Paper

THE U.S. GOVERNMENT'S MEDICAL COUNTERMEASURE PORTFOLIO MANAGEMENT FOR NUCLEAR AND RADIOLOGICAL EMERGENCIES: SYNERGY FROM INTERAGENCY COOPERATION

Marcy B. Grace,* Kenneth D. Cliffer,† Brian R. Moyer,§ C. Norman Coleman,‡ Joanna M. Prasher,† Richard Hatchett,** John Mercier,*** Ronald G. Manning,* Judith L. Bader,‡ Gary L. Disbrow,* and Gerald R. Kovacs*

Abstract—**Following the attacks of 11 September 2001, emergency preparedness within the U.S. Department of Health and Human Services, as well as at the Department of Defense and other federal agencies, received higher visibility, new mandates and increased funding. Emergency deployment teams increased the frequency of drills to enable better response to the health consequences of mass-casualty incidents. Interagency coordination has also continued to increase to more efficiently and effectively leverage federal resources toward emergency medical preparedness for both civilian and military populations.**

Health Phys. 101(3):238–247; 2011

INTRODUCTION

In September 2004, the Secretary of the U.S. Department of Homeland Security (DHS) determined that radiological and nuclear agents posed a "material threat" to national security (USDHHS 2008b). Examples of challenges that must be addressed by emergency preparedness personnel would include radiation from

- a radiological exposure device (RED);
- a radiological dispersal device (RDD, which can be either non-explosive or explosive); and
- a nuclear detonation of an improvised nuclear device (IND).

The U.S. Department of Health and Human Services (HHS) has developed a comprehensive strategy (USDHHS 2007a) and implementation plan (USDHHS 2007b) to address the medical consequences of chemical, biological, radiological and nuclear (CBRN) threats, including from a radiological or nuclear attack. Programs of development and acquisition under Project BioShield and associated efforts have been described in Project BioShield Annual Reports (USDHHS 2007d, 2008b, 2009, 2011). These papers collectively describe an overview of approaches, programs and assets that have been in development or are available through HHS and other key federal agencies and that could be brought to bear to prevent, mitigate or treat the adverse health effects following a significant nuclear or radiological incident. The assets that will be considered here do not constitute all the available federal resources for this purpose, particularly omitting many non-HHS assets described in the Nuclear/Radiological Incident Annex (USDHS 2008c) of the National Response Framework (USDHS 2008b). Furthermore, the emphasis here is on resources addressing radiation dose assessment for which HHS has a role in development and acquisition.

STRATEGIC NATIONAL STOCKPILE

The Strategic National Stockpile (SNS) has allocated large quantities of pharmaceuticals and medical

* Division of CBRN Countermeasures, Biomedical Advanced Research and Development Authority (BARDA), Office of the Assistant Secretary for Preparedness and Response, Office of the Secretary, Department of Health and Human Services, 330 Independence Avenue SW, Room 644G, Washington, DC 20201; † Division of Medical Countermeasure Strategy and Requirements, Office of Policy and Planning, Office of the Assistant Secretary for Preparedness and Response, Office of the Secretary, Department of Health and Human Services, Washington, DC 20201; § (contractor in support of BARDA) Tunnell Consulting, Inc., King of Prussia, PA 19406; ‡ Office of Preparedness and Emergency Operations, Office of the Assistant Secretary for Preparedness and Response, Office of the Secretary, Department of Health and Human Services, Washington, DC 20201; and National Cancer Institute, National Institutes of Health, Bethesda, MD 20892; ** Biomedical Advanced Research and Development Authority, Office of the Assistant Secretary for Preparedness and Response, Office of the Secretary, Department of Health and Human Services, Washington, DC 20201; *** Armed Forces Radiobiology Research Institute, Uniformed Services University of Health Sciences, Bethesda, MD 20889; current address: PO Box 420, Fairfax Station, VA 22039.

Author to whom inquiries should be sent: Marcy B. Grace; email marcy.grace@hhs.gov.

(*Manuscript accepted* 31 *January* 2011)
0017-9078/11/0

DOI: 10.1097/HP.0b013e3182135fba

supplies to protect the American public against known threats in situations in which local capabilities are not available or will be exhausted. HHS has made substantial progress in procuring products for the SNS, both before and under the Project BioShield Act of 2004 (P.L. 108-276), for responding to radiological and nuclear incidents. The SNS current inventory of medical countermeasures for radiation incidents includes:

- the chelating agent Prussian blue, which mitigates internal absorption of ^{137}Cs (a possible component of a dirty bomb);
- the decorporation agents Ca- and Zn-DTPA (diethylenetriaminepentaacetate) for the chelation of isotopes of the transuranic elements curium, plutonium and americium;
- cytokine growth factor, G-CSF (granulocyte-colony stimulating factor), which may be useful (under an Investigational New Drug protocol or Emergency Use Authorization from the FDA [USDHHS 2007c]) for addressing life-threatening neutropenia associated with acute radiation syndrome (ARS); and
- medical supplies to treat the complex array of medical problems following a radiological or nuclear attack, including antibiotics, anti-nausea drugs and supplies to treat burn and blast injuries.

PUBLIC HEALTH EMERGENCY MEDICAL COUNTERMEASURES ENTERPRISE

In July 2006, HHS established the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) to serve as the primary conduit for communication among entities involved in medical countermeasure development, acquisition and deployment (USDHHS 2006). The PHEMCE is a coordinated, intra- and interagency effort led by the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR). The PHEMCE membership includes three other HHS agencies: the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA) and the National Institutes of Health (NIH). Additionally, as illustrated in Fig. 1, the PHEMCE collaborates with the U.S. Department of Defense (DoD), the DHS, the U.S. Department of Veterans Affairs (VA), the U.S. Department of Agriculture (USDA) and other interagency stakeholders. The PHEMCE, through the Enterprise Senior Council, leads the civilian mission

1. to define and prioritize requirements for public health emergency medical countermeasures;

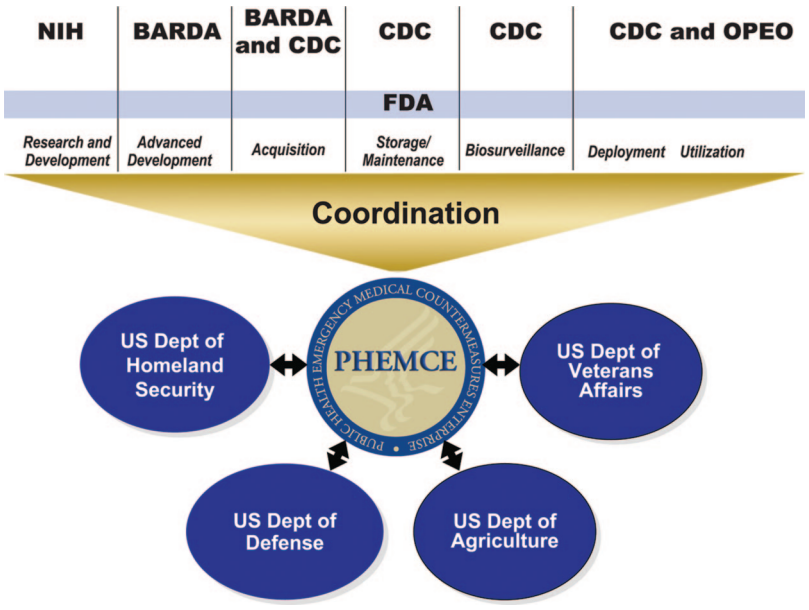

Fig. 1. HHS employs a diverse, balanced portfolio of medical radiation countermeasures through agency coordination. Within the HHS, the Biomedical Advanced Research and Development Authority (BARDA) in the Office of the Assistant Secretary for Preparedness and Response (ASPR), the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH), the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) all collaboratively support research and development of new and improved diagnostics and medical treatments for radiation casualties. The Office of Preparedness and Emergency Operations (OPEO) within ASPR is responsible for developing operational plans, analytical products and training exercises to foster preparedness at all levels to respond to domestic and international public health and medical threats and emergencies. OPEO coordinates with CDC for deployment and use of medical countermeasures.

2. to coordinate research, early and late stage product development, and procurement activities addressing the requirements; and
3. to set deployment and use strategies for medical countermeasures held by the HHS.

The PHEMCE has taken a comprehensive approach to the medical countermeasure mission, including research, development, acquisition, storage, maintenance, deployment and utilization. The 2007 *HHS PHEMCE Implementation Plan for CBRN Threats* (USDHHS 2007b) identified the top-priority targets for medical countermeasure research, development and acquisition that, in collaborative agreement with its interagency partners, were judged to have the greatest potential to improve public health emergency preparedness. Among the high priorities were the following types of agents and tools to address effects of radiological or nuclear attacks.

- Medical countermeasures to address ARS, the medical consequence of exposure of the whole body (or a large proportion of the body) to a relatively large dose of radiation (above 1–2 Gy) usually delivered from an external source over a short period of time, and to address the delayed effects of acute radiation exposure (DEARE), which includes late radiation-induced effects in multiple organ systems
- Radionuclide-specific medical countermeasures, which are chelating and blocking agents to manage the medical consequences of internalized radioisotopes
- Radiological dose assessment capabilities for on-scene triage and subsequent medical management of ARS/DEARE following a large radiological incident

In support of these PHEMCE goals, NIH, BARDA and the DoD each contributes its own expertise and assets.

NATIONAL INSTITUTES OF HEALTH

NIH is the lead agency within the federal government for conducting and supporting basic biomedical research relating to the causes, diagnoses, treatments, control and prevention of diseases. Since 2005, the National Institute of Allergy and Infectious Diseases (NIAID), in collaboration with colleagues from the National Cancer Institute, has led a program focused on radiological/nuclear medical countermeasure research and development. NIAID has developed a broad and comprehensive basic and translational research program to identify mechanisms of radiation injury; to identify targets of radiation injury mitigation and treatment; and to identify, evaluate and characterize candidate medical countermeasures (Grace et al. 2010; USDHHS 2010c). The NIAID program thereby currently supports a broad portfolio of projects focused on research toward and development of medical countermeasures for ARS/DEARE and for radionuclide internal contamination. NIAID awarded 38 grants in these areas in fiscal year (FY) 2008, 24 grants in FY 2009 and 10 grants in FY 2010, for a total of over $125 million over the three years. Furthermore, in August 2010 NIAID renewed funding of seven Centers of Excellence as part of its Centers for Medical Countermeasures against Radiation (CMCR) Program, dedicating $105 million to the program over five years.

Key to NIAID's ability to foster the development of safe and effective medical countermeasures for radiological and nuclear threats has been establishing the broad range of product development expertise, capabilities, facilities and services needed to support FDA approval through initiation of a product development support services contract. The contract provides for all the elements of drug development, including Good Laboratory Practices (GLP) research as described in 21CFR58, and animal safety testing facilities, manufacturing facilities, and regulatory and clinical study support. The contract also allows NIAID to perform efficacy studies and to fill in other data gaps for medical countermeasures.

To address the need for diagnostic and dosimetric tools that are sufficiently accurate and precise to enable appropriate triage and treatment decisions, NIH is supporting research and development of high-throughput approaches to radiation dose assessment, including biodosimetry and identification of biomarkers of radiation exposure, through its CMCR Program. High-throughput technology is required to enable thousands to tens of thousands of human samples to be acquired, processed and reported quickly, accurately and easily to clinicians during triage and definitive care. This capacity is currently not available.

BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY

The Pandemic and All-Hazards Preparedness Act established the Biomedical Advanced Research and Development Authority (BARDA) to promote innovation, reduce development risk to both medical countermeasure developers and the federal government and invest in advanced development that will carry products through the crucial and costly middle to late phases of development between basic research and acquisition of final products (Grace et al. 2010; USDHHS 2010e). BARDA seeks to facilitate advanced research and development (culminating in FDA licensure or approval) of promising medical countermeasures identified through the NIH, DoD and other pipelines and to build a robust portfolio of medical countermeasures in the SNS that can be called

upon in response to a radiological incident. In September 2008, HHS/BARDA awarded seven advanced development contracts worth more than $19 million to support therapies to address hematopoietic syndrome, bone marrow stromal cell loss and vascular injury resulting from acute exposure to ionizing radiation. In December 2009, HHS/BARDA awarded base contracts through the Broad Agency Announcement (BAA) mechanism for a total of $35 million to nine universities and companies to fund development of biomarker technologies to assess absorbed radiation dose. Performance-based options can be exercised for up to five years. Several of these contracts arose from the CMCR Program of NIAID, noted above. As biodosimetry requirements are shared worldwide, international partnerships are working collaboratively wherever appropriate and possible. Much remains to be done globally in development and acquisition of these critical tools to address radiological or nuclear threats of terrorism and in planning for the effective deployment and use of biodosimetric capabilities. BARDA also supports acquisition of other types of medical countermeasures, including acquisition contracts funded through the Project BioShield Act of 2004. This support is summarized in Project BioShield Annual Reports to Congress (USDHHS 2007d, 2008b, 2009, 2011).

Current funding opportunities at BARDA or other HHS or partner agencies can be found through the stakeholders' portal at www.MedicalCountermeasures.gov (USDHHS 2010b). BARDA developed MedicalCountermeasures.gov on behalf of HHS to facilitate communication between HHS and stakeholders involved in the research and development of medical countermeasures to enhance public health emergency preparedness. This Web site serves as the single point of entry for stakeholders to submit a request to meet with appropriate personnel within HHS regarding advanced development and acquisition of their products. Whether the product is in the early stages of development or has already been approved, the Web site helps stakeholders connect with the appropriate personnel within the federal government for meetings regarding their products. An open BAA is available through www.fbo.gov (USDHHS 2010d).

DEPARTMENT OF DEFENSE

The Joint Science and Technology Office at the Defense Threat Reduction Agency (DTRA-JSTO) manages programs aimed at early development of radioprotectants (pre-treatments and therapeutics), as well as radiation exposure biodosimetry diagnostic technologies. DoD's Chemical Biological Medical Systems Joint Project Management Office (CBMS JPMO) supports advanced development of therapeutics to address the gastrointestinal sub-syndrome of ARS and diagnostic hand-held devices for self-assessment of radiation exposure that can be carried by the individual warfighter. These devices are being designed to be interpreted immediately by the affected individual for efficient and appropriate triage and subsequent treatment of potential radiation casualties. Meanwhile HHS is pursuing development of therapeutic agents to address the hematopoietic sub-syndrome of ARS and assessment tools and devices for use for the civilian population not directly addressed by DoD efforts, including for pediatric and geriatric populations.

Also within DoD, the Armed Forces Radiobiology Research Institute (AFRRI) has a tri-service laboratory that was established in 1961 (USUHS 2011a). AFRRI is a joint entity of the military departments and of the Uniformed Services University of the Health Sciences under the Assistant Secretary of Defense for Health Affairs (USUHS 2011a). AFRRI executes the DoD Medical Radiological Defense Applied Research Program. AFRRI's civilian and active duty military personnel conduct exploratory and developmental research to identify and develop medical countermeasures against ionizing radiation. Core areas of study include prevention, dose assessment and treatment of radiological injuries. The Institute provides services and performs cooperative research with other federal and civilian agencies and institutions. Useful triage, treatment and dosimetry products are available for download from AFFRI's Web site (USUHS 2011c). These products include the Emergency Radiation Medicine Response Pocket Guide, the Medical Management of Radiological Casualties handbook, Prussian blue treatment and the Biodosimetry Assessment Tool (BAT; a similar tool is available through the REMM Web site; USDHHS 2010a). The BAT is a multiparameter dose-recording and biodosimetry assessment software tool, as is a newer software product called First Responder Assessment Triage (FRAT) (Blakely et al. 2005; Waller et al. 2009; USUHS 2011b). A FRRI has widespread collaborations with other DoD and HHS government facilities to leverage its work for common goals and receives funding for research from an intramural program, interagency agreements, grants from various funding agencies and cooperative agreements with commercial enterprises.

INTERAGENCY SYNERGY IN MEDICAL COUNTERMEASURE DEVELOPMENT

Through the PHEMCE, HHS and DoD coordinate medical countermeasure development and acquisition

efforts to ensure that FDA-approved medical countermeasures for assessing and treating injury from ionizing radiation are available for both the civilian and military populations. This integrated approach makes for both fiscal as well as programmatic efficiency in supporting the development and acquisition of the necessary drugs, therapeutics and diagnostic tools for addressing the public health consequences of radiological emergencies (Wagar 2007).

For example, HHS and DoD are coordinating efforts to support development of the suite of FDA-approved products that will be needed to address the complexity of ARS injury (Wagar 2007). A recent DoD development and acquisition program focuses on the gastrointestinal component of ARS, while recent HHS activities have been focused on addressing the hematopoietic component of ARS. With such coordination, federal resources can be most efficiently and effectively leveraged to ensure preparedness in both the civilian and military populations for radiological and nuclear threats.

HHS is also coordinating its dosimetry efforts with those of DHS. DHS provides radiation dosimetry technologies to measure the environmental exposure conditions for emergency responders following a potential terrorist release of radioactive material in densely populated metropolitan areas. DHS is supporting programs for several dosimetry technologies, including electronic warning dosimeters and passive personnel badges or wallet cards, as indicators of potential exposure. In a complementary effort, HHS is focusing on the technologies determining the *absorbed* dose of radiation for civilians exposed to ionizing radiation, which will be critical for diagnosis and treatment decisions.

CONCEPTS OF OPERATIONS

To analyze medical countermeasure needs and to ensure that tools that are developed can be effectively utilized, federal emergency medical response planning is "scenario-based." Scenarios 1 and 11 of the 15 National Planning Scenarios involve INDs and RDDs (both explosive and non-explosive), respectively (USDHS 2007). These scenarios help direct planning for the types of casualties and infrastructure problems that would be associated with these kinds of incidents. Using computer models of these scenarios and their medical and public health consequences, a concept of operations (CONOPS) is developed that guides the medical response.

The HHS operational planning for medical response is the responsibility of the Office of Preparedness and Emergency Operations (OPEO) within ASPR. This planning includes detailed preparations, working closely with intra-agency partners in HHS such as CDC and FDA, as well as interagency partners. Efforts are synergized to answer questions such as these:

- How will the medical response be organized?
- How will triage and transport be accomplished?
- What types of medical resources and other resources will be needed?
- Where will victims be sent?

The radiation incident CONOPS are organized into a time-oriented "playbook" to be used by HHS responders, including the Secretary, during an incident. Versions of these "playbooks" will be available online to assist HHS partners. Periodic exercises are staged to test the plans and responses and to determine modifications to be made based on "Lessons Learned" records, on theoretical and actual results of field test exercises, and on real-life incidents.

HHS is also involved in interagency efforts to develop "Protective Action Guidelines" and recommendations for emergency responders during such incidents. Thus, the radiological/nuclear planning is conducted in an environment with a broad range of experts in disaster planning, disaster response operations, international collaboration, and public health policy. Many OPEO response plans, as well as its products and tools, are available through the OPEO Web site (USDHHS 2010f).

The federal government interagency cooperation process led to the publication of *Planning Guidance for Protection and Recovery Following Radiological Dispersal Device (RDD) and Improvised Nuclear Device (IND) Incidents* (USDHS 2008a). However, this guidance is intended as an interim resource on the applicability of existing Protective Action Guides to RDDs and INDs, pending further consideration and guidance regarding responses to RDDs and INDs with respect to a wider range of circumstances (e.g., high doses and dose rate zones). Additional guidance superseding this document will be forthcoming from the U.S. Environmental Protection Agency (EPA). The federal government has also released the *Planning Guidance for Response to a Nuclear Detonation* (EOP 2010), which contains detailed descriptions of the consequences, zones of damage and response concepts, while recognizing that in an incident, the decisions will be made by local, regional and tribal responders in collaboration with federal agencies. The National Council on Radiation Protection and Measurements has released an updated publication on *Management of Persons Contaminated with Radionuclides* (NCRP 2008), establishing clinical decision guide (CDG) units for radionuclide amounts of concern for one-time internal contamination with radionuclides.

Non-federal governmental entities are participating in radiation preparedness efforts, especially including

medical professionals in hematology, oncology, radiation oncology and tissue/organ transplant sciences; medical and health physicists; professional societies disciplined in veterinary and clinical medicine; and international organizations and governments, including colleagues in the International Atomic Energy Agency (IAEA) and the World Health Organization (WHO).

RADIOLOGICAL DOSE ASSESSMENT FOR RADIATION TRIAGE, TREATMENT AND TRANSPORT

A radiation mass-casualty incident will trigger typical mass-casualty medical triage responses from local authorities. Although an all-hazards approach is part of the response, issues specific to a radiation incident will also require attention. Rapid, accurate dose assessment will be critical to the medical response to an incident involving radiation exposure, particularly after an IND when potentially hundreds of thousands of people will be concerned that they may have received dangerous doses of radiation, and tens of thousands of people could benefit from ARS mitigation.

Table 1 describes current capabilities for dose assessment. Current dosimetric tools are not adaptable to all incidents, largely because of the numbers of casualties expected. Advances in preparedness will require the development of multiple new approaches and tools. Individual victim triage and treatment decisions depend on many factors, especially:

- clinical medical evaluation—physical exam and history, tracking signs and symptoms over time;
- assessment of the victim's physical location during and after the incident, to be correlated with post-incident radiation levels;
- physical dosimetry, if the victim was wearing a dosimeter; and
- biodosimetry—absorbed-dose determination using bioassays.

Developing the capabilities in the "Rapid biodosimetry" column would complement, replace and/or enhance the current capabilities listed in the other sections of Table 1.

HHS has developed the "RTR system" (Radiation TRiage, TReatment, and TRansport) as a potential model for emergency responder handling of radiation exposure risks in the aftermath of a nuclear or radiological incident (Hrdina et al. 2009). Within this RTR system, biodosimetry information is critical to victim assessment. Initial victim triage will separate people into those who need (1) immediate treatment, (2) medical attention for possible ARS in the next few days to weeks, (3) monitoring for long-term risk, and/or (4) no medical intervention or monitoring. Triage decisions will depend on the size and type of incident, and medical history will be critical. As a broad guideline, immediate treatment will be considered important for those who have received estimated doses greater than 4 Gy; those who have received estimated doses between 2 and 4 Gy and will be considered to require expert care for ARS in the next few weeks; and those with under 2 Gy of estimated exposure, with a lower boundary not determined, who will be triaged for long-term risk assessment. Long-term risk assessment and epidemiological studies would be coordinated among public health authorities in the involved region in consultation with the CDC and radiation epidemiology experts from the Division of Cancer Epidemiology and Genetics at the National Cancer Institute. Mitigation therapy for ARS would be limited to those with estimated doses of greater than 2 Gy, or possibly higher. HHS medical response planning provides access to up-to-date, just-in-time medical management information for medical responders, using the "Radiation Emergency Medical Management" (REMM) Web site (Bader et al. 2008; USDHHS 2010a) developed by ASPR/OPEO and the National Library of Medicine, with input from numerous subject matter experts worldwide.

This approach structures the medical response in coordination with the HHS MedMap Project, which

Table 1. Dosimetry approaches employed by type of radiologic incident, method of triage, and dose assessment.[a]

Incident type	Radioisotope assay (identity and amount of a radionuclide)	Triage by hematology (N/L ratio; depletion kinetics) (Parker and Parker 2007)	Rapid biodosimetry (*biomarkers in development*)	Cytogenetics (dicentrics and translocations)
RDD, explosive	++++	+	++	+++
RDD, non-explosive	++++	+	++	+++
RED	+	++	+++	++
IND	+++	++++[b]	++++	++++
Used for concerned citizens or uncertain history	++++	+	+++	++

[a] Key: + = practical but not primary; ++++ = primary method (number of pluses indicates relative importance). [b] Hematology for IND requires two samples at different times; RDD, radiological dispersal device ("dirty bomb"); RDD, non-explosive (e.g., the incident in Goiânia, Brazil); RED, radiological exposure device (e.g., ^{192}Ir industrial weld-checking source); IND, improvised nuclear device (includes conventional military nuclear device).

provides useful mapping information correlating potential sites for medical, logistic and sheltering functions with changing environmental contamination information. The key information can be selectively shared and will be used by federal and local emergency managers in a single, up-to-date situational map. Details are available (Hrdina et al. 2009), and this model has been incorporated in the *Planning Guidance for Response to a Nuclear Detonation* (EOP 2010).

BIODOSIMETRY LABORATORY CAPACITY

At present, only limited biodosimetry laboratory capacity exists in the U.S. The classical dicentric method is considered as the gold standard in biological dosimetry. In this technique, a small sample of blood is taken from an individual and cultured for 48 h to assess metaphase chromosomes for specific radiation-induced dicentric chromosomes. Improvements in speed and efficiency need to be made for emergency response. Conceptual plans for a new Radiation Laboratory Response Network (Rad-LN) are shown in Fig. 2. The particular resources needed will evolve with automation of current biodosimetry techniques (e.g., lymphocyte kinetics, cytogenetics) and the introduction of new techniques. Physical dosimetry and biodosimetry will provide only a portion of the basis for medical assessment and decisions regarding the management of radiation victims. International experts in hematology, transplantation and radiation injury are collaborating to develop common methods for victim assessment and management based on use of the REMM algorithms and the METROPOL (medical treatment protocol) system (Fliedner et al. 2009).

The Rad-LN concept is being developed by an interagency working group coordinated through the Federal Emergency Management Agency (FEMA) and HHS. The Rad-LN is not yet established and has different proposed functionality from that of another laboratory network with some related capabilities, the CDC Laboratory Response Network, although aspects of infrastructure could be shared. The Rad-LN would provide four major components to assist medical response to a radiological incident, recognizing that this network will likely be largely virtual with many functions coming from existing hospitals and other partner organizations.

1. Radionuclide bioassay capability for all radionuclides of concern would be centered around the CDC Radiobioassay Laboratory and its network of state laboratories but also could involve nuclear medicine and radiation safety programs (such as those at NIH) for assistance with incidents in their regions and also for high-throughput scintillation counting for screening (depending on the radionuclide).
2. Enhanced cytogenetic biodosimetry assay throughput would include automated sample preparation and surge capacity through satellite readers. Artificial intelligence approaches to cytogenetics and other rapid screening procedures are being studied to facilitate surge capacity. International networks are being

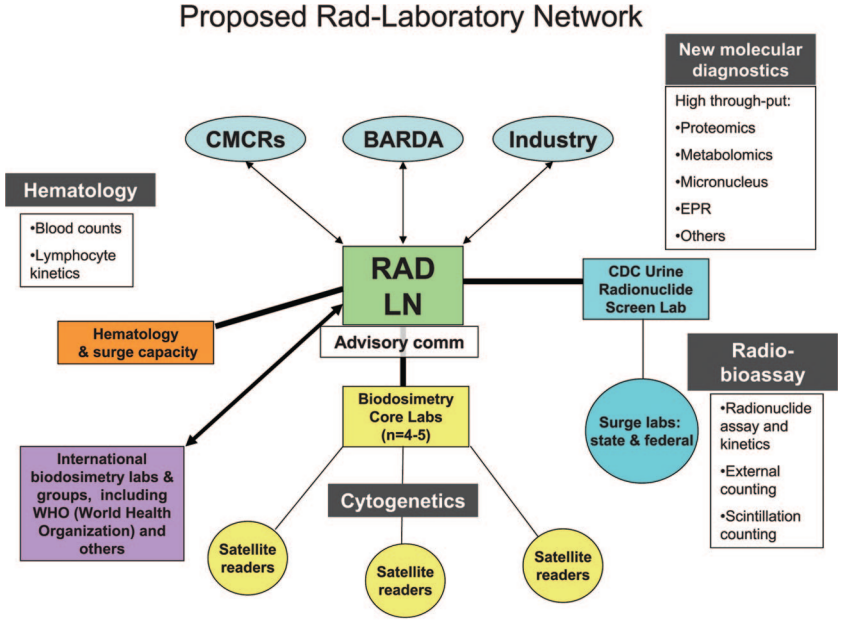

Fig. 2. HHS and interagency/multisector partner concept of a Radiation Laboratory Response Network (Rad-LN).

developed through the WHO, the IAEA and the Global Health Security Initiative (GHSI 2010).
3. Hematology surge capacity would include serial studies to assess lymphocyte decline and potentially newer algorithms to measure a neutrophil/lymphocyte ratio that might facilitate the initial triage of victims into risk groups for ARS.
4. A test bed would provide for assessment and interlaboratory comparison of novel high-throughput approaches to measuring molecular markers of radiation exposure. Many new molecular techniques are being explored that would need validation against a "gold standard" that the Rad-LN could provide.

The WHO BioDoseNet is a global network of biodosimetry laboratories whose role is to support management and decision-making in cases of large radiation emergency incidents in which the capacity of individual laboratories is likely to be overwhelmed. In preparedness for such incidents, the BioDoseNet focuses on harmonization of methodology, quality assurance, knowledge-sharing and inter-comparison exercises. Expert Consultancy includes Canada, China, France, Germany, Japan, Korea, United Kingdom, Ukraine and the U.S. A second biennial coordination meeting in conjunction with the BioDose conference was held in France (October 2010) to report on progress made and to plan future activities toward a larger inter-comparison study using a simulation of a mass-casualty scenario.

CONCLUSION

Interagency interaction, cooperation and support are required for long-term goals to be met effectively and efficiently within and across the civilian and military sectors. In the face of substantial yet limited resources and a panoply of potentially catastrophic threats requiring public health emergency preparedness, whether the threats are natural, accidental, or intentional, a vast range of activities and needs must be coordinated and prioritized at all levels of government.

HHS and DoD are dedicated to developing and implementing medical countermeasures, including dose assessment tools for triage, diagnosis, and treatment of acute radiation syndrome in large populations of civilians and warfighters. This paper describes many of the on-going efforts at the federal level to support and encourage coordination in addressing development and acquisition of these resources. These efforts will be critical to allocate and dispense medical countermeasures to those who will need them to prevent, mitigate and/or treat the harmful effects of ionizing radiation and particularly to enable the most appropriate allocation of limited funding. Close cooperation with international partners, as is being explored in the development of the Rad-LN concept, in addition to strong relationships among agencies and departments within the federal government, will lead to the most effective results. The goal is to leverage synergistically the unique capabilities of various departments and agencies to accomplish the ultimate objectives of saving the greatest possible number of lives and preserving or restoring health to the greatest extent possible among those that are saved.

Acknowledgments—We acknowledge the dedicated leadership of W. Craig Vanderwagen, the first Assistant Secretary for Preparedness and Response (ASPR). Nicole Lurie is currently the ASPR, the Secretary's principal advisor on matters related to bioterrorism and other public health emergencies. The ASPR also coordinates interagency activities among HHS; other federal departments, agencies and offices; and state and local officials responsible for emergency preparedness and the protection of the civilian population from acts of bioterrorism and other public health emergencies. The mission of the ASPR is to lead the nation in preventing, responding to and recovering from the adverse health effects of public health emergencies and disasters.

Note added in proof: During the publication of this paper in 2011, a series of papers on allocation of scarce resources after a nuclear detonation pertinent to dose assessment, triage, treatment, and transport appeared in a special Nuclear Preparedness supplement to Disaster Medicine and Public Health Preparedness, accessible at http://www.dmphp.org/content/vol5/Supplement_1/index.dtl. Accessed on 17 July, 2011.

REFERENCES

Bader JL, Nemhauser J, Chang F, Mashayekhi B, Sczur M, Knebel A, Coleman CN. Radiation Event Medical Management (REMM): new web site guidance for health care providers during mass casualty events. Prehospital Emergency Care 12:1–11; 2008.

Blakely WF, Salter CA, Prasanna PG. Early-response biological dosimetry—recommended countermeasure enhancements for mass-casualty radiological incidents and terrorism. Health Phys 89:494–504; 2005.

Executive Office of the President. Homeland Security Staff and Interagency Policy Coordination Subcommittee for Preparedness & Response to Radiological and Nuclear Threats. Planning guidance for response to a nuclear detonation [online]. 2010. Available at www.remm.nlm.gov/PlanningGuidanceNuclearDetonation.pdf. Accessed 31 October 2010.

Fliedner TM, Chao NJ, Bader JL, Boettger A, Case C Jr, Chute J, Confer DL, Ganser A, Gorin N-C, Gourmelon P, Graessle D, Krawisz R, Meineke V, Niederwieser D, Port M, Powles R, Sirohi B, Weinstock DM, Wiley A, Coleman CN. Stem cells, multiorgan failure in radiation emergency medical preparedness and assistance: a US/European consultation workshop. Stem Cells 27:1205–1211; 2009.

Global Health Security Initiative [online]. 2010. Available at www.ghsi.ca/english. Accessed 31 October 2010.

Grace MB, Moyer BR, Prasher J, Cliffer KD, Ramakrishnan N, Kaminski J, Coleman CN, Manning RG, Maidment BW, Hatchett R. Rapid radiation dose assessment for radiological public health emergencies: roles of NIAID and BARDA. Health Phys 98:172–178; 2010.

Hrdina CM, Coleman CN, Bogucki S, Bader JL, Hayhurst RE, Forsha JD, Marcozzi D, Yeskey K, Knebel AR. The "RTR" medical response system for nuclear and radiological mass

casualty events: a functional TRiage-TRansport-TReatment medical response model. J Prehosp Disaster Med 24:167–178; 2009.

National Council on Radiation Protection and Measurement. Management of persons contaminated with radionuclides. Bethesda, MD: NCRP; Report No. 161 (Volume 1); 2008.

Uniformed Services University of the Health Sciences. Armed Forces Radiobiology Institute. A United States Department of Defense research laboratory. About AFRRI [online]; 2011a. Available at www.usuhs.mil/afrri/organiza/about_afrri.htm. Accessed 25 June 2011.

Uniformed Services University of the Health Sciences. Armed Forces Radiobiology Research Institute. A United States Department of Defense research laboratory. Biodosimetry tools [online]; 2011b. Available at www.usuhs.mil/afrri/outreach/biodostools.htm#software. Accessed 25 June 2011.

Uniformed Services University of the Health Sciences. Armed Forces Radiobiology Research Institute. A United States Department of Defense research laboratory. Medical/operational guidance for managing radiation casualties [online]; 2011c. Available at www.usuhs.mil/afrri/outreach/guidance.htm. Accessed 25 June 2011.

U.S. Department of Health and Human Services. Office of Public Health Emergency Preparedness; statement of organization, functions, and delegations of authority. Federal Register 71:38403–38405; 2006.

U.S. Department of Health and Human Services. Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) strategy for chemical, biological, radiological and nuclear (CBRN) threats. Federal Register 72:13109–13114; 2007a. Available at www.upmc-biosecurity.org/website/resources/govt_docs/agents_disease/hhs/hhs_phemce_strategy.html. Accessed 25 October 2010.

U.S. Department of Health and Human Services. Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) implementation plan for chemical, biological, radiological and nuclear (CBRN) threats. Federal Register 72:20117–20128; 2007b. Available at www.upmc-biosecurity.org/website/resources/govt_docs/agents_disease/hhs/hhs_phemce_implementation_plan.html. Accessed 25 October 2010.

U.S. Department of Health and Human Services. Food and Drug Administration. Guidance—emergency use authorization of medical products [online]. 2007c. Available at www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm. Accessed 31 October 2010.

U.S. Department of Health and Human Services. Physical and biological dosimetry techniques and devices useful in initial triage after radiologic and nuclear events [online]. 2008a. Available at www.fbo.gov/index?s=opportunity&mode=form&tab=core&id=3e7743eb353597091efeb4194cb685b4&_cview=1. Accessed 31 October 2010.

U.S. Department of Health and Human Services. Office of the Secretary, Office of the Assistant Secretary of Preparedness and Response, Biomedical Advanced Research and Development Authority, Office of Policy, Planning, and Requirements. Project BioShield annual report to Congress: August 2006–July 2007 [online]. 2008b. Available at www.medicalcountermeasures.gov/BARDA/documents/bioshieldannualreport2006.pdf. Accessed 25 October 2010.

U.S. Department of Health and Human Services. Office of the Secretary, Office of the Assistant Secretary of Preparedness and Response, Biomedical Advanced Research and Development Authority, Office of Policy, Planning, and Requirements. Project BioShield annual report to Congress: August 2007–December 2008 [online]. 2009. Available at www.medicalcountermeasures.gov/BARDA/documents/bioshieldannualreport2008.pdf. Accessed 25 October 2010.

U.S. Department of Health and Human Services. Radiation emergency medical management: guidance on diagnosis and treatment for healthcare providers [online]. 2010a. Available from www.remm.nlm.gov/index.html. Accessed 31 October 2010.

U.S. Department of Health and Human Services. MedicalCountermeasures.gov [online]. 2010b. Available at www.medicalcountermeasures.gov. Accessed 11 November 2010.

U.S. Department of Health and Human Services. National Institutes of Health, National Institute of Allergy and Infectious Diseases. Medical countermeasures against radiological and nuclear threats [online]. 2010c. Available at www3.niaid.nih.gov/topics/radnuc. Accessed 25 October 2010.

U.S. Department of Health and Human Services. Office of the Secretary, Office of the Assistant Secretary for Preparedness and Response (ASPR), Acquisitions Management, Contracts, & Grants (AMCG). BARDA broad agency announcement for the advanced research and development of chemical, biological, radiological, and nuclear medical countermeasures [online]. 2010d. Available at www.fbo.gov/index?s=opportunity&mode=form&tab=core&id=ca181720fbf3804361552820b5e58b62&_cview=0. Accessed 11 November 2010.

U.S. Department of Health and Human Services. Office of the Secretary, Office of the Assistant Secretary for Preparedness and Response. Biomedical Advanced Research and Development Authority [online]. 2010e. Available at www.medicalcountermeasures.gov/BARDA/BARDA.aspx. Accessed 31 October 2010.

U.S. Department of Health and Human Services. Office of the Secretary, Office of the Assistant Secretary for Preparedness and Response (ASPR), Office of Preparedness and Emergency Operations (OPEO). Public health emergency [online]. 2010f. Available at www.phe.gov/about/opeo/. Accessed 31 October 2010.

U.S. Department of Health and Human Services. Office of the Secretary, Office of the Assistant Secretary of Preparedness and Response. Project BioShield annual report to Congress: January–December 2009 [online]; 2011. Available at www.medicalcountermeasures.gov/BARDA/documents/2009%20BioShield%20Report%20FINAL.pdf. Accessed 24 June 2011.

U.S. Department of Health and Human Services. Office of Public Health Emergency Preparedness, Office of Public Health Emergency Medical Countermeasures. Project BioShield annual report to Congress: July 2004–July 2006 [online]. 2007d. Available at www.medicalcountermeasures.gov/BARDA/documents/bioshieldannualreport.pdf. Accessed 25 October 2010.

U.S. Department of Homeland Security. National preparedness guidelines [online]. 2007. Available at www.dhs.gov/xlibrary/assets/National_Preparedness_Guidelines.pdf. Accessed 31 October 2010.

U.S. Department of Homeland Security. Federal Emergency Management Agency (FEMA). Planning guidance for protection and recovery following radiological dispersal device (RDD) and improvised nuclear device (IND) incidents [online]. Docket ID FEMA-2004-0004. Federal Register 73:45029–45048; 2008a. Available at edocket.access.gpo.gov/2008/E8-17645.htm. Accessed 31 October 2010.

U.S. Department of Homeland Security. Federal Emergency Management Agency. National response framework [online]. Washington, DC: USDHS; 2008b. Available at www.fema.gov/pdf/emergency/nrf/nrf-core.pdf. Accessed 31 October 2010.

U.S. Department of Homeland Security. Federal Emergency Management Agency. Nuclear/radiological incident annex of the national response framework. Washington (DC); [Internet]. 2008c. Available at www.fema.gov/pdf/emergency/nrf/nrf_nuclearradiologicalincidentannex.pdf. Accessed 31 October 2010.

U.S. Library of Congress, Federal Research Division. Military support to civil authorities: the role of the Department of Defense in support of homeland defense [online]. Washington, DC: U.S. Library of Congress; 2007. Available at www.loc.gov/rr/frd/pdf-files/CNGR_Milit-Support-Civil-Authorities.pdf. Accessed 25 October 2010.

Wagar E. Interagency cooperation in development of medical countermeasures. Chem-Biodefense Q 4:10–12; 2007.

Waller E, Millage K, Blakely WF, Ross JA, Mercier JR, Sandgren DJ, Levine IH, Dickerson WE, Nemhauser JB, Nasstrom JS, Sugiyama G, Homann S, Buddemeier BR, Curling CA, Disraelly DS. Overview of hazard assessment and emergency planning software of use to RN first responders. Health Phys 97:145–56; 2009.

White House, Office of the Press Secretary. Homeland Security Presidential Directive/HSPD-21; Public health and medical preparedness [online]. Washington, DC: OPS; 2007. Available at www.fas.org/irp/offdocs/nspd/hspd-21.htm. Accessed 25 October 2010.

■ ■