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MEETING REPORT

WHO 1st Consultation on the Development of a Global Biodosimetry Laboratories Network for Radiation Emergencies (BioDoseNet)

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The World Health Organization (WHO) held a consultation meeting at WHO Headquarters, Geneva, Switzerland, December 17–18, 2007, to develop the framework for a global biodosimetry network. The WHO network is envisioned to enable dose assessment using multiple methods [cytogenetics, electron paramagnetic resonance (EPR), radionuclide bioassays, etc.]; however, the initial discussion focused on the cytogenetic bioassay (i.e., metaphase-spread dicentric assay). Few regional cytogenetic biodosimetry networks have been established so far. The roles and resources available from United Nations (UN) agencies that provide international cooperation in biological dosimetry after radiological emergencies were reviewed. In addition, extensive reliance on the use of the relevant International Standards Organization (ISO) standards was emphasized. The results of a WHO survey of global cytogenetic biological dosimetry capability were reported, and while the survey indicates robust global capability, there was also a clear lack of global leadership and coordination. The expert group, which had a concentrated focus on cytogenetic biodosimetry, formulated the general scope and concept of operations for the development of a WHO global biodosimetry laboratory network for radiation emergencies (BioDoseNet). Follow-on meetings are planned to further develop technical details for this network. © 2009 by Radiation Research Society

INTRODUCTION

The worldwide use of ionizing radiation for beneficial purposes has also led to hundreds of instances in which one or more persons were accidentally overexposed (*1*). Because of recent terrorist activities and intelligence information, there is strong sentiment that it is not a question of if but rather when a radiological or nuclear terrorist attack will occur (*2*). The practice of radiation protection dictates the establishment of response capability for rapid medical diagnosis and management of overexposed individuals. The accepted generic multiparameter and early-response approach includes measuring radioactivity and monitoring the exposed individual, observing and recording prodromal signs/symptoms and erythema, obtaining complete blood counts with white blood cell differentials, sampling blood for the chromosome aberration cytogenetic bioassay using the ''gold standard'' dicentric assay for dose assessment, bioassay sampling, if appropriate, to determine radioactivity contamination, and using other available dosimetry approaches (e.g., dose assessment by measurement of free radicals in solid matrix materials using electron paramagnetic resonance, EPR) (*3–6*). Many nations have established reference expert cytogenetic biodosimetry laboratories. Early clinical medical decision needs associated with potential mass casualty events prompted Lloyd and colleagues to advocate the diagnostic role and utility of cytogenetics for triage of radiation casualties (*7*). In cases of an urgent need for assessment in radiological exposures,

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individual nations often rely on international cooperation facilitated by United Nations (UN) agencies [i.e., WHO and the International Atomic Energy Agency (IAEA)] (*8*). Reference expert cytogenetic laboratories have recently established regional (e.g., reference national cytogenetic laboratories among the respective institutes from the United Kingdom, Germany and France) and national (*9–11*) networks to enhance their capabilities.

Dr. Zhanat Carr (WHO) presented the rationale for the WHO 1st consultation meeting on the development of a global biodosimetry laboratory network for radiation emergencies held at WHO Headquarters, Geneva, Switzerland, on December 17–18, 2007. WHO has a unique advantage and is best placed to work directly with health authorities in the UN 193 Member States to (1) provide medical support and public health advice in case of radiation accidents or nuclear emergencies and (2) build capacity and provide technical assistance and information to support national programs in the field of radiation protection and radiation health. The global biodosimetry laboratory networks envisioned by WHO would involve laboratories with cytogenetics, electron paramagnetic resonance (EPR), and radionuclide bioassay expertise, with the view of expanding the network's scope as new biodosimetry methods become available. Global international cooperation and networking with clear standard operating procedures (SOP) for preparedness and emergency response are needed to ensure that laboratories have the capacity to respond to mass-casualty events.[2] International cooperation will facilitate sharing common protocols, criteria for quality assurance, guidance on certification, and common operational plans and reagent stockpiling to aid international cooperation. A global network of biodosimetry laboratories would also promote regular intercomparison studies (*12–14*), training and exercises for sustainable expertise.

An expert group that had focused on dose assessment by cytogenetics was charged at the WHO 1st consultation meeting with the following objectives:

1. identification of the needs and criteria for laboratories to be included into the network,
2. development of terms of references for the network setup and operation,
3. establishment of standard operating procedures for network activities (i.e., emergency network activation, sample collection and transportation, sample tracking, sample processing, reporting and data sharing),
4. defining the role of quality management, certification, intercomparison studies, training and exercise in network activities, and
5. mapping strategy and recommendations for next steps in network development.

[2] At the 2007 Washington, DC, meeting of the Global Health Security Advisory Group (GHSAG), the need of biodosimetry networks was also emphasized as one of the key current tasks before the international community [see Global Health Security Initiative (GHSI) website: http://www.ghsi.ca/english/index.asp]. GHSAG is a committee comprising high level representatives of the national health authorities for the G-8 block of countries.

BIODOSIMETRY AND INTERNATIONAL AGENCIES' ROLES IN RESPONSE TO RADIOLOGICAL AND NUCLEAR EMERGENCIES

WHO

Dr. Zhanat Carr described WHO's role in the response to radiological/nuclear emergencies and preparedness-strengthening activities. WHO has a mandate to provide and coordinate technical assistance on public health and medical response issues to its member states in case of radiation emergencies. This mandate is established in both Emergency Conventions (*15, 16*) and International Health Regulations (IHR) (*17*). The IHR reviewed in 2005 and in force since 2007 are a legally binding framework for all WHO member states for notification and verification of events of public health concern, risk assessment and rendering assistance as well as for building the capacity of member states to be prepared for public health emergencies regardless of their origin, including chemical and radionuclear events. The establishment of an international biodosimetry network is a part of WHO's IHR implementation plan.

Multiple-parameter dosimetry methods were reviewed along with guidelines for applications of biodosimetry after acute radiation exposure incidents. WHO's Radiation Emergency Medical Preparedness and Assistance Network (REMPAN) functions were also described. WHO REMPAN consists of more than 40 medical and research centers specializing in radiation emergency medicine and related fields including biodosimetry laboratories with expertise in cytogenetics, EPR, bioassays and molecular biology located worldwide. A 2006 survey of 35 REMPAN centers indicated that significant EPR capabilities are present or will be established in the near future in these centers.

Dr. May Chin-May Chu (WHO) presented a talk that addressed building core capacity under IHR and the role of laboratory networks. Citing the WHO report entitled *A Safer Future* (*18*), Dr. Chu stressed the importance of preparedness and international cooperation to mitigate threats from natural, accidental and deliberate public health emergencies. WHO supports Member States' efforts to improve their response capabilities. Individual countries face challenges in strengthening their laboratory systems. Regionalized and individualized approaches can be considered with local ownership enhanced with network involvement. WHO operates an effective event management process for public health emergency response. WHO guidance for national capacity assessment for public health response to the deliberate use of biological, chemical and radioactive (BCR) materials has been developed (*19*). Using WHO's Global Laboratory Directory Network (GLaDNet) as a basis and expanding it further to include threat-specific lab-

oratory services, several initial steps in establishing an effective global biodosimetry laboratory network could be considered, including

1. creation of a ''network of networks'' directory for ''one-stop shopping'' for expertise,
2. providing a platform for improving preparedness and surge capacity,
3. developing a partners benefit package for network members, and
4. encouraging applied research between partners for the public good.

A presentation from Dr. Renu Dayal-Drager (WHO) provided an extensive overview of the WHO expertise on working with global networks and using networks as a tool for international cooperation and coordination of activities. The WHO Global Epidemics Preparedness and Response network of WHO Collaborating Centers (CC) is focused on epidemic-prone infectious and zoonotic diseases and emerging and dangerous pathogens (see website: www.who.int/csr/en/). In the case of the WHO Global Influenza Programme, there are two networks, one focusing on surveillance and the second on research support. One hundred and fifteen member nations participate in the National Influenza Centre's program, with objective actions including early detection, notification and response to cases to contain new viruses, delay spread and implement surge capacity. This network is composed of several types of laboratories (e.g., global specialized, regional reference, national and sub-national) that share samples and data and cooperate in training. Based on the GLaDNet model and experience, additional recommendations for the next steps toward establishment of an effective global biodosimetry network were provided, including (1) use of a questionnaire survey to map potential participants and develop a ''yellow pages'' directory for the laboratory network, (2) development of guidelines for collaboration that protect individual and national rights to intellectual property, and (3) engaging neighbors by promoting joint activities (i.e., biosafety biosecurity awareness workshops, quality assurance, transport).

International Atomic Energy Agency (IAEA)

Dr. Kenzo Fujimoto (IAEA) presented a talk on IAEA's interest and activities in biodosimetry. The IAEA Incident and Emergency Centre (IEC) serves as an international global focal point for preparedness, communication and response for nuclear and radiological safety or security-related incidents, emergencies, threats or events of media interest (*20*). The IEC's activities are founded in statutory and legally binding obligations, including Emergency Conventions (*15, 16*). In 2000 IAEA established the Response Assistance Network (RANET), previously called the Emergency Response Network (ERNET), of national capabilities including teams and services suitably qualified to respond rapidly and, in principle, on a regional basis to nuclear or radiological emergencies (*21*). RANET's areas of expertise include assistance as advisors and with assessment and evaluation, monitoring and recovery. The responsibilities within RANET include assistance in response to nuclear accidents, radiological emergencies, or other nuclear or radiological events. The national assistance capabilities (NAC) included in RANET scope consist of 12 special fields of expertise (see Table 1), including biodosimetry capability. Member states of the IAEA are encouraged to enlist their national capabilities within the scope of RANET. As of December 2007, there was one biodosimetry laboratory among the countries that had registered their national capabilities with RANET.

TABLE 1
IAEA's National Assistance Capabilities

Aerial survey	Public health protection
Radiation monitoring	Biodosimetry
Environmental measurements	Internal dose assessment
Source search/recovery	Bioassay
Assessment and advice	Histopathology
Medical support	Dose reconstruction

Typically the types of assistance involving qualified experts consist of a Field Assistance Team as a part of the Joint Assistance Team and external base support personnel. External base support personnel provide support to the JAT, IEC or the requesting state and expert advice on assessment from another location, such as the donor country offices.

In 2001 IAEA published *Cytogenetic Analysis for Radiation Dose Assessment—A Manual* (*22*). Dr. Fujimoto also reviewed numerous radiation accidents and illustrated the use of biodosimetry for retrospective dose reconstruction; accident reports from these incidents are available from IAEA's website (www.pub.iaea.org/MTCD/publications/accres.asp). IAEA has a long-standing interest and involvement in biological dosimetry, including Coordinated Research Programmes, regional training courses and fellowships under IAEA's Technical Cooperation programs, and provision of equipment to the developing Member States. In addition, IAEA's ongoing activities and interest in biodosimetry include strengthening a Latin-American biodosimetry network within the IAEA Technical Cooperation project RLA 9054 and planning seminars, workshops and intercomparsion activities for 2008–2009.

In summary, IAEA, in close collaboration with WHO, encourages interested biodosimetry laboratories to register with RANET (*23*), engage in intercomparison studies to ensure skills, to maintain qualified staff, and to improve skills, attend training courses, seminars and workshops, and be involved in emergency exercises to ensure prompt assistance in emergencies.

International Standards Organization (ISO)

Dr. Phillipe Voisin, Institut de Radioprotection et Sureté Nucléaire (IRSN), France, chairman of ISO Working Group

(WG) 18, presented a talk on the efforts of ISO WG 18 to standardize biological dosimetry for both reference and triage applications. Examples of the practical diagnostic utility of cytogenetic biodosimetry to confirm exposures and provide dose assessments were presented. In 2004 ISO established an international standard: *Performance Criteria for Service Laboratories Performing Biological Dosimetry by Cytogenetics* (*24*). This standard addresses quality assurance and quality control to permit accreditation of biological dosimetry by cytogenetics (*25*). Revisions of ISO standard 19238 are in progress to improve the precision of description of the methodology, calculations of the dose–response curves, and inclusion of an accreditation protocol.

An example of a radiation accident in Africa that involved population triage was presented. The rationale for the use of a cytogenetic biodosimetry network in this type of emergency response was (1) to support the clinical triage of those persons who are potentially involved, (2) to identify highly irradiated patients who will require clinical intervention and also to identify wrongly diagnosed, false positive cases, (3) to provide long-term assistance, notably for selected cases that would be analyzed to produce more accurate evaluation of the effects of high partial-body exposure, and (4) to handle a potentially large number of casualties after a major event given the limited surge capacity of individual laboratories that have only a restricted number of trained staff. The mutual assistance of several laboratories would be required in mass casualty cases to increase the number of samples that can be handled and to provide results more quickly.

ISO WG 18 has initiated the development of an ISO standard for ''Radiation Protection—Performance for Service Laboratories performing 'cytogenetic triage' of mass casualties in radiological or nuclear emergencies—General principles and application to Dicentric Assay'' (draft ISO Standard 21243).[3] Cytogenetic triage is the use of chromosome damage to approximately and rapidly evaluate radiation doses received and the percentage of the body exposed in persons suspected of being exposed to supplement the early clinical categorization of casualties. The purposes of this standard are to (1) provide guidelines to all laboratories performing the dicentric bioassay and cytogenetic triage for dose assessment using documented and validated procedures, (2) facilitate the application of cytogenetic biodosimetry networks to permit comparison of results obtained in different laboratories, and (3) guide laboratories newly commissioned to carry out cytogenetic triage reproducibly and accurately. The document is directed to either an experienced biological dosimetry laboratory working alone or a network of collaborating laboratories. The standard gives an overview of the minimum requirements of the process and quality control (QC) components of the cytogenetic response for triage of mass casualties. Technical aspects of the dicentric assay are referred to in the earlier ISO Standard 19238 for use by reference laboratories for definitive dose assessment by cytogenetics. The new ''triage'' standard concentrates on organizational aspects of applying the dicentric assay for operation in a triage mode. Dr. Voisin illustrated several features of the new ISO standard, including emergency response of the reference laboratory, laboratory network activation, preparedness of the laboratory/network, and quality assurance (QA) and QC of the laboratory/network.

[3] International Standard Organization (ISO), Radiation protection—Performance criteria for service laboratories performing cytogenetic triage assessment of mass casualties in radiological or nuclear emergencies—General principles (ISO 21243), personal communication with Dr. Phillipe Voisin (IPSN, France).

WHO'S SURVEY RESULTS ON NATIONAL CYTOGENETIC BIODOSIMETRY CAPABILITIES

WHO executed a survey of nation/state capacities, facilities and resources in dose assessment by cytogenetics. Mr. Michael Hopmeier (Innovative and Unconventional Concepts, Inc., Arlington, VA) presented a summary report from this survey. WHO sent the questionnaire to over 50 laboratories/facilities around the world. Responses were received from 32 laboratories. Questions asked were: (1) How many staff do you have who are skilled in culturing lymphocytes and scoring dicentrics? (2) Do you have automated systems (e.g., metaphase finders) available; how many workstations do you have? (3) How many blood samples can you process in response to a sudden request to respond to a multi-casualty event, taking account of your normal holdings of consumables (medium, serum, plasticware, etc.), and are consumables easy to renew/obtain in your country? (4) For what types of radiation does your laboratory have dose–response calibration curves? (5) Which statistical methods do you use for curve fitting and calculating uncertainty on dose estimates? (6) If asked to score 50 metaphases per patient (triage mode), how many samples could you realistically score in a week taking into account your available trained staff, who would also be doing the ''wet work''? (7) Are you in a QA and QC compliance program, and do you have written procedures? (8) How is the collection of blood samplings (field to laboratory) for biological dosimetry in your country organized, and do you have a prearranged organized relationship between medical doctors and the biodosimetry laboratory? (9) What do you expect of and how do you see your participation in the establishment and the maintaining of a biological dosimetry network?

Table 2 provides a summary of the responses to the WHO survey. Based on the survey results, a typical reference cytogenetic biodosimetry laboratory consists of mean number of 8–12 staff members per facility. Most laboratories have three or four, and the mean number is biased to be rather high because one laboratory (Health Canada) included their network of staff located in clinical laboratories throughout their nation. Most laboratories make use of automated metaphase finders. Almost every laboratory has

TABLE 2
Summary of WHO's November 2007 National Survey Results from Biodosimetry Capacity Mini-survey

No.	Question[a]	Responses
1	Staffing	Staff/facility
	lymphocyte culturing	8.6; most have 3–4
	dicentric scoring	12.3; most have 3–4
		Note. Same people may do both culturing and scoring
2	Automation	
	little or none	9 out of 25 responding laboratories
	automated metaphase finders	most
		Note. Unclear what access laboratories have to data automation and internet
3	Emergency sample processing capacity	
	average number per laboratory	170; ranged from 10 to 1800; some with no capability
	time frame	hours to weeks
	access to consumables	varied responses, generally available in days to weeks
4	Radiation quality	Most: ^{60}Co and various X-ray energies
		Many: ^{137}Cs, fast neutrons
		Few: Tritium, thermal neutrons, plutonium, ^{241}Am, fission neutrons
5	Statistical methods	Most laboratories used standard statistical methods based on IAEA standards or methods shared by UK and German laboratories. Other specialized statistical software included DOSGEN, PolyFitA and IRLS.
6	Triage sample throughput in 1 week	Number per responding laboratories/facility
	<30	11 of 25
	30–50	7 of 25
	>50	7 of 25; some ranged up to 1000
7	QA and QC compliance	3—ISO 9000/9001; 2—ISO/IEC 17026; 2—ISO 19238; 1—ISO 14001; 2—CLIA; 12—custom standard; 7—none
8	Blood sampling coordinated	most—ad hoc; 12—plans in place; rest—in development
9	Expectations of network	varied responses

[a] See text for a more complete description of the survey questions.

some form of written procedures and in-house calibration curves for photon-type radiations. Emergency response surge capacity varied among the laboratories, with 14 of the 25 responding facilities reporting triage sample throughput capability of ≥30 cases in 1 week.

Mr. Hopmeier made several general observations from the survey. The survey had a wide potential for misunderstanding, and a selection of prepared standardized answers might have avoided confusion. There were no questions as to whether any of these answers have ever been verified by exercises, validations or experiences in emergency dose assessment by cytogenetics. There were also no discussions of international cooperation during operations, except for the laboratory's involvement in intercomparison studies. The survey results did not provide sufficient details to properly analyze answers and their meaning. For example, limited information was provided on the ease to obtain/reorder consumable supplies.

Mr. Hopmeier also concluded that there is an enormous opportunity for a network, with a vast array of untapped potential resources. At present there is no leadership or institutional organization in this area, and there is a significant need for validation and improvement of doctrine and assumptions. WHO could assist in the establishment of a global biodosimetry laboratory network because it is principally a public health issue.

EXPERT GROUP'S RECOMMENDATIONS ON THE DEVELOPMENT OF A BIODOSIMETRY LABORATORIES NETWORK FOR RADIATION EMERGENCIES BIODOSIMETRY (BioDoseNet)

Reference Laboratory Capabilitiy Criteria

In BioDoseNet, a reference laboratory is required to have experience in the lymphocyte metaphase-spread dicentric bioassay for dose assessment. Experience in other cytogenetic bioassays (e.g., cytochalasin B blocked micronucleus assay, premature chromosome condensation assay, fluorescence *in situ* hybridization–chromosome translocation) used for dose assessment is an advantage. Laboratories must also have established in-house radiation calibration curves, ideally for multiple radiation qualities (i.e., γ rays, X rays and neutrons). QA and QC programs with clearly written protocols are essential. Reference laboratories should have a publication record to attest to their experience in the performance of dose assessment by cytogenetics. A training program to ensure sustained expertise is an essential feature of a qualified reference laboratory. Documentation of compliance with appropriate national laws and regulations is a plus. In addition, the reference laboratory should have independence from WHO funding.

Reference Laboratory Capacity Criteria

The criteria for reference laboratory capability are very technical by their nature. The expert panel discussed this concept in depth and suggested criteria in the context of the participation of a reference laboratory in a global network of cytogenetic laboratories. The expert panel agreed that a reference laboratory's throughput must be 30 triage cases per week and that it must be sustainable for 4 weeks, although higher throughput and longer sustainability is a plus. Documentation of the demonstrated capacity to process 30 triage samples or more per week in an emergency would be helpful. A stockpile of available consumable resources (e.g., reagents, plasticware) to process and analyze 120 samples in 4 weeks is needed. After the initial triage time window (1–4 weeks), the reference laboratory needs to be able to commit to follow-up with a more suitable detailed analysis (i.e., scoring up to 500 metaphase spreads per case) for those cases that need further dose refinement to support clinical management.

Emergency Scenarios for Activation of Network

A significant radiological event of any origin can activate BioDoseNet. Use of the network would be justified in those cases where a nation lacks biological dosimetry capacity or in a large-scale emergency event that exceeds the national capacity for biological dosimetry. Nations need to request international assistance and accept the offer of assistance from BioDoseNet.

Major Steps in Using the Network in Emergencies

The expert panel agreed that the network should be organized to retain a high degree of flexibility to respond to radiological emergencies. Here we present one scenario for activation of the network. The detection of a significant radiological emergency in a given country can be derived from media or formal notification channels. For example, typically UN member nations, under agreements from Conventions, notify WHO offices. When national emergency response is activated and the assessment of the scale of the emergency requires international assistance, the existing international arrangements will be applied (*15, 16, 26*). If necessary, international agencies (WHO, IAEA) will assist with medical and public health responses, including the biological dosimetry needs. In this case or when requested, BioDoseNet would be activated. Depending on the scale of emergency, national and regional capability, and the geographic situation, one of the reference laboratories could then be appointed as the core laboratory for coordinating the biological dosimetry response and reporting for this specific event. WHO would facilitate the interactions between the requesting nation's health authorities and assisting in communication with BioDoseNet through a designated core reference laboratory with health care facilities throughout the entire period of response. A medical diagnostic information-based process would be the basis for patient selection and prioritization for dose assessment by biological dosimetry. The biological dosimetry assessment processes (sample collection, labeling, transportation, performance of a cytogenetic laboratory, reporting, etc.) (Fig. 1) would comply with guidance established by relevant international standards[3] (*20, 27*).

Rationale of a Network in Case of Emergency Response

The expert group adopted the rationales for the use of BioDoseNet in the case of an emergency response as presented earlier by Dr. Voisin in his report on ISO activities. Briefly, these include (1) support for clinical triage to confirm highly irradiated persons and identify false positives (e.g., worried healthy or concerned public), (2) more accurate analysis, after the initial cytogenetic triage assessment, in selected high-dose partial-body exposure cases, and (3) the potential for large numbers of casualties that exceed the requesting nation's capacity. Clearly the mutual assistance of several coordinated laboratories is required in such mass radiological casualty events to provide rapid assessment of large numbers of samples.

Patient Selection Criteria for Biological Dosimetry Testing

Victims of severe radiation overexposures are in critical need of confirmatory cytogenetic-triage dose assessment; they exhibit pronounced clinical symptoms during the initial or prodromal phase (*28, 29*) and would represent high-priority cases. A secondary priority for the BioDoseNet would be the large number of "concerned persons" who may need dose assessment by cytogenetic triage to provide initial confirmation that they have not been exposed to a life-threatening dose. BioDoseNet advocates the generically and internationally accepted medical diagnostic evidence-based process for patient selection and prioritization for dose assessment by biological dosimetry. This process used knowledge from the accident history, clinical signs and symptoms of the suspected exposed victim, physical measurements of radiation or radioactivity, and resource availability. The responsibility for patient selection for biological dosimetry testing is with the responding experts in the field; however, BioDoseNet may make recommendations. Responders should be informed about biological dosimetry, its role as well as its limitations. Responders need to be able to correctly collect and ship samples for dose assessment by BioDoseNet.

Cytogenetic Sample Collection Kit

Sample collection kits for dose assessment consist of materials to permit blood collection by venipuncture and shipment to the selected reference laboratory [see the Armed Forces Radiobiology Research Institute's (AFRRI) example in Fig. 2]. BioDoseNet recommends that a similar sample collection kit for small- and large-scale events be added to WHO's Radiological/Nuclear stockpile (*30*). A BioDoseNet

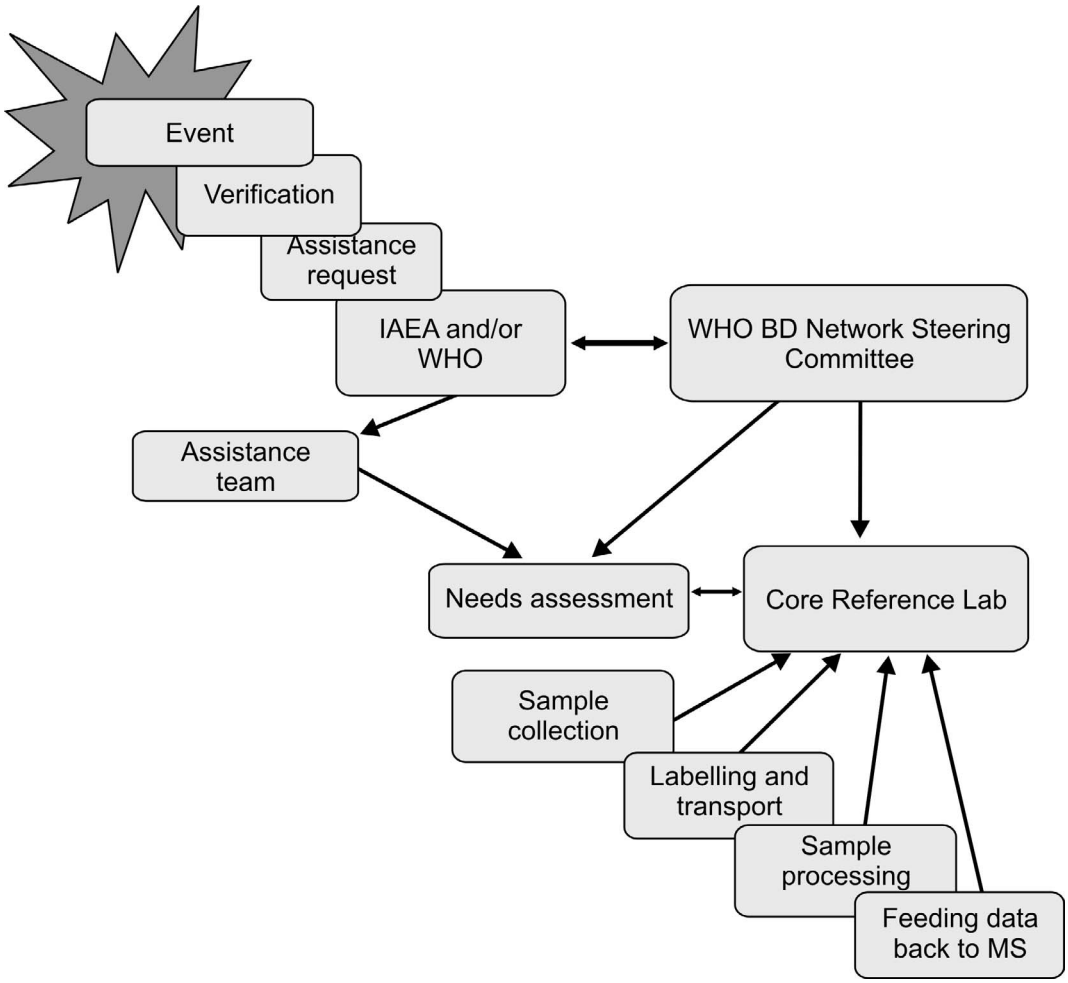


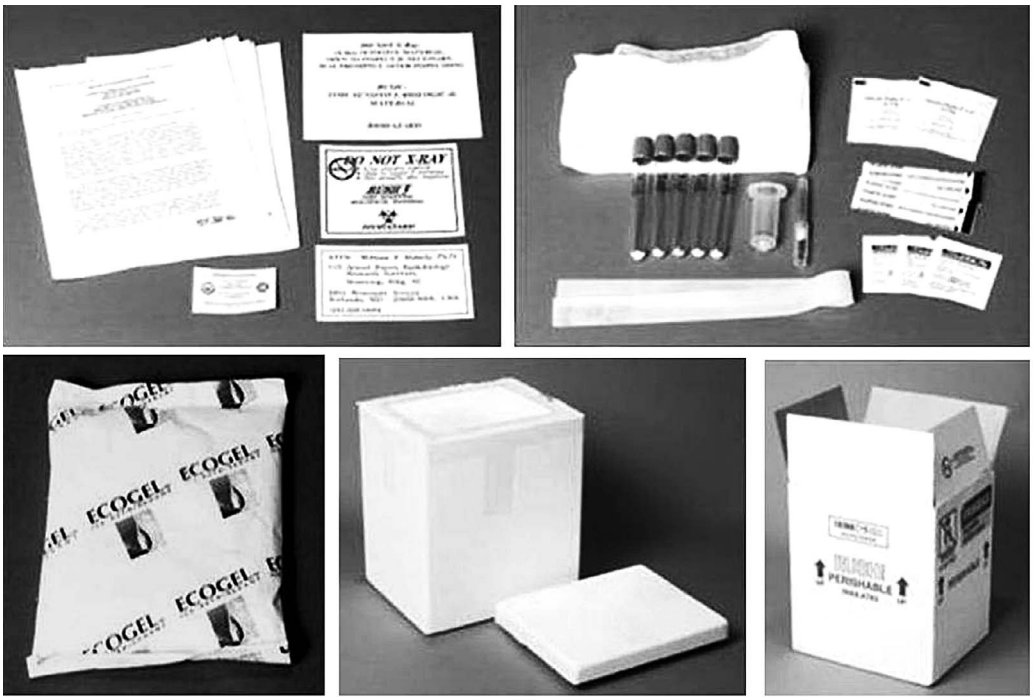
FIG. 1. Illustration of the potential process for use of the BioDoseLabNet in a radiation emergency.

steering committee will be charged to write consensus procedures for sample collection with clear guidance on sample labeling in the field with unique identifiers. The knowledge necessary to prioritize analysis of samples for dose assessment needs to be conveyed to BioDoseNet with links between individual samples and suspected radiological victims. A biodosimetry worksheet for dynamic recording of exposure and clinical data similar to that available on AFRRI's website (www.afrri.usuhs.mil) (*31*) will be developed and will accompany the sample collection kit or will be made available for downloading from the WHO's BioDoseNet website.

Sample Transportation

The expert panel recognized that sample transportation can be complex during radiological events; however, planning, advanced preparations and exercising for such events can significantly improve performance during real events. In an ideal situation, sample transportation will be in compliance with the UN sample shipment regulations (*32*); detailed information will be made available on WHO's network website. Of key importance is the intention to have a prearranged process for sample shipment between national customs and the BioDoseNet laboratory receiving the blood samples to avoid (1) potential delays in delivery due to weight or volume limitations or other causes, (2) radiation exposure of the sample from screening devices during transportation (a radiation detector can be included to monitor potential radiation exposures), and (3) extremes in temperatures (a temperature monitor could also be included to track the sample temperature during transportation) that could affect the cytogenetic bioassay results. BioDoseNet envisions that distribution of samples among the network laboratories can occur by at least three ways: (1) Samples can be shipped by the responders directly to different designated reference laboratories; in this case the reference laboratory has no responsibility for the shipment. (2) Samples and/or slides can be forwarded by the designated reference laboratories to affiliated or satellite laboratories; in this case, the reference laboratory is responsible for shipment. (3) Electronic images can be sent from the sample processing laboratory to several network partners for scoring.[4]

[4] Personal communication from Dr. Gordon K. Livingston (REAC/TS, Oak Ridge, TN).



1. Consent form & procedure for collecting blood
2. Swabs containing 70% alcohol
3. Tourniquet
4. One vacutainers sleeve and sterile needle
5. Five 8-ml sterile vacutainers containing lithium heparin
6. Band-aids
7. Coolant packs for return shipment
8. Protective packing materials
9. Address labels
10. Recyclable freight boxes with styrofoam insulation

FIG. 2. Illustration of component of AFRRI's cytogenetic biodosimetry blood sample collection and shipment kit.

This sample transportation process can be used both for emergencies and for intercomparison studies. Again, a BioDoseNet steering committee will be charged to write consensus procedures and guidelines for sample transportation.

Sample Coding and Prioritization

Sample coding for each reference laboratory in BioDoseLabNet will be performed consistent with standard protocols as defined by the relevant ISO standard (*24*). Reference laboratories may use their associated or satellite laboratories, which would use the same coding of their respective reference laboratory for communication purposes. Dynamic clinical feedback on suspected victims typically evolves during a radiological event. This and other knowledge contributing to an evidence-based selection and prioritization should be communicated to the designated core BioDoseNet laboratory and would be used to create a dynamic prioritization for sample analysis.

Output of Biological Dosimetry-Cytogenetic Triage Needed by a Physician

The output of biological dosimetry-cytogenetic triage for BioDoseNet is modeled from the scope of the relevant ISO standard in preparation to provide diagnostic information for early clinical treatment decisions.[2] Rapid and early dose assessments based on initial triage scoring of dicentrics in up to 50 metaphase spreads is provided in dose intervals (i.e., 0–1 Gy, 1–3.5 Gy, 3.5–5.0 Gy and >5 Gy). In addition, estimates of exposure distributions (i.e., partial-body non-homogeneous, whole-body homogeneous) are also provided. The reporting form will be in compliance with this new cytogenetic-triage ISO standard.

Laboratory Definitions

The expert panel agreed to adopt the laboratory definitions as used by the relevant ISO standards. In BioDoseNet, a reference laboratory with expertise in cytogenetic biodosimetry or alternative methodologies (e.g., radiobioassay, EPR) must be identified before the radiological emergency and must be in compliance with the relevant ISO standards and an established QC/QA system. WHO's cytogenetic BioDoseNet would be comprised of several reference laboratories, typically representing national expert cytogenetic biodosimetry laboratories (Fig. 3). The country requesting assistance from the network may request a specific reference laboratory, or alternatively WHO would create a BioDoseNet Steering Committee that at the time of the ra-

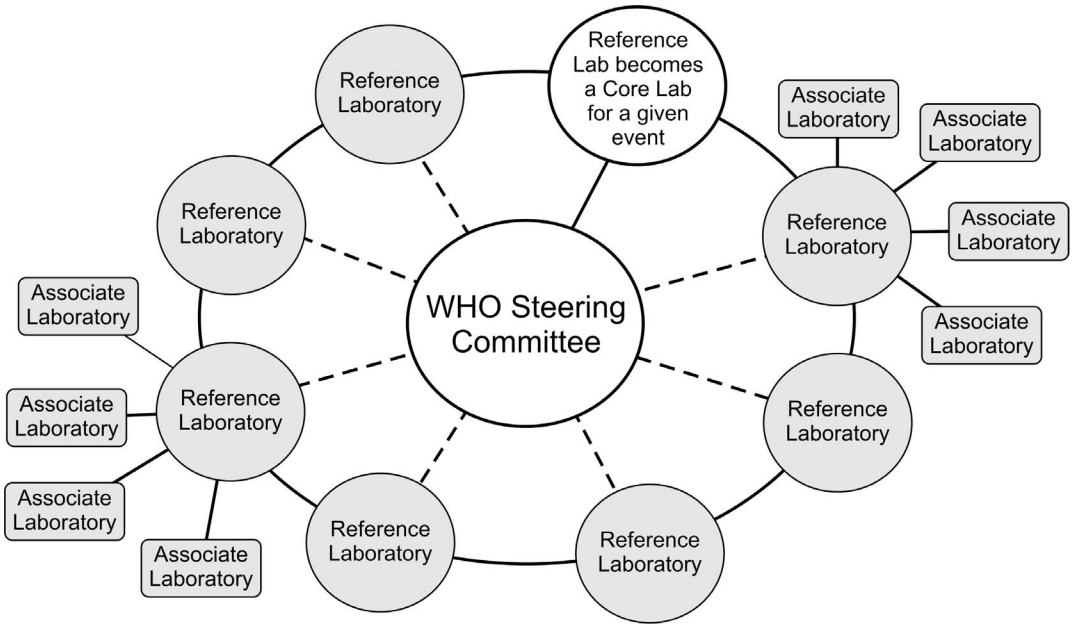


FIG. 3. WHO BioDoseNet structure, roles and functions of laboratories in case of emergency. Any Reference Laboratory may become a Core Laboratory in a given event, depending on geographical factor, scale of accident, etc. The WHO Steering Committee will assign a Reference Laboratory to take up the role to coordinate all reference laboratories for a given event. Reference Laboratories' efforts can be supplemented with contributions from their pre-established Associate Laboratories.

diological emergency would designate one of these reference laboratories, preferably located in the region of the incident, to be the event ''core'' reference laboratory to facilitate coordination of sample distribution, processing, analysis, collating of results from other reference and satellite laboratories, and interpretation and reporting of dose assessment by cytogenetics to the designated medical authorities of the requesting nation. An associate laboratory must be affiliated with a specific reference laboratory and must have been qualified previously to perform one or more specific tasks for the reference laboratory. The reference laboratory is responsible for their associate laboratories' performance.

Core Laboratory Tasks in Emergency

In BioDoseNet, a core reference laboratory is one of the reference laboratories that may be designated by the country in which the accident occurs or alternatively by WHO's Steering Committee upon activation of the network for an emergency radiological event response. Once activated by WHO, the core reference laboratory is required to provide 24-h/7-day response capability. The designated core reference laboratory will be responsible for receiving and coding samples as well as for coordination of outsourcing of samples to alternative reference laboratories in the BioDoseNet. The core reference laboratory will process samples and score chromosome aberrations along with other reference laboratories in BioDoseNet involved in the event response. The core reference laboratory will be responsible for receiving and tabulating exposure assessment on a case-by-case basis from all laboratories involved in the event, provide interpretation of results, and providing these results in a timely manner to the designated medical authorities of the requesting nation.

Reference Laboratory Tasks in ''Stand-by'' Time

Expert reference laboratories established by national authorities for dose assessment purposes are typically involved in a variety of activities to sustain proficiency and QC/QA in time windows when they are not engaged in an emergency response (i.e., quiet time). Reference laboratories in WHO's BioDoseNet would be expected to be similarly engaged. Examples of these activities include (1) establishing protocols and radiation calibration curves compliant with ISO standards; (2) evaluation of new diagnostic and analysis tools; (3) conducting intercomparison studies; (4) regularly testing communication channels; (5) participating in exercises (e.g., at least once every 2–3 years to hold all-network exercises with some 10 samples per laboratory; more frequently perform other smaller type of exercises and tests like desktop exercises, communication drills, national and regional exercises); each reference laboratory is responsible for single-laboratory exercise programs and staff qualifications; (6) providing biological training for laboratory personnel and contributing in training programs; and (7) auditing of network laboratory performance.

Candidate Reference Laboratories

The expert group at the WHO 1st consultation meeting provided WHO a potential list of laboratories that they rec-

ognized as candidate reference laboratories for performance of dose assessment by cytogenetics. These laboratories typically are established and funded by their nations as expert cytogenetic biodosimetry service laboratories with documented performance and experience in dose assessment by the metaphase spread-dicentric bioassay in radiological accidents.

Benefits of Network Membership

Requesting nations clearly would benefit from WHO's BioDoseNet responses; however, individual network laboratories also benefit from network membership and participation. Harmonization of protocols will lead to standardization and a greater ability to compare results among laboratories. Linking partners within regions and globally by action provide a surge response capability that would otherwise exceed an individual reference laboratory's response capability. BioDoseNet membership will facilitate access to (1) training programs, (2) mediation services, (3) standardized templates (memorandum of understanding or MOU, material transfer agreements or MTA, informed consent forms, etc.), (4) reagent and consumables sharing, (5) multicenter study templates, and (6) international intercomparison studies. It is expected that membership will also foster collaboration among members in applied research areas and career enhancements for individual scientists involved in BioDoseNet activities. Finally, a reference laboratory participation in BioDoseNet would result in increased visibility and recognition, and it could also facilitate the laboratory's ability to secure funds to sustain the laboratory's performance.

Framework for the Network Membership

The BioDoseNet is coordinated by WHO with support of the Steering Committee. Templates for MOUs, other agreement documents and letters will be made available by WHO. An MOU requires permission/approval of the head of the participating reference and/or satellite laboratory's Institution and expires every 4 years. Neither being a formal member of the WHO REMPAN network nor registration with IAEA's RANET is required for WHO's BioDoseNet membership. Participation in both UN agencies' networks (REMPAN, RANET) is not mutually exclusive and is encouraged.

BioDoseNet Terms of Reference

The expert group at the WHO 1st consultation meeting discussed the scope of the BioDoseNet Terms of Reference (ToR). Major features for the ToR should include: (1) commitment of participating network laboratories to provide services in an emergency; (2) network laboratories perform emergency biological dosimetry assessment of exposure according to standard protocols consistent with the relevant ISO standard and approved by the steering committee; (3) a consensus and common form of information sharing among the network will be identified (e.g., secured website as an interactive resource center, reports, meetings, etc.); (4) appropriately collated and tabulated data will be shared/discussed within the network; (5) reporting of data is done only through the WHO-designated core reference laboratory using a standard template; (6) no public release of information by network members; requests for information are to be redirected to the core reference laboratory during a radiological event; (7) all laboratories are required to inform the WHO BioDoseNet immediately about any changes in network laboratory's contact information (names, positions, phone and fax numbers, and e-mail addresses); (9) steering committee will develop audit criteria and protocols for undertaking periodic peer reviews of network laboratories and of others wishing to join.

Exercises

An active exercise program is essential to improving standard operating procedures (SOP) and identifying weak points of a network or individual laboratory response. The BioDoseNet will run intercomparison exercises (i.e., blood sample processing, and/or slide scoring and data analysis), coordinated by the Steering Committee, at least once a year. In addition, intracomparison exercises should be run in individual reference laboratories as part of their QC/QA programs. An emergency service response and intercomparison exercise for all BioDoseNet laboratories will occur once every 2 to 3 years with national exercises performed as required in each nation. Table-top simulation exercises will also be considered as an option to exercise communication and reporting responses.

Education and Training

Education and training of members are considered essential for the sustainment and performance of the BioDoseNet. Reference laboratories should report regularly to BioDoseNet about their existing laboratory training programs, including laboratory technician training on the job for new recruits and radiation cytogenetic biodosimetry specialist training. Education and training provided by network reference laboratories support the entry of a new laboratory into BioDoseNet. Reference laboratories are expected to provide technical contributions to the curriculum of training for medical response personnel. Peer learning through workshops, seminars and scientific meetings is encouraged.

Auditing and Recognition

Laboratories in WHO's BioDoseNet are not required to have ISO certification by the appropriate standard, but having it is an advantage. Strict compliance with protocols and QC/QA procedures as defined by the relevant ISO standard are expected. Laboratories are also encouraged to obtain national certification as applicable.

WHO's BioDoseNet membership certificate will be

awarded to reference laboratories after external evaluation by an ad hoc committee appointed by WHO in consultation with the BioDoseNet Steering Committee. WHO will also recognize the network laboratories fulfilling a performance audit using criteria defined by the Steering Committee with the ''WHO Laboratory of Excellence'' award. In addition, WHO will establish and recognize members of the roster of experts derived from the reference laboratory members.

Consumables Sharing Process

A catalogue of consumables supporting use of the cytogenetic biodosimetry assays is available in the recent IAEA manual (*22*). Laboratories in less-developed nations often experience supply shortages that may represent a significant constraint during an emergency radiological response involving mass casualties. WHO's BioDoseNet anticipates this problem and plans to work toward several possible solutions, including (1) asking network members to pledge to share their inventory resources, (2) asking manufacturers to pledge to donate key limiting consumables, and (3) exploring access to WHO's stockpile as an option. A subcommittee of BioDoseNet will be established to develop a concept of operations for reagent sharing process.

Recommendations

The 1st consultation expert group discussed at length the scope of recommendations to WHO with respect to the development of BioDoseNet. Briefly, these included (1) facilitating the establishment of BioDoseNet through the development of ToR, SOPs and model MOUs, (2) overseeing and coordinating operations during ''quiet times'', (3) in a radiological emergency, in cooperation with IAEA, facilitating provision of biodosimetry assistance, (4) supporting intercomparison studies and exercise programs within the BioDoseNet laboratories, (5) setting up a stockpile of consumables, including sample collection and shipping kits, (6) supporting and establishing a knowledge-sharing platform for the network (secure internet server, scientific meetings, reports, etc.), and (7) advocating for strengthening national biological dosimetry capabilities as a part of IHR implementation of national programs.

The expert group also made recommendations regarding the features and functions of WHO's BioDoseNet. This cytogenetic network should adopt the ISO emergency cytogenetic triage procedures. It should also contribute to facilitating harmonization of QA criteria and programs. BioDoseNet can endorse an existing worksheet or develop a consensus biological dosimetry worksheet for information collection to facilitate better interaction between responders/clinicians and biological dosimetry laboratories. Qualified reference laboratories should be identified and recruited to participate in the network. The design, establishment and coordination of an external peer-review mechanism among the laboratories in the network will contribute significantly to the sustainment and overall effective performance of individual laboratories and the network in general. Finally, network members are especially qualified to identify gaps and research needs and provide a platform for information exchange to share results from the evaluation of new diagnostic tools. For example, in a recent interlaboratory comparison study involving five laboratories in four countries, it was shown that scoring electronic metaphase cell images on the computer monitor produced radiation dose estimates equivalent to those obtained by conventional scoring under the microscope (*33*). This result demonstrates that a strategy of scoring chromosome images using multiple websites would allow many analysts in multiple time zones to reduce the turnaround time for test results.[4]

WHO'S NEXT STEPS IN THE DEVELOPMENT OF A GLOBAL BIODOSIMETRY LABORATORY NETWORK FOR RADIATION EMERGENCIES

The WHO Secretariat circulated the meeting report/minutes for comments that formed the basis of this report and a subsequent list of participants for a meeting at WHO headquarters in Geneva, Switzerland. A model MOU will be shared with the expert group. Individual modified MOUs will be exchanged with laboratories applying for BioDoseNet membership. Laboratories meeting the criteria for a cytogenetic ''Reference Laboratory'' will be identified and recruited to apply for BioDoseNet membership. A Steering Committee will be set up and its role defined. This committee will consist of representatives of reference laboratories and will meet regularly. Working Groups will be set up with topic specific focuses (automation, harmonization, new tools evaluation, peer-review evaluations, etc.).

WHO will compile a BioDoseNet ''Yellow Pages'' directory listing worldwide expertise, according to the WHO GlaDNet model. WHO uses color in these directories to provide a visual cue to help explain the three pillars making up a network and helping networks sustainability (Fig. 4): The yellow color is a directory and the blue color indicates the benefits to participants. The combination of yellow and blue forms green, which is used when partners from the ''yellow side'' (directory) join in through the ''blue side'' benefits to work on joint projects and to act together in emergencies.

WHO plans to follow the 1st consultation meeting with the first coordination meeting in association with another international biodosimetry scientific conference. A secure website for WHO's BioDoseNet will be developed through one of the participating laboratories' institutional portals. All members were encouraged to send citations of relevant publications to Dr. Voisin (ISPN) for posting on this website. Based on the feedback from the initial WHO survey of biodosimetry capability, a modified and improved questionnaire will be developed, and another survey will be carried out in due time.

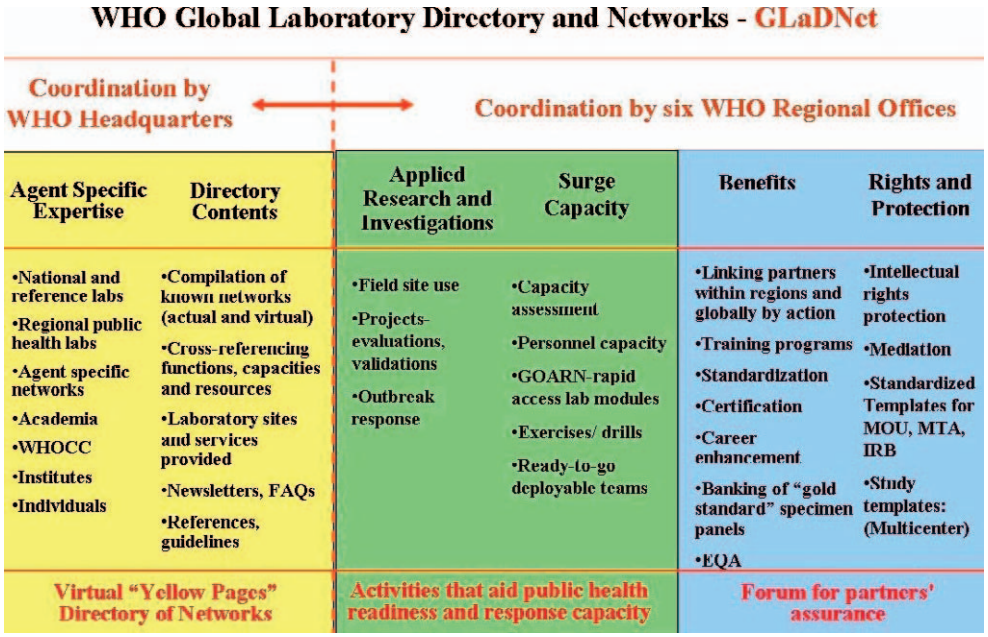


FIG. 4. Illustration of WHO's GLaDNet color-coded ''Yellow Page'' directory.

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REFERENCES

1. A. J. Gonzalez, An international perspective on radiological threats and the need for retrospective biological dosimetry of acute radiation overexposures. *Radiat. Meas.* **42**, 1053–1062 (2007).
2. W. C. Conklin and P. L. Liotta, Radiological threat assessment and the Federal Response Plan—a gap analysis. *Health Phys.* **89**, 457–470 (2005).
3. W. F. Blakely, C. A. Salter and P. G. S. Prasanna, Early-response biological dosimetry—recommended countermeasure enhancements for mass-casualty radiological incidents and terrorism. *Health Phys.* **89**, 494–504 (2005).
4. IAEA, *Generic Procedures for Medical Response during a Nuclear or Radiological Emergency.* EPR-MEDICAL, IAEA, Vienna, 2005.
5. G. A. Alexander, H. M. Swartz, S. A. Amundson, W. F. Blakely, B. Buddemeier, B. Gallez, N. Dainiak, R. E. Goans, R. B. Hayes and R. Wilkins, BiodosEPR-2006 Meeting: Acute dosimetry consensus committee recommendations on biodosimetry applications in events involving uses of radiation by terrorists and radiation accidents. *Radiat. Meas.* **42**, 972–996 (2007).
6. L. Lebaron-Jacobs, R. Fottorino, F. Barbry, P. Berard, F. Briot, P. Boisson, D. Cavadore, C. Challeton-de Vathaire, S. Distinguin and A. Miele, Dosimetric management during a criticality accident. *Nucl. Technol.* **161**, 27–34 (2008).
7. D. C. Lloyd, A. A. Edwards, J. E. Moquet and Y. C. Guerrero-Carbajal, The role of cytogenetics in early triage of radiation casualties. *Appl. Radiat. Isot.* **52**, 1107–1112 (2000).
8. I. Turai, B. Günalp, G. Köksal, F. Pala, F. Darroudi, D. Lloyd, A. Edwards, I. Sorokine-Durm and P. Voisin, Clinical and cytogenetic dose assessment for the Istanbul accident patients. In *The Medical Basis for Radiation-Accident Preparedness* (R. C. Ricks, M. E. Berger and F. M. O'Hara, Jr., Eds.), pp. 347–348. Parthenon, Pearl River, NY, 2002.
9. M. A. Yoshida, I. Hayata, H. Tateno, K. Tanaka, S. Sonta, S. Kodama, Y. Kodama and M. S. Sasaki, The Chromosome Network for Biodosimetry in Japan. *Radiat. Meas.* **42**, 1125–1127 (2007).
10. S. M. Miller, C. L. Ferrarotto, S. Vlahovich, R. C. Wilkins, D. R. Boreham and J. A. Dolling, Canadian Cytogenetic Emergency Network (CEN) for biological dosimetry following radiological/nuclear accidents. *Int. J. Radiat. Biol.* **83**, 471–477 (2007).
11. D. T. Wilkinson, T. Segura, L. Prud'homme-Lalonde, D. Mullins, S. Lachapelle, S. Qutob, E. Thorleifson, R. Wilkins, D. Morrison and D. Boreham, Canadian biodosimetry capacity for response to radiation emergencies. *Radiat. Meas.* **42**, 1128–1132 (2007).
12. L. Roy, V. Buard, M. Delbos, V. Durand, N. Paillole, E. Grégoire and P. Voisin, International intercomparison for criticality dosimetry: the case of biological dosimetry. *Radiat. Prot. Dosimetry* **110**, 471–476 (2004).
13. C. Lindholm, H. Romm, G. Stephan, E. Schmid, J. Moquet and A. Edwards, Intercomparison of translocation and dicentric frequencies between laboratories in a follow-up of the radiological accident in Estonia. *Int. J. Radiat. Biol.* **78**, 883–890 (2002).
14. O. F. Garcia, A. T. Ramalho, M. Di Giorgio, S. S. Mir, M. E. Espinoza, J. Manzano, N. Nasazzi and I. López, Intercomparison in cytogenetic dosimetry among five laboratories from Latin America. *Mutat. Res.* **327**, 33–39 (1995).
15. IAEA, *Convention on Early Notification of a Nuclear Accident.* INFCIRC/335, IAEA, Vienna, 1986. [Available online at www.iaea.org/Publications/Documents/Infcircs/Others/infcirc335.shtml; last accessed June 2008]
16. IAEA, *Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency.* INFCIRC/336, IAEA, Vienna, 1986. [Available online at www.iaea.org/Publications/Documents/Infcircs/Others/infcirc336.shtml; last accessed June 2008]
17. WHO, *Revision of the International Health Regulations.* WHO, Geneva, 2005. [Available online at www.who.int/csr/ihr/WHA58-en.pdf; last accessed June 2008]
18. WHO, *The World Health Report 2007—A Safer Future, Global Public Health Security in the 21st Century.* WHO, Geneva, 2007.
19. WHO, *Biological, Chemical and Radionuclear (BCR) Emergency*

Preparedness Strategies, Report of an Intercountry Meeting, Bangkok, Thailand, 17–20 March 2003. WHO, Geneva, 2003.

20. IAEA, *IAEA Response Assistance Network—Incident and Emergency Centre.* IAEA, Vienna, 2006.

21. IAEA, *RANET Assistance Action Plan—Arrangements for Providing International Assistance and Sample of Assistance Action Plan.* IAEA, Vienna, 2006.

22. IAEA, *Cytogenetic Analysis for Radiation Dose Assessment: A Manual.* Technical Report Series No. 405, IAEA, Vienna, 2001.

23. IAEA, *RANET Registry—Instructions and Application Form for Registration of National Assistance Capabilities.* IAEA, Vienna, 2006.

24. ISO, *Radiation Protection—Performance Criteria for Service Laboratories Performing Biological Dosimetry by Cytogenetics*. ISO 19238, ISO, Geneva, 2004.

25. P. Voisin, F. Barquinero, B. Blakely, C. Lindholm, D. Lloyd, D.C. Luccioni, S. Miller, F. Palitti, P. G. Prasanna and A. Wojcik, Towards a standardization of biological dosimetry by cytogenetics. *Cell Mol. Biol.* **48**, 501–504 (2002).

26. IAEA, *Joint Radiation Emergency Management Plan of the International Organizations—Emergency Preparedness and Response.* EPR-JPLAN 2006, IAEA, Vienna, 2007. [Available online at www-pub.iaea.org/MTCD/publications/PDF/JPLAN2006_web.pdf; last accessed June 2008]

27. ICAO, *Technical Instructions for the Safe Transport of Dangerous Goods by Air*, 2007–2008 edition. ICAO, Montréal, 2007.

28. T. M. Fliedner, I. Friesecke and K. Beyrer, *Medical Management of Radiation Accidents. Manual on the Acute Radiation Syndrome.* The British Institute of Radiology, London, 2001.

29. N. C. Gorin, T. M. Fliedner, P. Gourmelon, A. Ganser, V. Meineke, B. Sirohi, R. Powles and J. Apperley, Consensus conference on European preparedness for haematological and other medical management of mass radiation accidents. *Ann. Hematol.* **85**, 671–679 (2006).

30. M. Perez and Z. Carr, Eds., *Development of Stockpiles for Radiation Emergencies—Report of the Radio-Nuclear Working Group.* WHO, Geneva, 2007. [Available online at http://www.who.int/ionizing_radiation/a_e/emergencies/WHO_Stockpile_Report_2007_v2.pdf; last accessed June 2008]

31. AFRRI, Biodosimetry Worksheet—Medical Record of Radiation Dose, Contamination, and Acute Radiation Sickness Response AFRRI form 331, Armed Forces Radiobiology Research Institute, Bethesda, MD, 12/2007). [Available online at www.afrri.usuhs.mil/; last accessed March 3, 2008]

32. WHO, *Guidance on Regulations for the Transport of Infectious Substances 2007–2008.* WHO, Geneva, 2007. [Available online at www.who.int/csr/resources/publications/biosafety/WHO_CDS_EPR_2007_2.pdf; last accessed June 2008]

33. R. C. Wilkins, H. Romm, T. C. Kao, A. A. Awa, M. A. Yoshida, G. K. Livingston, M. S. Jenkins, U. Oestreicher, T. C. Pellmar and P. G. S. Prasanna, Interlaboratory comparison of the dicentric chromosome assay for radiation biodosimetry in mass casualty events. *Radiat. Res.* **169**, 551–560 (2008).