Overview of the Division of Laboratory Sciences National Center for Environmental Health

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

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Mission

Mission:

Provide laboratory support that improves the detection, diagnosis, treatment, and prevention of environmental, tobacco-related, nutritional, newborn, selected chronic, and selected infectious diseases.

Provide laboratory support that improves the rapid and accurate detection of chemical threats, radiologic threats, and selected toxins.

Planning Strategies

To accomplish its mission and goals, the Division of Laboratory Sciences (DLS) includes nine strategies in its planning process:

1. **Congressional, U.S. Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC), and National Center for Environmental Health (NCEH) requirements:** Meet mandates and requirements from Congress, HHS, CDC, and NCEH.
2. **Health impact:** Be certain that the public health impact of DLS laboratory efforts is substantive.
3. **Quality:** Assure consistent, high-quality laboratory measurements as part of every planned project.
4. **State support:** Assure that needs of state and local laboratories receive high priority.
5. **Gap analysis:** Regularly conduct gap analyses to identify public health laboratory needs not being met.
6. **Low-hanging fruit:** Regularly look for low-cost efforts that have a relatively high impact on health.
7. **Leverage efforts:** Leverage DLS efforts by collaborating with federal and other partners.
8. **Integrate efforts:** Integrate DLS efforts into NCEH/ATSDR, CDC, and HHS initiatives.
9. **Efficiency:** Use DLS resources more efficiently and effectively.

Goals

National Biomonitoring Program

Goal:
Provide laboratory science that improves the detection, diagnosis, treatment, and prevention of disease resulting from exposure to environmental chemicals.

Tobacco Laboratory

Goal:
Provide laboratory science that helps reduce individual and population exposure to addictive and toxic substances from tobacco products.

Nutrition, Chronic, and Infectious Disease Laboratories

Goal:
Improve the laboratory detection and diagnosis of nutrition-related disease, cardiovascular disease, and other chronic diseases and provide laboratory support for influenza and selected infectious disease projects.

Newborn Screening Laboratories

Goal:
Assure the early and accurate laboratory detection of treatable congenital disorders in newborns.

Chemical Threat Agents and Toxins Laboratories

Goal:
Provide effective laboratory support for the public health response to chemical threat agents and threats involving selected toxins.

Radiologic Threat Agents Laboratory

Goal:
Provide effective laboratory support for the public health response to radiologic threat agents.

National Biomonitoring Program

The National Biomonitoring Program provides laboratory science that improves the detection, diagnosis, treatment, and prevention of disease resulting from exposure to environmental chemicals.

The most comprehensive assessment of the U.S. population's exposure to environmental chemicals

DLS helps assess exposure to environmental chemicals by conducting biomonitoring (measurements in blood and urine) of participants in the ongoing National Health and Nutrition Examination Survey (NHANES). The *National Report on Human Exposure to Environmental Chemicals and Updated Tables* provide the most up-to-date exposure information for more than 300 environmental chemicals in a nationally representative sample of the U.S. population every 2 years. This DLS report helps identify at-risk population groups and assess the effectiveness of interventions to reduce harmful exposures by tracking the presence and amount of environmental chemicals in people over time.

Expanding and improving biomonitoring in states

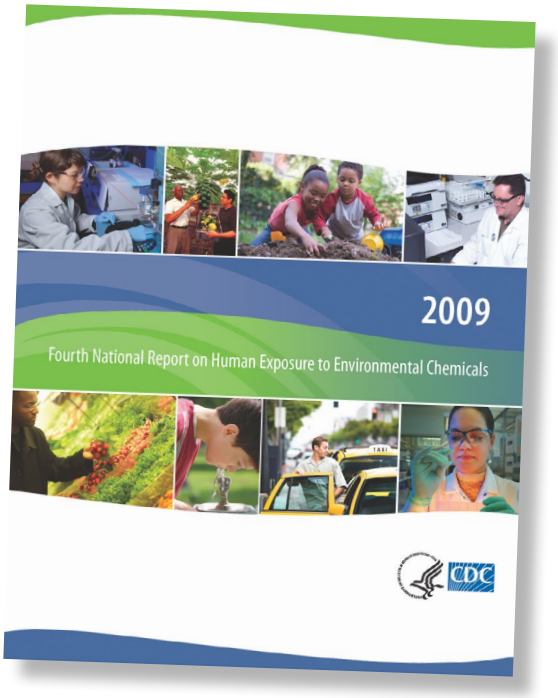
DLS helps states assess environmental exposures in their communities by funding public health laboratories to conduct high-quality biomonitoring. These awards establish substantial laboratory capability and support statewide biomonitoring surveys and projects to assess environmental exposures in vulnerable populations. New Hampshire, New Jersey, New York, Minnesota, Iowa, and Michigan currently receive 5-year funding. DLS also provides expertise, training, and method performance evaluation to state laboratories to support emergency investigations of potentially harmful exposures and improve the quality of biomonitoring nationwide.

Assessing exposures in vulnerable populations

DLS conducts or collaborates in more than 75 studies each year that examine exposures among vulnerable population groups or investigate the relationship between exposure levels and adverse health effects. For these investigations, DLS provides unique, high-quality measurements for priority environmental chemicals, such as poly- and perfluoroalkyl substances (PFAS), bisphenol-A (BPA), speciated arsenic and mercury, volatile organic compounds (VOCs), phthalates, perchlorate, and many others. For example, DLS used state-of-the-art biomonitoring methods to produce the first nationally representative information on exposure to PFAS among U.S. children 3–11 years of age. These baseline data helped identify higher exposures among pre-school and elementary-school aged children and confirmed widespread exposure even among children born a decade after discontinuation of certain PFAS. In addition, DLS is providing laboratory analysis for CDC and the Agency for Toxic Substance and Disease Registry's (ATSDR) flagship investigations of PFAS, which will help provide information about the human health effects of PFAS exposure.

Biomonitoring data impact public health

- **Triclosan removed from over-the-counter liquid soaps:** DLS measurements in human urine since 2003 consistently showed that triclosan, a common antibacterial agent used in many liquid soaps, was detectable in most people in the United States. These data informed the U.S. Food and Drug Administration's (FDA) 2016 rule stopping the use of triclosan and other active ingredients in over-the-counter antibacterial wash products.



Fourth National Report on Human Exposure to Environmental Chemicals, 2009

- **Warning labels on phthalate-containing drugs:** DLS measurements showed the use of certain time-release medications can cause exposures to di-n-butyl phthalate (DnBP) at levels higher than the Environmental Protection Agency's (EPA) reference dose. Since 2010, widely prescribed medications in the United States with DnBP-containing coatings now include cautionary labels about possible adverse effects from use during pregnancy and breastfeeding.

- **Certain phthalates prohibited in products for children:** In collaborative studies with national and international researchers, DLS showed associations between exposure to phthalates and health outcomes. Findings provided evidence for the 2008 Consumer Product Safety Improvement Act, which prohibits the manufacture, import, distribution, or sale of children's toys or care products containing di(2-ethylhexyl)phthalate (DEHP), DnBP, or benzyl butyl phthalate. Follow-up measurements by DLS show the U.S. population's exposure to these phthalates declining since 2001.

- **BPA-free, paraben-free, and phthalate-free consumer products:** DLS data revealed widespread exposure among the U.S. population to BPA, phthalates, and parabens, chemicals widely used in personal and consumer products. Public concern about the health effects of these compounds prompted manufacturers to develop "BPA-free," "phthalate-free," and "paraben-free" products. Subsequent DLS measurements demonstrated a substantial reduction in exposure to diethyl phthalate, a widely-used ingredient in fragrances, suggesting changes in the formulation or use of personal care products.

- **BPA removed from food packaging:** DLS measurements in human urine showed daily consumption of canned soup compared to fresh soup increases exposure to BPA by more than 10-fold. Within a few months, a major manufacturer of canned soup volunteered to eliminate BPA from its canned food packaging.

- **Polybrominated diphenyl ethers (PBDEs) removed from certain carpet and furniture uses:** DLS measurements in human blood identified higher exposures to PBDEs in carpet installers, polyurethane recyclers, and young children compared to other people. Public concern about possible health outcomes from such exposures prompted the voluntary phase out of PBDEs for these uses.

- **Identifying sources of arsenic exposure:** DLS measurements of various metals and species of arsenic helped ATSDR determine the extent of exposure among residents near the National Priority List site in Anaconda, Montana. These measurements helped provide the community with information to reduce harm by distinguishing exposures from drinking water, which can be toxic, from non-toxic exposures from food.

- **Identifying sources of mercury exposure:** DLS measurements of speciated mercury helped the state of California identify the source of mercury poisoning in a family as a skin lightening cream that contained methyl mercury at levels that were high enough to cause severe brain damage.

- **Primary exposure to perchlorate through foods:** DLS biomonitoring findings informed EPA's regulatory decisions designed to reduce human exposure to perchlorate by showing that diet, not drinking water, acts as the primary source of perchlorate exposure in the U.S. population.

Demonstrating the effectiveness of interventions to reduce exposure

- **Exposure to perfluorooctane sulfonic acid (PFOS) reduced:** DLS measurements demonstrated the impact of U.S. industry's voluntary end of PFOS production in 2002 by documenting an 84% reduction in PFOS concentrations in the U.S. population from 1999 to 2016.
- **Exposure to toxic phthalates reduced:** DLS biomonitoring data for six phthalates, including DEHP, showed a shift from exposure to relatively more-toxic phthalates (based on tolerable daily intake values) to relatively less-toxic phthalates among the U.S. population between 2005 and 2014.
- **Exposure to brominated flame retardants decreased:** DLS measurements in NHANES showed decreasing concentrations for several brominated flame retardants from 2005 to 2014, suggesting reduced exposure among the U.S. population. Nevertheless, DLS still detects these persistent organic compounds in a large proportion of the U.S. population years to decades after discontinuation of sale and registered use.
- **Exposure to certain organophosphorus (OP) insecticides decreased:** DLS measurements of six dialkylphosphate and four specific metabolites of OP insecticides in human urine suggested a major decline in the U.S. population's exposure from 1999 to 2008, a likely result of regulatory efforts to restrict agricultural and residential use of OP insecticides under the Food Quality Protection Act of 1996.
- **Exposure to carcinogens in wood smoke reduced by cook stove interventions:** DLS data demonstrated the potential health benefit of installing an improved stove with a chimney in homes in developing countries. Exposure to polycyclic aromatic hydrocarbons, carcinogens formed during burning of wood, declined approximately 30% in rural Peruvian women who previously used indoor open-pit stoves.
- **Exposure to polychlorinated biphenyls (PCBs) reduced by clean-up efforts:** DLS measurements of PCBs in residents of Anniston, Alabama, a former manufacturing site of PCBs, showed exposures in adults were two to five times greater than those in other U.S. adults. However, Anniston children's PCBs levels were similar to those in other U.S. children, suggesting cleanup and remediation interventions were effective.
- **Exposure to methyl tert-butyl ether (MTBE) reduced by regulations:** DLS measurements in household tap water and in the blood of residents showed reduced exposure to MTBE among the U.S. population, demonstrating the efficacy of EPA regulatory action banning the harmful fuel additive.
- **Exposure to trihalomethanes lowered by regulations:** DLS biomonitoring findings showed a decline in human exposure to carcinogenic bromodichloromethane associated with EPA regulatory action to reduce trihalomethanes in household tap water.

Improving the detection of harmful exposures

- DLS developed and applied state-of-the-art methods to assess people's exposure to 18 PFAS, including long- chain PFOS and perfluorooctanoic acid (PFOA), short-chain perfluorobutanoic acid, and the PFOA/PFOS replacements GenX and ADONA. Data show widespread exposure to long-chain PFAS, but limited exposure to short-chain PFAS and certain PFAS alternatives among the U.S. population.

- DLS develops methods for measuring "replacement" chemicals to monitor exposure trends among the U.S. population when alternatives to potentially harmful chemicals enter the consumer market. Examples include neonicotinoid insecticides replacing pyrethroid insecticides; bisphenol S and bisphenol F replacing BPA; DINCH, a non-phthalate plasticizer, and di-2-ethylhexyl terephthalate (DEHTP), a different type of phthalate, replacing DEHP and other phthalates; and organophosphorus flame retardants replacing PBDEs.

- DLS created laboratory tests for the most widely used insect repellent and 10 other herbicides and insecticides. These methods identify patterns in people's exposure following changes in use for vector-borne disease protection and under new EPA restrictions.

- DLS improved health investigations of metals by improving tests for measuring 29 toxic metals and metalloids in urine and 13 toxic or essential metals in blood. These methods identify participants with higher levels of inorganic elements such as lead, cadmium, arsenic, manganese, and uranium as a part of ATSDR's prospective birth cohort study of environmental uranium exposure in the Navajo Nation.

- DLS produced training resources to help health care providers and laboratorians reduce the risk of contamination when collecting blood samples from children for lead testing. Implementing these best practices helps ensure that children are tested for lead exposures with maximum accuracy.

- DLS developed laboratory tests that better identify people's exposures to the highly reactive and cancer-causing environmental chemicals formaldehyde and ethylene oxide. For example, DLS measurements found higher concentrations of ethylene oxide biomarkers, but not formaldehyde, in smokers' blood. These tests can help assess people's exposure over the prior 2 to 3 months, investigate how exposures affect the risk for developing cancer, and inform clinical and public health actions to reduce exposures.

- DLS is developing a new method for measuring fluoride in urine that assesses the U.S. population's exposure and informs public health efforts to improve oral health without increasing the risk of health effects from too much fluoride.

- DLS developed a new method for measuring iodine in salt that helps assess people's exposure and informs public health efforts to improve health without increasing the risk of health effects from too much iodine.
- DLS collaborated on the development of a portable blood lead analyzer that helps identify lead exposures and poisoning incidents around the world. DLS provided the analyzer and laboratory assistance for the investigation of lead poisonings in two mining villages in Nigeria. The instrument enabled life-saving medical treatment by rapidly identifying children with dangerously high blood lead levels and continues to allow ongoing exposure monitoring.
- DLS measurements of carcinogenic trichloroethylene (TCE) helped document the exposure pathway when TCE migrated from groundwater to soil gas to basement air to human blood.
- DLS developed a method for measuring the novel biomarker methylcyclopentane in blood . This method provides ongoing monitoring of exposures to a toxicant found uniquely in petroleum that can cause liver and kidney damage and impair the central nervous system.

Tobacco Laboratory

The Tobacco Laboratory provides laboratory science that helps reduce individual and population exposure to addictive and toxic substances from tobacco products.

Identifying and tracking trends in tobacco use and secondhand smoke exposure

DLS helps monitor tobacco use and exposure among the U.S. population by measuring the harmful and addictive ingredients of tobacco products in blood and urine from participants in the ongoing NHANES. Measurements of cotinine (a marker of nicotine) showed that 88% of the nonsmoking U.S. population were exposed to tobacco smoke in the early 1990s and prompted smoking restrictions in public buildings. Follow-up findings, highlighted in the 2014 Surgeon General's Report—The Health Consequences of Involuntary Exposure to Tobacco Smoke, showed a dramatic reduction in secondhand smoke exposure because of interventions. Ongoing DLS measurements of cotinine and 3-hydroxycotinine in NHANES help target public health efforts to further reduce exposure by identifying nonsmoker groups who are still exposed, including children and people with lower incomes.

Collaborating with FDA to support tobacco product regulation

DLS provides FDA with crucial laboratory measurements of addictive and toxic substances in tobacco products and smoke and in urine and blood from people who use tobacco or are exposed to secondhand smoke. These unique baseline measurements are crucial to FDA regulation of tobacco products. As part of the National Cigarette Survey, DLS completed the largest laboratory-based characterization of addictive, toxic, and enhancing substances in cigarettes and cigarette smoke from 50 major U.S. brands. In addition, DLS measures more than 70 markers of exposure in over 10,000 specimens each year for FDA's Population Assessment of Tobacco and Health (PATH) study monitoring the behavioral and health effects of the 2009 Family Smoking Prevention and Tobacco Control Act. DLS also collaborates with FDA's southeastern regional laboratory to enhance FDA's capability to test tobacco products for regulatory standards.

Identifying the cause of a national lung injury outbreak

In response to the outbreak of electronic cigarette, or vaping, product use-associated lung injury (EVALI), DLS rapidly developed and applied 22 laboratory methods for measuring priority potential toxicants in EVALI-associated product emissions and bronchoalveolar lavage (BAL) fluid. DLS data showed vitamin E acetate in product emissions and in BAL fluid from nearly all case patients. DLS subsequently worked collaboratively with external partners to show that mice exposed to e-cigarette emissions of vitamin E acetate cause lung injury. Taken together, these data conclusively establish inhaled e-cigarette emissions of vitamin E acetate as the cause of the outbreak.

Identifying exposures to harmful and addictive ingredients of tobacco smoke

- DLS measurements identified patterns in the U.S. population's exposure to more than 100 harmful ingredients or features of tobacco and tobacco smoke, such as hydrogen cyanide, pH, VOCs, nicotine, and others. These data established an important baseline for evaluating the effectiveness of future policy and regulatory changes to reduce tobacco use and exposure.

- DLS data showed that different types of tobacco products and smoking styles impact people's exposure to tobacco carcinogens. These findings influenced the design of NHANES surveys, which now track tobacco product types and use behaviors to monitor how changes in tobacco products affect human exposure.
- DLS measurements in human blood and urine identified tobacco smoke as the major source of the U.S. population's exposure to harmful VOCs such as propanal, butanal, isobutanal, isopentanal, and crotonaldehyde and showed that exposure increases with the number of cigarettes smoked per day.
- New DLS methods for measuring aluminum-, silicon-, and titanium-containing nanoparticles in mainstream tobacco smoke can help identify exposures from e-cigarette use and inform public health actions.
- DLS developed an improved laboratory method for measuring biomarkers of benzene, a ubiquitous human carcinogen. This new method enhances exposure assessment in large population-based studies.
- DLS performed an international, inter-laboratory method comparison study of nicotine and nicotine metabolites measurements in human urine. These efforts improve the comparability of findings across studies and enable effective meta-analyses.
- DLS performed three inter-laboratory studies of the levels of nicotine, tobacco-specific nitrosamines, and metals in a new National Institute for Standards and Technology tobacco standard reference material, which will help improve accuracy and precision of these analytical laboratory measurements.

Identifying harmful exposures from smokeless tobacco and little cigars

- DLS measurements documented decreases in human exposure from smokeless tobacco use, demonstrating the impact of manufacturing changes to reduce carcinogenic tobacco-specific nitrosamines in some smokeless products.
- DLS developed a highly sensitive method that identified contamination of smokeless tobacco products with aflatoxin B1, a potent carcinogen formed by mold.
- DLS identified patterns of addictive and toxic substances in smokeless tobacco products from around the world, helping inform effective cessation programs for users of different types of smokeless tobacco.
- DLS measurements of toxic metals in little cigar tobacco filler help distinguish exposures from other tobacco products and establish baseline information for evaluating regulations to reduce harmful exposures.
- DLS characterized patterns of exposure among users of conventional tobacco products, such as cigarettes, smokeless tobacco, and cigars, and emerging tobacco products, such as e-cigarettes and waterpipes. This information supports public health actions to distinguish types of users and identify appropriate interventions to reduce harm.
- DLS developed a new laboratory test for measuring hemoglobin adducts of acrylonitrile that better distinguishes tobacco smokers from users of other products such as e-cigarettes.

Demonstrating the impact of tobacco product design and additives on exposure

- DLS measurements show that cigarette design features vary by manufacturer, affecting delivery of dozens of harmful chemicals in cigarette smoke. These findings provide detailed exposure information that regulatory groups can use as they develop targeted approaches to reduce harm.
- DLS showed that roll-your-own cigarettes deliver as much as or more mainstream smoke as manufactured cigarettes, potentially increasing a smoker's exposure to toxic and addictive chemicals. Reusing partially-smoked cigarettes leads to additional exposure to harmful chemicals.
- DLS developed a new method for measuring seven carbonyls in tobacco smoke that can be used to evaluate how efficiently filters remove harmful chemicals.
- DLS characterized the harmful and addictive components of tobacco filler and mainstream smoke for all varieties of SPECTRUM reduced-nicotine-content cigarettes.This information helps researchers better understand how reducing addictive nicotine levels in cigarettes affects user exposure to other harmful chemicals.
- DLS data showed that reducing nicotine in cigarettes can lower addictiveness without causing users to adjust smoking behaviors in a manner that increases exposure to harmful constituents.
- DLS supports international laboratories analyzing addictive and toxic substances in tobacco by participating in the World Health Organization's (WHO) Tobacco Laboratory Network and developing standard operating procedures for measuring the nine tobacco constituents WHO recommends reducing in products.
- DLS created methods for measuring toxic metals, including chromium, nickel, copper, zinc, cadmium, tin, and lead, in e-cigarette liquids and aerosol that will improve assessment of these exposures from e-cigarettes.
- DLS measurements of menthol in cigarettes showed that even non-menthol cigarettes contain low levels of menthol. A follow-up clinical study of smoking behaviors found that mentholated cigarettes delivered higher levels of nicotine than non-mentholated cigarettes.
- DLS helped document minimal compensatory smoking of reduced-nicotine cigarettes by measuring solanesol in nearly 15,000 used cigarette filter butts from a collaborative study. These data provide FDA with a scientific basis to regulate nicotine in cigarettes to reduce population harm caused by smoking.

Identifying secondhand exposure to marijuana

- DLS developed a laboratory test for measuring five biomarkers of marijuana smoke in urine that improves health studies by identifying exposures in active smokers and people exposed to secondhand marijuana smoke, including children.
- DLS characterized secondhand marijuana smoke exposure in occupational and residential settings and, through collaborative studies, linked secondhand marijuana smoke exposure with increased rate of respiratory illness in children.

Nutrition, Chronic, and Infectious Disease Laboratories

The Nutrition, Chronic, and Infectious Disease Laboratories improve the laboratory detection and diagnosis of nutrition-related disease, cardiovascular disease, and other chronic diseases and provide laboratory support for influenza and selected infectious disease projects.

The most comprehensive assessment of the U.S. population's nutrition status

DLS measures nutrition indicators in blood and urine from participants in the ongoing NHANES to assess nutrition status. The Second National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population contains reference range information for 58 nutrition biomarkers, including fat- and water-soluble vitamins, iron-status indicators, iodine, and other dietary biomarkers that are important to human health. This DLS report helps physicians, scientists, and public health officials identify inadequate or excess intake of nutrients and informs studies on the relationship between biochemical indicators and health outcomes.

Identifying demographic, lifestyle, and physiologic factors influencing nutrition status

DLS expanded on the findings of the Second Nutrition Report by examining the association between 10 socio-demographic and lifestyle factors and 29 biomarkers of nutrition status. In eight articles published in *The Journal of Nutrition*, DLS showed that race-ethnicity, dietary supplement use, and smoking all affect U.S. population's levels of nutrition biomarkers.

Demonstrating the effectiveness of interventions to improve health

- **Effectiveness of folic acid fortification:** DLS developed a more accurate laboratory test that helped demonstrate the effectiveness of folic acid fortification, a public health intervention designed to reduce the risk of neural tube defects. DLS data documented that fortification led to a 50% increase in blood folate levels in all race/ethnic groups and a decrease in folate deficiency to less than 1%, both in the general U.S. population and in women of childbearing age. Nearly 20 years after the introduction of folic acid fortification, the folate status in the U.S. population is stable.

- **Trans-fatty acid levels decline in U.S. population:** A unique laboratory method developed by DLS measured blood levels of trans-fatty acids for the first time in the U.S. population. Findings showed a 50% decrease from 2000 to 2009 in adults and a similar decrease in children, documenting the effectiveness of efforts to reduce intake of trans-fatty acids and informing new regulations by FDA to further lower exposure.

Improving the diagnosis of nutrition-related disease

- **Better tests for vitamin D status:** DLS improves the diagnosis of bone diseases like osteoporosis, osteomalacia, and rickets by developing better tests for assessing vitamin D status. New laboratory methods helped harmonize U.S. population data from 1988–2010 to better track trends in vitamin D status over time. In addition, a new DLS method for measuring 24R, 25-dihydroxyvitamin D3 assigned orientation values to testing materials used by two major vitamin D proficiency testing programs, improving the quality of vitamin D results in laboratories around the world.

- **Harmonizing blood folate measurements worldwide:** DLS helped improve assessments of folate status, an indicator of neural tube defects, among women of reproductive age worldwide. For the folate microbiological assay, DLS trained scientists from nearly 10 countries over the last 5 years, produced a training video that helps scientists in low resource settings accurately perform the test, and demonstrated that using common critical reagents improved the comparability of data among laboratories.

- **Improving tests for bioactive dietary compounds:** DLS developed state-of-the-art tests for detecting urinary phytoestrogens and caffeine metabolites that provided the first national reference levels, improved national estimates of caffeine intake, and enhanced assessments of hormone-dependent cancer risk.

- **Improving international micronutrient testing:** DLS provides technical assistance, field training, and technology transfer to laboratories in developing countries to improve the detection of micronutrient deficiencies. DLS assures the quality of laboratory measurements in nearly 30 laboratories in more than 20 countries for 11 biochemical indicators of nutrition status.

- **Identifying trends in the U.S. population's salt intake:** DLS collaborated with other federal agencies to identify a sample collection approach suitable for determining sodium intake in population surveys. DLS measurements of sodium in U.S. population samples from 1988–2010 helped track trends over time and show a slight increase in sodium intake over the past two decades.

- **Improving the detection of iodine insufficiency:** DLS laboratory measurements identified vulnerable groups of the U.S. population with inadequate iodine levels, helping improve the prevention of iodine deficiency, especially in women of childbearing age. In addition, DLS improves the detection of iodine insufficiency and excess in people worldwide by ensuring the accuracy of global iodine measurements in more than 200 labs in over 90 countries.

Improving the detection, diagnosis, and treatment of cardiovascular disease (CVD)

- **Better methods to detect cholesterol:** DLS developed and maintains highly accurate and precise methods for measuring total cholesterol, other traditional blood lipids such as low-density lipoprotein (LDL) cholesterol, and new lipid biomarkers such as Lipoprotein-a (Lp(a)). These tests improve the accuracy and reliability of blood lipid testing in patient care and research and help to better identify people at risk for CVD that might not be identified with traditional lipid tests.

- **Better tests to assess CVD risk:** DLS developed a unique, reference-quality test for characterizing sizes of cholesterol containing lipid particles and is applying it to studies that establish levels and protein/lipid composition for healthy patients and patients with varying degrees of CVD. These studies will help define the health risks associated with different sizes high-density lipoprotein (HDL), LDL, and very low-density lipoprotein (VLDL) particles, which are promising diagnostic markers for heart disease.

- **Improving cholesterol and blood lipid tests in the United States and worldwide:** The DLS Lipid Reference Laboratory improves the accuracy and reliability of millions of tests for total cholesterol, HDL, LDL cholesterol and triglycerides performed annually worldwide by standardizing over 20 test manufacturers in 7 countries and over 130 laboratories in 11 countries. DLS is further improving test accuracy by leading the transition to new mass spectrometry-based technologies, expanding its international network of reference laboratories, and including new biomarkers such as lipoproteins.

- **Ensuring accuracy and reliability of laboratory tests for cholesterol and blood lipids in patient care and research:** The DLS Lipid Standardization Program helps over 300 clinical laboratories worldwide monitor and improve the measurement accuracy of their assays for total cholesterol, HDL cholesterol, triglycerides, apolipoprotein A and B, lipoprotein a, and non-HDL cholesterol, ensuring that measurements used in patient care and research are accurate and reliable.
- **Improving assessment of CVD risk:** DLS applied a new test for measuring fatty acids in red blood cells to samples from NHANES 2019–2020, helping provide information on the U.S. population's CVD risk through an omega-3-index.
- **Investigating CVD risk in populations exposed to tobacco smoke:** DLS is measuring high sensitivity C-reactive protein, a marker of chronic inflammation, in FDA's PATH study. Measurements will improve understanding of the impact of smoking tobacco and other products on CVD risk from inflammation.
- **Improving the detection of heart attacks and injury to heart muscle:** DLS is working with over 30 test manufacturers and other stakeholders to harmonize normal ranges for troponin measurements to improve the diagnosis of heart attack-associated heart muscle injuries.

Improving the detection, diagnosis, and treatment of chronic diseases

- **Better vitamin D tests used in research, public health and patient care:** The CDC Vitamin D Standardization Certification Program improves the analytical accuracy and precision of vitamin D tests by providing reference methods and materials to over 80 laboratories in 15 countries. The program helps laboratories and test manufacturers to identify potential causes of inaccurate measurements.
- **New laboratory methods for metabolic steroid profiles better assess health status:** A new, highly specific and sensitive method for measuring eight steroid hormones and metabolites in blood improves the diagnosis and treatment of breast cancer and supports studies to understand the associations between environmental exposures, steroid profiles, and health outcomes.
- **Improved testosterone measurements in patient care:** The DLS Hormone Standardization Program provides reference methods and materials to improve the accuracy and reliability of testosterone tests used for the diagnosis and treatment of hypogonadism and polycystic ovary syndrome.
- **New normal ranges for testosterone in men:** Using its standardized laboratory method, DLS established normal ranges for testosterone in men by analyzing samples from cohorts of major studies, including the Framingham Heart Study, European Male Aging Study, Osteoporotic Fractures in Men Study, and Male Sibling Study of Osteoporosis. Normal ranges help inform clinical practice guidelines for treating patients with testosterone deficiency.
- **Improving clinical measurements of estradiol:** DLS developed a highly accurate, sensitive, and specific reference method for measuring estradiol in blood that improves the diagnosis and treatment of patients with cancer and bone diseases. DLS applies this method to

calibrate and evaluate estradiol tests used in patient care and clinical research, reducing differences among them by two thirds and improving the reliability of estradiol tests.

- **Better detection and treatment of chronic kidney disease-mineral and bone disorder:** DLS is developing innovative methods for measuring parathyroid hormone, related compounds, and creatinine, which will enhance understanding of the causes of kidney diseases and bone disorders, improve diagnosis, and help better monitor patients on dialysis.
- **Helping clinical laboratories monitor the accuracy of tests in patient care:** DLS developed and implemented an Accuracy-Based Monitoring Program that helps clinical laboratories assess and monitor the accuracy and reliability of testosterone and vitamin D tests when testing patient samples.
- **Improving clinical testing for thyroid diseases:** DLS developed a highly accurate and precise method to measure free thyroxine (fT4), a biomarker for thyroid diseases, and is applying this method to improve the accuracy and reliability of fT4 tests used in patient care. Assessment of reference materials for thyroid stimulating hormones (TSH) will help improve calibration and comparability of TSH tests used to identify people with thyroid diseases.
- **New reference method for blood glucose:** DLS established a highly accurate and reliable method for measuring glucose in blood and is using this method to assess and improve the accuracy of glucose tests performed in patient care as well as tests performed by patients at home. DLS is the only U.S. laboratory offering such highly accurate measurements.

Improving influenza vaccines and diagnostics

- **Enhancing the quality of influenza vaccine:** DLS mass spectrometry methods have improved influenza vaccines by providing better measures of influenza proteins hemagglutinin and neuraminidase in the calibrators used for vaccine potency assays.
- **Increasing the speed of influenza vaccine distribution:** DLS developed better laboratory tests that rapidly identify faster growing influenza seed strains, which accelerates seed strain selection and production of vaccines for H1N1, H3N2, H7N9, and H5N1 influenza. DLS also developed an antibody-free potency test, which could accelerate the release of a vaccine to the public in the event of an influenza pandemic.
- **Identifying variability in diagnostic tests for influenza:** DLS helps ensure the use of accurate commercial rapid diagnostic tests for influenza when novel or variant viruses emerge by accurately quantifying nucleoprotein in influenza virus standards.

Newborn Screening Laboratories

The Newborn Screening Laboratories assure the early and accurate laboratory detection of treatable congenital disorders in newborns.

The nation's only newborn screening quality assurance program

The Newborn Screening Quality Assurance Program (NSQAP) improves the detection of treatable, newborn diseases by ensuring accurate laboratory testing for more than 98% of newborns in the United States. Each year, NSQAP creates and distributes over 700,000 dried blood spots to participating newborn screening (NBS) programs, helping assure the early, correct identification and treatment of more than 6,000 U.S babies that may have otherwise died or been severely disabled.

Supporting state laboratories with training, technical support, and funding

DLS works directly with laboratories in states as they conduct ongoing newborn screening and implement testing for new diseases. DLS provides training, technical assistance, test development, and quality assurance materials that help ensure accurate test results. In collaboration with partners, DLS develops and hosts yearly training courses to support state public health laboratories that use molecular and mass spectrometry methods for newborn screening. DLS also provides funding to help state laboratories implement testing for new conditions, including recent additions to the Recommended Uniform Screening Panel (RUSP), the list of conditions that guides states in selecting their newborn disease test panels.

Improving the quality of molecular tests in newborn screening

DLS and the Association of Public Health Laboratories (APHL) collaborate on the innovative Molecular Assessment Program, which provides guidance and technical expertise to newborn screening laboratories as they implement molecular testing techniques to better detect disease. Since 2011, the program has provided 29 on-site assessment visits to state NBS laboratories.

Improving the detection and diagnosis of severe combined immunodeficiency (SCID)

DLS helps increase the number of states and territories accurately testing babies for SCID, a deadly disease that is treatable if detected early. DLS funding to newborn screening laboratories helped states use innovative technologies to improve SCID tests and implement new tests to ensure early, life-saving treatment. CDC-funded programs served as models for other states implementing population-based screening. All states now conduct SCID testing, and CDC works directly with all these laboratories, providing training, technical assistance, and quality assurance materials that help ensure continued accuracy of test results.

Improving newborn screening for Spinal Muscular Atrophy (SMA)

DLS developed a new method for detecting SMA and combined it with an established test for detecting SCID, substantially reducing the additional cost of the new test. DLS funding to newborn screening laboratories helped states implement SMA testing to ensure early, life-saving treatment. DLS works directly with all laboratories in all phases of SMA screening to provide training, technical assistance, and quality assurance that help ensure continued accuracy of test results.

All three children in the photograph have glutaric aciduria type 1, an inherited metabolic disorder. Early detection and intervention prevented the two girls from becoming disabled.

Improving the detection and diagnosis of Adenosine Deaminase Severe Combined Immunodeficiency (ADA-SCID)

DLS developed critical quality assurance materials and mass spectrometry-based screening methods for ADA-SCID, which is deadly if not treated. The quality assurance materials were piloted successfully in the United States and Austria.

Accelerating implementation of screening for X-linked Adrenoleukodystrophy (X-ALD)

DLS is helping states implement population-based screening for X-ALD through on-site training of DLS-developed methods. DLS helped newborn screening programs in Michigan, Texas, Georgia, and other states implement the test. More than 12 states participated in a harmonization study that used CDC materials to harmonize X-ALD biomarker results and cutoffs among laboratories.

Expanding proficiency testing coverage using mass spectrometry

DLS helped newborn screening laboratories improve their tests by expanding proficiency testing services for mass spectrometry methods that detect 43 of the 61 core and secondary disorders on the Recommended Uniform Screening Panel.

Harmonizing newborn screening analytical results and cutoff values

DLS harmonized newborn screening cutoff values for biochemical tests measuring dozens of analytes among hundreds of newborn screening laboratories worldwide. Normalization of results and cutoffs enables comparison among peer laboratories and allows for the development of data analytics tools and algorithms to standardize newborn screening data.

Ensuring quality filter paper for blood collection

DLS has evaluated over 75 lots of filter paper used to produce blood collection cards for newborn screening since 1991. Manufacturers use evaluation results to ensure the quality of cards made for newborn screening programs nationwide.

Chemical Threat Agents and Toxins Laboratories

The Chemical Threat Agents and Toxins Laboratories provide laboratory support for the public health response to chemical threat agents and threats involving selected toxins.

Identifying people exposed to chemical threats using the Rapid Toxic Screen

DLS maintains 24/7 capability to quickly detect exposed people during a chemical emergency. DLS developed the Rapid Toxic Screen, which can identify the causative agent during an exposure event by measuring 150 specific chemicals in blood and urine from 40 exposed people within 36 hours. After identifying the chemical agent(s), DLS can measure up to 1,000 patient samples per day during an incident. This exposure information helps public health officials rapidly assess health risk, ensure effective treatment, and prevent additional exposures. DLS capacity and capability also serves as a deterrent to the use of chemical warfare agents. DLS has used the Rapid Toxic Screen in cases of sulfur mustard exposure, ricin poisonings, and potential exposures from chemical demilitarization sites.

Expanding laboratory capacity to respond to chemical threat incidents across the United States

DLS supports state, local, and territorial public health laboratories participating in the Laboratory Response Network for Chemical Threats (LRN-C) to improve national and regional responses to emergencies involving chemical threats. DLS develops and distributes quality control materials and provides quality assurance and performance testing to laboratories to assure high quality results during an emergency. DLS also transfers test methods and provides training to build laboratory capability in measuring chemical threat agents, including recent efforts to expand the network's ability to detect high threat organophosphate nerve agent and sulfur mustard metabolites in exposed people.

Developing crucial tests for emergencies and unknown illness

- DLS developed diagnostic methods for measuring stable protein adducts in blood that can identify people exposed to specific organophosphate nerve agents, sulfur mustard, and nitrogen mustards much longer after an event occurs.
- DLS developed the first method to measure biomarkers of exposure to chlorine, which will strengthen public health preparedness and response capabilities in cases of human exposure to this widely available toxic industrial chemical.
- DLS rapidly developed laboratory methods to identify and confirm exposure to Soapberry toxins as a part of CDC's emergency response to recurrent outbreaks of fatal, acute encephalopathy in Muzaffarpur, India. These methods provided the major information that identified the source of exposure and prevented additional disease and death in hundreds of young children.
- DLS developed the first method for the detection of human exposure to seven alpha conotoxins. The method enables rapid confirmation of accidental and intentional exposures to these harmful cone snail toxins.
- DLS helps improve worldwide readiness for responding to chemical incidents by serving as a designated biomedical testing laboratory for the Organisation for the Prohibition of Chemical Weapons. DLS developed and published diagnostic tests for nerve agent, sulfur mustard, and chlorine exposures and participates in proficiency testing and exercises that support international capabilities to detect these agents.
- DLS developed a novel protocol for reducing potential biological threats in clinical samples prior to chemical analyses. The implementation of this protocol improves safety of laboratory personnel and response time in public health emergencies.

Expanding surveillance capabilities for fentanyl exposure

- DLS developed a high throughput method for measuring 28 fentanyl analogs, synthetic opioids, and related metabolites in urine, plasma, and dried blood spots. These methods expand CDC's response capability to detect exposure to strong narcotic analgesics and distinguish fentanyl exposure from other opioids.

DLS distributed the methods to state public health laboratories supporting nationwide surveillance testing.

- DLS developed a high-resolution method and database for identification of 150+ synthetic opioids and related compounds in plasma and urine. This method enables laboratories to assess previously collected data for emerging fentanyls and identify new opioid threats.
- DLS partnered with five major manufacturers of commonly used opioid screening tests to improve the detection of fentanyl analogs in emergency situations.
- DLS designed laboratory reference materials (i.e., chemical reference standards) that will improve the public health response to the opioid overdose epidemic. These Traceable Opioid Material* Kits (or TOM Kits*) were provided free-of-charge to eligible U.S. laboratories to assure accurate and reliable fentanyl measurement across academic, public, and private sectors. To date, TOM Kits* have reached all 50 states, 2 territories, and the District of Columbia.

**TRACEABLE OPIOID MATERIAL, TOM KITS, and the TOM KITS logo are marks of the U.S. Department of Health and Human Services*

Identifying algal toxin poisonings

- DLS measurements confirmed several cases of human exposure to saxitoxin, a neurotoxin present in shellfish exposed to toxic algal blooms, by identifying saxitoxin in the urine of symptomatic persons. DLS also identified biomarkers of exposure to gonyautoxins in an individual known to consume seafood contaminated with paralytic shellfish poisoning toxins.
- DLS developed a method to confirm human exposure to tetrodotoxin, an extremely potent paralytic toxin found in puffer fish. These clinical measurements aid public health response by confirming poisoning by tetrodotoxin rather than by other paralytic toxins.

Developing unique diagnostic tests that improve the diagnosis and treatment of diseases from dangerous toxins

DLS develops unique, mass spectrometry-based methods to rapidly and accurately detect and diagnose diseases from dangerous toxins. DLS methods improve upon existing techniques to measure toxins and can detect and quantify toxins more quickly, handle many samples in an emergency, and identify infection during antibiotic treatment.

- **A rapid and accurate test for botulism that does not require animal testing:** DLS developed the first test for measuring medically-relevant levels of all botulinum neurotoxins, toxin mosaics, and their subtypes. DLS used these methods to analyze over 1,000 human, food, and environmental samples for botulism. DLS also evaluated the efficacy of a botulism vaccine, identified three previously unknown subtypes, and characterized a new botulinum neurotoxin hybrid of types F and A.

Clostridium botulinum

- **Improving botulism tests in state and international laboratories:** DLS provided training and transferred the botulinum neurotoxin test to state public health laboratories and international partners. Use of this more sensitive, rapid, and high-throughput method improves botulism diagnosis and lowers costs by reducing animal testing.
- **Identifying ricin in white powders:** DLS methods for detecting ricin in environmental samples measure both protein and biological activity, helping estimate how toxic a ricin sample is.
- **A test for anthrax that detects infection days before symptoms occur:** DLS developed a mass spectrometry test for measuring anthrax lethal factor that improves the diagnosis and treatment of anthrax. The method detects anthrax much faster than traditional culture methods, enabling essential early treatment, and is not affected by antibiotic interferences that can complicate culture-based diagnosis. DLS can analyze more than 1,000 samples per day and applied the method to evaluate the effectiveness of anthrax treatments and in anthrax outbreaks investigations worldwide.
- **Anthrax tests that predict stage of infection and need for advanced treatments:** DLS developed a suite of five tests that measure various anthrax toxins and their active toxic forms. These tests can help identify persons requiring specialized antitoxin treatments by determining the progression of disease.
- **A highly sensitive test for aflatoxin:** Provided critical laboratory testing for public health investigations of liver failure in several African countries by measuring aflatoxin-lysine adduct in serum. Results suggest that exposure to aflatoxins, likely through the food chain, may play a role in liver failure.

Radiologic Threats Agents Laboratory

The Radiologic Threats Laboratory provides effective laboratory support for the public health response to radiologic threat agents.

Identifying people exposed to radiologic threat agents using the Urine Radionuclide Screen

DLS maintains unique laboratory capability to rapidly detect exposed people from radionuclide poisoning, a "dirty bomb," or other radiologic incident. DLS developed the Urine Radionuclide Screen to assess people's internal exposure to important alpha-, beta-, and gamma-emitting radionuclides that frequently cannot be detected with external radiation equipment or clinical assessment. Using the Urine Radionuclide Screen, DLS can analyze more than 100 samples within 24 hours. DLS exposure information helps public health officials reliably differentiate people who are truly exposed from concerned citizens, ensure effective treatment with appropriate medical countermeasures, and prevent additional exposure.

Developing and improving rapid diagnostic tests for priority radionuclides

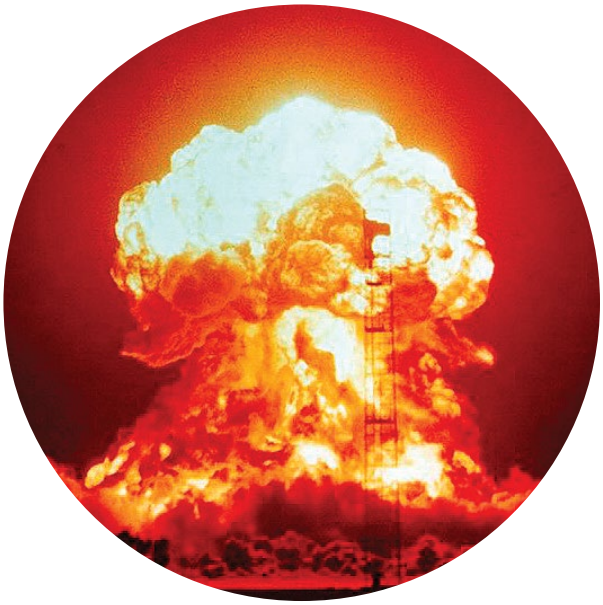
DLS improved the detection of human exposure to priority radionuclides by enhancing the speed and ruggedness of existing laboratory tests and developing new tests that can adequately respond to the high sample load of an emergency radiologic incident.

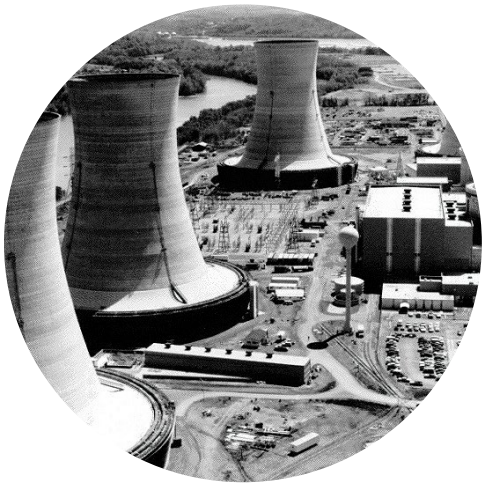
Measuring human exposures following accidental radiation releases

- DLS used the Urine Radionuclide Screen to measure radiation exposures in federal workers returning to the U.S. from Japan immediately following the Fukushima Daiichi Nuclear Power Plant radiation release. Test results showed low levels of radionuclides, posing no threat to health.
- DLS measurements in workers' urine provided reassuring results following a known release of plutonium-239 and americium-241 at a radioactive waste isolation plant.

Supporting global readiness for a radiologic emergency

DLS helps improve worldwide readiness to respond to a major radiological or nuclear incident by participating in Global Health Security Initiative exercises that test international laboratories' ability to identify radionuclides in human samples.





Three Mile Island Accident
Source: U.S. Department of Energy

The Division of Laboratory Sciences

Advanced laboratory science improving the detection, diagnosis, treatment and prevention of harmful exposures and disease

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national and international organizations.

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