Opportunities for Beryllium Health and Safety Research

Rank (1 is high)	Specific Goal	Objective and Description	Direct Benefit	Gap Categories	Yrs (S, M, L)	Likihood of Success	Topic Nos.	Est. $M/ Yr	Progress So Far	Extra- or Intr- Mural	Needed Peer Review Expertise	Possible Interest	Type of Research: Applied / Epi / Basic
									Exposure		Total for Exposure		4.850
Improve sampling methods													
Fine particulates sampling													
2	Develop sampling methods that characterize fine and ultra-fine beryllium particulate exposure.	Develop sampling methods for fine and ultra-fin particulates that deposit in lungs. This item addresses a current worker safety issue. The method would allow researchers to determine the health risk of exposure to fine and ultrafine beryllium particles and allow practitioners to better monitor and control these exposures in the workplace.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	Exposure Measurement Methods	S	H	2	0.4	Size-selective samplers are available but require a personal, high-volume pump. This pump will require an intensive development effort.	E, I	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH and NIOSH	Applied
	Develop sampling methods that characterize beryllium particulate exposure by mass, number, size fraction, chemical form, particle surface area.	Develop sampling methods that characterize beryllium particulate exposure by mass, numbe size fraction, chemical form, particle surface area. This item addresses a current worker safety issue. The method would allow researchers to determine the health risk of exposure measured by various particulate parameters and allow practitioners to better monitor and control these exposures in the workplace.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	Exposure Measurement Methods	M	M		1	NIOSH completed basic analysis of particle agglomeration and surface areas.	E, I	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH and NIOSH	Applied
Real-time monitoring													

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3	Develop promising near real-time monitoring instruments or sampling and analytical methods.	Develop promising intermediate-time, near real-time, and real-time (less than an hour to a few hours) monitoring instruments or sampling and analytical methods. These instruments and methods will improve worker and public protection, improve productivity through reduce production hold times and analytic costs, and reduce the cost of legacy and beryllium area cleaning and monitoring.	Identify and control exposures in the same shift that the exposure begins. Reduce analysis costs and hold times waiting for surface contamination sample results. Focus resources on controlling the greatest risks.	Exposure Measurement Methods	M	H	3, 8	1.15	A number of methods are available; some at prototype stage. Final development to specified sensitivity, specificity, reliability, portability, etc., and validation, is needed. New methods may be needed for some situations such as unique interferents.	E, I	Electrical and mechanical engineering, industrial hygiene, human factors, chemistry, instrument design, statistics, beryllium operations	NNAS, EH and NIOSH	Applied

Skin exposure

6	Develop a method for quantifying skin and mucous membrane exposure.	The method would allow researchers to determine body surface exposures that is necessary to determine whether these exposures contribute to sensitization and disease. The method also would allow practitioners to better control these exposures.	Reduce risk of sensitization and disease.	Exposure Measurement Methods	S	M	6	0.5	Methods are available but need standardization and validation for beryllium.	E, I	Chemistry, industrial hygiene, statistics	NNSA, EH, and NIOSH	Applied

Uncommon surface sampling

12	Develop standardized and validated sampling methods for uncommon surfaces and relevant media.	Develop standardized and validated sampling methods for general and porous surfaces, bulk samples, vacuuming, and other relevant media. Consistent and validated sampling methods for common as well as unusual types of surfaces will provide for better comparison of site conditions as they relate to beryllium exposure.	Improve consistency among sites on the validity of results and on and on identifying risks.	Exposure Measurement Methods	S	H	12	0.5	Methods are available but need standardization and validation for beryllium and for a variety of surface types.	E, I	Industrial hygiene, statistics, beryllium operations, chemistry	NNSA, EH, and NIOSH	Applied

Needed tools.-Exposure

Nanogram analysis

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	Develop and validate analytic methods sensitive to the 0.1 nanogram per sample level of quantitation.	Develop and validate analytic methods sensitive to the 0.1 nanogram per sample level of quantitation. Methods also must speciate between beryllium, beryllium oxide, and various beryllium alloys.	Improve worker exposure characterization by lowering detectable limit on samples.	Exposure Measurement Methods	S	H		0.25	LLNL reports promising new technology using accelerator mass spectrometry for quantifying femptogram amounts of Be isotopes.	E, I	Chemistry, radiochemistry, nuclear physics, industrial hygiene, statistics	NNSA, EH, and NIOSH	Epidemiology
Particle reference materials.													
	Establish the availability of aerosol and particle standard reference materials.	Establish the availability of aerosol and particle standard reference materials. Similar to NISTstandard reference materials. Various chemical forms, sizes, surface areas.	Needed to conduct research on improved sampling methods and beryllium toxicology in animal studies.	Exposure Measurement Methods	S	H		0.1		E	Metallurgy, industrial hygiene, statistics, particle physics, beryllium operations	NNSA, EH, and NIOSH	Epidemiology
Size-selective sampling.													
2	Identify or develop a high volume personal pump.	Provide a high volume personal pump.	Improve worker exposure characterization by collecting detectable amounts of fine particulate .	Exposure Measurement Methods	S	H	2	0.1	Demand has some vendors developing prototypes.	E, I	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH, and NIOSH	Applied
Use improved methods													
Different activities													

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	Determine the types of exposures that are generated by different types c activities.	Characterize the different types of exposures i concentrations in terms of mass, particle number, particle-size fractions, surface area, and chemical form.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	Exposure Measurement Methods	M	H		0.5	Limited progress with characterizing particle number exposure at Brush Wellman facilities.	E, I	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH and NIOSH	Epidemiology
Exposure correlates													
	Determine which exposure parameters correlate with each other at different times and workplaces.	Determine which exposure parameters correlat with each other at different times and workplaces so that the most convenient parameter can be monitored, e.g., mass, number, size fraction, chemical form, particle surface area.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	Exposure Measurement Methods	M	H		0.25	A great deal of mass exposure data exists and a very small amount of particle number exposure data exits.	E, I	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH, and NIOSH	Epidemiology
Risk characterization													
	Use of improved methods (e.g., sampling by mass, number, size fraction, chemical form, particle surface area and using real-time and nanogram analysis) to better characterize exposure risks in current DOE operations.	Use the improved methods to better characteriz exposure risks in current DOE operations. Includes conducting more effective (focused o highest risks and more timely) sampling of current beryllium operations across the complex. The information will be used to understand if operations are being controlled adequately and which operations are of greate concern.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	Exposure Measurement Methods	S	H		0.1	Size-selective samplers are available but require a personal, high-volume pump. This pump will require an intensive development effort.	E, I	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH and NIOSH	Applied

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Controls — Total for Controls 1.250

Develop improved controls.

DOE-wide controls

7	Develop improved engineering and administrative controls having DOE-wide application for beryllium operations, maintenance and construction activities.	Develop control technology for use by DOE complex. Document engineering controls and exposure data including efficiency and effectiveness. Operations that will benefit the most sites will be given preference. This item will provide better engineering controls for non-routine operations. For instance, a vacuum cleaner designed to prevent release of contaminants during maintenance would significantly reduce the risk of exposure to maintenance personnel at virtually all DOE beryllium sites.	Reduce exposure risk, increase worker safety.	Workplace Risk Factors	L	H	13	0.5	Efforts are on-going but need dedicated resources and recognition to continue.	E, I	Beryllium operations, metallurgy, variety of engineering (i.e., electrical, mechanical, ventilation) industrial hygiene	NNSA, EH, and NIOSH	Applied
15	Develop a coating technology to mitigate particulate aerosol releases from surfaces.	This research aims to limit worker exposure by coating beryllium-containing or beryllium-contaminated items with a film that prevents beryllium release from the item. It will limit both inhalation and skin exposure. The result of this research will be a form of engineering control (skin exposure which is preferable to the common administrative control of wearing glov	Increase worker safety and improve productivity by coating to reduce exposure and analysis costs and hold times needed to establish cleanliness.	Workplace Risk Factors	S	M	17	0.25	Some technologies are available for general sealing and waste disposal but they require validation. Other technologies may be need to be developec	E, I	Beryllium operations, metallurgy, coatings chemistry, industrial hygiene	EM and NNSA	Applied

Needed tools.-Controls

Surface level risk

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11	Determine the relationship between surface contamination and health risk.	This item will identify and/or develop models to determine the worker exposure that will result from various activities that disturb contaminatio on a surface. Existing models, e.g., for lead contaminated dust in dwellings and radioactive particulates in DOE facilities, will be evaluated for relevance. The relevant existing or newly developed models will be validated for beryllium contamination. This effort will determine what, any, surface levels constitutes a health risk.	Increase worker safety and provide the basis for health-based decisions for managing beryllium contaminated items and spaces.	Workplace Risk Factors	S	H	16	0.5	A few efforts failed t establish relationship. Additional effort is needed to either establish the relationship) or validate that none exist.	E, I	Physics, statistics, industrial hygiene, occupational medicine	NNSA, EH, and NIOSH	Applied

Health Effects — Total for Health Effects 8.500

Diagnosis.

Disease in general public.

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9	Determine the prevalence of sensitization and disease in the public. Include support personnel around beryllium operations. Consider smoking. Include natural and other non-occupational exposures.	This item will determine if individuals in the general population have sensitization or diseas and if that correlates with ubiquitous sources c exposure such as power plant flash or cigarett smoke. This will provide an understanding of th differences in worker occupational exposure versus ambient exposure to the general population and will allow for better deductive analysis of possible external sources when disease or sensitization is discovered and a plausible work exposure can not be found. Current data exists in several different progran both within and outside of DOE.	Provide basis for sound decisions for managing legacy issues and DOE groups with signs of disease but no plausible work exposure.	Necessary Levels of Protection	S	H	9, 20	0.5	Will require large scope project involving other agencies and cooperation of private clinics. Some exposures to the general population are documented. Additional exposures need to be sought. Correlation of non-occupational exposures to health effects	E	Occupational and public health epidemiology, industrial hygiene, statistics, environmental science, geology	EH and NIOSH	Epidemiology

Improved tests.

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1	Develop and validate improved screening and diagnostic tests, including the identification of genetic factors that relate to risk.	Develop tests that are less invasive to perform, and more predictive of sensitization and diseas than the current tests. Prevent progression to disease. Develop screening tests that are bett predictors of exposure, sensitization, disease. Develop screening tests that are not based on cell proliferation (e.g., accelerator mass spectrometry analysis of specific proteins in blood).	Reduce uncertainty of diagnosis and thereby improve the quality of subsequent decisions. Improve prognosis of disease.	Disease Process, Diagnosis, and Treatment	L	H	1	2.25	A potential improvement to the current screening test has been developed and needs validation. Other tests have yet to be developed. Very little recent progress has been made in therapeutic interventions or specific therapies.	E, I	Genetics, biology, immunology, statistics, pulmonary medicine, statistics, epidemiology.	SC , EH, NHLBI and NIOSH	Basic

Interventions and treatments

	Identify opportunities for therapeutic interventions (pre-CBD) or specific therapies for CBD.	This item is designed to develop new treatment for the disease that could slow or halt the disease process. Since death can occur in the mid-50's with quality of life issues resulting in the 40's, this would allow for patients to resum a more normal life and increase the life expectancy.	Improve quality of life for patients. Allow affected current workers to continue productive work for DOE. Minimize federal liability under EEOICPA.	Disease Process, Diagnosis, and Treatment	L	M	14	0.75	Removal from exposure and steroid treatments are available but do not appear to help many patients.	E	Genetics, biology, immunology, statistics, pulmonary medicine, statistics, epidemiology.	SC , EH, NHLBI and NIOSH	Basic

Disease process.

Dose-response.

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	Determine the dose response relationship for beryllium sensitization and disease for different exposure parameters, i.e., mass, number, size fraction, chemical form, particle surface area.	Determine the dose-response relationship for beryllium sensitization and disease for different exposure parameters, i.e., mass, number, size fraction, chemical form, particle surface area.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	Disease Process, Diagnosis, and Treatment	L	M		0.75	A number of workplace and community epidemiology studies have been published. All suffer from weak exposure data.	E	Pulmonary medicine, statistics, epidemiology, industrial hygiene	EH , NHLBI, and NIOSH	Epidemiology

Natural history of disease.

13	Determine the natural history of beryllium disease: sensitization to disease; different rates of progression; workers and public; include non-occupational exposures; risk factors e.g., genetics, underlying disease, gender, age, smoking.	Determine time frames of progression from initial exposure to disease using statistical analysis of existing clinical data. There are thre groups of patients, those that do not progress i symptoms, those who progress but CBD is not the reason for death, and those who progress rapidly and die of CBD. The reason for the differences is unknown. This research will provide the knowledge needed for developing intervention and treatment options to reduce or eliminate disease progression.	Improve disease management. Intervene to minimize or prevent symptoms.	Disease Process, Diagnosis, and Treatment	L	L	13	0.1	Some studies are completed but are for small populations. Some clinician experience is available but is not published. More and larger published studies are needed.	E, I	Pulmonary medicine, epidemiology, industrial hygiene	EH , NHLBI, and NIOSH	Epidemiology

Pharmacokinetic model.

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5	Characterize and determine the health significance of the physiochemical properties of beryllium. Determine the bioavailability of beryllium at different locations in the body; the health impacts at those locations and the impact on remote organ systems.	Develop and validate a pharmacokinetic model of beryllium in the body using both in-vitro and i vivo techniques. The model will describe the body's immunological response to beryllium. It will include exposure to skin, mucous membran and respiratory tract as well as lungs. It will assist in confirming that beryllium is deposited i lungs, in determining the location of the deposits, and possibly identify the form of beryllium that is deposited. The model will assist in developing improved diagnostic techniques, intervention and treatment options, and identifying the form of beryllium that is the most important workplace risk factor to control.	Provide better understanding of disease leading to better control, prevention, diagnosis, intervention, and treatment.	Disease Process, Diagnosis, and Treatment	M	M	5, 22	1.25	Some early research is complete. Efforts are hampered by lack of an animal model. Diagnostic techniques exist but are intrusive and not sufficiently reliable.	E, I	Cellular biology, physical chemistry, pharmacokinetics, biology, biopsy tissue analysis, pulmonary medicine	SC, EH, NIEHS, and NIOSH	Basic

Needed tools.-Health Effects

Animal model and cell line

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4	Develop an animal that models human CBD by contracting the disease after exposure to beryllium.	An animal model is needed to test hypotheses disease pathways for both skin and lung exposure, determine its natural history, understand genetic components of the susceptibility to disease, and to test intervention and treatment options.	Provide better understanding of disease leading to better control, intervention, and treatment.	Disease Process, Diagnosis, and Treatment	M	M	4	0.5	LBL has developed a genetically altered mouse that exhibits beryllium sensitivity. Testing for chronic beryllium disease (CBD) is needed. Other genes or animals may be needed if CBD does not develop in this mouse.	E, I	Genetics, immunology, statistics	SC and NIEHS	Basic

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	Develop a human cell line that responds to beryllium.	A human cell line is needed to test hypotheses of disease pathways for both skin and lung exposure, determine its natural history, understand genetic components of the susceptibility to disease, and to test interventio and treatment options.	Provide better understanding of disease leading to better control, intervention, and treatment.	Disease Process, Diagnosis, and Treatment	M	M	4	0.5		E, I	Genetics, immunology, statistics	SC and NIEHS	Basic
Definitions and protocols													
	Define the natural history of beryllium disease.	Establish standard definitions for sensitization and disease.	Provides essential accuracy and consistency necessary for researching and managing beryllium health effects.	Disease Process, Diagnosis, and Treatment	S	H	13	0.05	Some definition are available in references but are not widely accepted by clinicians.	E	Genetics, biology, immunology, statistics, pulmonary medicine, statistics, epidemiology.	SC , EH, NHLBI, NIEHS and NIOSH	Basic
	Establish standard clinical definitions and protocols for determining sensitization and disease.	Establish standard protocols for determining sensitization and disease.	Provides essential accuracy and consistency necessary for researching and managing beryllium health effects.	Disease Process, Diagnosis, and Treatment	S	H		0.05	Some protocols are available in references but are not widely accepted by clinicians.	E	Genetics, biology, immunology, statistics, pulmonary medicine, statistics, epidemiology.	SC , EH, NHLBI, NIEHS and NIOSH	Basic
Detection in tissue, biomarkers													

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	Develop in-vitro and in-vivo technologies for detecting beryllium in tissue.	Develop in-vitro and in-vivo technologies for detecting beryllium in tissue	Needed to conduct research into fate o beryllium in the body. Increase sensitivity of screening workers for beryllium exposure.	Disease Process, Diagnosis, and Treatment	M	H	21	0.5		E, I	Cellular biology, physical chemistry, pharmacokinetics, biology, biopsy tissue analysis, pulmonary medicine	SC , EH, NHLBI, NIEHS and NIOSH	Basic
	Identify biomarkers of exposure such as molecules in serum that indicate exposure, sensitivity, disease.	Detect beryllium in tissue or other body component. May require ultra-sensitive analyti methods such as accelerator mass spectrometry.	Increase sensitivity of screening workers for beryllium exposure. Needed to conduct research into fate o beryllium in the body.	Disease Process, Diagnosis, and Treatment	M	M	1	0.5	LLNL reports promising new technology using accelerator mass spectrometry for quantifying femptogram amounts of Be isotopes.	E, I	Chemistry, radiochemistry, nuclear physics, industrial hygiene, statistics	NNSA, EH, and NIOSH	Epidemiology
Disease registry													
	Develop a nationwide beryllium registry for all sensitized and CBD individuals.	Develop a nationwide beryllium registry for all sensitized and CBD individuals. This may aid in determining the genetic risk factors for increased risk among ethnic populations.	Allow DOE to inform workers of risk factors before the workers are exposed.	Disease Process, Diagnosis, and Treatment	M	L	16	0.25		E	Pulmonary medicine, statistics, epidemiology, industrial hygiene	EH , NHLBI, and NIOSH	Epidemiology
Risk communication													

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	Determine effective means for communicating beryllium risk.	Determine effective means for communicating beryllium risk so that workers obtain sufficient understanding to make informed decisions concerning employment and medical screening.	Maximize workforce productivity by workers understanding their risks.	Disease Process, Diagnosis, and Treatment	S	M		0.05	Occupational health risk models are available to evaluate and modify.	E, I	Pulmonary physicians, industrial hygienists, ethicists, editors, graphic artists, risk communication specialists.	EH, NNSA, EM	Epidemiology
Tissue repository													
1	Develop a nationwide tissue repository (library) of samples obtained from beryllium sensitized and diseased patients.	To have a library available so that all researche have access for various research projects. Access to tissues currently is limited to those who have patients with sensitization or disease or those who can obtain the tissue through collaboration. This item is designed to allow for any researcher to be able to work on the beryllium problem by providing samples of tissues obtained from sensitized and diseased patients. Bio-specimens also needed from people who were exposed but not sensitized o diseased, and are unexposed.	Improve understanding of disease by increasing the number of researchers who are able to work the problem.	Disease Process, Diagnosis, and Treatment	L	H	18	0.5	Funds have been transferred from DOE/EH to NIH/National Heart and Lung Institute to establish the repository. Cooperation of clinics and patients is needed.	E, I	Blood and tissue medicine.	EH and NHLBI	Epidemiology
				Total for All				14.600					