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GHSI Emergency Radionuclide Bioassay Laboratory Network - Summary of a Recent Exercise

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Abstract

The Global Health Security Initiative (GHSI) established a laboratory network within the GHSI community to develop collective surge capacity for radionuclide bioassay in response to a radiological or nuclear emergency. A recent exercise was conducted to test the participating laboratories for their capabilities in screening and *in vitro* assay of biological samples, performing internal dose assessment, and providing advice on medical intervention, if necessary, using a urine sample spiked with a single radionuclide, ^{241}Am. Laboratories were required to submit their reports according to the exercise schedule and using pre-formatted templates. Generally, the participating laboratories were found to be capable with respect to rapidly screening samples for radionuclide contamination, measuring the radionuclide in the samples, assessing the intake and radiation dose, and providing advice on medical intervention. However, gaps in bioassay measurement and dose assessment have been identified. The network may take steps to ensure that procedures and practices within this network be harmonized and a follow-up exercise be organized on a larger scale, with potential participation of laboratories from the networks coordinated by the International Atomic Energy Agency (IAEA) and the World Health Organization (WHO).

Keywords

nuclear emergency; radiological emergency; radioactive contamination; radionuclide bioassay; internal dosimetry; medical countermeasures

Introduction

The Global Health Security Initiative (GHSI) is an informal network of countries formed in 2001 to ensure health-sector exchange and coordination of practices in confronting risks to global health posed by chemical, biological and radio-nuclear threats, as well as by pandemic influenza[1]. The member countries/organizations of the GHSI are Canada, France, Germany, Italy, Japan, Mexico, the United Kingdom, the United States and the European Commission. The World Health Organization (WHO) is a technical advisor. As part of the GHSI partnership, an annual meeting of Health Ministers is held to foster dialogue on topical policy issues and promote collaboration. Other initiatives involving senior health officials as well as policy, technical and scientific personnel take place on a regular basis, focused on risk management; communications; chemical events; radio-nuclear threats; pandemic influenza; and global laboratory cooperation.

The GHSI Rad-Nuc Threats Working Group (RNWG) was created to facilitate sharing and collaboration on policies and capability development to enhance public health preparedness and response to radiological and nuclear threats. As a result of discussions and consultations, the RNWG decided to establish a laboratory network to improve our collective surge capacity for radionuclide bioassay within the GHSI community. Within this network, laboratories can share their expertise through training activities, exercise their preparedness through intercomparisons, develop new capabilities through collaborative R&D, and assist in bioassay analysis when multiple laboratories are required following an emergency.

In 2013, the network laboratories were surveyed on their current capabilities in emergency radionuclide bioassay and the technological and operational gaps they had identified in this area. Based on the survey results, an intercomparison exercise was organized in late 2014 to test the participating laboratories for their response capabilities in screening and *in vitro* assay of biological samples, performing internal dose assessment, and providing advice on medical intervention when necessary. Eight laboratories from seven countries (Canada, France, Germany, Italy, Japan, UK and USA) participated. In addition to testing, the exercise also provided an opportunity for countries to share and compare their policies and practices for assessing internal contamination, and for the network to identify common technological or operational priorities for future collaborative work.

Methods and Materials

Exercise Design

The exercise was designed to be an intercomparison of emergency capabilities for screening, bioassay, dose assessment and medical advice. While it was somewhat realistic, the scenario was deliberately designed to be manageable by most of the participating laboratories in terms of the required sensitivity for the measurement as well as resource demands (i.e. laboratories were not asked to work overtime).

Based on the consensus of the RNWG, it was decided to exercise the participating laboratories with a urine sample spiked with a single radionuclide that has been identified to be high-risk[2–4]. The following scenario and parameters were chosen or considered:

- Acute intake of ^{241}Am (1.50 MBq) via ingestion by a man with physical characteristics similar to a “Reference Man” described by the International Commission on Radiological Protection (ICRP)[5];
- Urine collection started 24 hours after the suspected intake and lasted for 24 hours. One 100 mL urine sample from this collection would be sent to each laboratory (to mimic a spot sample).
- Laboratories were required to report their results at short, pre-determined intervals in order to simulate an emergency response.
- The level of contamination in the scenario was chosen to accommodate the bioassay capabilities previously demonstrated by some of the participating laboratories[6], as well as to approach the dose thresholds for medical intervention recommended by national or international authorities[4, 7].

Sample Preparation and Distribution

Based on the above design, a calculation using IMBA Plus® (version 4.0.36, provided by ACJ & Associates, Inc., 129 Patton Street, Richland, WA, USA) determined that the spiking level for ^{241}Am in urine should be 4.3 Bq/L. Blank urine was collected from one healthy unexposed individual, preserved and spiked with ^{241}Am (RM S2/22/10, Amersham, Buckinghamshire, UK) following the standard procedure of the National Calibration and Reference Center for Bioassay and *In Vivo* Monitoring, Health Canada, which is certified to the International Organization for Standardization (ISO) 9001:2008 standard[8]. The spiked urine sample was then divided into 100 mL aliquots; one was sent to each participating laboratory by a commercial carrier.

Scheduled Reports

Table 1a and Table 1b summarize the messages sent to the participating laboratories and the questions to be addressed in the scheduled reports. “Message No 1” was sent out soon after the urine samples were picked up by the commercial carrier along with questions for the laboratories to address when submitting the “6-Hour Report” and the “72-Hour Report”. This message was sent by email to each laboratory individually with a designated confidential lab code provided. Considering the time required for sample delivery and potential delay over the weekend, laboratories were advised to start the exercise at a convenient time; they were not required to start the exercise at a specific time or immediately after receiving the samples. The “6-Hour Report” and the “72-Hour Report” were required to be submitted no later than 6 hours and 72 hours, respectively, once the exercise started.

“Message No 2” was sent by email to each laboratory soon after its “72-Hour Report” was received along with questions for the laboratories to address when submitting the “96-Hour Report”. This message provided essential information for the assessment of intake and radiation dose. The “96-Hour Report” was due in 24 hours after receiving “Message No 2”.

Results and Discussions

Response to Reporting Schedule

Overall, participating laboratories submitted most of the required reports as scheduled although the starting time varied from lab to lab due to the difference in the time required for sample delivery and customs clearance, time zone issues, and/or a schedule conflict with other work commitments. All laboratories submitted the required “6-Hour Report” on time indicating that the laboratories are capable of screening samples in a short time period. Three laboratories delayed the submission of the “72-Hour Report” due to either the bioassay method(s) requiring more time or the bioassay work was paused over the weekend. One laboratory slightly delayed the submission of its “96-Hour Report” due to issues related to weekend communication. Lab 003 exited the exercise after submitting its “72-Hour Report”.

Results for “6-Hour Report”

All participating laboratories reported that the sample was “radioactive” and provided a brief description for the techniques used for sample screening (Table 2). Four screening methods/techniques were used by the laboratories, with gamma spectrometry and liquid scintillation counting being the most widely employed. Within a short counting period (2–3 hours), gamma spectrometry would show a small but visible peak at 60 keV which indicates the possible presence of ^{241}Am in the sample. Liquid scintillation counting using a small fraction of the sample, with or without alpha/beta discrimination, would indicate above-background radioactivity in the sample and the presence of alpha emitter(s). Gross alpha/beta analysis is a very popular technique for sample screening, however, in this exercise only Lab 007 used it. Interestingly, inductively coupled plasma mass spectrometry (ICP-MS) was also used for screening (lab 002 and Lab 005). ICP-MS measurement does not tell if a detected mass is for a radionuclide, but it does indicate the potential presence of the radionuclide with such a mass. Lab 003 used a whole body counter to screen the sample, as the above mentioned four techniques were not available.

Results for “72-Hour Report”

For the bioassay measurement, diverse methods/techniques for sample treatment, separation, measurement, QA/QC, and estimation of uncertainties were used by the participating laboratories (Table 3). Alpha spectrometry was used by four laboratories (Lab 004, Lab 005, Lab 006, Lab 007) for the measurement of ^{241}Am in the urine samples following separation using chromatographic methods (solid phase extraction or anion exchange) and electro-deposition. Lab 002 also separated ^{241}Am from the sample using a chromatographic method but measured it by ICP-MS. Lab 008 and Lab 009 quantified ^{241}Am in the sample using gross alpha liquid scintillation counting and gamma spectrometry, with a counting time of 17 hours and 68 hours, respectively. The advantages and disadvantages of different methods/techniques for emergency bioassay have been discussed previously[6]; however, it is worthwhile to note that bioassay methods that deliver results in hours rather than days are always desired for emergency population monitoring and management as early medical interventions, if indicated necessary by bioassay results, help reduce radiation induced health risks more effectively.

Table 4 summarizes the bioassay results reported by the participating laboratories with uncertainties at 95% confidence interval (CI). As mentioned above, the spiked testing level for the ^{241}Am is 4.3 Bq/L. The calculated bias from the reported results in Table 4 falls between −12% and +19%, which is well within the acceptable range of −25% to +50% recommended by ISO 28218[10], an international standard developed for occupational bioassay. Currently, there is no international standard for emergency bioassay available. Lab 005 and Lab 007 reported the measurement results for other radionuclides although only ^{241}Am was spiked in the sample. These results indicate potential contamination from impurities in the tracers and chemicals used by the laboratories, or more possibly interferences to the measurements from background radiation depending on the techniques employed. Post-exercise discussion revealed that the reported ^{241}Pu signal by Lab 007 was actually caused by the presence of ^{40}K in the urine sample.

Results for “96-Hour Report”

Table 5 summarizes the assumptions, methods, and tools used by each laboratory when performing the intake and dose assessment. All laboratories inferred from “Message No 2” that the ICRP “Reference Man” model[5] could be used for intake and dose assessment, while some of the laboratories also recognized the limitation of using it. ICRP biokinetic and dosimetric models were used by all laboratories, in the form of national or international guidelines or as computerized tools (IMBA, AIDE, MONDAL, DCAL). Some laboratories used multiple tools to verify the assessment which is a very good practice.

Table 6 presents the reported intake and the 50y committed effective dose (CED) from each laboratory. As mentioned above, the exercise was designed starting with an acute intake of 1.50 MBq ^{241}Am through food ingestion. The calculated 50y CED for a “reference man” is 306 mSv. Table 6 shows that for all but one laboratory, the reported intake of ^{241}Am and the resulting committed effective dose are very close to 1.5 MBq and 306 mSv, respectively, with a bias no more than ±20%. Although the bioassay result reported by Lab 005 (Table 4) is very close to the testing level, the reported intake and dose values are substantially different than the expected values. Post-exercise discussion revealed that this was due to a mistake regarding the date the urine sample was collected. The results for intake and committed effective dose obtained from re-calculation (not shown in this paper) are very comparable to those submitted by other laboratories. Lab 005 and Lab 007 also reported the calculated intake and dose for radionuclides other than ^{241}Am. As discussed above, these are the results of tracer impurities, contamination, or background interference.

Table 7 presents the medical advices provided by the participating laboratories. All recommended treatment (immediate or not) with diethylene triamine penta acetate (DTPA) (with or without specified dosage) in reference to a dose threshold recommended by one or more national or international guidance documents. The role of qualified physicians and other factors were also identified by some laboratories as important considerations when a decision on treatment needs to be made. Some laboratories mentioned the need for further monitoring to evaluate the treatment efficacy. Note that some guidance documents recommend the use of a dose threshold of 250 mSv for treatment[4], while others recommend the use of 200 mSv[7].

Conclusion

Overall, this mini-exercise demonstrated that the participating laboratories are capable of rapidly screening bioassay samples for radionuclide contamination, measuring the radionuclide in the samples, assessing the intake and radiation dose, and providing advice on medical intervention. However, in some areas, improvements are needed. For example, some methods used in the exercise required more time than is ideal for emergency bioassay, as demonstrated by the delay in submitting the "72-Hour Report" by three laboratories. Rapid bioassay methods are very important for timely delivery of results following an emergency.

The RNWG may consider organizing a technical workshop to facilitate exchange and learning in the GHSI community, arrange inter-laboratory hands-on training among network laboratories, and/or organize another exercise involving a multiple radionuclides scenario. In addition, to ensure the success of this laboratory network, the RNWG may consider developing and formalizing emergency response plans and protocols for the activation, coordination, sample shipment, and use of this laboratory network. These plans/protocols would supplement the IAEA RANET (Response and Assistance Network)[15] and the WHO REMPAN (Radiation Emergency Medical Preparedness and Assistance Network)[16], and need to be integrated into national emergency preparedness and response plans. Collaborations between this GHSI laboratory network and the RANET and REMPAN networks may be considered in the future.

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Table 1

a: Messages sent to the participating laboratories	
Message No 1 “A urine sample has been shipped to your lab for screening and bioassay of a radionuclide in it. Once you receive the sample, you may start working at a time convenient to you.” (sent soon after samples were picked up by the commercial carrier)	Message No 2 “The urine sample (100 mL) you received is from a man (70–80 kg, 170–180 cm) of mid-twenties who was suspected to have had a single intake of the radionuclide through food consumption. Urine collection from this person started 24 hours after the suspected intake and lasted for 24 hours. The sample you received is a fraction of this 24-hour urine collection.” (sent immediately after receiving the “72-Hour Report”)

b: Questions for participating laboratories to address when submitting their reports		
6-Hour Report	**72-Hour Report**	**96-Hour Report**
When did you start? Is the sample radioactive? How did you know? (<100 words)	Which radionuclide is in the sample? What is the activity of this radionuclide in the sample? and the uncertainty associated with the activity at 95% CI? How the analysis was conducted (method and procedure, method for estimating uncertainty)? (<200 words)	What is the intake activity? (Bq) What is the projected 50y committed effective dose to the person from this intake? (mSv) Which methods/tools did you use when conducting intake and dose assessment? (<100 words) Would you recommend any medical intervention to this person? What intervention? Which guideline did you follow when you make the recommendation? (<200 words)

Table 2

Methods/techniques used for sample screening in the participating laboratories

Lab Code	Screening Techniques
002	Gamma spectrometry (HPGe) showed a small peak of 60 keV; Liquid scintillation counting for gross alpha showed a result slightly above the background; ICP-MS screening showed the possible presence of ^{241}Am
003	Gamma emitter(s) indicated using a whole body counter; No alpha emitters indicated because of small volume of sample
004	Gamma spectrometry indicated the suspected presence of ^{241}Am; Liquid scintillation counting for gross alpha/beta confirmed the presence of alpha emitter(s)
005	Gamma spectrometry (HPGe) found several small peaks around 59 keV, 63 keV and 92 keV with poor counting statistics; ICP-MS analysis found a significant amount of an element with a mass of 88
006	Gamma spectrometry indicated the presence of ^{241}Am; Liquid scintillation counting for gross alpha/beta measurement with 1 mL sample showed results <detection limit
007	Gamma spectrometry indicated the presence of ^{241}Am; Gross alpha/beta analysis (using 20 mL of the sample) gave results of 4.2 ± 0.4 and 28.5 ± 3.4 Bq/L for alpha and beta, respectively. The beta spectrum suggests the presence of ^{90}Sr/^{90}Y
008	Gamma spectrometry on the sample (3 hours counting) showed a peak at 59.5 keV, characteristic of ^{241}Am; Liquid scintillation counting for gross alpha/beta measurement with 5 mL sample (2 hour counting) indicated the presence of alpha emitter(s) but not beta emitter(s)
009	Gamma spectrometry; Liquid scintillation with alpha/beta discrimination

Table 3

Methods/techniques used for bioassay in the participating laboratories

Lab Code	Bioassay Methods
002	Solid phase extraction separation using DGA column (Eichrom®); Measurement using HR-ICP-MS (Thermo Element XR); QA/QC: tracer application (^{243}Am), creatinine correction, method validation using NIST traceable QC materials.
003	Failed. Activity is too low to be measured by using a whole body counter
004	Sample mineralization using nitric acid and H_2O_2; Anion exchange column separation (Dowex 1×8 Cl form) and solid phase extraction (DGA); Electro-deposition of Am and Pu on stainless steel discs; Measurement using alpha spectrometry; QA/QC: tracer application (^{243}Am and ^{242}Pu).
005	Sample mineralization using nitric acid; Anion exchange column separation (Dowex 1×8 Cl form); Electro-deposition of Am on a counting disk; Measurement using alpha spectrometry; QA/QC: tracer application (^{243}Am, ^{232}U, ^{242}Pu),
006	Sample mineralization using nitric acid and H_2O_2; Solid phase extraction separation using TRU column (Eichrom®); Electro-deposition of Am on a counting disk; Measurement using alpha spectrometry; QA/QC: tracer application (^{243}Am)
007	Measurement of ^{241}Am and ^{239}Pu using alpha spectrometry following ion exchange separation and electro-deposition; Measurement of ^{90}Sr using liquid scintillation counting following phosphate isolation and extraction chromatography; Measurement of ^{241}Pu (suspected) using gross beta liquid scintillation counting
008	Measurement of a sub-sample (5 mL) using gross alpha liquid scintillation counting (17 hours); QA/QC: A urine sample from a healthy donor was counted similarly for blank correction.
009	Measurement using gamma spectrometry (HPGe, 68 hours counting); GUM[9] for uncertainty estimation

Table 4

Bioassay results reported by the participating laboratories

Lab Code	Bioassay Results at 95% CI (Bq/L)
002	^{241}Am: 3.8 ± 0.41
003	-
004	^{241}Am: 4.12 ± 0.44
005	^{241}Am: 4.1 ± 0.45; ^{242}Cm: 0.13 ± 0.04
006	^{241}Am: 4.4 ± 0.7
007	^{241}Am: 4.1 ± 0.5; ^{239}Pu: 0.1 ± 0.05; ^{90}Sr: 2.2 ± 0.4; ^{241}Pu: 26 ± 5
008	^{241}Am: 4.2 ± 0.2
009	^{241}Am: 5.1 ± 1.4

Table 5

Intake and dose assessment methods and tools used by the participating laboratories

Lab Code	Assumptions, Methods, and Tools
002	DCAL: urinary excretion fraction ICRP: ingestion dose coefficient; “reference man” (1.6 L urine per day) AIDE: for confirmation
004	ICRP: “reference man” (1.6 L urine per day); acute intake; ingestion dose coefficient
005	ICRP: “reference man” (1.6 L urine per day) IMBA Professional Plus: acute intake, ingestion, Day-2 sample, intake and dose calculation
006	A national guideline based on ICRP data
007	ICRP: “reference man” (1.6 L urine per day), GI Tract model, radiation and tissue weighting factors, reference bioassay and biokinetic models; f1 values IMBA Professional Plus: intake and dose calculation Other assumption: presence of ^{90}Y from the decay of ^{90}Sr intake
008	IMBA Professional Plus: intake and dose calculation
009	ICRP: biokinetic and dosimetric models; Day-2 urine from “reference man” (1.6 L urine per day) IMBA: intake and dose calculation MONDAL 3: for confirmation

Table 6

Intake and dose assessment results from participating laboratories

Lab Code	Intake (MBq)	50y CED (mSv)
002	1.3	270
004	1.44	297
005	^{241}Am: 0.22 ^{242}Cm: 0.007 ^{234}Th: 27	^{241}Am: 45 ^{242}Cm: 0.08 ^{234}Th: 92
006	1.53	306
007	^{241}Am: 1.4 ^{239}Pu: 0.006 ^{90}Sr: 0.00016 ^{241}Pu: 16 (not certain)	^{241}Am: 290 ^{239}Pu: 16 ^{90}Sr: 0.0044 ^{241}Pu: 76
008	1.46	300
009	1.8	360

Table 7

Medical advices provided by the participating laboratories

Lab Code	Medical Advice
002	This person would be a candidate for treatment as the CED is above 250 mSv. However, other parameters than CED should be considered as well. DTPA would be the proper countermeasure; Reference: NCRP 161[4]
004	Treatment is recommended as soon as possible with decorporation agent DTPA by intravenous administration together with the use of binding agents to enhance fecal excretion. Further monitoring of the urinary and fecal excretion to obtain more reliable evaluation on intake and to verify the effectiveness of the treatment; References: NCRP 166[11], ICRP 96[12]
005	It is recommended to initiate DTPA treatment immediately as the estimated dose from both Th and Am are within the range to consider intervention. Daily administration of 1g Ca-DTPA in 100 mL normal saline via drip infusion for the first day, followed by 1g Zn-DTPA in the next days, is recommended. The termination of treatment should be based on the treatment efficacy monitored by bioassay. Because one week has passed since ingestion of these radionuclides, GI tract clearance using laxatives may not be effective. Absorption of these radionuclides from GI tract (f1) is thought to be low. Laxatives such as sorbitol can be the choice to further reduce the absorption; Reference: IAEA EPR-Medical 2005[13]
006	Treatment with DTPA therapy should be applied immediately as the committed 50y effective dose exceeds 250 mSv and side effects of the treatment are low. However, the risk-benefit assessment must be made by a highly specialized physician. Further incorporation monitoring should be performed; References: ICRP 109[14], NCRP 166[11], NCRP 161[4], and the TMT Handbook[7]
007	As the committed 50y effective dose exceeds the action level of 200 mSv recommended by the TMT Handbook, the person should be referred for immediate medical assessment. Treatment with DTPA-Ca and/or DTPA-Zn is suggested. Further monitoring (24-hour urine, *in vivo* measurement of ^{241}Am in liver and bone over the next 15 days), information gathering (chemical forms, appropriate RBE values for organ dose assessment), and reassessment of organ doses for the individual rather than the Reference Worker using state-of-the-art models (i.e. the ICRP Human Alimentary Tract Model, and OIR systemic models) may be considered; Reference: The TMT Handbook[7]
008	Treatment is recommended with chelation therapy (DTPA-Zn or DTPA-Ca) under the supervision of a qualified physician; Reference: NCRP 161[4]
009	Treatment is recommended with chelation therapy (daily intravenous administration of 1g of DTPA in 250 mL normal saline. The duration and administration pattern will depend on bioassay results performed every day during the first week; Reference: The TMT Handbook[7]