The Radioactive Drug Research Committee (RDRC): A 2006 Update

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The Radioactive Drug Research Committee (RDRC)

- Title 21 Code of Federal Regulations (CFR) 361.1

- Conditions for RDRC Research
  - Basic Science Research — “…not intended for immediate therapeutic, diagnostic, or similar purposes or to determine the safety and effectiveness of the drug…”
  - No pharmacologic effect
  - Radiation dose limits

- FDA approves committee members

- RDRC Responsibilities
  - Reviews and approve each research protocol per regulations, with IRB* concurrence
  - Submit variety of regulatory reports to FDA

* Institutional Review Board
RDRC Profile

- Typical committee
- Type of radionuclides
- Types of research
- Research subjects
Currently there are 74* active RDRC’s

- If a committee files its annual report, it is considered active by FDA.
- In 2003 there were 84 “active committees”
- Ten (10) committees have voluntarily inactivated because they have not conducted any studies.
- RDRC protocols average 10 subjects each.
  
  284 protocols employed 2797 subjects
  (10 subjects/protocol) **

* June, 2006
** 2003
### Most RDRC Research conducted at Major Medical Institutions

<table>
<thead>
<tr>
<th>RDRC’s In 2003</th>
<th>Studies Conducted</th>
<th>Human Subjects</th>
<th>All RDRC Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>31</td>
<td>266</td>
<td>9.5%</td>
</tr>
<tr>
<td>B</td>
<td>34</td>
<td>251</td>
<td>9.0%</td>
</tr>
<tr>
<td>C</td>
<td>14</td>
<td>242</td>
<td>8.7%</td>
</tr>
<tr>
<td>D</td>
<td>14</td>
<td>214</td>
<td>7.7%</td>
</tr>
<tr>
<td>E</td>
<td>16</td>
<td>211</td>
<td>7.5%</td>
</tr>
<tr>
<td>F</td>
<td>25</td>
<td>193</td>
<td>6.9%</td>
</tr>
<tr>
<td>G</td>
<td>15</td>
<td>162</td>
<td>5.8%</td>
</tr>
<tr>
<td>H</td>
<td>12</td>
<td>154</td>
<td>5.5%</td>
</tr>
<tr>
<td><strong>Top 8</strong></td>
<td><strong>161</strong></td>
<td><strong>1693</strong></td>
<td><strong>61%</strong></td>
</tr>
</tbody>
</table>
77% of RDRC Research uses PET Imaging

<table>
<thead>
<tr>
<th>Year</th>
<th>% PET nuclides</th>
<th>% gamma</th>
<th>% beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>5</td>
<td>77</td>
<td>18</td>
</tr>
<tr>
<td>1981</td>
<td>12</td>
<td>32</td>
<td>56</td>
</tr>
<tr>
<td>1986</td>
<td>30</td>
<td>14</td>
<td>56</td>
</tr>
<tr>
<td>1991</td>
<td>37</td>
<td>8</td>
<td>55</td>
</tr>
<tr>
<td>1996</td>
<td>55</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>2001</td>
<td>80</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>2003</td>
<td>77</td>
<td>5</td>
<td>18</td>
</tr>
</tbody>
</table>
96% of PET* Research Protocols conducted under RDRC Authority**

- RDRC PET protocols average 8 subjects.
  218 protocols employed 1756 subjects = 8 subjects/protocol**

- IND*** PET protocols average 62 subjects.
  8 protocols employed 496 subjects = 62 subjects/protocol

RDRC Special Summaries required when n > 30

* Positron Emission Tomography
**2003
***Investigational New Drug application
Types of RDRC Research Studies*

- Neuroreceptor – 45%
- Cancer – 15%
- Diabetes – 12%
- Cardiac – 9%
- Other** – 22% (Exercise, pain, obesity, acupuncture, prostheses, GI, pulmonary, auditory, bone physiology, etc.)

* 2003

** Each less than 2%. Sum total is greater than 100% because some studies had more than one research subject.
Pediatric studies rarely conducted under RDRC authority

<table>
<thead>
<tr>
<th>Year</th>
<th>Pediatric/Total Studies</th>
<th>Pediatric/Total Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>3/18 (16.7%)</td>
<td>39/531 (7.3%)</td>
</tr>
<tr>
<td>1981</td>
<td>12/224 (5.4%)</td>
<td>58/2099 (2.8%)</td>
</tr>
<tr>
<td>1986</td>
<td>8/207 (3.9%)</td>
<td>80/2310 (3.5%)</td>
</tr>
<tr>
<td>1991</td>
<td>9/245 (3.7%)</td>
<td>80/2833 (2.8%)</td>
</tr>
<tr>
<td>1996</td>
<td>6/243 (2.5%)</td>
<td>32/1958 (1.6%)</td>
</tr>
<tr>
<td>2001 - 2003</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2004</td>
<td>1 study</td>
<td>4 subjects</td>
</tr>
</tbody>
</table>
FDA 2915
Study Summary

**A. GENERAL INFORMATION**
- Title of Research Project
- Study ID Number
- Original Study Approval Date
- Study Termination Date
- Name of Responsible Investigator (Note: Also name the principal investigator or other than the responsible investigator)
- Complete and Complete Description of the Purpose of the Research Project

**B. SPECIFIC INFORMATION**
- Pharmacological Dose (Based on pharmacological data available from studies in human subjects the dose should be known to cause any directly measurable pharmacological effect in human beings)
  - Name of the radioisotope
  - Dose

**C. ROUTINE INFORMATION**
- Name of Issuer
- Study Number
- Date of Approval
- Date of Submission

**D. FOR A SPECIAL SUMMARY:** Enter information below for a representative subject (refer to page 7 for more information)
- Age
- Sex
- Activity of Radioactive Drug Administered and Other Associated Procedures
- Absorbed Dose Per Single Administration
- Total Dose Per Organ Per Year

**E. RADIATION ABSORBED Dose**
- List reference, if any, (e.g., ICNP) and attach calculations used to estimate the radiation absorbed dose.
Changes in Forms

Membership (2914)    Study Summary (2915)

Old Forms                      New Forms

- No instructions
- No reference of qualifications
- Use of “dose” confusing
  “Maximum amount (i.e. mg) of nonradioactive moiety administered per subject, per single dose and/or the minimum specific activity (i.e. mCi/mg) of drug at the time of administration.”
- Terms not only confusing, but incorrect: “mR/whole body”

- Instructions
- Referenced by date
- Dose terms clarified
  Pharmacological dose, the NOEL*
  dose, and the radiation absorbed dose requested individually..
  MBq, uCi, mCi, mSv, Rem
  * No Observed Effect level (NOEL)
New FDA Reporting Forms
Membership (2914) and Study Summary (2915)

Posted on FDA RDRC website:

1. Go to www.fda.gov
2. Search on “RDRC”
3. Click on Radioactive Drug Research Committee (RDRC) Program
4. Click on RDRC Forms and Checklist

or go directly to:

http://www.fda.gov/cder/regulatory/RDRC/default.htm#forms

http://www.fda.gov/opacom/morechoices/fdaforms/FDA-2914.DOC

http://www.fda.gov/opacom/morechoices/fdaforms/FDA-2915.DOC
Status of RDRC Regulatory Initiatives

- Draft Guidance – in process
- Regulations
  - Radiation dose limits outdated
  - Feedback on FR notice and stakeholder meeting
  - Impact of Exploratory IND
- Reinstated Inspection Program
RDRC Inspections

- Drug Quality and Purity Issues
- Safety Issues
- Administrative Issues

“Do what you say, say what you do!”
Annual Report Reviews
Noteworthy Observations

- RDRC not associated with a medical institution.
- Medical institution did not know they had an RDRC.
- An RDRC chair who tried to convince their administration that the RDRC members were surrogate FDA employees and therefore operate independently of the medical institution.
- An RDRC that believed their role was to review their institution’s IRB actions.
- Radiation doses reported inconsistently, or not reported at all.
Other Activities

- RDRC Website
  www.fda.gov/cder/regulatory/RDRC

- Presentations in 2006
  American Pharmacy Association
  Society of Nuclear Medicine

If you need assistance:

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Vision: FDA Campus
@ White Oak, Maryland
Reality: FDA campus and RDRC program still works-in-progress