the Registry Sponsor and result in delays to site setup.

Inexperienced reviewers

- Registry studies are typically held to differing regulatory requirements compared to Investigational Medical Product (IMP) trials.
- The review board members may understand regulatory requirements of an IMP trial, but may not be experienced in the requirements of a registry study.
- This may cause delays in registry study approvals due to incorrect regulation being applied, resulting in Registry Sponsors undertaking additional work to clarify their study.

Other challenges

- Length of regulatory processes
- Supporting clinical data entry
- Providing global translation and language support
- Achieving informed consent in a timely way

RECOMMENDATIONS

Harmonise regulatory requirements

- Create regulations that are applicable to all countries where a registry study would be undertaken.
- The impact would encourage the creation of new patient registries, assist current Registry Sponsors to recruit centres in new countries and allow patients to join a registry without the barrier of geography.

Clearly define approval process for each site/region/country

- Review bodies of centres, regions and countries should be encouraged to develop a comprehensive resource to clearly define their research approval process.
- The creation of such a resource should allow the Registry Sponsor to understand which review bodies must be approached, the requirements of each review body and how to interact with each review body.
- To encourage interest from patient organisations, the language used should be jargon-free.

CONCLUSION

The necessity of research regulation is clear: to ensure that research protects the rights and safety of research participants. Indeed, this principle is enshrined into many organisations, including the EU (2) and the United Kingdom (3). However, research regulations and approval processes can introduce barriers to the creation of and participation in patient registries. As patient registries can fulfill a number of roles, including collecting data regarding disease natural history, post-marketing surveillance tool and patient quality-of-life register, regulatory bodies should look to where the approval of patient registries can be expedited.

For further information please visit: inpdr.org, and for our latest updates please follow us on Facebook @INPDR

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