



University of Rochester and FDA Partnership for the Improvement of Cardiac Safety

The Telemetric and Holter ECG Warehouse

Governance Structure

Version: 2.0 _____
Date: __9/3/2008

1-Rational

Cardiac safety remains a major public health concern. It is also one of the most challenging hurdles in the development of new molecular entities (NME) and biomedical products. For instance, sudden cardiac death (SCD) is the largest cause of natural death in the U.S. causing about 325,000 adult deaths each year and SCD is responsible for half of all heart disease deaths¹. Despite the increased availability and advances in medical imaging, the surface ECG remains a routinely used test because it is inexpensive, non-invasive and provide useful information for the diagnostic and risk stratification of cardiac patients. With the escalating cost of the health care system in US, and world-wide, an optimal cost-benefit ratio of any medical investigation is required. So under such economic pressure and with the spread of ECG technologies in clinical and research settings, the surface electrocardiogram is expected to remain widely used and the incentive to develop new ECG technologies is strong.

Drug-induced adverse cardiac events is another significant public health concern. It has been estimated that as many as 86% of all NMEs tested in pharmaceutical development show specific inhibitory activity of potassium ion kinetics and thus have a potential to prolong the heart's ventricular repolarization (VR), which in some cases can lead to Torsades de Pointes (TdPs) and potentially to SCD.² According to the FDA, the main reason for the inability of the current pharmaceutical development process to effectively screen out potentially harmful drugs, while bringing safe and efficacious medicines to market is the fact that companies “are forced to use the tools of the last century to evaluate this century's advances.” In order to address this problem “a new product development toolkit is urgently needed to improve predictability and efficiency along the critical path.”³ The US Food and Drug Administration (FDA) supports the development of better technologies for the assessment of device and drug safety under its public health mission.

The Telemetric and Holter ECG Warehouse (THEW) is supported by a working group consisting of staff members from the FDA, the University of Rochester (UR), scientific societies and institutes as well as other public and private partners. The THEW is being developed to provide services to public, private and other scientific organizations world-wide by fostering and distributing the resources (data and tools) needed to conduct ECG-related research activities. The THEW Initiative will deploy appropriate information technologies and computer processing power to benefit the overall scientific community. Specifically, the THEW will provide access to continuous electrocardiographic data to for-profit and not-for-profit organizations for the design and validation of analytic methods to advance the field of quantitative electrocardiography with a strong focus on cardiac safety.

2-THEW Value Proposition:

To promote cross-fertilization of scientific knowledge, expertise and to leverage resources that will advance the field of quantitative electrocardiography, THEW will strive to:

¹ Gillum RF. Sudden coronary death in the United States: 1980-1985. *Circulation*. Apr 1989;79(4):756-65.

² Shah RR. Drug-induced QT interval prolongation--regulatory guidance and perspectives on hERG channel studies. *Novartis Found Symp*. 2005;266:251-80; discussion 280-5.

³ Innovation/Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products; Food and Drug Administration; March 2004.

- Develop specific projects to implement the THEW data warehouse and algorithm development and testing;
- Facilitate collaborative discussions, leveraging resources to implement joint projects among FDA, UR, and other public and private stakeholders;
- Identify and evaluate new electrocardiographic markers of cardiovascular risk related to management of patient care and evaluation of new molecular entities;
- Incorporate, as appropriate, scientific findings from the THEW into the pre-market evaluation process for ambulatory electrocardiographic devices, and into the total product life cycle.

By using advanced software tools, internet capabilities and database functionalities (described in APPENDIX A), the THEW Client Application (THEWCA) will ensure connection between users' computer and the THEW servers. The THEWCA will provide access to a large set of ECG recordings and their associated clinical information (See APPENDIX B). The THEW users will have the ability to improve accuracy and reproducibility of their ECG-based technologies by accessing large set of ECGs and associated metrics and to implement clinical research using the information available in the THEW.

3-Governance Structure:

The THEW will be organized into a number of committees drawn from members of the University of Rochester Medical Center, the FDA, national/international industries and national/international Academic Centers/Universities. All individuals/organizations involved in the THEW must review and sign the "Acknowledgement of the Agreement with the Telemetric and Holter ECG Warehouse Initiative" (provided in APPENDIX C)

The THEW structure consists of four groups: the Executive Committee (EC), the Scientific Committee (SC), the Data Review Committee (DRC) and the Translational Research Group (TRG). The constituencies of these groups are provided below.

The Executive Committee – (EC)

Composition:

- URMC Heart Research follow-up Program (3- including chair and co-chair)
- FDA (3 - non voting)
- UR (1)

Responsibilities:

- Define and ensure the objectives of the THEW program in accordance with its mission
- Ensure the development of logistics and operational infrastructure of the THEW
- Review, approve and execute plans
- Establish and oversight the Scientific Committee (SC), Data Review Committee (DRC) and the Translational Research Group (TRG).

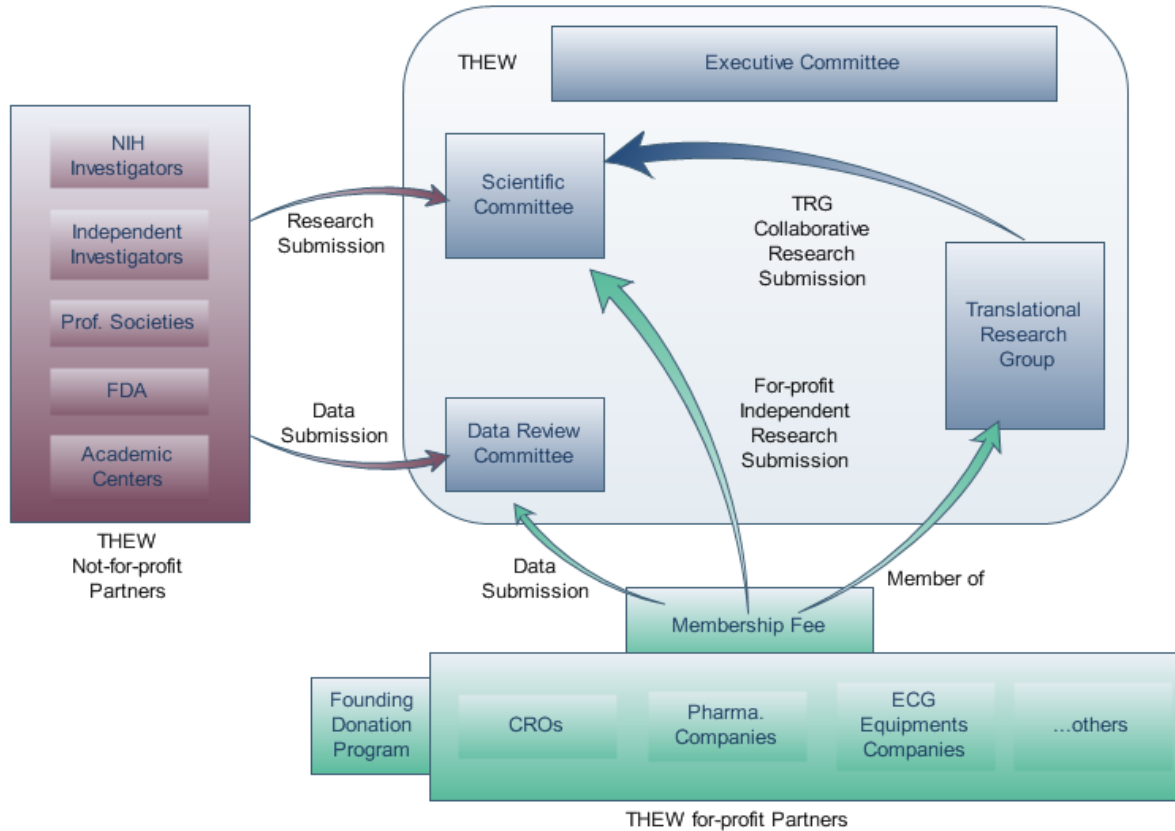


Figure 1: Governance Structure of the Telemetric and Holter ECG Warehouse. This figure schematizes the various players and the associated interactive mechanisms.

The Scientific Committee – (SC) Elected members

Composition:

- URMH Heart Research follow-up Program (1, chair)
- FDA US Human Health Department (1- non voting)
- Independent Academic Individuals (3 – including co-chair)

Responsibilities:

- Review, critique, approve or reject scientific proposals submitted to the THEW,
- Ensure cohesion of the overall research activities around the THEW database,
- Evaluate the financial and scientific feasibility of submitted research projects,
- Refuse/grant the access to the THEW datasets,
- Form ad hoc project-specific advisory groups as needed and define their objectives.

The members of the SC will serve renewable 1-year terms and they will meet on a monthly or as needed basis.

The Data Review Committee – (DRC) *Elected members*

Composition:

- URMH Heart Research follow-up Program (1)
- FDA (1 - non voting)
- Independent Experts (3- including Chair and Co-chair)

Responsibilities:

- Define and periodically update process associated with data submission to the THEW,
- Review and assess quality of submitted data.

The members of the DRC will serve non-renewable 1 year terms. The DRC will meet on a monthly or as needed basis when ECG dataset are submitted to the THEW.

The Translational Research Group – (TRG) *Elected Chair*

The access to the TRG is obtained through the THEW membership. Member of the TRG receives periodic newsletters about the activities of the various research activities in the THEW including new ECG datasets, new granted research proposals, update of members of the EC and the DRC.

Composition:

- URMH Heart Research follow-up Program (1 - Chair)
- FDA US Human Health Department (1 – non voting)
- US and European Corporations (contributors to the THEW)

Responsibilities:

- Discuss and propose technology solutions related to digital quantitative electrocardiography in general that can include drug safety ECG markers.
- Define and write translational research proposal involving multi-partnerships.
- Present commercial technology solutions to the Agency and to the THEW for-profit partners.

The TRG will meet periodically to identify and develop preliminary project proposals, to inform and to obtain feedback from the FDA on research and development strategies. Proposal for research projects from for-profit organizations can be submitted independently from the TRG directly to the SC, or to the TRG to generate synergistic arrangements with other for-profit members of the TRG. All types of projects will be submitted to the SC to assess the alignment between the research project and the THEW objectives.

The members of the DRC will be based on a yearly membership. The TRG meeting will communicate via conference calls and face-to-face meetings organized during international scientific events.

4- Antitrust Guidelines:

All activities with the THEW should be done to advance the mission of the THEW and shall not deter competition among the THEW members and other participants. Generally, the collaborations contemplated by the THEW are expected to be precompetitive in that the technological advancements that are anticipated should enable private companies to move potential new products and services more quickly and efficiently to research and development. In order to ensure the foregoing, the following guidelines shall apply to the THEW activities:

1. All private companies may freely conduct activities that do not infringe the intellectual property of others (see Data Sharing Guidelines and Intellectual Property Guidelines).
2. No member or participant in the THEW shall take or seek action relating to the THEW for the purpose of restraining competition in the marketplace. Any concerns in this regard shall be brought to the attention of the Governing Council for appropriate review and action.
3. No member or participant in the THEW shall communicate to, or exchange with the THEW or any of its governing committees, any information concerning: (a) pricing or pricing policies for any product or service offered by and members, participants or their competitors; (b) market share or the establishment of terms or conditions relating to the sale of products or services; (c) any agreement or arrangement to not sell or not buy from, or to withhold products or services from certain individuals or companies

5- Data sharing Guidelines:

1. Any data sharing activities with the THEW will be governed by the signature of the THEW Data Sharing agreement (see APPENDIX D)
2. The THEW Data Sharing agreement stipulates the type of data and the legal framework under which the data can be used by the THEW members.
3. The submission of data should be sent to the Chair of the Data Review Committee (see THEW website: www.thew-project.org) using the Data Submission form provided in APPENDIX I
4. No “reach through IP” rights can be claimed in the THEW Data Sharing Agreement as described in Section 8.
5. The sharing of data must fit the antitrust guidelines described in section 5.
6. The DRC will provide a response to the submitting organization using the Form attached in APPENDIX I

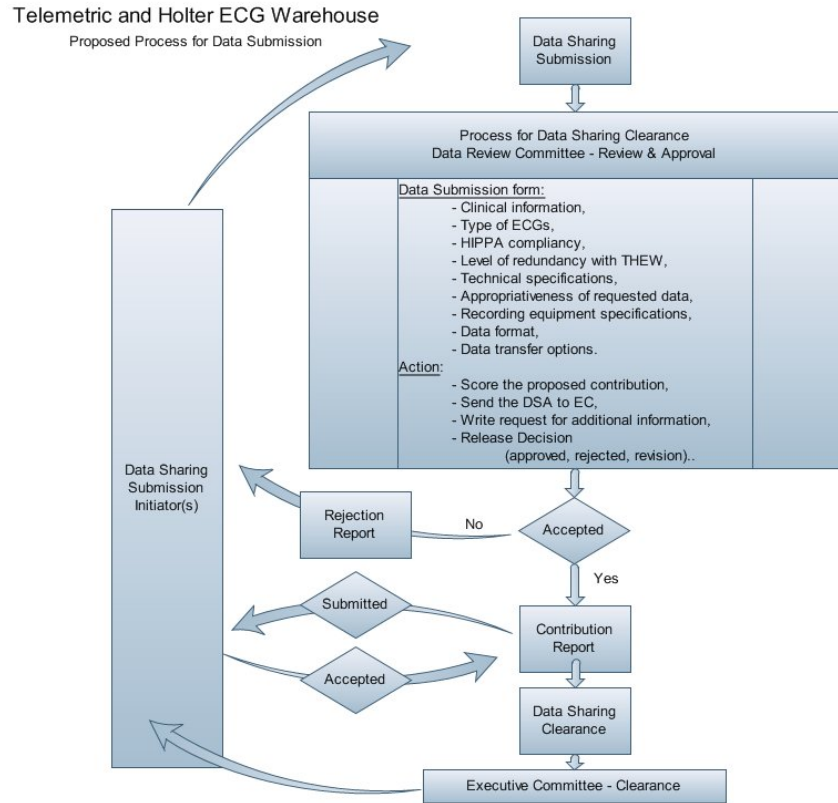


Figure 2: Proposed process for data submission to the THEW.

6- Technology Sharing Guidelines:

1. Any technologies shared with the THEW should be done after the signature of the THEW Non-exclusive technology sharing agreement (see APPENDIX E for the Software Sharing Agreement)
2. Shared technologies will not be distributed to or accessed by external entities which are not official members of the THEW.
3. Sharing of technologies must abide by the antitrust guidelines and IP guideline described in section 4 and 7.

7- Intellectual Property Guidelines:

To accomplish the goals and objectives of THEW, all participants contributing data to the THEW shall retain no claim or right to any intellectual property that may result from the use of their data by others. All data provided to THEW shall be placed in the THEW server and shall be available for use by THEW members under the current options described in section 9. By providing information and data to THEW, all providers acknowledge the terms of this policy and have ensured that there are no rights to the data provided that would conflict with these terms.

8- Data Usage Guidelines:

1. The access to the data cannot be granted before the awarded users have signed the THEW Data Use Agreement (see APPENDIX F)
2. The THEW Data Sharing agreement stipulates the type of data and the legal framework under which the data can be used by the THEW members.
3. The sharing of data must fit the antitrust guidelines described in section 5.

9- Membership and Data Access Fees:

Any for-profit organization is eligible to be part of the THEW by charitable contribution to the program and/or purchasing the access to the THEW databases.

1. The proposed fee for access is dependent on the organization size. We define three types.

$[\geq 100]$ employees: large companies
 $[20-100]$ employees: medium company
 ≤ 20 employees: small company

The THEW will function under a “cost center” structure. Fees for membership and data access will be used to cover maintenance and development of the THEW. These fees will be adjusted on a yearly basis based on number of members and the changes in content of the warehouse. This costing structure will be in accordance with the costing structure described in the circular A-21 of the US Office of Management and Budget for specialized service facilities. No intellectual property restrictions apply to the use of this data.

2. The access to database for regular membership depends on the database and their development and maintenance costs.

The fees for membership and database access for year 2008-2009 are described in the following table. We defined two types of yearly memberships:

- 1) Full access membership providing access to all databases available in the THEW at the time of the membership purchase and
- 2) Regular membership with which additional data access purchase is required to access specific database.

| THEW Full Access Membership | | |
|--|--------------------|-----------|
| Small company | (<=20 employees) | \$ 23,000 |
| Medium company | (20<employees<100) | \$ 33,000 |
| Large company | (>=100 employees) | \$ 43,000 |
| THEW Regular Membership | | |
| Basic Yearly Membership (Regular) | | |
| Small company | (<=20 employees) | \$ 10,000 |
| Medium company | (20<employees<100) | \$ 20,000 |
| Large company | (>=100 employees) | \$ 30,000 |

10- Proposed Mechanism for THEW Activities:

We define 3 independent but combinable types of activities within the THEW: data sharing/exchange, technology contributions and collaborative research projects.

1. Data Sharing: we defined a process around the submission of ECG data to the THEW described in Section 6. The quality of the submitted data will be reviewed by the THEW Data Review Committee to decide whether the data is appropriate and bring scientific value to the warehouse. Data contribution to the THEW will provide to the contributor a THEW account, a licence for the Client Application and the access to one (or a set of) database(s) at the time of the signature of the Data Sharing Agreement (DSA). The list of awarded accesses will be defined by the DRC and mentioned in the DSA. The DSA stipulates that the contributing organization cannot claim “reach-through” intellectual property (IP) right on any technology developed by the THEW users. Eliminating the link between data ownership and IP rights is required in order to enable incentives for users to develop valuable technologies and to facilitate translational research (see Section 8). For for-profit organizations, data contribution will provide data access under the condition that this company is a THEW member and has purchased, at least, a basic yearly membership.
2. Technology Contribution: we invite organizations to share their technologies to improve and grow the initiative. This type of contribution can be either technologies supporting the

warehouse infrastructure or technologies related to the analysis of ECG signals. The submission process for technology sharing will be done through the Executive Committee of the THEW and described in their Non-exclusive Software/Technology Sharing Agreement (see APPENDIX E for the Software Agreement). Technology sharing can be considered as in-kind contribution toward the purchase of membership and data access when the EC consider this is appropriate.

3. Collaborative Research Project: one of the objectives of the THEW project is to facilitate collaborative initiatives and spawn research activities by initiating, supporting, and fostering research grant proposals. Thus, the THEW will provide a set of documents to help its users and potential users to apply for private, governmental and federal research funding programs. The description of the process involved in these submissions is schematized in Figure 3. A research proposal cannot be submitted more than three times

Research Proposal (RP): the RP should provide the rationale for the research work and information about the resource allocation for the implementation of the project. The THEW Form for research proposal submission (see APPENDIX G) should be submitted to the Chair of the SC. The contact of this person is available on the THEW website (www.thew-project.org). The RP is a short document describing the objective(s) of the research and the research hypothesis. It includes a section for requesting partnerships with for-profit or/and non-for-profit organization.

The RP will be reviewed by the RC and a review report (see APPENDIX H) will be sent back to the authors. Collaboration involving for-profit organizations will require these organizations to purchase, at least, a basic membership to the THEW.

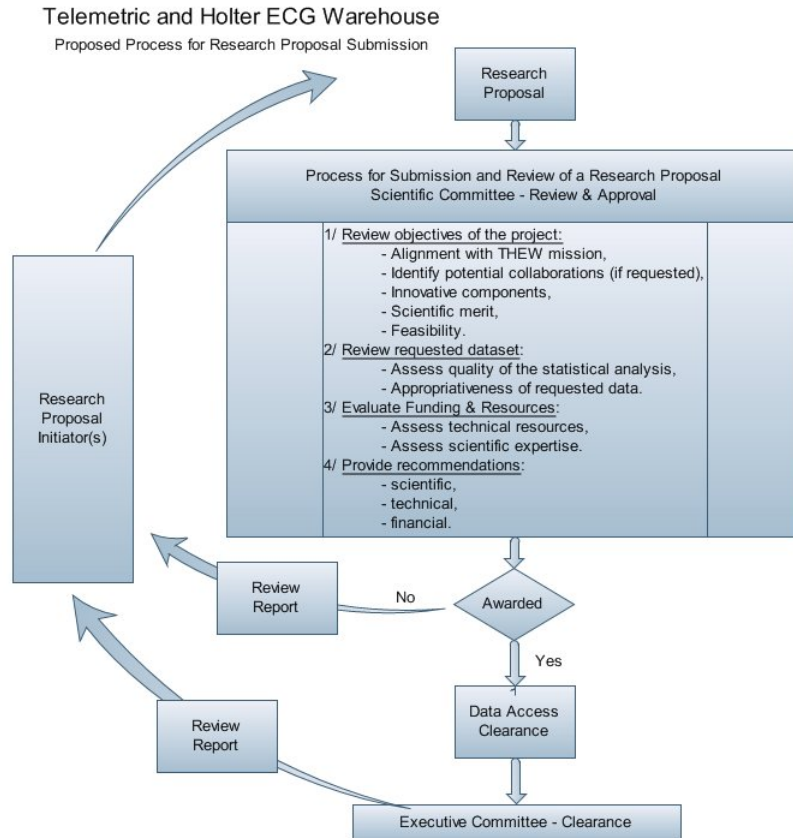


Figure 3: The SC is the only consistency involved in the approval of the research proposal. The final clearance for data access will be granted only when the Data Sharing Agreement signature has been received by the EC.

For not-for-profit organizations, the access to the THEW database will be granted to award investigators without the need for any other contributions.

Note: the THEW forms are currently being evaluated and might be changed over time. To obtain the most updated version of these forms please visit the THEW website and download the forms from the "content" area. (www.thew-project.org)

APPENDIX A:

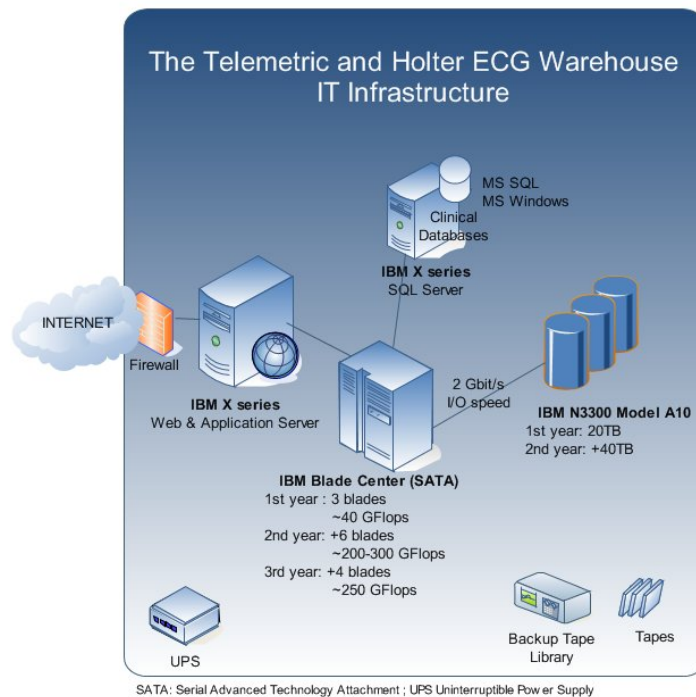
THEW Information Technology infrastructure

THEW Infrastructure

The infrastructure of the THEW is described in Figure 1. The THEW structure includes 3 servers. First, the web server hosts the website of the THEW (www.THEW-project.org). In addition, it will include the application server and the management tools for the THEW user accounts. Second, the data server will host all the ECG files, this server will have the ability to host a large amount of storage (~50 Tb). Finally, the SQL server will host the Holter Management System storing and managing the clinical information and ECG metrics.

THEW Content

The THEW includes several large databases of de-identified Holter ECG recordings. The majority of these recordings are fully annotated. Most of them have been acquired using digital recorders. The recordings are from healthy individuals exposed to cardiac and non-cardiac drugs, from patients with the congenital and the acquired form of the long QT syndrome, from post-myocardial patients and from patients with coronary artery disease. A more detailed description of the THEW content is described in Table I, it includes the name of the database, the number of recordings, the number of leads recorded in each Holter and a brief description of the content of each database.



THEW architecture and basic foundation. This structure does not include the Computing Center that will be added later on.

- **Storage:** The Center will host digital Holter, telemetric and standard electrocardiograms. These recordings can be continuous 2-12 lead 24-hour high-resolution signals. A single file can contain 500Mb of data (1,000Hz, 16-bit resolution, 12 leads). A study can contain 500 to 5,000 recordings. We expect to host a total number of ECGs requiring 50Tb of storage during the year 2009.

- **Computation Power:** Because the ECG files are too large to be sent over the internet in a timely fashion, the Center will incorporate a Data Processing Server to which the algorithms of scientific partners will be uploaded in order to process a large set of ECG data.

APPENDIX B:

THEW Client Application (THEWCA)

A client application will be available for download on the THEW website (www.THEW-project.org). This application requires Microsoft XP and a high-speed internet connection. This client side application is a direct bridge to the data of the THEW. It provides numerous features:

- **Setup tools:**
 - Access to user account information,
 - Database selection,
 - Plugins registration,
 - Connection setup.
- **ECG tools:**
 - Browsing ECG lists,
 - Selection of ECG files,
 - Browsing continuous Holter data,
 - Selection of ECG interval for client-side processing,
 - Accessing to specific metrics.
- **Development tools:**
 - System Development Kit (SDK),
 - Examples of simple plug-in codes.

A full specification document for the THEW CA will be released at later date.

APPENDIX C:

Please download and read the governance document of the THEW initiative and then sign the following form to be sent to the Chairman of the Executive Committee of the THEW.

Acknowledgement of the Governance of the THEW Initiative

As a member of the Telemetric and Holter ECG Warehouse (THEW), I have received and understand the conditions for participating to the THEW initiative program as described in the Governance document of the THEW.

Name: _____

Title: _____

Organization: _____

Date: _____

APPENDIX D:

DATA SHARING AGREEMENT
between
TELEMETRIC AND HOLTER ECG WAREHOUSE
at the
UNIVERSITY OF ROCHESTER
and

This Agreement is made and entered into this ___ day of _____, 200_ between the Telemetric and Holter ECG Warehouse (“THEW”) of the University of Rochester and _____ (“PROVIDER”).

THEW is a data warehouse used as a repository of ECG datasets comprised of large amounts of digital ECG signals that will be useful for the development of novel ECG technologies related to the development of ECG markers that can help in the assessment of cardiotoxicity.

PROVIDER has developed one or more data sets of digital ECG signals as more fully set forth below (the “Data”). PROVIDER is the full owner of such Data and is providing the Data to THEW on the terms set forth herein.

Therefore, PROVIDER agrees to share the following Data to THEW:

1. Description of Data :

2. The Data was obtained pursuant to the (name of study) _____ research study under the following conditions:

- a. PROVIDER certifies that it has all necessary rights, power and authority to transfer the Data to THEW for use in the THEW database.
- b. PROVIDER certifies that no personal health identifiers are included in the Data or that appropriate patient consent and HIPAA authorization or IRB/HIPAA board waiver has been obtained for all identifiable Data.
- c. If Data is comprised of ECG signals obtained from patients outside of the U.S., PROVIDER certifies that all applicable laws and regulations for the transfer of the Data to THEW have been complied with; and
- d. In the event PROVIDER becomes aware of any inadvertent disclosure of personal health information as provided under HIPAA regulation, PROVIDER will promptly inform THEW and PROVIDER and THEW agree to take all commercially reasonable measures to remove such information from the Data and the THEW database.

3. PROVIDER represents that no intellectual property pre-commitments exist for the Data that would interfere with the incorporation of the Data into the THEW database. PROVIDER understands that Users of the THEW database (which will include the Data), will be entitled to access and use the Data for any commercial or non-commercial research purpose without any intellectual property obligations to THEW or PROVIDER.

4. PROVIDER has made reasonable efforts to ensure that the Data is accurate.
5. PROVIDER acknowledges that THEW is not responsible for the content of the THEW database, including the Data or for monitoring the use of the database, including the Data by users.
6. This Agreement shall cover the Data shared hereunder and shall continue indefinitely unless earlier terminated at the request of either party. If PROVIDER elects to terminate this Agreement, THEW will use commercially reasonable efforts to remove the Data from the database but any access to the Data by Users prior to the date of removal shall continue to be permitted pursuant to the terms hereof.
7. Nothing in this Agreement is intended to, or shall, create any agency, partnership or exclusive relationship between the parties. Subject to the parties' obligations specified herein, each party shall be free to independently pursue related or similar business opportunities. Nothing in this Agreement shall be construed as any representations or commitment that either party will engage the services of the other for any future arrangement.
8. This Agreement is expressly made subject to all laws and regulations of the United States, without regard to any choice of law principles.
9. The terms and provisions of this Agreement represent the entire understanding of the parties with respect to the transfer of the Data by PROVIDER to THEW.

IN WITNESS WHEREOF, the parties have caused this Agreement to be executed as of the first date written above.

UNIVERSITY OF ROCHESTER
on behalf of THEW

PROVIDER

By : _____
Name:
Title:

By: _____
Name:
Title:

APPENDIX E:

NON-EXCLUSIVE SOFTWARE LICENSE AGREEMENT

THIS NON-EXCLUSIVE LICENSE AGREEMENT (“Agreement”) is a legal agreement between _____, a business corporation with offices at _____ (the “Licensor”) and University of Rochester, an educational institution chartered by the State of New York, having its business office at 601 Elmwood Avenue., Rochester NY (“Licensee”) and governs the license of certain software as more fully set forth herein (the “Software”).

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2. LICENSE RESTRICTIONS.

(a) Licensee agrees to use the Software for the use of the University of Rochester’s *Telemetric and Holter ECG Warehouse (THEW)*, and not for any other purpose not specifically stated in this Agreement. Licensee may make copies of the Software only for internal archival or back-up purposes. Title in all copies shall be reserved by Licensor. Software Licensee may not modify, translate, reverse engineer, de-compile, disassemble (except to the extent that this restriction is expressly prohibited by law) or create derivative works based upon the Software or any related documentation. Licensee may not remove any proprietary notices or labels on the Software or any related documentation.

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(c) Licensee agrees to only use the Software and any related documentation in a manner that complies with all applicable laws in the jurisdictions in which it uses the Software and documentation, including, but not limited to, applicable restrictions concerning copyright and other intellectual property rights.

3. LICENSE PERIOD. The license granted in this Agreement shall remain in full force for a minimum term of five years unless terminated prior to that time as provided herein.

4. PAYMENT. In payment for the license granted under this Agreement, Licensee shall pay Licensor the total sum of \$0.00 as a license fee, due and payable in full upon the execution of this Agreement. Licensee shall pay all taxes that may be assessed on the Software or its use, including personal property taxes, sales and use taxes and excise taxes.

5. DELIVERY AND ACCEPTANCE OF SOFTWARE. The Software shall be deemed to have been accepted by Licensee upon delivery. Upon any refusal by Licensee to accept the Software, Licensee must return the Software to Licensor and report reasons of unacceptability of the Software.

6. PROPERTY RIGHTS. Licensee acknowledges and agrees that the Software is the confidential and proprietary property of Licensor, and except to the extent expressly authorized under this Agreement, Licensee

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9. INDEMNIFICATION BY LICENSOR. Licensor agrees to, at its own expense, hold harmless, indemnify and defend Licensee against any claims that the Software infringes any copyright or patent in existence on the date the Software was initially provided to Licensee.

10. TERMINATION. This License Agreement will automatically terminate upon the occurrence of any of the following: (i) Licensee fails to comply with any term of this Agreement; (ii) Expiration of the term specified in this Agreement or (iii) cessation of business by Licensee or any successor or assign to whom the Software has been legitimately transferred.

11. NO ASSIGNMENT. You may not assign, sell, transfer, delegate or otherwise dispose of this Agreement, whether voluntarily or involuntarily, by operation of law or otherwise. Any purported assignment, transfer or delegation by you will be null and void. Subject to the foregoing, this Agreement will be binding upon and will inure to the benefit of the parties and their respective successors and assigns.

12. TECHNICAL SUPPORT. Licensor has no obligation to provide support, maintenance, upgrades, modifications or new releases for the Software or any related documentation under this Agreement.

13. ALTERATIONS. This Agreement may NOT be altered, supplemented or amended by the use of any other document(s) unless otherwise agreed to in a separate written agreement signed by both Licensee and Licensor.

18. PRODUCT. Licensor’s software is updated and revised from time to time. Licensor may revise and discontinue products at any time without notice to you.

19. MISCELLANEOUS.

(a) Arbitration & Jurisdiction. Licensee and Licensor agree that the exclusive remedy for all disputes and claims relating in any way to, or arising out of, this Agreement, or Licensee’s use of the Software, (including the arbitrability of any claim or dispute and the enforceability of this paragraph), or to any other alleged act or omission by Licensee or Licensor toward the other, shall be final and binding arbitration. The arbitration shall be conducted under the Commercial Arbitration Rules of the American Arbitration Association (“AAA”) before a

panel of three arbitrators and conducted in the United States of America, State of New York, pursuant to the laws of the State of New York.

(b) Complete Agreement. This Agreement shall constitute the complete and exclusive agreement between Licensee and Licensor. The terms and conditions contained in this Agreement may not be modified by Licensee except in a writing duly signed by Licensee and Licensor. If any provision of this Agreement is held to be unenforceable for any reason, such provision shall be reformed only to the extent necessary to make it enforceable, and such decision shall not affect the enforceability of such provision under other circumstances, or of the remaining provisions hereof under all circumstances.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

LICENSOR

LICENSEE:

University of Rochester

By: _____

Name:

Marjorie Hunter

Title:

Director

Office of Technology Transfer

APPENDIX F:

DATA USE AGREEMENT

1. This agreement is between the Telemetric and Holter ECG Warehouse managed by the University of Rochester (THEW), and _____, hereinafter termed "User". Both parties mutually agree to enter into this agreement to comply with the following specific paragraphs.

2. This Agreement addresses the conditions under which THEW will disclose and the User will obtain and use the data file(s) specified in section 5. The parties agree further that any additional instructions or interpretations concerning this Agreement or the data specified herein but not specified in this agreement shall not be valid unless issued in writing by the THEW point-of-contact specified in section 4 or the THEW signatory to this Agreement shown in section 14.

3. The parties mutually agree that the User does not obtain any right, title, or interest in any of the data furnished by THEW. The User recognizes that there may be errors in the Data. I will review the THEW Policies (www.THEWproject.org/policies/) for a discussion of the limitations of the Data and will not hold THEW or the University of Rochester liable for any such errors.

4. The parties mutually agree that the following named individual will be designated as "point-of-contact" for the Agreement on behalf of THEW.

_____[Name]
_____[Title]
_____[Address]
_____[Tel.]
_____[E-mail address]

5. The User represents and warrants that such data file(s) will be used solely for the following purpose(s):

The User represents and warrants further that the User shall not disclose, release, sell, rent, lease, loan, or otherwise grant access to the data covered by this Agreement to any person. The User agrees that, within the User's research group, access to the data covered by this Agreement shall be limited to individuals on a need-to-know basis only.

The following THEW data file(s) is/are covered under this Agreement
Files:

6. The User agrees to establish appropriate administrative, technical, and physical safeguards to prevent unauthorized use or access to the data.

7. As described in the THEW Policies {www.THEWproject.org/policies/}, all Data contained in the THEW is intended to be de-identified for the purposes of the Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and the regulations promulgated thereunder. In the event of an inadvertent disclosure of "protected health information" as defined in 45 CFR Section 164.501, User agrees to (a) fully comply with HIPAA and the regulations promulgated thereunder with respect to the use of such protected health information, and (2) report in writing to the name and address specified in Section 5 of this Agreement any protected health information that is contained in the THEW data files accessed by User.

8. In an effort to avoid simultaneous submission of similar articles to scientific journals, the User **agrees to notify THEW upon the submission of any and all manuscripts submitted for publication based on findings from analysis of the THEW Data**. Notification shall include the title of each manuscript, an abstract for each manuscript, and the name(s) of the journal(s) to which the manuscript(s) will be submitted. Notification shall be directed to the THEW point-of-contact specified in section 4 or the THEW signatory to this agreement shown in section 14. The User agrees to send a reprint of the manuscript that uses the THEW Data to the THEW point-of-contact specified in section 4 or the THEW signatory to this agreement shown in section 14 whenever the manuscripts are published.

9. The User agrees that the following credit line and disclaimer will be used on all reports, publications and other materials resulting from use of THEW Data:

Data used for this research was provided by the Telemetric and Holter ECG Warehouse of the University of Rochester (THEW), NY.

10. The User agrees that in the event THEW determines or has a reasonable belief that the User has made or may have made disclosure of the aforesaid file(s) that is not authorized by this Agreement, or has used the aforesaid files for commercial purposes, THEW in its sole discretion may require the User to: (a) promptly investigate and report to THEW the User's determinations regarding any alleged or actual unauthorized disclosure and/or uses, (b) promptly resolve any problems identified by the investigation; (c) if requested, submit a formal response to an allegation of unauthorized disclosure and/or use; (d) if requested, submit a corrective action plan with steps designed to prevent any future unauthorized disclosures and/or uses; and (e) if requested return data files to THEW. The User understands that as a result of THEW's determination or reasonable belief that unauthorized disclosures and/or uses have taken place, THEW may refuse to release further data to the User for a period of time to be determined by THEW.

11. User will indemnify, defend and hold harmless THEW and the University of Rochester from and against any claim, cause of action, liability, damage, cost or expense (including, without limitation, reasonable attorneys fees) arising out of or in connection with the use of all or any portion of the THEW data by the User or any of its subcontractors, agents, employees or other assigns.

12. By signing this Agreement, the User agrees to abide by all provisions set out in this Agreement for protection of the data file(s) specified in section 5.

13. On behalf of the User the undersigned individual hereby attests that he or she is authorized to enter into this Agreement and agrees to all the terms specified herein. There are no intended third party beneficiaries to this Agreement.

(Name and Title of Individual - Typed or Printed)

(Company/Organization)

(Street Address)

(City/State/ZIP Code)

(Phone and Fax No., and E-Mail Address)

Signature (Date)

14. On behalf of THEW the undersigned individual hereby attests that he or she is authorized to enter into this Agreement and agrees to all the terms specified herein.

(Typed or Printed Name and Title of THEW Representative)

(Signature) (Date)

APPENDIX G:

**Proposed Submission Form for Research Proposal
For the Scientific Committee of the THEW**

- Research Proposal ID #:

-Research Proposal Title:

- Investigators (names and organizations):

- Submission for collaborative proposal: Yes No

- Will the data be used to obtain grant/financial support from federal agency? Yes No

- Will the data be used to obtain grant/financial support from for-profit organization? Yes No

- Will the data be used to obtain grant/financial support? Yes No

(if yes in any of the 3 previous questions, provide contact name and address of the solicited organization)

- Describe the Objectives of the Research proposal and how it is aligned with the mission of the THEW

- Describe the Innovative aspect of the Research Proposal

A two page proposal should accompany this form. These two pages should be organized as follow:

1/ Background,

2/ Working Hypothesis,

3/ Method,

4/ Prior experience in the domain,

5/ Financial support,

6/ Conclusions,

7/ Five to six references related to the field.

APPENDIX H:

Review Report Form from the Scientific Committee of the THEW

- Research Proposal ID #: Approved Revised Reject
- Research Proposal Title:

- Investigator(s) (name(s) and organization(s)): _____

- Submission for a collaborative proposal (inviting other parties to join): Yes No

- Is the research proposal aligned with the THEW mission statement? Yes No

(If no please explain)

- Is the proposal includes innovative medical and/or technical concepts?

- Is the main question relevant to the field of quantitative electrocardiography?

- Are the research objectives realistic? Yes No

(If no please explain)

- Are the statistical analyses appropriate and likely to demonstrate the working hypothesis? Yes No

(If no please explain)

APPENDIX I:

Data Submission Form to the THEW (* required)

1. *Data Sharing Agreement #: _____ Associated THEW Research Proposal (optional): _____

2. *Data Description (same as in DSA):

3. *Initiators(s) (name(s) and organization(s)): _____

4. *Do the submitted data include patient clinical information? Yes No
-if 'yes' to item 4:

Please provide detailed description of the clinical information (documents can be attached):

What is the format of the file including clinical information?

5. *Is the submitted data HIPPA compliant? Yes No

6. *Were the individuals consented using approved consent form and did they agreed on sharing their ECGs for research purpose? Yes No

7. Is the submitted data similar to database already hosted in the THEW? Yes No
(If 'Yes' please explain the uniqueness or interest of adding this dataset to the warehouse)

8. Type of ECG recordings submitted to the THEW? (please insert all information you may have about the dataset)
(The THEW does not require the submitted data to be converted in any specific format)

Digital data Analog data Paper tracings Other: _____

How many leads? _____

What are the recorded leads? _____

ECG sampling frequency (Hz):

180 Hz 200 Hz 250Hz 1000Hz Other: _____

ECG amplitude resolution (insert unit)? _____

Holter 24-hour

Standard 12-lead Strips

Telemetric

Other: _____

9. *ECG equipment brand name: _____

10. ECG recordings type: _____

11. Number of ECGs: _____

12. Number of Patients: _____

13. Recordings duration (if variable provide average): _____

14. Size of the set of files: _____

15. Recommended method for sharing the data (recommended size):

- FTP transfer (<1Gb)
- mailed DVDs/CDs (≤40 Gb)
- mailed USB Hard drive (>40Gb)
- Others: _____

16. Is a copy of the Study protocol shared? Yes No

17. Does the dataset include information related to marketed drugs? Yes No

(If 'Yes' please describe)

18. *Description of the ECG Dataset (any documents can be attached):

19. *Did the organization/individual signed and forwarded the THEW DSA to the THEW DRC? Yes No

Section reserved to the THEW Data Review Committee

- Did the DRC receive the THEW DSA related to this submission? Yes No

Approved

Recommended method for sharing the data:

- FTP transfer
- mailed DVDs/CDs
- mailed USB Hard drive
- Others: _____

Revised

Reject

Comments:

Chairman of the THEW Data Sharing Committee:

Signature: _____

Date: _____