COMMUNITY HEALTH ASSURANCE MONITORING PROGRAMS

CHAMP

Technical and Feasibility Assessment of CHAMP as part of a Sustainable Long-term Stewardship Vision

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EXECUTIVE SUMMARY

Community Health Assurance Monitoring Programs are designed to identify evidence of exposure or early health status changes in communities living in proximity to hazardous waste sites or industrial accidents. This report evaluates CHAMP as a component of a long-term stewardship system for residual radioactive or chemical waste at Department of Energy facilities. CRESP examined both the technical feasibility of various approaches to monitoring humans for exposure, as well as the context in which such a program could be implemented.

*Goal of a CHAMP: community reassurance or early notification of exposure.

*Incorporates human biomonitoring as an outer ring in the CRESP vision of sustainable protection as a series of concentric monitoring rings.

*Suitable for detecting offsite migration of radionuclides and heavy metals from residual contamination in the event of barrier failure.

*Whichever components are chosen, we conclude that they are not sufficient or cost effective to mount as independent programs, but should be integrated into existing health monitoring programs undertaken by health agencies and/or providers.

*A variety of biomarkers, clinical tests, and epidemiologic systems have been evaluated to determine their technical feasibility and utility for incorporation in a CHAMP.

*Specific radionuclide or heavy metal monitoring in urine, hair, and teeth can be effective for sites where these are present in residual contamination.

*We were unable to identify a suitable biomarker for detecting organic solvent exposure at the low levels expected in the community. Markers of pesticide or organics lack sensitivity and specificity.

*Sensitivity and specificity must be taken into account when implementing CHAMP, and predictive value is crucial in interpreting results to individuals or agencies.

*Stakeholders, including not only DOE and its regulators, but the affected community as well as medical providers, should participate in designing any site-specific CHAMP.

*CHAMP's main usefulness will be to contribute to peace of mind of individuals residing in proximity to residual nuclear waste, but also offers another ring to CRESP's sustainable model of stewardship----periodic assessments to determine if there is an indication of human exposure to contaminants migrating from a containment facility. It should also offer peace of mind to regulators as well as to the DOE.

OVERVIEW

CRESP undertook this investigation of a Community Health Assurance Monitoring Program as an integral part of its overall sustainability initiative, helping the U.S. Department of Energy (DOE) develop a comprehensive long-term stewardship program for residual contamination from legacy waste that cannot be adequately or cost-effectively removed or remediated. It supports DOE's commitment to have a "continuing cycle of planning, implementing, evaluating, and improving processes and actions" to protect public health and the environment as well as to prevent pollution and comply with environmental requirements (DOE Order 450.1). Residual waste with long radiologic halflives may be contained by barriers that are subject to eventual failure, while other materials may be undergoing monitored natural attenuation.

Moreover, DOE has had a substantial interest and concern with the issues of medical surveillance and biomarkers, applied to both workers and communities. In 1997 DOE sponsored the conference *Biomarkers and Occupational Health: Progress and Perspectives*, to produce a state-of-the-art volume (Mendelsohn et al. 1998). The first chapter of which examines the historical use of biomarkers (Gochfeld 1998). Several papers in that conference, for example, Desrosiers and Romanyukha (1998) examined biomarkers of radiation exposure or effect, including DOE-funded studies of genetic responses to ionizing radiation.

This review is, therefore, directly relevant to a long-line of DOE studies, and focuses on the potential role of human biomonitoring, both for early detection of exposure to hazards and for reassurance. In addition to examining the technical feasibility of various biomedical and epidemiologic approaches, the authors recognize that communities in proximity to contaminated sites, industrial facilities, or other technological hazards, often desire human studies, human data, and personal monitoring to provide peace of mind, and confidence, that they are not in danger (Greenberg et al, 2005).

DOE, in part assisted by CRESP, has made great strides in stakeholder involvement. This includes its Citizens Monitoring and Technical Assessment fund, which supports independent environmental monitoring studies around various DOE sites. These assessments include environmental and ecological sampling, but not human sampling.
CRESP takes into account that humans are part of ecological systems and social communities. For both natural and anthropogenic chemicals, there are potential pathways from environmental media to the body, and that exposure, rather than proximity alone, is an essential feature of risk evaluation.

The design of any screening program should conform insofar as possible to the World Health Organization guidelines set down 50 years ago. These are paraphrased below:
1. The condition or exposure should be important.
2. Screening tests should have adequate sensitivity and specificity.
3. Tests should be acceptable to participants and providers
4. The natural history of the condition should be known
5. There should be an effective preventive intervention and a commitment to achieving intervention.
6. Benefits of the program should outweigh the harm

A CHAMP can conform to all of the above guidelines.

GOAL OF THE CRESP II CHAMP PROJECT

The goal of the CHAMP project is to examine the environmental factors, biomarkers and biomedical considerations, and organizational features necessary for implementing a CHAMP, contributing to the sustainable protection of the public from the potential health risks of residual contaminants at or near DOE sites, in the event that there is inadequate containment in the future. This project would have general relevance to medical monitoring for any community exposed to hazardous waste.

INTRODUCTION

Long-term stewardship of potentially hazardous situations involves a combination of engineering and institutional controls, and this combination is essential for the sustainability of the program. Sustainability is a social issue, more than a technical issue, but poses a significant challenge in the present, to assure protectiveness in the future. Engineering and institutional considerations are not discrete entities, for viable institutional controls are needed to assure the integrity of engineered systems. Likewise, land-use decisions made today, cannot be assumed to hold true indefinitely, and demographic changes that are already visible today, can be expected to continue in the future. Any program designed today must assume iterative changes in the future----even on the scale of years.

Thus any long-term stewardship program must include evaluation and quality control components to assure that any potential pathways between residual contamination and receptors are effectively interdicted, and that the monitoring rings: engineering, environmental, ecological, and human, are functioning effectively. These are well-illustrated by CRESP's concentric ring model of sustainability (Figure 1). Human biomonitoring and clinical assessments represent the outer rings of an integrated program.

Figure 1. CRESP's Conceptualization of a sustainable stewardship program for monitoring residual contamination (Powers, 2005). The inner ring represents the first line of protection against residual contaminants (i.e. inspection of engineered barriers), while the outer rings of human biomonitoring represent the highest level of detection and reassurance.

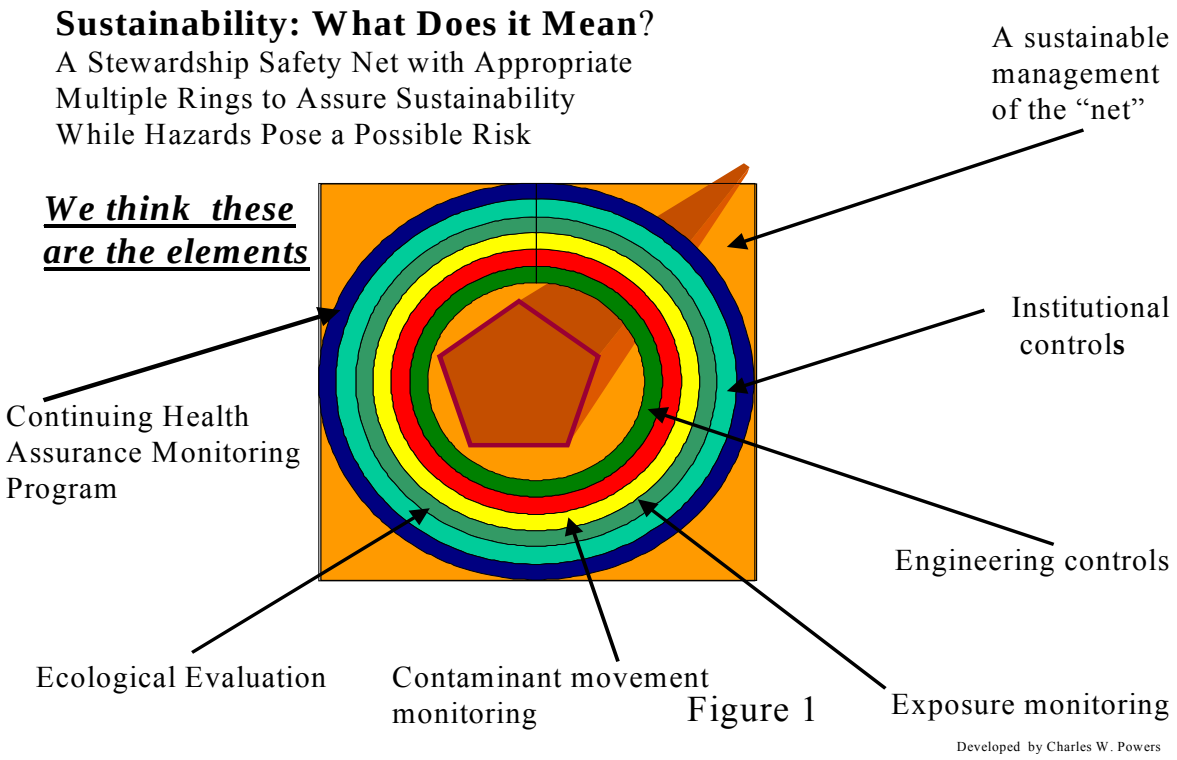
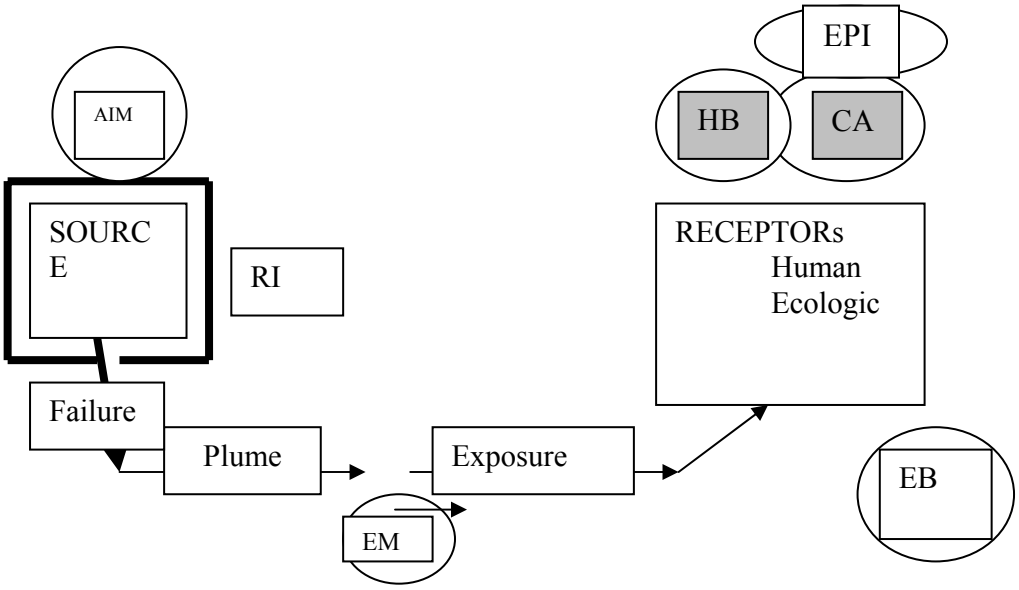


Figure 2 illustrates the role of source containment, automatic integrated monitoring and inspection, environmental monitoring, ecological biomonitoring, human biomonitoring, and clinical assessment in the detection of failure, plumes and exposure. The shaded boxes represent two potential aspects of CHAMP, with the current paper focusing on the technical feasibility and potential value of supplementing engineering and management controls with human exposure biomonitoring (HB).

Fig 2. Overview of monitoring components of Long-term stewardship



AIM=Automated integrated monitoring
RI=Regular inspection
EM=Environmental Monitoring (air, water, soil)
EB=Ecologic biomonitoring (plants, animals)
HB=Human biomonitoring
CA=Clinical Assessment
EPI=Epidemiologic approaches including syndromic surveillance

* * *

DISCLAIMER

This paper does not address risk assessment. We do not examine the risk or probability of containment failure, nor the probability of exposure and magnitude of health risks, in the event of failure. It focuses more narrowly and more practically on a preventive health system designed to supplement other components noted in figure 2 by seeking to detect low levels of exposure that might result from failure of source containment and on the reassurance of a target population in the absence of exposure.

BACKGROUND

The challenges of stewardship for residual contamination are several, but the overall goal is to assure protection of humans and the environment in perpetuity. The time frame of "perpetuity", itself is controversial----whether dozens, hundreds, thousands, or millions of years. We confine ourselves to a more modest hundred year time horizon, where we can make some meaningful assessment of technology, and during which some of the most important radionuclides from both a monitoring and health perspective (^{137}Cs, ^{90}Sr, ^{3}H) will have decayed significantly.

In public health we divide prevention into different levels:

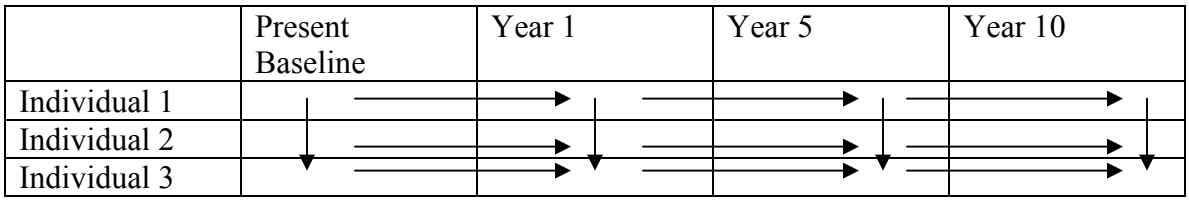
Primary prevention: stopping an exposure from occurring
Secondary prevention: early detection of an exposure before damage occurs
Tertiary prevention: detection of damage and halting progression.

Engineering controls and containment represent primary prevention. CHAMP is a good example of secondary prevention. It aims at detecting whether there is exposure in the human population to chemicals that may have migrated from the source. Primary prevention aims at removal of sources or effective containment. In principle CHAMP can play three functions: 1) it can provide early detection of exposure, hence failure of containment, 2) it can provide early detection of disease, and 3) it can provide reassurance to both receptor individuals and responsible parties, hence a quality control function, that containment and monitoring are effective. This report examines these issues. Any program involving human biomonitoring must take into account the ethical and psychological issues of privacy and apprehension. Human monitoring programs can create a Sword of Damocles situation, enhancing rather than alleviating concerns. Communities may choose to forget or ignore the nearby contamination, as in the case of the Love Canal community, which in changed its name as the first step in erasing its past.

CHAMP embodies elements of both screening and surveillance (Gochfeld 1992). Screening is defined as the cross-sectional assessment of a population, usually at one point in time, and often for a particular condition. Well-known screening programs include portable chest xrays for tuberculosis, mammography for breast cancer, occult blood for colon cancer, etc. Surveillance is longitudinal tracking or observation of a individuals or a population, looking for changes over time. Table 1 illustrates the combination of screening and surveillance, tracking individuals over time, while performing periodic population-based analyses. Medical surveillance focuses on individuals, while public health surveillance (Halperin 1992) focuses on detecting events in populations, for example, infectious disease reporting.

The distinction between screening and surveillance in a hypothetical CHAMP program is illustrated in Table 1. Horizontal arrows signify longitudinal surveillance of each individual over time, and while vertical arrows signify cross-sectional screening of a group of individuals occurring at a point or period of time. The optimal program includes both elements.

Table 1: Screening and Surveillance. The vertical arrows represent screening a population cross-sectionally at different times. Horizontal arrows indicate surveillance examinations of individuals. The same examination can serve both functions.



FROM CONTAINMENT TO ENVIRONMENT

Radioactive waste is not chemically inert, and the challenges for achieving permanent, or at least very long-term containment materials, are dealt with in separate CRESP reports. Residual waste, whether contained in perpetuity by engineering barriers or allowed to undergo monitored natural attenuation, has the potential of migrating, leading to exposure to humans or other organisms. DOE has long been sensitive to public concerns about actual or potential contamination of ground water (RWMA 2004), and the environmental monitoring ring will focus on detecting any ground water contamination. In the event of containment failure, material may seep out slowly, carried by surface water filtering through the upper soil levels and carrying contamination downward.

Characterizing the residual contamination, identifying both the radionuclides or chemicals that remain on site, is fundamental to choosing when and how to develop a site-specific CHAMP. This will be investigated in a subsequent CRESP report.

SUSTAINABILITY

Figure 1 illustrates the CRESP concept of Sustainability. Wherever DOE (or for that matter other industries) have residual chemical or radiological contamination that cannot be completely remediated for reasons of accessibility (underground nuclear test sites) or technological feasibility or cost, it is necessary to contain the residual contamination so it does not reach or impact "receptors". Receptors can refer to humans working or living in proximity to such organisms or ecosystems, or even abiotic targets, particularly ground water. The design and construction of a containment system involves engineering control, but the monitoring and maintenance of containment bridges institutional and engineering controls. Although one would hardly suggest relying on human exposure as the means for monitoring the integrity of containment or detecting failure, human biomonitoring does offer an additional opportunity for detecting failure. Thus human monitoring is an adjunct to the inspection and maintenance of barriers, testing environmental media, and biomonitoring organisms.

CRESP has viewed the sustainability of controls as a series of concentric circles (Figure 1), where the first (innermost) circle is the design itself. Monitoring the integrity of containment, the surrounding environmental media, possible ecologic receptors, and ultimately human receptors, represent the additional circles. It is this outermost circle, that provides the most reassurance to humans, but is also the most difficult to design and assess. Each of these circles has its methodologies, and CHAMP will link most strongly to the environmental monitoring of air, soil, and water and to ecotoxicologic monitoring (Hoffman et al. 1995).

Monitoring can occur at many levels (each of the concentric circles in the figure). Environmental monitoring can be highly specific, detecting a particular target analyte in a

particular medium. Biomonitoring includes both ecologic monitoring and human monitoring. Whereas environmental monitoring requires measurement of a contaminant in air, water, soil, and food, at a specific sampling location at specific time points, biological monitoring provides temporal and spatial integration of exposure.

TECHNICAL CONSIDERATIONS

CONTAMINANTS OF CONCERN

Table 1 provides examples of some contaminants at three selected DOE sites. These have been assessed in environmental media or in biota including wildlife, domestic animals and their products, and crops. The radionuclides detected in deer harvested at the *Paducah Site* in 2003 include a maximum concentration of 11.6 Bq/kg (liver) for Tc-99, 7.2 Bq/kg (bone, liver, muscle) for Th-230, and 0.7 Bq/kg (liver) for U-235 (Paducah, 2004; Paducah, 2004a). The concentrations for other radionuclides in deer at the Paducah Site in 2003 were below the minimum detection level.

Analyses of the Peconic River for evidence of environmental contamination at *Brookhaven National Laboratory* (BNL) have detected mercury and PCBs in fish, VOCs and tritium in river and groundwater, Cesium-137 in sand filter beds near the BNL sewage treatment plant, and Sr-90 and tritium contaminants in the aquifer (Brookhaven RBES, 2003). Ecological assessments (Brookhaven Site Environmental Report, 2003) of biological samples of deer identified Cs-137 average meat concentrations of 55.5 Bq/kg-ww for samples taken at locations under one mile off-site, versus 4.1 Bq/kg-ww for samples taken greater than a mile off-site. The onsite deer meat Cs-137 average concentration is 41 Bq/kg. Strontium-90 concentrations for deer show greatest concentrations on-site, at 97.3 Bq/kg-dw, followed by 87.7 Bq/kg-dw for samples taken within one mile off-site, and lowest values averaging 63.6 Bq/kg-dw at distances greater than one mile off-site. Squirrels sampled on-site ranged from 11 to 121 Bq/kg, while off-site samples were considerably lower, 2 to 11 Bq/kg. Sr-90 was not identified in squirrel bones. Concentrations of Cs-137 and Sr-90 were found in fish from both the Peconic River System (several proximate ponds) – with Cs-137 concentrations generally three to seven times higher than those found in further off-site control samples and with Sr-90 not detected in control samples but averaging about 35 Bq/kg-dw in the Peconic River ponds of Swan, Donahue's and Forge Pond (Brookhaven Site Environmental Report, 2003).

Table 1. Common radionuclides and contaminants (Bq/kg-ww for muscle or liver, dw for bone and for fish at BNL) measured at three DOE sites and the targets in which they are measured. This listing is not exhaustive but exemplifies the range of substances, the variation in half lives, and some differences among sites.

Contaminant	Half-life	Paducah	Brookhaven	INEEL
H-3 (tritium)	12.3 Y		water	
Co-60	5.3 Y			
Sr-90	28.7 Y	Deer – ND	Deer meat – 97 ave site; Fish 35 ave	Milk – 26 to 52 Bq/m^3 Marmots – 0.7 to 6 Bq/kg In Wheat, lettuce, potato Waterfowl max of 670 Bq/kg
Tc-99	6h/213kY[a]	Deer liver, max of 11.6		
Nb-95	35d			
I-129	16m Y			
I-131	8 d			Pronghorn
Cs-134	2.1 Y			
Cs-137	30.2 Y	Deer – ND	Deer, ave 55 Squirrels, max 121 Fish, 230 Bq/kg-dw	Lettuce, on-site sheep, mule deer, pronghorn, marmots, waterfowl
Ce-141	32.5 D			Marmots Waterfowl
Th-230		Deer (bone, liver, muscle max of 7.2		
Np-237		Deer – ND		
U-234	246k Y	Deer – ND		
U-235	700 m Y	Deer liver, max of 0.7		
U-236				
U-238	4.5 b Y	Deer – ND		
Pu-238	87.7 Y			Marmots
Pu-239,240	24k Y/6.6k Y	Deer – ND		Marmots; Waterfowl
Am-241	432 Y			Marmots Waterfowl

Mercury			fish	
Lead		Yes		
Cadmium				
TCE		Yes		
Other chlorinated solvents		Yes	water	

H=hours D=days Y=years k=thousand m=million b=billion
Yes= has been detected;
If list "Deer, Fish, etc."= has been detected in that biota, unless states ND
ND = tested, but not detected

Selected Radionuclides

Two of the most widely occurring radionuclides in the environment are ^{137}Cs and ^{90}Sr. Both occurred in large amounts in fallout from atmospheric testing, as well as in effluent from nuclear weapons production. Both have a half-life of about 30 years, so will be attenuated substantially over the next century. Meanwhile, however, because of high bioavailability and a propensity to concentrate in soft tissue (Cs) and bone (Sr), both need to be considered. Indeed, although INL showed a substantial decline of ^{90}Sr in soil from 1975 to 2002 (from 34 to 4 nCi/m^2), there was virtually no change of ^{90}Sr in lettuce or wheat over the 1998 to 2003 period (INEEL 2004 Fig 7.3,Tables 7-2 and 7-3). ^{241}Am increased substantially from 1975 to 2002 and Pu species increased slightly. ^{131}I is a major fission product released during power plant accidents (Three Mile Island, Chernobyl), but its short (8 day) half-life, renders it an unlikely candidate for detection in a long-term monitoring program. Another fission product, ^{129}I has a very long half life and may be incorporated e into a monitoring program, for example, for underground test sites. In 2005, a survey of marine biota around Amchitka, did not detect ^{129}I in any organisms (CRESP 2005).

Various DOE sites have monitored environmental media including biota for a wide range of radionuclides including the following naturally occurring species: Ac-228, Be-7, Bi-214, Pb-214, K-40, Ra-226, Th-228, Th-230 Th-232, U-234, U-235, U-236, U-238, Np237. The utility of any one of these as a biomarker of containment failure is complicated by their natural presence and no evidence of failure could be assumed if comparable levels or frequencies of detection were found for on-site and off-site biota. On the other hand, Am-241 and Pu-239,240 are isotopes that are rarely if ever found in nature, and this makes it feasible to incorporate detection into a human biomonitoring program.

Metals

Metal contamination can be as serious a health threat as radionuclide contamination, since several metals are carcinogenic and also may have significant other toxicities to specific target organs, such as the kidney or nervous system. Many sites have identified metal contamination as a problem, and monitor metals routinely. For example, Oak Ridge reports monitoring for As, Be, Cd, Cr, Pb, and total uranium, but especially for mercury. The possible offsite migration of mercury is also a concern at Brookhaven.

Other Substances

Polychlorinated biphenyls (PCBs) were widely used in electrical equipment such as transformers and capacitors, and were often discarded casually when equipment was repaired. PCB levels in the general population have decreased over the past 30 years since most uses were banned. PCBs are prominent contaminants at several DOE sites (DOE 1994). DOE remediation is accomplished by removal and bioremediation.

POPULATIONS OF CONCERN

Selected DOE Sites: Areas and Populations

Contamination is particularly relevant to human health if populations have the potential for exposure. Site RBES documents describe contaminant plumes of greatest concern from a control perspective. While specific populations are often not defined as potential receptors should plumes or other contaminant aggregates theoretically breach safeguards and move offsite, it is important to assume certain scenarios so that the concentric series of protective circles can be evaluated for effectiveness. The following table (Table 2) provides some rudimentary information regarding several main DOE sites. The area of each site is noted, as is the population of the primary county (Census estimates, 1996-2000) containing the largest segment of the site, the population of the standardized metropolitan (used freely here) most associated with the site, and a rough estimate of the average annual number of workers employed at the site during the 1996-2000 time frame. These population estimates would be refined to census tracks or other defined areas proximate to the edge(s) of site most likely having the greatest post-clean=up residual contamination concentrations in groundwater, soil or air.

Table 2. Examples of demographic information around selected DOE sites, indicating the different scales. Planning a CHAMP will require more refinement, probably at the census tract level. This will be addressed in a subsequent CRESP report.

SITE	AREA OF SITE sq.miles	COUNTY POPULATION[a]	SMSA POPULATION[b]	WORKERS[c]
SRS	310	167,000	650,000	14,000
Hanford	560	190,000	600,000	7,000
Oak Ridge	53	120,000	800,000	7,500
Rocky Flats	10	500,000	2,500,000	3,500
INEEL	890	145,000	250,000	6,000
Los Alamos	40	140,000	950,000	19,300
Nevada TS	1,350	30,000	1,500,000	3,000
Pantex	25	7,000	250,000	?
TOTALS	3,238	1,299,000	7,500,000	60,300

a. County population figures include the primary county within which Site resides – but do not include surrounding counties. County figures are Census estimates from 1996-2000.

b. SMSA = standardized metropolitan statistical area, which for some Sites includes a wide area.

c. Excludes subcontractor populations, which can be considerable at some sites.

Future Land Use and Demographic Changes

Designing any long-term stewardship and monitoring plan must take into account population changes that will occur in the future. To some extent these can be projected by examining data for the past 50 years, and most sites have developed some projections as part of their Risk-based EndState vision documents (2002-2005). Designing a CHAMP for a future (as opposed to an historic) exposure, requires recognition that the potential receptor population is likely to grow.

Comparison Populations

Interpreting the possible occurrence of contamination in a group of people close to (downwind or down-gradient) of a residual contamination site, may be facilitated by reference to a comparable population residing further from the potential source, or upwind or upgradient. Designing a CHAMP would require identifying such possible reference populations. The NHANES samples appear to represent an additional set of potential comparisons on a national basis. A process exists for incorporating additional tests in the battery of examinations provided by NHANES, given adequate justification and clearance time for such changes.

BIOMONITORING

Urinalysis and Mass Spectroscopy

Urine samples have been used to monitor population exposures to several radionuclides. Plutonium in urine of Marshall Islanders is used to track the degree of potential exposure that they may have had to residues from Pacific test site detonations in prior decades. Earlier analytic approaches, including fission track analyses, were found to have many deficiencies, not the least of which included contamination issues, low chemical yields, and errors in quantification (LLNL, 2005). More recent plutonium urine assessments have utilized accelerator mass spectrometry. Mass spectroscopy surveillance finds levels of 1 to 3 uBq of plutonium (LLNL, 2005) in 24 hour urine collections of Marshall Island residents and it provides individual isotopic assessment of ^{238}Pu and ^{240}Pu. The isotopic ratios are of value in helping to determine the source of radionuclide exposure. Neither fission track analysis nor alpha spectrometry can identify and quantify plutonium isotopes, so the accelerator mass spectrometric techniques offer great advantages in sensitivity, specificity and eventual data utility. The impact of inhaled radionuclide route of exposure was assessed in Mayak nuclear reprocessing workers in Russia (Khokhryakov et al, 2004), through a study of the concentration of total plutonium in urine and feces as a function of time of last exposure. In this study, using somewhat less sensitive alpha spectrometry, the MDA of plutonium was about 2 mBq/day.

Because depleted uranium has been used as a wartime component of armor-penetrating ammunition, there have been some studies of indirect and inadvertent exposure to military participants and civilian bystanders (Durakovic et al, 2002; Durakovic et al, 2003; Bishop, 2004). It appears that many of the reported analyses are from the same analyst (Hari Sharma) and laboratory (located at the University of Waterloo, Canada) that has reported Strontium-90 in the tooth fairy studies. Uranium isotopes, including ^{234}U, ^{235} U, ^{236}U and ^{238}U, were assessed in military populations through the use of multi-collector inductively coupled plasma ionization mass spectrometry (MC-ICP-MS) techniques (Durakovic, 2005). Reported results for 8 civilian men in Afghanistan include 100 fold increases, compared to a “reference range” in average total

urinary uranium concentrations (275 ng/L; SD 137.8). There was no detection of ^{236}U, and isotopic ratios were consistent with what might be expected from natural uranium exposures (Durakovic, 2005).

The United States Centers for Disease Control and Prevention, Division of Environmental Health Sciences Laboratory Sciences, studied total uranium analyses on 500 randomly selected spot urine samples collected in the Third National Health and Nutrition Examination Survey (Ting et al, 1999). The CDC used a "magnetic-sector inductively coupled argon plasma mass spectrometer (ICP-MS)". Results were reported as both ng of uranium /L of urine and, correcting for urinary dilution, as ng of uranium /g of creatinine. Of interest is that nearly all urinary samples (96.6%) had uranium above the detection limit of 1.0 ng/L, and the median concentration was 6.32 ng/L or 5.57 ng/ g of creatinine. The range, from the 5th to 95th percentile was 1.42 to 34.5 ng/L or 1.48 to 34.9 ng/g creatinine. This data set is particularly of value, since it can be used "as a basis for comparing concentrations in subjects who have suspected or known exposure to a point source" (Ting et al, 1999).

Radiochemical Analysis

Many studies have analyzed specific radionuclides in specific tissues, blood or urine. Radionuclide studies offer the advantage of a high level of specificity, but the analytic costs can be high. The detection levels show an approximately linear relationship to the mass of the sample, and a curvilinear relationship to the time in the counter. Gamma counting offers a higher cost-effectiveness. Some examples of existing biomonitoring programs are as follows:

Cord Blood

At birth, cord blood draining from the placenta, is routinely collected and stored in many hospitals. It is used in a variety of studies, and would be available for periodic surveys, including anonymous surveys, if there were a marker. Unlike Tooth Fairy Monitoring, cord blood provides almost instant gratification, but also allows archiving for future study. It may be valuable for retrospective epidemiologic study, but is only moderately useful for a CHAMP.

Placenta Tissue

Placental tissue which is expelled during child birth is readily obtained and often routinely archived for analysis measure maternal exposure levels. There appears to be no evidence for a placental barrier for the natural radionuclides U-238 and Th-232. Very similar concentrations, between 2 and 7 mBq/kg, were found in both fetal and placental samples from English studies (Bradley and Prosser, 1993; Bradley and Ewers, 1995). These findings are important, since they suggest that placental concentrations may provide an indication of fetal exposure for at least some radionuclides. Because placental concentrations of anthropogenic radionuclides are often very low, typical alpha spectrometric analyses may not be sensitive enough to be of practical value. For example, Prosser et al (1994) did not detect Pu-239 in placental tissue by using alpha spectrometry but, utilizing mass spectrometry, found concentrations from 4 to 90 uBq/kg. Russian studies of populations near a weapons test site, identified Pu-239 concentrations in placentas at much higher concentrations, up to 70 mBq/kg (Lund and Tkatchev, 1996). Pb-210 and P0-210 are likely to be found at higher concentrations than many other radionuclides. They have been detected in placental tissue through alpha-particle tracking, with concentrations up to 260 mBq/kg in UK (Henshaw et al, 1995). While placental tissue may be a useful community indicator of recent radionuclide exposure, its utility

may be minimized by maternal and social acceptance, legal considerations, and the limited number of placental samples that may be available to study.

Tooth Monitoring

The propensity of strontium to replace calcium in the hydroxyapatite crystals of teeth has long been used to monitor ^{90}Sr exposure. This can be accomplished by radiochemical analysis or by measuring electroparamagnetic resonance (Appendix D). Since children naturally shed their deciduous teeth, these are readily available for study, through a "tooth fairy" project where parents collect and contribute the teeth. This proved invaluable in demonstrating the behavioral effects of lead (Needleman 1977). Teeth can also be collected from dentists and orthodontists.

Three techniques have been compared: *in vivo* beta counting, radiochemical analysis, and electron paramagnetic resonance. Tolstykh et al. (2003), reported that in vivo beta counting of residents in the Techa River Valley of Russia showed very similar peak uptake in the 1949-1950 period. They found the former both easier, less costly, and more reliable as an estimate of exposure. The Techa River contamination from the Mayak plant (mainly in 1950-51), pre-dates global fallout from atmospheric testing which began around 1953.

Children shed their deciduous teeth beginning around age 5. These teeth developing during the first year of life have the advantage of archiving exposure that occurred over a period of months, and the disadvantage of representing a time about four years before present. Although teeth have been studied in several ways, the most famous is the Needleman (1979) study showing that dentine lead correlated with poor school performance and behavioral disturbances. Teeth can be analyzed chemically for elemental contaminants, or by electron paramagnetic resonance (EPR), for the record of radiation exposure secured therein. Arguing for the need for routine monitoring of the U.S. population, Mangano et al. (2003) reported an unexpected rise beginning in the late 1980s of ^{90}Sr in baby teeth from persons living within 40 miles of nuclear reactors in several states. This was long after the peak exposure from fallout as was attributed to nuclear plant emissions, a contention challenged by the Nuclear Regulatory Commission (NRC 2005).

***In vivo* beta counting for ^{90}Sr.**

We reviewed the existing literature. Teeth develop at different rates and roots and crowns accumulate strontium differentially (Tolstykh et al. 2003). The tooth beta count data given in their paper, reveal that teeth formed prior to 1943 were all below 40 counts per minute (cpm). Of these 50% were 10 cpm or less and 50% were between 10 and 40 cpm. All values in excess of 40 cpm were clearly part of the peak rise which culminated around 1950, and then declined, although atmospheric testing continued beyond that date.
A cpm > 40 would clearly indicate a non-background exposure. Tolstykh et al. (2003) report using 9cpm as a criterion from a previous study (not available), but the data they present would not support such a criterion.

Electron Paramagnetic Resonance

EPR measures absorbed radiation dose from all sources including background radiation. When radiation strikes the hydroxyapatite crystals of tooth enamel, CO_2^- radicals are generated within the enamel. This highly stable product allows teeth to serve as stable dosimeters of exposure that occurred from internal exposure during tooth formation. Once mature, external radiation can still generate the radical formation, albeit slowly, and even UV exposure from sunlight contributes to these changes (El-Faramawy 2005). There is an extensive literature on

EPR dosimetry, particularly for 90Sr, and interlaboratory comparisons show a high agreement (Wieser et al. 2005) indicating that this is a mature and effective method. EPR has been used to measure background radiation in India, based on the gradual accumulation of exposure with year (El-Faramawy 2005). In Russian radiation workers at the Mayak Plant, EPR exposure estimates had a 0.97 correlation with film badge exposure data. Incorporation of strontium in teeth continues up until the dentition is fully formed in early adolescence (Tolstykh et al. 2003).

With new equipment EPR can be conducted *in vivo*, but the equipment illustrated (Iwasaki et al. 2005) does not appear suitable for routine monitoring. Tolstykh et al. (2003) conclude that EPR is not sufficiently sensitive for reconstructing ^{90}Sr exposure. Interpretation of EPR data is complicated by the contribution of dental Xrays (El-Faramawy 2005). The combination of EPR with thermoluminescence using ultra thin layered aluminum oxide thermoluminescent dosimeters (which only measures the internal dose contribution) can help interpretation.

Radiochemical Analysis of Teeth

Radiochemical analysis involves digesting the tooth, and then conducting analysis for the beta emissions of ^{90}Srm and Acar and Acar (2000) were able to obtain detection limits of 0.9 Bq/kg for ^{90}Sr, counting for 16 hrs. The radiochemical analysis is costly, and for monitoring purposes a high level of sensitivity is required. It has less utility than EPR if that were to become readily available.

Autoradiography Imaging

A fourth technique is to measure distribution of ^{90}Sr in teeth using a photostimulable phosphor imaging detector, which is highly sensitive or aluminum oxide thermoluminescence dosimetry. The former has very high sensitivity is non-destructive and is fast and inexpensive (5 min to read an imaging plate for up to 50 teeth). It is currently experimental and our assessment is that it will be useful for improving the accuracy of dose reconstruction. It can be a very sensitive means for screening large numbers of teeth.

Data are also available for $^{239+240}$Pu in children's teeth. O'Donnell et al. (1997) found a decrease in Pu (but not total alpha) in teeth with distance from Sellafield, but there was not a statistically significant difference between concentrations in the Sellafield vicinity versus the rest of England, due to high variance. The levels reported were in the mBq/kg range (very low), and this limits the sensitivity of teeth as a Pu biomarker. However, with large enough sample size, the Pu determination could detect a failure signature. The main limitation once teeth are collected, is the cost of conducting specific actinide analysis.

Analytic sensitivity notwithstanding, the temporal resolution of tooth testing limits the value of this approach. On a long time scale, where monitoring is conducted at 5 or 10 year intervals (DOE LTS), this temporal issue doesn't detract from its utility.

Hair Analysis

Uranium ratios measured in hair, nails, and urine by multi-collector inductively coupled plasma mass spectrometry (MC-ICPMS) have been found to be effective biological indicators of the primary source of exposure. Recently published work, based upon an assessment of 45 individuals, found a 97% correlation between the U-234/U-238 ratios in hair and drinking water (Karpas et al, 2005). The collaborators of the study (from the Nuclear Research Center in Beer-Sheva, Israel and the Radiation and Nuclear Safety Authority of Finland) concluded: "These results conclusively demonstrated that the uranium found in the bioassays can be traced to

drinking water, thus providing a direct link to the source of exposure. Hair may serve as an excellent indicator of occupational or environmental exposure to uranium and provide information regarding its source" (Karpas et al, 2005).

The advantages of hair analysis include the ease of sample collection and long-term storage without refrigeration, the integrated value of hair measurements, the high level of sensitivity provided by ICPMS (assuming meticulous handling of the hair sample digestion phase and the use of an efficient nebulization device), and the very short analytic measurement time of approximately one minute. The use of multicollector-ICPMS in measuring low concentration ratios of radionuclide isotopics in different matrices has been previously reported (Ehrlich et al, 2001; Platzner et al, 2001; Karpas et al, 2005a).

Whole Body Counting

Whole body counting is widely used in research and sometimes clinically. Whole body counting has been used to measure the biological uptake of ^{137}Cs. It has been applied to assess to the radionuclide burden in individuals who may have ingested high-energy gamma-emitting radionuclides in foods potentially grown in contaminated soil. Whole-body counters typically consist of large volume sodium iodide radiation detectors positioned in a chair-like device in which seated volunteers are measured. Whole-body counting has been described as "a simple and effective method of determining the quantity of gamma emitters in the body" (http://eed.llnl.gov/mi/wbc.php). Dose estimates for ^{137}Cs assume a biological half-life of 110 days. The biological half-life is an estimate of the time needed for 50% of ingested radionuclide to be excreted from the body via biological routes, such as urine, feces, or respiration.

Whole-body counting has been used to assess the ^{137}Cs doses in populations potentially exposed to nuclear test site conditions in the South Pacific and elsewhere. For example, it has been provided to residents of Enewetak Island and to resettlement workers on Rongelap Island. Data from 2001 surveillance of Enewetak Island residents showed the following concentrations (table 3), in mrem units:

Table 3: Cs-137 Concentrations in Enewetak Island residents

	Number tested	Annual Ave ^{137}Cs	Std deviation
Adults	358	0.4 mrem	0.4
Teenagers	41	0.2 mrem	0.2
Children	6	<0.1	-

Ref: Whole-Body Counting, Lawrence Livermore National Laboratory. http://eed.llnl.gov/mi/wbc.php. Last modified, December 10, 2002.

Other applications of whole-body counting are evident in the United Kingdom, where studies between 1990 and 2001 of 136 non-occupationally exposed residents of Oxfordshire and

Berkshire found 23.5% of residents with Cs-137 whole-body measurements greater than the detection limit (18 Bq whole body, or about 0.3 Bq/kg for a 70 kg person), with detected levels ranging between 18.5 and 55 Bq (Ham et al, 2003). The Cs-134 whole-body detection level was 12 Bq (or about 0.2 Bq/kg for a 70 kg person), and 5.9% of the population had results above the detection limit – ranging from 12.6 to 18 Bq. These measurements appeared to be relatively stable from year to year, and were similar to results prior to the Chernobyl event of 1986.

In addition to cesium, some of the UK surveys have measured I-131 (thyroid scans), Am-241 (skull scans), Cs/K activity ratios, Zr-95 (lung measurements), Tc-99m, and other radionuclides (Dendy et al, 1992; Ham et al, 2003; Rundo and Newton, 1962; Rundo and Newton, 1965).

Genetic Markers

Standard techniques in genetic toxicology have examined chromosomal aberrations, micronucleus formation, and sister chromatid exchange. Since ionizing radiation causes genetic mutations, and since this is the basis for the major health concern from radiation----cancer, great interest has focused on the feasibility of genetic dosimetry. The Department of Energy supports research on several possible markers, including chromosomal translocations (Tucker 1998).

DNA Adducts

Many environmental chemical contaminants, react with the DNA of cells to form adducts. The chemicals actually attach themselves to one of the nucleotides, and potentially disrupt the DNA replication and the subsequent life history of the cell. This has been proposed as a mechanism of chemical carcinogenesis. Although this has been considered a very promising approach for dosimetry applied to chemical carcinogens, because it is on the main line of the cancer causing mechanisms, it has proven difficult to provide consistent results. Partly, many of adducts are transient, eliminated by DNA repair mechanisms. However, even if the interpretation of DNA adducts or protein adducts, were systematized, current methods make it unlikely that this method could move from the screening laboratory to the clinical laboratory. The utility of adducts in screening will depend on new technologies and research. (Hemminki et al. 1998)

Glycophorin A (GPA) assay

The GPA is a somatic mutation assay that uses flow cytometry to measure the mutation rates as reflected in N0 and NN mutant red blood cells in individuals who were heterozygous for the M and N GPA alleles. The assay measures the number of red blood cells that have mutated from their M N heterozygous allele state of the GPA gene to either N0 (deletion or inactivation of M allele) or NN (loss of M allele and replacement with N). The measurement has been useful for assessing the impact of acute high-dose, high dose rate radiation exposures, such as in Japanese atomic bomb survivors and in Chernobyl workers sent in to clean up the site soon after the accident (Heller, 1999). Studies of radiation workers at Sellafield (Tawn et al, 2003) and uranium miners (Shanahan et al, 1993) have failed to find significant dose-related GPA changes and suggest that "the GPA mutation assay is insufficiently sensitive to be used as a biological marker of low-dose chronic exposure " (Tawn et al, 2003).

STATISTICAL ISSUES: SAMPLING, POWER SENSITIVITY SPECIFICITY

Sampling Plan

A first step in a CHAMP will be to identify a target population that might be exposed in the event of containment failure. These are people for whom the existence of an exposure pathway can reasonably be anticipated. The main pathways would be groundwater plumes affecting drinking water or less likely airborne releases. However, recreationists may encounter contaminated soil or may consume contaminated fish and wildlife. Realistic scenarios need to be constructed and analyzed to project the size and location of such population(s). At the same time the comparable reference population needs to be identified.

Power and Type I Versus Type II Errors

Power refers to the ability of a survey to detect a difference in the sampled population. This difference can be in comparison to the same population sampled at an earlier point (previous year or decade) or in comparison to a similar reference population sampled at a point in time.

If a substance is rarely detected in the human body, for example ^{241}Am then simply finding a detectable level in one person, could trigger an investigation. But more ubiquitous radionuclides such as ^{238}U would require careful statistical analysis and larger sample size. If the level discovered is only slightly higher than previously or than in the reference population, one would need to have a large number of people to be sure that the detected increase is significant. Power thus depends on how much of a difference has occurred and on the number of people (sample size) in the two populations or sampling period. There will be communities where the total number of potentially exposed people is too small for any effect to be interpreted.

Sensitivity-Specificity-Predictive Value

Interpreting any test or study hinge on sensitivity and specificity. These are broad ranging concepts which have particular impact on interpreting any kind of screening program. Sensitivity is the ability of a program or test to detect whatever it is looking for. Specificity is the ability of a program or test to detect only what it is looking for. In other words, sensitivity is the ability of a test to be positive when it should be positive (i.e. a true positive, when the condition or exposure actually exists), and specificity is the ability of a test to be negative when it should be negative (i. e. a true negative is when the condition or exposure does not exist).

These are often depicted as follows (table 4) with the **boldfaced entries** being desirable outcomes.

Table 4: Screening attributes

	Exposure has occurred	Exposure has not occurred	
Test for exposure is positive	**TRUE POSITIVE**	FALSE POSITIVE	All positives
Test for exposure is negative	FALSE NEGATIVE	**TRUE NEGATIVE**	All negatives
	TP + FN	FP + TN	

Sensitivity is defined as TP/(TP+FN)
Specificity is defined as TN(TN+FP)

Actually we can only measure sensitivity and specificity accurately when we have an independent measure of whether the exposure has or has not occurred (or whether a particular

condition is or is not present). This independent measure is called a gold standard. Often it is another kind of test that is either more inconvenient, more invasive, or more expensive, than the screening test that is being compared. Often, however, there is not gold standard, and one can only make an educated guess about sensitivity and specificity.

But there is another measure that is actually of greater immediate interest. If there is a positive test, how likely is it that it is a true positive. This is called the positive predictive value, or the proportion of all positives that are true positives

Positive Predictive value is TP/(TP+FP).
Negative Predictive value is TN/(TN+FN)

There is a fourth consideration that influences predictive- value, that is the underlying prevalence or frequency of the condition being sought. When the condition occurs in half the population, then the predictive value is quite high, but when the condition is rare, then the proportion of positive tests that are false positives, inevitably rises. This is illustrated in Appendix C.

Any test that is incorporated as part of a CHAMP has to be evaluated with regard to these concepts. This is important both to assess its utility for detecting exposure (containment failure) and for conveying reliable information to the participant. It is apparent from Appendix C that when exposure is rare and infrequent, the negative predictive value becomes almost infinite, allowing the clinician to provide confident reassurance. It is also apparent that one needs collective screening, to distinguish whether positives are likely to be true positives or false positives.

EXISTING FEDERAL HEALTH AND EXPOSURE SURVEILLANCE SYSTEMS

A. Systems that focus on collecting and assessing exposures

1. National Report on Human Exposure to Environmental Chemicals

- Biomonitoring of subset of 2690 NHANES general population participants for 148 environmental chemicals (in 2000-2001 samples), including urinary total uranium and total cesium (with and without creatinine correction, which adjusts for urinary concentration).
- Comparison data is provided for 1999-2000 samples.
- Further statistical adjustments are made for race/ethnicity, age, gender, log serum cotinine, and urinary creatinine.
- Data is provided in percentiles, with 95% confidence intervals.
- Chemicals analyzed include 13 metals, 23 polycylic aromatic hydrocarbons, 12 phthalates, 16 organochlorine pesticides, 12 organophosphate insecticides or metabolites, 7 heribicides, 5 pyrethroid pesticides, 5 other pesticides, and cotinine.

2. BioWatch

An early detection and response system to assist federal, state and local agencies monitor the air of major urban centers for evidence of releases of biological agents, and, if present, to estimate their geographic extent.

- Under the U.S. Department of Homeland Security.
- Operational since 2003, often linked with the EPA Air Quality Monitoring Network and partnering with state, local and tribal environmental agencies.
- Over 500,000 air samples have been analyzed, with no false alarms through the first complete year of operation (Washington Technology, 2004).

B. Systems that focus on collecting and assessing health measures or disease reports

Primarily Infectious Diseases:

1. National Electronic Disease Surveillance System (NEDSS)

- Replaces: NETSS (the National Electronic Telecommunications Systems for Surveillance), the HIV/AIDS reporting system, the vaccine preventable diseases systems, and systems for tuberculosis and infectious diseases
- Enhances "ability to identify and track emerging infectious diseases (including potential bioterrorism attacks), investigate outbreaks, and monitor disease trends."
- It "provides the foundation upon which state and program areas needs, data collection, and processing can be built."
- Includes modules for core demographic data and nationally notifiable diseases.
- NEDSS base system (Version 1.1.3) completed in May, 2004.
- Includes all nationally notifiable conditions, case management for over 140 diseases or conditions (including food borne and enteric disease surveillance).
- Has option for developing "customized fields".

2. Public Health Information Network (PHIN) Preparedness

PHIN is a consistent national network of preparedness systems, with functional requirements, specified standards/specifications (HL7, SNOMED, LOINC, etc), interconnected across the public health structure, for the following six capabilities:

- Early event detection and syndromic surveillance
- Outbreak management
- Linking of laboratory systems
- Administration of response and countermeasures
- Communicating/alerting
- Cross-functional components

The PHIN architecture includes BioSense, a national program that channels health data through analysis and visualization algorithms to provide a monitoring approach for infectious disease outbreaks, evidence of biological or chemical attacks, and for impacts of natural emergencies.

Primarily Non-Infectious Disorders:

1. National Ambulatory Care Survey (NAMCS)

- Annual utilization data on visits for a number of cancer prevention tests provided in an ambulatory setting.
- Data on mammography, skin biopsies, Pap tests, colonoscopy, flexible sigmoidoscopy.

2. National Hospital Discharge Survey (NHDS)

- Annual report on a national probability sample of non-Federal, short-term hospitals.
- Includes diagnoses, diagnostic and surgical procedures, and hospitalization characteristics (i.e., patient demographics, length of stay, costs, vital status at discharge, payment source, etc.)

3. National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results Program (SEER) Registries

- Population-based cancer registry in 9 states and 6 metropolitan areas, from 1973 to the present (Wingo et. al., 2005)
- Contains population demographics, tumor characteristics (including histology, staging, site, etc.), treatment, and outcome (including follow-up survival data).
- Maintains rigid standards for quality and comprehensiveness of data.
- Such data are used to describe trends in cancer incidence, mortality and survivorship statistics and have mined to determine whether an aggregation of cancer cases merits denotation as a cluster.

4. Centers for Disease Control and Prevention (CDC) National Program of Cancer Registries (NPCR)

- Consists of cancer registries from 45 states, the District of Columbia, and three U.S. territories.
- Similar types of data as SEER, but variable standards of quality and comprehensiveness.
- Types of Cancer data associated with radiation are listed in Table 5.

Table 5: Cancers with high, moderate and low association with radiation as a cause (based on Mettler and Upton 1995.)

LEVEL OF ASSOCIATION	CANCER SITE	SCREENING
High association	Leukemia (marrow)* Female breast Salivary glands Thyroid	Not routine Routine Not routine, but apparent Not routine, but in physical
Moderate association	Urinary bladder Colon Stomach Liver Lung Ovary Skin	UA routine, cytology not Occult blood, colonoscopy Not routine Liver enzymes, not routine Only in high risk groups Not routine Routine recommended
Weak Association	Bone Brain Connective Tissue	Not routine Not routine Not routine

	Kidney Larynx Nasal Sinuses	Urinalysis Smokers with symptoms Not routine

* Excludes chronic lymphocytic leukemia.

5. Population-based cancer registries (combination of SEER and NPCR registries which meet NAACCR high quality data standards).

- Includes registries meeting high quality data standards.
- Similar data as SEER, including geographic patterns, diagnostic criteria, staging of disease, socioeconomic status, and demographics (including a standardized identification of individuals of Hispanic origin).

6. National Cancer Data Base (NCDB)

- A private database developed by the American College of Surgeons and supported by the American Cancer Society.
- Is a hospital-based cancer registry operating continuously since 1987.
- Includes diagnoses, stage at diagnosis, treatments, recurrences, specific data on surgical procedures and outcomes, and will include co-morbidity conditions.

7. Birth Defects Registries

C. Systems that collect, assess and integrate health measures and indicators of exposure

Acute Exposures:

1. Toxic Exposure Surveillance System (TESS) – American Association of Poison Control Centers.

- 64 Participating Centers, serving 295 million people, with 2.4 million human exposures in 2003 (Watson et al, 2004).
- This system records personal exposures (including route of exposure and type of agent) reported to Poison Control Centers, recommendations, and, for certain cases, an indication of outcome.

Chronic Exposures:

1. National Health and Nutrition Examination Survey (NHANES)

- Report on Human Exposure to Environmental Chemicals (described above)
- Is conducted by the National Center for Health Statistics (NCHS) of DHSS
- Is an in-depth evaluation of health status and biomarkers in statistically valid probability samples of the United States.
- The survey, as currently constructed, is limited to analyses of cross-sectional relationships between clinical findings and exposure to environmental chemicals available on a subset of participants.

Comment:

NHANES could support CHAMP objectives by:

1. Including a probability sample of populations proximate to DOE sites.
2. Supporting the application of NHANES methodologies and laboratory tests modified to meet critical DOE site needs by state health departments or others to DOE target populations, and

using similar NHANES tests in a general population sample to provide both national trend data and external comparison data for DOE sites.

The procedure for modifying NHANES is specified (Johnson memo 2005). CDC has also published criteria for adding new environmental chemicals for inclusion in a *National Report on Human Exposures to Environmental Chemicals* (CDC 2002). The criteria are:
1. Whether independent scientific data suggests the potential for exposure is changing or persisting
2. The seriousness of potential health effects
3. The proportion of US population likely to be exposed to significant exposure levels
4. The validity of public health actions to reduce exposure
5. The existence of analytic methods
6. The incremental analytic cost to perform the analyses

NCHS periodically can add new or revised questionnaire material, laboratory assessments, and examination components to surveys, but, naturally, programmatic, feasibility, prioritization and logistical considerations that must be taken into consideration.

2. National Environmental Public Health Tracking Program (EPHT)

- Under CDC's National Center for Environmental Health's Environmental Health Tracking Branch (EHTB)
- Builds upon current efforts within the public health and environmental health sectors to develop an integrated network of hazard monitoring, exposure and health effects surveillance data that is to be used to improve community health.
- Identifies "areas and populations most likely to be affected by environmental contamination" (CDC, 2005)
- Utilizes biomonitoring as a method to assess the potential exposure of individuals, communities or populations groups
- To apply routine and standardized data collection/reporting procedures, quality control, defined geographic coverage, and timeliness of analyses
- Collaboration includes: the Environmental Council of the States (ECOS), the National Association of County and City Health Officials (NACCHO), the National Environmental Health Association (NEHA), the Association of State and Territorial Health Officials (ASTHO), and the Environmental Health Tracking Branch (EHTB) of the Centers for Disease Control and Prevention (CDC)

3. National Human Exposure Assessment Survey (NHEXAS)

An Environmental Protection Agency funded multicenter exposure assessment program, designed to surmount the limitations of single-chemical and single-media exposure studies. The data on several hundred individuals provided a basis for validating exposure models. The types of measurement methods and variables in NHEXAS are outlined in table 6. The study emphasized several important principles which will inform the design of CHAMP.

Table 6: Measurement methods and variables in NHEXAS

Measurement methods	Measurement variables
Questionnaires	Sociodemographic variables

Diaries	Activity patterns
Interviews	Exposure and Residential factors
Household environmental monitoring	Environmental concentrations
Personal monitoring	Environmental concentrations
Human tissue biomarkers	Body Burden

The degree of public participation in NHEXAS screening programs is noted later in this report: see the Acceptability Section under Social Issues.

4. Syndromic Surveillance

Public health departments have conducted various forms of syndromic surveillance for a century. This has included making certain diseases reportable, relying on doctor networks and hospital emergency rooms, obtaining reports from clinical laboratories. Electronic networks have expanded the reach of such systems, but it was not until the Anthrax Attack of 2001, that syndromic surveillance became a national priority. There is now a National Syndromic Surveillance network developing in the United States. The network itself focuses first on acute infectious diseases and toxic syndromes, but its existence offers a model for syndromic surveillance of community contamination. Such systems are best suited to exposures that have rapid and dramatic manifestations. A stewardship program could include syndromic surveillance, but this is clearly a last resort----tertiary prevention.

SOCIAL ISSUES

In addition to the biomedical issues that determine the technical feasibility of CHAMP, there are major social issues regarding acceptability, trust, perception and communication, ethics and privacy, and cost-effectiveness. CRESP considered each of these items.

Prevention in Health Care

Although many studies have shown the benefits of prevention in many aspects of health maintenance, it is remarkable that for the most part traditional indemnity insurance provides no coverage for preventive activities. The ascendancy of Health Maintenance Organizations in the United States in the 1990s, provides a radical change in this situation, where many preventive activities are encouraged and incentivized. Despite the varying economic viability of different HMOs, the overall direction is to increase the number of preventive services that are covered. The importance of this is that insured individuals are increasingly likely to undergo periodic preventive examination and testing. This is cost effective both for insurers and for society, and it provides a context into which CHAMP can be integrated. Thus a number of clinical tests and biomarkers that are deemed informative, can be incorporated into existing preventive programs, with negligible increase in cost, time, or inconvenience. This trend provides great optimism that a CHAMP can be sustainable.

Acceptability and Trust

In the 1980s and 1990s Gochfeld and others at the Environmental and Occupational Health Sciences Institute, developed screening programs for residents who had been exposed to industrial waste. Two of these are still ongoing. The experience in interviewing practitioners in their affected community as well as potential participants in the screening, provides some guidance in planning for the integration of CHAMP as a function of community health services. Such programs must be acceptable to both the public and providers.

Acceptability by the public and patients

People who know or believe themselves to be in harms way,(i.e. in the case of containment failure), vary in their interest or willingness to participate in targeted medical screening programs. Current experience in a New Jersey population indicates that where legal settlements provide free screening, only about 20% of people who were likely exposed, participate in a screening program. Reasons given for non-participation are: 1) moved away and no longer considered part of exposure group, 2) believe that personal exposure was low, 3) don't like the idea of living under a cloud (Sword of Damocles), and 4) inconvenience.

Participants, on the other hand, are effusive in their support of the screening programs, most returning year after year. Positive reinforcement----news that the screening has detected a cancer----did not encourage non-participants to participate, nor alter the participation of others. Some community residents requested that they not receive newsletters in the future. The highest potential for acceptability emerges when a screening program is incorporated into existing health care systems.

Participation rates in screening and surveys vary greatly from study to study. Some of the best participation rates are reported by NHEXAS (see above) and Table 7.

Table 7. Participation rates for various components of the NHEXAS study		
Component	Eligibles	Participation rate
Questionnaire	884	72%
Personal & Indoor Air	326	58% and 80%
Urine samples	326	65%
Blood Samples	326	50%
Food measurements	326	68%

Source: NHEXAS web site. http://www.epa.gov/nerl/research/2003/g5-3.html

A recent review of literature on health study participant recruitment and retention noted the following participation rates (table 8) for several major studies in the United States, a few of which are summarized below (Pierce and Hartford, 2004):

Table 8: Participation Rates in Selected Health Studies

Study	Initial Response Rate	Reference	Comments
Framingham Heart Study	69%	DHHS, 2002.	Middle aged adults, longitudinal study. Support of local physicians and hospitals.
National Health and Nutrition Examination Survey (NHANES)	83%	Khare et al, 1994	Interviews and questionnaires, biological samples, Medical exam. Probability samples.
(CPP) Collaborative Perinatal Project	95%	NIH, 1983	Obstetric hospital-based. Obstetricians recruited their patients.
Tucson Epidemiologic Study of Chronic Obstructive Lung Disease	55%	Lebowitz et al, 1975	Older study, with 1655 households participating.
NHEXAS Maryland	35%	Callahan et al, 1995	Based on only 80 study participants. Included diary, questionnaire, food environmental, and blood samples.

Acceptability by the Providers

Providers, mainly physicians practicing in a community, vary in their willingness to incorporate new tests into existing protocols. In many cases resistance arises from uncertainty over who will pay for additional tests, but more importantly, physicians do not feel comfortable in interpreting unfamiliar tests or in explaining their import to patients. Thus assurance of guaranteed payment and distribution of guidelines for interpreting each new test, should improve the comfort level and participation level for both individual practitioners, and groups or clinics which provide periodic health assessments. Furthermore, if provider communities (medical societies, hospitals, etc.) see and discuss the results (publications or reports) of CHAMP in protecting their patients and properties, they will more likely foster participation in such efforts. Medical practices that already conduct a wide scope of preventive services, indicated a willingness to participate in the community monitoring program, while fee-for-service practitioners considered this screening an added burden for both themselves and their patients. Practitioner acceptance is a critical feature of a sustainable CHAMP.

Trust

If reassurance is a major objective, the CHAMP has to be trusted. Integrating it into an existing health care program or provider relationship, will achieve the necessary trust. However, the reliability of information conveyed to participants by providers, depends on their access to accurate information on sensitivity, specificity, and predictive value.

Ethics and Privacy

There have been many papers and symposia on the ethical issues of biomarker research and application. There is an important distinction relevant to CHAMP. Many of the ethical dilemmas arise in the application of biomarkers of susceptibility, and this was extensively investigated in the DOE-funded symposium (Mendelsohn et al. 1998). Biomarkers of effect raise few ethical obstacles (Sharp and Zigas 2002).

A major challenge to the use of biomarkers in programs such as CHAMP is imposed by the issue of privacy. This has become a growing issue in the United States, influencing both research and practice. The problem is well-known to DOE, and has been extensively addressed in the DOE policy on protection of human subjects (DOE 2000). This is not an issue for the provider who informs a patient about a finding, but it does influence how such information could be used collectively to identify a source of exposure.

Although many diseases have been reportable to public health agencies, the role of physicians in initiating reports has long-been recognized as weak. In the case of sexually-transmitted diseases physicians were reluctant to provide sensitive information to an impersonal Health Department. In other cases it is simply inertia and lack of incentives for monitoring.

Health Departments have circumvented this problem for heavy metals, for example, by requiring clinical laboratories to report all test results that exceed certain levels. This has resulted in the accumulation of substantial data, and has a higher rate of compliance than physician-based systems.

Health Insurance Portability and Accountability Act (HIPAA)

Passage of the Health Insurance Portability and Accountability Act of 1996 included the requirement for the Department of Health and Human Services to address the issue of privacy, particularly regarding electronic medical records. In December 2000 DHHS promulgated the *Standards for Privacy of Individually Identifiable Health Information* which has had a dramatic (some would say a "chilling") impact on the sharing of medical information. Although the act was primarily concerned with allowing people to keep health insurance when they changed employment, the regulation addresses protected health information. However, it is also often misinterpreted. There are many kinds of sharing of health information which do not require the consent of the patient, for example, providing information to insurance companies. The DHHS specifically states: "The flow of your medical information is beyond your control when the disclosure is made by a covered entity to or in connection with any disclosure required by federal, state, or local regulation, regardless of the scope of the disclosure or the purpose of the disclosure." including "Public health authorities." Indeed, more than a dozen other exclusions are provided. http://www.hhs.gov/ocr/hipaa/. Although HIPAA does allow patients to complain to their doctors or to DHHS if they believe their medical information has been misused, patients do not have the right to sue under HIPAA. Thus, health information obtained as part of medical screening examinations can legally be used for the public health purpose of monitoring exposure, and this does not require that individual patients be notified when the results are shared. However, the performing of additional tests, even if not billed to the patient, does require patient approval. Thus the CHAMP needs to embrace a comprehensive directive to physicians and patients alike to obtain willing participation and sharing. The agency that monitors CHAMP results, most likely a state health department, already has guidelines regarding privacy. Difficulty would arise if the responsibility for monitoring the CHAMP data were assigned to a 3rd party. Who would then have the responsibility for assuring privacy of protected health information.

Risk Perception and Communication

The sustainability and effectiveness of a CHAMP hinges on a rational risk perception by DOE (and its successors), health officials, health providers, and target populations. All of these undergo change, and in some cases (i.e. medical insurance) the change is so rapid that predictions beyond a decade are highly speculative. On the other hand the basic principles of risk perception (Slovic 2000), albeit influenced to some extent by the growing body of scientific understanding, are remarkably stable, and form the basis for planning risk communication programs (Tinker et al 1998). Risk communication will continue to progress, and new formats will be developed for helping people arrive at reasonable personal decisions regarding health hazards, both environmental and lifestyle (Burger et al. 2003).

IMPLEMENTATION ISSUES

To provide a meaningful contribution to a stewardship program, CHAMP has to provide value added, contributing information that cannot be obtained elsewhere.

Quality control: the engineered system involving containment and monitoring has to be sensitive enough to detect failure at the earliest stage and has to be sustained at an effective level. There is high likelihood of future breakdowns in maintenance and inspection hence CHAMP provides a backup assessment that can identify a quality control breakdown.

A Home for a CHAMP

Our assessment of CHAMP leads to the conclusion that it cannot be a stand alone program but must be integrated with one or more existing health programs. Accordingly we examined how CHAMP could relate a variety of existing programs, for example, the National Health and Nutrition Examination Survey (NHANES) conducted annually by the National Center for Health Statistics of the Centers for Disease Control and Prevention. The NCHS has proven sustainable over the past 40 years, despite political attempts to weaken it, and NHANES has become a valuable and widely used source of information on health status and biomarkers in a representative population.

CHAMP could also become part of routine medical care and preventive services provided by private practitioners in a target area. This would require briefing the physicians on the importance of such a program, and assurance of appropriate funding to perform and interpret the test results. The Institute of Medicine Committee chaired by B.D.Goldstein (one of the founders of CRESP) (IOM 1988) foresaw an increased role for primary care physicians in the recognition and prevention of illnesses related to the environment. This recognized the existing fragmentation of preventive medicine, as well as the lack of incentives for expanding the very small cadre of physician specialists. IOM (1988) recommended incentives to increase the recognition of environment in medical education, training and practice. Although realization of the recommendations has been slow, it remains true today, about 20 years later, that the number of specialists is static, and that any improvements in screening populations for exposure or effects, will have to come from primary care physicians. Therefore the movement to expand medical training in the areas of clinical prevention, including environmental medicine, offers the promise of better trained physicians in the future.

The feasibility of the latter depends in large measure on the health care environment in the vicinity of a site. Health care varies greatly across the country. The financing of health care and the rise of manage care has claimed to increase reliance on preventive services as a means of reducing overall health costs. Although the success of this venture remains to be seen (Gochfeld et al. 2000), the opportunity afforded by a prevention-oriented medical care system, would be a fertile base for CHAMP.

Selection of Biomarkers

DOE has invested substantial research funding into developing biomarkers, particularly for worker populations (Mendelsohn et al. 1998). In its broadest sense a biomarker is anything that can be measured (even semi-quantitatively) to provide information. Biomarkers are divided into three classes: biomarkers of susceptibility, biomarkers of exposure, and biomarkers of

effect. One of the best known examples is lead. Measurement of lead in the blood is a biomarker of exposure. Measurement of erythrocyte protoporphyrin or delta-amino levulinic acid in urine are biomarkers of effect. Biomarkers of susceptibility are mainly genetic, and are not currently used in monitoring programs, although the rapid advances in toxicogenomics is likely to change this within the next generation.

For radionuclide exposures, the actual measurement of the radionuclide or its decay product are the usual biomarkers of exposure. For most radionuclides the effects of concern are cell damage or cancer initiation related to the alpha, beta, or gamma emissions, the pathophysiologic effects will be common to all radionuclides (non-specific), dependent mainly on the dose and the energy of their emissions.

New technologies have greatly expanded the kinds of biomarkers that can be measured in individuals and populations (table 8), and many are described in the review volume edited by Wilson and Suk (2002). Although none of the 37 papers deal with radiation or radionuclides, but many of the techniques, for instance proteomics and signal transduction pathways, may prove suitable for radiation monitoring in the future. The biomarkers offer great promise for most metals, for polychlorinated aromatics and for polyaromatic hydrocarbons, with growing attention paid to neurotoxic and endocrine disruptive chemicals.

Table 8. Summary of selected biomarkers and their utility for providing reassurance or detecting exposure.

Exposure Biomarkers	**Obtaining specimens and compliance**	**Sensitivity**	**Specificity**	**Utility**
Whole-body counting	not easy, use for known exposure	good	high to detect gamma but doesn't distinguish	Low
Urinalysis and mass spectroscopy	Easy	good, depends on MDA	high	high
Glycophorin-A	Simple blood test but storage and testing can be complicated	Moderate for total radiation; used at Sellafield. Must be heterozygote to being with	Moderate	Low
Radiochemical Analysis of teeth	Relatively easy	Moderate	High for rad, lower for type	Moderate
EPR of teeth	Relatively easy	Moderate	High for rad but low for type	High
Hair analysis	Easy	Moderate	Good for uranium, also total alpha screening	High
Outcome Biomarkers				
Genetic markers	Difficult for population studies, many legal and ethical issues.	Good for total radiation, not for specific radionuclides	Double-strand breaks are relatively specific to radiation	A future topic – not ready for general population surveys
Cancer registry	All states collect data,	Very low and after the fact	High for radiation-caused cancers	Low, but data are collected anyway
Birth Defect Registries	Routinely collected	Low	Low	Not good early indicator

Site Specific Source Identification

In the event that the CHAMP detects increased concentrations or frequencies of detection of radionuclides or other key targeted analytes, in its human biological sampling, these data must be linked to the other monitoring elements in the sustainable vision (Figure 1). A standardized

process for investigating the potential source is necessary, to assure that concerns are adequately evaluated, and that the pathway is identified and corrected. This may require coordination with DOE, local and/or state health and environmental authorities, ATSDR, EPA and members of the public.

The process, while targeted to potential DOE-offsite contamination, should also consider the possibility of a non-DOE source of contamination (i.e., global or regional fallout, contaminated food from non-local sources, etc.). It should include data triggers for investigation and communication, as well as information triggers for investigation closure or need for continued monitoring. The investigative process may include a) validation of initial findings in the index cases, b) assessment of exposure concentrations in other family members of the same household; c) geospatial and temporal mapping of off-site findings – of both positive and negative samples – for evidence of clustering, d) assessment of DOE on-site pathways and barriers known to be proximate to the off-site findings; e) evaluation of drinking water sources of positive cases (well water and/or community water); f) assessment of dietary habits of positive cases and, if local milk or crops are potentially involved, assessment of those items for the presence of contamination; and g) analysis of patterns in comparative groups (NHANES, "sister cities", etc.). The process should be designed to minimize time and cost, yet maximize information needed to identify source or resolve the issue – both from scientific and public relations perspectives.

Clinical Findings

Experience gained from a number of community monitoring programs indicate the clinical findings gained during the history, physical examination, and office testing (as distinguished from laboratory testing), are useful for certain types of exposure. History can reveal changes in exposure, for example, changes in the taste or discoloration of tap water particularly emanating from private wells. Physical examination may detect skin conditions, related to direct exposure to irritants or allergens. Palpation of the thyroid may be the first indication of a change in size and function or the presence of a cancerous nodule. Moreover, the clinical encounter provides the opportunity for the exchange of information which may alert the practitioner to a nascent exposure or condition---and prompt inquiries directed to subsequent patients from the same community. On the other hand the exigencies of medical practice and financing, have constrained the amount of time allotted to a medical history or to the non-targeted physical examination. This places a burden on a patient to become informed about potential exposure-related findings and bring them to the attention of the physician.

Cost

In general a medical monitoring program can be costly, particularly if it relies on high level, high paid professionals. The costs can be divided into two components: the cost of obtaining a sample and performing the analysis, and the cost of incorporating the screening into existing programs and follow up on both negative and positive results. This phase of CHAMP did not analyze the costs.

CONCLUSION

As secondary prevention a CHAMP would play a quality assurance role, a last line of detection, for the primary preventive engineering and monitoring controls. Due to sensitivity constraints, human monitoring alone does not suffice to assure the early detection of failure or leakage. But human monitoring is essential to provide the assurance and peace of mind that the public, or certain large segments of the public, require. A stand alone CHAMP is unreasonable and unsustainable, but CHAMP can be incorporated into existing epidemiologic and health care systems, and predicted changes in the health care system will increase the feasibility of CHAMP. The expansion of routine clinical monitoring of patients to include some CHAMP biomarkers, will require that clinicians of the future understand the role of these markers and how to interpret them, both to their individual patients, and to those responsible for Long-term Stewardship. Thus a CHAMP must include a built-in, ongoing education component, with appropriate materials for both clinicians and patients. And there must be procedures for reviewing and revising both the materials and the biomarkers, in the light of new knowledge.

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APPENDICES

APPENDIX A NHANES

The National Health and Nutrition Examination Survey

1. Organization: The National Health and Nutrition Examination Survey (NHANES) is a Program within the National Center for Health Statistics (NCHS), which is part of the Centers for Disease Control and Prevention (CDC) OF THE U.S. Public Health Service.

2. Major **NHANES** objectives *(italics* added):
    - To estimate the number and percent of persons in the U.S. population and *designated subgroups* with selected diseases and *risk factors*;
    - To monitor trends in the prevalence, awareness, treatment and control of selected diseases;
    - To *monitor the trends* in risk behaviors and environmental exposures;
    - To analyze *risk factors* for selected diseases;
    - To study the relationship between diet, nutrition and health;
    - To explore *emerging public health* issues and new technologies
    - To establish a national probability sample of genetic material for future genetic research;
    - To establish and maintain a national probability sample of baseline information on health and nutritional status.

3. Operation: **NHANES** studies the health and nutritional status of adults and children in the United States. It was preceded by the U.S. National Health Survey program, established in 1956, was a series topical health surveys that has evolved into interviews, physical examinations and laboratory testing of a representative sample of about 5,000 to 5,500 people per year (there are 11,039 people in the 2001-2002 survey). It performs surveys through mobile examination stations that are moved to the target populations – and also provides household assessments for the convenience of individuals who have impaired mobility.

4. Survey Design: stratified, multistage probability sample. Utilizes concept of primary sampling units (PSUs), which consist of counties or groups of adjoining counties. PSUs are further refined into segments, households within segments, and one or more participants within the selected households.

5. Content of the assessment:

Detailed interviews (demographic, socioeconomic, reproductive, occupational, dietary, health status);
*General Examinations (*medical, dental*);*
Mental Health Assessment (anxiety, depression, panic disorders, eating disorders*, ADHD*, conduct disorders*)*
*Physiologic measurements (*bioelectrical impedence, ankle brachial blood pressure index, peripheral nerve conduction, selected muscular strength measures, visual acuity and fields, pulmonary function, auditory acuity, etc.);
Laboratory Tests – hematology, clinical chemistry, hormone profiles, nutritional biochemistries, environmental* biomonitoring (including VOC badge, blood and urine tests, hair analyses, etc.), smoking indicators (cotinine) latex allergy test, infections and diseases**

A host of health risk factors are routinely evaluated – including smoking, alcohol, medications, fitness (including the wearing of a physical activity monitor), weight, diet (food frequency questionnaire), occupation, family history general environment, and prior disorders.

*Common chemical environmental indicator tests (#of chemical measured) include:

Blood lead
Erythocyte Protoporphyrin
Mercury (hair, urine, blood)
Acrylamimde
Selenium
Arsenic (urine)
Iodine (urine)
VOCs in 48 hour personal air sampling badges (13), in home tap water (5), and in blood samples (32)
Phthalates (7)
Organophosphate metabolites
Metals (13)
Nonpersistent pesticides
Persistent pesticides
Phytoestrogens (8)
PAHs (16)
Dioxins
Lead Dust

**Infection-related tests include:

HIV antibody and CD4 counts
Measles/Varicella/Rubella Abs
Toxopolasma
Cryptosporidium
Helicobacter pylori
Hepatitis (A,B,C,D HbSAg, AntiHBs)
Chlamydia (urine)
Gonorrhea (urine)
BV/Trich
TB skin test (PPD S-1 and the non-tuberculous mycobacterial antigen PPD-B)

APPENDIX B USPSTF and BMJ

The New U.S. Preventive Services Task Force (USPSTF)
http://www.ahrq.gov/clinic/uspstfab.htm
and BMJ: Clinical Evidence from British Medical Journal
http://www.clincalevidence.org

The U.S. Preventive Services Task Force (USPSTF), first convened by the U.S. Public Health Service in 1984, and since 1998 sponsored by the Department of Health and Human Service's Agency for Healthcare Research and Quality (AHRQ), is the leading independent panel of private-sector experts in prevention and primary care. The USPSTF conducts rigorous, impartial assessments of the scientific evidence for the effectiveness of a broad range of clinical preventive services, including screening, counseling, and preventive medications. Its recommendations are considered the "gold standard" for clinical preventive services.

The mission of the USPSTF is to evaluate the benefits of individual services based on age, gender, and risk factors for disease; make recommendations about which preventive services should be incorporated routinely into primary medical care and for which populations; and identify a research agenda for clinical preventive care.

The BMJ Clinical Evidence identified itself as "The international source of the best available evidence for effective health care." It goes far beyond screening into the realm of therapeutics.

Both of these sources epitomize evidence-based medicine, and both tend to be very conservative, before advocating particular screening approaches. CRESP has reviewed both sources to ascertain that neither emphasizes screening for exposure in general, much less to environmental contaminants such as radionuclides. The principles that govern these processes remain important, but neither has demonstrated relevance to detection of radiation of chemical exposures.

APPENDIX C Sensitivity, Specificity and Predictive Value

The following text has been included in the body of the report, but the examples are given here.

Interpreting any test or study hinge on sensitivity and specificity. These are broad ranging concepts which have particular impact on interpreting any kind of screening program. Sensitivity is the ability of a program or test to detect whatever it is looking for. Specificity is the ability of a program or test to detect only what it is looking for. In other words, sensitivity is the ability of a test to be positive when it should be positive (i.e. a true positive, when the condition or exposure actually exists), and specificity is the ability of a test to be negative when it should be negative (i. e. a true negative is when the condition or exposure does not exist).

These are often depicted as follows with the **boldfaced entries** being desirable outcomes.

	Exposure has occurred	Exposure has not occurred	
Test for exposure is positive	**TRUE POSITIVE**	FALSE POSITIVE	All positives
Test for exposure is negative	FALSE NEGATIVE	**TRUE NEGATIVE**	All negatives
	TP + FN	FP + TN	

Sensitivity is defined as TP/(TP+FN)
Specificity is defined as TN(TN+FP)

Actually we can only measure sensitivity and specificity accurately when we have an independent measure of whether the exposure has or has not occurred (or whether a particular condition is or is not present). This independent measure is called a gold standard. Often it is another kind of test that is either more inconvenient, more invasive, or more expensive, than the screening test that is being compared. Often, however, there is not gold standard, and one can only make an educated guess about sensitivity and specificity.

But there is another measure that is actually of greater immediate interest. If there is a positive test, how likely is it that it is a true positive. This is called the positive predictive value, or the proportion of all positives that are true positives

Positive Predictive value is TP/(TP+FP).
Negative Predictive value is TN/(TN+FN)

There is a fourth consideration that influences predictive value, that is the underlying prevalence or frequency of the condition being sought. When the condition occurs in half the population, then the predictive value is quite high, but when the condition is rare, then the proportion of positive tests that are false positives inevitably rises. This is illustrated in Appendix C.

Scenario 1. The biomarker test for exposure has 99% sensitivity and 99% specificity, and the population of 2000 people has 50% exposed. The test is given to identify who is exposed and who is not exposed so appropriate treatment can be given

SCENARIO 1	Exposure has occurred in 1000 people	Exposure has not occurred in 1000 people	
Test for exposure is positive	99% test positive=990 TRUE POSITIVE	1% test positive =10 FALSE POSITIVE	1000 positives of which 990 are True Positives
Test for exposure is negative	1% test negative=10 FALSE NEGATIVE	99% test negative=990 TRUE NEGATIVE	1000 negatives of which 990 are True Negatives
	TP/(TP + FN)=99%	TN/(FP + TN)=99%	

Of 1000 positives tests 990 are true positives yielding a positive predictive value of 99%.
Of 1000 negative tests 990 are true negatives yielding a negative predictive value of 99%.

Scenario 2. Sensitivity and Specificity are only 90%, but there are still 50% exposed in a population of 2000.

SCENARIO 2	Exposure has occurred in 1000 people	Exposure has not occurred in 1000 people	
Test for exposure is positive	95% test positive=950 TRUE POSITIVE	5% test positive =50 FALSE POSITIVE	1000 positives of which 950 are True Positives
Test for exposure is negative	5% test negative=50 FALSE NEGATIVE	95% test negative=950 TRUE NEGATIVE	1000 negatives of which 950 are True Negatives
	TP/(TP + FN)=95%	TN/(FP + TN)=95%	

In this case the positive and negative predictive values are 95%.

Scenario 3. Again we will use 99% sensitivity and specificity, but we will reduce the underlying prevalence of exposure from 50% to 10%.

SCENARIO 3	Exposure has occurred in 100 people	Exposure has not occurred in 1900 people	
Test for exposure is positive	99% test positive=99 TRUE POSITIVE	1% test positive =19 FALSE POSITIVE	118 positives of which 99 are True Positives
Test for exposure is negative	1% test negative=1 FALSE NEGATIVE	99% test negative=1881 TRUE NEGATIVE	1882 negatives of which 1881 are True Negatives
	TP/(TP + FN)=99%	TN/(FP + TN)=91%	

When the exposure is uncommon, the positive predictive value declines from 99% to 84% even though sensitivity and specificity remain high.

Scenario 4. Takes the prevalence from 10% to 1% i.e. exposure is now rare.

SCENARIO 4	Exposure has occurred in 10 people	Exposure has not occurred in 1990 people	
Test for exposure is positive	99% test positive=10 TRUE POSITIVE	1% test positive =20 FALSE POSITIVE	30 positives of which only 10 are True Positives
Test for exposure is negative	1% test negative=0 FALSE NEGATIVE	99% test negative=1970 TRUE NEGATIVE	1970 negatives of which all are True Negatives
	TP/(TP + FN)=95%	TN/(FP + TN)=95%	

It is apparent that when exposure becomes rare the positive predictive value of a single test declines even to the point where most positives are false positives.

APPENDIX D Paramagnetric Resonance and Tooth Dosimetry for Ionizing Radiation

Electron paramagnetic resonance (EPR) provides the opportunity for retrospective dosimetry of ionizing radiation. The technique was first recognized in the late 1960s, and its first application to human populations was for atom bomb survivors in Japan (Ikeya et al. 1984). The technique is also called electron spin resonance. It depends on the following properties of the hydroxyapatite (HA) matrix of bone and teeth. Since hydroxyapatite forms about 95% of dental enamel, it is tooth enamel that is the most reliable basis for EPR. During mineralization, carbonate ions replace phosphate ions in the crystalline structure of HA. Ionizing radiation striking the tooth causes the carbonate ions to capture electrons to form free-radicals with unpaired electrons in the matrix. The number of free radicals is directly correlated with the radiation dose. Radicals generated in soft tissue disappear, but those generated in a calcifying tooth are trapped essentially permanently. When the tooth is exposed to electromagnetic energy in the microwave range, there is a change in energy state of the unpaired electrons, resulting in a signal, which is linear over much of the ionizing radiation dose (i.e. from 200 mGy to 10 kGy).

The advantages of EPR in teeth is the relative ease with which teeth can be collected, either in the process of tooth replacement in children, or through dental practices including orthodontia. In the appropriate laboratory there is a high degree of analytic precision. Preparation requires cutting the tooth, washing with sodium hydroxide, and pulverizing it. The analytic procedure is sensitive to the geometry of the target, which must be considered in calibration. This is sufficiently sensitive that adult molars and incisors require separate calibration. Since the front teeth are exposed to sunlight, which can contribute a cumulative dose of up to 200 mGy, they are not considered appropriate for dosimetry. Application of EPR to the Techa River population near the Mayak fuel recycling facility in Russia, allowed not only dose reconstruction, but separate information on background, internal, and external radiation exposure.

There are significant limitations whether in any locality there would be sufficient background information to reveal a signal from a low level environmental source and the lack of test specificity. EPR will detect effects of Xray, alpha, gamma, beta and protons. Individual history of medical and dental Xrays may overwhelm any environmental signal, particularly since Xrays are about 2.5 times more potent than gamma rays in producing the radicals. The free radical generation occurs at the time that the tooth is forming and calcifying, so each tooth provides a historic record that depends on the age of the participant at the time of exposure. Nakamura et al. (1998) compared the EPR signal in the front of teeth (exposed to dental Xrays) and the back of teeth (not directly exposed), and found no difference in molars, suggesting that dental Xrays were not a major contributor to the signal in molars.

There are two “background” issues during EPR. One is the non-specific background signal generated when the microwave irradiation strikes the target. The second is the actual effect, or radicals, generated by historic radiation exposure. The first can be identified by reading the signal using both low and high microwave energies. The second is part of the signal and can be identified by analyzing teeth from an unexposed population.

Although the main problem recognized by Desrosier and Romanyukha (1998) was to perform dose reconstruction for individuals, the use of EPR in CHAMP would actually be simpler. Any exposure above background, occurring in multiple individuals with a target population, would point to an exposure. This would then alert the environmental scientists and engineers to seek the source of radiation.

RESEARCH QUESTION: EPR AND RISK
In the light of the BEIR VII report that the linear non-threshold model is still the best model for radiation risk, a signal above background would signify a risk above background (BEIR VII).

Improvements in electronics and the comparison of two or more spectra derived from two different microwave frequencies, has improved the signal to noise interpretation of EPR. However, its application to individual dosimetry remains to be demonstrated. The most likely application of EPR would be to establish dose in a population with a known likelihood for radiation exposure above background, for example, atom bomb survivors, Chernobyl liquidators and surrounding population, and Mayak workers and communities. EPR could then be used to circumscribe an exposed population.

Application of EPR in a CHAMP context would require
1) Identify the target population within an agreed upon area around a legacy waste management site.
2) Establish background levels by obtaining a representative sample of teeth (preferably molars or pre-molars.
3) Identify source(s) of exposure

The utility of EPR lies in periodic resampling of a population. Since the power of a tooth surveillance program depends on the magnitude of the change (i.e. the likelihood of distinguishing signal from noise), it is difficult to determine an a priori sample size. One could argue conversely, that unless the signal is large enough to be seen in a small population, it is not likely to be significant or traceable to a containment failure.

EPR has mainly been used to quantify dose in a population with known exposure. But it can also be used to detect exposure in a population whose background signals are well established, through a comprehensive baseline assessment. This would require obtaining at least one hundred teeth from a putative target population and 100 teeth from an unexposed population. At point 0, the readings should be the same.

Repeating the survey at 5 or 10 year intervals, would be one technique, but it would be more reasonable to conduct a Tooth Fairy project in which all deciduous teeth are collected from parents, the age and residence of the children documented, and the teeth archived, until a time when the EPR study can be conducted.

BEIR VII – Phase 2. 2005. Health Risks From Exposure to Low Levels of Ionizing Radiation. Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation, Board of Radiation Effects Research, National Research Council. National Academy of Sciences.

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