CHTN
COOPERATIVE HUMAN TISSUE NETWORK

APPLICATION (Part 1)

The Principal Investigator (PI) responsible for overseeing the project and controlling the laboratory and personnel who will receive, use and process the requested specimens should complete this application.

Patient identity is confidential. Samples and accompanying clinical data will be identified by a code, which will not be released under any circumstances.

The PI is responsible for remission of processing fees to the originating CHTN division for each specimen provided, including fees for any additional services performed and any shipping costs not directly billed to the applicant's courier account. Please refer to our website for the current fee table. Payment is required within 60 days and an account is considered delinquent after 90 days.

Any transfer of samples, aliquots, derivatives or associated clinical data to collaborating personnel or laboratories that are not under the direct supervision of the indicate PI requires the following:

- A written justification of the need to transfer the materials and benefit to the applicant's research.
- Copies of the AGREEMENT FOR USE OF TISSUE and DATA USE AGREEMENT signed by the collaborator.
- Documentation of the collaborator's IRB approval or exemption unless the collaborator is covered under the IRB approval granted for the project proposed in this application.

The PI initials in the box below acknowledging on behalf of their institution that they will not reach out to any of the CHTN division's institutional physicians or staff that are not directly associated with the CHTN.

PI Initial:

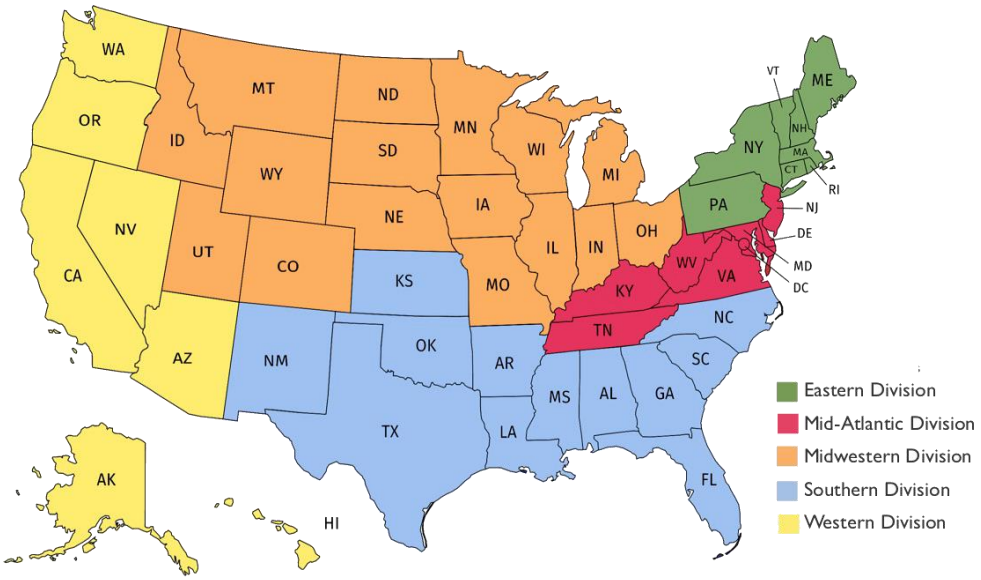
DIRECTIONS

The CHTN does not supply samples to specimen banks whose purpose is distribution to third-party researchers; those researchers should be encouraged to apply to the CHTN directly.

Directions to complete this form:

1. **Please remember to fill out the Request Information Form (Part 2) before submitting your application.** You should have two documents to submit: Application (Part 1) and Request Information Form (Part 2).
2. Please be specific about your requirements, including those for storing and handling tissue samples from the time the specimens are collected until they are delivered to your lab (i.e. transport media, refrigeration status, etc.).
3. If requesting specimens from more than one specific anatomic site or disease, please complete separate copies of the Request Information Form (biospecimen, donor and preparation details) as necessary.
4. PIs must document human subjects review for their project by their institution to receive specimens from the CHTN. Full or expedited approval, exemption or non-human subjects research determination for your project can be obtained from your Institutional Review Board (IRB). **A copy of the approval or review documentation must be returned with this form**. Documentation of continuing review, if necessary, must be forwarded to the CHTN to maintain eligibility to receive tissue. If your institution does not have internal review, contact your divisional coordinator. **NOTE:** Tissue microarrays are fully anonymized and do not require documentation of IRB approval or exemption.
5. Please provide a signed copy of the Agreement for Use of Tissue and Data Use Agreement (Agreements included below). **The language in the application and agreements are NOT to be altered.**
6. The CHTN is divided into five geographic regions as identified on the map below. PIs should submit their application to the appropriate primary division based on his/her geographic location. **PIs from any geographic area requesting pediatric specimens only** should forward their completed application directly to the Pediatric Division at The Abigail Wexner Research Institute at Nationwide Children's Hospital.
7. If you have any questions or need additional information, please contact your primary division based on your geographical location or the CHTN Central Coordinator.

GEOGRAPHIC REGIONS/DIVISIONS & DIVISONAL CONTACTS



Pediatric Division serves pediatric requests throughout all of the U.S. & Canada.

Eastern Division	**Mid-Atlantic Division**	**Midwestern Division**
PI: Dr. Kathleen Montone Division Coordinator: Dee McGarvey dfitzsim@pennmedicine.upenn.edu 3400 Spruce St. 566 Dulles Hospital of the University of Pennsylvania Philadelphia, PA 19104 Tel: 215-662-4570 Fax: 215-614-0251	PI: Dr. Christopher Moskaluk Division Coordinator: Rebecca Blackwell chtn-midatl@hscmail.mcc.virginia.edu CHTN-Mid-Atlantic Division University of Virginia Dept. of Pathology Box 800904 Charlottesville, VA 22908 Tel: 434-924-9879 Fax:434-924-9438	PI: Dr. Anil Parwani Division Coordinator: Randy Mandt randy.mandt@osumc.edu CHTN Midwestern Division Innovation Centre 2001 Polaris Parkway Columbus, OH 43240 Tel: 614-293-5119 Fax: 614-293-7013 **Primary for Canada*
Pediatric Division	**Southern Division**	**Western Division**
PI: Dr. Nilsa Ramirez Division Coordinator: Sara Coppens pCHTN@nationwidechildrens.org The Abigail Wexner Research Institute at Nationwide Children's Hospital 700 Children's Drive Rm WA1340 Columbus, OH 43205 Tel: 614-355-1546 Fax: 614-722-2897	PI: Dr. Shannon McCall Division Coordinator: Kate Frankey Path-CHTN@duke.edu Duke University Department of Pathology DUMC 3712 Durham, NC 27710 Tel: 919-684-6928 **Primary for Mexico*	PI: Dr. Kay Washington Division Coordinator: Kerry Wiles kerry.wiles@vumc.org Vanderbilt University Medical Center 1161 21st Ave S MCN D7201 Nashville, TN 37232 Tel: 615-322-7486 **Primary for U.S. Territories*

CHTN Central Coordinator
Kiley Radin
kradin@chtn.org
Tel: 317-620-1026
**Primary for International (besides Mexico and Canada)*

PRINCIPAL INVESTIGATOR INFORMATION

First Name: Middle Name: Last Name:

Salutation: Degree: Title:

Institution Type: ☐ Academic/Non-Profit ☐ Government Lab ☐ Commercial

Have you been a CHTN Investigator before? ☐ Yes ☐ No

Mailing address:

Institution:

Department:

Address 1:

Address 2:

City: State: Zip code: Country:

Tel#: Alt. Tel#: Fax#:

Email:

LABORATORY CONTACT INFORMATION

First Name: Middle Initial: Last Name: Title:

Tel#: Alt. Tel#: Fax#:

Email:

First Name: Middle Initial: Last Name: Title:

Tel#: Alt. Tel#: Fax#:

Email:

SHIPPING INFORMATION

Preferred Shipping Courier: Courier Account# (required):

Shipping address same as mailing address: ☐

Attention:

Institution:

Department:

Address 1:

Address 2:

City: State: Zip Code: Country:

Tel#: Alt. Tel#: Fax#:

Email:

BILLING AND PAYMENT INFORMATION

Billing contact:

First Name: Middle Initial: Last Name: Title:

Tel#: Alt. Tel#: Fax#:

Email:

Billing address:

Same as mailing address: ☐

Attention:

Institution:

Address 1:

Address 2:

City: State: Zip code: Country:

Tel#: Alt. Tel#: Fax#:

Email:

Payment details: ☐ Purchase Order (PO#) ☐ Credit Card *Do not provide card account information on this form. CHTN will call the billing contact for account information at the time of each shipment.*

Purchase Order (PO)#: PO Expiration Date: PO Amount:

Bill to Grant: Billing Ref#:

Copy of Bill to Investigator: ☐ Yes ☐ No

Is PO intended for: ☐ Use by any CHTN Division ☐ Use by only the primary CHTN Division

PROJECT INFORMATION

Project Title:

IRB Review Type (IRB documentation required to show IRB review decision):

☐ Full ☐ Expedited ☐ Exempt ☐ Not Human Subjects Research

☐ Human Use Agreement ☐ Not required (TMA's only)

IRB#: IRB Expiration Date: Exempt-no expiration ☐

PUBLICATION INFORMATION

CHTN'S Research Resource Identifier (RRID): SCR_004446

If applicable, please enter your Open Researcher and Contributor ID (ORCID):

If you do not have an ORCID but would like to obtain one, please click this link and you can follow the steps to apply.

To help determine your priority, please include your major research grant. Institutional and other funding sources may also be listed.

Funding Source #1:

Grant#:

Grant Start Date: Grant End Date:

Extramural peer-reviewed: ☐ Yes ☐ No

Funding Source #2:

Grant#:

Grant Start Date: Grant End Date:

Extramural peer-reviewed: ☐ Yes ☐ No

Currently unfunded: ☐ Please explain:

Please provide below a short research summary of the proposed research on the tissues you are requesting from the CHTN: (please click on the field to start typing)

How did you hear about the CHTN:

- AACR - Smaller Conference
- Colleague
- NCI Specimen Resource Locator
- NCI Website
- New CHTN Investigator/Contact
- Current CHTN Investigator/Contact
- Previous CHTN Investigator/Contact
- CHTN Presentation/Poster Session
- Google Search
- Publication
- Other (write in space below)

AGREEMENT FOR USE OF TISSUE

The recipient/investigator agrees that the tissues provided by the Cooperative Human Tissue Network (CHTN) grantees (Duke University, The Ohio State University, University of Pennsylvania, University of Virginia, Vanderbilt University Medical Center and Nationwide Children's Hospital) will be used only in the laboratory of the recipient principal investigator for the research and/or educational purposes specified in this application and shall be used for no other purpose. The recipient agrees not to attempt to obtain information identifying the individuals providing tissues to the CHTN. The recipient agrees that it shall not sell any portion of the tissues provided by the CHTN, or products directly extracted from these tissues (e.g. protein, mRNA or DNA). The recipient agrees that the principal investigator shall not transfer tissue (or any portion thereof) supplied by the CHTN to internal or external third parties without the prior written permission of the CHTN. Transfer of specimens to a third party specifically for analyses pursuant to the experiments named in the initial application do not need to be reported to the CHTN. If the investigator has created a self-replicating experimental model system (cell line, xenograft tumor line) the transfer of the model system does not need permission from the CHTN. Transfer of primary derivatives of CHTN specimens that are not established self-replicating model systems (organoids, extracted nucleic acids, etc.) for purposes not covered by this investigator agreement do not require prior written permission from the CHTN.

The recipient understands that while the CHTN attempts to avoid providing tissues that are contaminated with highly infectious agents such as hepatitis and HIV, all tissues should be handled as if potentially infectious. The individuals who have supplied tissue to the CHTN have not agreed to have clinical tests performed on this tissue (e.g. for the presence of infective agents such as hepatitis), therefore, the recipient agrees not to perform such tests on the tissues supplied by the CHTN. The recipient acknowledges that the institution where the tissue will be used follows OSHA regulations for handling human specimens and will instruct their staff to abide by those rules. The recipient further agrees to assume all responsibility for informing and training personnel in the dangers and procedures for safe handling of human tissues.

Tissues are provided as a service to the research community without warranty of merchantability or fitness for a purpose or any other warranty, express or implied. Neither the CHTN nor the grantees outlined above accepts any responsibility for any injury (including death) damages or loss that may arise either directly or indirectly from their use by recipient.

The recipient agrees to acknowledge the contributions of the CHTN in all publications resulting from the use of these tissues. Recommended wording for the methods or acknowledgment section is as follows: *"Tissue samples were provided by the Cooperative Human Tissue Network (CHTN), which is funded by the National Cancer Institute. Other investigators may have received specimens from the same subjects."*

When tissue is to be used at State Institutions: The institution agrees to be responsible for any claims, costs, damages, or expenses resulting from any injury (including death), damage or loss that may arise solely from the receipt, handling, storage and use of tissues received from the CHTN to the extent permitted under the laws of this State. The undersigned certify that they have authority to execute this agreement on behalf of the recipient institution.

When tissue is to be used at U.S. Government Agencies: The US government assumes all risks and responsibilities about the receipt, handling, storage and use of tissues received from the CHTN. The United States assumes liability for any claims, damages, injury or expense arising from the use of the material or any derivative, but only to the extent provided under the Federal Tort Claims Act (28 U.S.C. Chap. 171).

When tissue is to be used by all other institutions: The institution agrees to assume all risks and responsibility about the receipt, handling, storage and use of tissues from the Cooperative Human Tissue Network. It further agrees to indemnify and hold harmless the CHTN, the grantees outlined above, and the United States Government from any claims costs, damages or expenses resulting from the use of the tissues provided by the CHTN. The undersigned certify that they have authority to execute this agreement on behalf of the recipient institution.

BY MY SIGNATURE I AGREE TO THE TERMS SET FORTH IN THE ABOVE AGREEMENT

Name of PI Recipient _____

Acknowledgement of PI Recipient _____ Date _____

Name of Official Authorized to Sign for Agency _____

Signature of Agency Official _____ Date _____

Upon receipt of these signed understandings and the information requested above, the CHTN will consider this request and all future requests for tissue. Specific questions about your application should be directed to your regional coordinator. Any other questions should be directed to the NCI Program Director, Dr. Sanita Bharti at 240-276-5909.

DATA USE AGREEMENT BETWEEN COOPERATIVE HUMAN TISSUE NETWORK (CHTN) INSTITUTIONS PROVIDING A LIMITED DATA SET AND LIMITED DATA SET RECIPIENTS

This Data Use Agreement ("Agreement") is designed to permit the use of a Limited Data Set for research pursuant to the Standards for Privacy of Individually Identifiable Health Information, (Privacy Rule) 45 CFR Parts 160 and 164. All terms used in this agreement are as defined in the Privacy Rule.

This Agreement is made and entered into as of this of , 20 by and between the Duke University, the University of Pennsylvania Health System and the University of Pennsylvania School of Medicine, The Rector and Visitors of the University of Virginia for the University of Virginia Medical Center, The Ohio State University, The Abigail Wexner Research Institute at Nationwide Children's Hospital and Vanderbilt University Medical
Center, ("CHTN divisions"), which operate as various divisions of the Cooperative Human Tissue Network (CHTN) and ("Data Recipient").

1. This Agreement sets forth the terms and conditions pursuant to which the CHTN divisions will disclose certain Protected Health Information (PHI) to the Data Recipient. PHI may include associated histopathologic, demographic, and clinical data that have been rendered a Limited Data set in compliance with 45 CFR 164.514(e) (1).
2. Except as otherwise specified herein, the Data Recipient may make Uses and Disclosures of the Limited Data Set consistent with the purpose of the research as described within their research application to the CHTN.
3. The individuals, or classes of individuals, who are permitted to use or receive the Limited Data Set include the Data Recipient and other researchers or individuals directly involved with the research project described within their research application to the CHTN.
4. The Data Recipient agrees to not Use or Disclose the Limited Data Set for any purpose other than the Research Project or as Required by Law.
5. The Data Recipient agrees to use appropriate safeguards to prevent Use or Disclosure of the Limited Data Set other than as provided for by this Agreement.
6. The Data Recipient agrees to report to the CHTN divisions any Use or Disclosure of the Limited Data Set not provided for by this Agreement, of which it becomes aware, including without limitation, any Disclosure of PHI to an unauthorized subcontractor.
7. The Data Recipient agrees to ensure that any agent, including a subcontractor, to whom it provides the Limited Data Set, agrees to the same restrictions and conditions that apply through this Agreement to the Data Recipient with respect to such information.
8. The Data Recipient agrees not to attempt to identify or contact the individual(s) to whom the Limited Data Set applies.
9. This agreement may be terminated by the CHTN divisions upon five (5) days written notice to the Data Recipient if the Data Recipient materially breaches any provision contained in this Agreement and such breach is not cured within the five (5) day period. The Data Recipient acknowledges that if efforts to cure the breach are unsuccessful, the CHTN Divisions may discontinue disclosure of Protected Health Information and report the problem to the Secretary of the Department of Health and Human Services.
10. The terms of this agreement cannot be changed.

DATA RECIPIENT

Name and Title of Principal Investigator_____ Date_____

Authorized Signature _____ Date_____

If whole genome sequencing, whole exome sequencing or assays using other genetic identification technologies will be performed on the specimens being requested from the CHTN or if the specimens being requested will be used for generation of cell lines, patient-derived xenografts (PDX) or similar models, please indicate this below so samples can be screened for appropriate consent status prior to distribution. Biospecimens collected by the CHTN come from a wide range of academic hospitals and allied health care entities and are collected under local human subjects (IRB) approvals which allow minimal-risk research to be performed. However, not all specimen donors give consent for genomic DNA sequencing, to be involved in studies of genetic inheritance, use of their specimens to create cell lines or for sharing of their genomic data in public databases. Therefore, the CHTN will not give blanket assurance that tissue or biofluid specimens provided to our investigators can be used for genetic/genomic studies. The CHTN does not re-contact specimen donors, so such permissions cannot be obtained retrospectively. All CHTN specimens are either fully anonymized or coded-linked but considered permanently de-identified to recipient investigators. CHTN investigators are responsible for the use of the specimens according to the requirements placed on their research by their local IRB and the requirements for publication of any genomic data generated by their studies.

Investigator Policy Acknowledgment

***Please read the policy below and check the box**

☐ I understand and acknowledge that, unless specifically requested, specimens provided by the CHTN may be collected under Waiver of Consent or Surgical Consent and that those specimens are not considered appropriately consented for genomic research, creation and sharing of cell lines or other model systems, publication of genomic research data, or deposition of genomic research data in public databases.

Please check which item(s) below relate to your project.

☐ No, I will not be performing whole genome and/or whole exome sequencing on specimens requested from the CHTN or using these specimens for generation of cell lines or other model systems.

☐ Yes, I will be performing whole genome and/or whole exome sequencing on specimens requested from the CHTN and require specimens from appropriately consented donors. Note that this may significantly reduce the number of available specimens.

☐ Yes, I will be generating cell lines, PDX, or other models using specimens requested from the CHTN and require specimens from appropriately consented donors. Note that this may significantly reduce the number of available specimens.

DO NOT FORGET to fill out the Request Information Form (Part 2) before submitting your documents.

Deidentification, Anonymization and Coded Data and Biospecimens in Human Tissue Research and the Impact on Biorepositories and Research and Discovery

Deidentification (either by anonymization or coding) is a method used to protect the privacy and confidentiality of individuals whose data or samples are procured, stored, or distributed by the Cooperative Human Tissue Network (CHTN), but they have distinct meanings and implications.

Deidentification involves the removal or alteration of personal identifiable information (PII) from data or samples to prevent the identification of individuals. This typically includes personally identifiable information such as names, addresses, social security numbers, and dates of birth (MM/DD/YYYY). Deidentified data or samples may still retain certain indirect identifiers such as age and gender, but they may be modified or generalized to reduce the risk of reidentification. The PII can be irreversibly anonymized (anonymization) or coded (reversibly anonymized).

Anonymization irreversibly removes all PII from the data and samples. This means that there is no way to link the data or samples back to the individual from whom they were obtained. Anonymization typically involves more extensive modification to the data or samples, such as removing all direct and indirect identifiers and ensuring that the remaining information cannot be used to identify the individuals by any means. This means that once the data or samples have been anonymized, they are no longer considered to be linked to any specific individual, and they can be used for research or other purposes without the need for consent. The anonymization process provides a higher level of privacy protection, but it may limit the utility of the data or samples for certain types of research that may generate results that can potentially be re-identified in certain circumstances (e.g., whole genome sequencing).

Coded samples are those in which PII (names, addresses, or medical record numbers) are replaced with a code that allows for tracking and management of the sample without revealing the identity of the individual. A key or code list is maintained separately from the samples, linking the codes to the individuals' identities. This allows researchers or authorized personnel to access additional information associated with the samples if necessary. Coded samples still retain the link to the individual's identity through the code, but the actual identifying information is kept separate and protected by an "honest broker". A code is sometimes also referred to as a "key," "link," or "map".

The "honest broker" is a neutral intermediary (person or system) between the patient's data and/or biospecimens being collected and the investigator. The CHTN acts as the honest

broker as it collects and collates pertinent information regarding the tissue source, replaces identifiers with a code, and releases only coded information to the investigator.

To learn more the following references discuss the concepts noted above in the context of human tissue biorepositories:

1. El Eman, K., Jonker, E., Arbuckle L., Malin, B. (2011). A Systematic Review of Re-Identification Attacks on Health Data. PLoS ONE, 6(12), e28071.
2. Ohm, P. (2009). Broken Promises of Privacy: Responding to the Surprising Failure of Anonymization. UCLA Law Review, 57(6), 1701-1777. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=1450006
3. Gkoulalas-Divanis, A., Loukides, G., Sun, J., Zhang, Y. (2016). Advances in Anonymization: Integrating Evolutionary Game Theory with Data Heterogeneity. IEEE Transactions on Knowledge and Data Engineering, 28(9), 2366-2379.
4. National Cancer Institute. (2018). Best Practices for Biospecimen Resources.
5. NIST Special Publication NIST SP 800-188 De-Identifying Government Datasets: Techniques and Governance (https://doi.org/10.6028/NIST.SP.800-188)

Please check the box to verify you read the Deidentification Document. ☐

DO NOT FORGET to fill out the Request Information Form (Part 2) before submitting your documents.