

# Case Studies: Multicenter Clinical Trials "Development of a Clinical Trials Network by SNM"

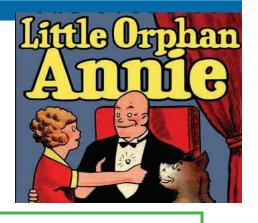
Michael Graham, PhD, MD President, SNM Co-chair, Clinical Trials Network



## Drugs without IP

- FDG
- FLT
- FDOPA
- FMISO
- C-11 acetate

- No company owns the rights
- No company will solely benefit
- No company will sponsor the trials
  - SNM?
  - NCI?
  - Industry consortium?



From SNM-FDA meeting April 20, 2008



# SNM is Looking to Develop Best Practices for Clinical Trials with Imaging Biomarkers

- Imaging biomarker production standards
- Patient selection/prep standards
- Image acquisition standards
- Vendor platform standards for display and analysis
- Standard analytical approaches
- Phantoms
- Hybrid technologies

From SNM-Pharma meeting November, 2008

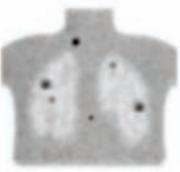


## Network 2008 Accomplishments

#### Phase I Baseline Work

- September '08
  - Approved multicenter IND for FLT
  - Round 1 of Imaging Site Registry Applications (130+)
- October '08
  - Launch of phantom program (alpha phase)
- November '08
  - Detailed 3 year plan with budget was developed & approved by the SNM Board of Directors





Oncology chest phantom & scan with mock lesions

Images courtesy of Paul E. Christian



## The Beginning

- In October 2008, SNM leadership announced the creation of the SNM Clinical Trials Network with notification that FDA approved SNM's first IND (F-18 Fluorothymidine)
- Two-day Workshop in Clearwater Beach, Florida.
  - Provided an opportunity to learn how SNM's new Clinical Trials Network can facilitate faster and more cost-effective drugs and biologics development through the improved integration and standardization of imaging biomarkers into therapeutic clinical trials.
- Following the Mid-Winter Meeting, SNM has continued to further define the structure of the Clinical Trials Network. Committees are being organized to cover the general areas of Quality Overview, Site Validation, Trial Design, Education, and Databases.



## Organization



From SNM Annual meeting June, 2009



### Poster at SNM Annual Meeting, June 2009



## Molecular Imaging in Clinical Trials: The SNM Clinical Trials Network Database Initiative

John Sunderland, Saranya Thirumoolan, Elkhair Elkhair, University of Iowa



Data Flow

#### Clinical Trials Network

In October, 2006, SNM leadership amounced the creation of the SNM Clinical Trials Network (CTM) for the expressed purpose of developing an immediate molecular imaging program to accelerate clinical trials for investigational florapsection and to immease the number of imaging frameriers available for clinical use.

Since this time, the CTN has apply evolved from concept to gottal early with over 200 eightered adoptermaceuthal product bins less and PET imaging sizes in 21 countries around the world.

The CTN has two major intlatives being addressed in

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(2)The CTN is creating a rigorous imaging site qualification system, including

- aphanominaging programal modal assessing:
- Imagequalityunderdiricalimaging conditions
   Issign detectabilityundercontrolled conditions
- / quantitateunitomiandissonSIN messurement
- adlessessmentprogram to identify necessary passioned and equipment inhast uctue-requirements.

Also being contemplated is a cross-vendor PET/CT image termonitation initiative designed to minimize image qualty and image quantitation differences inherent multicenter tribb using scanners with different vendors and models.

To better harness the potential power of this growing network, the design and construction of a web-lessed relational database has been initiated with the intension of linking the diverse information heing collected for the CTN project.

#### The Database

Software Choices: The database is being designed and constructed using Microsoft SQL Server 2005, with programming performed using Microsoft Visual Basic using 2008 Visual Studio. Demographic and geographic information is interfaced to Google Maps for a familiar, flexible, and robust interactive

The database and programming language were chosen so as to match software versions presently used in SNM corporate offices so as to enable a seamless hand-off of the project at the end of the development period.

Timetable: The database project is in its first month of its scheduled 3 month development period. The Database Subcommittee is receiving recommendations for fields and structure from SNM leadership and four CTIN subcommittees:

- The Phantom Subcommittee,
- The Site Validation Subcommittee,
- The Manufacturers Subcommittee.
- The Trial Design Subcommittee.



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### Database Organization DatabaseOrganization: Thepresentrative offe

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#### Google Maps Interface

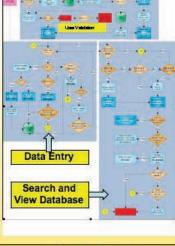
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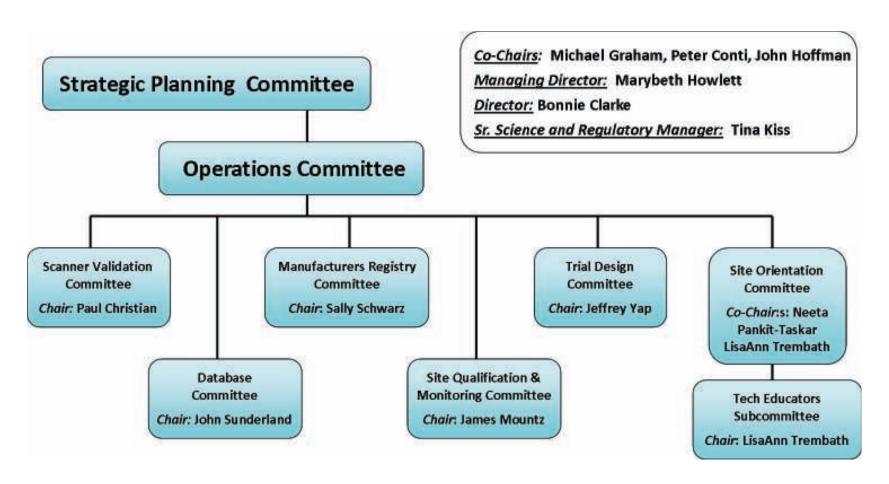
Figure 5. The world-wide presence of the CTN as of 6105. The map can be zoomed out for a world view.



Conclusions



## **CTN Organizational Chart**



From SNM Mid Winter meeting January, 2010



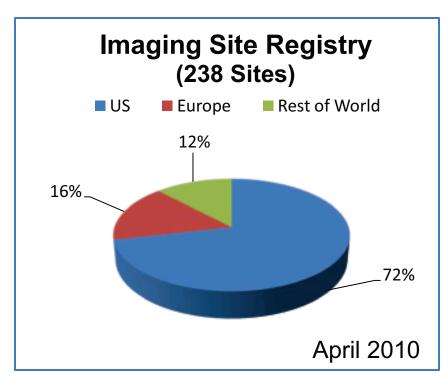
## Accomplishments

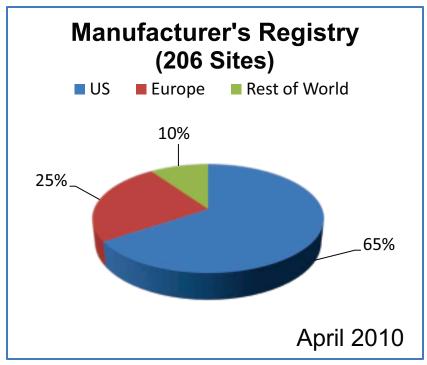
- First SNM multicenter IND for an investigational imaging biomarker
- First three founding members from the pharmaceutical development community on board
- 200+ members of both the imaging site and manufacturers registries
- Over 25% participation from outside the U.S.
- Development and launch of a clinical oncology phantom program
- Many on-going educational activities to inform about the Network and advance the awareness and understanding of the "Practice of Clinical Trials" within the imaging community
  - Community Workshop to be held Feb 1-2, 2010 in Albuquerque



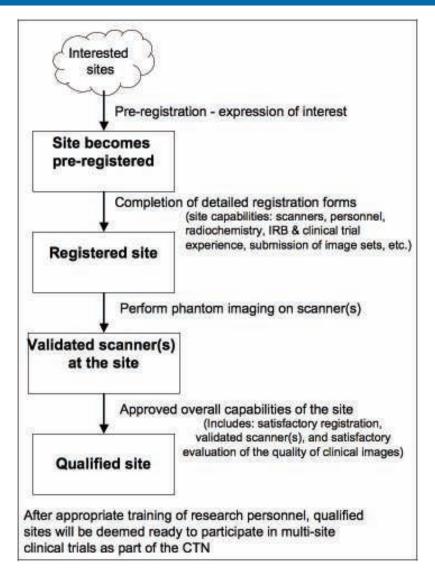
## CTN Registries (April 2010)

### Consistent Interest and Growth









### Site Qualification Process

- Registration in CTN site database: online completion of site-specific information
- Scanner Validation
- Sites must meet a set of minimum requirements related to research infrastructure, access to experimental imaging agents, validated equipment and experience of imaging personnel



# Problems Discovered During Scanner Validation Process

- Extreme time delays at certain sites (>65%)
  - Find time in clinical schedule (>20%)
  - Personnel unable to correctly prepare DICOM CD of images (44%)
- Sites filled phantom incorrectly (7%)\*
- Dose calibrators not working properly (3%)

**Lesson Learned:** Instructions are being revised to include step-by-step guide for burning images scanned on each of the three main vendor's equipment to reduce site errors in CD preparation and time delays.

<sup>\* &</sup>lt;1% since online video demonstration became available in Jan 2010.



## **CTN Scanner Validation**



•	Validated scanners	31
•	Sites currently imaging phantoms	19
•	Sites waiting for phantoms	>17



## Training and Education

### Curriculum courses offered for all imaging site personnel:

- Following clinical research imaging protocols
- Improving image quality / troubleshooting
- Monitoring QC and QA: equipment and imaging procedures
- Source documentation and CRF completion
- Accurate documentation and reporting of violations, deviations and AEs/SAEs



CTN recognizes key role of molecular imaging technologists in promoting and improving imaging in clinical research



## CTN Long-Term Goals

- One new IND per year based on pharmaceutical & community need
- Expand phantom program to include cardiac and brain scenarios; can be designed to be study-specific
- Reach beyond PET biomarkers
- Assist with developing standardized imaging acquisition guidelines, processing and data analysis, and improved protocol development
- Work with imaging CROs to develop global standardized site qualification process; baseline and study specific capabilities



## Long-Term Goals, cont.

- Expand multicenter IND capability for imaging biomarkers
  - Non-proprietary Proprietary
  - Individual academic investigator-driven
- Facilitate quantitative imaging in biomarker clinical trials
  - Phase I, Phase II assessing chemotherapy agents with Pharma
  - Multicenter NIH-sponsored similar trials
  - Proprietary agents in Oncology, Cardiology, Neurology

