FAQ for CCHS Network One World Registry "CCHS NOW Registry" Natural History Study

1. What is a Patient Registry?

A patient registry is a collection of standardized information about a group of patients who share a condition and is used for a variety of purposes such as conducting natural history studies and supporting disease specific clinical trial recruitment. *The CCHS Network One World Registry (CCHS NOW Registry) will collect patient information, securely and confidentially (see more below), to study CCHS.*

2. What is a Natural History Study?

A natural history study is a study designed to track the course of a disease over time and includes people who have a specific medical condition or disease and those who are at risk of developing such. This method of research explores the disease in a comprehensive way and identifies demographic, genetic, environmental, and other variables that correlate with the disease and its outcomes. Natural history studies have many potential uses such as patient care best practice developments and clinical trial recruitment.

3. What is a Longitudinal Study?

A longitudinal study is a research method in which data is gathered for the same subjects repeatedly over a period of time. Longitudinal research projects can extend over years or even decades.

4. What is a Research Study Sponsor?

An individual, company, institution, or organization that takes responsibility for choosing appropriately trained and experienced researchers as well as the initiation, management, and/or financing of a clinical trial. The study sponsor ensures that the study is conducted in a reputable manner and upholds regulations as they apply to the study.

5. Who is CCHS Network?

The CCHS Network, founded in 1989, is a non-profit, tax-exempt patient advocacy organization registered in the United States. The CCHS Network promotes communication across physician - patient communities in the US and around the world, while our CCHS Foundation and Research Advisory Board focus upon funding and facilitating critical CCHS research in the US and abroad. We have learned that sharing our CCHS challenges and successes through the CCHS Website and online discussion pages is an important source of inspiration and improved medical support for CCHS patients. Family discussions of high-tech homecare, medical issues and coping challenges have also yielded ideas for new areas of research on this rare disorder. By sharing

patient experiences, new research and healthcare strategies and information with families, physicians, and researchers around the US and the world, the CCHS Network provides the CCHS community with a meaningful and powerful voice.

6. Who is NORD® – the National Organization for Rare Disorders, Inc.?

The National Organization for Rare Disorders, Inc. (NORD®), an independent nonprofit, is leading the fight to improve the lives of rare disease patients and families. We do this by supporting the rare community, its people, and organizations. We work together to accelerate research, raise awareness, provide valuable information, and support, and drive public policy that benefits the estimated 25-30 million Americans impacted by rare diseases.

Learn more about NORD at https://rarediseases.org/.

7. What is a Principal Investigator?

The Principal Investigator is the research group leader or, the person with the primary responsibility for the design and conduct of the research project or study. Vandana Dole PhD (PI), Linda Dokas, PhD (Archivist), and Melinda Riccitelli, PhD (System Administrator) are sharing responsibility duties for the CCHS NOW Registry. If you have questions *at any time* about this Registry, please contact them at cchsnowregistry@cchsnetwork.org

8. What is an Institutional Review Board (IRB)?

Any board, committee, or other group formally designated by an institution or investigator to review, approve the initiation of, and to conduct periodic review of research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. Also known as Ethics Committee (EC).

9. What is a Registry Advisory Board?

A Registry Advisory Board/ or committee, that may include scientists, doctors, and patient advocates, will be assembled to oversee the conduct of the study. The Advisory Board will review aggregate registry data and the use of this registry, ensure proper evaluation of protocols requesting to use registry data and/or contact registry participants, and will review any protocol or confidentiality deviations on a case-by-case basis and ensure that any such deviations are reported to the IRB.

10. What is the purpose of the CCHS NOW Registry?

One of the most important purposes of the CCHS NOW Registry is to bring the CCHS community together and collect data which could be used to create therapeutics and improve the quality of life for patients. Some other goals of the CCHS NOW Registry are to:

- Conduct a prospectively-planned natural history study that will result in the most comprehensive understanding of CCHS and its progression over time.
- Characterize and describe the CCHS population as a whole.
- Assist the CCHS community with the development of recommendations for standards of care.
- Assist researchers studying the pathophysiology of CCHS.
- Assist researchers studying interventional outcomes.
- Support the design of clinical trials for new treatments.

11. What types of data will be collected in the CCHS NOW Registry?

The data collected is uniform and includes but is not limited to:

- Socio-demographics
- Medical and diagnostics
- Treatment and disease progression
- Management of care
- Quality of life

12. What might be some benefits of this study to me?

Because CCHS is a rare disorder, effective research into the phenotype, pathophysiology, effectiveness of treatments, etc., requires the accumulation of data from a broad cohort of participants. There are no direct benefits associated with participation in the CCHS Network One World Registry and individual participants should not expect a direct benefit. The CCHS NOW Registry will facilitate collaboration between clinicians at multiple sites as well as assist in recruitment of participants for clinical trials. Conceivable benefits include the potential for future studies that will significantly increase understanding of therapeutic options for CCHS patients. The use of information contained within the CCHS NOW Registry for retrospective research analyses may be of future benefit to patients with CCHS. In addition, participants in the CCHS NOW Registry will be informed of future research studies involving CCHS for which they may be eligible. Certain participants may directly benefit from inclusion in future treatment studies that result from the registry, and for which separate informed consent will be obtained.

13. What are some risks of the study?

There are no risks of physical harm associated with participation in the study. The registry surveys may ask questions about the impact of CCHS on your daily life, your economic status, mood, and other topics that you may find unpleasant or disquieting. Participation in the CCHS NOW Registry does involve the potential risks of a breach of confidentiality of medical

information and associated privacy of participants. Such risks will be minimized by ensuring adherence to applicable regulations and data security measures and by performing the following: (1)removing direct participant identifiers from information and data shared or released from the registry; (2)limiting access to linking codes assigned to the CCHS NOW Registry information; (3)and limiting access to information contained within the CCHS NOW Registry to registry investigators and researchers approved by the Advisory Board, and (4) Maintaining the Privacy and Confidentiality of Registry information as described below.

14. How is the data collected?

Data is collected through a secure web-based system developed by the National Organization for Rare Disorders, Inc. (NORD®), an independent non-profit committed to the identification, treatment, and cure of all 7,000 rare diseases. Study participants respond to questions grouped within a series of surveys developed per study standards and in collaboration with disease specific experts.

15. How is the Patient Registry maintained?

The registry is maintained by NORD who hosts the registry on its cloud-based Platform and provides oversight and ongoing support of the system. CCHS Network provides the day-to-day management of their patient registry, including the development and adherence to the study procedures.

16. Who is a Study Participant?

A study participant is the individual who takes part in a research study and whose information is collected for that research. Study participants may consent to enter and share their own personal data. *In the CCHS Now Registry the CCHS patient is the study participant.*

17. Who is a Reporter/Respondent?

A reporter/respondent is an individual who completes the surveys on behalf of the patient/study participant, when they are unable to do so on their own behalf. *In the CCHS NOW Registry a CCHS parent or Legal Representative (see more below) of a minor CCHS patient or a CCHS patient who cannot answer for him/herself is the reporter/respondent.*

18. What is a Legally Authorized Representative (LAR)?

An individual who is authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial. The LAR may be a parent, grandparent, spouse, caregiver, or guardian who has the legal authority to grant consent on behalf of another who is eligible to participate in research. When a LAR acts on behalf of a study participant, they are considered to be the reporter/respondent in the research.

19. What is an Informed Consent?

An informed consent is a document that provides potential participants in a research study information about the study so that participants can make a voluntary, knowledgeable decision to join the study or not. Some (not all) of the information that an informed consent includes are the risks and benefits of the research project, how data will be handled, ethical considerations, the duration of the study, economic considerations, how the study will be conducted, and how data will be used.

20. Do I have to sign the CCHS NOW registry informed consent to participate in the study?

Yes, in order to participate in the CCHS NOW Registry you must sign the informed consent. Two consents are available: one for adult CCHS patients and one for minor/dependent CCHS patients. If you are a CCHS adult, you will sign the informed consent for adults. If the CCHS patient is a minor or a dependent, the legal representative of the patient (most of the time a parent) will sign the Legally Authorized Representative (LAR) consent form.

If after reading the informed consent you are confused or have questions about the CCHS NOW Registry informed consent process or research project, please direct these inquiries to study investigators at, cchsnowregistry@cchsnetwork.org.

Participation in this research project is completely voluntary.

21. Who can join the Registry?

This registry is open to anyone who has a Congenital Central Hypoventilation Syndrome (CCHS) diagnosis.

For the purpose of this registry, CCHS is defined as:

- Disease status by genetic testing to confirm PHOX2B mutation, OR;
- Disease status by clinical diagnosis

To participate you must also be:

- Willing to provide informed consent
- Able to comply with web-based study procedures and data collections

22. Is there a cost to participate?

There is no cost to the patient to join this study. The CCHS Network absorbs the cost of the registry for its members.

23. How long will this study last?

This registry will be open for at least five years with the option to renew registration. There is

no date of termination or closure at this time.

24. How long will it take to complete questionnaires?

You should anticipate each survey section taking between 10 and 30 minutes to complete.

25. Do I have to answer all survey questions asked?

Participation in this registry is completely voluntary. Although some questions are required, as a study participant you have the right to not answer survey questions that make you uncomfortable and/or you choose not to answer.

26. Can data be collected worldwide?

The patient registry uses an online platform which allows participants to contribute data from anywhere in the world. Individuals from other countries who enter data into the registry should be aware that data and privacy laws are different in the U.S. from other countries. This U.S. based registry will protect data and privacy according to U.S. requirements.

27. Where is the data stored?

The data is stored on NORD's registry platform system which adheres to industry standards regarding security protections.

28. Is the data safe?

The registry follows strict government guidelines to assure patient information is protected. The platform is served over HTTPS, which provides traffic encryptions so as to prevent eavesdropping and man-in-the-middle attacks. Communications between the registry platform application server and the database are also encrypted. As with any information you provide electronically, there is a risk that your privacy could be compromised, however the registry is designed to minimize the chance of this occurring.

29. Is the data collected by the CCHS NOW Registry kept confidential?

Yes, your data is kept confidential from the public. Confidentiality is protected by limiting access to data and keeping Personal Health Information (PHI) data password protected on a secure server. Access to PHI in the database will be limited to the sponsor's registry research team (see above – "What is a Principal Investigator") via password protected security measures. Data will be maintained on the NORD Natural History Studies platform, which meets or exceeds current guidelines for maintaining security of PHI. **Only** aggregated, de-identified data will be shared with the public as general descriptive statistics regarding database contents. De-identified data will be shared with NORD. PHI will be associated with a unique identifier that is assigned by registry staff to further obscure patient identity. The file linking the unique identifier and the PHI will be kept in a separate password protected database.

While data is kept confidential, a unique feature of the CCHS NOW Registry is that participants, can see the data collected as it is being collected (in an anonymous format, once 10 patients have enrolled), empowering patients with information in real time. This feature is not typical of most registries where data collected is concealed from participants until the time the researcher published the results.

30. Who owns the data?

The identifiable and de-identifiable data are owned by the study sponsor, **CCHS Network**. CCHS Network decides how and with whom to share the data. A subset of the pseudonymized data collected across the NORD Registry Platform is available to NORD to support cross disease analysis and advocacy activities to members of the rare disease community as a whole. Participants are able to withdraw from the study at any time, however, the researchers may still use the information that they have collected prior to changing your mind in order to complete the research that has already started. Information that has already been shared with collaborative groups or sent to a researcher for a specific study prior to your request for removal cannot be retrieved or removed.

31. Who will be able to use this data?

One of the goals of this registry is to gather and disperse CCHS information as quickly and securely as possible. In agreement with the standards set by NORD and the IRB, we intend a free sharing of de-identified data with any researcher who asks for it for a legitimate reason. The CCHS Network in collaboration with the CCHS NOW Registry Advisory Board (comprised of CCHS clinical and research experts, CCHS patients, and CCHS family advocates) will review request for access to de-identified data from researchers. Investigators wanting to use the registry or contact participants will need to apply to the CCHS NOW Advisory Board for access. The application will require information concerning: Principal Investigator, aims and hypotheses of the proposed research, and where the research will be performed, and how the research will be funded. The CCHS NOW Advisory Board will review and approve applications based on study quality, potential, and value to CCHS.