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

From SNM BOD meeting March, 2009
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.

From SNM Annual meeting June, 2009
Organization

From SNM Annual meeting June, 2009
**Molecular Imaging in Clinical Trials: The SNM Clinical Trials Network Database Initiative**

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

<table>
<thead>
<tr>
<th>Clinical Trials Network</th>
<th>The Database</th>
<th>Database Organization</th>
<th>Database Security</th>
<th>Data Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Software Choices:</strong> 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 integrated to Google Maps for a familiar, facile, and visual interactive experience.</td>
<td><strong>Database Organization:</strong> Registration and investigator recruitment database. Data entry and data review and approval.</td>
<td><strong>Data Entry:</strong> Data entry and reviewed for accuracy by the Investigator. Data quality assurance and data entry.</td>
<td><strong>Search and View Database:</strong> Data entry and reviewed for accuracy by the Investigator. Data quality assurance and data entry.</td>
<td><strong>Conclusions:</strong> Data entry and reviewed for accuracy by the Investigator. Data quality assurance and data entry.</td>
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<td><strong>Google Maps Interface:</strong></td>
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**From SNM Annual meeting June, 2009**
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

From SNM Mid Winter meeting January, 2010
Consistent Interest and Growth

CTN Registries (April 2010)

Imaging Site Registry (238 Sites)
- US: 72%
- Europe: 12%
- Rest of World: 16%

Manufacturer's Registry (206 Sites)
- US: 65%
- Europe: 25%
- Rest of World: 10%
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%)

* <1% since online video demonstration became available in Jan 2010.

**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.
CTN Scanner Validation

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