

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)

GloBE-Reg

1. Is your project research?

Yes No

2. Select one category from the list below:

- Ionising Radiation for combined review of clinical trial of an investigational medicinal product
- Ionising Radiation and Devices form for combined review of combined trial of an investigational medicinal product and an investigational medical device
- Clinical investigation or other study of a medical device
- Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
- Basic science study involving procedures with human participants
- Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- Study involving qualitative methods only
- Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- Study limited to working with data (specific project only)
- Research tissue bank
- Research database

If your work does not fit any of these categories, select the option below:

Other study

3. In which country of the United Kingdom is the database established?

- England
- Scotland
- Wales
- Northern Ireland

3a. In which countries of the United Kingdom will centres collecting and/or supplying data to the database be located?
(tick all that apply)

- England
- Wales
- Scotland
- Northern Ireland

4. Which applications do you require?

- Social Care Research Ethics Committee
- Research Ethics Committee
- Confidentiality Advisory Group (CAG)

6. Do you plan to include any participants who are children?

- Yes No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

- Yes No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

- Yes No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

- Yes No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

- Yes No

RESEARCH DATABASE



Health Research Authority

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
GloBE-Reg

Please complete these details after you have booked the REC application for review.

REC Name:

West of Scotland REC 4

REC Reference Number:

22/WS/0074

Submission date:

09/05/2022

A management protocol or similar document should be enclosed with this application. This should be a comprehensive outline of the purpose, operation, methods, policies and governance of the database.

Part A: Core Information

Administrative information

1. Title of the Database

Global Registry For Novel Therapies In Rare Bone & Endocrine Conditions

2. Name and address of the establishment (i.e. the legal entity responsible for storage of the data)

Organisation	The University of Glasgow
Address	IT Services Sir James Black Building
Postcode	G12 8QQ
Telephone	01413302813
Fax	

3. Name of the Applicant *The applicant should be the person with overall responsibility for the management of the Database and will be regarded as the Data Controller.*

	Title	Forename/Initials	Surname
	Professor	S. Faisal	Ahmed
Address	Royal Hospital for Children Office Block, RHC & QEUH campus Glasgow		
Postcode	G51 4TF		
E-mail	Faisal.Ahmed@glasgow.ac.uk		
Telephone	0141 451 5841		

Mobile 07765422553
Fax

A copy of a current CV (maximum 2 pages) for the applicant should be enclosed.

4. Name of the Data Custodian *This should be a senior person at the establishment, other than the applicant, who is independent of the research database team and able to provide assurance that appropriate information governance is in place.*

	Title Forename/Initials Surname
	Mr Paul McLaughlin
Address	IT Manager Room 203 Sir James Black Building
Postcode	G12 8QQ
E-mail	paul.mclaughlin@glasgow.ac.uk
Telephone	01413302813
Mobile	
Fax	

5. Has this database (or any part of the database) previously been the subject of an application for ethical review?

Yes No

Purpose of the Database

6. Summarise the types of data to be stored. *Please state the population base and the selection criteria for inclusion of data in the Database. Indicate what data is already held and summarise the plans for further data collection from patients, service users or care records. Indicate whether any particularly sensitive data will be held.*

The Global Registry For Novel Therapies In Rare Bone & Endocrine Conditions (<https://globe-reg.net/>) is a new project that has been launched in January 2022. GloBE-Reg is developing a platform that can support post-regulatory approval studies for several novel endocrine therapies in children. This level of involvement reflects the global interest in developing a single registry and common data fields that can be completed for a wide range of drugs within a common class. The data fields are divided into the core data fields that have been recommended by the European rare Disease Registry Infrastructure (https://eu-rd-platform.jrc.ec.europa.eu/erdri-description_en) and which have been included in the applicant's other successful registry projects including I-DSD (19/WS/0131) and EuRRECa (18/WS/0205). Amongst this dataset, the only identifiable field is the date of birth. In addition, depending on the class of drug being studied, a set of customised fields shall be available based on the guidance of specific scientific study groups in GloBE-Reg. These specific fields will be divided into four categories - diagnosis, therapy, clinician reported outcomes including adverse events and patient reported outcomes. All children who are prescribed therapy as part of routine clinical management that is included within the scope of the scientific study group will be eligible to be included. The first class of drugs that will be included in GloBE-Reg is Long Acting Growth Hormone. Centres that participate will need to be a member of one of the participating professional paediatric endocrine societies.

Please enclose a list of all data items to be stored. Enclose a copy of any questionnaire to collect data from donors which is additional to data collected in the course of normal healthcare provision.

7. Justify the collection of this data and describe how it will be used for research. *Summarise the overall policy of the establishment for use of the data, including release to other researchers or research organisations. Say what other research databases already exist in this field. What will this database add to existing resources and what will be the potential benefits?*

Patient registries are organised systems that collect uniform data to identify a wide range of outcomes for a population defined by a particular disease, condition or exposure. In the field of endocrinology we have performed a mapping exercise (Ali SR, et al The current landscape of European registries for rare endocrine conditions. Eur J Endocrinol.

2019 Jan 1;180(1):89-98) which showed that the majority of exercise that exist collect natural history data on a narrow range of endocrine conditions. Registries can also provide valuable data that can support regulatory decision making on medicinal products by providing evidence on the efficacy/effectiveness and safety of medicinal products in the frame of non-interventional studies at a post-authorisation level. In endocrinology, most of the existing registries have not been designed for this purpose and even if they are redesigned their scope is guided by the conditions they cover, rather than the drugs that require post-regulatory approval surveillance. The registries that do exist for this purpose have been developed by industry for one specific drug and the long-term utility of these industry registries becomes limited as industry loses interest after the period that is required for a post-approval surveillance. In paediatrics and, particularly, paediatric endocrinology, the combination of outcome and safety can only be judged after a follow-up period of three to four decades as a minimum. Thus, there is an increasing realisation that registries that are developed in partnership between industry, academic organisations, health care professionals and patients are more likely to succeed in the long-term as effective tools for non-interventional studies of medical therapies that have already been approved. These issues were discussed in detail at an EMA workshop in 2016. More recently in 2020, the agency performed a survey of existing registries in its database and although the full results are yet to be published, the survey showed that only a small percentage of the surveyed registries collect systematic information on adverse events and those that do collect these data, do not have standardised processes for sharing data with industry and regulators for post regulatory surveillance.

The Registry platform will be developed using the .net framework which is currently being used for the EuRRECa Core Registry and will adhere to the high standards of registry management and governance that the applicant has adhered to over the last decade and a half for the other projects. The cornerstones of the I-DSD/CAH model are site autonomy and the detailed definition and enforcement of standard operating procedures on access, usage and contribution of data to the registry. Details of the standard operating procedures for other projects are available at <https://home.i-dsd.org/protocol-for-using-the-registry/>. The registry will be driven by security, incorporating both the needs of the clinical community and ethical oversight required on information governance with inclusion of pseudoanonymized data only. Patients will also have access to their data and will also be able to submit patient reported outcomes in their own language. The project will be overseen by a Steering Committee that will consist of representatives from all participating professional societies and industry partners. Access to data shall be overseen by a separate Data Access Committee that will also have patient representation. Data will be provided to study groups following approval by the Data Access Committee.

8-1. How have you actively involved, or will you involve, patients, service users, or members of the public in establishing the database and its policies?

Patients and patient groups will be present in the Scientific Study Groups and the Data Access Committee. For the long-acting growth hormone Scientific Study Group, Endo-ERN have already been approached and has identified patient groups who have agreed to join the project. In addition, Obtaining PROs will be an essential feature of the registry platform. The applicant has extensive experience of this at a local level in Glasgow (PRO-DSD, 20/WS/0099) and the EuRRECa project mentioned earlier. In EuRRECa, the platform has the ability to collect language specific PROs.

9. How will you inform data subjects and other patients, service users and members of the public of the results of research?

This will be performed through multiple mechanisms

- a dedicated website - <https://globe-reg.net/>
- a twitter feed https://twitter.com/GloBE_Reg
- all outputs of GloBE-Reg will be open access
- links to the websites of partner societies
- at scientific meetings
- at education and consultation meetings for patients
- by building a dedicated patient module. We have done this already for the I-DSD and EuRRECa projects. Patients can see their own details and this space will also allow patients to complete patient reported outcomes
- 6-monthly newsletters
- a leaflet

10. How will the Database be managed, financed and sustained to ensure the potential benefits are realised?

The project has currently been funded by Novo Nordisk for an initial period of three years from January 2022 onwards with a likelihood of being funded for another 8 years after that. Other companies who are also in the same field as Novo Nordisk have expressed an interest in supporting the platform and discussions are ongoing with Ascendis, GenSci, LG-Chem and Pfizer. It is anticipated that this will be a long-term project which will require approval on a 5-

yearly cycle. In addition to industry funding, the project will also be sustained by fees that will be charged for data provision to study groups. However, from past experience with the I-DSD Registry, this income stream is never sufficient for sustaining a registry project. Thus the project will remain dependent on external funding. As new classes of drugs are included over time, no single industry will remain the sole funder of the project. In addition, study groups will be encouraged to apply for funding that will allow the development of new modules. The steering committee of GloBE-Reg met for the first time in late 2021 and consists of members of industry as well as official representatives from a wide range of paediatric endocrine organisations across the globe. These organisations include the Asia Pacific Pediatric Endocrine Society, the Australasian Paediatric Endocrine Group, the Arab Society for Pediatric Endocrinology and Diabetes, the Chinese Society of Pediatric Endocrinology, the European Society for Paediatric Endocrinology, the European Reference Network for Rare Endocrine Conditions, Latin American Society for Pediatric Endocrinology and the Pediatric Endocrine Society of North America. The project will be overseen by this Steering Committee that will consist of representatives from all participating professional societies and industry partners. Access to data shall be overseen by a separate Data Access Committee that will also have patient representation. The Project Management Group will be based in Glasgow and will be led by the applicant.

Information governance

11. What personal identifiers will be held with the data records? *Please tick all that apply.*

- Initials
 Full name
 Address
 NHS or CHI number
 Hospital ID no.
 GP registration
 Date of birth
 Year of birth
 Date of death
 Postcode
 Other geographical identifiers

please specify

- The hospital and health care provider where the patient receives endocrine care
- Access to 'the patient space' in the Core Endocrine Registry will require the email of the patient or the patient's carer. This will be an optional exercise which the patient will need to choose on the consent form.
- The date of birth is necessary to calculate several time dependent outcome indicator

Purpose for which postcode/geographical identifiers required:

- Deprivation scoring
 Lifestyle analysis
 Geographical analysis
- Gender
 Occupation
 Ethnicity
 Other identifiers

12-1. What systems will be in place to ensure the confidentiality of personal data? *What will be your policy for limiting access to identifiable data within the establishment. Say who will have access and for what purposes, what training they will have and how the confidentiality policy will be monitored and enforced.*

No personally identifiable data except those mentioned above shall be stored on the Core Endocrine Registry. All those involved in the running and development of the Registry will have to be up to date with the General Data Protection Regulations and will complete the University of Glasgow online course (<http://www.gla.ac.uk/services/dpfoioffice/dataprotectiononlinetrainingmodule/>) and familiarise themselves with the

University's policies on data protection and management at
<https://www.gla.ac.uk/myglasgow/openresearch/researchdatamanagement/>

13. What security and audit measures will be in place to secure access to identifiable data held by the Database?

IT Services at the University of Glasgow have a body of projects associated with fine-grained security. In restricting access to the registry and its contents, roles based access control (RBAC) and identity based access control (IBAC) mechanisms are applied. The X509-based digitally signed roles (attribute certificates) are maintained in a secure attribute server. The assignment and revocation of roles and hence privileges to individuals involved in either entering cases to the registry or accessing cases will be through agreement with the GloBE-Reg project office. Authentication to the portal and delivery of attribute certificates for local authorisation at the portal level is made through a dedicated Identity Provider. This same standard will be maintained for the GloBE-Reg project.

14. What arrangements will be in place for monitoring the Database's systems and procedures?

Access to the GloBE Registry will be perpetually monitored and information logged on its usage. Basic internet-based monitoring tools shall be used for recording patterns of interactions (including ensuring that only recognised client IP-addresses are used when accessing the registry). Finer grained auditing and logging of access and usage of the registry contents will be maintained through portal-based solutions which leverage the RBAC and IBAC mechanisms. Feedback on access and usage of the registry will be regularly discussed at project meetings. This is the system we have used for the other successful registries that we have run from Glasgow. In addition to internal governance systems and procedures, GloBE-Reg will also be governed by its Steering Committee.

Use of data by the Research Database team or other researchers**15. Do you wish to seek generic ethical approval for research projects using the stored data, under conditions agreed with the REC, without requirement for researchers to apply individually to the REC for approval?**

Yes No

16. What types of research will be undertaken and in what field(s) of health or social care?

The overall objective of the registry is to collect clinician and patient reported outcomes in patients with a rare endocrine or bone condition starting on a novel drug as part of routine clinical care. The data in the Registry shall be analyzed to provide a summary update on the contents of the Registry to funding bodies as well as to groups interested in using the Registry for their research.

- Research will also be performed on the use of the Registry and its development.
- The Registry will also report on the distribution of cases and their epidemiology
- Aggregate data on outcomes such as clinical effectiveness, adverse events and patient reported outcomes shall be also analyzed.
- The development of new study groups will be promoted so that new classes of drugs are also incorporated on the platform
- While the class of drug may change and the outcomes may change accordingly, the same form of analysis will be performed irrespective of the drug.
- The Registry will also perform internal quality assurance checks.

17. Give summary details of the research team. It is not necessary to name individuals, but please give an indication of the types of researchers who are likely to be involved and the expertise available within the team, including IT and other support staff. Include any external research organisations or units you plan to collaborate with, if known.

The research team that is developing GloBE-Reg is based at the The Office for Rare Conditions (www.officeforrareconditions.org) and is part of the University of Glasgow. It was launched in January 2017 and it has two broad groups of activities, those that are Glasgow facing and those that have a national and international direction. The international activities of the Office for Rare Conditions are overseen by Professor Faisal Ahmed who was appointed to the Samson Gemmell Chair of Child Health at the University of Glasgow in 2012. In addition, he was appointed as Professor of Endocrine Registries at the University of Leiden in 2019. Amongst the international activities, the Office for Rare Conditions has a strong track record in developing web-based registries. Its first international registry was the Euro-DSD Registry launched in 2008 and this was succeeded by the I-DSD Registry in

2011 and joined by I-CAH in 2014 and I-TS in 2021. In addition, the Office has developed registries that support European Reference Networks, Endo-ERN and ERN-BOND through registry projects, EuRRECa which was launched in 2018 and EuRR-Bone, launched in 2020. The development of these registries has also allowed the Office to develop guidance for core outcomes, patient friendly practice, data governance and quality improvement for existing endocrine registries. Other members of the local team include project managers, project administrators, a database developer, clinical research fellow and a senior research fellow with statistical input. It is anticipated that a data steward with overall responsibility for data quality will be appointed over the next year. The project is supported by the legal and contracts team as well as IT services at the University of Glasgow. The Project Management Group is overseen by the GloBE-Reg Steering Committee as explained further in the supporting documents.

18. Will any types of research or research organisation be excluded from receiving data?

Yes No

19. What arrangements will be made to consider applications from researchers for access to the data? How will decisions on access be made and who will be involved? Include details of arrangements for ensuring adequate scientific critique of research proposals.

The procedure for obtaining data will be transparent and posted on the GloBE-Reg website and follow the same process as the other projects (I-DSD and EuRRECa). Searching the Registry for data at centres other than the user's own centre shall only be possible by the project management team. Depending on the amount of work involved data searches will incur a fee and researchers shall be advised to get in touch with the project management team for further information. This process has allowed the I-DSD project to share data widely with the majority of the projects leading to several peer-reviewed publications https://scholar.google.co.uk/citations?hl=en&user=K-9hmkwAAAAJ&view_op=list_works&sortby=pubdate. The Office for Rare Conditions in Glasgow can provide more extensive study support depending on the investigator's needs and this may include advice on study process and design, liaising with Registry users on behalf of the study investigators or developing study specific modules. Prospective investigators shall be advised to contact the office before embarking on, developing, or seeking funding for the study so that the costs of this proposed work can be clarified. The applicants shall complete a Data Request Form and a Data Sharing Agreement. The data fields that are collected in GloBE-Reg shall be included in a data dictionary that will be available on its website so that applicants will have full knowledge of the fields that the Registry collects. Once submitted all study documents shall be sent to the Data Access Committee for approval. Once approved, all participating centres shall be informed of the Data Request and asked whether they would like to contribute to the new study. The Data Access Committee shall include members of the Project Management Group, the Steering Committee and the Scientific Study Groups. They will have a fixed tenure and declare all conflicts of interest. All approved requests shall be posted on the GloBE-Reg website as active projects and annual study reports will be requested from all investigators for the Data Access Committee. If a new application for data is similar to an active study or to another application, the investigators shall be asked to explore the overlaps and collaborate with each other.

20. Please give details of how the data will be effectively anonymised or pseudonymised to protect the confidentiality of subjects. What measures will you take to prevent possible re-identification by linking to other databases?

The data held in the GloBE-Reg Registry will be pseudoanonymised. The clinician entering the case data shall hold the NHS, CHI or Hospital ID number separately at their local centre. On completing the core dataset within the Registry, the clinician shall be provided with a unique registry number. The clinician shall store this registry number and the link to local case details (NHS,CHI number) in their local institution physically separate from the Registry. The Registry office will not be able re-identify the patient. The clinical user will have strict instructions not to enter personally identifiable data (except for Date of Birth, Date of Death, Gender and Health Care Provider) in any section of the Registry. Access to 'the patient space' in the Registry will require the email of the patient or the patient's carer. This will be an optional exercise which the patient will need to choose on the consent form.

21. What conditions will apply to the sharing of data with researchers? Please summarise the terms of any data access or data sharing agreement and say how these will be monitored and enforced.

All prospective researchers will be asked to provide details of the proposed project including the need for funding, dissemination, patient and public involvement, clinical impact, publication policy at outset with specific timelines. They will also be asked to complete a data sharing agreement. They will be informed of the conditions of ethics approval of the data and instructed that any information or biomaterials that the investigators intend to collect which is over and above the information that is routinely collected as part of normal clinical care will require further ethics review. Approved researchers will be provided the data that they are seeking by the Project Management Group and contact with clinicians will be initiated by the Project Management Group. Progress reports will be required at 12 monthly

intervals. Those investigators that do not provide progress reports will not be eligible to apply for further data requests. Further details of the Data Sharing Agreement as well as the Data Request form that have been used for other registry projects are available at <https://home.i-dsd.org/procedure-for-obtaining-registry-data-for-research/> These procedures shall be replicated for GloBE-Reg.

22. Is it possible that the research could produce findings of direct clinical significance for individuals? (This may include relatives as well as data subjects.)

It is possible that patient centred outcome measures collected on individual patients may have some direct clinical significance. These data will be deposited in the individual's own web space and can be accessed by the patient. There will be clear guidance in this section that these data need to be discussed by the individual with their clinician. The clinician will receive a notification when a patient has completed an outcome and the clinician's dashboard will show when an outcome has been completed. This approach has been adopted in other registries including EuRRECa and from personal experience in the clinical setting, these features have strengthened the patient-doctor relationship and increased the patient's interest in their own condition.

23. Where research data is of direct clinical significance for individuals, will arrangements be made to notify the individuals concerned?

Yes No

If No, please justify. If Yes, say what arrangements will be made and give details of the support or counselling service.
As discussed above, the data that will be collected as patient reported outcomes will reflect clinical care and will be discussed at the clinic that the individual attends. In addition aggregate data shall be posted on GloBE-Reg website when the data are analysed and disseminated as study outputs. However, centre specific and patient specific data shall not be publicly available.

24. Will data be released to individuals/organisations conducting research outside the UK?

Yes No

If Yes, please give details and describe any additional safeguards you will put in place:
The data will be provided to all researchers approved by the Data Access Committee. The information sheet will clarify this and explicitly state that the data can be shared with any researcher. We have used this approach over the last decade and a half and over 90% of the participants have allowed for the data to be accessed by any approved researchers in the world. This is very important in the field of rare conditions where the research may be performed at a site very far away from the patient. In addition, meaningful data from aggregates may only be possible when data are shared across international geographical boundaries. The Data Sharing Agreement that has been developed with the help of the legal team at the University of Glasgow can be adapted for the purpose of the Office for Rare Conditions acting as a data processor (when receiving data from a centre) or data controller (when providing data to a researcher).

25. What policies will apply to further storage and use of data by researchers when studies are complete? What mechanisms will be in place for approving further studies?

All cases will have a record of what Registry data have been used for which study. New researchers will be provided specific case's data which have been used. A new researcher who proposes a study which overlaps with an active study will be put into contact with the other researchers. Researchers will be encouraged to consider new studies on the data that will be stored in the Registry. As long-term outcome as a critical aspect of this Registry, it is proposed that the data shall be stored for a period of 30 years but an approval will be sought every 5 years.

Data collection and informed consent arrangements

Question 26 applies to existing collections of data only.

26. Has informed consent already been given to use the data for research?

Yes No Not applicable

If Yes, please describe what arrangements were made to seek informed consent and for what purposes. A copy of the information sheet and consent form should be enclosed. Confirm that the consent covers the uses of personal data now proposed by the Research Database team.

If No, or if existing consent does not cover the purposes now proposed, say whether consent will now be sought. Please include details of the arrangements for seeking consent in your answer to questions 28 - 30. If consent will not be sought, please justify.

Informed consent will be obtained from each patient (or their legal carer) who is entered into the registry. See questions 28-30.

Question 27 relates to identification of the data cohort. It applies to all new data collection from patients, service users or health records.

27-1. How and by whom will records be identified?

Patient identifiable records will be kept separately in the local hospital records by the clinician who is entering the data. The pseudoanonymized data will be accessible to the clinician and the patient as well as the coordinating centre.

27-2. Will this involve reviewing or screening identifiable personal information of potential data subjects?

Yes No

27-3. Please give details of how identification will be carried out and what resources will be used?

The clinician and their team who are responsible for entering the data shall have access to the locally held NHS/CHI/Hospital number and shall be able to link these to the unique Registry ID. This clinician and their team will identify cases locally, obtain consent and enter data into the Registry.

27-4. Will individuals other than the direct healthcare team have access to identifiable personal information of potential data subjects for this purpose?

Yes No

Questions 28 - 30 apply in all cases except where the application relates to an existing data collection and consent has already been obtained.

28. How and by whom will data subjects first be approached? Indicate whether this will be in the course of healthcare provision or whether additional procedures will be involved. In the case of additional procedures, what burdens could arise for participants?

Data subjects will first be approached as part of routine healthcare.

29-1. Will you obtain informed consent from or on behalf of data subjects?

Yes No

If you will be obtaining consent from adult data subjects, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

If you will not be obtaining informed consent, please complete question 29-3.

To obtain consent and for providing information about the Registry, the clinician or their respective team shall approach the patients and their legal guardians, if applicable, at the routine hospital visit. Alternatively, the clinician or the team can also provide information and obtain consent remotely by means such as tele or video consultation. An electronic copy of the signed consent form will need to be sent to the clinician's centre for local records and for the purpose of

auditing.

For the purpose of quality assurance, 10% of cases (or a minimum of one case) under the care of any one reporting clinician at any participating centre shall be audited each year. The exercise shall be performed remotely by uploading source documents into the registry where all the personal identifiers have been redacted. In the case of a new case that has been entered, the quality assurance exercise shall also include a check of the informed consent form. This check will not be performed by uploading the ICF document into the Registry but will simply be checked through a remote un-recorded video appointment between the Project office and the clinician. In those cases, where the patient has already activated their access to the patient section of the Registry, this video appointment shall not be performed.

Please enclose a copy of the information sheet(s) and consent form(s).

29-2. Will you record informed consent in writing?

Yes No Not applicable

30-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information in English, or who have special communication needs? (e.g. translations, use of interpreters)

Information sheets will be created in as many languages as possible. This has been a standard policy in the international registry related projects led by the applicant. Furthermore, the patient user interface in the Registry shall be able to be customised by the patient for their preferred language. This has been achieved in the EuRRECa project. Furthermore, for some regions, such as China, the clinician, it is anticipated that the clinician interface may also be customised for a local language.

30-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to data subjects in Wales?

As the Registry becomes more widely adopted throughout the UK including Wales, there will need to be an appraisal of its use across the UK and how its use can be further extended. The development of information sheets in Welsh and other minority languages in the UK as well as other parts of the world remains an important consideration for this international registry.

Questions 31 - 32 apply to all applications:

31. Will any financial or other incentives be offered to data subjects?

No

32. What steps will be taken where data subjects subsequently withdraw consent to the use of their data? What information will data subjects be given about this?

The information sheet will clearly state that the data can be removed by the data subjects or their legal guardians. In addition, the Registry will develop a patient dashboard which patients will have access to and within which they can alter their settings and notify their clinician that they would like to delete their data.

Summary of the application

33. Please provide a brief summary of the application in a form suitable for publication, using language easily understood by patients and public. The summary will be published on the website of the National Research Ethics Service following the ethical review. You may cut and paste from answers to other questions.

Title of the database: Global Registry For Novel Therapies In Rare Bone & Endocrine Conditions

Establishment responsible for management of the database:

Organisation The University of Glasgow

Address	IT Services Sir James Black Building
Postcode	G12 8QQ
Telephone	01413302813
Fax	

Data to be stored and data collection arrangements (maximum 200 words): All data shall be stored on secure servers in the University of Glasgow and will be kept strictly confidential and all information will be handled through very secure electronic systems. The Registry users will not be able to make contact any patient because the name, address and hospital number will not be recorded. Only the hospital doctor and their team will be able to contact the patient as they can link the data in the Registry to the hospital records. To access the data from the Registry, investigators will need to apply to the Data Access Committee and once the application has been approved, the data shall be provided to the investigators with strict data sharing agreement. The provision of data will also occur through secure electronic systems rather than just by email. Again, the data that are provided will not contain any information that can allow the investigator to link the information to the actual patient. A progress report will be obtained every year to understand the research progress of the investigators.

Research programme/community supported by the database (maximum 200 words): GloBE-Reg has been developed with the needs of people with rare endocrine conditions who are starting on new therapies in mind. The initial focus is on children and especially a group of children who are starting on a drug called growth hormone (GH). There are currently no international registries for children starting GH therapy that are independent of industry. The registries that exist are limited to one region, or limited for specific conditions or run by individual companies. GloBE-Reg intends to develop one single registry for all children receiving GH. This approach has been welcomed by patients, doctors, industry as well as the regulators who monitor the use of these drugs. However, if the registry works well, then the platform can be used for other endocrine therapies in children as well as adults.

PART B: Section 7 - Children**1. Please specify the potential age range of children under 16 who will be included and give reasons for carrying out the research in this age group.**

Children from the age of birth onwards will be eligible to be included in the Registry. Given that a large proportion of rare endocrine conditions present in childhood and their therapy is started in childhood, there is a considerable focus on this research in children, their management and their long-term outcome.

2. Indicate whether any children under 16 will be recruited as controls and give further details.

No. The Registry will only recruit children who are starting therapy for a wide range of rare conditions. In time, it is anticipated that children on different forms of therapy may start to act as a control' group for another group of children but they are more likely to be considered to be a comparator group rather than a control group.

3-2. Please describe the arrangements for seeking informed consent from a person with parental responsibility and/or from children able to give consent for themselves.

Consent shall be obtained from the person with parental responsibility. Whilst it is appreciated that many children under the age of 16 yrs can provide consent for themselves, it is possible that a number of children are not under regular followup from late childhood. Leaving it to the clinicians to ensure whether a child is mentally ready to provide consent was considered to be logistically difficult, especially as this project will cover several centres across the world. We have, therefore, opted for a blanket approach of covering every young person at a standard age of 16 yrs. The reading age of the information sheet has been kept low enough for older children above 14 to be able to understand the document and it can therefore, be used for a child presenting for the first time around that age. Within the electronic registry a system shall be developed for sending a reminder to the clinician to obtain consent from a young person over 16 whose information was entered before the age of 14. We have used this process effectively in the I-DSD and EuRECa registries.

4. If you intend to provide children under 16 with information about the research and seek their consent or agreement, please outline how this process will vary according to their age and level of understanding.

Children under the age of 16 years and their parents shall be provided with the single information sheet. An additional sheet has been developed for the child between the ages of 8 and 14 years, as attached.

Copies of written information sheet(s) for parents and children, consent/assent form(s) and any other explanatory material should be enclosed with the application.

Part C: Data Collection Centres

Please enter details of the organisations (NHS or other) in the UK that will act as data collection centres for this research database.

Data collection centre	Local collaborator
Greater Glasgow & Clyde NHS Board	Dr M Guftar Shaikh
Greater Glasgow & Clyde NHS Board	Dr S Ching Chen

Part D: Declarations**D1. Declaration by the applicant:**

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. If the application is approved I undertake to adhere to the terms of the application of which the REC has given a favourable opinion and any conditions set out by the REC in giving its opinion.
3. I undertake to seek an ethical opinion before implementing substantial amendments to the terms of the application of which the REC has given a favourable opinion.
4. I undertake to submit annual progress reports to the REC.
5. I understand that the information contained in this application, any supporting documentation and all correspondence with NHS Research Ethics Committees or their operational managers relating to the application:
 - ◊ Will be held by the main REC indefinitely (or until 3 years after the closure of the Database).
 - ◊ May be disclosed to the operational managers or the appointing body for the REC in order to check that the application has been processed correctly or to investigate any complaint.
 - ◊ May be seen by auditors appointed by the National Research Ethics Service to undertake accreditation of the REC.
 - ◊ Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
 - ◊ May be sent by email to REC members.
6. I understand that a summary of this application will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication

NRES would like to include a contact point with the published summary of the application for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- Applicant named at A3
 Other – please give details
 None

Optional – please tick as appropriate:

I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to the establishment and other research units and collaborators would be removed.

This section was signed electronically by Professor SF Ahmed on 09/05/2022 12:52.

Job Title/Post:

Organisation:

Email:

Part D: Declarations**D2. Declaration by Data Custodian**

1. I confirm that the information in this application is accurate to the best of my knowledge and belief and I approve the application.
2. I confirm that the establishment has Data Protection Registration appropriate to the purposes described in this application.
3. I confirm that the establishment has an appropriate System Level Security Policy in place for the systems used by the Database.
4. If the application is approved, I confirm that I will take responsibility for ensuring that the arrangements described in the application are adhered to and any agreed conditions of ethical approval are complied with.

This section was signed electronically by Mr Paul McLaughlin on 09/05/2022 16:06.

Job Title/Post: IT Manager
Organisation: University of Glasgow
Email: paul.mclaughlin@glasgow.ac.uk