TELEMETRIC *and* HOLTER ECG WAREHOUSE

UNIVERSITY *of*
ROCHESTER

www.THEW-project.org

TELEMETRIC and HOLTER ECG WAREHOUSE

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Pharmaceutical companies:

Abbott,
Astra-Zeneca,
Inspire Pharmaceuticals, Inc.
Johnson&Johnson,
Pfizer,
Roche,
Shire Pharmaceuticals,
Wyeth Research.

CROs

Cardiocore,
CardioDx
Duke Clinical Research Institute,
eResearch Technology,
iCardiac Technologies,
MDS Pharma Services,
Medifacts International,
Quintiles,
SpaceLabs.

ECG-related companies & others:

AMPS,
Biosigna,
Cardionet,
Digital Oxygen Corp.,
Entelligent Solutions,
GE-Health Care,
Global Instrumentation,
Monebo,
Mortara Instruments,
Nabios,
NewCardio,
Philips Health Care,
Zoll-LifeCor

Academic & NPO

CCTS, Columbia
Critical Path Institute,
FDA (CDER, CDRH),
Harvard University,
ISI (Czech Republic),
Jefferson Heart Institute,
Social & Scientific Systems,
St. George's University of London,
St. Paul's Cardiac Electrophysiol.,
Uniform Services University Health,
University of California (SF),
University of Marche (Italy)
University of Rochester (NY),
University of Utha,
University of Zaragoza (Spain)

Registered Organizations

8:00 AM Welcoming
8:10-9:30 The Telemetric and Holter ECG Warehouse: 2009 update
9:30-10:45 Enabling Research Activities (Academic Perspectve)

Dr. Christine Garnett (Silver Spring, CDER, FDA):
CSRC White Paper: QT/QTc evaluation for drugs with autonomic effects
Dr. Mark Haigney (Uniform Services University Health, MD):
QT variability and drug safety
Dr. Marek Malik (London University, UK):
QT measurements and heart rate corrections
Dr. Richard Verrier (Harvard University, MA):
T-wave alternans and Drug Safety
Dr. Wojciech Zareba (University of Rochester, NY):
Repolarization Morphology and Cardiac Safety

10:45-11:15 Break

11:15-12:30 Enabling Research Activities (Industry perspectives)

Dr. Fabio Badilini (AMPS, NY, USA):
Optimized ECG extractions in clinical trials
Dr. Anthony Fossa (iCardiac Technologies, NY, USA):
Prospective Evaluation of advanced ECG/Holter markers to differentially assess the QT Interval with drugs that affect autonomic state vs. impair repolarization
Dr. Adel Nada (Abbott, IL, USA):
Thew Initiative: A valuable resource to large pharmaceutical company in managing cardiac safety in clinical development
Dr. Jeremy Rice (IBM, NY, USA):
Combination in vitro and in silico methodology for risk assessment of Long QT type 1 patients
Dr. Larry Satin (Cardiocore, MD, USA):
The Value of Holter Arrhythmia Analysis in Thorough QT Trials

12:30-12:45 FDA Perspectives (Dr. N. Stockbridge)
12:45-13:00 Discussion

Agenda

TELEMETRIC and HOLTER ECG WAREHOUSE

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THEW Executive Committee:


Jean-Philippe Couderc, PhD (Chair, URMC)


Benjamin Eloff, PhD (Commissioner Office- FDA)


Arthur J Moss, MD (URMC)


Gail Norris (URMC)


Wendy R. Sanhai, PhD (Commissioner Office- FDA)


Norman Stockbridge, PhD (CDER-FDA)


Wojciech Zareba, PhD, MD (co-Chair, URMC),

The objective of the *Telemetric and Holter ECG Warehouse (THEW)* is to provide access to 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.

Mission Statement

- Not-for-profit Organization - 501(c)(3)

- Costing structure is in accordance with the Circular A-21 costing for specialized service facilities from the Office and Management and Budget.

-Cost Center: Donation Program, Membership, Data Access Fees, Grants

Legal Status

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FDA and University of Rochester Partnership

•Facilitate collaborative discussions, leveraging of resources for the implementation of **joint projects among FDA, UR, and other public and private stakeholders**;

•**Develop, identify and evaluate new electrocardiographic markers** of cardiovascular risk related to management of patient care and evaluation of new molecular entities;

•As appropriate, **incorporate scientific findings from the THEW into the pre-market evaluation process** for ambulatory electrocardiographic devices, and into the total product life cycle.

UR-FDA Agreement

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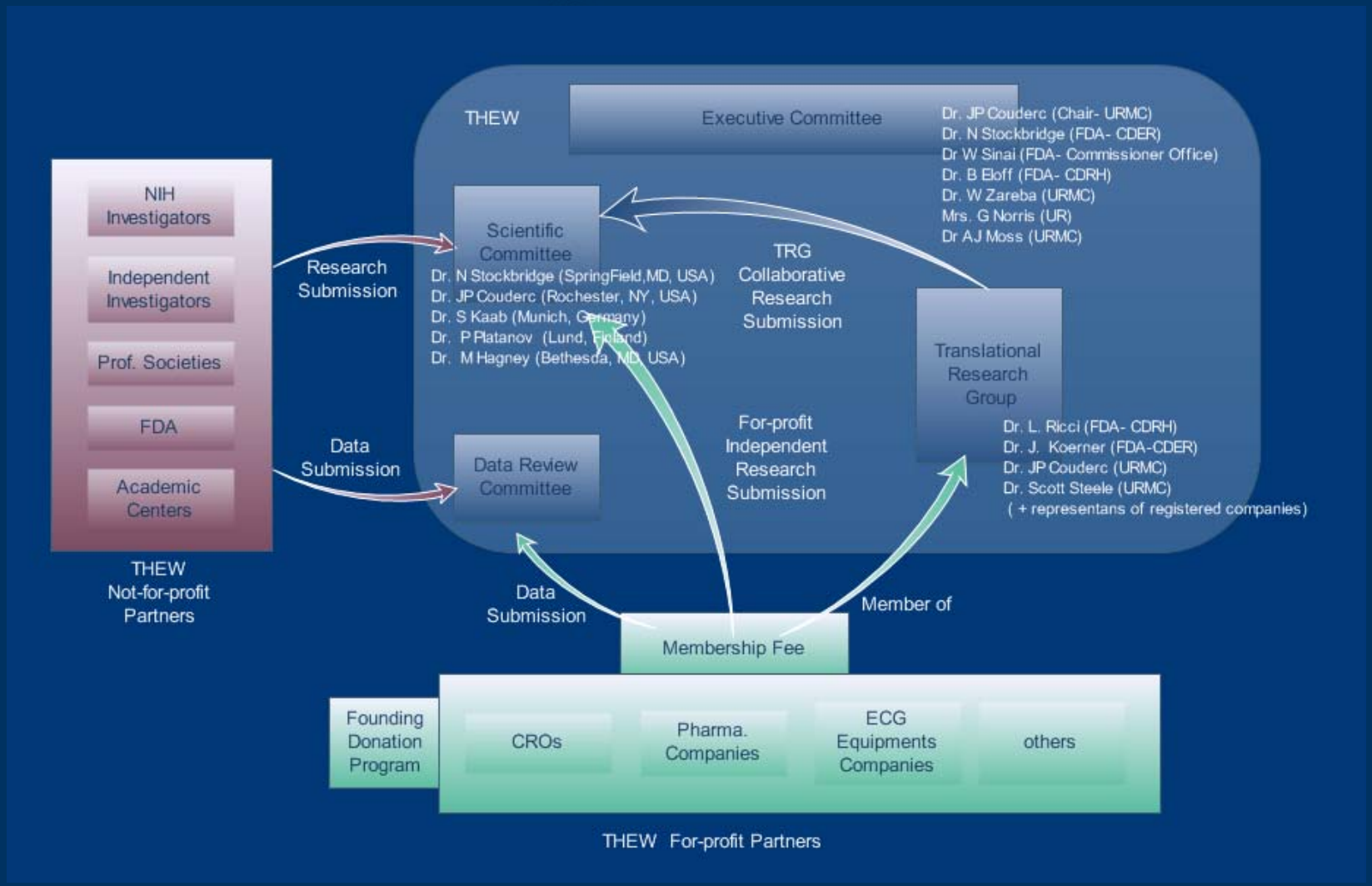

Governance Structure

TELEMETRIC and HOLTER ECG WAREHOUSE

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Founding Donation Program:
AMPS, LLC, NY, USA
GE-Health Care Inc., WI, USA
Global Instrumentations, LLC, NY, USA
iCardiac Technologies Inc., NY, USA
Mortara Instruments, WI, USA
Philips Medical System, CA, USA
Schiller America Inc., FL, USA

Cardiocore

Roche DSA DUA (TQT)

Global Instrumentations TSA

Governance Structure

FDA/URMC Agreement:

12-2007 01-16-2008 MAY 05-27-2008 07-01-2008 JULY 07-15-2008 09-03-2008 SEPTEMBER 09-10-2008 09-15-2008 OCTOBER 10-06-2008 10-30-2008 DECEMBER 12-04-2008

FIRST THEW EVENT:
FDA CAMPUS, SilverSpring , MD

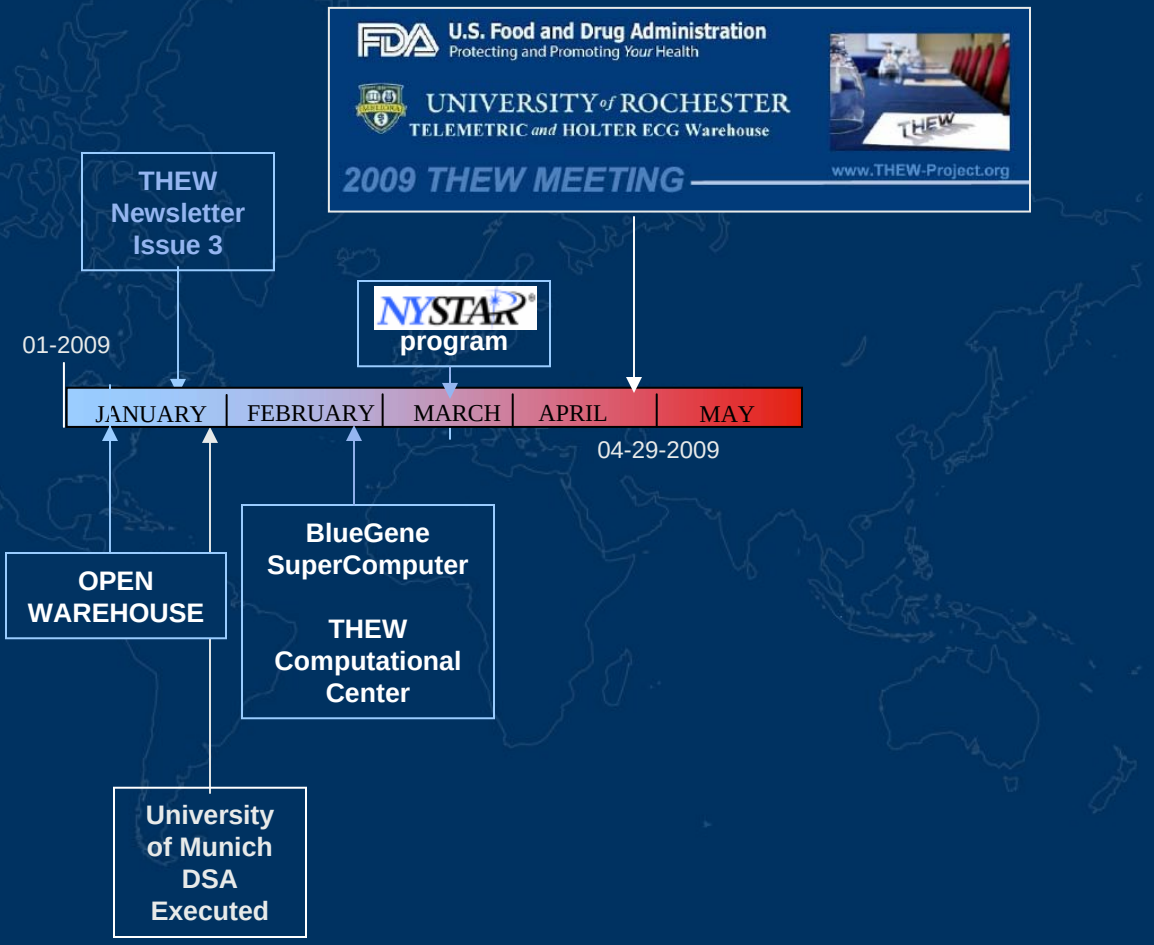
THEW Newsletter Issue 1

Pfizer DSA (TQT)

THEW Newsletter Issue 2

AMPS TSA

2008 THEW Milestones



2009 THEW Milestones

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Promoting cross-fertilization of scientific knowledge, resources, and ideas that will advance the field of quantitative electrocardiography

DATA : ECGs for R&D activities

- Cardiac patients
- Healthy individuals
- Drug–induced arrhythmias
- Congenital LQTS

EXPERTISE:

- Academic Network
- Private Partners
- Regulators,

Others….

TOOLS:

- ECG data access / visualization / APIs (Client Application)/ SFTP
- Computing Centers for development/validation of ECG algorithm on large database.

THEW : Data, Expertise and Tools

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	Study	ECG type	Contributor	# recordings	Population	
2008	**IDEAL 1**	24-hour Holter	HRFUP	206	Acute Myocardial Infarction	
	IDEAL 2	24-hour Holter	HRFUP	265	Healthy Individuals	
	Moxifloxacin	24-hour Holter	Roche	142	Thorough QT study	1,082
	Moxifloxacin	24-hour Holter	Pfizer	175	Thorough QT study	
	IDEAL 3	24-hour Holter	HRFUP	294	Coronary Artery Patients	
2009	**Acqu. LQTS**	24-hour Holter	Munich University	3	Drug-induced torsades de pointes	
	Cong. LQTS	24-hour Holter	Munich University	4	Genotyped, torsades de pointes	
	Sotalol	24-hour Holter + standard ECGs	Pfizer Inc. [1]	99+1600	Baseline, single and double dose of sotalol (160/320 mg)	4,131
	ED patients	24-hour Holter ECGs	UCSF	1308 (189 HR)	24 hour following ED admission for chest pain	
	Cardiac patients with TdPs	10-min ECGs	Munich University	34	Cardiac patients with a history of drug-induced TdPs	
	Healthy Volunteers	24-Holter ECGs	Abbott [1]	TBD	Pre-competitive data	
2010	**Dofetilide**	24-hour Holter	Pfizer Inc.[1]	5,000	Drug-induced arrhythmias	9,131

[1] these companies agreed on sharing the data with the THEW, legal aspect around the data sharing are being discussed.

THEW data: the warehouse content

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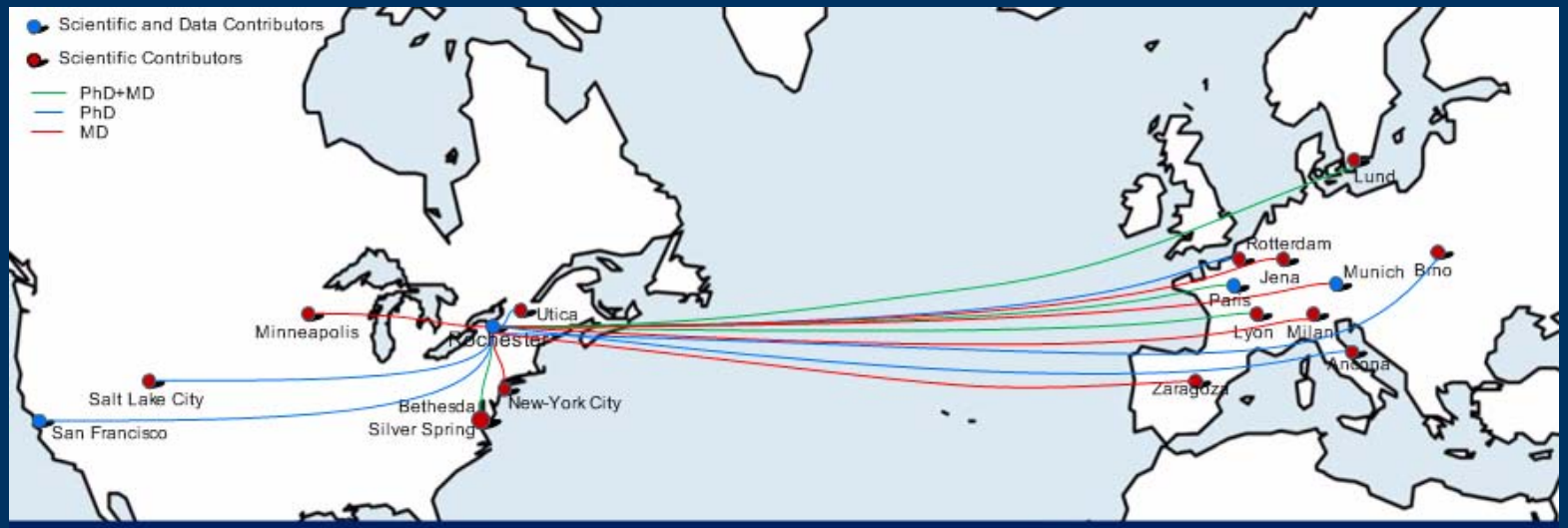


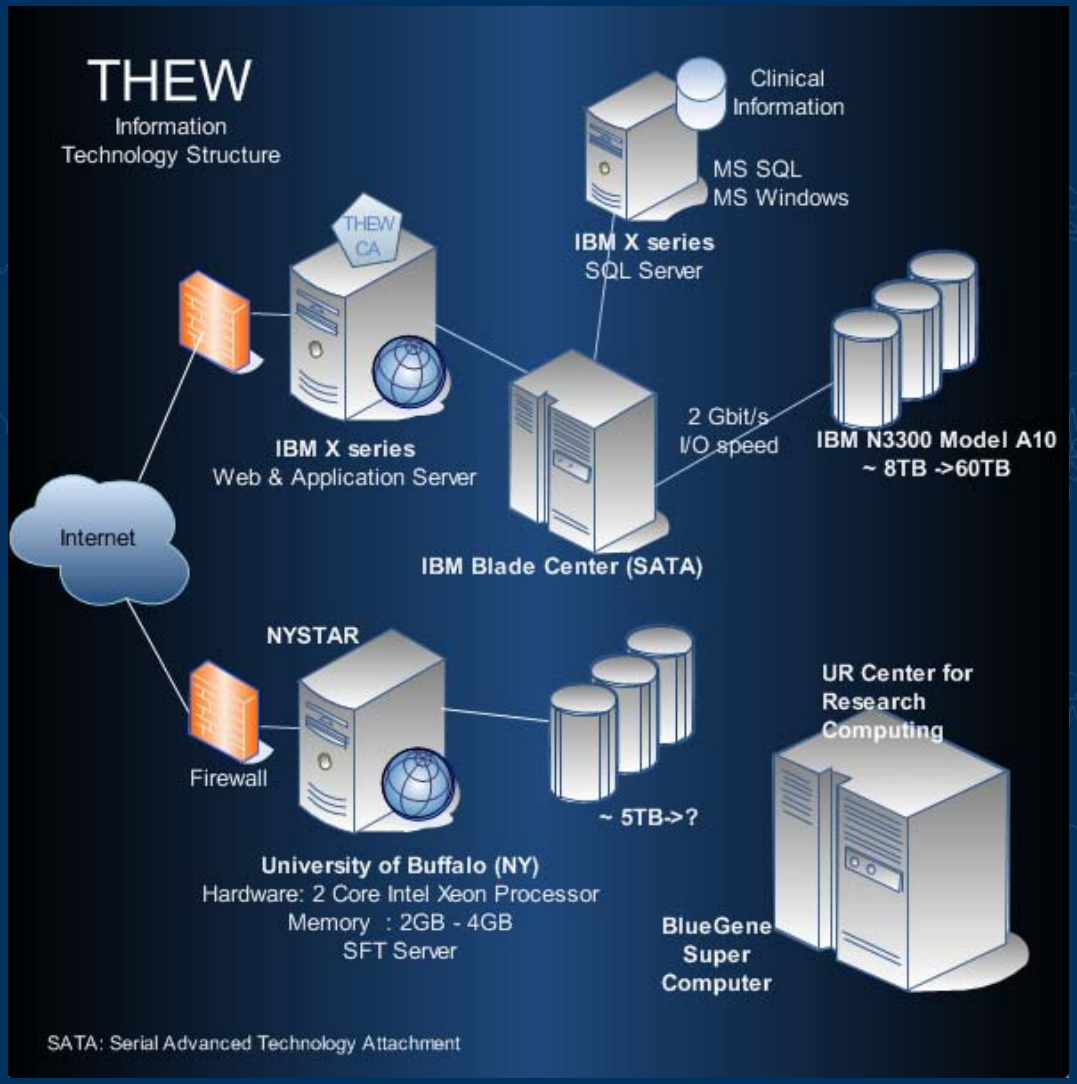
US Committed Scientific Investigators:

(MD) Bethesda, MD - Dr. Mark Haigney, Division of Cardiology, Department of Medicine, Uniformed Services University of the Health Sciences;
(MD) Minneapolis, MN - Dr. Morrison Hodges, University of Minesota;
(PhD) Utica, NY - Charles Antzelevitch, Masonic Medical Research Laboratory;
(PhD) Salt Lake City, UT - Robert Lux, CRVTI, University of Utah;
(PhD) Silver Spring, MD - Norman Stockbridge, CDER, FDA, US Human Health Department
(PhD) Rochester, NY - Mark Bocko, University of Rochester
(PhD) Rochester, NY - Jean-Philippe Couderc, University of Rochester Medical Center
(MD) New-York City - Eric Rashba, Stony Brook University Medical Center
(RN, PhD) San Francisco - Barbara Drew, University of California

European Committed Scientific Investigators:

(MD) Paris, France- Pierre Maison-Blanche, Hospital Lariboisiere
(PhD) Milan, Italy - Alberto Porta, University of Milan
(PhD) Rotterdam, Netherland - Jan Kors, Erasmus MC
(PhD) Jena, Germany - Andreas Voss, University of Applied Sciences
(MD) Lyon, France - Philippe Chevalier, Hopital Louis Pradel
- Paul Rubel, INSA
(MD,PhD) Lund, Sweden - Pyotr Platonov and Dr. Fredrik Holmqvist, Lund University Hospital
(PhD) Ancona, Italy - Laura Burratini Polytechnic University of Marche
(PhD) Brno, Czech Republic, Josef Halamek , Academy of Science of Czech Republic
(PhD) Zaragoza, Spain, Pablo Laguna Centro Politécnico Superior. Universidad de Zaragoza

THEW Expertise: Academic Network



THEW Tools: IT structure

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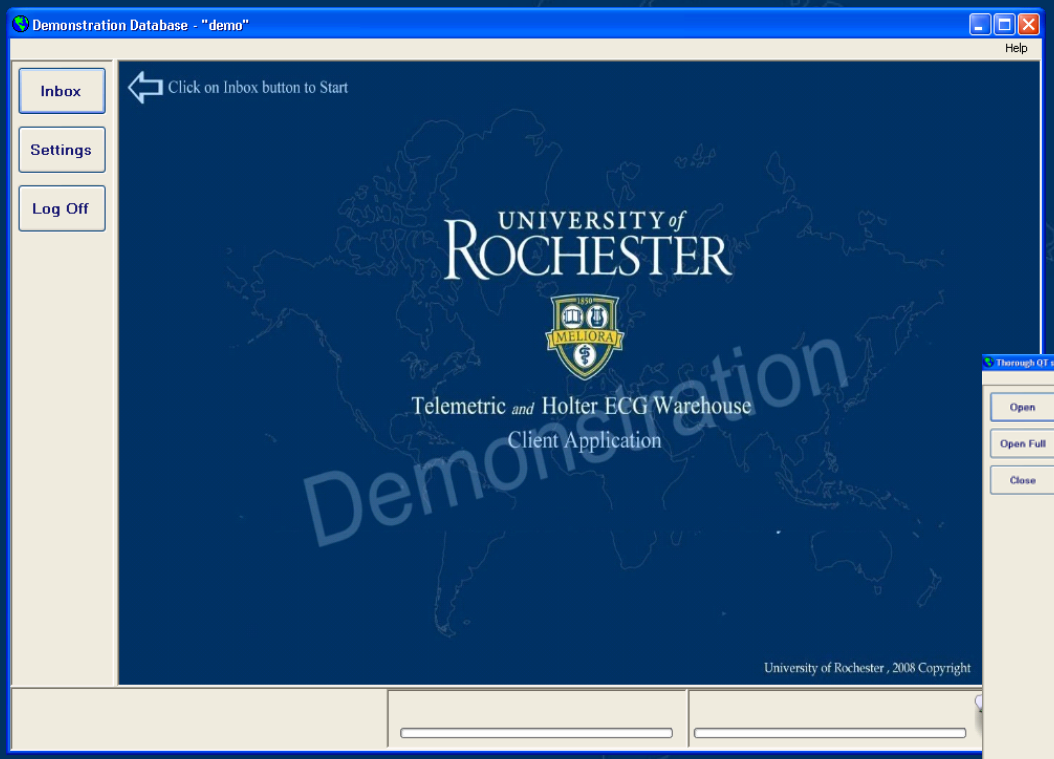
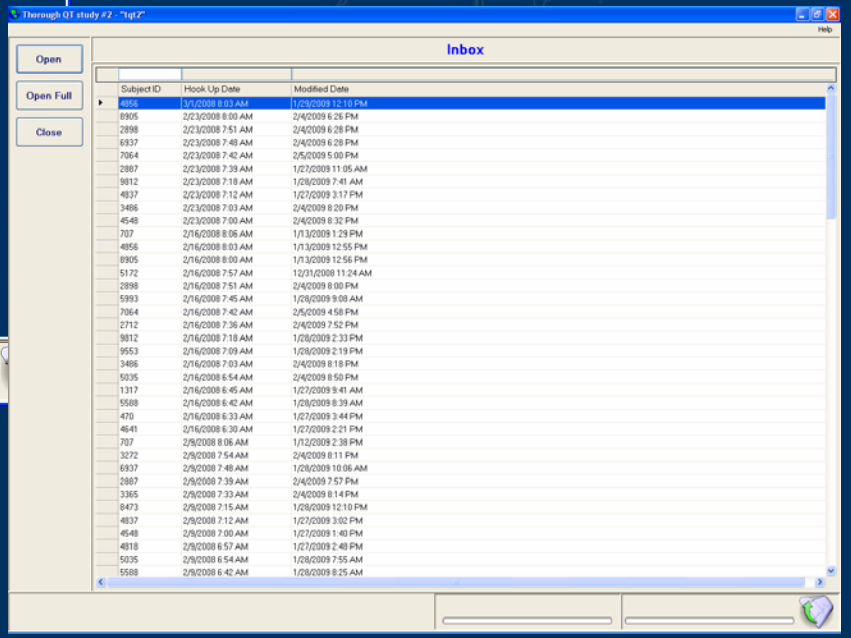


- -Visualize ECG signals and annotations
- -Download ECG signals and annotations
- -Password protected access/database
- -APIs empowered application
- -SDK available
- -Enable local machine epoch generation



The version of the THEW Client Application (V1.4) was tested on site at the FDA and in 20 sites in the U.S. and in Europe.

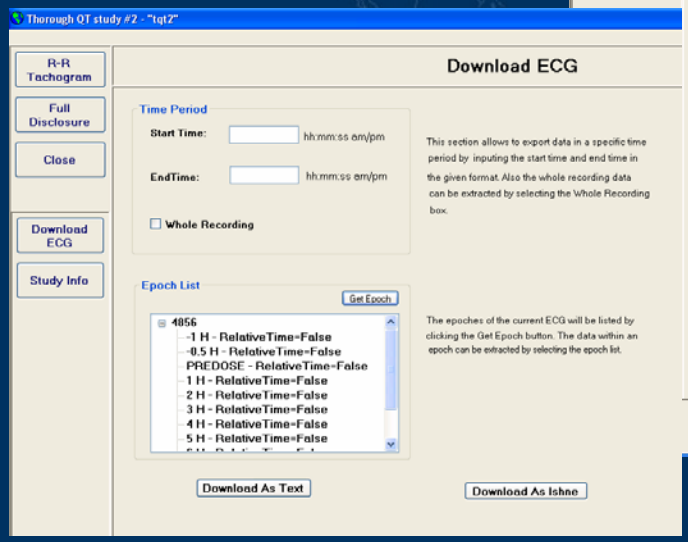
Free demo version available at www.thew-project.org

THEW Tools: the Client Application

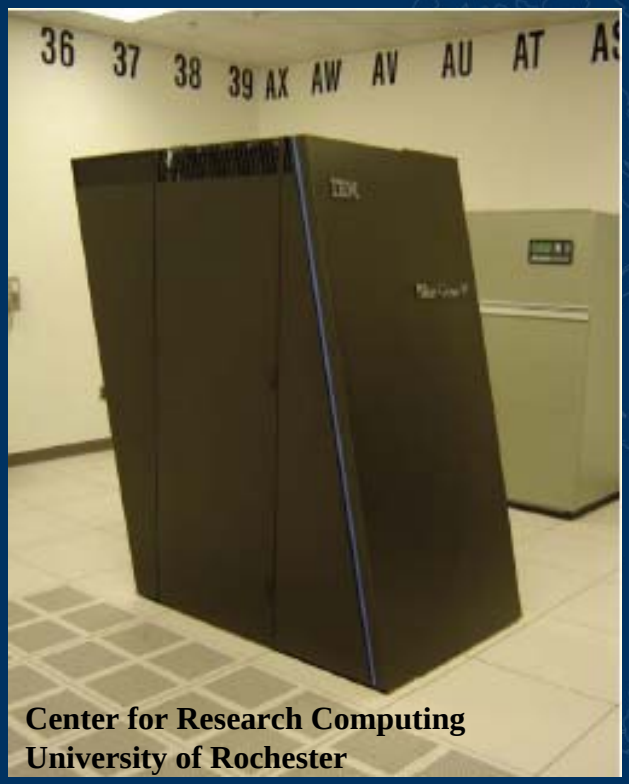
Thorough QT study: E-HOL-12-140-008

File format for ECG signal and annotation:
1/ ASCII format
2/ ISHNE format
3/ FDA-XML (available soon)

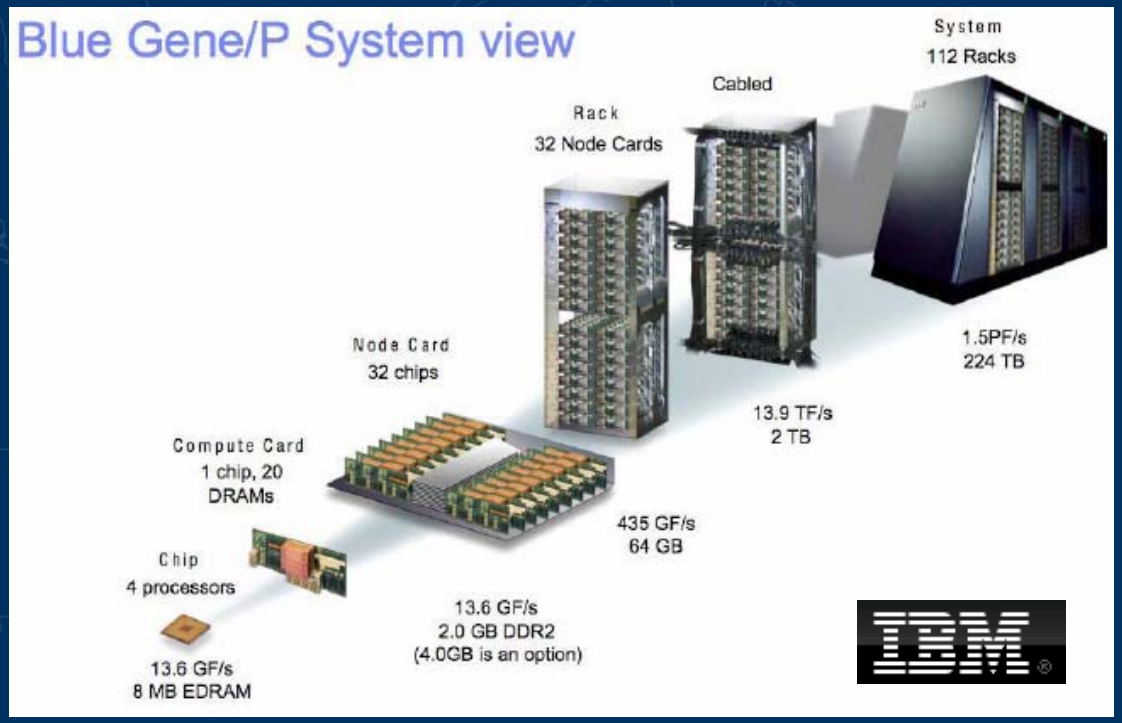
Selection of extracted period, no limitation in duration.



Computational power: THEW and UR Center for Computing Research

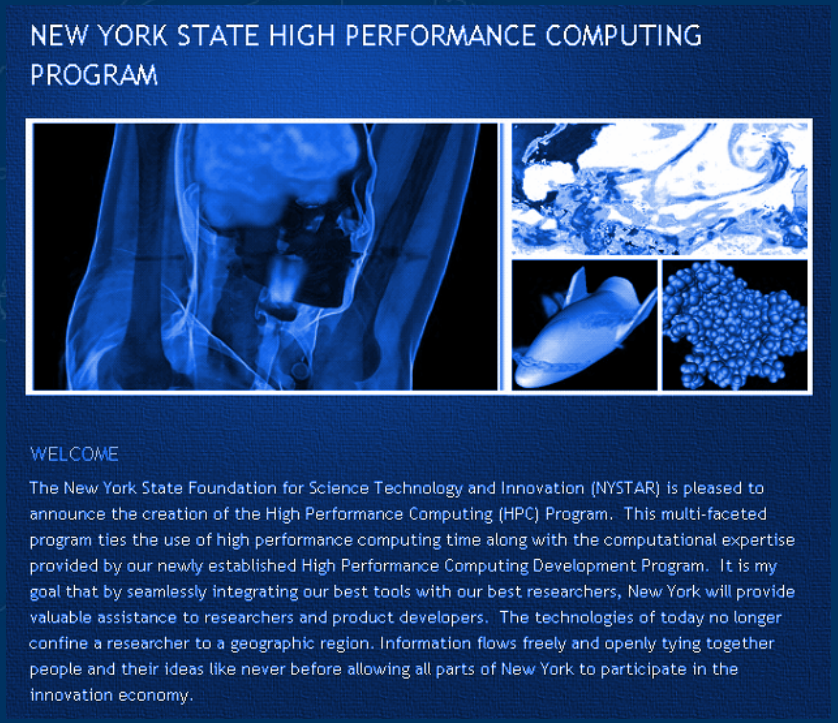


Center for Research Computing
University of Rochester



- **4,096 cores**
- **13.9 TFLOPS**

Alliance with the New York State Foundation for Science Technology and Innovation (NYSTAR)
- Hyper Computing program



<u>The NYSTAR HPC provides storage for the next three years to the THEW initiative.</u>

1- Integrating a Research Platform providing opportunities for:

- Developing Research/ collaborative projects
- Synergistic Alignment with THEW Partners
  - Pharmaceutical, CROs and ECG equipments
- Interaction with the regulators (CDER, CDRH)
  - THEW/FDA events and research project review

2- Accessing datasets for validation of ECG metrics (legal framework):

Availability of large set of ECGs (continuous and standard 12-lead)

- Healthy
- ECGs with QT prolongations (moxifloxacin, sotalol)
- ECGs with drug-induced TdPs,
- …. more ….

3- ECG:

- QT intervals (dataset of reference: moxi. + cardiac patients)
- Holter ECG annotation
- Reproducibility analysis

- **Our heritage** is the Heart Research Follow Up Program that has extensive experience in the design, conduct, and analysis of world-wide, multicenter, clinical research studies ranging from 100-3,500 subjects (MADIT I, MADIT II, MADIT CRT, LQTS and ARVD registries).

- **Our alignment** with the Critical Path Initiative has been officially expressed by a partnership agreement between the University of Rochester and the FDA - a 3-year partnership for the development of ECG technologies within the drug safety arena.

- **Our objective** is to promote cross-fertilization of scientific knowledge, resources, and ideas that will advance the field of quantitative electrocardiography.

The THEW will play an important role in the development of novel ECG technologies by helping the access to scientifically relevant ECG recordings and their clinical information.

Conclusions

9:30-10:45 Enabling Research Activities (Academic Perspectives)

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