eRESEARCH | REGULATORY MANAGEMENT

Date: Monday, December 5, 2022 3:35:57 PM Print Close

View: 01. General Study Information
Section: 01. General Study Information

01. General Study Information

The forms menu on the left displays all sections and pages of the application. Pages in **bold** are required. Pages in *italics* may not apply to your project. Use the "Continue" button to advance through the smartform, as it will only display the sections that must be completed.

All questions marked with a red asterisk (*) are required. Questions without a red asterisk may or may not be required, depending on their relevance to the study.

1.1* Study Title:

OUR HHT Registry

1.1.1 Full Study Title:

Hereditary Hemorrhagic Telangiectasia (HHT) Research Outcomes Registry

1.1.2 If there are other U-M studies related to this project, enter the eResearch ID number (HUM#) or IRBMED Legacy study number. Examples of related projects include, but are not limited to:

- Projects funded under the same grant
- IRBMED Legacy study being migrated into eResearch
- Previously approved Umbrella applications (such as Center Grants or approvals for release of funding)
- Previously approved projects for which this is a follow up study

1.1.3* Does this application include the study of COVID-19?

For example:

- **testing or studying the COVID-19 virus,**
- **exploring treatment options,**
- **studying the impact of the COVID-19 pandemic (This could included epidemiological, social, behavioral, or educational research).**

Note: Answer "Yes" only if this project includes the study of COVID-19. Inclusion of study procedures solely intended to allow the research to be conducted under pandemic constraints, such as remote interactions with subjects, remote consenting, or at-home drug delivery are not considered the study of COVID-19.

○ Yes ● **No**

1.2* Principal Investigator:

Suman Sood
Note: If the user is not in the system, you may Create A New User Account...

1.3 Study Team Members:

Study Team Member	Study Team Role	Appointment Dept	Appointment Selection Complete?	Student	Friend Account	COI Review Required	Edit Rights	Accepted Role?	PEERRS Human Subjects?
Suman Sood	PI	MM Int Med-Hematology/Oncology	Yes	no	No	no	yes	N/A	yes
James Munn	Co-Investigator	MM CW Hemophilia/COAG CMS	Yes	no	No	no	yes	Yes	no
Melissa Pynnonen	Co-Investigator	MM Otolaryngology - HNS	Yes	no	No	no	no	Yes	yes
Neil Sheth	Co-Investigator	MM Int Med-Gastroenterology	Yes	no	No	no	yes	Yes	yes
Mark Zacharek	Co-Investigator	MM Otolaryngology - HNS	Yes	no	No	no	yes	Yes	yes

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Study Team Member	Study Team Role	Appointment Dept	Appointment Selection Complete?	Student	Friend Account	COI Review Required	Edit Rights	Accepted Role?	PEERRS Human Subjects?
Zachary Tigani	Study Coordinator/Project Manager	MM CW Hemophilia/COAG CMS	Yes	no	No	no	yes	Yes	yes

1.8* Project Summary:

HHT has an estimated prevalence of 1 in 5000, affecting children and adults, in multiple organs. The disease is characterized by the presence of vascular malformations (VMs), including arteriovenous malformations (AVMs) of the lung, liver, brain, spinal cord and smaller mucosal lesions (telangiectasia) of the nose, mouth and GI tract.

The purpose of this study is to prospectively and longitudinally characterize major outcomes of Hereditary Hemorrhagic Telangiectasia (HHT), including frequent symptoms (epistaxis, migraines, etc.) as well as severe complications (death, stroke, heart failure, anemia, etc.), and identify their determinants. Furthermore, to identify predictors of epidemic/pandemic infections amongst HHT patients and the effects on; epistaxis (severity, topical nasal medication, nasal intervention, etc); disease severity (hospital admission, requiring ventilation, venous thromboembolism, death); HHT outcome and care (health care utilization, access to care, screening, preventative treatment).

Baseline clinical and demographic data will be collected from participating HHT patients along with annual outcomes data, and entered into the Our HHT registry. For subjects who agree to give a saliva sample, the goal is to create a DNA repository of HHT subjects as a resource for future genetic, pharmacogenetics and targeted therapy studies and replicate and further characterize genetic associations with HHT phenotypes

1.9* Select the appropriate IRB:

IRBMED

1.11* *Estimated* Duration of Study:

10 years

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Section: 01. General Study Information

Study Team Detail

1.4 Team Member:

Suman Sood

Preferred email: sumisood@umich.edu
Business phone 734-615-2681
Business address: UMH Int Medicine-Hem/Onc MIB C351A 48109-5848

1.5 Function with respect to project:

PI

1.6 Allow this person to EDIT the application, including any supporting documents/stipulations requested during the review process:

Yes

Credentials: Required for PI, Co-Is and Faculty Advisors

Upload or update your CV, resume, or biographical sketch.

Name	Version
Suman Sood M-CV 032322.pdf(0.12)	0.12

Conflict of Interest Detail: Required for all roles except Administrative Staff

Current Disclosure Status in M-Inform: *This study team member has disclosed outside interest(s) or relationship(s) in M-Inform.*

D1 Do you or your family members **have an** outside activity, relationship, or interest **with a** non-UM entity**, where the non-UM entity:**

- Provides financial or non-financial support for this project;
- Supplies a product used in this project (e.g., an app, device, compound, drug, software, survey, evaluation) either for free or at a cost (e.g., purchased);
- Holds an option or license to intellectual property used in this project (e.g., a device, compound, drug, software, survey, evaluation, code, data, schematics, algorithms) that you or your family member developed;
- Will perform work on this project (e.g., subcontract, service agreement, unfunded agreement); or
- Has a financial stake in the outcome of this research?

No

D2 If "Yes" to the question above, provide the name of the outside entity or entities and a brief description of the interest/relationship(s):

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Section: 01. General Study Information

Study Team Detail

1.4 Team Member:

James Munn

Preferred email: jmunn@umich.edu
Business phone 734-764-9311
Business address: UMH Hemophilia/Coag Program L2110 Womens SPC 5238 48109-4257

1.5 Function with respect to project:

Co-Investigator

1.6 Allow this person to EDIT the application, including any supporting documents/stipulations requested during the review process:

Yes

1.7 Include this person on all correspondences regarding this application: (Note: This will include all committee correspondence, decision outcomes, renewal notices, and adverse event submissions.)

Yes

Credentials: Required for PI, Co-Is and Faculty Advisors

Upload or update your CV, resume, or biographical sketch.

Name	Version
CV-jim.doc(0.05)	0.05

Conflict of Interest Detail: Required for all roles except Administrative Staff

Current Disclosure Status in M-Inform: *This study team member has disclosed outside interest(s) or relationship(s) in M-Inform.*

D1 Do you or your family members **have an** outside activity, relationship, or interest **with a** non-UM entity**, where the non-UM entity:**

- Provides financial or non-financial support for this project;
- Supplies a product used in this project (e.g., an app, device, compound, drug, software, survey, evaluation) either for free or at a cost (e.g., purchased);
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- Will perform work on this project (e.g., subcontract, service agreement, unfunded agreement); or
- Has a financial stake in the outcome of this research?

No

D2 If "Yes" to the question above, provide the name of the outside entity or entities and a brief description of the interest/relationship(s):

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Study Team Detail

1.4 Team Member:

Melissa Pynnonen

Preferred email: pynnonen@umich.edu
Business phone 734-936-8050
Business address: UMH Otorhinolaryngology 1904 TC SPC 5312 48109-5312

1.5 Function with respect to project:

Co-Investigator

1.6 Allow this person to EDIT the application, including any supporting documents/stipulations requested during the review process:

No

1.7 Include this person on all correspondences regarding this application: (Note: This will include all committee correspondence, decision outcomes, renewal notices, and adverse event submissions.)

Yes

Credentials: Required for PI, Co-Is and Faculty Advisors

Upload or update your CV, resume, or biographical sketch.

Name	Version
Melissa A Pynnonen DV 2017(0.06)	0.06
Pynnonen Biosketch 2012(0.01)	0.01
Pynnonen CV(0.03)	0.03
Pynnonen CV10_23_09.doc(0.02)	0.02

Conflict of Interest Detail: Required for all roles except Administrative Staff

Current Disclosure Status in M-Inform: *This study team member has disclosed outside interest(s) or relationship(s) in M-Inform.*

D1 Do you or your family members **have an** outside activity, relationship, or interest **with a** non-UM entity**, where the non-UM entity:**

- Provides financial or non-financial support for this project;
- Supplies a product used in this project (e.g., an app, device, compound, drug, software, survey, evaluation) either for free or at a cost (e.g., purchased);
- Holds an option or license to intellectual property used in this project (e.g., a device, compound, drug, software, survey, evaluation, code, data, schematics, algorithms) that you or your family member developed;
- Will perform work on this project (e.g., subcontract, service agreement, unfunded agreement); or
- Has a financial stake in the outcome of this research?

No

D2 If "Yes" to the question above, provide the name of the outside entity or entities and a brief description of the interest/relationship(s):

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Study Team Detail

1.4 Team Member:

Neil Sheth

Preferred email: neilshet@umich.edu
Business phone 734-647-9252
Business address: Gastroenterology 3912 Taubman Ctr 48109-5362

1.5 Function with respect to project:

Co-Investigator

1.6 Allow this person to EDIT the application, including any supporting documents/stipulations requested during the review process:

Yes

1.7 Include this person on all correspondences regarding this application: (Note: This will include all committee correspondence, decision outcomes, renewal notices, and adverse event submissions.)

Yes

Credentials: Required for PI, Co-Is and Faculty Advisors

Upload or update your CV, resume, or biographical sketch.

Name	Version
M-CV NSheth Current July 2020.pdf(0.01)	0.01

Conflict of Interest Detail: Required for all roles except Administrative Staff

Current Disclosure Status in M-Inform: *This study team member has indicated in M-inform that they do not have any outside interests to disclose.*

D1 Do you or your family members **have an** outside activity, relationship, or interest **with a** non-UM entity**, where the non-UM entity:**

- Provides financial or non-financial support for this project;
- Supplies a product used in this project (e.g., an app, device, compound, drug, software, survey, evaluation) either for free or at a cost (e.g., purchased);
- Holds an option or license to intellectual property used in this project (e.g., a device, compound, drug, software, survey, evaluation, code, data, schematics, algorithms) that you or your family member developed;
- Will perform work on this project (e.g., subcontract, service agreement, unfunded agreement); or
- Has a financial stake in the outcome of this research?

No

D2 If "Yes" to the question above, provide the name of the outside entity or entities and a brief description of the interest/relationship(s):

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Study Team Detail

1.4 Team Member:

Mark Zacharek

Preferred email: zacharek@umich.edu
Business phone 734-232-0120
Business address: Otoloryngology 1904 TC 48109-5312

1.5 Function with respect to project:

Co-Investigator

1.6 Allow this person to EDIT the application, including any supporting documents/stipulations requested during the review process:

Yes

1.7 Include this person on all correspondences regarding this application: (Note: This will include all committee correspondence, decision outcomes, renewal notices, and adverse event submissions.)

Yes

Credentials: Required for PI, Co-Is and Faculty Advisors

Upload or update your CV, resume, or biographical sketch.

Name	Version
M_Zacharek%2520Updated%2520CV%2520December%25202012%2520[1][1].doc(0.01)	0.01
Mark Zacharek, MD CV 12-2010(0.01)	0.01
Zacharek CV - 23SEP2021(0.01)	0.01

Conflict of Interest Detail: Required for all roles except Administrative Staff

Current Disclosure Status in M-Inform: *This study team member has disclosed outside interest(s) or relationship(s) in M-Inform.*

D1 Do you or your family members **have an** outside activity, relationship, or interest **with a** non-UM entity**, where the non-UM entity:**

- Provides financial or non-financial support for this project;
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- Will perform work on this project (e.g., subcontract, service agreement, unfunded agreement); or
- Has a financial stake in the outcome of this research?

No

D2 If "Yes" to the question above, provide the name of the outside entity or entities and a brief description of the interest/relationship(s):

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View: VIEW000072_customAttributes._attribute186_Study Team Detail
Section: 01. General Study Information

Study Team Detail

1.4 Team Member:

Zachary Tigani

Preferred email: zyj@umich.edu
Business phone
Business address: 48109

1.5 Function with respect to project:

Study Coordinator/Project Manager

1.6 Allow this person to EDIT the application, including any supporting documents/stipulations requested during the review process:

Yes

1.7 Include this person on all correspondences regarding this application: (Note: This will include all committee correspondence, decision outcomes, renewal notices, and adverse event submissions.)

Yes

Credentials: Required for PI, Co-Is and Faculty Advisors

Upload or update your CV, resume, or biographical sketch.

Name	Version
There are no items to display	

Conflict of Interest Detail: Required for all roles except Administrative Staff

Current Disclosure Status in M-Inform: *This study team member has not yet disclosed in M-Inform.*

D1 Do you or your family members **have an** outside activity, relationship, or interest **with a** non-UM entity**, where the non-UM entity:**

- Provides financial or non-financial support for this project;
- Supplies a product used in this project (e.g., an app, device, compound, drug, software, survey, evaluation) either for free or at a cost (e.g., purchased);
- Holds an option or license to intellectual property used in this project (e.g., a device, compound, drug, software, survey, evaluation, code, data, schematics, algorithms) that you or your family member developed;
- Will perform work on this project (e.g., subcontract, service agreement, unfunded agreement); or
- Has a financial stake in the outcome of this research?

No

D2 If "Yes" to the question above, provide the name of the outside entity or entities and a brief description of the interest/relationship(s):

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View: 01-1. Application Type
Section: 01. General Study Information

01-1. Application Type

1-1.1* Select the appropriate application type.

	Application Type	Description
☑	Human Subjects research **involving interaction or intervention** *(formerly Standard, non-exempt research project - or - Exempt)*	Studies that involve either or both of the following: • Interaction, including communication or interpersonal contact between investigator and subject • Intervention, including both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or subject's environment that are performed for research purposes Interaction/Intervention studies may also have a "secondary research" component.

Does the research involve any of the following:

a. more than minimal risk to participants?
b. use of drugs or medical devices?
c. target prisoners as research subjects?
d. collection of biospecimens from subjects (including blood, saliva, cheek swabs)?

● **Yes** ○ No

☐	**Secondary research** uses of private information or biospecimens	"Secondary research" are studies that involve ONLY re-using private information and/or biospecimens that are collected for some other "primary" or "initial" activity, such as other earlier research studies, a biorepository holding specimens obtained with "broad consent," clinical care, or educational records. Includes Exemption 4 and "not regulated" projects. **Do NOT use this application type for:** • Studies that **also** have an interaction/intervention component, such as primary collection of information or biospecimens for the purposes of the study. (Choose instead "Human subjects research involving **interaction or intervention**.") • Projects involving secondary use of information/biospecimens for **only non-research purposes**, such as QA/QI, case studies on one or two individuals, or use in a class to teach research methods. (Choose instead "Activities **not regulated** as human subjects research.")
☐	Activities **Not Regulated** as human subjects research	Not all activities that involve people, their data, or specimens are covered by the regulations governing human subjects research (45 CFR 46 or 21 CFR 50/56). **IRB review is required** for the following activities **ONLY** to assess compliance with **HIPAA** or other regulations or institutional policies: • Research on existing data or specimens that have been coded before the researcher receives them, but identifiers still exist. • Research Involving Deceased Individuals Only • Pre-review of Clinical Data Sets Preparatory to Research • Standard Public Health Surveillance or Prevention Activities **IRB review is not required for the following activities**, but researchers may wish complete this brief application to generate a determination letter for funding or publication purposes, or to

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		request IRB review to confirm the "Not Regulated" determination: • Case Studies • Class Activities • Journalism/Documentary Activities • Oral History • Quality Assurance and Quality Improvement Activities • Research on Organizations • Research using Publicly Available Data Sets
☐	Projects **lacking immediate plans for involvement of human subjects**, their data, and/or their specimens	Activities such as training grants, program projects, center grants, or multi-phase studies not involving human subjects until later years. Before release of funding, some agencies may require IRB acknowledgement of the future use of human subjects. These projects are sometimes referred to as "umbrella projects" or "dry applications."
☐	**Single-patient Expanded Access Drug or Biologic (Emergency Use or Non-Emergency/Compassionate Use)**	Use of an investigational drug or biologic, outside of a clinical trial, under a single-patient IND issued by the FDA for a patient faced with a serious or life-threatening disease or condition. • Contact the IRB Chair-on-Call as soon as possible once the decision to use the investigational drug or biologic is made. • Submission for IRB review and approval is required, prior to use if feasible. **If this was an emergency use, submit no later than five days after use of the investigational agent.** • This includes both one-time use and continuing therapy.
☐	**Single-patient Expanded Access Device Use (Emergency Use or Non-Emergency/Compassionate Use)**	Use of an investigational device, outside of a clinical trial, when this is the only option available for a patient faced with a serious or life-threatening disease or condition. • Contact the IRB Chair-on-Call as soon as possible once the decision to use the investigational device is made. • Submission for IRB review and approval is required, prior to device use if feasible. **If this was an emergency use, submit no later than five days after use of the investigational device.** • This includes both one-time use and continuing therapy.
☐	**Humanitarian Use Device** (HUD) under a HDE	Non-research, on-label use of an HUD under a Humanitarian Device Exemption (HDE)
☐	Requesting Review by a **Non-UM IRB**	Use ONLY to request deferral of IRB oversight for UM activities to a non-UM IRB or when UM is a performance site in a multisite research project where UM is the lead site.
☐	**Multi-site Research** where U-M is a Coordinating Center and/or IRB of Record	Do not use Multi-site Research application type when U-M is **only** a performance site - select Standard application type. Select when U-M is any of the following: • Data Coordinating Center; • Clinical Coordinating Center; or • IRB of Record for non-U-M sites (for U-M to be IRB of Record you must contact your IRB for prior acknowledgement). When U-M is **also** a performance site, a separate application is required for local site considerations. Refer to special requirements at the IRB website.

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View: 01-2. Standard Study Information
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01-2. Standard Study Information

1-2.1* Who initiated this study?

National cooperative group (clinical)

1-2.2* Are you or any students working on this project being paid from a federally funded training grant?

◯ Yes ● **No**

1-2.3 This study is currently associated with the following department. To associate this research with a different department, click Select. If the department has defaulted to "student", click select to specify the department through which this application is being submitted.

Unknown

1-2.4 Will the study utilize resources from the following centers?

Select all that apply:

There are no items to display

1-2.5* Is the study related to cancer, cancer risk, or cancer care delivery?

◯ Yes ● **No**

1-2.6* Does this study require review by the Rogel Cancer Center Protocol Review Committee (PRC)?

◯ Yes ● **No**

1-2.7* Has the scientific merit of this study already been peer reviewed (i.e., reviewed by one or more recognized authorities on the subject)?

● **Yes** ◯ No

1-2.7.1* List the peer-review organization(s).

Peer Review Organization
External sponsor review process (e.g. study section)
Other (explain below)

Peer Review By CureHHT Foundation

IRB approved by St. Michael's Hospital Research Ethics Board

1-2.8* Is this a clinical trial?

◯ Yes ● **No**

1-2.9* Would the integrity of this research study be compromised if the subject were able to view results of their research tests or medications in the Patient Portal of MyUofMHealth.org? Research results displayed to the subject in MyUofMHealth.org will include: lab results, radiology examinations and outpatient medication lists. Contracts and protocols should be assessed by the Principal Investigator for specific language regarding blinding of subjects and their research results.

(NOTE: Additional actions are required in order to limit the subject's view into their electronic medical record. Contact the IRB for additional information or see additional guidance for blinded studies at** https://az.research.umich.edu/medschool/guidance/guidance-blinded-studies**)

◯ Yes ● **No**

1-2.10* Does the study involve administration of a cell therapy product?

◯ Yes ● **No**

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View: 02. Sponsor/Support Information
Section: 02. Sponsor/Support Information

02. Sponsor/Support Information

The following sections request details about the current or pending sponsorship/support of this study. Consider all of the choices below and complete the appropriate sections.
*** Note: At least one of the following sections must be answered. Multiple forms of funding or support must be added one at a time.**

2.1 Please select all Proposal Approval Forms (PAFs), Awards (AWDs), and/or Unfunded Agreements (UFAs) associated with this study.

☐ **Click here to indicate that a PAF(s) has not been initiated.**

Related PAFs:

ID	Title	PI	Direct Sponsor	Prime Sponsor	State	Has SUBKs?	Related Awards
18-PAF08760	Multidisciplinary HHT Care through Hemophilia Treatment Centers: A Pilot Project	Suman Sood	Cure HHT		Awarded	no	AWD016993 (9/30/2019 - 9/29/2021) AWD012515 (9/30/2015 - 9/29/2020)

Related AWDs:

Award ID	Title	PI	Direct Sponsor	Prime Sponsor	State	Has SUBKs?	Project Period	Awarded PAFs
There are no items to display								

Related UFAs:

UFA ID	Title	PI	State	Category	Start Date	End Date
22-UFA01123	OUR HHT Registry	Suman Sood	Active	Data Use Agreement	11/1/2021	1/1/2030
22-UFA01143	OUR HHT Registry	Suman Sood	UFA Hold	Material Transfer Agreement		

2.2 Internal UM Sponsor(s)/Support: [Including department or PI discretionary funding]

Type	Department Sponsor	Support Type
There are no items to display		

2.3 Check here if the proposed study does not require external or internal sponsorship or support:

☐

2.4* Is there any other financial or non-financial sponsorship or support not covered in the sections above?

○ Yes ● **No**

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View: 03. UM Study Functions
Section: 03. Performance Sites

03. UM Study Functions

3.1* Indicate all functions that will be performed at University of Michigan locations.

Select all that apply:
Recruitment (including screening)
Interaction (e.g., information gathering, survey, interview, focus groups, etc.)
Intervention (e.g., use of drug or device, medical procedures, educational intervention, group intervention, social/psychological intervention etc.)
Secondary data collection (e.g., medical chart review, data abstraction from existing records, etc.)
Primary or secondary analysis (data/specimen)

If other, please specify.

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View: 03-1. Performance Sites
Section: 03. Performance Sites

03-1. Performance Sites

3-1.1* Performance Sites:

Location	Country	"Engaged" in the research?	Performance Site Type	Site Function
University of Michigan	USA	yes		Intervention,Interaction,Analysis,Secondary data collection,Recruitment

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View: Performance Site Detail
Section: 03. Performance Sites

Performance Site Detail

3-1.2* Location or Institution:

University of Michigan

3-1.3 Address:

City
State
Country* USA

3-1.4* Function of this location with respect to this study:

Select all that apply:
Recruitment (including screening)
Interaction (e.g., information gathering, survey, interview, focus groups, etc.)
Intervention (e.g., use of drug or device, medical procedures, educational intervention, group intervention, social/psychological intervention etc.)
Secondary data collection (e.g., medical chart review, data abstraction from existing records, etc.)
Primary or secondary analysis (data/specimen)

If other, please specify:

3-1.5* Will this site be "engaged" in the conduct of the research?

● **Yes** ○ No

3-1.6 If known, provide the Federalwide Assurance (FWA) number for this location.

FWA00004969

3-1.7 If applicable, indicate what organization, agency or government office has reviewed this research and provided its approval (e.g., IRB, ethics committee, school district office, prison official, nursing home administrator).

3-1.8 Upload any location site approval documentation here:

Name	Version
There are no items to display	

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View: 05. Research Design
Section: 05. Research Design

05. Research Design

5.1* Is there a stand-alone scientific protocol document and/or research plan associated with this application?

● **Yes** ○ No

5.1.1* Click ADD to attach the document(s) electronically.

Name	Version
OUR Registry Protocol(0.03)	0.03

5.1.2* Indicate the section where each of the following are covered in the attached protocol:

Objective	2.0 Study Aim
Specific Aim/Hypothesis	2.0 Study Aim
Background Information	1.0 Background and Rationale
Methodology	4.0 Recruitment Enrollment and Study Design 5.0 Data Collection 7.0 Sample Collection and Processing 11.0 Data Analysis
Statistical Design	3.0 Registry Design 4.0 Recruitment Enrollment and Study Design 5.0 Data Collection

5.1.3* Study team Experience: Briefly outline the experience and competence of the study team to pursue the proposed study.

Zach Tigani - 5 years collecting and inputing patient data into registries for CDC funded research. Experience consenting patients for research studies.

Suman Sood, MD - PI- > 10 years experience as a PI on registry studies, experienced clinician in the care of patients with HHT

5.2* Will the involvement of ANY subjects in this study be limited to analysis of their existing data or specimens?

○ Yes ● **No**

5.3* Will the study involve recruitment and/or participation of subjects in order to produce new data (e.g., surveys, interaction, intervention)? *[Require sections 8-1 and 11-3]*

● **Yes** ○ No

5.4* List the inclusion and exclusion criteria for this study population and/or data set. (If covered in attached protocol, indicate section)

Inclusion Criteria:
Patients diagnosed with HHT by the Curacao criteria (either 3+ clinical diagnostic criteria or genetic diagnosis).
Capable of giving informed consent in person or via a substitute decision maker
>18 years

Exclusion Criteria:
Patients unable to give informed consent either in person or with a substitute decision maker

5.5 Identify any racial, ethnic, or gender group(s) that will be specifically excluded from participation in this research study and provide a compelling justification for such exclusion:

none

5.6* Indicate the age range (in years) of the subject population in this study.

Minimum Age: 18
Maximum Age: 999If no upper limit, enter "999"

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View: 06. Benefits and Risks
Section: 06. Benefits and Risks

06. Benefits and Risks

6.1 * Describe the potential benefits of this research to society.

The benefit of this research is that it will allow the HHT community and researchers to further their knowledge and understanding of HHT, the symptoms and complications it causes ("outcomes") and how the disease impacts people's lives.

There is a remote chance that new information could be discovered from DNA sequencing, participants will have a choice of receiving the new information and findings. The discovery of new information accidental or targeted will be returned to a participant who chooses to receive the new information.

Additionally, while there may be no direct benefit to a participant, their information will help researchers to quickly identify individuals who may be suitable for a particular future research study.

6.2 * Will results of the research be communicated back to the subjects?

● **Yes** ○ No

6.2.1 * Explain the plan and process.

There is a remote chance that new information could be discovered from DNA sequencing, participants will have a choice of receiving the new information and findings. The discovery of new information accidental or targeted will be returned to a participant who chooses to receive the new information. The DNA sequencing site (St. Michael's), will receive anonymized data. The coordinating site will use the master linking log on site to identify the participant. The study doctor will discuss the findings with the participant. Since receiving information regarding the discovery of inherited changes in DNA may cause the participant or family members psychological distress, to mitigate any distress, the study team will connect the participant or family members to genetic counselors for support if required

6.3 * Describe any direct risks to the public or community, which could result from this research?

There are no harms to participating in this registry. However, there is a small risk of the unintentional release of information. The chance that this information will be accidentally released is small.

6.4 * Does this project involve study arms that have differing levels of benefit or risks to subjects?

○ Yes ● **No**

6.5 * Benefits and Risks:

Click "Add" to begin entering the benefit and risk level detail information associated with this study.

	Name	Risk Level	Direct Benefit
View	HUM00198400	No more than minimal risk	no

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View: Benefits and Risks Detail
Section: 06. Benefits and Risks

Benefits and Risk Level Detail

If a study involves multiple arms or phases that pose different levels of risk or direct benefits to subjects, then create an entry for each arm or phase using the "OK and Add Another" option at the bottom of this page. Only one entry is necessary if the risk level and the direct benefit to subjects is the same for the entire project, even if the study involves multiple arms or phases.

6.5.1 * Name of Arm (experimental group, study wave, etc.)

HUM00198400

6.5.2 * Description of Arm (experimental group, study wave, etc.)

6.6 * Are there potential direct benefits of this research to the subjects?

○ Yes ● **No**

6.7 * Provide a description of the foreseeable risks to subjects. For studies involving multiple arms or phases, enter the risks for this arm or phase only.
Provide a description of the foreseeable risks to the subjects.
For EACH identified risk, include:

- **Likelihood of the risk,**
- **Seriousness to the subject; and**
- **What measures will be taken to minimize the risk (for example, study design includes the substitution of procedures already being performed on the subject for diagnostic or treatment purposes, or in a study of Post-Traumatic Stress Disorder, the investigator takes steps to identify, manage, or refer as appropriate, subjects for whom the study may evoke very difficult emotions)**

If possible, please use the following categories to assess the likelihood:

- **"Common" (i.e., approximate incidence > 25%)**
- **"Likely" (i.e., approximate incidence of 10-25%)**
- **"Infrequent" (i.e., approximate incidence of 1-10%)**
- **"Rare" (i.e., approximate incidence < 1%):**

Privacy
- Rare
- Patients will be de-identified from any data and saliva sample collected.

Section 8.5 in Protocol and listed under Section 5 in the consent

6.8 * What is the level of risk of harm to the subjects, resulting from this arm of the research? For studies involving multiple arms or phases, enter the level of risk for this arm or phase only.

	Risk Level	Description
●	**No more than minimal risk**	**A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of a routine physical examination. (Note: The definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults.) Refer to the Risk Grid for more information.**
○	Minor increase over minimal risk	While this risk category may be used to classify research involving adult subject populations, it must be considered in the evaluation of risk in research involving children as defined in 45 CFR 46 sections 404-407*** Risks are more severe than those defined as “No more than minimal risk” and less severe than those described as “Moderate” on the Risk Grid.
○	Moderate risk	Refer to the Risk Grid for more information.
○	High risk	Requires scrutiny in regards to the likelihood of direct benefits, and whether or not benefits clearly outweigh risks. Refer to the Risk Grid for more information.

6.9 * Discuss why the risks to the subjects are reasonable in relation to the anticipated benefits.
Will provide researchers with invaluable data into comorbidities suffered in those with HHT, allowing future treatments and interventions to be developed. For many of these patients, any new developments in the treatment of their disorder, HHT, will outweigh the potential risk of privacy concerns.

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View: 07. Special Considerations
Section: 07. Special Considerations

07. Special Considerations

7.1* Does this study involve human tissue or biological specimens (use, collection, or secondary analysis) (e.g. blood, urine, bone marrow, skin, etc.)? [Require Section 18]

● **Yes** ○ No

7.1.1* Will genetic analysis be performed on any specimens acquired in conjunction with this study? [Require Section 20]

● **Yes** ○ No

7.2* Does this study involve the secondary analysis of a pre-existing data set, including data associated with any specimens identified in response to question 7.1? [Require Section 24]

○ Yes ● **No**

7.3* Will the research involve the access, collection, use, maintenance, or disclosure of protected health information (PHI)? PHI is:

- **information about a subject's past, present, or future physical or mental health, the provision of healthcare to a subject, or payment for the provision of healthcare to a subject; AND**
- **maintained by a HIPAA-covered entity (e.g. healthcare provider, healthcare plan, or healthcare clearinghouse).**

[Require Section 25]

● **Yes** ○ No

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View: 07-1. Special Considerations - Continued
Section: 07. Special Considerations

07-1. Special Considerations - Continued

7-1.1* Will subjects receive payment or other incentives for their participation in the study? [Require Section 13]

○ Yes ● **No**

7-1.2* Will subjects undergo healthcare-related treatments or procedures (standard of care and/or research) as part of the study? [Require Section 14]

○ Yes ● **No**

7-1.3* Does this study involve the deception or concealment of subjects? [Require Section 27]

○ Yes ● **No**

7-1.4* Excluding routine email correspondence, does this study involve the use of the Internet or email as an integral part of the research design or will sensitive information be transmitted by e-mail? [Require Section 28]

○ Yes ● **No**

7-1.5* Will the study collect data using surveys, interviews, or focus groups? [Require Section 29]

● **Yes** ○ No

7-1.6* Does this study require subjects to listen to an audio recording or view images? [Require Section 31]

○ Yes ● **No**

7-1.7* Will any drugs, biologics, radiopharmaceuticals, nutritional (e.g., herbal or alternative medication) supplements or other material be administered, implanted, or applied to the subjects as the object of the study? [Require Section 15]

○ Yes ● **No**

7-1.8* Will the study involve a placebo (drug, device, procedure, intervention, surgery, etc.) control group? [Require Section 17]

○ Yes ● **No**

7-1.9* Will the study involve human embryonic stem cells (hESCs) or induced pluripotent stem cells? [Require Section 19]

○ Yes ● **No**

7-1.10* Will the study have a Data and Safety Monitoring Plan (DSMP)? [Require Section 32]

○ Yes ● **No**

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View: 07-2. Special Consideration - Continued
Section: 07. Special Considerations

7-2. Special Consideration - Continued

7-2.1* Will any devices be used, administered, implanted, or applied to the subjects, or will human specimens be used to test in vitro diagnostic devices? [IRBMED Applications Require Section 16]

◯ Yes ● **No**

7-2.2* Is the research testing or utilizing a health-related mobile software application that is:

- Designed for a handheld (e.g., smartphone) or wearable mobile device (e.g., exercise tracking), or
- Tailored to a mobile platform (i.e., a handheld commercial or off-the-shelf computing platform, with or without wireless connectivity) but executed (run) from a server

and the mobile software application/platform performs any of the following:

- Uses a built-in feature of a device such as light, vibration, or camera to perform a medical device function.
- Connects or links to an existing device to control its operation, function, or energy source.
- Uses patient-specific data from a connected device including a sensor or electrode to monitor, manipulate, calculate, or analyze information.
- Conveys diagnostic information, or provides education materials or encouragement.
- Performs calculations, conversions, measurements or interpretations.

◯ Yes ● **No**

7-2.3* Will the subjects be exposed to any ionizing radiation during the course of this study? [Require Section 21]

◯ Yes ● **No**

7-2.4* Will any organs, tissues, or cells from humans (including fetal tissue) or animals be administered to the subjects for the purposes of this study? [Require Section 22]

◯ Yes ● **No**

7-2.5* Does this study involve a gene transfer intervention or an intervention based on recombinant DNA technology? [Require Section 23]

◯ Yes ● **No**

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View: 08. Subject Participation
Section: 08. Subject Detail

08. Subject Participation

8.1* Please indicate the number of subjects to be enrolled from ALL study locations to achieve the goal of the study:

10000

8.2* Enter the estimated number of subjects to be enrolled at each University of Michigan site:

Location or Institution	Total
University of Michigan	
Adults	100
Children	0
Total from all University of Michigan sites:	**100**

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View: 08-1. Subject Recruitment
Section: 08. Subject Detail

08-1. Subject Recruitment

8-1.1* At what point in the study are you planning on beginning the recruitment of subjects?

0-2 years after approval

8-1.2* Indicate which of the following established subject pools, if any, will be used for recruitment.

Select all that apply:

Patients or their medical records from the UM Health System or any other UM health care provider (e.g., School of Dentistry, University Health Service, University Center for Language and Literacy)

Provide Related UM IRB Project Number or Subject Pool Description:

8-1.3* Describe the manner in which potential study subjects will be recruited. List how, when, who will recruit and where they will be recruited. Include any provisions to protect or maintain subject privacy.

Potential study subjects will be recruited during their routinely scheduled clinic visit with their HHT provider. Potential subjects will be noted as eligible prior to their visit by the study coordinator, who will also be responsible for consenting subjects and collecting the necessary data. Eligibility will be made aware to their physician the date of their visit. Potential study subjects will be approached in private patient clinic rooms to maintain privacy.

8-1.3.1 If applicable, how will prospective subjects' healthcare providers (e.g., physician, dentist, etc.) be involved in the recruitment and/or be notified of their individual patients' participation in the study?

The study coordinator will note to the physician which subjects are eligible the day of the potential subjects visit. The physician will be the first individual to discuss with the potential subject their eligibility for the study and help gauge their interest in further details, which will then be passed along to the study coordinator.

8-1.4* Explain how the recruitment strategy is equitable and represents the population required for the study. If the information is covered in the attached protocol, please indicate section.

3.1 Setting and Patient Population

8-1.5* Does the recruitment strategy involve contacting individuals multiple times in an effort to secure their initial enrollment into the study?

○ Yes ● **No**

8-1.6* Indicate which methods will be used for recruitment?

Check all that apply:

Face-to-face contact (e.g. during a health care visit or an interview at a home address, etc.)

Other

If other please specify:

Contact during a virtual healthcare visit.

8-1.7 How will any email, address, and/or telephone lists be obtained?

N/A

8-1.8* What materials will be used for recruitment? The IRB must approve all recruitment materials.

See Help for important information regarding the requirements for recruitment materials

Check all that apply:

None

If other please specify:

If Web pages will be used, provide the Web address (URL) for the location where the pages will be posted (also upload the content of the pages below):

Upload recruitment materials here:

See Help for more information about working with documents (e.g. uploading, downloading, and editing).

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Name	Version
There are no items to display	

☐ **Check here if any of the materials are not available electronically.**

Note: Study Teams are encouraged to scan and upload documents. See Help for a list of sites with scanning facilities

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View: 09. Survey Populations
Section: 09. Subject Populations

09. Survey Populations

9.1* Is the study limited to a survey of either:

- The general adult population (aged 18 or older); or
- A subgroup of the general population which does not specifically target:

- Pregnant women and/or fetuses
- Lactating women
- Women of child-bearing potential
- Prisoners
- Cognitively impaired adults
- College students
- Economically or educationally disadvantaged persons
- Patients of the study team
- Employees, students or trainees of the study team
- Family members of the study team

where the survey is the sole interaction with the subject and does not pose more than minimal risk?

○ Yes ● **No**

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View: 09-1. Subject Populations
Section: 09. Subject Populations

09-1. Subject Populations

9-1.1* Is the research designed to include or allow the following populations?

Select all that apply

- [ ] **Normal, healthy subjects**
- [x] **Adults** *age 18 and older*
- [ ] **Minors able to consent** *to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted (e.g. emancipated minors or minors seeking treatment for certain conditions.)*
- [ ] **Children and/or Viable Neonates** *(i.e. persons who have not yet reached the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted) [Require Sections 33 and 41]*
- [ ] **Neonates of uncertain viability and/or nonviable neonates** (do not check this box if the research is solely retrospective. For retrospective research regarding neonates of uncertain viability, check the box for 'Children'. See Help for additional information.) [Require Section 34]
- [ ] **Individuals and/or products involving human in vitro fertilization**
- [ ] **Pregnant women and/or fetuses** [Require Sections 35 and 41]
- [ ] **Lactating women** [Require Section 36]
- [x] **Women of child-bearing potential** [Require Section 37]
- [ ] **Prisoners** (If the research includes a study population that is likely to become incarcerated during the conduct of the research, also select this category) [Require Section 38 and 41]
- [x] **Cognitively impaired adults** [Require Sections 39 and 41]
- [ ] **College students** [Require Sections 40 and 41]
- [ ] **Economically or educationally disadvantaged persons** [Require Section 41]
- [x] **Patients of the study team** [Require Section 41]
- [ ] **Employees, students or trainees of the study team** [Require Section 41]
- [ ] **Family members of the study team** [Require Section 41]
- [ ] **Unknown, unspecified population**

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View: 10. Informed Consent - Adults
Section: 10. Informed Consent

10. Informed Consent - Adults

10.1* What type of informed consent will be obtained from adults or minors legally able to consent to treatments or procedures involved in the research?

With signature:

- [x] **Comprehensive written**
- [x] **Written assent for cognitively or decisionally impaired adults**

Without signature (waiver of documentation):

- [ ] Comprehensive written
- [ ] Comprehensive oral consent script
- [ ] Assent for cognitively or decisionally impaired adults

Waivers of informed consent:

- [ ] Request for waiver of informed consent/parental permission/legally authorized representative consent (Note: no longer required for screening/recruitment)
- [x] **Request for waiver of assent for cognitively or decisionally impaired adults**

Other:

- [ ] Short form, comprehensive oral script, and witness
- [ ] Request for alteration of informed consent requirements
- [ ] Pre-existing consent(s) covers this activity
- [ ] Re-consent/assent subjects for use of existing data/records/specimens for a new research purpose

10.1.1* Waiver of assent is requested because:

Select all that apply:

- Research presents no more than minimal risk, assent is not practicable, waiver will not impact the rights and welfare of subjects, and as appropriate, subjects will be provided with additional pertinent information after participation.
- Capabilities of some or all adults are so limited they cannot be consulted
- Study offers important benefit unavailable outside of the research

10.1.2* Describe the process to seek and obtain informed consent and/or assent from adults. If requesting a waiver of documentation of assent, provide justification here.

During the potential subject's regularly scheduled clinic visit, the study coordinator will approach the individual with an explanation of the study, its goals. The potential subject will be presented the consent form to look over, with the option to read the study consent absent the presence of the study coordinator. The potential subject will then have the opportunity to ask the study coordinator any questions they have about the study and to address any concerns. If the questions and concerns are answered to the potential subjects satisfaction, and they agree to consent to the study, the study coordinator will then obtain the subjects consent, providing them with a copy of the signed consent form and the number to contact the study coordinator if any further questions arise or the subject chooses to be removed from the study.

A waiver of assent would be needed if the subject has an altered mental status due to medication(s), an illness resulting in an impaired mental state (dementia), or for any other reason that results in the subject having an altered or impaired mental state. The PI or CI, in conjunction with the substitute decision maker, will determine if the subject is cognitively capable to sign the consent. In the cases where the subject is not cognitively capable, we would use a substitute decision maker to consent. With the assent being part of the consent document, if the subject is able to assent they will sign the Consent/Assent form.

In all instances, our initial attempt is to get the signed consent or assent from the subject if we are able, otherwise a substitute decision maker will be used.

10.1.3* Is the cognitive capacity of the subjects expected to change significantly during the study?

○ Yes ● **No**

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View: 10-1. Informed Consent
Section: 10. Informed Consent

10-1. Informed Consent

10-1.1* All documents related to consent, assent, permission, and or debriefing documents, including oral scripts must be uploaded here. If you are requesting a waiver of documentation of informed consent, upload a copy of any written materials to be provided to participants, and provide a written description of any information to be provided orally.

Name	Version
Consent - Clean_ Ame00128376(0.04)	0.04
Consent-Tracked(0.06)	0.06

10-1.1.1* Does the Informed Consent use the sentences required for Applicable Clinical Trials: "A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by US law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time."?

○ Yes ● **No**

10-1.2* Will the subjects be audiotaped, videotaped, or photographed (identifiable images of subject) during the research?

○ Yes ● **No**

10-1.3* Is there a substantial likelihood that the research will be conducted among a non-English-speaking population?

○ Yes ● **No**

10-1.4* Indicate which anticipated costs could be the full or partial responsibility of the subject.

Check all that apply:

Cost of routine health care that would be incurred for this condition if the subject were not participating in the research study

If other, please specify:

10-1.5* Is the study designed to collect identifiable information from primary research subjects about other individuals, including family members?

○ Yes ● **No**

10-1.6* At the conclusion of this study, will specimens and/or data be retained for future research use?

● **Yes** ○ No

10-1.7* Does the informed consent document explicitly notify subjects that their data and/or specimens will be stored for future research?

● **Yes** ○ No

10-1.8* Are subjects required to agree to retention of their data and/or specimens as a condition of participating in the research?

● **Yes** ○ No

10-1.8.1* Provide a justification for this requirement. If the information is included in the attached protocol, please indicate section.

The purpose of the OUR HHT Registry is to collect data on HHT patients about their current condition, with the hope that future research and eventually treatments can be developed. Not retaining a patient's data or specimen beyond their initial consent would prevent researchers from being able to track and analyze trends and determine potential links in disease progression, severity, and outcomes over time in relation to an individual, or group of individuals, with gene mutations determined from DNA sequencing, if specimen collection is allowed by the patient in addition to the standard data collection. Not having access to this information could prevent researchers from being able to develop new therapies, treatments, or formulating further research studies.

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View: 11. Confidentiality/Security/Privacy
Section: 11. Confidentiality, Security and Privacy

11. Confidentiality/Security/Privacy

11.1* Will the study team access any data that is linked to a subject's identity by name or other identifier or code? [Require Section 11-1]

● **Yes** ○ No

11.2* Explain how the subjects' privacy will be protected.

The participants will receive a local ID code. The data and sample entered in to the data base will receive a new randomly generated code. The codes will be filled and stored separately in a secure location and the data will be password-protected and securely stored. In addition, access to records and data will be limited to authorized persons and transmission of the data will be secure. All persons involved in the study, are committed to respecting the privacy of the participants.

The study team will have access to the subject's hospital chart and will have that privacy protected by standard HIPAA guidelines. All data will be kept in a secured database and a locked office.

11.3* How will the study team protect research records, data, and/or specimens against inappropriate use or disclosure, or malicious or accidental loss or destruction in order to protect the confidentiality of subject data?

Select all that apply:

Locked office
Locked cabinet or storage unit
Restricted access
Access rights terminated when authorized users leave the project or unit
Secure laptop
Individual ID plus password protection
Network restrictions
No non-UM devices are used to access project data, or any that are used to access project data use secure connections to communicate with U-M services (e.g. VPN – “virtual private network”)
Security software (firewall, anti-virus, anti-intrusion) is installed and regularly updated on all servers, workstations, laptops, and other devices used in the project
Safe disposition/destruction of data or devices, as appropriate (e.g., shredding paper documents, destroying disks or thumb drives, secure erasure of electronic media)

If other please specify:
Section 12 of the Protocol discusses Data Security

11.4* Does either statement apply to this research:

Research has NIH, CDC, or FDA funding, or other federal funding from an agency that automatically issues a Certificate of Confidentiality as part of the terms of the award:

The study will include identifiable sensitive information, identifiable biospecimens, individual human-level genomic data/biospecimens, or any information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

or

Research does NOT have NIH, CDC, or FDA funding, or other federal funding from an agency that automatically issues a Certificate of Confidentiality as part of the terms of the award:

The study will include identifiable, sensitive information or identifiable biospecimens that, if revealed, might place the subjects at risk for personal safety, criminal or civil liability, or damage to their financial standing, employability, insurability, or reputation.

[Require Section 11-2]

○ Yes ● **No**

11.5* Will data be provided to a repository as part of a data sharing agreement?

● **Yes** ○ No

11.5.1* Please indicate the repository:

Select all that apply:

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Select all that apply:

Other

If Other, please specify:
Geisel School of Medicine, USA - Data, and University of California, San Francisco (UCSF), USA - Saliva sample and its analysis

11.6* What will happen to the data and/or any specimens at the conclusion of this study?

Select all that apply:

Retain for study recordkeeping purposes

Retain for future research use - requires Section 11-4

11.6.2* If the data and/or specimens will be retained for study recordkeeping purposes, provide the following information (if covered in the attached protocol, please indicate section):

- expected duration of the retention period,
- any changes in the conditions or arrangements for storage of research data/specimens during the retention period, if different from those listed above in question 11.3.

9.0 Record Retention

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View: 11-1. Identifiable Data
Section: 11. Confidentiality, Security and Privacy

11-1. Identifiable Data

Completion of this section is required based on the response provided to question 11.1.

11-1.1* Indicate how subjects are identified in the research records.

Select all that apply:

Coded or Indirect Identifiers - data record includes a link to direct identifiers (e.g., name, initials, phone number, SSN, or medical record number linked to data record but stored separately)

11-1.2* Explain the necessity for collecting or maintaining data linked to subjects' identities. If the information is covered in the attached protocol, please indicate section.

Allows for study team members to update the subject's health information in the registry. Only study team member at Michigan Medicine will have access to any identifiable information.

11-1.3* How long will the identifiers be retained?

For up to 13 years.

11-1.4* Will individually identifiable sensitive data be accessed, collected, used, maintained, or disclosed in the study?

○ Yes ● **No**

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View: 11-3. End of Subject Participation
Section: 11. Confidentiality, Security and Privacy

11-3. End of Subject Participation

11-3.1* What specific criteria will be used to prematurely end a particular subject's participation in the study (If covered in attached protocol or informed consent, indicate specific location).

None, except withdrawal by choice of subject.

11-3.2* If a participant withdraws from the research, what is the plan to use, disclose, store, or destroy the participant's data and/or specimen?

Participants may withdraw from the study at any time and the collected information will be removed from the registry. The ongoing registry information will be retained until it is closed.

Participants can request withdrawal of DNA sample collected and housed at UCSF at any time. Withdrawal request before sample shipment to UCSF will be done prior to DNA analysis and samples can be withdrawn and destroyed (according to institutional policy) at the site. For withdrawal request after sample has been sent to UCSF the unused portion of the sample will be destroyed.. For withdrawal request after DNA analysis, data already obtained up to the point of request cannot be withdrawn or destroyed.

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View: 11-4. Retention of Data and/or Specimens Detail
Section: 11. Confidentiality, Security and Privacy

11-4. Retention of Data and/or Specimens Detail

Retention may be for future research by the investigator and/or the creation of a bank or repository.

Completion of this section is required based on the response provided to question 11.6.

11-4.1* What is the intent or purpose of retaining the data and/or specimens?

OUR HHT registry will allow collection of the natural history data in HHT, with characterization of clinical outcomes and DNA sequencing, to provide information and generate research questions for future studies related to HHT. The collection of the saliva sample needed for this DNA sequencing is optional. Based on the information provided for and collected in the registry, via the information uploaded into the registry by members of the study team or uploaded by study subjects themselves in the OUR HHT Registry patient-entry portal, eligible subjects, with their consent, may be contacted to participate in future research studies.

11-4.2* Where will you store the data and/or specimens?

Other Institutions

If Other Institutions, please specify:
Geisel School of Medicine, USA - Data

University of California, San Francisco (UCSF), USA - Saliva sample and its analysis

11-4.3* Describe the arrangements for the storage conditions, management, and security of the data and/or specimens. Include the following as applicable:

- ***Personnel access to data and/or specimens***
- ***Whether identifiers will be removed and the key to any code destroyed***
- ***For coded data and/or specimens, indicate who holds key to the code and where it is stored in relation to the data and/or specimens***
- ***Storage plan***
- ***Plan to protect privacy in transfer to other collaborators.***

The participants will receive a local ID code. The data and sample entered in to the data base will receive a new randomly generated code. The codes will be filled and stored separately in a secure location and the data will be password-protected and securely stored. In addition, access to records and data will be limited to authorized persons and transmission of the data will be secure.

Saliva specimens for DNA extraction will be collected from each participant and shipped from various enrolling sites to a limited access facility at the University of California, San Francisco (UCSF) and stored in an ethics approved storage facility. The saliva collection kits will be identified by unique barcode stickers prior to collection, to track the sample throughout the collection and DNA isolation process.

Both the data and remaining specimen will store for future research.

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View: 18. Biological Specimens
Section: 18. Biological Specimens

18. Biological Specimens

Completion of this section is required based on the response provided to question 1-1.2.1, 4-1.1, or 7.1.

18.1* List all of the human biological specimens that will be used in the study.

18.1.1 Blood obtained directly from subjects for the purpose of this research.

Only key fields are displayed. Click on the link below to view all details.

Collection Schedule

There are no items to display

18.1.4 Non-blood specimens obtained directly from subjects for the purpose of this research study, NOT from specimens removed for medically indicated reasons.

Only key fields are displayed. Click on the link below to view all details.

Kinds Of Specimens
View Saliva

18.1.9 Blood or non-blood residual or to-be-discarded specimens.

Only key fields are displayed. Click on the link below to view all details.

Kinds Of Specimens

There are no items to display

18.1.15 Blood or non-blood existing, banked, human biological specimens.

Only key fields are displayed. Click on the link below to view all details.

Kinds Of Specimens

There are no items to display

18.2* Will the investigators receive or record direct or linked subject identifiers for ANY biospecimens?

● **Yes** ○ No

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View: VIEW000608_customAttributes._attribute191.customAttributes._attribute2_Direct Collection Non-Blood Specimen
Section: 18. Biological Specimens

Direct Collection Non-Blood Specimen

18.1.5* What kinds of biological specimens will be used?

Saliva

18.1.6* By what method will the biological specimens be collected?

Oragene OGR-500 Saliva Collection Kit (DNA Genotek).

18.1.7* Who will collect the biological specimens from the subjects? Specify source name and primary contact (e.g., directly from physician, UMHS clinical pathology labs, UMHS delivery rooms, remote institutions, etc.)

The patient will be given in clinic or sent to their home the kit detailed above, which will then be sent to the research facility by the patient.

18.1.8* Describe the specimen collection schedule, including frequency, duration (first to last collection), and amount (size, weight, or volume). Indicate the total amount to be collected from each subject and show how this amount was calculated from the frequency, duration, and amount per collection as indicated.

One collection obtained, via saliva swab, that follows consenting to the study.

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View: 20. Genetic Analysis
Section: 20. Genetic Analysis

20. Genetic Analysis

Completion of this section is required based on the response provided to question 1-1.2.1.2 or 7.1.1.

20.1* Indicate on which biological specimens the genetic analysis will be performed.

Saliva

20.2* What is the specific purpose of the genetic analysis?

The samples will be used for a genome wide association analysis and whole exome sequencing, to look for genetic influences on vascular malformations in HHT patients, both sporadic and inherited.

20.3* What particular genetic information will be acquired?

The samples will be used for a genome wide association analysis and whole exome sequencing for HHT.

20.4* Will any genetic information or specimens be shared with colleagues outside the study? If Yes - This must be disclosed in the informed consent.

● **Yes** ○ No

20.4.1* How will the privacy of the subject be protected in the transfer? Indicate whether identifiable information will be included in the transfer.

Researchers who are interested in using information from this registry in the future will have to apply for approval from HHT Foundation International as well as their Institutional Review Boards.

20.5* Are the special risks associated with genetic analysis disclosed in the informed consent document?

● **Yes** ○ No

20.6* Will the subject be given the opportunity to specifically indicate in the informed consent document (e.g. via checkbox) his/her desire to receive these results?

● **Yes** ○ No

20.7* Will the results of the genetic testing be shared with the research subject?

● **Yes** ○ No

20.7.1* Justify why the results will or will not be shared with the research subject.

If as in 20.6, the patient states they want to receive the results then they will be made available to them.

20.7.2* Will the testing be performed in clinical diagnostic laboratories?

○ Yes ● **No**

20.7.3* Will genetic counseling be available to subjects to explain the findings?

● **Yes** ○ No

20.7.3.1* Will the cost of providing the counseling be covered by the study?

○ Yes ● **No**

20.7.3.1.1* Justify why the study has not made provisions to pay these costs.

Through our multidisciplinary center, genetic counseling is available to our HHT patients as a resource for questions arising from HHT related genetic testing.

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View: 25. HIPAA Covered Components
Section: 25. Protected Health Information/HIPAA

25. HIPAA Covered Components

Completion of this section is required based on the response provided to question 1-1.2.8, 4-1.1, 5-1.3, 7.3, or 7-3.2.

25.1* Select all sources of HIPAA-regulated data used, received, or analyzed in the study:

Entity
Michigan Medicine hybrid covered entity *Examples: Michigan Medicine electronic medical record; Medical School Office of Research services such as Data Office for Clinical and Translational Research or Central Biorepository; University Health Service; School of Dentistry Provider Clinics; U-M Group Health Plan*

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View: 25-1. Protected Health Information/HIPAA
Section: 25. Protected Health Information/HIPAA

25-1. Protected Health Information/HIPAA

Completion of this section is required based on the responses to questions 4-1.1, 5-1.3, 7.3, or 7-3.2 and question 25.1.

25-1.1* Identify the PHI to be used.

Select all that apply:

- Hospital/doctor's office records, including test results and dental records
- Genetic counseling/genetic testing records
- Any records relating to condition, the treatment received, and response to the treatment
- Demographic information
- Personal identifiers

If other, please specify:

25-1.2* Explain why the PHI listed above is the minimum necessary to conduct the study.

The goal is to better understand HHT, the symptoms and complications it causes (“outcomes”) and how the disease impacts people’s lives. In order to observe this, the PHI listed above is needed to allow researchers to see how the disorder is currently medically affecting suffers and how that suffering changes through interventions and treatments over the course of the study.

25-1.3* Will HIPAA authorization for access to the PHI be obtained for all or some subjects?

Yes, sometimes - HIPAA authorization will not be obtained from some subjects or from some candidates for recruitment before their records are reviewed for eligibility determination or to obtain contact information

25-1.3.1* If HIPAA authorization for access to the PHI will be obtained from some or all subjects before their data is collected, used or disclosed (including for eligibility determination or recruitment), indicate the document/process to be used:

Integrated with informed consent document/process (All IRBMED apps must select this)

If other, please specify:

25-1.3.2* If HIPAA authorization for access to the PHI will NOT be obtained from some or all subjects/candidates for recruitment, indicate what alternative(s) will be used:

Select all that apply:

- Request for full or partial waiver of HIPAA authorization to be approved by U-M IRB or Privacy Board

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View: 25-2. HIPAA Authorization Waiver Request
Section: 25. Protected Health Information/HIPAA

25-2. HIPAA Authorization Waiver Request

Completion of this section is required based on the response provided to question 25-1.3.2

25-2.1* Waiver of HIPAA authorization requested for:

Select all that apply:

Recruitment portion only

If other, please specify:

25-2.2* To ensure that this research use of the PHI involves no greater than minimal risk to privacy, describe the plan to protect patient-subject identifiers from improper use or disclosure.

The participants will receive a local ID code. The data and sample entered in to the data base will receive a new randomly generated code. The codes will be filled and stored separately in a secure location and the data will be password-protected and securely stored. In addition, access to records and data will be limited to authorized persons and transmission of the data will be secure. All persons involved in the study, are committed to respecting the privacy of the participants.

25-2.3* To ensure that this research use of PHI involves no greater than minimal risk to privacy, describe the plan to destroy patient-subject identifiers at the earliest opportunity consistent with the research. Indicate at what point in the research the patient-subject identifiers will be destroyed. If applicable, provide a health, research or legal justification for retaining the identifiers.

All registry records will be held indefinitely in this data base. The investigator at St. Michael's Hospital in Toronto, Canada will be responsible for retaining all records and supporting documentation pertaining to this registry for 7 years after study completion. After data verification and analysis all identifiable data will be destroyed in accordance with St. Michael's Hospital policy. The de- identified data will be kept indefinitely.

25-2.4* To ensure that this research use of the PHI involves no greater than minimal risk to privacy, provide assurance that this information will not be reused or disclosed to any other person or entity (i.e., outside the research study team), except as required by law, for authorized oversight of the research study, or for other research for which the IRB has granted a waiver of the HIPAA authorization.

Non de-identified information collected will only be accessible to members of the study team located at Michigan Medicine.

25-2.5* Why could this research not practicably be conducted unless the waiver of HIPAA authorization is granted [45 CFR 164.512 (i)(2)(ii)(B)]?

We are only requesting waiver of HIPAA authorization for recruitment portion only.

25-2.6* Why could this research not practicably be conducted without access to and use of the PHI [45 CFR 164.512(i)(2)(ii)(C)]?

The goal of the study is to better understand HHT, the symptoms and complications is causes, and how the disease impacts people's lives through the collection and analysis of long-term data collected over a number of years. The PHI collected, e.g. age, race, gender, etc., will help investigators understand how different groups of people are affected by HHT throughout the course of the study. Not having access to this PHI would make it difficult for investigators to see health trends in the affected groups and potentially miss opportunities to develop new targeted treatments and therapies for these groups.

25-2.7* Will data containing PHI be shared outside of the U-M covered component? (If yes review the guidelines from UM HIPAA office)

● **Yes** ○ No

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View: 29. Survey Research
Section: 29. Survey Research

29. Survey Research

Completion of this section is required based on the response provided to question 7-1.5.

29.1* Provide a list of all surveys and interviews used in the study:

Name	# of Questions	Duration	Sensitive?	Disturbing?
OUR HHT Registry	38	20 minutes	no	no
OUR HHT Registry Patient Portal	23	15-20 minutes	no	no

29.13* Will the research involve the use of focus groups?

○ Yes ● **No**

29.14* Is any of the material disturbing?

○ Yes ● **No**

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View: VIEW000619_customAttributes._attribute234.customAttributes._attribute8_Survey Detail
Section: 29. Survey Research

Survey Detail

29.2* Survey or interview name:

OUR HHT Registry

29.3* Is the design or development of this survey instrument dependent on receipt of funding or hiring of personnel?

◯ Yes ● **No**

29.4* In what manner will the survey or interview be conducted (e.g., in-person, Internet, mail, telephone, etc.)? *Special Note: For electronic surveys, the eResearch ID number must be included in the informed consent document (uploaded in section 10-1) or other material that serves as the informed consent.*

In person or via the HHT Patient Portal

Survey located on pages 13-15 in the Protocol.

29.5* What is the predicted response rate?

100 %

29.6* What is the total number of questions?

38

29.7* What is the anticipated cumulative amount of time required for each subject?

20 minutes

29.8* What is the total number of interviews/data collection interactions with an individual subject?

Yearly until end of study

29.9* Does the survey or interview contain questions of a sensitive nature (e.g., mental illness, sexual abuse, illicit drug use, etc.)?

◯ Yes ● **No**

29.10* Is the survey or interview likely to produce psychological discomfort or negative feelings in the subjects?

◯ Yes ● **No**

29.11* Has the survey instrument been validated or used in standard practice?

● **Yes** ◯ No

29.11.1* If yes, describe the origin of the instrument.

Developed by the founders of the registry and is in use by other HHT Centers of Excellence currently enrolling patient into the OUR HHT Registry.

29.12* Upload the survey instrument here.

Name	Version
OUR HHT Registry Questions(0.01)	0.01

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View: VIEW000619_customAttributes._attribute234.customAttributes._attribute8_Survey Detail
Section: 29. Survey Research

Survey Detail

29.2* Survey or interview name:

OUR HHT Registry Patient Portal

29.3* Is the design or development of this survey instrument dependent on receipt of funding or hiring of personnel?

○ Yes ● **No**

29.4* In what manner will the survey or interview be conducted (e.g., in-person, Internet, mail, telephone, etc.)? *Special Note: For electronic surveys, the eResearch ID number must be included in the informed consent document (uploaded in section 10-1) or other material that serves as the informed consent.*

Patients would enter data into their OUR HHT Registry Patient Portal.

29.5* What is the predicted response rate?

60 %

29.6* What is the total number of questions?

23

29.7* What is the anticipated cumulative amount of time required for each subject?

15-20 minutes

29.8* What is the total number of interviews/data collection interactions with an individual subject?

Every 3 months

29.9* Does the survey or interview contain questions of a sensitive nature (e.g., mental illness, sexual abuse, illicit drug use, etc.)?

○ Yes ● **No**

29.10* Is the survey or interview likely to produce psychological discomfort or negative feelings in the subjects?

○ Yes ● **No**

29.11* Has the survey instrument been validated or used in standard practice?

● **Yes** ○ No

29.11.1* If yes, describe the origin of the instrument.

Developed by the founders of the registry and is in use by other HHT Centers of Excellence currently enrolling patient into the OUR HHT Registry.

29.12* Upload the survey instrument here.

Name	Version
Patient Portal Screenshot(0.01)	0.01

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View: 37. Women of Child Bearing Potential
Section: 37. Women of Child Bearing Potential

37. Women of Child Bearing Potential

Completion of this section is required based on the response provided to question 9-1.1.

37.1* Is there a potential that any of the study procedures pose significant physical or psychological risks to women who are or may be pregnant, or to a fetus?

○ Yes ● **No**

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View: 39. Cognitively Impaired Adults
Section: 39. Cognitively Impaired Adults

39. Cognitively Impaired Adults

Completion of this section is required based on the response provided to question 9-1.1.

39.1* Explain the manner and extent to which the adult subjects are cognitively impaired.

If patients are cognitively impaired for any reason, i.e.: Dementia, we will ask for a substitute decision maker for the patient. We are not expecting subjects to be cognitively impaired due to having HHT (the focus of this protocol).

39.2* How will competency be assessed for the purpose of obtaining informed consent?

The subject's family, legal guardian, or designated substitute decision maker will make the decision about the subject's competency.

39.3* What measures will be taken to provide the cognitively impaired adult subjects the opportunity to understand that they have been enrolled in the study and have the right to object.

Through the involvement of family members or other substitute decision maker.

39.4* Should a cognitively impaired adult subject desire to withdraw from the study, describe the process for managing the transition.

Same process that would be taken when a cognitively intact adult decides to withdraw from the study.

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View: 41. Subjects Vulnerable to Coercion
Section: 41. Subjects Vulnerable to Coercion

41. Subjects Vulnerable to Coercion

Completion of this section is required based on the response provided to question 9-1.1 or 9-2.1.

The following subject populations, vulnerable to coercion or undue influence, have been identified for inclusion in the study.

Cognitively Impaired Adults

Patients of Study Team

41.1* What is the justification for the inclusion of these subject populations?

All patients approached to be entered into the registry and have their saliva samples taken will be Patients of Study team, which may include Cognitively Impaired Adults. Inclusion of these subjects is important for the diverse recruitment of subjects and will provide researchers with a larger more representative cohort of subjects from whom to collect data.

41.2* Describe the additional safeguards that have been included in this study to protect the rights and welfare of these subjects.

Patients of Study Team, which will include Cognitively Impaired Adults, will be reassured their decision to be included, excluded, or chose to be disenrolled at a later date will not have any impact on or affect the quality of care they receive from members of or those associated with the Study Team involved in their care. Cognitively Impaired Adults will have further reassurance from their primary decision maker.

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View: 44. Additional Supporting Documents
Section: 44 Additional Supporting Documents

44. Additional Supporting Documents

44.1 Please upload any additional supporting documents related to your study that have not already been uploaded. Examples include, but are not limited to, data collection sheets, newsletters, subject brochures, and instructional brochures.

Name	Version
There are no items to display	

44.2 Enter any information that should show in a "Supporting Documents" list on the current submission's approval notice, such as document names and version numbers or version dates. Text entered here will AUTOMATICALLY appear word-for-word on the approval letter.

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View: 45. End Of Application
Section: 45. End of Application

45. End of Application

The form was successfully submitted. Click 'Exit' or 'Finish' to leave the form.

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