the FULL/LONG TITLE OF THE STUDY

An integrated clinical research platform and 'next generation registry' in patients with Interstitial Lung Disease

SHORT STUDY TITLE / ACRONYM

AccessILD: A Next Generation Registry in Interstitial Lung Disease

PROTOCOL VERSION NUMBER AND DATE

Version: 2.0

Date:10th October 2023

SPONSORS:	Cohort Science Ltd
FUNDERS:	Cohort Science Ltd

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the chief investigator agrees to conduct the study in accordance with the current Good Clinical Practice (GCP) regulations and in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, 21 Code of Federal Regulations (CFR) Parts 11, 50, 54, and 56, the Sponsor's standard operating procedures and other regulatory requirements. Any changes in procedure will only be made if necessary to eliminate immediate hazards and/or to protect the safety, rights, or welfare of participants.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest, accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

I agree to keep records on all subject information collected during the study in accordance with the current GCP, local and national regulations.

For and on behalf of the Study Sponsor:

Signature: Date:
..../...../.....

Name (please print): Anil S Jina, MD

Position: Secretary, Cohort Science Ltd

Chief Investigator:

Signature: Date:
..../...../.....

Name (please print): Timothy Dempsey, MD

Position: Pulmonary & Critical Care Specialist,
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DOCUMENT HISTORY

Document	Date of Issue	Summary of Change
AccessILD protocol	22.08.2023	Initial version 1.0
AccessILD protocol	10.10.2023	Protocol version 2.0

LIST of CONTENTS

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REGISTRY SUMMARY

Registry Title	An integrated clinical research platform and 'next generation registry' in patients with Interstitial Lung Disease
Internal ref. no. (or short title)	AccessILD: A Next Generation Registry in Interstitial Lung Disease
Study Design	Remote, longitudinal, observational study @cohort.science Research database and registry Integrated clinical research platform
Study Participants	Patients with a diagnosis of Interstitial Lung Disease coded in health records.
Planned Size of Sample	No upper limit Target in year 1: up to 500 participants
Follow up duration	20 years
Planned Study Period	20 years
Research Question/Aim(s)	1) To build a registry of participants with a diagnosis of Interstitial Lung Disease to access new research opportunities. 2) To create a core clinical dataset including questionnaire data, genetic and other linked clinical data.

FUNDING AND SUPPORT IN-KIND

FUNDER(S)	**FINANCIAL AND NON-FINANCIAL SUPPORT GIVEN**
Cohort Science Ltd 8 Warner Yard, London, EC1R 5EY Email: info@cohort.science Phone: +44 (0) 2033 030329	Sole funder of registry

LIST OF ABBREVIATIONS

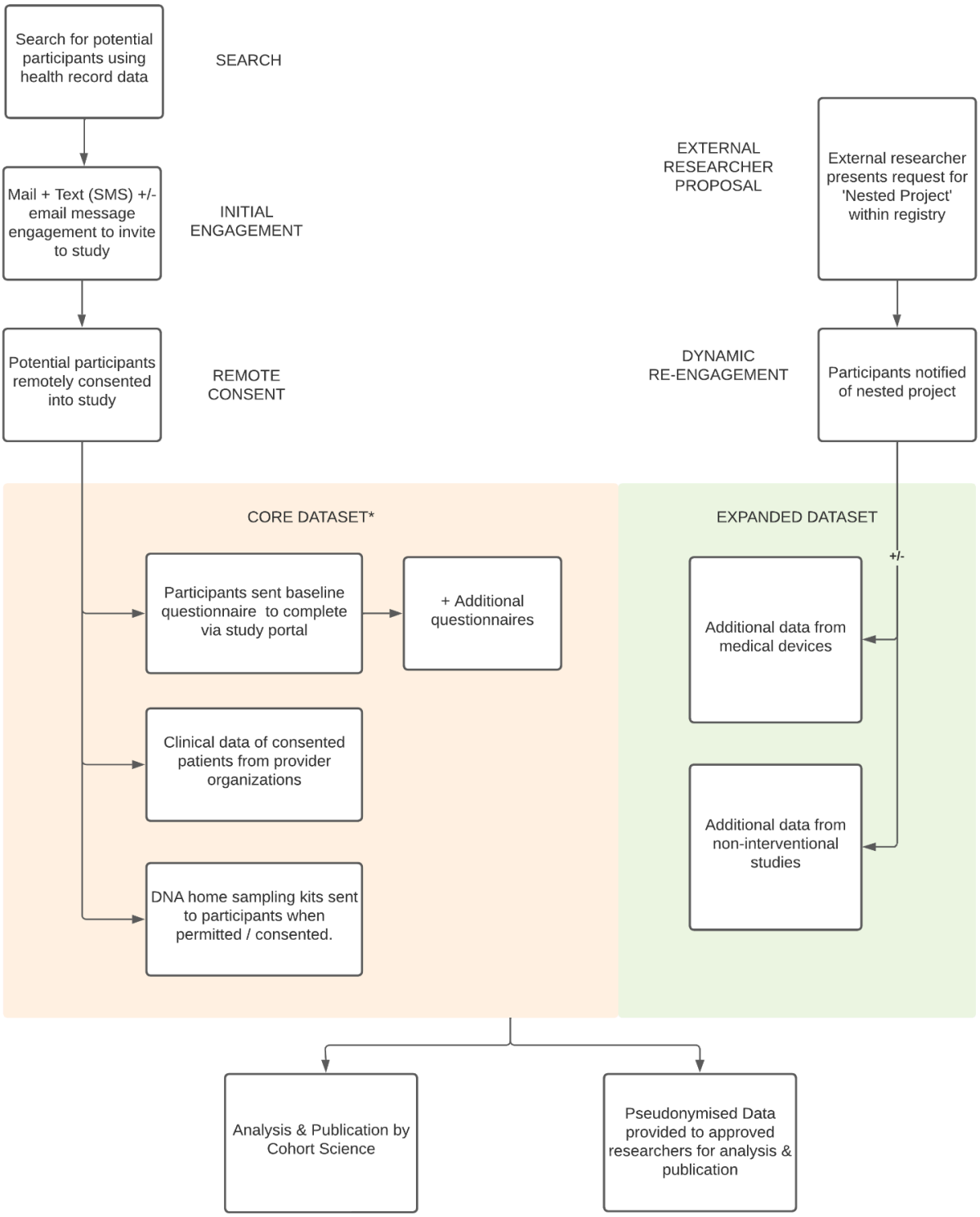
Table 1. List of abbreviations and definition of terms

Abbreviation	Definition
CCD	Core Clinical Data
GCLP	Good Clinical Laboratory Practice
CS	Cohort Science
DPA	Data Processing Agreement
DSA	Data Sharing Agreement
EHR	Electronic Health Record
FAQ	Frequently Asked Questions
GCP	Good Clinical Practice
GP	General Practitioner (or GP Practice)
HCP	Healthcare Providers (GP, GP Practice or Group of Practices)
ICF	Informed Consent Form
ICH	International Council on Harmonisation
IPF	Idiopathic Pulmonary Fibrosis
NHS	National Health Service
PCP	Primary Care Physician
ILD	Interstitial Lung Disease
CI	Chief Investigator
PF	Pulmonary Fibrosis
PPI	Patient and Public Involvement
PRO	Patient Reported Outcome
REC	Research Ethics Committee
SOP	Standard Operating Procedure

KEY WORDS

Pulmonary Fibrosis, Interstitial Lung Disease, registry, research database, tissue bank, observational studies, clinical trials, medical devices

REGISTRY FLOW CHART (Figure 1)



REGISTRY PROTOCOL

An integrated clinical research platform and 'next generation registry' in patients with an Interstitial Lung Disease

1. BACKGROUND

Interstitial lung diseases (ILD) comprise a group of heterogeneous respiratory diseases that lead to damage of the lung tissue [1]. Due to difficulties in diagnosing and treating the diseases, as well as the vast range of subtypes covered under this umbrella term, there is limited epidemiological data available that describe the global prevalence and incidence of the diseases. Kaul et al reported an incidence of ILD ranged from 1 to 31.5 per 100,000 person-years and a prevalence ranged from 6.3 to 71 per 100,000 people in a recent systematic review [2]. Among the subtypes, idiopathic pulmonary fibrosis (IPF) is considered the most common and archetypal form of ILD, especially in Europe and North America where the incidence is estimated to range between 2.8 and 18 cases per 100,000 people per year [2], [3]. Much of our current knowledge on ILD is based on studies of patients with IPF.

Immunomodulatory treatment options are available for ILDs other than IPF due to their inflammatory component. However, since the subtypes differ in their presentations and pathogenesis, there is no single guideline for the treatment of all ILDs [4]. In 2014, the anti-fibrotic drugs pirfenidone and nintedanib were approved for use in the United States for patients with IPF given trials showing their ability to slow the decline in lung function for patients with IPF compared to placebo [5], [6]. Despite literature continuing to support the effectiveness of the antifibrotics for both IPF and other forms of fibrotic lung disease, additional therapeutics with superior efficacy, improved tolerability, and reduced cost are desperately needed for patients with pulmonary fibrosis [7], [8]. Additionally, there remain unmet needs in early diagnosis of the diseases, stratification of patients into appropriate subtypes and development of other effective treatments tailored to the individual and their specific ILD type [9].

While randomised control trials remain the gold standard for evaluation of the efficacy for treatments, designing trials for rare, deadly diseases like IPF and other ILDs have proven challenging. Attempts to improve our understanding of different ILDs through disease registries have been made and many seem promising. However, many of the current ILD and/or pulmonary fibrosis registries are only available through large tertiary care centres in the US or do not include all subgroups of ILD, thus limiting their generalizability across different demographics and impacting their ability to gather data on the rarer disease types [10].

2. RATIONALE

The main aim of this project is to develop a 'next generation registry' (a longitudinal, observational, fully remote study utilising technology to collect both electronic clinical records and patient-reported outcomes) for participants with ILD. The fully remote and observational study will be used to build a cohort of participants with ILD for longitudinal study of that population. This cohort can also be involved in further research opportunities with additional consent, including (medical) device studies and clinical trials of investigational or approved medicinal products. Through consultation with patients and patient organisations, we recognise the limitations of the current methods of recruitment to clinical research studies. These limitations lead to selection bias and inadequate generalisability of data, as well as poor practice around consent and data handling. Through AccessILD, participants with a

diagnosis of ILD will be approached remotely and invited to consent to join a ILD-specific research registry. This approach has the following advantages:

a) **Fairness** – By directly approaching patients on behalf of their recognized provider, AccessILD will seek to include all patients with an ILD diagnosis, not just those who are treated by research-driven respiratory physicians or those being seen at tertiary academic medical centres. The uMed platform can also target and customise outreach to minority populations, ensuring that the study dataset better reflects the overall population of ILD patients.

b) **Efficiency and cost** – by identifying potential participants via clinical records, a huge volume of data can be used to select participants for studies with precision and populate research databases, reducing the 'human' effort and costs that are currently required (either by the participant or researcher). Participation accruals will become automated and research data shared across studies (with express consent) so that questionnaires and demographic information does not need to be completed repeatedly if participants are taking part in multiple studies.

c) **Scale** – the registry will recruit prospectively and remotely, enabling more patients to register over time and for the size of the resource to grow. As the process of identification, engagement and consent into AccessILD is automated and utilising remote technology on behalf of participating GPs, the rate of recruitment can be substantially increased in comparison to other observational studies.

d) **Control** – participants will be given full control over how their data is used and the studies in which they wish to participate.

3. THEORETICAL FRAMEWORK

Healthcare providers and other bodies face significant practical, legal and ethical challenges when leveraging patient data assets for direct patient care, as well as secondary use for research. A key unmet need is the facility to allow third parties (e.g., research teams) other than a patient's regular healthcare provider to target, engage and monitor specific sub-groups of patients without burdening clinical staff.

The uMed platform acts on behalf of the patient's healthcare provider to automate the process of conveying engagements to specific patient groups, and collating data for third parties, but ONLY when appropriate authority has been sought and obtained from the patient's healthcare provider and – where necessary – the individual patient.

The current model of participant recruitment is through the type of healthcare organisations with which Umedeor has partnered. Recruitment therefore depends on clinician willingness to have their patients involved in research (bias at the clinician level) and finite site selection due to resource limitation (a further source of bias). By engaging patients directly, much of this bias is removed and the result is improved access to research opportunities in an equitable manner.

Recognising the need for transparency and accountability, Umedeor created a subsidiary company (Cohort Science Ltd) to act as the registry sponsor and funder for AccessILD. This allows clear separation of the responsibilities and data within the registry workflow.

Umedeor Ltd is a research enabler and service provider to healthcare providers/organisations within the Umedeor network, using the uMed technology platform. Umedeor has access to participant identifiable data through a data processing agreement (DPA) with Healthcare Providers.

Cohort Science (CS) is the registry sponsor and manager of the registry and associated datasets. CS manages the registry dataset and has access only to the data provided by participants that have consented to join AccessILD. CS will provide services to facilitate access and analysis of registry data for external researchers.

AccessILD leverages the uMed technology platform to support the targeted engagement of potential research participants on behalf of the Healthcare Provider (HCP).

Cohort Science (sponsor and data controller) will engage with Umedeor (data processor) through a signed services agreement. Umedeor also acts as a data processor for HCPs, that are in turn data controllers for data held at their practices.

A Research Tissue Bank Participation Agreement between the HCP and Umedeor, will enable the contact with specific groups of patients based on searches of the medical record data held by their HCP (see Appendix 2).

The uMed platform has been successfully used in a range of different studies to support recruitment and remote consent of participants on behalf of HCP's. Through this model, AccessILD will be able to overcome some of the key challenges that are usually associated with conducting a large-scale observational research program, without compromising well- established registry governance, as well as maintaining the highest standards for participant control over use of their data. AccessILD will serve as an example of how registries can be created at scale without placing burden on an already stretched healthcare delivery system. Simultaneously AccessILD will allow the research community to better understand the natural history of the disease and use the 'next generation registry' as a platform to rapidly re-engage participants in order to test new hypotheses and develop new therapies.

A summary of the data protection provisions and governance workflow for AccessILD can be found in **section 9.**

The intent of AccessILD is to create a 'next generation registry' that collects a core clinical set of data from consented patients (AccessILD Core Clinical Data [CCD]), consisting of clinical data from their Electronic Health Records (EHR) and relevant Patient Reported Outcomes (PRO) and other information obtained via questionnaires. Umedeor ensures patient identifiable information is always separated from health data via an encrypted layer which prevents complete patient records from being inappropriately accessed. Depending on the data sharing agreements between different parties, data will be shared either anonymised or pseudonymised (see Appendix 2).

It will also bring research opportunities to patients with which they can participate. Decisions regarding the ongoing conduct of the study, inclusion of new research opportunities ('nested projects'), data and participant access requests, manuscript writing and dissemination of results will be taken by the AccessILD Management Committee.

3.1. Open Access to the Core Clinical Data

The CCD will be made openly available to any academic researcher providing their credentials as a researcher and project proposals are approved by the AccessILD Management Committee. Access to

the registry dataset will not be unduly restricted and the AccessILD Management Committee must provide written response to any researcher who has been denied access, stating the reasons access has not been granted.

3.2. Nested Projects

Academic and commercial research teams may also submit proposals for ‘nested projects’ to the AccessILD Management Committee. A nested project is defined as a project that is undertaken with a researcher external to Cohort Science that requires the collection of additional data and/or samples from participants in line with the existing AccessILD protocol. Any nested project that is not covered by the existing AccessILD protocol, will require a submission of a ‘substantial amendment’ to the REC. Final decisions regarding the conduct of these nested projects will be made by the AccessILD Management Committee. Where participants are included in such a nested project, they will be proactively informed by text message and/or email about the nature of the project.

Depending on the type of nested project being undertaken this may require the participant to explicitly opt-out (Type A projects which utilise the existing pseudonymised dataset), opt-in (Type B projects which go beyond the existing pseudonymised dataset) or re-consent (Type C projects which require an amendment to the AccessILD protocol with subsequent REC approval). Further details of the governance model for different types of nested projects can be found in **Appendix 1**.

Any clinical trials or other interventional studies using participants identified through AccessILD will be conducted as standalone trials with separate protocols and will undertake independent ethics committee review prior to commencement.

Appendix 2: Schematic of stakeholders involved in AccessILD.

4. ROLES AND RESPONSIBILITIES

4.1. Study Sponsor

Cohort Science Ltd is the sole sponsor and funder of AccessILD.

4.2. Registry Management Committee

After initial setup, the AccessILD Management Committee will control the final decisions about the conduct of the registry, the inclusion of ‘nested projects’, data analysis and interpretation, manuscript writing and dissemination of results. Applications to view and/or process data from AccessILD will be made directly to the AccessILD Management Committee. Applications must state the reason for the request and the expected outcome(s) of data use. Applications will be reviewed and a decision communicated within 30 days. Reasonable requests for access will not usually be declined. Data will be shared in a GDPR compliant manner. Initially this will be an anonymised, password protected CSV file transferred via an SFTP secure download or secure access to the uMed platform. In time, we anticipate that data access will be through a dedicated analytics platform. Use of data will be governed by a data use agreement which will capture the purpose and duration of data use, and will be signed by the applicants.

The proposed members of the Management Committee are:

- Chief Investigator: Timothy M. Dempsey, MD, MPH
- Cohort Science: Anil S Jina, MB BCh
- Umedeor representative: Matt Wilson, MB BCh
- GP representative: Dr. Elango Vijaykumar, FRCGP
- Participant representative: TBD
- Industry representative: Dana Ball
- Clinical Site representative: TBD

4.3. Protocol Contributors

- Chief Investigator: Timothy M. Dempsey, MD, MPH
- Cohort Science Ltd

5. RESEARCH QUESTION/AIM(S)

The principal **aim** of this project is to develop a new platform for research (described throughout as a 'next generation registry' and called AccessILD), which will establish a core clinical dataset for ILD and help streamline widespread, equitable access to additional research opportunities for patients with ILD.

5.1. Objectives

a) To establish a new integrated clinical research platform/ 'next generation registry' for ILD.
b) To provide information, obtain consent and recruit patients to the AccessILD platform.
c) To collect a core clinical set of data from consented patients (AccessILD Core Clinical Data [CCD]), which would consist of clinical data from their EHR and relevant PRO's and other information obtained via questionnaires.
d) To link the platform to other 'nested projects' and offer these new opportunities to participants who are registered with AccessILD. Nested projects may require protocol amendments and/or additional REC approval.
e) To develop a notification system for clinicians about potential patient participation in additional research. Additional research may be conducted under separate protocols with separate REC approvals.

5.2. Outcome

The main outcome of this project is to build an engaged and active group of participants registered with the AccessILD platform, contributing to the AccessILD CCD, who are also exposed to a range of additional research opportunities, which will streamline progress in ILD research and drive better outcomes for patients.

6. REGISTRY DESIGN and METHODS of DATA COLLECTION and DATA ANALYSIS

Potential participants will be identified from EHR according to the participant inclusion and exclusion criteria outlined below (Section 8.1). The initial contact will be via short message service (SMS)/text sent by Umedeor on behalf of the patient's recognized healthcare provider (see figure 1), which will invite potential participants to view information about AccessILD in their smartphone or computer browser. Potential participants may also receive a letter sent by Umedeor as a precursor to receiving SMS communications about AccessILD. This letter would include the participant information leaflet (**Appendix 6**).

Information will be presented about the aims of the registry and steps required to participate, which include volunteering consent to enrol with the registry and expressing willingness to be approached for additional research opportunities.

AccessILD will invite participants to complete PRO's and other medical questionnaires to generate a set of core clinical data for research (AccessILD CCD).

A list of initial PRO's and questions is provided below. Additional PRO's and questionnaires which may be administered in the future will require protocol amendments and/or REC approval.

6.1. Clinical Assessment

All participants recruited will have the following information extracted from their EHR or answer questions to provide more details:

- Demographics (Age, sex, ethnic group, race, education (level/years))
- Comorbidities (including acid reflux)
- Vital signs (weight, height, blood pressure, heart rate, oxygen saturations)
- Current and previous medications
- Date of symptom onset and first symptom
- Specific ILD diagnosis
- Date of ILD diagnosis and setting (primary or secondary care)
- Name of ILD specialist and/or treatment centre
- Other personal medical history
- Family medical history (including genetic conditions)
- Social history (including occupation, diet, physical activity, smoking, alternative medicine, exposure to pesticides and insecticides, postcode, Townsend Score of social deprivation)
- Pulmonary function testing data
- CT chest and other imaging data
- Biopsy data (if applicable)
- Oxygen utilisation
- Six-minute walk test data
- Pulmonary rehabilitation attendanceQuestionnaires related to ILD, including patients' symptoms and treatment experiences of ILD and exposure to risk factors (see **Appendix 3**)

- Other ad-hoc questions related to experience of ILD, its treatment and participant reported outcomes
- Other outcome measures which will be included (see **Appendix 3**):
    - Mortality
    - Hospitalisation rate
    - Exacerbation rate
    - Progression of disease

It is anticipated that many of these data fields will be populated by record linkage. The maximum completion time for questionnaires administered at any one time is not expected to exceed 20 minutes.

Depending on the 'nested projects' that are linked to AccessILD, participants may be invited to complete additional scales and questionnaires. These may be self-reported or involve remote or in-person clinical assessment. A list of potential clinical scales is provided in **Appendix 3.**

After enrollment, participants may be invited to participate in additional research studies relating to ILD. These studies may be initiated by Umedeor, their academic partners, or independent academic and/or commercial entities. Participants will retain full control over their participation and how their data is used. Additional research will be conducted under a protocol amendment (or a separate protocol) and REC approval, if it is not covered in this protocol.

Examples of additional research opportunities include:

1) **Longitudinal or cross-sectional observational studies** (nested projects)

- Questionnaires about ILD status administered periodically
- Questionnaires about ILD risk factors
- Objective tests such as pulmonary function testing, CT chest imaging, and biopsy results (as applicable)
- Virtual or in-person clinical assessments

2) **Medical device studies** – medical devices for measuring symptoms of ILD or providing treatment.

3) **Clinical trials** of approved or investigational medicinal products (using a traditional or decentralised model).

4) **DNA collection and analysis**

Participants may be invited to submit a saliva or blood sample for DNA extraction and analysis. An at-home saliva sample collection kit will be dispatched in the mail to participants that consent to saliva collection and returned to a central lab for DNA extraction and storage. Blood

samples would be taken at a participant's healthcare centre and analysed by an accredited laboratory with relevant licences (e.g HTA licence where required).

Analysis (genotyping and/or sequencing) will take place at an approved laboratory (UK or international) that meets GDPR requirements. Saliva is covered by the Human Tissue Act 2004 (HTA) but DNA falls outside the remit of the HTA and can be shared with explicit consent and when GDPR requirements are met. DNA may be shared with approved collaborators (academic and commercial), in the UK or outside the UK (worldwide) to further understanding of ILD. Genotyping and/or sequencing data and clinical data may be shared in aggregated or de-aggregated forms, with approved collaborators (academic and commercial), in the UK or outside the UK (worldwide) to further understanding of ILD. Researchers receiving samples and/or data must have a written usage agreement. Samples will be stored for as long as deemed useful for research purposes.

7. REGISTRY SETTING

Most engagement with participants will happen remotely and online. The initial approach will be made by an SMS message sent by Umedeor on behalf of the patient's GP (+/- written material sent via mail), after identifying patients with a diagnosis of ILD from clinical records. Registration, information provision, consent to participate and research activities will all be managed and accessed via the online AccessILD portal.

8. SAMPLE AND RECRUITMENT

8.1. Eligibility Criteria

8.1.1. Inclusion criteria

A principal goal of this project is to establish a core clinical dataset for ILD and to improve representativeness in ILD research. Hence the inclusion criteria are:

- All individuals with a coded diagnosis of ILD (see **Appendix 4**).
- Aged ≥18 years old.
- Identified through a HCP participating in AccessILD in the United Kingdom.
- Able to provide consent to participate.

8.1.2. Exclusion criteria

- Patients who have recorded a preference in their medical record that they do not wish to be considered for research or contacted regarding research opportunities.
- Patients who have recorded a preference not to share data for research.

8.2. Sampling

The uMed platform has already been employed in the UK through agreements with the United Kingdom National Health Service (NHS). Through its network of agreements with NHS primary care providers in the UK, Umedeor currently has access to approximately 5 million patients' EHR.
Based on initial modelling of available patients in the Umedeor network (as of July 2023) in the UK, there were 2272 patients with ILD in a population of 3 million (patients over the age of 20, alive and still registered at their GP practices) based on a coded diagnosis of ILD alone. This number increases to 2371 if the case definition incorporates a coded diagnosis of ILD OR an approved anti-fibrotic drug for the treatment of ILD **(Appendix 4)**.

8.2.1. Size of sample

Due to the aim of the project (e.g. to develop a new platform for research, establish a CCD for ILD and help facilitate access to research opportunities for patients with ILD, whilst improving equitability), the sample size will be as high as possible and is not based on statistical power calculations. Recruitment is currently planned in the US and the UK and Canada, with an overall goal to enrol up to 10,000 individuals with ILD between these countries. Separate Ethics Committee approval will be obtained from each country as per local regulations.

8.2.2. Sampling technique

As above, the aim is to offer participation to all patients with a diagnosis of ILD identified through a healthcare provider participating in AccessILD within the Umedeor network in the United Kingdom.

8.3. Recruitment

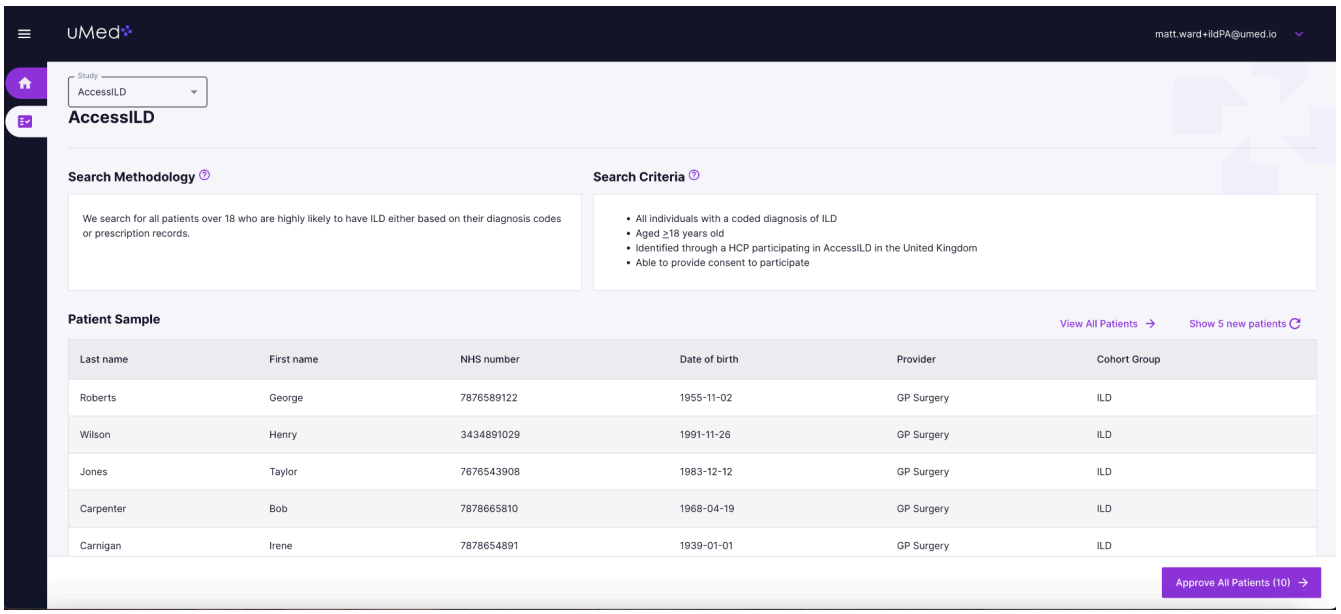
Potential participants will be identified from EHR at GP practices with whom Umedeor have a partnership agreement, based on the inclusion and exclusion criteria above.

8.3.1. Sample identification

This will involve the following steps:

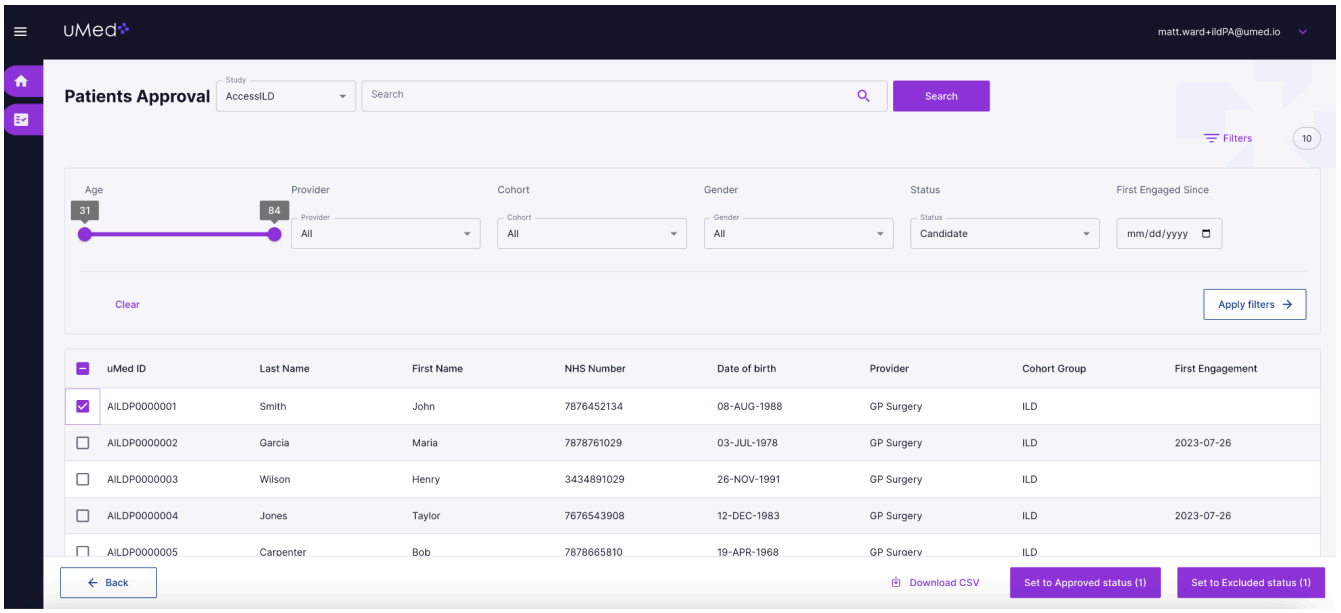
a) A search will be undertaken to identify potential participants using clinical data from the EHR of HCP's who have agreed to participate in the Umedeor network. This search of clinical data will identify potential participants in line with the inclusion /exclusion described above.
b) When potential participants have been identified, HCP's will be notified via the uMed platform and presented with all relevant information about AccessILD (illustrative example of HCP user interface provided below in Figure 3).

Figure 3: HCP User Interface Example



c) HCP's will be able to sign clinical registry agreements and supporting registry documentation via the user interface using integration with DocuSign.

d) Once onboarded, HCP's will be able to review the list of potential participants identified via the clinical data search and exclude any patients they believe should not be contacted for the registry.



e) Once approved by their HCP, potential participants will be automatically contacted via mail, SMS, and/or email and provided a participant specific link to sign up for AccessILD. The consent questions can be found in **Appendix 8A**, and the full participant onboarding workflow can be found in Appendix 8B.

8.3.2. Consent

In accordance with relevant regulations, an informed consent agreement explaining the procedures and requirements of the study, details on how individuals' confidentiality will be maintained, and potential hazards/risks, will be presented to potential participants. Potential participants will be shown a short video along with a clickable participant information leaflet, a list of frequently asked questions (FAQs) and contact details (email, web-form) in case of questions. They will then view the consent form which includes a list of statements, including a request for consent to linkage of data to GP records and relevant datasets held by NHS England (e.g. HES). They will select the statements that they agree to and submit these.

After consenting, consented participants will be able to complete the core clinical data questionnaires outlined above and view other research opportunities, including reading relevant registry information and, if interested, participate in those studies.

The precedent of gathering web-based consent alongside provision of information is well established. Capacity in clinical settings is decision-specific and assumed unless there is evidence to the contrary. It is unlikely that ILD patients with loss of capacity to participate in research would be actively responding to SMS messages inviting enrolment in a registry. However, the nature of data being collected and the non-invasiveness of the research undertaken in AccessILD mean that there is minimal risk posed to participants

9. ETHICAL AND REGULATORY CONSIDERATIONS

The Health Research Authority has a UK Policy Framework for Health and Social Care Research. The Policy Framework begins with an outline of the aspects that contribute to delivering research of the highest quality and to which the HRA is committed. Selected examples are listed below, along with a description of how the Access-ILD project has taken these into consideration.

Regulatory/ethical consideration	**AccessILD**
Patients, service users and the public are given, and take, the opportunity to participate in health and social care research and to get involved in design, management, conduct & dissemination.	Patients, patient representatives and patient advocacy groups will be involved in the project design, scoping and priority setting. A PPI group is planned before commencement of AccessILD and will continue to advise as the project progresses.
Safer, more efficient or more effective treatments, care and other services are developed and tested through ethical and	AccessILD will enhance access for patients to research opportunities and the ILD research community to a unique dataset that combines

scientifically sound research for the benefit of patients, service users and the public.	clinical data, participant reported data and biosamples. Together this will drive better understanding of aetiology, manifestation, progression and potential therapeutic targets, as well as efficient recruitment for clinical trials.
Ensure that study populations better reflect the patient populations who could ultimately benefit from the research in clinical practice.	AccessILD will enhance access for patients to research opportunities, and make it easier for researchers to reach out to underserved populations. The use of clinical data also promotes more efficient recruitment of a diverse population and supports identification of participants for whom traditional referral centres are not accessible.
Researchers find it straightforward to do high-quality, ethical research.	AccessILD will dramatically improve efficiency when it comes to identifying eligible participants for research and offering the opportunity to participants in a highly equitable manner.
Industry sees the UK as a great place to do health and social care research, and increases its investment for the benefit of patients and service users.	Industry-led and academic-led research projects will be offered in the platform, increasing efficiency and breadth of opportunities, with increasing investment from those stakeholders.
Money from foundations and other research funders goes into carrying out research, not into navigating burdensome bureaucracy or duplicating previous work.	The AccessILD model creates a platform which allows an ever growing dataset to be created and accessed by researchers. In doing so this dramatically reduces the cost and burden associated with creating bespoke programs that still remain the status quo.
Research projects get registered, the data and biosamples they collect can be made available for future analysis, with adequate consent and privacy safeguards, and research findings get published and summarised for those who took part in them.	AccessILD is committed to an open science framework and sets a new standard for privacy safeguards by ensuring a broad based consent for secondary use of registry data is balanced through proactive engagement (and the ability to opt out) of specific secondary use projects. The platform also enables efficient sharing of publications and research summaries with participants.

9.1. Assessment and management of risk

Potential risks that have been identified:

Risk	**Describe source of risk and nature of potential impact on individuals.** Include associated compliance and corporate risks as necessary.	Likelihood of harm	Severity of harm	Overall risk
1	Malicious action by an external party to access sensitive pseudonymised health data from the registry system.	Low	Significant	2
2	Malicious action by an external party to access personal data from the registry system.	Low	Major	3
3	Malicious action by an external party to access identifiable sensitive data from the registry system.	Low	Major	3
4	Malicious action by Umedeor employee to access, alter or exploit data held on the registry system.	Low	Major	3
5	Patients receive unwanted solicitation to engage in research.	Medium	Low	2
6	A participant's health data is shared with a third party organisation by a *Member* using the registry system against their expectations or wishes.	Medium	Significant	2
7	A participant is misidentified in communications leading to preferences and/or responses being associated with another record.	Medium	Significant	2
8	A third party research group (e.g. Pharmaceutical company) who access sensitive data via the registry system utilise this data for purposes beyond those stated in the data sharing agreement.	Low	Major	3
9	Participant preferences listed in registry conflict with those held by the participant's healthcare provider.	Medium	Significant	2
10	Umedeor fails to meet compliance requirements for information and security governance.	Low	Major	3

11	Umedeor becomes insolvent while holding sensitive data within the registry system.	Very Low	Catastrophic	3
12	A change in privacy/data legislation invalidates registry system processes.	Very Low	Catastrophic	3
13	Incidents or outages may result in business interruptions and inaccessibility or loss of registry data	Medium	Considerable	3

Mitigating Actions

Risk	Options to reduce or eliminate risk	Effect on risk	Residual risk	Measure approved
1	Pseudonymised sensitive data is encrypted at rest and hosted in a certified AWS environment in line with or exceeding the standards set by NHS England. Penetration testing and external security certification reports available on request.	Reduced	Low	Yes
2	Personal data is encrypted at rest and hosted in a certified AWS environment in line with or exceeding the standards set by NHS England. Access control managed by job role with permissions audited reviewed periodically.	Reduced	Low	Yes
3	The registry system uses a de-linked and encrypted identifier to connect pseudonymised and identifiable datasets which are held in separate AWS instances. The encryption key itself is held in a separate Key Management Service. Malicious actors would have to simultaneously gain access to multiple distinct AWS instances as well as the Encryption Key Service to attempt re-identification. This level of security far exceeds those standards set by NHS England and many of the existing cloud hosted integrated care records.	Reduced	Low	Yes
4	The registry system has implemented SOPs and security controls to address this risk including: ● Confidentiality policy acknowledge by employees	Reduced	Low	Yes

	● Employee induction and continuous security and compliance training ● Prospective employee vetting ● Password management ● Assignment of unique identifier to employees to allow for tracking of access ● Dual factor authentication procedures to verify person accessing participant protected health information is approved employee ● Employee offboarding process in place that includes confidentiality clauses The registry system exceeds the requirements of the NHS DSP toolkit (Umedeor Ltd-ODS 8K677 and Cohort Science Ltd-ODS F2F6L); both businesses are ISO9001:2015 and ISO27001:2013 certified.			
5	All correspondence makes clear to the subject why they are being contacted and how to change preferences to prevent unwanted further correspondence.	Eliminated	Low	Yes
6	When using the registry system, participants associated with a specific DPA will be informed even when sharing does not require consent as a legal basis. This allows participants to 'opt-out'.	Reduced	Low	Yes
7	Participant identity will be confirmed before any consent is obtained. This is achieved by asking the participant to confirm DOB which is cross referenced with the DOB held against the record associated with the contact information in question. This contact information is obtained from the *Member* which supports another implicit layer of identity verification.	Reduced	Low	Yes
8	If the registry system is used to facilitate data transfer/sharing with a third party, access is only granted once the data transfer/sharing agreement is in place. Audit logs give an immutable record of activity and any access by named individuals within a 3rd party. Like all other agreements, breach of this could result in legal action by the *Member.*	Reduced/ Accepted	Low	Yes

9	The registry system will flag any participants with preferences that conflict from those documented within the participant record. The registry system will default to declining third party engagement until the discrepancy has been remedied.	Reduced	Low	Yes
10	In the unlikely event Umedeor Ltd becomes insolvent, all data created from participant engagement including metadata and logs will be returned to the provider organisations associated with their participant population. All copies of sensitive and personal data will be destroyed and access granted to *Members* and / or independent auditors to demonstrate this.	Eliminated	Low	Yes
11	Umedeor continuously reviews current and planned data legislation. If a change in data legislation is likely to affect Umedeor operations, then this will be highlighted alongside the mitigating measures planned by Umedeor to ensure ongoing compliance.	Reduced	Low	Yes
12	Policies are in place regarding final disposition of electronic protected health information and disposal of hardware/electronic media associated with storage of such data.	Eliminated	Low	Yes
13	Business Continuity Policy and Process is in place and is annually tested and independent externally audit. This includes a backup and restore policy.	Reduced	Low	Yes

9.2. Potential Benefits

Participants will not benefit directly from being in this research study.

9.3. Research Ethics Committee (REC) and other Regulatory review & reports

Before the start of the registry, approval will be sought from a REC (researchers should check if they are required to gain a favourable opinion from the UK Health Departments Research Ethics Service NHS REC) for the registry protocol, informed consent forms and other relevant documents e.g. advertisements. In addition:

- Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site.
- All correspondence with the REC will be retained.

- It is the Sponsor's responsibility to produce the annual reports as required.
- The Sponsor will notify the REC of the end of the registry.
- An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the registry is declared ended.
- If the registry is ended prematurely, the Sponsor will notify the REC, including the reasons for the premature termination.
- Within one year after the end of the registry, the Sponsor will submit a final report with the results, including any publications/abstracts, to the REC.

9.4. Regulatory Review & Compliance

Before any site can enrol patients into the registry, the Sponsor will ensure that appropriate approvals from participating organisations are in place. Specific arrangements on how to gain approval from participating organisations are in place and comply with the relevant guidance. Different arrangements for NHS and non-NHS sites are described as relevant.

For any amendment to the registry, the Sponsor, in agreement with the Chief Investigator, will submit information to the appropriate body for them to issue approval for the amendment. The Sponsor will work with sites (R&D departments at NHS sites as well as the registry delivery team) so they can put the necessary arrangements in place to implement the amendment to confirm their support for the registry as amended.

9.5. Amendments

Amendments to the protocol, participant information and consent forms will be made as required, for example, if the nature of information/data being collected from participants were to change. Amendments will be led and coordinated by the Chief Investigator (with support from administrative staff), and with the agreement of the sponsor (CS Ltd). The decision about when to make an amendment will be taken by the Chief Investigator, who will also determine whether the amendment is substantial or non-substantial. Amendments will be notified via email to relevant stakeholders and the amendment history (along with all supporting documentation by version number and date) will be retained.

9.6. Peer review

Independent expert peer review has been undertaken by:

- Toby Maher, MD, PhD, Professor of Clinical Medicine, USC, Keck School of Medicine
    - former Professor of Interstitial Lung Disease and Head of the Fibrosis Research Group at the National Heart and Lung Institute, Imperial College, London. British Lung Foundation Chair in Respiratory Research and National Institute for Health Research (NIHR) Clinician Scientist. Honorary Consultant Respiratory Physician on the Interstitial Lung Disease Unit, Royal Brompton Hospital and Director of the NIHR Respiratory CRF and Director of Respiratory Research at Royal Brompton Hospital)

9.7. Patient & Public Involvement Group

AccessILD will undertake regular PPI group consultation to capture broader feedback on the activity taking place within the registry. A patient representative will also be nominated to sit on the Management Committee.

A PPI group was convened for patients with ILD before the start of the study. We obtained holistic feedback from patients on the protocol, patient information leaflet, patient engagements and study structure. A quarterly newsletter providing patient updates will also be sent to participants, and feedback will always be encouraged and welcomed. Participants of the PPI group will receive an attendance expense payment.

9.8. Protocol compliance

This protocol provides a written guide for the conduct of the project. Deviations from the protocol (if they occur) will be recorded by date, alongside a description of the deviation and will be available for audit.

9.9. Data protection and participant confidentiality

Data protection has been a key consideration since the conception of the uMed platform and has been developed further when constructing the AccessILD protocol. For clarity, this section has been split into data protection and participant confidentiality considerations that relate to Umedeor vs those that relate to Cohort Science Ltd.

9.10. Cohort Science Ltd and Umedeor Ltd

Both businesses comply with UK GDPR, the UK Data Protection Act 2018, and the Common Law Duty of Confidentiality. Both businesses are also compliant with the NHS Data Protection & Security Toolkit, the ISO27001:2013 Information Security Management System, and hold a Cyber Essentials Plus certification.

The core principle applied throughout AccessILD and across the wider uMed Platform is that Umedeor always acts as a data processor on behalf of the investigator sites (GP practices) involved in the registry.

This data processing agreement (aka platform agreement) allows Umedeor to access and utilise EHR data from the practice to provide services to support delivery of studies. Umedeor therefore cannot use or share provider data with any third party without the permission from the GP practice (data controller). Consequently, the uMed platform includes provision for an authorisation workflow to enable the practice to give permission(s) for engagement and/or sharing of data in-line with the Access-ILD protocol. This process also ensures that an audit trail is created such that the sponsor is able to confirm all required permissions have been given by each site.

Cohort Science data will be extracted as encrypted files that are sent to AWS S3, and then decrypted and ingested by the CS AWS account.

Further detail can be found in **Appendix 5: Umedeor IG Whitepaper.**

9.11. Health Record Data Security

Umedeor applies the latest cloud-based security principles to ensure that data is held securely on our Amazon Web Service (AWS) infrastructure. In addition to conforming to the standards set by NHS Digital, the uMed platform goes beyond this to create a gold standard for information security of health data. It achieves this by ensuring patient identifiable information is always separated from health data via an encrypted layer which prevents complete patient records from being inappropriately accessed.

Additional information relating to the Umedeor business processes that ensure information security can be found in the Umedeor Information Management Security System documentation which is available on request. DSP Toolkit registration data can be found at:

https://www.dsptoolkit.nhs.uk/OrganisationSearch/8K677

https://www.dsptoolkit.nhs.uk/OrganisationSearch/f2f6l

9.12. Data Retention

As Umedeor provides services to GPs requiring access to GP data, Umedeor holds this data until the data processing agreement between Umedeor and the GP site expires or is terminated.

9.13. Data Encryption & Transmission of Data to Study Sponsor

Umedeor only transfers data to a third party once the data controller and the participant has given permission for the transfer in line with requirements set out in the AccessILD protocol.

The following data must be always encrypted using minimum 2048-bit encryption:

- Data backups - encrypted using high grade secure keys.
- Data in transit uses public/private certificate key pairs for exchange of data.

Any exchange of data with external systems uses unique key pairs per source/destination.

Encryption keys are stored on a separate secure key management system (KMS) that uses FIPS 140-2 validated hardware security modules (HSMs) to generate and protect keys.

Access to private keys is restricted to specific users with appropriate security clearance and access is logged. The Head of Security must approve access requests for any encryption keys.

9.14. Cohort Science Ltd

Prior to transfer of any registry data to Cohort Science (CS), permission of the registry site (data controller) and participant consent will have been sought and obtained in line with the requirements of:

a. The registry protocol.
b. CS - Site clinical trial agreement.
c. Umedeor - GP data processing agreement.

All data transferred to CS by Umedeor on behalf of the registry site will be pseudonymised[1] prior to transfer. All participant identifiers will be removed and an encrypted pseudo-ID will be used that can be passed back to Umedeor if participant re-identification / re-engagement was required.

All registry data will be held in CS AWS infrastructure and no individual will have common access to CS as well as Umedeor data infrastructure.

All transfers between the Umedeor and CS will be logged and reports made available to external auditors on request. All access to CS datasets will also be logged with access restricted only to the CS research team and external researchers approved by the registry Management Committee.

9.15. Data Retention

In line with MRC guidance, registry data will be retained for a period of 20 years after the registry has been completed.

9.16. Access to the registry dataset

AccessILD aims to balance the goals of 'open science' alongside creating a sustainable registry model that incentivises academic and commercial researchers to engage with the registry and develop new ideas, diagnostics and therapies that can improve the lives of patients with ILD.

A: Any access to AccessILD data or samples will require approval by the registry Management Committee *(see **Appendix 10**)*

B: Access to DNA samples

Access to samples may be provided to researchers for the purpose of genotyping/sequencing. It is a requirement that data from this analysis of DNA will be provided back to Cohort Science and integrated into the Core Clinical Dataset. Researchers requesting access to DNA samples will be required to provide evidence to the registry Management Committee of affiliation to a bona fide research institution that has the requisite governance in place to manage DNA samples and the resulting genotype/sequencing data.

C: Open Access to Core Clinical Data

All academic researchers will be provided access to the CCD once their credentials have been validated and a description of the intended project that will use the registry data has been provided to the registry Management Committee. The AccessILD CCD includes:

a. Baseline and scheduled questionnaire data.
b. Linked clinical health record data.
c. DNA genotype/sequencing data.

[1] Pseudonymisation refers to techniques that replace, remove or transform information that identifies individuals, and keep that information separate. Umedeor carries out pseudonymisation in accordance with Article 4(5) of the UK GDPR

d. Any additional data collected as part of a supported registry or nested project where the funder of that registry/project has agreed for that data to be included in the open data.

D: Additional data captured under AccessILD protocol

To preserve incentives for industry engagement, Cohort Science or the funders of 'nested projects' that capture additional data from registry participants will be able to request that access to this subset of data is restricted to specific users.

Unless exceptional reasons are presented to the registry Management Committee, access to this additional data will not be restricted for more than 1 year after publication. After which, the previously restricted data will be made available as part of the CCD.

Importantly, participants associated with 'nested projects' will be proactively engaged and presented information explaining who is funding the project and if access to data from this nested project will be restricted. Participants are given a clear means to then opt out of further engagement with the 'nested project'.

9.17. Subject Withdrawals

Subjects will be advised in the informed consent that they have the right to withdraw from the study at any time without prejudice. In instances where participants want to withdraw their data/biospecimens from the study, the uMed platform has the capability to identify and remove the data linked to specific individuals.

If a participant wishes to withdraw their data/biospecimens from the study, the participant may submit such a request to the study team via phone or email. The study team will make every effort to remove the participant from the registry and have his or her samples destroyed. However, in some cases, it may be impossible to locate and stop such future research on your specific sample if all identifiers were stripped from your sample prior to the sample being provided to other investigators.

10. DISSEMINATION POLICY

10.1. Dissemination policy

- Cohort Science Ltd will manage and be responsible for the pseudonymised CCD.
- Any external researcher wishing to publish based on data from AccessILD will need approval from the registry Management Committee.
- Study protocol will be made available via appropriate web portals (e.g. HRA website, clinicaltrials.org) within 6 months of commencing registry recruitment.
- Participants will automatically be notified of any publication that arises as a result of their participation in AccessILD. This will be achieved using the uMed platform and notifications will be sent via email or SMS in line with the participants' stated preferences. Participants will be provided with a layperson language summary of the publication alongside a link to the article.

10.2. Authorship eligibility guidelines and any intended use of professional writers

Cohort Science and Umedeor will be acknowledged as the sponsor and facilitating technology platform respectively in any publication using registry data.

11. REFERENCES

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12. APPENDICES

Appendix 1: Governance of Nested Projects within AccessILD

Appendix 2: Stakeholder Relationship Schematic

Appendix 3: Examples of questionnaires and scales for 'nested projects'

Appendix 4: SNOMED-CT codes for inclusion & exclusion criteria

Appendix 5: Umedeor Information Governance White Paper

Appendix 6: Participant Information Sheet

Appendix 7: Schedule of Activities (Example)

Appendix 8A: Consent Questions

Appendix 8B: Engagement screen flow

Appendix 9: Previous success with Access-PD

Appendix 10: CS Data access application

Appendix 1: Governance of Nested Projects run within AccessILD

Nested projects will be categorised into 3 types.

Type A: Nested project using the existing pseudonymised study dataset.

Type B: Nested project requiring additional PRO's, questionnaires, or observational data. All data provided to external researchers will be pseudonymised.

Type C: Nested project using wearable technologies.

Type A nested project will enable research teams external to AccessILD to access the existing pseudonymised study dataset only. Access will be granted subject to review of the request by the AccessILD Management Committee.

As Type A projects only utilise existing data and consent is already obtained for this secondary use, the participant does not need to opt-in. Umedeor will still proactively engage participants when AccessILD intends to share data with external research teams and participants will be given the opportunity to opt-out for access by specific external researchers.

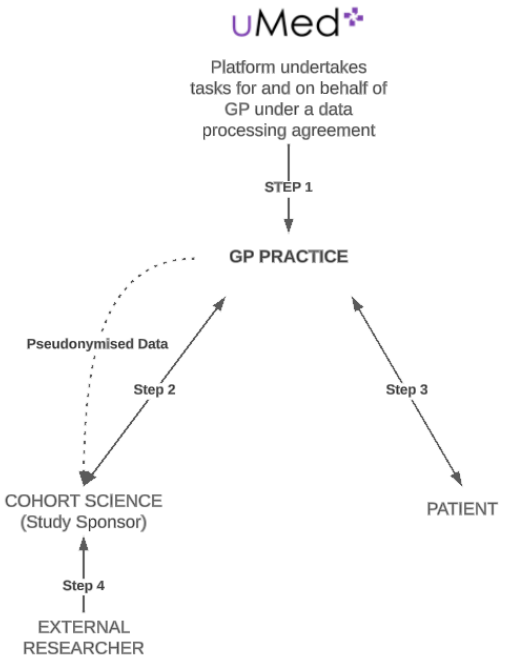
Type B nested projects are defined as those that will seek to capture additional PRO's, questionnaires or observational data collected through in-person or remote visits with the study team. Participants presented with the opportunity to provide additional data will be required to opt-in to such activities. Data will always be pseudonymised prior to access by external researchers. These projects may require a protocol amendment and/or REC approval.

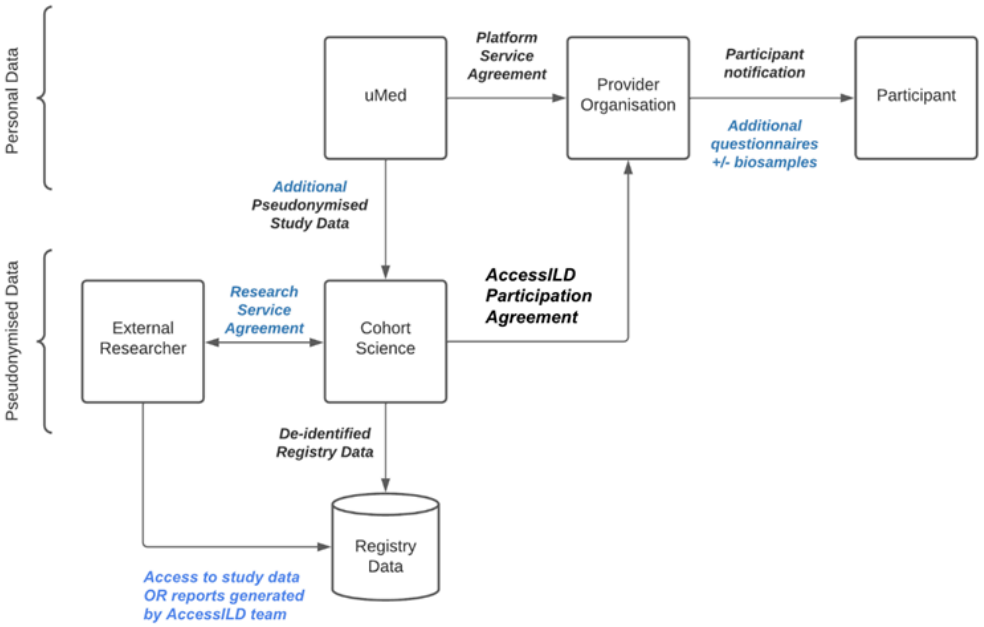
Type C nested projects allow sub-groups of patients within AccessILD to be recruited for studies using wearable technologies. In these types of studies, any wearable technologies used will only be used for measurement. These type C nested projects would be submitted as an amendment to the AccessILD protocol with subsequent REC approval. Participants within AccessILD who wish to engage with the opportunity to be part of Type C nested projects will be required to re-consent.

Note. Any interventional or clinical drug studies recruiting participants identified through AccessILD will be conducted as standalone trials with their own protocols and will undertake independent REC review prior to commencement.

Appendix 2: Stakeholder Relationship Schematic

Process Flow:





Step 1:
Umedeor has a data processing agreement with the HCP and a Study Research Tissue Bank Participation Agreement. This allows Umedeor to undertake tasks including search of health records to identify potential participants and engagement of those potential participants once this list of individuals has been reviewed and approved by the healthcare provider within the uMed platform.

Step 2
The study sponsor (Cohort Science) enters into an agreement with Umedeor to process study specific data agreement with GP. Umedeor's technology helps identify suitable healthcare provider sites and supports the providers in completing the relevant study onboarding documents (eg, study agreement)

Step 3
Umedeor, with the approval and on behalf of the provider organisation, will contact potential participants and ask them to enrol in AccessILD. This includes a link to the participant information sheet, information videos and an electronic consent workflow. Umedeor acts on behalf of the provider to automate this outreach via text, email, and letter. The consent questions that potential participants receive can be viewed in Appendix 8 of the protocol.

Once consented, the participants will be sent study questionnaires and other data collection (e.g. DNA tests) over several months. Data collected from participants is consolidated with health record data and shared with the study sponsor (Cohort Science) in pseudonymised form.

Step 4
External researchers can engage with AccessILD through 'nested projects' which enables access for those external researchers to pseudonymised data and additional data collected from subgroups within the AccessILD population to support analyses of specific research questions.

When an external researcher wishes to engage in a nested project, the pseudo-IDs of relevant participants will be shared with the provider's practice. Acting on behalf of the provider and the sponsor, Umedeor will then reidentify those participants and engage them to collect the additional data required for that nested project.

All nested projects that provide access to data and/or samples will need to be approved by the AccessILD Registry Management Committee. Further information on how access is managed can be found in section 8.8 of the protocol.

Appendix 3: Questionnaires and scales for ‘nested projects’

Name	Domain	Duration
Chronic Respiratory Disease Questionnaire (CRQ)	Symptoms, HRQOL	20 minutes
St George’s Respiratory Questionnaire (SGRQ)	Symptoms, HRQOL	3 minutes
36-item short form” (SF36)	HRQOL	5 minutes
Transitional Dyspnea Index (TDI)	Symptoms	
Living with Pulmonary Fibrosis (L-PF)	Symptoms, HRQOL	20 minutes
Pulmonary Fibrosis Impact on Quality of Life Scale (PF-IQOLS)	Symptoms, HRQOL	10 minutes
Hospital Anxiety and Depression Score (HADS)	Mood	5 minutes
CHEST Interstitial and Diffuse Lung Disease Patient Questionnaire	Risk factors/medical history	15 minutes
King’s Brief Interstitial Lung Disease Questionnaire	Symptoms, HRQOL	10 minutes
Quality of life in patients with idiopathic pulmonary fibrosis (QPF)	HRQOL	15 minutes
Leicester Cough Questionnaire (LCQ)	Symptoms, HRQOL	5 minutes

Appendix 4: SNOMED-CT codes for Inclusion & Exclusion Criteria

Appendix 4.1: ILD Diagnosis codes

SNOMED-CT code	term
1017196003	Interstitial pulmonary fibrosis due to inhalation of substance
1017197007	Interstitial pulmonary fibrosis due to inhalation of drug
10713006	Diffuse interstitial rheumatoid disease of lung
129451001	Respiratory bronchiolitis associated interstitial lung disease
129452008	Nonspecific interstitial pneumonia
129458007	Bronchiolitis obliterans organizing pneumonia
14700006	Bauxite fibrosis of lung
155621007	Rheumatoid lung
17385007	Graphite fibrosis of lung
17996008	Pneumoconiosis caused by inorganic dust
192658007	Giant cell interstitial pneumonitis
196027008	Toxic bronchiolitis obliterans
196051003	Drug-induced interstitial lung disorder
196053000	Chronic drug-induced interstitial lung disorders
196125002	Diffuse interstitial pulmonary fibrosis
196132006	Rheumatoid lung
196133001	Lung disease with systemic sclerosis
196136009	Lung disease co-occurrent with polymyositis
201794001	Rheumatoid lung
201813004	(Rheumatoid lung) or (Caplan's syndrome) or (fibrosing alveolitis associated with rheumatoid arthritis)
22607003	Asbestosis
233673002	Drug-induced bronchiolitis obliterans
233692000	Cryptogenic pulmonary eosinophilia
233703007	Interstitial lung disease
233713004	Seasonal cryptogenic organizing pneumonia with biochemical cholestasis
233723008	Bronchiolitis obliterans with usual interstitial pneumonitis
233724002	Toxic diffuse interstitial pulmonary fibrosis
233725001	Drug-induced diffuse interstitial pulmonary fibrosis

233748006	Simple pneumoconiosis
233749003	Complicated pneumoconiosis
233750003	Erionite pneumoconiosis
233751004	Metal pneumoconiosis
233754007	Cerium pneumoconiosis
233755008	Nickel pneumoconiosis
233756009	Thorium pneumoconiosis
233757000	Zirconium pneumoconiosis
233758005	Mica pneumoconiosis
233759002	Mixed mineral dust pneumoconiosis
233760007	Acute silicosis
233761006	Subacute silicosis
233762004	Chronic silicosis
233764003	Wollastonite pneumoconiosis
233770009	Stage 4 pulmonary sarcoidosis
236302005	Acute interstitial pneumonia
239297008	Lymphomatoid granulomatosis of lung
239794002	Fibrosing alveolitis associated with rheumatoid arthritis
24369008	Pulmonary sarcoidosis
26511004	Pneumoconiosis caused by sisal fiber
277844007	Pulmonary lymphangioleiomyomatosis
29422001	Coal workers' pneumoconiosis
30042003	Confluent fibrosis of lung
319841000119107	Rheumatoid lung disease with rheumatoid arthritis
32139003	Mixed dust pneumoconiosis
32544004	Chronic obliterative bronchiolitis caused by inhalation of chemical fumes AND/OR vapors
34371004	Subacute obliterative bronchiolitis caused by inhalation of chemical fumes AND/OR vapors
35037009	Primary atypical interstitial pneumonia
3514002	Peribronchial fibrosis of lung
36599006	Chronic fibrosis of lung
37711000	Cadmium pneumonitis
385479009	Follicular bronchiolitis

398640008	Rheumatoid arthritis with pneumoconiosis
398726004	Rheumatoid lung disease
40100001	Obliterative bronchiolitis
40122008	Pneumoconiosis
40218008	Carbon electrode makers' pneumoconiosis
40527005	Idiopathic pulmonary hemosiderosis
405570007	Pulmonary fibrosis due to and following radiotherapy
40640008	Massive fibrosis of lung co-occurrent and due to silicosis
426437004	Familial idiopathic pulmonary fibrosis
426853005	Pneumoconiosis caused by silicate
427046006	Drug-induced pneumonitis
427123006	Interstitial lung disease due to collagen vascular disease
430476004	Diffuse panbronchiolitis
44274007	Lymphoid interstitial pneumonia
47515009	Simple silicosis
47938003	Chronic obliterative bronchiolitis
51615001	Fibrosis of lung
54867000	Rheumatoid arthritis with fibrosing alveolitis
56841008	Massive fibrosis of lung
58691003	Antimony pneumoconiosis
59903001	Acute obliterating bronchiolitis
62371005	Pulmonary siderosis
64667001	Interstitial pneumonia
700249006	Idiopathic interstitial pneumonia
700250006	Idiopathic pulmonary fibrosis
700251005	Chronic idiopathic pulmonary fibrosis
700252003	Subacute idiopathic pulmonary fibrosis
704345008	Chronic interstitial pneumonia
707434003	Pulmonary fibrosis due to Hermansky-Pudlak syndrome
708537005	Acute idiopathic pulmonary fibrosis
711379004	Interstitial lung disease due to connective tissue disease
71193007	Fibrosis of lung caused by radiation
719218000	Cryptogenic organizing pneumonia
72270005	Collagenous pneumoconiosis

73144008	Pneumoconiosis caused by talc
733453005	Congenital nephrotic syndrome, interstitial lung disease, epidermolysis bullosa syndrome
737181009	Interstitial lung disease due to systemic disease
737182002	Interstitial lung disease due to granulomatous disease
737183007	Interstitial lung disease due to metabolic disease
737184001	Interstitial lung disease co-occurrent and due to systemic vasculitis
789574002	Acute exacerbation of idiopathic pulmonary fibrosis
805002	Pneumoconiosis caused by silica
836478002	Subacute obliterative bronchiolitis caused by chemical fumes
836479005	Subacute obliterative bronchiolitis caused by vapor
840350008	Chronic obliterative bronchiolitis caused by chemical fumes
840351007	Chronic obliterative bronchiolitis caused by vapor
8549006	Desquamative interstitial pneumonia
866103007	Interstitial lung disease due to juvenile polymyositis
870573008	Interstitial pneumonia with autoimmune features
87909002	Hard metal pneumoconiosis
684633371000119107	Diffuse pulmonary meningotheliomatosis
556179491000119104	Interstitial lung disorder due to vaping
470101491000119107	Interstitial lung disorder due to dabbing
328661000119108	Interstitial lung disease of childhood
328641000119109	Genetic disorder of surfactant dysfunction
1284850005	Interstitial lung disease caused by ionising radiation due to and following radiation therapy
1228876007	Severe early-onset pulmonary alveolar proteinosis due to MARS deficiency
1222679006	Autoimmune interstitial lung disease, arthritis syndrome
1222678003	Interstitial lung disease due to ABCA3 deficiency
1222677008	Interstitial lung disease due to surfactant protein C deficiency
1172606002	Idiopathic pleuroparenchymal fibroelastosis
860890006	Fetal interstitial neoplasm of lung
846637007	Chronic pulmonary fibrosis caused by chemical vapors
783182004	Chronic respiratory distress with surfactant metabolism deficiency

770760006	16q24.1 microdeletion syndrome
723829000	Pulmonary fibrosis, hepatic hyperplasia, bone marrow hypoplasia syndrome
708026002	Chronic pneumonitis of infancy
707551007	Pulmonary interstitial glycogenosis
707541006	Acute respiratory distress in newborn with surfactant disorder
707435002	Neuroendocrine cell hyperplasia of infancy
707433009	Lymphangioleiomyomatosis due to tuberous sclerosis syndrome
302913000	Diffuse pulmonary calcinosis
240629003	Malarial shock lung
233717003	Diffuse pulmonary neurofibromatosis
233623000	Mononuclear interstitial pneumonia
233621003	Rickettsial pneumonia
196116008	Pulmonary hypostasis
196115007	Pulmonary congestion and hypostasis
196052005	Acute drug-induced interstitial lung disorder
196028003	Chronic pulmonary fibrosis due to chemical fumes
195896004	Pneumonia due to pleuropneumonia-like organism
89687005	Postimmersion-submersion syndrome
77690003	Interstitial emphysema of lung
76090006	Pittsburgh pneumonia
67782005	Acute respiratory distress syndrome
60125001	Perinatal interstitial emphysema
7548000	Rheumatic pneumonia

Appendix 4.2: Drug codes for Nintedanib and Pirfenidone

SNOMED CT code	**Term**
712494002	Nintedanib (substance)
776919004	Product containing only nintedanib (medicinal product)
863993005	Nintedanib esilate (substance)
28790311000001108	Nintedanib 150mg capsules (product)
28790211000001100	Nintedanib 100mg capsules (product)
715613009	Product containing nintedanib (medicinal product)
30768211000001100	Nintedanib 100mg capsules 60 capsule (product)

28782511000001100	Nintedanib 150mg capsules 60 capsule (product)|
28782211000001103	Nintedanib 100mg capsules 120 capsule (product)|
780015009	Product containing only nintedanib in oral dose form (medicinal product form)
715614003	Product containing nintedanib in oral dose form (medicinal product form)
863992000	Product containing precisely nintedanib (as nintedanib esilate) 150 milligram/1 each conventional release oral capsule (clinical drug)
865888008	Product containing precisely nintedanib (as nintedanib esilate) 100 milligram/1 each conventional release oral capsule (clinical drug)
777222000	Product containing only pirfenidone (medicinal product)
439581000	Pirfenidone (substance)
34625611000001106	Pirfenidone 801mg tablets (product)
34625511000001107	Pirfenidone 267mg tablets (product)
22343011000001103	Pirfenidone 267mg capsules (product)
840654008	Product containing precisely pirfenidone 801 milligram/1 each conventional release oral tablet (clinical drug)
	Product containing precisely pirfenidone 267 milligram/1 each conventional release oral tablet (clinical drug)
438240001	Product containing pirfenidone (medicinal product)
840655009	Product containing precisely pirfenidone 267 milligram/1 each conventional release oral capsule (clinical drug)
34623111000001104	Pirfenidone 801mg tablets 84 tablet (product)
41497811000001102	Pirfenidone 801mg tablets 90 tablet (product)
34623011000001100	Pirfenidone 267mg tablets 63 tablet (product)
34622911000001108	Pirfenidone 267mg tablets 252 tablet (product)
22332911000001107	Pirfenidone 267mg capsules 63 capsule (product)
40959811000001105	Pirfenidone 267mg tablets (Sandoz Ltd) (product)
22333111000001103	Pirfenidone 267mg capsules 270 capsule (product)
41497711000001105	Pirfenidone 801mg tablets (Amarox Ltd) (product)
40960111000001102	Pirfenidone 801mg tablets (Sandoz Ltd) (product)
22333011000001104	Pirfenidone 267mg capsules 252 capsule (product)
40710711000001108	Pirfenidone 801mg tablets (Teva UK Ltd) (product)
40710411000001102	Pirfenidone 267mg tablets (Teva UK Ltd) (product)
840659003	Product containing only pirfenidone in oral dose form (medicinal product form)
40359611000001103	Pirfenidone 267mg tablets (Celix Pharma Ltd) (product)

40363911000001102	Pirfenidone 801mg tablets (Celix Pharma Ltd) (product)
41440011000001102	Pirfenidone 801mg tablets (Axunio Pharma GmbH) (product)
41439611000001102	Pirfenidone 267mg tablets (Axunio Pharma GmbH) (product)
840658006	Product containing pirfenidone in oral dose form (medicinal product form)
41497911000001107	Pirfenidone 801mg tablets (Amarox Ltd) 90 tablet (product)
40640211000001104	Pirfenidone 267mg tablets (Accord Healthcare Ltd) (product)
40640811000001103	Pirfenidone 801mg tablets (Accord Healthcare Ltd) (product)
41296311000001109	Pirfenidone 267mg tablets (Viatris UK Healthcare Ltd) (product)
41362711000001102	Pirfenidone 801mg tablets (Lupin Healthcare (UK) Ltd) (product)
41296711000001108	Pirfenidone 801mg tablets (Viatris UK Healthcare Ltd) (product)
41362511000001107	Pirfenidone 267mg tablets (Lupin Healthcare (UK) Ltd) (product)
41439711000001106	Pirfenidone 267mg tablets (Axunio Pharma GmbH) 63 tablet (product)
41440211000001107	Pirfenidone 801mg tablets (Axunio Pharma GmbH) 84 tablet (product)
41439911000001108	Pirfenidone 267mg tablets (Axunio Pharma GmbH) 252 tablet (product)
40874511000001102	Pirfenidone 801mg tablets (Dr Reddy's Laboratories (UK) Ltd) (product)
40874211000001100	Pirfenidone 267mg tablets (Dr Reddy's Laboratories (UK) Ltd) (product)
41487911000001106	Pirfenidone 267mg tablets (Glenmark Pharmaceuticals Europe Ltd) (product)
40960211000001108	Pirfenidone 801mg tablets (Sandoz Ltd) 84 tablet 4 x 21 tablets (product)
40959911000001100	Pirfenidone 267mg tablets (Sandoz Ltd) 63 tablet 3 x 21 tablets (product)
41487711000001109	Pirfenidone 801mg tablets (Glenmark Pharmaceuticals Europe Ltd) (product)
40710511000001103	Pirfenidone 267mg tablets (Teva UK Ltd) 63 tablet 3 x 21 tablets (product)
40710811000001100	Pirfenidone 801mg tablets (Teva UK Ltd) 84 tablet 4 x 21 tablets (product)
40960011000001103	Pirfenidone 267mg tablets (Sandoz Ltd) 252 tablet 12 x 21 tablets (product)
40710611000001104	Pirfenidone 267mg tablets (Teva UK Ltd) 252 tablet 12 x 21 tablets (product)
40360011000001106	Pirfenidone 267mg tablets (Celix Pharma Ltd) 63 tablet 3 x 21 tablets (product)
40364011000001104	Pirfenidone 801mg tablets (Celix Pharma Ltd) 84 tablet 7 x 12 tablets (product)
40360411000001102	Pirfenidone 267mg tablets (Celix Pharma Ltd) 252 tablet 12 x 21 tablets (product)
40640411000001100	Pirfenidone 267mg tablets (Accord Healthcare Ltd) 63 tablet 3 x 21 tablets (product)

40640911000001108	Pirfenidone 801mg tablets (Accord Healthcare Ltd) 84 tablet 4 x 21 tablets (product)
41296411000001102	Pirfenidone 267mg tablets (Viatris UK Healthcare Ltd) 63 tablet 9 x 7 tablets (product)
41362911000001100	Pirfenidone 801mg tablets (Lupin Healthcare (UK) Ltd) 84 tablet 7 x 12 tablets (product)
41619411000001107	Pirfenidone 267mg tablets (Lupin Healthcare (UK) Ltd) 63 tablet 3 x 21 tablets (product)
41296811000001100	Pirfenidone 801mg tablets (Viatris UK Healthcare Ltd) 84 tablet 6 x 14 tablets (product)
41296511000001103	Pirfenidone 267mg tablets (Viatris UK Healthcare Ltd) 252 tablet 18 x 14 tablets (product)
40640711000001106	Pirfenidone 267mg tablets (Accord Healthcare Ltd) 252 tablet 3 x (4 x 21 tablets) (product)
40874611000001103	Pirfenidone 801mg tablets (Dr Reddy's Laboratories (UK) Ltd) 84 tablet 4 x 21 tablets (product)
41362611000001106	Pirfenidone 267mg tablets (Lupin Healthcare (UK) Ltd) 252 tablet 3 x (4 x 21 tablets) (product)
40874311000001108	Pirfenidone 267mg tablets (Dr Reddy's Laboratories (UK) Ltd) 63 tablet 3 x 21 tablets (product)
41488011000001108	Pirfenidone 267mg tablets (Glenmark Pharmaceuticals Europe Ltd) 63 tablet 9 x 7 tablets (product)
40874411000001101	Pirfenidone 267mg tablets (Dr Reddy's Laboratories (UK) Ltd) 252 tablet 12 x 21 tablets (product)
41487811000001101	Pirfenidone 801mg tablets (Glenmark Pharmaceuticals Europe Ltd) 84 tablet 6 x 14 tablets (product)
41488111000001109	Pirfenidone 267mg tablets (Glenmark Pharmaceuticals Europe Ltd) 252 tablet 18 x 14 tablets (product)

Appendix 5: Umedeor Information Governance White Paper

See accompanying document.

Appendix 6: AccessILD Participant Information Leaflet

See accompanying document.

Appendix 7: Schedule of Activities (Example)

Procedures	**Visits (insert visit numbers as appropriate)**			
	Screening	**Baseline**	**Every 6 Months**	**Unscheduled**
Informed consent	x			
Demographics (Limited as captured via EMR)		x		
Medical history (Limited as captured via EMR)		x		
Symptom / QOL Questionnaire		x	x	
Oxygen utilisation		x	x	
Pulmonary function testing data		x	x	
CT Chest imaging data		x	x	
Six-minute walk data		x	x	
Biosample Collection				x
Supplementary Questionnaires/Objective tests				x
Contact for participation in 3rd party studies				x

Appendix 8A : Consent Questions

Title of the Study: AccessILD
Sponsor: Cohort Science, Warner Yard, London EC1R 5EY
IRAS: 333380
Date: 14 Aug 2023

Potential participants will receive information on AccessILD (an introduction and a link to the Patient Information Leaflet). After reading the materials they will be asked the following questions in the form of an electronic remote consent. Potential participants will also be provided with an email address and nursetelephone number of the helpdesk and study nurse team for any questions they may have.

	Question	**Response**
Q1	I have read and understood the AccessILD Participant Information Sheet	YES/NO (Yes to proceed)
Q2	I consent for the use of my primary care record (GP record) to create my profile with AccessILD and to identify my suitability for further research opportunities.	YES/NO (Yes to proceed)
Q3	I agree to my data being stored by the sponsor of the study, Cohort Science Limited (the data controller)	YES/NO (Yes to proceed)
O4	I understand that information collected about me will remain confidential	YES/NO (Yes to proceed)
Q5	I understand that I may be offered the opportunity to participate in other research studies	YES/NO (Yes to proceed)
Q6	I understand that I will be invited to undertake activities or actions that aim to build a database of information that can be used to support Interstitial Lung Disease's research. These activities will not cost me anything and may be conducted in person or remotely, depending on the circumstances. Examples include: questionnaires, genetic tests, wearable devices, physical examinations by a doctor or nurse (or other healthcare professionals), lung function tests, etc..	YES/NO (Yes to proceed)
Q7	I consent that data collected as part of this study, including but not limited to my NHS identifiers, may be shared with NHS England to obtain my hospital health records. This applies to both my past medical data (data held by NHS England before I join AccessILD and any future data, for the duration of my participation on AccessILD.	YES/NO (Yes to proceed)

Q8	I understand that anonymised non-identifiable population data from AccessILD may be used for medical publications or shared with specific approved investigators (including those in the UK and worldwide) for further understanding of and research into Interstitial Lung Disease.	YES/NO (Yes to proceed)
Q9	I will be informed which research organisations have requested access to data which includes my pseudonymised person-level data, and I will be given the opportunity to opt out if I do not want that specific research organisation to have access.	YES/NO (Yes to proceed)
Q10	I understand that my involvement is voluntary. I will retain full control over my consent to participate in AccessILD and associated studies, and I can revoke this at any time, without providing a reason	YES/NO (Yes to proceed)
Q11	I would like to participate in this study. I consent to be part of the AccessILD registry	YES/NO (Yes to proceed)

Appendix 8B: Engagement screen flow

See accompanying document.

Appendix 9: Previous success with Access-PD

See accompanying document.

Appendix 10: CS Data access application