A Patient-Centric Outcomes Registry of Patients with Known or Suspected Novel Coronavirus Infection SARS-COV-2 (COVID-19)

Protocol Number:	XC-PCOR-COVID19
Version Number:	V1.0
Version Date:	March 20, 2020
IND Number:	N/A
NCT Identified Number:	TBD
Sponsor:	
Funded by:	xCures
Central IRB:	Genetics Alliance IRB
IORG Number:	IORG0003508
Principal Investigator:	Mark Shapiro VP, Clinical Development xCures, Inc.

Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale
N/A	N/A	N/A – Initial Draft

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STATEMENT OF COMPLIANCE

This registry study will be carried out in accordance with applicable guidelines and regulations. The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted for Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form will be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Study Sponsor:	xCures, Inc.
Study Title:	A Patient-Centric Outcomes Registry of Patients with Known or Suspected Novel Coronavirus Infection SARS-CoV-2 (COVID-19)
Study Acronym:	TBD
Study Description:	This study is a patient-centric outcomes registry enrolling patient with known or suspected COVID-19 infection. This study includes enrollment via on-line informed consent to participate in a data registry, including remote collection of symptoms, treatments, and outcomes.
Study Number:	XC-COVID19-2020
IND Number:	N/A
NCT Identified Number:	TBD
General Study Design:	Patient-centric outcomes registry
Objectives:	To collect demographic and medical history information from patients with known or suspected COVID-19 infection with a daily e-diary that includes symptoms, treatments.
Secondary Objectives:	• Define natural history of COVID-19 infection among different demographic and medical subgroups • Assess the impact of different comorbid conditions and treatment regimens on the duration and severity of COVID-19 infection.
Endpoints:	The purpose of this study is to understand at the population level the symptomatic course of known or suspected COVID-19 patients while sheltering-in-place or under quarantine. Symptoms will be measured using a daily report derived from the CTCAE-PRO as well as free response. Outcomes will be assessed based on the duration and severity of infection, hospitalization, lost-to-follow-up, or death. As a patient-centric registry, patients themselves may propose, suggest, and/or submit evidence or ideas for relevant collection. The registry should provide real-world data on the course of COVID-19 among patients under quarantine or sheltering-in-place and will supplement information collected by others in formal clinical trials, which are currently focused on the inpatient population.
Study Population:	This study will initially include up to 100,000 adults with known or suspected COVID-19 infection or others who are present in the United States.
Key Inclusion Criteria:	Adult men and women currently in the United States and willing to provide written informed consent and: • who are feeling sick but have not tested positive for COVID-19 • who are feeling sick and have tested positive for COVID-19 • People who are not feeling sick but want to participate

Key Exclusion Criteria:	Patients unwilling or unable to provide informed consent.
Phase:	Not applicable.
Sites Enrolling Participants:	This is a patient-centric, real-world data registry. Patients will be enrolled over the Web at a dedicated web site (URL to be determined) using electronic informed consent.
Study Duration:	The longitudinal, observational study will run for an initial period of one year for patient recruitment with up to one year of observation of enrolled patients or until community transmission of COVID-19 has ended. If community transmission continues, the duration of enrollment and data collection may be extended.
Participant Duration:	Patients will be asked to complete a baseline information questionnaire at registration and will be sent daily diary questionnaires until the COVID-19 outbreak has resolved. Patients will be asked to provide authorization for future follow-up contacts related to outcomes confirmation and medical record access under HIPAA.

2 STUDY RATIONALE

2.1 Disease Setting and Trial Context

The COVID-19 pandemic is an urgent, global public health crisis. In addition to non-treatment interventions underway, there is urgent need for detailed information about the natural history and course of the disease in non-hospitalized patients, in particular to develop an understanding of the nature, duration, and severity of symptoms in various demographic and medical subgroups.

2.2 Objectives and Aims

The objective of this project is to develop a patient-centric registry for participants from before the development of symptoms through the course of the illness by tracking symptoms, treatments, and outcomes of patients with known or suspected novel coronavirus-19 (COVID-19) through the prospective collection of symptoms information from non-hospitalized participants who are or may become infected with COVID-19 infection. This dataset will provide valuable information for researchers trying to understand the natural history of COVID-19 in different population in the community setting. Additional aims include understanding differences between subgroups and obtaining authorization for future collection of medical records information for inclusion in the disease registry and obtaining the permission of registry participants to be contacted in the future for follow-up information related to their COVID-19 diagnosis and/or treatments.

2.3 Risk/Benefit Assessment

2.3.1 Known Potential Risks

This is a non-interventional study. The purpose is to develop case-histories for patients with known or suspected COVID-19 infection while they are sheltering-in-place or under quarantine.

2.3.2 Known Potential Benefits

Ongoing insights and findings from this registry will be made available to participants and their medical providers, as well as to the wider public health community. Such information may be helpful to COVID-19 patients directly, or to patients with medical conditions who may be at increased risk. Through participation in this registry patients, healthcare providers and public health officials may receive information that supports management of COVID-19.

2.3.3 Assessment of Potential Risks and Benefits

The only risk of this project is potential loss of participant confidentiality. To mitigate this risk, xCures uses a secure data architecture that follows commercially reasonable and customary procedures to secure participant confidentiality. The risks minimal in accordance with the definition of Minimal Risk in 21 CFR 50 and 56 and outweighed by the potential benefits to individuals and society.

3 OBJECTIVES

During the current COVID-19 pandemic there is urgent need for information about the natural history of the infection in non-hospitalized patients, including the severity and duration of symptoms, and outcome from early in the infection, among different subgroups of patients. In addition, a large, real-world data registry can provide information about how different concomitant medications may differentially affect symptoms among patient subgroups. Such information can be invaluable for clinicians managing chronic diseases during this pandemic, as well as identify interventions undertaken in a naturalistic setting that have differential effects. Such factors may include patient diet, over the counter or prescription medications, and herbal and alternative treatments, among others. Identifying the natural disease history in patients from different demographic and disease subgroups will be important for identifying at-risk patients and effectiveness of interventions undertaken in the community.

4 STUDY DESIGN

4.1 OVERALL DESIGN

This is a patient-centric outcomes registry prospectively enrolling healthy volunteers and those who know or suspect they may have the COVID-19 infection. This study includes enrollment and consent through a secure Web page and completion of on-line surveys for inclusion into a data registry, including remote collection of symptoms, treatments, and outcomes. Additional retrospective data collection, including chart review of medical records for select cases is included. Cases selected for additional records collection will be contacted and their authorization for records collection will be conducted under HIPAA.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The purpose of a patient-centered registry is to serve one or more predetermined scientific or clinical purposes. In this case, the purpose is to develop a longitudinal, observational dataset of people before, during, and after infection with COVID-19 in the community. Such data is currently lacking and will provide useful information about the natural history of the disease, treatments administered in the community, and outcomes, particularly among demographic and medical subgroups. This data may provide useful prognostic regarding characteristics of people at greater risk for more severe infection as well as comparative analysis of the effects of treatments or concomitant medications used in the general population. Registries are valuable for providing information about the safety and effectiveness of treatments in patients that are not part of clinical trials, for example by evaluating the effectiveness of off-label therapies used during routine clinical practice and dietary interventions.

4.3 END OF STUDY DEFINITION

This is a longitudinal, observational study that will run for an initial period through the end of the current pandemic, which is anticipated to be approximately one year from initial approval, but may be extended should the outbreak continue or for long term follow with infected patients.

5 STUDY PROCEDURES

5.1 REGISTRATION AND CONSENT OF PARTICIPANTS

Patients will be registered for through the study Web site, covid19-registry.org (or the redirect site, beat19.org). Following Web site registration, patients will receive an electronic informed consent form (Appendix A). Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-approved and the participant will read and review the document electronically. A FAQ page will be on the Web site (Appendix C) and an email address will be available for additional questions. Participants must sign the informed consent document prior to participating in the registry. Participants will be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice by emailing the study team or simply unsubscribing from study emails.

5.1.1 SELECTION OF PATIENTS

5.1.2 INCLUSION CRITERIA

As a real-world data registry, any adult men and women currently in the United States and willing to provide written informed consent and:

- who are feeling sick but have not tested positive for COVID-19, or?
- who are feeling sick and have tested positive for COVID-19, or?
- who are not feeling sick but want to participate can enroll?

5.1.3 EXCLUSION CRITERIA

Patients unwilling or unable to provide informed consent will be excluded.

6 DATA MANAGEMENT

6.1 DATA HANDLING AND RECORD KEEPING

6.1.1 DATA MANAGEMENT

A registry database will be maintained with identified registry data elements captured into the REDCap Cloud EDC system, a commercial eClinical Platform that is 21 CFR Part 11 Validated, HIPAA & FISMA compliant, and WHODrug and MedDRA certified. All access and activity in the system is tracked and can easily be monitored by the Administrator. The system has a login audit feature that tracks who has logged into the system, the date and time of login, and the IP address of the connection. The system also tracks failed logins and automatically locks a user's account after several failed attempts. The REDCap Cloud system has a robust audit trail that shows all changes to any records within the system including who made the change, the date and time of the change, the field that was changed, the old value of the field and the new value of the field. Access can be monitored via a dashboard or email alerts. Data management activities will follow standard operating procedures.

6.1.2 STUDY RECORDS RETENTION

In the event that patient authorize the collection of additional medical records, those records will be maintained in xCures' HIPAA compliant box storage platform hosted on Amazon's HIPAA-compliant cloud servers. Source information, including medical records will be abstracted into a study database and not made available in their original format outside the study team. Study data including source records and case reports forms will be maintained in electronic format indefinitely. De-identified databases derived from the study records may be made available to other researchers and may be retained by those organizations indefinitely based on the terms of the agreement under which the data was provided.

6.1.3 SOURCE DOCUMENTS

Source data can include clinical findings and observations, or other information incorporated into the registry database to support analysis of data. Source data is all information from which information in the registry database is derived in original form (or certified copies of an original record). Examples of these original documents and records include but are not limited to the following: electronic medical records, clinical and office charts, laboratory notes, memoranda, correspondence, subjects' diaries or patient-reported questionnaires, data from automated instruments, such as ECG machines, photographs and other imaging (DICOM) files, slides, pharmacy records, and the reports documenting medical interpretation of those files.

Data may be entered into the eCRF either manually by the study team performing data abstraction from the EMR or electronically using direct entry of data into the or from an electronic import of data. Patients may also enter information directly into the eCRF using a patient-facing survey functionality either over the Web or using a smartphone app. Data elements originating in EMR may be automatically transmitted directly into the eCRF using a suitable API. Source data derived in that manner may have an intervening process, such as abstraction by third-party including software including processing using machine learning algorithms prior to transferring to the eCRF. xCures will retain source records in a secure that will be maintained separately and securely from the

eCRF. However, metadata tagging may be employed to electronically map source data back from the eCRF to the source data record to create an audit trail.

6.2 Discontinuation of Participation

Participants can withdraw from the registry at any time by sending a written request to xCures. Withdrawal from the study means that no additional data will be collected from the patient and does not constitute revocation of the right to use the data collected prior to withdrawal for the purposes described herein. xCures may discontinue the study at any time for any reason. In the event the registry is discontinued enrolled participants may receive an email notification and a public posting on the study Web site will be made, if possible.

6.3 Unanticipated Problems

6.3.1 Definition of Unanticipated Problems (UP)

Unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

6.3.2 Unanticipated Problem Reporting

xCures will report unanticipated problems (UPs) to the Genetic Alliance Institutional Review Board (GAIRB) in accordance with the IRB's policies and procedures. The UP report will include the following information:

- Study identifying information: protocol title and number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported within 10 working days of xCures identifying or learning of the event.

6.3.3 Reporting Unanticipated Problems to Participants

Unanticipated problems will be reported to registry participants that are affected by the UP within 30 days of xCures becoming aware of the problem.

7 ANALYTIC METHODS AND STATISTICAL CONSIDERATIONS

7.1 Overview of Analytic Methods

The patient-focused outcomes research outlined in this registry protocol is focused on generating a large dataset for hypothesis identification and testing using machine learning or other analytic models. Participants and external researchers may suggest hypotheses for testing and qualified researchers may receive a de-identified dataset.

The analysis of the registry data should lead to new information about emerging signals from treatments used in the community, as well as the role of comorbid conditions and concomitant medications as risk factors for COVID-19 infection.

8 SUPPORTING DOCUMENTATION AND CONSIDERATIONS

8.1 REGULATORY AND ETHICAL CONSIDERATIONS

8.1.1 REGULATORY CONSIDERATIONS

As a patient-centric, non-interventional prospective, observational study, the proposed research program meets the regulatory criteria under 21 CFR 312.2(b)(1) for an exemption from the requirement for the submission and FDA-acceptance, of an IND application. Specifically:

1. The investigation is not intended to be reported to the FDA as a well-controlled study in support of a new indication for the use of an FDA-regulated product, nor intended to be used to support any other significant change in the labeling of an FDA-regulated product.

2. The investigation is not intended to support a significant change in the advertising for an FDA-regulated product. The purpose of this study is to use machine learning to identify factors which may be predictive of treatment response at the level of individual patients and disseminate that information to patients, physicians, and public health officials.

3. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of an FDA regulated product. Specifically, this is a data-collection registry, treatment of patients will continue at the discretion of their physician. xCures may provide information to the public based on public information related to therapeutic options and/or clinical trials for which the participant may be eligible.

4. The investigation is subject to prior approval by the Genetic Alliance IRB, based in, which operates in compliance with the FDA regulations including 21 CFR Parts 50 and 56 and is registered with OHRP as IRB Organization number IORG0003358.

5. Neither the participants in this clinical investigation, nor their insurance providers, will be charged for the procedures associated with participation in the study. Patients in this registry will be treated according to their institution's normal standards of practice and at their oncologist's discretion.

xCures maintains strong data security procedures has procedures in place to comply with the FTC Health Breach Notification Rule (16 CFR 318) in the event of an unauthorized breach of confidentiality of patient information. Such an incident would be reported to the Genetic Alliance IRB in accordance with the procedures for UP reporting. As a patient-centric outcomes registry, we encourage patients to communicate publicly about their conditions and to share information. Disclosures are made by patients and are not considered unauthorized disclosure.

This registry study will comply with sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) (42 U.S.C. §§ 282(i) and (j)), which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85, 121 Stat. 904) by registering and reporting results in the Clinicaltrials.gov database.

8.1.2 CONFIDENTIALITY, PRIVACY, AND DATA SECURITY

Participant confidentiality and privacy is strictly held in trust by xCures, their staff, partners, and affiliates. xCures maintains the confidentiality of records and that confidentiality extends to cover test results of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study data will be stored in secure electronic format and personally identifiable information will not be disclosed without the express permission of the participant, however authorized representatives of xCures and representatives of the Genetic Alliance IRB, as well as regulatory agencies may inspect records in certain circumstances without prior approval.

Research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored by xCures in a research study database within the REDCap EDC system. REDCap is a secure, cloud-based system that is HIPAA, FISMA, GDPR, Annex 11, and 21 CFR 11 compliance system for the collection and storage of clinical research and survey information. Services Data related to the provision of information services or management of the study Web site will not be considered Research Data under this protocol and will be maintained separately.

For both Research Data and Services Data, sensitive personal information will be stored in a secure database using a role and permission-based system for access. Sensitive data elements, including PHI or other sensitive or identifiable information will be stored in encrypted-at-rest format. Research Data will identify participants only by a unique study identification number. The decode list for this information will be maintained securely and not disclosed to recipients of the Research Data. Research Data may be disclosed outside of xCures and their agents and affiliates for the purposes of research and education, public health, or to further the development of treatments for COVID-19.

8.1.3 Future Use of Stored Data

Data collected for this study will be analyzed and stored by xCures and their designated data/technology provider(s). In the event the study is terminated for any reason, the de-identified, archived data will be retained for future use by other researchers possibly including those outside of the study. Access to the study data will require agreement to comply with the privacy policies herein.

8.1.4 Publication and Data Sharing Policy

This study will be conducted in accordance with the ICMJE publication and data sharing policies. xCures and their partners are responsible for submitting manuscripts for publication. Every attempt will be made to publish results in a suitable, peer-reviewed journal. External researchers may publish articles based on access to the de-identified or limited study data following agreement to comply with applicable regulations.

8.1.5 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership at xCures has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

8.1.6 Ethical Considerations

The research protocol and consent form will be provided to the Genetic Alliance IRB for review and approval prior to implementation.

All patients must provide informed consent. The process will be conducted electronically using the secure e-consent process. Documentation of the consent will be maintained. Participants will receive an electronic copy of their consent. Further, participants may discontinue participation at any time in accordance with the procedures outlined in the consent form. All data collected up to the point of withdrawal will remain in the Research Database and may be included in de-identified data for future analyses.

8.2 Study Oversight and Other Considerations

8.2.1 Financial Considerations

xCures is a for-profit organization and will be responsible for the costs associated with implementing and maintaining the registry.

8.2.2 Study Discontinuation and Closure

This study may be suspended or prematurely terminated at any time for any reason, at the discretion xCures. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants at their provided contact email and via public notice on the study Web site, if possible, as well to the IRB, and regulatory authorities, if required.

8.2.3 Quality Assurance and Quality Control

xCures will perform internal quality management of study conduct, including collection, handling and analysis of data. A quality management system will be implemented and written Standard Operating Procedures (SOPs) will be followed.

Quality control (QC) procedures will be implemented within the data collection and storage systems with quality control procedures. Any missing data or data anomalies will be investigated.

Noncompliance events that meet the IRB's reporting requirements must be reported to the IRB office within 10 working days of xCures becoming aware of the event.

8.2.4 Key Roles and Study Governance

VP, Clinical Development	**Lead Data Scientist**	**Legal and Compliance**
Mark Shapiro, MA, MBA	Asher Wasserman, PhD	Christopher Porter, JD, MBA
xCures, Inc.	xCures, Inc.	Porter Advisory Services
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Director of Research	**VP, Clinical Operations**	**CTO**
Jeff Schrager, PhD	Bryan Federowicz	Glenn Kramer, PhD
xCures, Inc.	xCures, Inc.	xCures, Inc.
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8.3 PROTOCOL AMENDMENT HISTORY

The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A Summary of Changes table for the current amendment is located in the Protocol Title Page.

Version	Date	Description of Change	Brief Rationale

9 REFERENCES

Gliklich RE, Dreyer NA, eds. Registries for Evaluating Patient Outcomes: A User's Guide. 2nd ed. (Prepared by Outcome DEcIDE Center [Outcome Sciences, Inc. d/b/a Outcome] under Contract No. HHSA29020050035I TO3.) AHRQ Publication No.10-EHC049. Rockville, MD: Agency for Healthcare Research and Quality. September 2010

Lim L, Pullenayegum E, Moineddin R, Gladman D, Silverman D, Feldman B. Methods for analyzing observational longitudinal prognosis studies for rheumatic diseases: a review & worked example using a clinic-based cohort of juvenile dermatomyositis patients. Pediatric Rheumatology 2017; 15:18

Sherman R, Anderson S, Dal Pan G, Gray G, Gross T, Hunter N, LaVange L, Marinac-Dabic D, Marks P, Robb M, Shuren J, Temple R, Woodcock J, Yue L, Califf R. Real-World Evidence: What Is It and What Can It Tell Us? NEJM 2016 Dec; 375(23):2293-7.

APPENDIX 1: INFORMED CONSENT AND ASSENT TEXT

xCures COVID-19 Registry Informed Consent

xCures is conducting a research study of people who may have the novel coronavirus COVID-19. This study involves many thousands of people. To be in the study you must be in the United States or US territories. If you sign up on the Web site, you can participate.

By signing up for this study, you will receive a series of emails with questions about your health. These are focused on symptoms thought to be caused by COVID-19 as well as any treatments or actions that you take to manage your health. You can share information that you think is important. We will collect the data and present summaries of how the COVID-19 virus affects people differently. No one will be individually identified, but reports may be created on how groups of people of different ages or with different health conditions experience the infection. We will also ask for geographic location (Zip Code) to understand how changing weather may alter the transmission of COVID-19.

Being in the study should not put you at risk, but because we collect some of your information, there is a risk of breach of confidentiality. To reduce this risk, your research information is stored in a secure and encrypted database. Information may be shared with other researchers in the future, but your identifying information will not be shared or disclosed outside of study team.

If you on longer want to be contacted or change your mind about being in the study, you can stop participating at any time by contact xCures via email or through an opt out on the study Web site. If you ask to stop, we will no longer contact information about you, but they will keep the information that has been collected for research purposes.

If you have questions about the study, you can ask COVID19-Registry@xcures.com. For questions about your rights as a participant in research, you can contact the Genetic Alliance IRB at 202.966.5557 or by email at info@geneticalliance.org.

By entering your information, clicking "I Agree" below and signing you are agreeing to the electronic consent form and to get important information about the study online. This process takes the place of traditional paper forms.

xCures is responsible for the study and for giving you notices, forms, and other information about your participation in the study. That information is already in this consent document (collectively, the "required information"). By electronically initialing this document, you are confirming that you agree:

(1) to receive online the required information, notices and other disclosures related to taking part in this research study;

(2) to continue to receive online any records, documents or other notices regarding the study until and unless you change your mind and withdraw your agreement by notifying xCures in writing; and

(3) to use an electronic signature in place of a handwritten signature to sign the form agreeing to participate in the study.

By entering your information and clicking on the "I agree" button, you confirm and agree to the above terms and conditions and agree that your electronic consent is the same as signing a paper consent form.

Agree to Participate? *Make one selection*

I have read the consent document and I wish to participate in the study

I have read the consent document and I DO NOT wish to participate in the study

I am the legally authorized representative for the participant listed below and have reviewed the study with them and they have verbally assented to be in the study

Participant First Name: **Participant Last Name:**

Legally Authorized Representative First Name (*if applicable*):

Legally Authorized Representative Last Name (*if applicable*):

Signature of Participant or Legally Authorized Representative:

Date of Signature:

APPENDIX 2: WEB SITE CONTENT

What is the COVID-19 Registry?

The COVID-19 Registry is a patient-centric research study designed to help us all of learn about how people experience the COVID-19 infection, including characteristics associated with risk and severity of infection.

What is xCures?

xCures is a precision medicine company based in Los Altos, California and Chapel Hill, North Carolina. We are a team of data scientists, software engineers, and biomedical scientists working to find out what treatments work for individual patients. Our team supports many non-profit patient advocacy organizations with their efforts to encourage and find treatments for the patients that they represent.

Why is xCures doing this?

There are a number of urgent and unanswered questions about COVID-19. While many small clinical trials are happening in hospitalized patients, there is an urgent need to understand the natural history and look for signals in a large dataset. We are all in this together and we need a large de-identified dataset made publicly available for qualified researchers and data scientists in real time.

How does xCures' COVID-19 Registry Work?

The COVID-19 Registry works by asking people to register online, contribute data about themselves, their health and any symptoms, and provide consent for the use of their data in this research study. People in the study will complete a daily survey by email. The information that is collected will be analyzed and shared with all study participants through updates at the Web site. Findings from the study will be submitted for peer review in medical or scientific journals.

Who can be in this study?

1.) *People who are feeling sick but have not tested positive for COVID-19*
2.) *People who are feeling sick and have tested positive for COVID-19*
3.) *People who are not feeling sick but want to participate*

What information will participants receive during the COVID-19 Registry?

We will present daily summary information at our Web site on where and how different groups experience symptoms, as well as treatments they are using to manage symptoms, other health conditions, and any interaction between symptoms and treatments. If sufficient information is available, we will present heat maps of symptoms at a geographic level that does not risk identifying individuals (First three numbers of Zip code).

How Participants provide data to the COVID-19 Registry?

Questions will be emailed to patients daily. In some cases, the research team may contact patients for additional information or to request permission to collect medical records associated with COVID-19 treatment or to contact their medical care provider to ask questions related to their treatment. Such requests will utilize a separate patient agreement providing legal authorization under HIPAA to access such records.

How will your data be kept secure?

All your personal information will be kept private and stored in encrypted form. Extensive efforts are undertaken to ensure data security including the use of validated systems that are HIPAA, FISMA, and 21 CFR 11 compliant. Analysis of data will be at the aggregate and/or group level and individually identifying information will be removed from analysis dataset.

What do I get from joining the COVID-19 Registry?

When you join the COVID-19 Registry you will get access to:

1.) A curated fact sheet that details current evidence potential treatments under study for COVID-19. This will be updated and available at the study website as knowledge emerges.

2.) Access to the combined data from all the study participants shared on an online dashboard

3.) An opportunity to collaborate to help us all learn quickly about what to do about COVID-19

Appendix 3: Planned Data Elements

1. Demographics
    a. Name: First, MI, Last
    b. Current age and Year of Birth (parity check (+/- 1-year accuracy) Or, 18 – 20, 21 – 29, 30 – 39, etc.…
    c. Gender M, F, Other
        i. If F, are you pregnant?
        ii. If F, are you nursing?
    d. Ethnicity: Are you Hispanic or Latino, Not Hispanic or Latino, Not Reported/Not Known
    e. Race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White or Caucasian, Other, Decline to answer
    f. Participant Contact
        i. Email address for surveys:
        ii. Phone number
        iii. May we contact you by phone or email for follow-up questions? Y/N
    g. Would you like to provide an alternate contact: Y/N, If Y:
        i. Name
        ii. Email
        iii. Phone
        iv. Relation: parent, guardian, other

2. Environment
    a. Are you currently in an area with under shelter-in-place recommendation? Y/N
        i. Do you leave the home regularly for work?
        ii. Do you work in any of the following settings? [List Clinic, Hospital, Nursing Home, Senior Care Facility, Other health or medical facility]
    b. In what city and state are you currently residing? (This may not be your home address but is the location where you are staying during the outbreak.)
    c. What is the Zip code where you currently reside?
    d. With how many people do you currently reside (not counting yourself)?
        i. Are any people in your household under age 18?
    e. Have you had contact with anyone known or suspected to have COVID-19 within the last two weeks?
    f. NEW Question: Are you feeling sick today? Y/N
        i. IF Y, when did you start feeling sick? Calendar widget. Note: we will start sending you surveys about your symptoms once you complete this intake form.

3. Health status
    a. Height and weight

b. For your age, how healthy are you 1-5 (much less than average, less than average, average, better than average, much better than average)
c. Do you smoke?
d. Do you exercise regularly?
e. Do you have or have you ever had any of the following problems with your:

i. (let's do a two-column table with a check box for things that they have in the med hx, and another column for currently taking medication for this condition).

ii. Lungs:
iii. Asthma
iv. COPD
v. Emphysema
vi. Lung disease or tuberculosis

vii. Immune system:
viii. Allergies
ix. HIV/AIDS
x. Transplant

xi. Heart and blood:
xii. Bleeding
xiii. High blood pressure
xiv. Heart disease
xv. Arrythmia or pacemaker
xvi. Stroke

xvii. Other medical conditions:
xviii. Alzheimer's Disease
xix. Cancer
xx. Kidney disease
xxi. Diabetes (T1 or T2)
xxii. Arthritis
xxiii. Liver disease or hepatitis
xxiv. Other medical conditions: free text

4. Do you take any prescription medications?
5. List (free text OK, we'll do NLP)

6. Daily Survey Questions:

7. Activity: Are you in an area under a shelter-in-place recommendation?

8. Travel: Did you go to work or school outside the house today? IF Y, how did you travel, walk, bicycle, bus, taxi/rideshare service, personal vehicle, subway/rail/train, air travel?

9. With how many people outside your immediate family did you interact today? 0, 1-3, 4-10, 10-20, 20+

10. Is anyone in your household sick with known or suspected COVID-19? Y/N

11. Physically, how have you been feeling today on a scale of 0-10?

12. What is your stress right now level on a scale from 0-10? (0 = no stress, 10 = as stressed as you can possibly imagine).

13. Are you concerned that you may be getting sick?

14. Have you sought care for or been tested for COVID-19? Y/N

15. If yes, did you have a rapid flu test? Was the flu test positive or negative? (not known)

16. Did you have a COVID-19 test? Result positive or negative? (not known)

17. Have you had any problems with the following (draw terms and rubric from validated scales CTCAE-PRO, TCS):

Your head, eyes, ears, nose and throat: Y/N, if Y:

a. Headache 0-3 scale (none, mild, moderate, severe)
b. Sore throat
c. Runny
d. stuffy nose
e. gritty/itchy eyes
f. watery eyes
g. Other problem:

Problems with your stomach, like nausea, vomiting, or diarrhea? Y/N if y:

h. Nausea
i. Vomiting
j. Diarrhea
k. Other:

Problems with your chest or lungs? Y/N, if Y

l. Sneezing:
m. Coughing: If mild+ symptoms then ask: wet or dry cough, if wet: blood in phlegm?
n. Shortness of breath
o. difficulty breathing:
p. Pain or pressure in your chest

q. Other problems:

r. Have you had other problems like fever, chills, aches and pains, or feeling tired/fatigued: Y/N, if Y:

s. Fever y/n if y: what was your temperature _ _ _. _
t. Chills
u. Body aches
v. Fatigue
w. Other issues: Free text_____ (NLP)

18.	no symptoms = 0	mild symptoms = 1	moderate symptoms = 2	severe symptoms = 3
19. runny nose				
20. stuffy nose				
21. sneezing				
22. itchy nose				
23. gritty/itchy eyes				
24. watery eyes				

25. Note: any serious scores should prompt them to contact medical assistance immediately.

26. Have you taken any of the following medications today?

	No	Yes
Did you use an oral antihistamine (e.g., Zyrtec, Allegra, Claritin, Benadryl, etc.) today?		
Dis you use eye drops (Visine, Clear Eyes, etc.) today?		
Did you use a nasal corticosteroid (Flonase) today?		

Did you use an over-the-counter multi-symptom cold/cough medication (Dayquil, Nyquil, Robitussin, etc.)		
Did you use a fever reducing medication (Advil, Tylenol, Aleve, or similar)?		

27. Are you taking other medications? Free text

28. Has a doctor prescribed any medications for your symptoms? Y/N if Y, type or upload photo of the label.

29. Are you using any nutritional supplements or other remedies? Y/N If Y: free text

30. Is there other information that you think is important to share? Y/N if Y free text for NLP.