THE INTERNATIONAL DISORDER OF SEX DEVELOPMENT REGISTRY

I-DSD REGISTRY

PROTOCOL FOR A RESEARCH DATABASE

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1. Background

The I-DSD Group is a group of clinicians and academics who deal primarily with patients with abnormalities of gonadal, adrenal or hormonal function that lead to a DSD. Most of these patients are identified in childhood and often present in early infancy with an abnormality of the development of the external and/or internal reproductive organs. There is a large amount of variation in how these patients are managed across the UK as well as across the world. In addition, there are enormous gaps in our knowledge about the aetiology of these conditions and the long-term outcome in adults with these conditions.

Until quite recently, there was little consensus about data collection in patients with a disorder DSD. In 2006, a group of international experts attempted to reach a consensus on terminology. The SGAN dataset adopted this terminology and the dataset has also been scrutinised by a working group within the European Society of Paediatric Endocrinology, ESPE (www.eurospe.org/about/ working groups/DSD) and the current version has now been adopted by this special interest group of ESPE and was used as the core dataset within the EuroDSD project − a programme of research between 2008 and 2011 which was funded by the EU Framework Project 7 grant (www.eurodsd.eu). As part of the EuroDSD programme, the core dataset was transformed into an electronic web based registry by experts at the National E−Science centre. The web based EuroDSD registry has been scrutinised by the ethics advisers of the EuroDSD programme (www.eurodsd.eu/en/wp−01−virtual−research−environment−vre.php). This registry, funded by the EuroDSD programme was originally open to programme partners but its transformation into the International DSD Registry supported by the MRC UK from 2011 to 2016 will lead to increasing its access to a larger group of approved clinicians and researchers.

As the core dataset has achieved a very high level of consensus between professionals and there is current funding and support for the web based registry, this seems to be the right moment to consider extending the use of the registry. A high level of enthusiasm exists in in Europe and many countries outside the EEA have also expressed an interest in this collaborative work.

The data contained in the research database shall purely be observational data. The primary goal of the database is to act as a source of observational data that will facilitate research into the aetiology of DSD and long-term outcome of patients with DSD. Researchers whose study proposals are reviewed and approved in advance by the Panel may use data for a fixed period.

The following are broad examples of studies in which these data could be used.
• What is the molecular aetiology of cases of DSD?
• Do associated abnormalities occur in DSD and do they help with identifying a genetic problem
• Long-term outcomes
• What kind of support do patients with the same severity of condition receive around the world?
• Are there any differences in investigating patients with DSD?
• Variability of clinical and biochemical phenotypes within each molecular aetiology

2. Eligibility of Users of Registry

2.1. I-DSD Panel

The I-DSD Panel are DSD experts representing the funding streams of the Registry. Group. Users shall apply to this panel for approval. There will be two broad categories of users of the Registry– clinical partners and research partners.

2.2. Clinical partner

Clinical partners shall be eligible to enter data into the Registry and will seek approval from the I-DSD Panel to seek this privilege. Only members of a national or international clinical professional society shall be allowed to become a clinical partner and will need to show proof of membership. In addition, application for more than one clinical partner from the same institution shall be discouraged but not barred. Each clinical partner can identify other members of their team who will require access. Thus, the clinical partner will remain responsible and accountable for data entry. The clinical partner and approved members of the team shall be able to enter, search, edit, and delete data on all the cases that are entered under that clinical partner. Details of the clinical partner and their local institution should be entered on the information sheet.

2.3. Research partner

Research partners shall need to apply to the I-DSD Panel with details of their proposed study. Research partners are required to demonstrate that they have obtained ethics approval. The Panel will approve the use of the Registry by the research partner for a fixed period of time. An administration fee may be levied depending on the required duration of access. In addition, any form of research output that results from the use of the Registry shall acknowledge its use using a standard sentence. Each research partner can identify other members of their team who will require access for that same period. The research partner and approved members of the team shall be able to search data on all the cases that can be shared by the clinical partner.

2.4. Joint Clinical & Research Partners

Some partners may have joint clinical and research partner status. These partners shall need to continue renewing their research partner status.

3. Eligibility of Cases in Registry

3.1. Eligibility Criteria

Any individual with a disorder of sex development at a centre with an approved clinician is eligible to be included in the Registry. This includes adults and children. Participating clinicians shall be informed about new studies that are approved by the I-DSD Panel and this will encourage them to approach and register suitable patients.

3.2. Provision of Information

Patients and their legal guardians (if patient less than 16yrs old) shall be approached by the clinical partner or a member of their team for approval to include the patient's details on the Registry. Information and the approval form can be provided at the clinic.

3.3. Obtaining Consent

Although the Registry contains non-identifiable data and there may be no need to obtain informed consent in the UK to share data with EEA members, it is recognised that some countries within the EEA as well as outwith EEA may have different national regulations which require opt-in. For uniformity as well as to comply with the feedback received from patient and user support groups, it is felt that the opt-in system should be adhered to as a basic minimum standard of consent. Completion of data entry into the electronic Registry can only occur if these national regulations have been adhered.

3.4. Minor Assent
As the Registry includes children, an information sheet should be provided for those under the age of 14 years. Over the age of 14 years, these young adults should be provided with the adult information sheet. The minor (under 16 years) may only participate if the minor and a parent or legal guardian both do not raise any objections. If either the parent/legal guardian or the minor declines participation, the minor shall not be enrolled into the Registry. If the minor lacks the capacity to provide assent, parent or legal guardian permission is sufficient. On turning 16 years old, the patient who is already on the Registry should be sent an adult information sheet. The Registry will remind the clinical partner to do this.

3.5. Participant Withdrawal from Registry
At any time a participant may request that his or her data or their child's data no longer be made available in the Registry. The participant shall make this request to their local clinician who is the clinical partner and who will inform the Panel. The participant can also make this request directly to the Panel. A confirmation of withdrawal shall be sent to the clinical partner.

4. Local Approvals

The current DSD Registry has been approved by the local Caldicott Guardian in Glasgow and has also been approved by the UK Research Ethics Committee and the Ethics Committee of the EuroDSD programme. All information stored in the registry, and access to that information, conforms to the UK Data Protection Act (1998). However, all participating clinical partners and research partners should follow their own national regulations and provide assurance to the I-DSD Panel that national regulations are being followed for data handling as well as research. The information sheet and consent forms should include the name of the local clinical partner, local institution and local institutional contact. The CAH support group and the AIS Support Group in the UK have also been consulted on the development of the Registry.

5. Using The Registry

5.1. Flow of Information
Appendix 1 summarises how information shall flow in the Registry as well as the checks that will be employed for the purpose of security

5.2. The Core Dataset
Details of the fields that are included in the core dataset are in Appendix 2. Those marked with an asterisk are mandatory. There is no need to place a local identifier. Further details about the dataset can be obtained by visiting https://tethys.nesc.gla.ac.uk/.

5.2. Accessing and Navigating the Registry
Every approved user shall be provided with a unique log in and choose their own password. Users shall only log on with their username. For research partners, the log in shall be time limited. Further details of how to access and use the Registry website in general can be obtained by visiting https://tethys.nesc.gla.ac.uk/.

5.4. User Tracking
Audit tracking software monitors access patterns, machine locations and user IDs. With this information, it is possible to accurately track and identify any illegal usage. The Registry shall not store or capture any personal information, but will log the user's IP address, which is automatically recognised by the web server. The website and server logs are hosted by the National e-Science Centre at the University of Glasgow using Shibboleth Single Sign-On (SSO) technology and the IP information is accessed through tools provided by Google Analytics. We shall not use cookies for collecting user information from the site and will not collect any information about users except that required for conducting research within the consortium, enforcing consortium privacy rules, or for system administration of the registry.

6. Data Confidentiality

Access to all information in the Registry is tightly controlled with passwords and logins set at multiple levels. Access to the Registry is limited to named people who have specific job responsibilities related to the Registry. There are no patient identifiable data on the Registry. Every participant on the Registry shall have a unique identifier. This identifier will have a link local ID which does not need to be entered on the Registry depending on local regulations. This local ID shall be kept by the clinical partner, physically and electronically, separately to the Registry. The unique identifier contains no identifying information within it. This number is used to track all information about the participant in the Registry. The identity of participants in the Research Database is kept confidential at all times. Data released to research partners does not include identifying data either such as birth date. The only way for research partners to find out more is to contact the clinical partners whose details shall be linked to the unique identifier. All research staff at the National eScience Centre at the University of Glasgow maintain up-to-date training in protection of human subjects.

7. Funding

The I-DSD Registry is currently funded by a network project grant by the Medical Research Council. This funds a 0.5wte Database Developer at the National E-Science Centre and a 0.5wte Project Manager. The fees that will be charged to access the Registry shall be directed towards the maintenance and administration costs of the Registry. Cofunded studies that include the I-DSD Registry will not be subject to any fees.