The meeting was called to order by Dr. Nelson Chao at 1:35 p.m. Eastern Daylight Time at the Marriott Bethesda. This report summarizes the information that was gathered and the agreements that were reached:

1. **OVERVIEW OF WHO-REMPAN**

   Dr. Zhanat Carr covered the role of the World Health Organization (WHO) and the Radiation Emergency Medical Preparedness and Assistance Network (REMPAN).

   1-1 WHO’s role in a radiation emergency is to respond to and assist member states (192 countries) when a population is exposed to radioactive material in an uncontrolled manner intentionally or by accident. Its role is integrated in the international system of emergency response led by the International Atomic Energy Agency (IAEA). WHO’s mandate is to:

   - Develop and implement evidence-based policy for public health authorities of member states aimed at reduction of risks and protection of public health from the exposure of ionizing radiation.

   - Build national capacity for preparedness for nuclear emergencies and radiological accidents through education, training, provision of guidelines and assistance in infrastructure development.

   - Provide intervention support, public health and medical assistance to member states in preparedness and response to radio-nuclear accidents or terrorist situations.

   - Provide information to the public during and after emergencies.

1-2 It was pointed out that *The World Health Report 2007 - A safer future: global public health security in the 21st century* marks a turning point in the history of public health, and signals what could be one of the biggest advances in health security in half a century. The report explains how the revised International Health Regulations (2005), which came into force this year, helps countries work together to identify risks and act to contain and control them. The regulations are needed because no single country, regardless of capability or wealth, can protect itself from catastrophic hazards without the cooperation of others.
1-3 WHO-REMPAN responds to radiological and nuclear emergencies:

<table>
<thead>
<tr>
<th>Radiological Emergencies</th>
<th>Nuclear Emergencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Accidental over-exposure (industrial, medical)</td>
<td>o Operational failures at a nuclear power plant</td>
</tr>
<tr>
<td>o Orphan sources</td>
<td>o Attack on a nuclear facility</td>
</tr>
<tr>
<td>o Isotope transportation accident</td>
<td>o Detonation of an improvised or weapons grade nuclear device</td>
</tr>
<tr>
<td>o Malicious use of radioactive substance</td>
<td></td>
</tr>
</tbody>
</table>

Dr. Carr reviewed the scale of radiation emergency events. In addition, a number of Irridium 192 and medical over-exposure accidents were covered.

1-4 WHO-REMPAN’s activities include:

- Enhancing medical preparedness to radiation accidents within WHO member states through guidelines, education training and exercises.
- Providing public health and medical assistance to individuals and populations affected by radiation accidents.
- Providing information to public decision makers.
- Promoting harmonization in treatment and public health response in cases of radiation accidents.
- Providing a clearing-house for information on experience gained from management of accidents and treatment of victims.

The ongoing work of REMPAN was covered.

1-5 WHO is providing consultation on development of a radiation emergency stockpile. Consultation activities include:

- Defining scenarios (accidental, deliberate).
- Defining conditions under which the stockpile would be used and the overall strategy and goals for its use:
  - To equip WHO response teams.
  - To assist member states by providing emergency supplies.
- Determining the content and size of the stockpile (material and personnel).
- Estimating the initial cost and sources of supply.
- Defining the type of skills necessary for maintenance and support of the stockpile.
- Defining operational interface of WHO:
  - With WHO regional offices.
  - Other international organizations.
  - National authorities.
- Defining a method for assessment and revision of the stockpile and its relevance to evolving treatment protocols and the world environment.
- Developing an outline of WHO guidelines for establishment and use of stockpiles in member states.
2. RADIATION EVENT MEDICAL MANAGEMENT

Dr. Judith Bader provided a demonstration and an update on the Radiation Event Medical Management (REMM) program.

2-2 The chronology of REMM’s development was covered:

- REMM was launched on March 8, 2007.
- The Adult order set was critiqued and approved by FDA and RITN.
- REMM requested RITN guidance on acyclovir and the pediatrics order set.
- REMM requested FDA guidance on acyclovir doses and the pediatrics order set cleared by RITN pediatricians.
- A four month review hiatus was received from FDA.
- The scope of FDA’s critique was much greater than guidance on acyclovir.
- Dr. Bader responded to the issues outlined by the FDA. However, the FDA still requires evidence-based information which makes the document too large. The solution was removing drug names and doses from REMM.
- New generic orders without drug names and doses were uploaded.
- Acute radiation syndrome (ARS) doses are still present: for cytokines.

2-3 Dr. Bader led a discussion on the issues pertaining to FDA and RITN objectives:

- FDA’s mission calls for evidence-based guidance.
- The REMM site goal is different: "Cliff Notes" for non-specialist clinicians:
  - Quickly accessible guidance.
  - Readable only.
  - Link back to primary text documents including Package Insert.
- “Emergency Use Authorization” in a declared Public Health Emergency would be sought for off-label indications (which must be noted online).
- Providing all the contraindications, drug interactions, sliding drug doses and clinical caveats would make the online order set unusable.
- REMM could link to RITN documents, if they incorporate FDA guidance.
- Pediatric and Adult documents are needed, especially for those who lack expertise.

2-4 ACTION ITEM: It was agreed that Dr. Chao would coordinate communication with the FDA to see what modifications they would be receptive to. Dr. Bader will submit a new response covering adult orders first and then, based on acceptance, pediatric orders. The back-up position would request REMM to provide a link to the RITN Web site.
3. DATA COLLECTION

Dr. Confer covered data collection issues. He indicated that collection of data on patients treated by RITN centers is critical and that data collection systems should be developed and ready for deployment. Data entry should be Web-based with paper backup and research consent is required.

3-1 The status of the implementation plan was covered:

<table>
<thead>
<tr>
<th>Approach</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modify the existing IRB-approved data collection protocol to include patients with marrow toxic injuries.</td>
<td>Completed</td>
</tr>
<tr>
<td>Modify the existing IRB-approved data collection protocol to include patients with marrow toxic injuries.</td>
<td>Scheduled</td>
</tr>
<tr>
<td>Add radiation-specific data forms to the FORMS Net data collection.</td>
<td>Scheduled for completion FY 08 – 09</td>
</tr>
<tr>
<td>Add RITN data elements to NCI caDSR public warehouse.</td>
<td>TBD</td>
</tr>
</tbody>
</table>

3-2 Required data elements were reviewed:

<table>
<thead>
<tr>
<th>No Hematopoietic Cell Transplantation</th>
<th>Hematopoietic Cell Transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Registration (demographics)</td>
<td>✓ Use existing CIBMTR research report forms</td>
</tr>
<tr>
<td>✓ Exposure data</td>
<td>✓ Develop a new disease specific insert</td>
</tr>
<tr>
<td>✓ Exposure symptoms</td>
<td></td>
</tr>
<tr>
<td>✓ Medical history - comorbidities</td>
<td></td>
</tr>
<tr>
<td>✓ Laboratory (blood, marrow, cytogentic, imaging, etc.)</td>
<td></td>
</tr>
<tr>
<td>✓ Therapy</td>
<td></td>
</tr>
<tr>
<td>✓ Follow-up</td>
<td></td>
</tr>
</tbody>
</table>

3-3 ACTION ITEM: A committee was selected to draft HCT data elements. Members included Drs. Dan Weisdorf, Theodore Fliedner, George Selby and Nancy Kernan. The goal is to develop a reasonable set of forms that identify the patient, symptoms, exposure and treatment.

4. PREPARATORY REGIMEN

Dr. Weisdorf reviewed conditioning for Hematopoietic Stem Cell Transplantation after radiation or marrow toxic exposure. Conditioning considerations should include performance status, co-morbid injuries (trauma/burns), pre-existing infections and immunocompetence. He suggested having **two alternative regimens** based on patient conditions.

4-1 The likely conditioning regimen for radiation victims should be:

- Cyclophosphamide 50 mg/kg/d x 1 \( (d -2) \)
- ATG (thymoglobulin) 3 mg/kg \( (d -4,-3,-2) \) = 9 mg/kg
- Fludarabine 30 mg/m2/d \( (d -5,-4,-3,-2)\) = 120 mg/m2
- CSA or Tac (to d 100-180) plus MMF (to day 30)
4-2 The proposed modified regimen for radiation victims is outlined below. It Limits mucosal injury (no TBI or high dose alkylator), assures potent immunosuppression and engraftment, limits likelihood of GVHD and is suitable for matched (related or URD) or partially matched (UCB) donors.

- Modest dose cyclophosphamide
  - 50 mg/kg/d x 1 (or none)
- ATG (thymoglobulin) 3 mg/kg -4,-3,-2 = 9 mg/kg
- Fludarabine 30 mg/m2/d -5,-4,-3,-2 = 120 mg/m2
- CSA or Tac (to d 100-180) plus MMF (to day 30)

4-3 The proposed conditioning regimen should follow these guidelines:

- Defined regimen and GVHD prophylaxis:
  - Suitable for universal application
  - Permit future reassessment and modification
- Defined donor matching and selection process.
- Defined supportive care.
- Defined data collection plans.

5. **Adjournment**

The meeting was adjourned at 4:45 pm Eastern Daylight Time.

Submitted by:
Bob Krawisz