Updated Guidelines for the Control of *Legionella* in Western Pennsylvania

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PREFACE

Legionnaires’ disease (LD) is a pneumonia caused by different varieties of Legionella bacteria. Pennsylvania is within the U.S. region that has the highest incidence of reported LD. Following several local outbreaks of LD in health care institutions, Allegheny County Health Department (ACHD) convened a task force in June 1992 of members of the medical, public health, plumbing, and drinking water regulatory agencies to develop practical guidelines for health care institutions to use as recommendations for minimizing the occurrence of Legionella bacteria in their water systems and reducing the incidence of LD among patients. In 1993, ACHD issued a first set of guidelines, “Approaches to Prevention and Control of Legionella Infection in Allegheny County Health Care Facilities.” The guidelines were subsequently revised and reissued in 1997. The scientific community has two decades of additional experience with Legionella since the original ACHD guidelines were issued.

In 2013, the Pittsburgh Regional Health Initiative (PRHI) and ACHD decided to update the county’s guidelines, and they received encouragement from the Centers for Disease Control and Prevention (CDC) to do so. In late 2013 and on behalf of the local stakeholders, PRHI contracted with the RAND Corporation to facilitate this process. The purpose of these updated guidelines is to provide interested persons and organizations in western Pennsylvania—especially community hospitals, nursing homes, assisted living and high-rise retirement facilities—with updated information on Legionella and how to minimize its occurrence and impact in people and in the environment.

These updated guidelines were developed in consultation with experts representing a range of organizations, disciplines and expertise (Appendix 1). They draw from information and guidelines from local, state, federal and international health agencies, e.g., ACHD, the Pennsylvania Department of Environmental Protection (DEP), CDC, the VA Veterans Health Administration, the World Health Organization (WHO), and various countries that have issued guidelines related to Legionella control. Most experts feel that more scientific evidence is needed on which to ground definitive recommendations, especially those related to management of Legionella risk in the environment. Therefore, readers are well advised to consult guidelines issued subsequent to these, because they will provide more detailed information not available as evidence for the present guidelines, and will address specific areas in more detail than here (e.g., legionellosis outbreak investigation, environmental remediation, engineering design), including national level recommendations or regulations. Readers are also advised that new scientific reports will eventually enable more confident and precise evidence-based recommendations.

For questions specific to legionellosis in Western Pennsylvania, readers may contact ACHD or DEP (see contact information in Appendix 10). For questions regarding the development of the guidelines, readers may contact the RAND research team: Dr. Melinda Moore (703-413-1100, ext. 5234; mmoore@rand.org) or Ms. Shoshana Shelton (412-683-2300, ext. 4262; sshelton@rand.org)
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LEGIONELLOSIS refers to the diseases caused by *Legionella* bacteria. The most severe of these diseases is a pneumonia known as Legionnaires’ disease (LD), which typically requires hospitalization. Pontiac fever is a milder infection that, like many other “colds,” can resolve without treatment.

*Legionella* bacteria are considered ubiquitous and grow in natural and manmade freshwater environments, *surviving* in relatively cold to relatively hot temperatures and *thriving* in sources that maintain warm temperatures. Water sources that can transmit *Legionella* and thus pose a risk to human health typically meet three key conditions: heat, stasis and aerosolization. Examples include drinking water systems (e.g., faucets or showers), hot tubs, other recreational water systems such as pools or decorative fountains, and air conditioning systems that use cooling towers or other evaporative condenser mechanisms. Occasional exceptions to this general rule occur, for example a case of healthcare-associated LD traced to a hospital’s ice machine. People become infected when they inhale *Legionella* as aerosol, spray, or mist dispersed from contaminated sources, or when they choke on water (e.g., in respiratory therapy equipment) that has been contaminated with the bacteria. *Legionella* is spread strictly from such environmental “point” sources, and not from person to person.

Risk factors for LD include older age, male sex, a history of smoking, chronic lung disease, or compromised immune system. Effective treatment is available for LD, especially if treatment is initiated as early as possible during the illness. Patient history and physical examination may suggest a diagnosis of LD; in some patients, such as those who are severely ill, laboratory testing is indicated so that definitive diagnosis can be made and optimal antibiotic therapy given. The tests for *Legionella* are different from routine tests and specific to this microbe, so the clinician must suspect LD and order those specific tests. For less severely ill patients treated on an outpatient basis, physicians

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**EXECUTIVE SUMMARY**

These updated guidelines were developed based on review of available evidence and consultation with experts. They provide information for health-care related facilities that house or serve persons at greatest risk for legionellosis and practical information on what they can do to reduce the risk and impact of legionellosis among those they serve:

- Such facilities should be aware of how legionellosis presents clinically, suspect LD in persons who meet the LD profile, and manage or refer ill persons for diagnosis and treatment. As per DOH regulation, health care providers and laboratories will report diagnosed cases to the local health authorities for further investigation and to help identify sources of infection. Additionally, the Allegheny County Health Department welcomes reports of laboratory-confirmed cases or multiple potential cases from facilities that house or serve them, since this may enable more timely responses to investigate the causes and prevent further cases.

- The water systems of some facilities will fall under government regulation, and some will not. All facilities should take a risk management approach regarding their water systems. This involves development of a water safety plan, in which a facility will specify monitoring and control measures that are appropriate to their own facility and clientele, for preventing or reducing *Legionella* growth.

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Risk factors for LD include older age, male sex, a history of smoking, chronic lung disease, or compromised immune system. Effective treatment is available for LD, especially if treatment is initiated as early as possible during the illness. Patient history and physical examination may suggest a diagnosis of LD; in some patients, such as those who are severely ill, laboratory testing is indicated so that definitive diagnosis can be made and optimal antibiotic therapy given. The tests for *Legionella* are different from routine tests and specific to this microbe, so the clinician must suspect LD and order those specific tests. For less severely ill patients treated on an outpatient basis, physicians
will typically treat clinical pneumonia without ordering laboratory testing to confirm the specific cause.

The first signal of a *Legionella* problem can be clinical—when someone is diagnosed with LD—or environmental—when monitoring reveals *Legionella* contamination in a water system that disperses aerosol, fine mist or spray into the air. Unfortunately, scientific evidence has not yet identified a dose-response relationship that indicates a “safe” level of contamination; thus, there is no established threshold for an environmental “signal.” Whether in response to a clinical case or environmental contamination, the goal of environmental intervention measures is to reduce the concentration of *Legionella* in the water system or to ensure that it cannot disperse the bacteria into the air where people will breathe it, thereby reducing the health risk associated with *Legionella* bacteria.

Various domestic government agencies (federal, state, local), non-government organizations (e.g., professional associations), and international authorities (e.g., World Health Organization, national and sub-national governments), each with its own mandate and perspective, have issued guidelines that address different aspects of legionellosis prevention and control. Some of these date back to the 1990’s and early 2000’s (see summary in Appendix 2). As of September 2014, the VA had just issued an updated directive for “Prevention of Healthcare-Associated *Legionella* Disease and Scald Injury from Potable Water Distribution Systems”, and a number of other agencies in the United States—the Environmental Protection Agency (EPA), Occupational Safety and Health Administration, Centers for Disease Control and Prevention (CDC)—were in the process of developing new or revised guidelines that are expected to be issued within just a few months to years following the present guidelines.

These updated guidelines for Western Pennsylvania provide practical information aimed at meeting the needs of health care-related facilities that house or serve persons at risk for LD and have water systems that may harbor and disperse *Legionella*—especially community hospitals, nursing homes, assisted living and high-rise retirement facilities—so they know what they can do to help minimize the risk and impact of LD.

Specifically, the guidelines provide information to raise awareness and suggest practical actions related to:

- Managing *Legionella* in people
  - In individuals: Clinical aspects – how legionellosis presents clinically and how it is diagnosed and treated
  - In populations: Public health aspects – general information on how public health professionals collect information on and respond to cases of LD
- Managing *Legionella* in the environment
  - Environmental sources (types of water system) and settings (for such systems) where *Legionella* can pose a risk to human health
  - Approaches to management of *Legionella* in the environment, including a risk management approach
  - Routine operation and maintenance of water distribution systems
  - Regulated routine control measures for prevention of *Legionella*
  - *Legionella* treatment methods
Environmental management in response to a confirmed LD case or outbreak
Collection of water samples for microbiological testing
Interpretation of laboratory results

These guidelines for Western Pennsylvania incorporate updated information and recommendations as well as new features not included in the 1997 ACHD guidelines:

- The scope is broadened beyond health care facilities to include other facilities that house or serve persons at highest risk for legionellosis.
- The range of water sources addressed is similarly broadened.
- There is more detailed and updated information on the clinical and public health aspects of legionellosis, including the role of clinical surveillance as part of an overall legionellosis risk management approach.
- A risk management approach replaces previous more prescriptive recommendations related to environmental control of Legionella.
- New features include an updated list of published guidelines and topical references (Appendix 2), glossary of key terms (Appendix 3), clinical diagnosis including a tool that clinicians may use to help distinguish LD clinically from other clinical diseases (Appendix 4), current laboratory tests for Legionella (Appendix 5), the updated surveillance case definition for legionellosis (Appendix 6), a summary of recent legionellosis surveillance trends (Appendix 7), general steps in the investigation of a legionellosis outbreak (Appendix 8), federal and state regulations related to Legionella (Appendix 9), and where to call for more information (Appendix 10).

The recommendations offered here reflect varying levels of confidence, based on the evidence available in 2014, existing guidelines from authoritative sources, and inputs from the experts consulted.

**MANAGING LEGIONELLA IN PEOPLE**

**Individuals**

1. **Suspect Legionella in ill persons who fit the LD profile:** Consider the possibility of Legionella infection in elderly or other vulnerable persons who develop symptoms compatible with LD, such as fever, cough, headache, muscle pain, chills, shortness of breath, chest pain, gastrointestinal symptoms, and/or confusion. This may be a single individual, or multiple individuals, in the hospital, residential, or other facility.

2. **Manage or refer such persons promptly for medical attention:** A health care facility will manage ill persons, and other facilities should refer them for medical diagnosis and treatment, mentioning that legionellosis is suspected. The treating health care facility or laboratory will report any laboratory-confirmed LD cases to the county health department, which will take care of further investigation,
including efforts to identify the source of infection, and they will report the case to the CDC.

3. **Verify the diagnosis of persons returning to residential facility:** For a patient from a residential facility who has received medical attention for pneumonia, it will be important for the facility to verify the diagnosis, in particular to ascertain whether microbiological laboratory testing was undertaken and *Legionella* was diagnosed. If so, investigation of the facility’s water system may be warranted.

4. **Respond to suspected or confirmed LD case(s) associated with a residential or health care facility.** Every confirmed LD case should be considered an alert, for follow up both on the human health and environmental side. For the former, facilities can review their records to determine if potentially linked cases have occurred in the past two years. On the environmental side, the occurrence of a case of LD should prompt facilities to at least review their water system(s), control measures, and routine monitoring of those measures.

5. **Contact the health department with any further questions about ill persons:** For any further questions or need of help, call the Allegheny County Health Department at 412-687-ACHD (2243) or contact them online via [http://www.achd.net/newweb/contactForm.html](http://www.achd.net/newweb/contactForm.html). While reporting of cases to ACHD is officially the responsibility of health care providers and laboratories, ACHD welcomes you to contact them about laboratory-confirmed cases, to enable their rapid response and investigation.

**Populations**

6. **Health care providers and laboratories will report suspected or confirmed LD cases to the local health department (in Pennsylvania, through the Pennsylvania-National Electronic Disease Surveillance System).**

7. **The local health department will follow up to investigate such cases and recommend appropriate control measures.**

**MANAGING LEGIONELLA RISK IN THE ENVIRONMENT**

8. **Take a risk management approach to environmental monitoring and control of Legionella:** Consistent with federal (EPA, VA), state (Pennsylvania Department of Environmental Protection—DEP) and international (World Health Organization—WHO) guidelines, these guidelines recommend that facilities take a risk management approach to environmental monitoring and control of *Legionella*, not only in health care facilities but also in other facilities that house or serve persons at greatest risk including community hospitals, nursing homes, assisted living facilities, and high-rise retirement facilities. Such an approach applies to both regulated and non-regulated drinking water systems and is the basis for Pennsylvania drinking water regulations. One practical way to
implement a risk management approach is through a water safety plan. As described in more detail later, the key steps are to:

- Document and describe the building’s water system(s).
- Assess hazards and characterize risk.
- Identify water system management points and engineering control strategies.
- Implement, monitor and document engineering control measures.
- Validate the effectiveness of engineering control measures.
- Take corrective action when warranted.

9. **Implement routine water system operation and maintenance best practices.** Regardless of whether a facility’s water system falls under government regulatory control, facilities should implement routine maintenance and control measures for their water system(s). Operation and maintenance best management practices that do not require a DEP permit (but that may be included in permitting) include:

- Thermal control
- Routine inspection and cleaning
- Routine flushing

10. **Implement appropriate treatment methods to prevent *Legionella* growth or when otherwise warranted.** A number of approaches have been recommended or taken to prevent or reduce *Legionella* contamination in the environment, whether on a routine basis to prevent contamination or in response to documented environmental contamination or the occurrence of an LD case linked to the facility’s water system. Some of the measures described below can be used for system-wide disinfection, and others are more appropriate for focal treatment, including disinfection. Some are used routinely and others for emergency disinfection. As described in more detail later, such measures include:

- **Thermal disinfection (thermal eradication; superheating/flushing):** Flushing the entire system with water at 70°C (158°F), allowing this to flow for at least 5 minutes (or an equivalent temperature-time combination) from every outlet.

- **Instantaneous steam heating:** Flash heating water to temperatures greater than 88°C (190°F) and then blending hot water with cold water to attain designated water temperature.

- **Hyperchlorination:** Involves shock or super-chlorination at dosages of 50-100 mg/L. Hyperchlorination is different from continuous disinfection using chlorine at much lower dosages. **One-time hyperchlorination for remedial purposes does not require a DEP Public Water System permit.**

- **Chlorine:** Continuous disinfection using free chlorine, aiming to maintain residual free chlorine level of 0.3-0.5 mg/liter (0.3-0.5 ppm) throughout the distribution system, from intake to all distal outlets. Note that current DEP standards are lower (must have detectable free residual chlorine; current instrumentation can detect down to 0.02 mg/L), but higher
minimum standards are under consideration. Very effective and relatively simple to use. Requires a DEP Public Water System permit.

- **Monochloramine**: Generated onsite by combining chlorine and ammonia. Ammonia addition quenches residual chlorine and minimizes formation of disinfection byproducts; monochloramine penetrates biofilms. Aim for monochloramine concentration of 1.5-3.0 mg/liter. Requires a DEP Public Water System permit.

- **Chlorine dioxide**: Generated onsite as a gas (sodium chlorite and a strong acid); concentration at sentinel taps and representative outlets should be at least 0.1 mg/liter. Requires a DEP Public Water System permit.

- **Copper-silver ionization**: Distorts the permeability of the *Legionella* cell, denatures proteins, and leads to cell breakdown and cell death. Requires monitoring of copper and silver ion levels in water system. Not listed by EPA as a treatment technology that can be used to comply with federal regulations. DEP does not issue permits for its use in potable water supply.


- **Ultraviolet light sterilization**: UV reactor generates short wavelength UV light on site. Provides no residual. Does not require a DEP Public Water System permit.

- **Point of use filter**: Physical barrier to prevent exposure to contaminated water. Does not require a DEP permit, but must meet NSF standards for safety and efficacy.

11. **Call the department of health and/or environmental protection if you have further questions**: If you have further questions about monitoring for *Legionella* in the environment, you can call the local health department [ACHD: 412-687-ACHD (2243)], the relevant appropriate DEP regional Office [see Appendix 10; RA-epcontactus@pa.gov], or consult other references provided in Appendix 10.
INTRODUCTION AND BACKGROUND

- Legionnaires’ disease, the most severe form of infection by certain species of *Legionella* bacteria, is a pneumonia that should be treated as early as possible.
- *Legionella* bacteria are commonly found in natural and manmade water sources, but they proliferate and can pose greatest risk to human health in water sources that meet three key conditions: heat, stasis, aerosolization. Examples of such sources include potable water systems (showers, faucets), hot tubs, decorative fountains, cooling towers, and nebulizers.
- People become sick after inhaling or aspirating (choking on) contaminated aerosol, fine spray or mist from such sources.
- Different government and non-government agencies have issued detailed guidelines and standards related to legionellosis. As of 2014, many of these agencies were in the process of updating their guidelines.

Legionellosis\(^1\) refers to two distinct syndromes caused by Gram-negative *Legionella* bacteria. The more severe one is Legionnaires’ disease (LD), a pneumonia caused by various serogroups of *Legionella pneumophila* and other *Legionella* species. LD can be severe enough to cause 5-30 percent of patients to die. The other clinical disease is Pontiac fever (PF), a non-fatal influenza-like illness with fever, chills and malaise, but without pneumonia. Not all *Legionella* have been demonstrated to cause human disease, but they are all theoretically capable. Only 18 of the 42 identified species have been linked to patients with pneumonia.\(^2\) The most common cause of LD is *Legionella pneumophila*, which has been linked to 90 percent of all LD cases, and especially serogroup 1 which is the causative agent of 70-80 percent of LD cases. The Centers for Disease Control and Prevention (CDC) estimates that fewer than five percent of persons exposed to *Legionella* will develop the severe form of illness, LD, and more than 90 percent of those exposed will develop Pontiac fever. However, more than 99 percent of legionellosis cases reported to CDC are LD, since reporting is required only for LD, and no one gets definitively diagnosed with Pontiac fever except as part of an outbreak investigation.

LD was first identified (and named) following an outbreak of severe pneumonia in 1976 among persons who had attended an American Legion conference in Philadelphia. The outbreak was attributed to airborne spread of an unidentified pathogen from water cooling towers serving a particular hotel, with main exposure in the hotel’s lobby.

Since LD became a nationally notifiable disease in 1976 and continuing into the new millennium, the number of cases—and the population-based incidence rate—has increased.\(^3\) CDC estimates that 8,000-18,000 hospitalizations for LD occur each year in the United States. However, the true incidence of LD is difficult to determine because it is under reported to national surveillance systems and depends on clinician awareness of

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\(^1\) Terms in red font are defined in Appendix 3, “Glossary of key terms used”
\(^2\) Bangsboro 1997
\(^3\) Neil and Berkelman 2008; CDC - [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6032a3.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6032a3.htm)
the disease and resources available to diagnose it. Persons at higher risk for LD include those who are older, are current or former smokers, have chronic lung disease, and/or have weak immune systems due to disease or drug therapy. The Legionella species are ubiquitously found in nature, primarily in aquatic environments. They can survive in varied water conditions, in temperatures 0-63°C (32°F-145.4°F) and a pH range of 5.0-8.5. They thrive in water that is warm but not too hot (25°C-42°C, or 77°F-107.6°F). Water sources that can transmit Legionella and thus pose a risk to human health meet three key conditions: heat, stasis and aerosolization. Examples of such sources include institutional hot water distribution systems, hot tubs, decorative fountains or misting devices. Legionella is spread mainly via airborne transmission (inhalation) of contaminated water in the form of aerosol, fine spray or mist emanating from these sources, or from choking on water (e.g., in respiratory therapy equipment) that has been contaminated with the bacteria. Healthcare-associated LD has also been traced to a hospital’s ice machine. LD has been associated with drinking and/or recreational water systems in settings such as health care facilities, nursing homes and assisted living facilities, hotels/motels, and cruise ships. In the United States, legionellosis is more common in summer-fall months and in Atlantic seaboard states, especially the Middle Atlantic Region that includes New Jersey, New York and Pennsylvania. There is no scientifically established "safe" dose of Legionella, i.e., a threshold for human health risk. While it is likely impossible to eradicate Legionella colonization altogether in water systems, the key approach to LD prevention is risk management, which aims to prevent or minimize Legionella growth in water systems and to take action to reduce Legionella when indicated. Outbreaks in healthcare facilities may receive the most media attention, but such facilities may account for only about 10-20 percent of all reported LD cases. These updated guidelines for Western Pennsylvania were developed in consultation with experts representing a range of organizations, disciplines and expertise (Appendix 1). They are intended to provide clear, practical, and actionable information to health care and residential facilities (among others) that both serve persons at risk for LD and have water systems that may harbor and disperse Legionella—especially community hospitals, nursing homes, assisted living and high-rise retirement facilities. The guidelines are organized into the following major sections:

- **Managing Legionella in people: Clinical and public health aspects**: clinical presentation, clinical and laboratory diagnosis, treatment, public health surveillance, outbreak detection and investigation
- **Managing Legionella risk in the environment**: approaches to management of Legionella in the environment, risk management approach, drinking water regulation and monitoring, public water system

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4 See [http://www.cdc.gov/legionella/about/people-risk.html](http://www.cdc.gov/legionella/about/people-risk.html)
5 Nguyen et al., 1991
7 Graman 1997
regulation at federal and state level, routine maintenance and operations practices, treatments to prevent or reduce *Legionella* contamination including disinfection methods, collection of water samples for microbiological testing, interpretation of laboratory results

- **Appendices:** List of contributors, published guidelines and topical references, LD clinical diagnosis, glossary of key terms used, diagnostic testing, surveillance case definition, steps in epidemiological investigation, federal and state regulation and monitoring of drinking water, where to call for more information

Various domestic government agencies (federal, state, local), non-government organizations (e.g., professional associations), and international authorities (e.g., World Health Organization), each with its own mandate and perspective, have issued guidelines that address different aspects of legionellosis prevention and control. Some of these date back to the 1990’s and early 2000’s (see Appendix 2). As of August 2014, the VA had just issued an updated directive for “Prevention of Healthcare-Associated *Legionella* Disease and Scald Injury from Potable Water Distribution Systems”, and a number of other agencies in the United States were in the process of developing new or revised guidelines or reference materials:

- Environmental Protection Agency (EPA): revised guidance document based on review of the current knowledge of *Legionella* treatment technologies (expected in spring 2015)
- Occupational Safety and Health Administration (OSHA): updated technical guidelines for occupational health and safety (target date uncertain, but revision process underway during 2014)
- CDC outbreak investigation guidelines (expected in early 2015)
- American Society of Heating, Refrigerating, and Air Conditioning Engineers (ASHRAE) guidelines for prevention of legionellosis associated with drinking water systems (next round of public review in January 2015)

These updated guidelines for Western Pennsylvania were developed based on review of numerous published reports and guidelines and in consultation with most of the agencies listed above, and with the Pennsylvania stakeholder agencies contributing to the 1997 ACHD guidelines. However, readers are well advised to consult guidelines issued subsequent to these because they will provide more detailed information not available as evidence for the present guidelines, and will address specific areas in more detail than here (e.g., legionellosis outbreak investigation, engineering design and environmental remediation), including national level recommendations or regulations. Readers are also advised that new scientific reports will eventually enable more confident and precise evidence-based recommendations.
Managing *Legionella* in people involves medical management of disease in individuals and public health management of disease in populations. This chapter is organized into the following sections:

### Managing *Legionella* in individuals—clinical:
- Clinical presentation of LD
- Diagnosis (more details are provided in Appendixes 4 and 5)
- Treatment
- Follow-up

### Managing *Legionella* in populations—public health:
- Epidemiology
- Disease surveillance and reporting (more details are provided in Appendixes 6 and 7)
- Outbreak detection and investigation (more details are provided in Appendix 8; implementation of appropriate public health control measures is based on findings from the investigation)

The symptoms and signs of Legionnaires’ disease are similar to those of pneumonia caused by other microbes.

Especially in severely ill patients, it is important to make a specific diagnosis so that the most appropriate treatment can be given.
- Laboratory testing should ideally include both the urine antigen test and culture of a respiratory specimen such as sputum.
- The drugs of choice for Legionnaires’ disease are a *macrolide* such as azithromycin or a respiratory *fluoroquinolone* such as moxifloxacin.

Cases of Legionnaires’ disease can arise in the community (*community-acquired*), health care facilities (*nosocomial*), or in association with travel (*travel-associated*).

Disease surveillance involves the monitoring and reporting of cases among patients (*clinical surveillance*) and the broader population (*public health surveillance*) so that investigation can be undertaken to identify the source of infection and inform actions to reduce further transmission and risk to human health.
LD in Individuals: Clinical Aspects

Clinical Presentation

It is important to understand the clinical picture of LD in order to suspect Legionella in ill persons who fit the LD profile. A person can begin to feel ill within two to ten days after exposure to Legionella. Exposure means breathing in air containing water that is contaminated with Legionella, in the form of aerosol, fine mist or spray, or choking on (“aspirating”) contaminated fluid (e.g., in respiratory therapy equipment).

On the first day, a person may feel:

- headache
- muscle pain (“myalgia”)
- chills
- fever that may reach as high as 104° F (but may also begin as a low grade fever)

By the second and third day, the person may develop:

- cough (dry cough, or cough with mucus, only occasionally with blood)
- shortness of breath
- chest pain (that either does or does not hurt more with breathing movement—“pleuritic” pain)
- gastrointestinal symptoms (for example, nausea, vomiting, watery diarrhea, abdominal pain)
- confusion

It is important to manage or refer such persons for medical attention promptly, because LD often requires hospitalization, and treatment will be more effective when started as early as possible.

Diagnosis

The clinician will take a careful history, examine the patient, and determine whether to order specific diagnostic tests to help determine the cause of the patient’s illness and point to the best initial treatment. For example, in its guidelines for prevention of healthcare-associated pneumonia, CDC recommends diagnostic testing for legionellosis in “suspected cases, especially in patients who are at high risk for acquiring the disease [such as] patients aged ≥65 years; or patients who have chronic underlying disease.” More general CDC guidance recommends diagnostic testing of patients with suspected healthcare-associated pneumonia and also pneumonia patients who have failed outpatient antibiotic therapy, are immunocompromised, have a relevant travel history, or whose pneumonia occurs in the setting of an outbreak. On the other hand, widely used consensus guidelines for community-acquired pneumonia note the controversy surrounding recommendations for diagnostic testing, but suggest such testing in patients who are severely ill (as defined in the guidelines) or for whom the testing would alter individual antibiotic management.

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8 CDC 2003 (Preventing Health-Care Associated Pneumonia)
9 See http://www.cdc.gov/legionella/clinicians.html
10 Mandell 2007
not recommend routine diagnostic testing for persons with clinical pneumonia who are treated as outpatients, unless the outpatient therapy fails. Definitive diagnosis of more cases of pneumonia would be helpful to public health by enhancing our understanding of specific diseases like LD. As such, clinicians might consider the merits of ordering diagnostic testing for Legionella even in the outpatient environment, in relation to the public benefits. Appendix 4 provides more details on the clinical diagnosis of LD, and Appendix 5 provides details of diagnostic testing, including the different laboratory tests used to detect Legionella infection. It is important to note that laboratory diagnosis of Legionella requires specialized tests that may not be routinely performed on every patient with pneumonia, so the clinician must suspect LD in order to diagnose it and to treat it appropriately. Diagnostic testing is especially important in more severely ill patients.

**Treatment**

After making a clinical diagnosis of pneumonia, the clinician will usually start treating the patient based on the most likely diagnosis (or range of diagnoses) gleaned from history and physical examination including vital signs, i.e., before definitive diagnostic test results (if performed) are available. This is called “empiric” or “presumptive” treatment. As suggested in the previous section, empiric treatment is the norm for pneumonia treated as an outpatient, since routine diagnostic testing is not recommended. When LD is suspected, whether or not diagnostic testing is performed, initial empiric therapy should include a drug that is effective against Legionella, for example either a respiratory fluoroquinolone or a macrolide. Empiric treatment with an antibiotic effective for LD is critical, since delaying initiation of LD treatment increases the risk of death. It is important to note, however, that treatment for pneumonia without or before diagnostic testing may result in cases of LD or other pneumonias not being diagnosed specifically or reported to health authorities, and hence, significant under-reporting of these diseases.

Historically, erythromycin, a macrolide antibiotic, was the drug of choice for LD. In more recent years, other macrolide antibiotics and other groups of drugs such as fluoroquinolones and a new glycylcycline drug have displaced erythromycin as the drugs of choice for LD, including:

- **Macrolides**: including azithromycin, clarithromycin
  - Subclass – ketolides: telithromycin
- **Fluoroquinolones**: including levofloxacin, moxifloxacin (these are considered “respiratory fluoroquinolones”, i.e., effective against respiratory infections)
- **Tetracyclines**: including doxycycline
- **Glycylcycline**: new class of drugs that includes tigecycline (approved by FDA in 2005)

A respiratory fluoroquinolone drug should be used for the most severely ill patients, for whom, as noted above, laboratory diagnostic testing is recommended. A 10-14-day course of antibiotic treatment is typically given intravenously at first, until the patient becomes demonstrably better (e.g., afebrile and breathing comfortably), and then

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11 Mandell 2007
12 CDC - [http://www.cdc.gov/legionella/diagnostic-testing.html](http://www.cdc.gov/legionella/diagnostic-testing.html)
completed with oral dosing; immunocompromised patients may require a 21-day course of treatment. Specialized medical consultation may be needed if a patient does not improve with treatment.

Hospitalized LD patients may require additional oxygen and even mechanical ventilator assistance (“respirator”) to maintain adequate oxygenation.

**Follow-up**

If the LD patient lives in a residential facility, it will be important for the facility’s staff to verify their diagnosis when they return to the facility. In particular, it will be important to ascertain whether *Legionella* or some other pathogen was identified. Facilities should respond to suspected or confirmed LD case(s) associated with their facility. Practically speaking, this means notifying the local health department, e.g., ACHD, if LD has been diagnosed (through laboratory testing) in one or more residents and the exposure may have occurred at the facility.

In Pennsylvania, laboratory-diagnosed LD cases should be reported (mainly by providers and laboratories) through the Pennsylvania-National Electronic Disease Surveillance System (PA-NEDSS), and information will automatically go to both the local and state health departments. Because “suspected” or “confirmed” LD means that laboratory testing has implicated *Legionella*, even a single case indicates environmental contamination that could infect others, and thus warrants investigation and potential action, just as an outbreak does. The health department will likely investigate further and report the case(s) to the state health department and on to CDC, as described in the next section.

In principle, treatment facilities are responsible for reporting cases of notifiable diseases (described in the next section) to the health department, but staff or others should feel free to contact the health department if they have further questions about ill persons or any other questions about legionellosis.

<table>
<thead>
<tr>
<th>Recommendations for Managing <em>Legionella</em> in Individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Suspect <em>Legionella</em> in ill persons who fit the LD profile.</td>
</tr>
<tr>
<td>2. Manage or refer such persons for medical attention promptly.</td>
</tr>
<tr>
<td>3. Verify the diagnosis of persons returning to a residential facility (to ascertain whether LD was diagnosed).</td>
</tr>
<tr>
<td>4. Respond to suspected or confirmed case(s) of LD associated with a residential or health care facility.</td>
</tr>
<tr>
<td>5. Contact the local health department with any further questions.</td>
</tr>
</tbody>
</table>

13 See [http://www.portal.state.pa.us/portal/server.pt/community/pa_national_electronic_disease_surveillance_system%28pa-nedss%29/14215](http://www.portal.state.pa.us/portal/server.pt/community/pa_national_electronic_disease_surveillance_system%28pa-nedss%29/14215) or contact ACHD or the PA Department of Health (see Appendix 10 for contact information)
LD in Populations: Public Health

Epidemiology

Epidemiology is the study of the distribution and determinants of diseases and health conditions in the population. The determinants of a disease are based on the relationship between host, agent, and the environment, known as the “epidemiologic triad.” For legionellosis, the host (a person) becomes infected if the agent (*Legionella*) is present, and if the environment (water source and setting) is conducive to *Legionella* growth and aerosolized dispersion to people. People become infected from the environment; unlike many respiratory diseases, LD is not spread from person to person. Cases are often described in terms of where they arise and the type of occurrence:

*Community-acquired:* Community-acquired infections arise from a variety of sources and settings other than hospitals or long-term care facilities.\(^{14}\)

*Nosocomial:* Nosocomial, or “healthcare-associated,” infections are those acquired in a health care facility. Specifically, a patient with laboratory-confirmed legionellosis who was hospitalized continuously for 10 days or more prior to onset of illness is considered a “definite” nosocomial case; a laboratory-confirmed infection that occurs within 2-9 days after hospitalization is considered a “possible” nosocomial case.\(^{15}\)

*Travel-associated:* Travel-associated infections are acquired from a source where a person spends at least one night away from home.

*Sporadic cases and outbreaks.* *Legionella* may cause single (“sporadic”) or multiple cases (“outbreaks”) from a contaminated source.

The epidemiology of a condition is usually described in terms of person, place and time. Based on more than three decades of surveillance, outbreak investigations, and analysis, legionellosis has the following epidemiologic characteristics:

*Person.* LD patients typically have one or more risk factors, including older age, history of smoking, chronic lung disease, compromised immune system; higher incidence rates are also associated with male sex and African American race, for reasons not yet fully explained.

*Place.* Within the United States, eastern seaboard regions have the highest reported incidence rates, especially the states in the Middle Atlantic region (New Jersey, New York, and Pennsylvania).\(^ {16}\) Infection may be acquired in the community; in a health care facility, via inhalation or choking—*aspiration*—on contaminated water (e.g., in respiratory therapy equipment); in a residential facility; or at a site associated with travel (e.g., hotel/motel, cruise ship). Such settings can pose a risk to human health if they have water sources conducive to *Legionella* proliferation, whether through contaminated potable water systems (including water both intended and not for drinking – e.g., faucets, showers) or contaminated recreational water (e.g., pool, spa) or a decorative water system (e.g., fountain).

\(^{14}\) Lutfiyya 2006  
\(^{15}\) CDC 1997  
\(^{16}\) CDC 2011 (*MMWR* 60[32])
Legionellosis tends to be seasonal, with nearly two-thirds of reported cases occurring during the five months from June through October.

**Disease Surveillance and Reporting**

**Clinical Surveillance**

Clinical surveillance for LD refers to monitoring for cases of disease, typically in a health care facility; this is contrasted with environmental surveillance, which refers to monitoring for *Legionella* contamination in the environment. Clinical surveillance for LD is primarily a secondary prevention approach, i.e., oriented toward preventing additional cases once a first case is detected. (In contrast, primary prevention—described in the next section—is oriented toward preventing any case from occurring, based on a risk management approach.) Secondary prevention of legionellosis is generally associated with health care settings but “[community-acquired] pneumonia from nonambulatory residents of nursing homes and other long-term care facilities epidemiologically mirrors hospital-acquired pneumonia and should be treated according to [guidelines for healthcare-associated pneumonia].”\(^{17}\) Clinical or other professional staff at facilities should maintain a high level of suspicion and immediately test anyone who becomes ill with potential *Legionella* disease. This is especially important if the infection might have been acquired in the facility (i.e., if the person resided in the facility continuously for 10 days or more before becoming ill—consistent with the time frame associated with nosocomial, or healthcare-associated, legionellosis). CDC guidelines in effect as of 2014 call for additional action upon identification of (a) one laboratory-confirmed case classified as definitely or possibly healthcare-associated, occurring in a high-risk patient setting such as a transplant unit), or (b) two or more laboratory-confirmed cases within six months of each other in patients who visited such settings for part of 2-10 days prior to illness. Specifically, such occurrences should trigger intensified clinical surveillance (“active surveillance”) to identify additional cases and epidemiologic investigation by the local health department to determine the source/cause of infection and inform appropriate actions to limit further transmission. Clinical surveillance is also important, for example in a hospital setting, if environmental monitoring indicates *Legionella* contamination of the facility’s water system.

**Public Health Surveillance**

Public health surveillance refers to detection and reporting of cases of disease or other conditions in the population. In the United States, public health surveillance is voluntary on the part of state and local health departments. Constitutionally, it is not, and cannot be, mandated by the federal government. However, the Council of State and Territorial Epidemiologists (CSTE) determines the list of “Nationally Notifiable Diseases” and their case definition for purposes of disease surveillance reporting. CSTE identified LD as one of approximately 70 nationally notifiable diseases reportable to CDC through the electronic “National Notifiable Disease Surveillance System” (NNDSS). Case reports (based on the CDC Legionellosis Case Report Form\(^{18}\)) include basic demographic information as well as travel and diagnostic information. Appendix 6 provides the details

\(^{17}\) Mandell 2007  
of the CDC case definition for legionellosis, and Appendix 7 summarizes legionellosis surveillance trends.

**Outbreak Detection and Investigation**

Outbreaks of LD may be detected locally through surveillance reports or ad hoc communications, e.g., a phone call from a hospital, nursing home, assisted living facility. CDC’s surveillance aims to follow trends in legionellosis and also to detect and respond to outbreaks. An “outbreak” is defined as two or more persons linked epidemiologically in place and time to a common source, based on an epidemiologic investigation. The 2005 CSTE updates for LD surveillance reporting enhance the timeliness of reporting travel-associated LD in particular, in order to detect outbreaks among persons who may return home to widely different locations after travel and leave an environmental source of risk undetected and unaddressed.

An epidemiological/environmental investigation is a systematic process for examining a cluster of cases of a suspected condition to identify, through statistical means supported by laboratory testing, the likely causative source. In the case of infectious diseases such as LD, these investigations help point to the source of disease transmission and the mode in which the disease is spread. This information in turn informs the appropriate control measures, usually environmental measures related to an implicated water system or source. Because of the environmental source of *Legionella* and the likely need for environmental control measures, it is important that the epidemiological investigation team include one or more environmental health professionals.

LD is distinctive as a disease whose causative organism is found in water (a water-borne disease) but is acquired by inhalation (air-borne transmission). Most water-borne diseases affect primarily the gastrointestinal tract, causing nausea, vomiting and/or diarrhea; they may be spread from either “point sources” (a contaminated water source) or from person to person (via hand-to-mouth, or “fecal-oral,” contamination). LD is spread through the air through inhalation of contaminated aerosolized water or aspiration (choking, e.g., on water in a contaminated medical device such as a nebulizer), but it is transmitted strictly from common environmental “point” sources, and not from person to person; most other respiratory infections are spread from person to person. Therefore, an epidemiologic/environmental investigation of a pneumonia outbreak must take into consideration whether LD is a possibility and examine the appropriate range of infection sources accordingly. Once a possible outbreak is detected, a trained epidemiologist/environmental health specialist will conduct an epidemiologic investigation. Appendix 8 outlines the steps in such an investigation, and the next section describes steps for investigation and management of *Legionella* in the environment in response to a confirmed case or outbreak.

### Recommendations for Managing *Legionella* in Populations

6. Health care providers and laboratories will report suspected or confirmed LD cases to the local health department (in Pennsylvania, through the Pennsylvania–National Electronic Disease Surveillance System).

7. The local health department will follow up to investigate such cases and recommend appropriate control measures.
Legionella bacteria are common in the environment. They thrive and may pose a risk to human health in water systems with heat, stasis, and aerosolization.

Water systems in facilities that house or serve persons at risk for legionellosis may fall under state regulatory control. The regulations are based largely on a risk-management approach to prevent or reduce Legionella contamination in the environment. For such systems, permits issued by the Pennsylvania Department of Environmental Protection will require the facility to comply with certain requirements of Title 25, PA Code Chapter 109, Safe Drinking Water Rules and Regulation, and any specific permit conditions.

These guidelines provide practical information for managing water systems commonly found in health care facilities and facilities housing, caring for or serving persons at particular risk for legionellosis, including monitoring and control measures.

Managing Legionella risk in the environment requires an understanding of where and how the organism grows in the environment and approaches for its control, including relevant regulations. This chapter is organized into the following sections:

- Legionella in the environment
- Approaches to management of Legionella in the environment
- Federal and state regulation of drinking water (more details are provided in Appendix 9)
- Taking a risk management approach
- Routine operation and maintenance of water distribution systems
- Regulated routine control measures for prevention of Legionella
- Legionella treatment methods
- Environmental management in response to a confirmed LD case or outbreak
- Collection of water samples for microbiological testing
- Interpretation of laboratory results
**Legionella in the Environment**

*Legionella* are found in the environment, usually in freshwater from natural or man-made sources. They can survive in temperatures from 0°C-63°C (32°F-145.4°F), but they thrive in warm water (25°C-42°C, or about 77°F-107.6°F), stagnant water, scale and sediment (including biofilms), and in the presence of certain free-living amoebae in the water. Biofilms facilitate nutrient exchange for *Legionella* and offer protection from adverse environmental conditions, including water disinfection.\(^{19}\) Because biofilms colonize drinking water distribution systems, they provide a habitat suitable for *Legionella* growth in such systems. Potable water, especially in hospitals and facilities with complex hot water systems, is considered to be the most important source of *Legionella* transmission.\(^{20}\) Table 1 presents a summary of water sources and settings that have been associated with LD outbreaks across the United States.\(^{21}\) Implicated sources include:

- pools or spas (e.g., hot tubs)
- reservoirs
- lakes
- wells
- creeks or springs
- rivers
- cooling towers
- mist devices
- fountains

Implicated settings for these outbreaks include:

- hotel/motel
- hospital & other health care facilities
- nursing homes
- assisted living facilities
- long-term facilities
- retirement homes
- personal care home
- apartments, other residential buildings
- membership clubs
- community settings
- factory, industry, office workplaces
- restaurant
- store
- prison/jail

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19 WHO 2007
20 Blatt et al. 1993; Stout and Yu 1997; Woo et al., 1992; Yu 1993
21 CDC *MMWR* 2013, CDC *MMWR* 2014
<table>
<thead>
<tr>
<th>Period Covered</th>
<th>Type of Water Source</th>
<th>Number of Outbreaks</th>
<th>Sources (# outbreaks)</th>
<th>Settings (# outbreaks)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Legionella</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2007-2008</td>
<td>Recreational</td>
<td>134</td>
<td>Pool &amp;/or spa (10)</td>
<td>Hotel/motel (7), assisted living facility (1), community (1), membership club (1)</td>
</tr>
<tr>
<td></td>
<td>Drinking + other non-recreational</td>
<td>48</td>
<td>Reservoir (6), lake (3), well (2), well/river (1)</td>
<td>Hospital (5), nursing home (3), residential building (2), hotel (1), assisted living facility (1)</td>
</tr>
<tr>
<td>1973-2002</td>
<td>Drinking + other non-recreational</td>
<td>70</td>
<td>Hospital/health care facility (31), community (13), hotel/motel (8), factory/industry (6), office (4), store (2), retirement home (1), club (1), event (1), restaurant (1), prison/jail (1)</td>
<td></td>
</tr>
<tr>
<td>2009-2010</td>
<td>Recreational</td>
<td>81</td>
<td>Pool or spa (4)</td>
<td>Club (2), apartment (1), hotel/motel (1)</td>
</tr>
<tr>
<td></td>
<td>Drinking</td>
<td>33</td>
<td>Lake/reservoir (8), well or spring (4), river/stream (2), well and river/stream (1), spring/creek (1), surface water (1), ground water (1), unknown (1)</td>
<td>Hotel/motel (6), hospital/health care facility (5), personal care home (2), apartment (2), long-term care facility (1), assisted living facility (1), membership club (1), prison/jail (1)</td>
</tr>
<tr>
<td></td>
<td>Other non-recreational</td>
<td>12</td>
<td>Cooling tower (2), mist device (1), ornamental fountain (1), unknown (1)</td>
<td>Long-term care facility (2), assisted living facility (1), health care facility (1), hotel/motel (1), factory/industry (1), military facility (1)</td>
</tr>
</tbody>
</table>

TOTAL          | 378                           | 91                  |                       |                        |

Sources: CDC MMWR 2011 (Vol 60[12]), CDC MMWR 2013, CDC MMWR 2014
Approaches to Management of *Legionella* risk in the Environment

There has been considerable debate over the years—still not fully resolved—regarding environmental management to prevent or reduce *Legionella* contamination, including appropriate control measures and where, when and how to monitor for *Legionella* in the environment. Most U.S. guidelines have not been updated for many years, but current guidelines from the Environmental Protection Agency (EPA) and the Pennsylvania DEP, the 2014 VA guidelines, and recent guidelines from other countries and the World Health Organization embrace a risk management approach rather than prescribing a fixed approach for all settings. Such an approach recognizes that environmental contamination may not be entirely eradicable, but environmental risks can be substantially minimized through a number of routine and ad hoc measures. The steps for management of *Legionella* in the environment are somewhat more standardized in response to a confirmed case or outbreak of LD.

In the United States, one school of thought, promulgated in particular by health officials in Western Pennsylvania, has focused on primary prevention of LD in health care facilities, specifically routine pre-emptive environmental monitoring and management in all hospital facilities, i.e., not just in response to an LD case. Directive 1061 issued by the VA in August 2014 also focuses on primary prevention, specifically the prevention of health care-associated legionellosis in VA-owned buildings in which patients, residents or visitors stay overnight. The Directive advocates a risk management approach, including risk assessment, environmental monitoring and appropriate engineering controls. Engineering controls include “ongoing monitoring of implemented controls, validating that the control measures are effective at inhibiting *Legionella* growth, and modifying implementation or type(s), as necessary.” This is similar to the risk management approach described in the 2007 WHO guidelines.

Another approach, embodied in CDC’s 2003 guidelines for preventing health care-associated pneumonias, orients LD-related monitoring around clinical surveillance to detect and respond to a case of LD that may have been acquired in the facility, i.e., secondary prevention. CDC has generally recommended that facilities maintain a high index of suspicion for LD among all healthcare-associated pneumonia cases, especially in individuals at high risk for the disease (e.g., immunocompromised patients such as those who have received bone marrow transplants), and conduct an environmental investigation upon confirmation of one definite case or two suspect cases. In those guidelines, CDC recommended routine environmental surveillance only in hospital units that provide transplantation services. As of 2014, several agencies—including CDC and the Occupational Safety and Health Administration, among others—were in the process of updating their legionellosis guidelines (and conceivably could include greater emphasis on primary prevention than before), but the present guidelines for Western Pennsylvania were completed before these revisions were finalized and issued.

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22 Stout et al., 2007, 1997 ACHD guidelines
23 VA 2014
24 WHO 2007
25 CDC 2003 (Environmental Infection Control in Health-Care Facilities)
Federal and State Regulation of Drinking Water

Some potable water systems fall under government regulation and others do not. By law, state environmental regulations must be at least as stringent as federal regulations. Appendix 9 summarizes drinking water regulation at federal and state levels.

Through its permitting process, the DEP regulates certain public water systems (PWS’s) as defined in the federal Safe Drinking Water Act (SDWA). A PWS is defined as having at least 15 service connections or regularly serving at least 25 individuals. A community water system (CWS) is a PWS that provides water on an ongoing year-round basis. Pennsylvania’s Safe Drinking Water Regulations also define a consecutive water system as “A public water system which obtains all of its water from another public water system and resells the water to a person, provides treatment to meet a primary MCL or provides drinking water to an interstate carrier. The term does not include bottled water and bulk water systems.”

Most facilities interested in these legionellosis guidelines probably have the type of public water system (at least 15 service connections or 25 users) that is also a community water system (year-round use) and consecutive water system (receives treated water from another public water system). All of these labels are important because some DEP regulations are defined in terms of more than just the broadest category of public water systems.

DEP regulates such systems unless they qualify for an exemption under the SDWA. For example, only systems that install treatment or add their own source of water supply trigger applicability under the SDWA and are subject to DEP regulation. Thermal treatment alone or one-time hyperchlorination (“shock chlorination”) for purposes of remediation do not subject a PWS/CWS to DEP regulation. However, DEP requires that super-chlorinated water must be properly flushed and cannot be served to the public. Other forms of treatment do trigger applicability under the SDWA - including when the treatment involves the addition of chemicals or causes a change to the water chemistry.

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Taking a Risk Management Approach

Consistent with guidelines from the Pennsylvania DEP, VA, and World Health Organization,^27 facilities should take a risk management approach to environmental monitoring and control of *Legionella*. This approach is appropriate not only for health care facilities but also for other facilities that house or serve persons at greatest risk including community hospitals, nursing homes, assisted living facilities, and high-rise retirement facilities. The DEP permitting process as well as the 2014 VA and 2007 WHO guidelines are all based on a risk management approach.

The recommendations here take advantage of the available, albeit not always sufficient or definitive, scientific evidence for the appropriate routine monitoring and control of water systems and compliance with state environmental regulations, as well as what actions to take to decontaminate water systems to minimize the risk to human health.^28

One practical way to implement a risk management approach is through a water safety plan (WSP). The key steps are to:

- **Document and describe the building’s water system(s).** Develop a schematic (line) diagram of the site distribution and building water systems (hot and cold water). The diagram should indicate how water is distributed, circulated, heated and cooled, treated and monitored.

- **Assess hazards and characterize risk.** This entails assessment of such factors as the number and vulnerability of patients/persons served by the facility and its water systems, the various water sources to which such persons might be exposed and the likelihood and intensity of exposure, past cases of LD linked to the facility, ability to implement and maintain engineering controls to prevent *Legionella* growth, and past lapses in engineering controls including past positive environmental testing results. The 2014 VA Directive for its own buildings calls for an annual risk assessment.^29

- **Identify water system management points and engineering control strategies.** This is based on the schematic diagram(s), identification of points where controls can be implemented and monitored, and identification of specific control strategies for both routine and remedial use. Specific description of such strategies includes setting target levels, e.g., for hot and cold water temperature or residual biocide level; establishing a schedule to routinely monitor implementation of the control strategies; establishing a plan to eliminate or prevent system dead-legs (where water can stagnate and favor *Legionella* growth).

- **Implement, monitor and document engineering control measures** including lapses identified and corrective actions taken. Water systems should be

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^27 See Appendix 2
^29 VA 2014
monitored from the entry point into the building (e.g., the municipal water supply entering the building), through key portions of the system to its distal outlets (e.g., shower heads and faucets). Given the relevance of the municipal water supplied to a building, facilities will want to communicate and coordinate relevant efforts with their water supplier, for example if the water entering the building does not meet minimum biocide standards or if the facility wishes the provider to flush the water hydrant closest to the building to move fresher water to the facility.

- **Validate the effectiveness of engineering control measures.** This involves both environmental and clinical validation approaches, including periodic testing for *Legionella* in the water system and monitoring for cases of LD (which may or may not be linked to the facility, depending on the persons involved and timing of their potential exposure). The 2014 VA guidelines call for at least quarterly testing for *Legionella pneumophila* in a building’s hot and cold water systems. Those guidelines specify testing water samples from at least 10 outlets each on the hot and cold water distribution systems. For routine testing, swab samples are not required but may be added to the testing of water samples. Also, International Standard Organization (ISO) 11731 is a voluntary monitoring method standard for the isolation and enumeration of *Legionella* organisms in water intended for human use. Access to ISO standards requires a paid subscription.

- **Take corrective action when warranted.** When routine monitoring indicates that engineering control measures fail to maintain water within specified limits (e.g., temperature, biocide level), those responsible should assess the reasons why the controls fell outside the established limits and take prompt corrective actions.

The general aim of the water safety plan is to minimize the proliferation and dispersion of *Legionella* in the environment and minimize exposure of vulnerable persons, but there are different practical options for achieving this. Current guidance on the development of water safety plans tend to cover water from source to consumer (i.e., are not limited to water distribution systems within buildings), and they are not specific to *Legionella*, but several useful guidance documents are referenced in Appendix 2. Based on overall risk assessment, some facilities will decide to undertake relatively frequent, routine environmental monitoring (including sampling and laboratory testing) of water systems/sources that are conducive to the growth and dispersal of *Legionella*. This will facilitate taking remedial environmental measures to reduce the risk of exposure and disease among vulnerable populations. Other facilities may choose to undertake environmental testing only if there is a confirmed case of LD linked to a source within the facility (see later section on environmental management in response to an LD case or outbreak).

The following sections describe non-regulated operation and maintenance best management practices for water distribution systems and then a longer list of treatment methods to control the growth of *Legionella* in the environment. Most of the latter are subject to regulation.

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Routine Operation and Maintenance of Water Distribution Systems

Whether or not a building’s water systems fall under government regulatory control, facilities should implement routine operation and maintenance best management practices for their water systems. Each facility will develop its own plan, based on a general risk management approach or as required through the DEP permitting process. In general, water distribution systems should maintain appropriate temperatures and flow and be designed or retrofitted to eliminate dead ends (e.g., proper installation and disinfection of new fixtures and water lines, cross connection control). Best management practices for the routine operation and maintenance of water systems, which do not explicitly require permitting, include the following:

- **Thermal control**: Specific guidelines vary somewhat across agencies and countries, but in general and if feasible within the design of the facility’s water system and permitted by local regulations, maintaining all elements of the water system at <20°C (68°F) or >50°C (>122°F) should inhibit Legionella growth. (For example, the 2014 VA guidelines specify that, to the greatest extent practicable, cold water should be maintained at or below 19.4°C, or 67°F.) Water in the hot water storage tank should ideally be maintained at a minimum of 60°C (140°F). A master thermostatic mixing valve can be installed to reduce temperature to around 54°C (130°F) before distribution. Hot water reaching the faucet or tap should be at least this temperature within two minutes. Pressure or thermostatic mixing valves can also be installed at the outlets and set to 45-49°C (113°F-120°F) to control temperature at the tap and reduce the risk of scalding. The 2014 VA Directive indicates a maximum temperature of 43.3°C, or 110°F, at the outlet, to prevent scalding. Hot water return should be at least 50°C (122°F). The water temperature in the hot and cold water distribution systems should be monitored continuously and documented. The points to be monitored include the incoming water supply to the building, water storage tanks, hot water discharge from the heating units, hot water return proximal to the hot water source equipment, water at the return of circulation loops, and water supplied to representative outlets (note that the 2014 VHA Directive indicates that details of the sampling scheme are forthcoming.)

  - Advantages: Simple, effective and easily monitored; little significant growth of Legionella below 20°C or above 50°C.
  - Disadvantages: Only applicable to drinking water systems (not ice machines or decorative fountains, for example); higher temperature limit does not eliminate Legionella; difficult to maintain in old systems; hot water limits require protection against scalding

- **Routine inspection and cleaning**: This includes control monitoring and physical inspection of the water system and its components. These are typically routine and relatively easy procedures.

  - **Inspection**: The number of sites to be monitored for temperature or biocide and the monitoring frequency should be based on risk. Illustrative examples from around the world suggest a monitoring frequency of daily to weekly, quarterly, six-monthly or annually, based on the system and
local risk. Hospitals and facilities that care for elderly or other vulnerable populations will likely want to monitor more frequently, e.g., weekly. This is reasonable, since monitoring of temperature and/or free residual chlorine is relatively simple.

- **Cleaning**: This involves removing and physically scouring or replacing parts, mainly distal outlets, to remove biofilms. The frequency will be specified in the building’s water safety plan (DEP does not have specific frequency requirements even for systems under their regulation). Showerheads, faucet aerators and hoses should either be replaced or cleaned on a regular basis. For cleaning, they should be dismantled, cleaned and descaled quarterly or more frequently, based on risk. Cleaning of showerheads can entail the use of disinfectants such as chlorine bleach (1,000 ppm free residual chlorine) for 10-15 minutes. Add 125 ml (about one-half cup) of proprietary chlorine bleach (which is typically around 4% free residual chlorine) to 5 liters of cold water, or 250 ml (about one cup) to 10 liters of cold water. If using liquid pool chlorine, which is typically 12.5% free residual chlorine: add 50 ml bleach to 5 liters of water, or 100 ml bleach to 10 liters of water. If using granular chlorine product, with 65% free residual chlorine, add 8 grams of bleach to 5 liters or 15 grams to 10 liters. Thermostatic mixing valves, if installed, should also be regularly serviced according to the manufacturer’s recommendations, and in any case at least annually.

- **Routine flushing**: Outlets on hot and cold water systems should be used regularly to maintain a degree of water flow that minimizes stagnation and reduces the potential for *Legionella* colonization. DEP regulations cite distribution system flushing as one of a handful of operational parameters to be monitored routinely. Routine flushing of outlets not used can be undertaken on a daily to weekly basis, based on risk. (For example, Ireland’s national guidelines suggest more than weekly routine flushing of unused outlets in hospitals and nursing homes. The 2014 VA guidelines call for flushing at least twice per week of hot and cold water at outlets that are not in routine use or which experience low water flow.) This entails running each unused outlet for six minutes: cold water at full flow for three minutes and then hot water at maximum temperature and full flow for three minutes. Increase the flow gradually to minimize aerosolization of potential *Legionella* and thus reduce the risk to personnel. Also, during periods when any system is undergoing a heating or flushing, all faucet aerators and shower heads should be removed and cleaned, as described above.

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31 Ireland 2009 (page 51)
32 DEP 2014
33 Ireland 2009 (page 49)
Specifically with regard to healthcare facilities, 2003 guidelines from CDC and the Healthcare Infection Control Practices Advisory Committee recommend a variety of routine control measures to help prevent *Legionella*. According to those guidelines:

- Cold water in hospitals should be stored and distributed at temperatures below 68°F (20°C). Where allowed by state regulations and codes, hot water should be stored at temperatures above 140°F (60°C) and circulated with a minimum return temperature of at least 124°F (51°C). Both the recommended cold and hot water temperatures are outside the range of optimal growth temperatures for *Legionella*.

- New shower systems in large buildings, hospitals, and nursing homes should be designed so that hot and cold water are mixed close to the shower head (not earlier in the system, where the mixed warm water would favor *Legionella* growth).

- When such systems cannot be retrofitted, they should be periodically flushed (a) at high temperatures (for at least five minutes with water that is at least 150°F/66°C at the point of use – e.g., faucet or showerhead) and/or (b) with additional chlorine (for at least five minutes with water containing at least 2 mg/L (2 parts per million [ppm]) free residual chlorine using an EPA-approved chlorine-based product. Facilities that are regulated as a PWS must use chemicals that are compliant with ANSI/NSF Standard 60 for safety. Common household bleach products that are typically available in grocery stores are not NSF approved, because their concentration is well below the required 12.5% solution.

- Sometimes, a facility performs emergency decontamination through either of these procedures (superheating or hyperchlorination); whether routine or on an emergency basis, it should try to maintain either the temperature conditions or sufficient chlorine levels (1-2 mg/L / 1-2 parts per million [ppm]) to impede new *Legionella* proliferation.

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34 CDC 2003 (Environmental Infection Control in Health-Care Facilities)
Regulated Routine Control Measures for Prevention of Legionella

Several routine control measures for the prevention of Legionella in water systems are regulated and require a permit, e.g., in Pennsylvania, from DEP. Routine treatment methods that are allowed by DEP and for which DEP must issue a permit include the following, all described in more detail in the section that follows:

- Chlorine – continuous disinfection using free chlorine
- Monochloramine
- Chlorine dioxide
- Ozone

Additional measures may be needed to remove accumulations of scale (including biofilms) and sediment that may impede the killing action of heat or chlorine on Legionella bacteria. Measures that have proven effective under laboratory and operational conditions include treating water with chlorine, monochloramine, chlorine dioxide, heavy metal ions (copper/silver), ozone, or UV light. (However, as noted in the next section, copper-silver ionization is not yet listed by EPA as a compliant treatment technology, and DEP does not issue permits for its use in regulated drinking water systems.) As an additional note, disinfection using ultraviolet light is allowed but may not require a DEP permit.

Legionella Treatment Methods

Facilities should implement appropriate treatment methods to prevent Legionella growth or when otherwise warranted, for example routine use or on an emergency basis following failure of engineering control measures, the occurrence of a LD case linked to the facility’s water system, or positive microbiological test results. The EPA lists best available technologies and treatment techniques under the Code of Federal Regulations (40 CFR Part 141 and 142). Currently listed treatment technologies for the inactivation of pathogens include chlorine, monochloramine, chlorine dioxide, ozone, and ultraviolet light (UV). Table 2 summarizes a number of treatment methods.
Table 2. Water System Treatment Methods

<table>
<thead>
<tr>
<th>Thermal disinfection / Thermal eradication / Superheating &amp; flushing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Summary</strong></td>
</tr>
<tr>
<td>● Hot water temperature elevated to &gt;70°C (158°F), while distal</td>
</tr>
<tr>
<td>sites (e.g., faucets, showerheads) are flushed for 30 minutes.</td>
</tr>
<tr>
<td>● Outlet water temperature during emergency thermal shock</td>
</tr>
<tr>
<td>treatment should not fall below 60-65°C.</td>
</tr>
<tr>
<td><strong>EPA/DEP requirements</strong></td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>● Effective against many microbial pathogens including <em>Legionella</em></td>
</tr>
<tr>
<td>● No special equipment necessary</td>
</tr>
<tr>
<td>● Relatively inexpensive</td>
</tr>
<tr>
<td>● Simple, effective and easily monitored</td>
</tr>
<tr>
<td>● Can be used to disinfect entire water distribution system</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>● Not easy or quick to implement</td>
</tr>
<tr>
<td>● Local codes/regulations may not permit, and/or the water system may not be designed to handle super-heating</td>
</tr>
<tr>
<td>● Potential for scalding</td>
</tr>
<tr>
<td>● Disinfection is only temporary so recolonization may occur within days to months if hot and cold water temperatures are not adequately maintained throughout the system</td>
</tr>
<tr>
<td>● Not applicable in cold water systems</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Instantaneous steam heating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Summary</strong></td>
</tr>
<tr>
<td>● Flash heating water to temperatures greater than 88°C (190°F) and then blending hot water with cold water to attain designated water temperature</td>
</tr>
<tr>
<td><strong>EPA/DEP requirements</strong></td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>● Cost effective</td>
</tr>
<tr>
<td>● Does not require specialized personnel to operate system</td>
</tr>
<tr>
<td>● Maintenance can be performed by regular building staff</td>
</tr>
<tr>
<td>● Useful as short-term remediation measure</td>
</tr>
<tr>
<td>● Simple to apply in hot-water installation</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>● Maintenance is more complex than conventional hot water tank</td>
</tr>
<tr>
<td>● Only controls <em>Legionella</em> in hot water supply system; does not disinfect cold water distribution system</td>
</tr>
<tr>
<td>● Does not affect <em>Legionella</em> that may have colonized downstream in the system, since high temperatures may not reach distal parts of the system</td>
</tr>
<tr>
<td>● Transient effect on <em>Legionella</em></td>
</tr>
<tr>
<td>● No limitation on biofilm formation</td>
</tr>
<tr>
<td>● Scalding risk</td>
</tr>
<tr>
<td>● Designed to disinfect only a specific portion of water distribution system</td>
</tr>
</tbody>
</table>
### Hyperchlorination / Shock chlorination

| Summary | • Available as a liquid, or can be generated on site  
• Injected into a pipe or tank/chamber (requires chlorinator)  
• Minimum CT of 100 is recommended throughout the distribution system to inactivate *Legionella*; CT = residual disinfectant concentration (C) in mg/L times the corresponding disinfectant contact time (T); e.g., CT of 100 could be achieved by 100 mg/L x 1 minute or 50 mg/L for 2 minutes  
• Flush each outlet to flow for at least 5 minutes, starting at distal outlets and working back toward central water heater  
• Flush all outlets individually; those on individual branches should be flushed simultaneously (e.g., hand basins and showers). |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>EPA/DEP requirements</td>
<td>None for one-time hyperchlorination for remediation purposes, however DEP requires that super-chlorinated water must be properly flushed to waste, i.e., cannot be served to the public</td>
</tr>
</tbody>
</table>
| Advantages | • Very effective for viruses & many microbes including *Legionella*  
• Relatively inexpensive and simple to use  
• Can be used to disinfect entire water distribution system |
| Disadvantages | • Does not penetrate biofilms well  
• *Legionella* present in amoebae may be resistant to chlorine  
• Disinfectant byproduct formation  
• Can affect corrosion and increase lead and copper levels in the distribution system  
• Not stable, particularly in hot water  
• Affects taste and odor |

### Chlorine (continuous disinfection using free chlorine)

| Summary | • Water from source (entering building) through to all distal outlets (e.g., faucets, shower heads) should be maintained at 0.3-0.5 mg/L free residual chlorine  
  o Upper limit of 0.5 mg/L is recommended by the American Water Works Association and Ten-State Standards  
  o Minimum DEP standard is “detectable” residual chlorine, or 0.02 mg/L (but DEP is planning to propose higher level standards, a process that will take two years)  
  o The forthcoming EPA review may result in new guidance for chlorine residual |
| --- | --- |
| EPA/DEP requirements | • Requires a DEP Public Water System Permit  
• National Public Drinking Water Regulations (NPDWR): Requires monitoring of disinfection byproducts and **Maximum Residual Disinfectant Level (MRDL)**  
• DEP requires operator certification and minimum residual; may require containment or separate structure for onsite storage of chemicals |
| Advantages | • Very effective for viruses & many microbes including *Legionella*
• Most commonly used biocide
• Easy to use and relatively inexpensive
• Can be used to disinfect entire water distribution system |
| --- | --- |
| Disadvantages | • Does not penetrate biofilms well
• *Legionella* present in amoebae may be resistant to chlorine
• Disinfectant byproduct formation
• Can affect corrosion and increase lead and copper levels in the distribution system
• Not stable, particularly in hot water
• Affects taste and odor |
| **Monochloramine** |  |
| Summary | • Generated onsite by combining chlorine and ammonia
• Ammonia addition quenches residual chlorine and minimizes formation of disinfection byproducts
• Aim for monochloramine concentration of 1.5-3.0 mg/liter<sup>35</sup> |
| EPA/DEP requirements | • Requires a DEP Public Water System Permit
• National Public Drinking Water Regulations (NPDWR): Requires monitoring of disinfection byproducts and Maximum Residual Disinfectant Level (MRDL)
• Other
  • Onsite storage of chemicals may require containment or separate structure and local permitting requirements
  • State requirements including operator certification and minimum residual |
| Advantages | • Appears to be more effective than chlorine against *Legionella*
• Can penetrate biofilm effectively
• Longer lasting and more stable residual in the distribution system |
| Disadvantages | • Can affect lead and copper levels
• Can result in nitrification in large distribution systems and problems with total coliform compliance
• Can impact plumbing components, especially rubber (gaskets, o-rings, seals)
• No commercial kit available for dosing small water systems |

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<sup>35</sup> Duda et al. 2014
### Chlorine Dioxide

| Summary                  | • Generated onsite as a gas (sodium chlorite and a strong acid)  
|                         | • Not stored  
|                         | • Concentration at sentinel taps and representative outlets should be at least 0.1 mg/liter |
| EPA/DEP requirements     | • Requires a DEP Public Water System Permit  
|                         | • NPDWR requires monitoring of disinfection byproducts (including daily chlorite levels) and daily monitoring of MRDL entering the distribution system  
|                         | • Other  
|                         |   o Onsite generation as a gas: isolation, separate structure, permitting requirements  
|                         |   o State requirements including operator certification and possibly chlorate monitoring compliance |
| Advantages               | • Very effective disinfectant for *Legionella*  
|                         | • Very effective for biofilms in shock treatment  
|                         | • Simple to use |
| Disadvantages            | • Generally not used for residual disinfection in the distribution system  
|                         | • Decomposes rapidly – may not maintain disinfectant residual in distribution system  
|                         | • Formation of chlorite |

### Copper-silver ionization

| Summary                  | • Distorts the permeability of the *Legionella* cell, denatures proteins, and leads to cell breakdown and cell death  
|                         | • Requires monitoring of copper and silver ion levels in water system (e.g., monitor sentinel taps monthly and representative sample annually, maintain silver ions at least 20 µg/l) |
| EPA/DEP requirements     | Not listed by EPA as a treatment technology that can be used to comply with federal regulations; DEP does not issue permits for this technology because it is not yet certified by National Sanitary Foundation (www.nsf.org) or American National Standards Institute (www.ansi.org) as safe and effective for use in potable water systems. However, as of 2014, one manufacturer had recently obtained NSF Standard 61 certification; efficacy validation was still pending. |
| Advantages               | • Commercial system can be easily installed  
|                         | • Provides residual protection throughout water distribution system  
|                         | • Described as effective in WHO 2007 guidelines |
| Disadvantages            | • Not yet certified nationally for use in potable water systems  
|                         | • Scale must be regularly removed from electrodes  
|                         | • pH of system must be maintained below 8  
|                         | • Extremely high concentrations of copper and silver ions will turn the water black in color |
### Ozone

**Summary**
- Generated onsite as a gas or liquid oxygen using an ozone generator.
- Ozone instantaneously inactivates *Legionella*

**EPA/DEP requirements**
- Requires a DEP Public Water System Permit
- NPDWR requires monitoring of disinfection byproduct bromate
- DEP requires operator certification; containment or separate structure and permitting for onsite generation as a gas; ambient air monitoring, scrubbers

**Advantages**
- Does not form disinfection byproducts associated with chlorine/monochloramine
- Very effective for inactivation of viruses and *Legionella* at much lower doses than chlorine

**Disadvantages**
- Designed to disinfect only a specific portion of water distribution system
- Decomposes rapidly, therefore inadequate residual concentrations
- Second form of disinfection (e.g., chlorine or monochloramine) may be required for residual protection
- Operational and maintenance demands significantly greater than chlorine and monochloramine

### Ultraviolet light sterilization

**Summary**
- UV reactor generating short wavelength UV light on site

**EPA/DEP requirements**
- May not require a DEP Public Water System Permit
- State requirements include operator certification

**Advantages**
- Produces no disinfection byproducts
- Effective for *Legionella* (also *Giardia*, *Cryptosporidium*, *Mycobacterium avium*, some viruses)
- Ultraviolet sterilization system can be installed easily
- Taste and odor of water are not affected

**Disadvantages**
- Does not provide residual protection
- No effect on biofilm formation
- Not suitable for turbid water
- Operational and maintenance demands significantly greater than chlorine and monochloramine
- Some studies with point-of-use UV (at fixtures) indicate effectiveness, but need continuous exposure (recirculating loop)

### Point-of-Use Filters

**Summary**
- Point-of-use filters are installed at distal outlets. They serve as a physical barrier to inhibit exposure to contaminated water.

**EPA/DEP requirements**
- Should meet NSF standards for safety and efficacy

**Advantages**
- Physical barrier
- Easy to install (may require some modification of the outlet)
- Suitable for hot and cold water systems
- Good for systems to which high-risk patients may be exposed

Sources: EPA presentation at May 2014 workshop in Pittsburgh; WHO guidelines (2007)
Environmental Management in Response to a Confirmed LD Case or Outbreak

As noted earlier, even a single confirmed case indicates environmental contamination that could infect others, and thus warrants investigation and potential action, just as an outbreak does.

For cases not classified as outbreaks:

1. Measure free and total chlorine where the water line enters the building or as close as possible.
2. Measure the hot and cold water temperature at all outlets sampled.
3. Collect two samples from hot water storage: one immediate and then one after flushing for 30-60 seconds.
4. Remove any faucet aerator prior to sampling.
5. Collect swab and water samples from all or most of the outlets in the residence or room where the patient was residing, i.e., those to which the patient was most likely exposed.
6. Randomly collect swabs and water samples from other parts of building. Note that swabs disrupt the biofilm that might otherwise not become dislodged when collecting a water sample alone.
7. Based on laboratory results, apply the appropriate (focal and/or systemic) treatment method(s) to the water system, and collect appropriate water and swab samples for retesting.

For outbreaks, follow the procedures above, including more extensive sampling of outlets to which all confirmed or suspected cases have been exposed. Also refer to CDC’s updated outbreak investigation guidelines (expected in 2015). In addition, under DEP regulations (109.301(a)(3)(iii)), if a facility with a public water system that is regulated by DEP becomes aware of a waterborne disease outbreak that is associated with their water system, the facility must report the circumstances to DEP within one hour. DEP would not ask for or need any confidential patient information. Rather, they just need to know that an outbreak involving a specified pathogen, including *Legionella*, has been linked to a specified water system that DEP regulates.
Collection of Water Samples for Microbiological Testing

The frequency and sampling scheme for microbiological testing should be included in a facility’s water safety plan, including those facilities whose water system is subject to DEP regulation and permitting. Samples should be collected by a person who is adequately trained to do so.

International guidelines recommend routine maintenance and monitoring of temperature and biocide over reliance on microbiological monitoring (i.e., routine culturing for Legionella). For example, the 2007 WHO guidelines note “potential for over-reliance on [microbiological test] results at the expense of risk management strategies.” However, the WHO guidelines do suggest microbiologic testing if there are signs that the water system is not under control, after periods of stagnation, after work on the distribution system, or other activities or signs that might favor Legionella proliferation. Ireland’s national guidelines suggest monthly monitoring as follows: at sentinel taps for cold and hot water temperatures; testing of sentinel thermostatic mixing valves if installed; temperature of water leaving and returning to the water heater/storage tank; those guidelines also suggest six-monthly temperature monitoring of incoming water at the inlet (at least once in winter and once in summer); they also suggest annual temperature testing of a representative number of taps on a rotational basis, to ensure that both cold and hot water temperatures meet standards.

Current evidence does not point to a specific number of specimens to collect. Facilities may make such decisions based on other risk factors such as past contamination and specific exposures of LD cases. They will likely choose to test central water system components (e.g., water heater, especially at levels in the tank below the heating unit) and a representative sample of peripheral water distribution points (e.g., showers, faucets).

- For example, facility managers may wish to establish an inventory/catalogue all distribution points and randomly select a small number from each floor of the building for sampling, on a rotating basis for any routine monitoring. When there is a suspected or confirmed LD case, water system sites for testing should be selected based on the patient’s potential exposures (e.g., the shower and faucet used by the patient).

- As another illustrative example, Ireland’s national guidelines refer to the Dutch guidelines in terms of the number of sites to sample: If the water system has <50 outlets – 2 samples; if 51-100 outlets – 4 samples; if 101-200 outlets – 6 samples; if 201-400 outlets – 8 samples; if 401-800 outlets – 10 samples; if 801-1,600 outlets – 12 samples; if >1,600 outlets – 14 samples.

CDC guidelines recommend taking swabs of faucet aerators and showerheads. This is particularly aimed at testing for Legionella in biofilms. Swab samples should be taken before collecting water samples if both are collected at the same outlet. Use pre-moistened sterile cotton wool swabs. After removing a faucet aerator (if present), the swab should be moved up the faucet as far as it will reach and rotated several times up and down around

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36 CDC, Procedures for the Recovery of Legionella from the Environment, 2005
the inner circumference, to cover the entire surface area of the swab. The swab should then be submersed in a tube with 3-5 milliliters of water to prevent drying during transport. For showerheads, rotate the swab over the entire surface of the showerhead four times.

After the swab sample is collected, the hot water outlet valve should be opened and a first-draw water sample collected. Pennsylvania’s drinking water regulations defines a first-draw sample as “a 1-liter sample of tap water …. collected without flushing the tap”. First-draw samples from the hot water system are the norm in Western Pennsylvania, in addition to swabs. Several international guidelines recommend sampling from both the hot water system and the cold water system, since *Legionella* can grow in either a hot water system that is not maintained sufficiently hot or in a cold water system that is not maintained sufficiently cold. If both hot and cold water samples are to be collected, the hot water sample should be collected first. In addition to first-draw samples, some of these same international authorities recommend that water samples usually or always be collected after running water through the outlets for at least 30-60 seconds (i.e., “post-flush” samples); such recommendations typically apply after disinfection of the local tap or tap fitting (as described earlier in the context of routine operation and maintenance). The flushing of the outlets prevents carryover of the disinfection agent (e.g., chlorine) into the post-flush water sample.

For microbiological testing of water, CDC guidelines recommend that “whenever possible, a collection of one liter is preferred.” Occasionally, larger volumes of water (up to 10 liters) are needed to detect *Legionella* in water that typically has very low concentrations of the bacteria such as municipal water supplies. If a liter cannot be collected from the sample source, a smaller volume is acceptable, though not preferred. Other CDC guidelines specify collection of at least the “minimum volume of water … sufficient to complete any and all assays indicated”, which those guidelines specify is 100 mL. Water samples should be collected from proximal and distal points in the water system and selected points in between. Selection of sites can be based on risk or routine/random determination based on the reason for testing water specifically for *Legionella* (e.g., case identified versus routine monitoring) and the design of the building’s water system. Each 1-liter sample of water should be collected in either a new container or one that has been “properly cleaned, washed and rinsed with distilled water and disinfected or sterilized.” The container should be capped, polyethylene (or similar material) with enough sodium thiosulfate (0.5ml of 0.1N sodium thiosulfate) to neutralize any chlorine or other biocide that might limit the growth of *Legionella* if present. Sampling containers provided by a local laboratory will typically contain this additive. If a 1-liter bottle will not fit under the fixture or water tank, use a sterile 125ml bottle without sodium thiosulfate and then transfer the sample to the 1-liter bottle containing the sodium thiosulfate.

Specimens collected from water sources/systems should be kept at a cold temperature (4°C or 39.2°F) and sent to a qualified laboratory. Those from regulated water systems must be

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37 DEP 2014
38 UK 2005 (pg 19); South Australia 2008 (pg 16); Ireland 2009 (pg 58)
39 UK 2005 (pg 22); WHO 2007 (pg 190); Ireland 2009 (pg 59)
40 CDC, Procedures for the Recovery of *Legionella* from the Environment, 2005
41 CDC, Guidelines for Infection Control in Health-Care Facilities, 2003 (pg 94)
42 UK 2005
tested by a qualified laboratory. In Pennsylvania, the ACHD recommends only those laboratories that have been certified by the CDC ELITE program.\(^{43}\)

**Interpretation of Laboratory Test Results**

The laboratory will culture the water sample and will provide results that specify (a) whether *Legionella* was found or not, (b) the species and serogroup(s) found, and (c) a quantitative estimate of the degree of contamination (e.g., number of colony-forming units per liter or milliliter as may be appropriate). While the laboratory results will be clear, scientific evidence remains insufficient to establish definitive criteria and thresholds of environmental contamination that should trigger remedial actions. Therefore, this is an area of continuing debate among experts. Some experts (and guidelines) recommend a water system safety and risk management approach, while others (including the 1997 ACHD guidelines) specify a minimum positivity rate (percentage of samples testing positive for pathogenic *Legionella*) that should trigger environmental disinfection measures.

According to the prior ACHD guidelines, a hospital should consider disinfection of the hospital water system if at least one of two conditions is met: (1) *Legionella* has been found in the water distribution system and prior cases of health care-acquired legionellosis have been observed or (2) *Legionella* has been found in the water distribution system and \(\geq 30\%\) of distal sites are positive for *Legionella*.\(^{44}\) The 30\% threshold continues to be the subject of much debate, mainly because there are few studies to support its use as the cut-off for decision making,\(^{45}\) and nosocomial transmission has occurred when less than 30\% of sites tested positive, specifically in highly susceptible patient populations such as transplant patients.\(^{46,47}\)

It is unrealistic to expect that a complex water distribution system could be entirely free of a ubiquitous and naturally occurring bacterium such as *Legionella*, even with continuous disinfection. While previous studies have demonstrated a correlation between the extent of colonization (percent positivity) and the risk of legionellosis,\(^{48}\) there is no established dose-response relationship for *Legionella* infection and the concentration of *Legionella* necessary to cause an outbreak is unknown – i.e., scientific evidence has not established a “safe” level of *Legionella* contamination.\(^{49}\) Furthermore, results of environmental monitoring can be affected by several factors, such as the type of sample collected (swab or water, and volume of water), the methods used for sample processing (acid pretreatment and filtration of water sample), and the media used for culture isolation.\(^{50}\) A few countries have established criteria for action based on microbiological testing, usually based on the number of colony-forming units per liter (cfu/l). In the

\(^{43}\) See [http://www.cdc.gov/legionella/elite.html](http://www.cdc.gov/legionella/elite.html)

\(^{44}\) Squier et al., 2005

\(^{45}\) Best et al., 1983.

\(^{46}\) Kool et al., 1999.

\(^{47}\) Kool et al., 1998.

\(^{48}\) Best et al., 1983.

\(^{49}\) WHO 2007.

\(^{50}\) Squier et al., 2005
absence of more definitive evidence or explicit U.S. federal guidance, guidelines from these countries could be considered:

- In piped potable water and water distribution systems in buildings, the UK, France and Netherlands have “targets” of <100 or 100 cfu/l for routine maintenance.
- At 100-1000 cfu/l, UK guidelines specify that action depends on whether just one or a majority of samples are positive for *Legionella*, i.e., focal or systemic colonization.
- At > 1000 cfu/l in such systems, the Netherlands recommends “immediate action … to prevent closure of (part of) the system involved” and the UK recommends “immediate review of control measures and risk assessment; possible disinfection.”
- The only U.S. guidance mentioned by the WHO 2007 report in this context had significantly higher threshold for action: North Carolina guidelines (2005) specify a trigger point of > 10,000 cfu/l that should lead to “prompt cleaning and/or biocide treatment of the system.”
- A water system should be retested three to seven days after it has been disinfected in response to a case or outbreak of LD or identified local or systemic colonization by *Legionella*.

Current evidence does not permit definitive judgment about risk to human health from samples that test positive, only when test results from a proficient laboratory are negative. For any questions about *Legionella* in a facility’s public water system, the facility should contact the DEP.  

51 DEP emergency response contact numbers can be found in Appendix 10.

### Recommendations for Managing *Legionella* Risk in the Environment

8. Take a risk management approach to environmental monitoring and control of *Legionella*.

8. Implement routine water system operation and maintenance best practices.

9. Implement appropriate treatment methods to prevent *Legionella* growth or when otherwise warranted.

10. Call the department of health and/or environmental protection with any further questions.

### CONCLUSIONS

The information and recommendations contained here reflect the best evidence available as of 2014 and expert inputs. The information is intended to help facilities that house or serve persons at greatest risk better understand legionellosis in people and in the environment. The recommendations are intended to serve as a practical guide to help facilities prevent and control the risk and impact of legionellosis in those they serve.

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51 For a list of PA Department of Environmental Protection emergency response contact numbers, see [http://www.portal.state.pa.us/portal/server.pt/community/report_an_incident/6010](http://www.portal.state.pa.us/portal/server.pt/community/report_an_incident/6010).
Appendix 1. List of experts consulted

Allegheny County Health Department

Director
- Dr. Karen Hacker

Epidemiology and Biostatistics
- Dr. Ron Voorhees
- Lauren Torso
- Dr. Kristen Mertz
- Dr. LuAnn Brink

Infectious Disease Program
- Sharon Silvestri

Public Drinking Water Program
- John Jeffries
- Robin Shaw
- David Schultise
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- Dr. Robert Wadowsky

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Pennsylvania Department of Environmental Protection
- Lisa Daniels (Bureau of Safe Drinking Water)

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- Dr. Janet Stout

Department of Veterans Affairs--Veterans Health Administration

Pittsburgh
- Dr. Ali Sonel

Central Office (Washington, DC)
- Dr. Gary Roselle
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Centers for Disease Control and Prevention

National Center for Infectious and Respiratory Diseases
- Dr. Laurel Garrison (epidemiology)
- Dr. Claressa Lucas (laboratory)

National Center for Environmental Health:
- Dr. Sharunda Buchanan
- Christopher Kochtitzky
- John Sarisky

Environmental Protection Agency
- Dr. Stig Regli (Washington, DC headquarters)
- Alysa Suero (Region III)
Appendix 2. Summary of published guidelines and other references

Published guidelines, regulations and codes

United States

- Legionella.org (nonprofit organization based in Pittsburgh)
  - Summary of legionellosis guidelines: http://legionella.org/guidelines/


- Pennsylvania Department of Environmental Protection
  - Maximum Contaminant Levels: http://files.dep.state.pa.us/Water/Drinking%20Water%20and%20Facility%20Regulation/lib/watersupply/pa-mcls_06.pdf
  - DEP template for an Operation and Maintenance Plan for Public Water Systems: http://www.elibrary.dep.state.pa.us/dsweb/View/Collection-8798
  - DEP template for an Emergency Response Plan: http://www.elibrary.dep.state.pa.us/dsweb/View/Collection-8776

- Centers for Disease Control and Prevention
  - Preventing Health-Care Associated Pneumonia (2003): http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5303a1.htm
• Guidelines for Environmental Infection Control in Health-Care Facilities (2003): [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5210a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5210a1.htm)


• EPA

  • Guidance on “treatment” regarding the triggers for applicability under the SDWA:
    - [http://water.epa.gov/lawsregs/guidance/sdwa/upload/wsg_8A.pdf](http://water.epa.gov/lawsregs/guidance/sdwa/upload/wsg_8A.pdf)


• Council of State and Territorial Epidemiologists (CSTE)


**International**


Engineering

• Pennsylvania Uniform Construction Code: 
  http://www.portal.state.pa.us/portal/server.pt/community/uniform_construction_code/10524

• International Plumbing Code (2012): 
  http://publicecodes.cyberregs.com/icod/ipc/2012/index.htm

• ASHRAE guidelines (2012, but still under review as of 2014): 
  https://osr.ashrae.org/Public%20Review%20Draft%20Standards%20Lib/Std-188P-PPR2%20Final%206%2010%202011.pdf

General references

• Legionella.org (Pittsburgh, PA): http://legionella.org

• CDC legionellosis homepage: http://www.cdc.gov/legionella/index.html

Topical references

**Legionella in people: Clinical and public health**

• Information on clinical diagnosis and treatment
  


  o Mayo Clinic: http://www.mayoclinic.org/diseases-conditions/legionnaires-disease/basics/symptoms/con-20028867


  o OSHA: https://www.osha.gov/dts/osta/otm/legionnaires/disease_rec.html


- **Diagnostic testing**
  - CDC: [http://www.cdc.gov/legionella/diagnostic-testing.html](http://www.cdc.gov/legionella/diagnostic-testing.html)

- **Public health (epidemiology)**
Legionella in environment

- Environmental Protection Agency (EPA)

- Environmental sampling, monitoring, screening, risk assessment

- Environmental laboratory testing
  - The ACHD endorses laboratories that have been certified as proficient by the CDC ELITE program: [http://www.cdc.gov/legionella/elite.html](http://www.cdc.gov/legionella/elite.html) (in Pennsylvania as of 2014, eight laboratories were listed on the CDC ELITE site)
• Environmental interventions
  o CDC guidelines for environmental infection control in healthcare facilities
    http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5210a1.htm and prevention
    of health-care associated pneumonia
    http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5303a1.htm
  o Best M., Stout J, Muder R, Yu V, Goetz A, & Taylor F. *Legionellaceae* in the
    hospital water-supply: epidemiological link with disease and evaluation of a
    method for control of nosocomial legionnaires' disease and Pittsburgh pneumonia.
    *Lancet* 1983. 322(8345), 307-310. At:
    of a new monochloramine generation system for controlling *Legionella*
    in building hot water systems. *Infect Control Hosp Epidemiol* 2014. 35(11).
    Forthcoming November 2014.
  o Kool JL, Bergmire-Sweat D., Butler JC, Brown EW, Peabody DJ, Massi DS, ...
    & Fields BS. Hospital characteristics associated with colonization of water
    systems by Legionella and risk of nosocomial legionnaires' disease: a cohort
    At: http://www.jstor.org/stable/10.1086/501587
  o Kool JL, Fiore AE, Kioski CM, Brown EW, Benson RF, Pruckler JM, ...
    & Breiman RF. More than 10 years of unrecognized nosocomial transmission of
    legionnaires' disease among transplant patients. *Infect Control Hosp Epidemiol*

• Water safety plans
    management for drinking-water suppliers.
    http://whqlibdoc.who.int/publications/2009/9789241562638_eng.pdf?ua=1
    quality from catchment to consumer.
  o Alberta Environment and Sustainable Resource Development. Drinking Water
    See also: www.environment.alberta.ca/apps/regulateddwq/dwsp.aspx (website
    includes Drinking Water Safety Plan template, guidance notes and manual)
  o UK Drinking Water Inspectorate (2005). A brief guide to drinking water safety
    plans. http://dwi.defra.gov.uk/stakeholders/guidance-and-codes-of-
## Appendix 3. Glossary of key terms used

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACHD</td>
<td>Allegheny County Health Department (Pennsylvania)</td>
</tr>
<tr>
<td>Active surveillance</td>
<td>Actively looking for new or additional cases, e.g., of LD; contrasts with “passive surveillance,” in which health authorities receive routine reports of cases</td>
</tr>
<tr>
<td>Alveoli</td>
<td>The air sacs within the lung where oxygen exchange takes place (i.e., where oxygen is transferred from inhaled air into the blood)</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>A drug used to treat bacterial infections by killing them (“bactericidal”) or inhibiting their further growth (“bacteriostatic”)</td>
</tr>
<tr>
<td>Antigen</td>
<td>Any substance that causes the body’s immune system to produce antibodies against it (e.g., as relevant here, a specific <em>Legionella</em> protein that stimulates antibody production against the infecting strain)</td>
</tr>
<tr>
<td>Aspirate / aspiration</td>
<td>To inhale/breathe liquid, food, saliva or other materials into the lungs; to choke on such materials</td>
</tr>
<tr>
<td>Bacteriostatic (drug)</td>
<td>An antibiotic that inhibits the growth but does not kill bacteria</td>
</tr>
<tr>
<td>Bactericidal (drug)</td>
<td>An antibiotic that kills bacteria</td>
</tr>
<tr>
<td>Beta lactam</td>
<td>A broad class of antibiotics (including penicillins, cephalosporins and others) defined by virtue of containing a “beta lactam” ring in their chemical structure</td>
</tr>
<tr>
<td>Biofilm</td>
<td>Microorganisms (such as <em>Legionella</em>) that stick together on a surface in the body or in the environment, often protected by a self-produced “slime”; biofilms are typically able to withstand efforts to kill (disinfect) the organisms and hence pose a great challenge to clinical treatment (relevant to some organisms but not <em>Legionella</em>) or environmental disinfection (relevant to <em>Legionella</em>)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>Slow heartbeat; “relative bradycardia” refers to a heartbeat that is slower than expected based on other patient characteristics, such as fever or rapid breathing</td>
</tr>
<tr>
<td>Case definition</td>
<td>The characteristics of a condition (e.g., a specific infectious disease) that constitute a “case” for purposes of either surveillance reporting or epidemiologic investigation.</td>
</tr>
<tr>
<td>Cell-mediated immunity</td>
<td>One of the two major types of immune response and the major response mechanism for <em>Legionella</em> infection; does not rely on antibodies but rather, on different kinds of white blood cell responses (cytotoxic T-lymphocytes and phagocytes)</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention, within the federal Department of Health and Human Services</td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>Pneumonia arising from a variety of sources and settings other than hospitals or long-term care facilities.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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</tr>
<tr>
<td>Community water system (CWS)</td>
<td>A public water system (PWS) that serves at least 15 service connections that are used by year-round residents or regularly serves at least 25 year-round residents.</td>
</tr>
<tr>
<td>Consecutive water system</td>
<td>As defined in Pennsylvania Safe Drinking Water Regulations, Chapter 109: A public water system which obtains all of its water from another public water system and resells the water to a person, provides treatment to meet a primary MCL or provides drinking water to an interstate carrier. The term does not include bottled water and bulk water systems.</td>
</tr>
<tr>
<td>CSTE</td>
<td>Council of State and Territorial Epidemiologists; professional association that, among other functions, agrees upon diseases to be reported by all states and the case definition of each</td>
</tr>
<tr>
<td>Culture</td>
<td>A diagnostic test to try to grow an organism (e.g., bacteria, such as <em>Legionella</em>) in the laboratory, using different types of growth media depending on the range of suspected organisms</td>
</tr>
<tr>
<td>DEP</td>
<td>Pennsylvania’s Department of Environmental Protection.</td>
</tr>
<tr>
<td>DFA</td>
<td>Direct fluorescent antibody test: a laboratory diagnostic test that uses a known <em>Legionella</em> antibody tagged with a fluorescent marker to test for the presence of <em>Legionella</em> antigen in a respiratory or other clinical specimen</td>
</tr>
<tr>
<td>Differential diagnosis</td>
<td>The initial range of plausible diagnoses based on patient history, vital signs, physical examination (to inform appropriate diagnostic testing and potentially initial treatment), and refined further as test results narrow the range of likely diagnoses</td>
</tr>
<tr>
<td>Disease surveillance</td>
<td>The monitoring of diseases in the population, to analyze trends and detect abnormalities such as outbreaks</td>
</tr>
<tr>
<td>Empiric treatment</td>
<td>Treatment based on best clinical judgment of the cause, in the absence of or prior to results of laboratory testing (see also “presumptive treatment”)</td>
</tr>
<tr>
<td>EPA</td>
<td>U.S. Environmental Protection Agency</td>
</tr>
<tr>
<td>Epidemiologic investigation</td>
<td>A systematic process for examining cases of a condition and comparing affected to non-affected persons to help determine, on a statistical basis, the likely source for those affected; in many instances, including the original 1976 LD outbreak, epidemiological investigation may point to the source of disease transmission and suggest effective control measures, even before the causative microbe is identified</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>A group of bactericidal antibiotics (within the original “quinolones”) that includes ciprofloxacin, levofloxacin, moxifloxacin and others – nine fluoroquinolones are currently licensed for use in the United States</td>
</tr>
<tr>
<td>Glycylcycline</td>
<td>A new class of drugs derived from minocycline (tetracycline family), currently less drug resistance than older tetracyclines; tigecycline was approved by FDA in 2005</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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<tr>
<td>Healthcare-associated pneumonia</td>
<td>Pneumonia acquired in a health care facility. CDC defines healthcare-acquired legionellosis as a patient with laboratory-confirmed legionellosis who resided continuously in the hospital or care facility for ten days or more prior to infection, or who becomes ill 2-9 days after leaving the facility. <em>See also “nosocomial”</em></td>
</tr>
<tr>
<td>Humoral immunity</td>
<td>One of two major types of immune response, based on development of antibodies to fight the infecting organism; not as important as cell-mediated immunity for <em>Legionella</em></td>
</tr>
<tr>
<td>Hypoxia</td>
<td>Condition in which the body, or a region of the body, is deprived of adequate oxygen</td>
</tr>
<tr>
<td>LD</td>
<td>Legionnaires’ disease: a pneumonia caused by <em>Legionella pneumophila</em> and related species of bacteria</td>
</tr>
<tr>
<td>Legionella</td>
<td>The single genus within the <em>Legionellaceae</em> family of bacteria; includes over 50 different species (more than 20 of which that have been associated with human disease); causes pneumonia (LD) and mild respiratory infection (Pontiac fever); the most common cause of LD is <em>L. pneumophila</em>, serogroups 1 (80-95% of community-acquired LD), 4 and 6.</td>
</tr>
<tr>
<td>Legionellosis</td>
<td>Refers to infection with <em>Legionella</em>, including both legionnaires’ disease and Pontiac fever (but, because the latter is rarely diagnosed or reported, mainly refers to LD)</td>
</tr>
<tr>
<td>Macrolides</td>
<td>A group of bacteriostatic antibiotics that includes erythromycin (the original drug of choice for LD) and newer drugs such as azithromycin (Zithromax), clarithromycin (Biaxin), and moxifloxacin</td>
</tr>
<tr>
<td>Macrophage</td>
<td>A cell derived from a specific type of white blood cell (“monocyte”), one type of “phagocyte” that is important in <em>cell-mediated immunity</em></td>
</tr>
<tr>
<td>Maximum Contaminant Level</td>
<td>MCL: The maximum permissible level of a contaminant in water which is delivered to any user of a public water system; MCL is an enforceable standard</td>
</tr>
<tr>
<td>Maximum Residual Disinfectant Levels</td>
<td>MDRL’s: Maximum residual allowed in the distribution system for chlorine, monochloramine, chlorine dioxide</td>
</tr>
<tr>
<td>Mixing valve</td>
<td>Class of devices used for tempering hot water in potable water systems, to meet relevant codes (e.g., International Plumbing Code)</td>
</tr>
<tr>
<td>Monocyte</td>
<td>The largest type of white blood cell, turn into <em>macrophages</em> when sent to replenish old ones or fight a new infection</td>
</tr>
<tr>
<td>Myalgia</td>
<td>Muscle pain</td>
</tr>
<tr>
<td>NNDSS</td>
<td>National Notifiable Disease Surveillance System: the electronic disease surveillance system which is managed by CDC and includes all diseases agreed upon by CSTE</td>
</tr>
<tr>
<td>Noncommunity Water System</td>
<td>Any public water system (PWS) that is not a community water system (CWS) is considered to be a noncommunity water system</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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</tr>
<tr>
<td>Nontransient water system</td>
<td>A noncommunity water system that serves at least 25 of the same people for at least 6 months of the year; examples are schools, hospitals, commercial establishments, and industrial parks</td>
</tr>
<tr>
<td>Nosocomial</td>
<td>Associated with a health care facility; nosocomial infections are those acquired in a health care facility (from Greek <em>nosokomĩ'o</em> = hospital). CDC defines nosocomial (or healthcare-associated) legionellosis as a patient with laboratory-confirmed legionellosis who resided continuously in the hospital or care facility for ten days or more prior to infection, or who becomes ill 2-9 days after leaving the facility. See also “healthcare-associated pneumonia”</td>
</tr>
<tr>
<td>Outbreak</td>
<td>The occurrence of two or more cases that are epidemiologically linked; for waterborne diseases including LD, (a) linked by time, location of water exposure and illness characteristics, and (b) epidemiologic evidence implicating water as the probable source of illness</td>
</tr>
<tr>
<td>Paired serology</td>
<td>Refers to comparing antibody levels in the blood serum very early during illness (“baseline”) and at least two to three weeks later, expressed as multiplicative magnitude of change; increases of more than four-fold for the specific antibody are generally considered diagnostic; a single level of at least 1:256 in a single specimen (referring to the highest level of dilution at which antibody can be detected) is considered positive in some instances, but is also found in 5-10% of the general population</td>
</tr>
<tr>
<td>Pathophysiology</td>
<td>The functional changes in the body (at the level of cells) associated with an abnormal condition; the “pathophysiology of LD” refers to how <em>Legionella</em> enter and infect the body and how the body responds to fight the infection</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase chain reaction: a type of laboratory test</td>
</tr>
<tr>
<td>Pleuritic pain, pleurisy</td>
<td>Chest pain due to inflammation of the thin tissue (“pleura”) covering the lung and lining the lung cavity; pain feels worse with breathing movement (particularly breathing in) because these inflamed tissues rub together</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Lung infection</td>
</tr>
<tr>
<td>Point-of-use filter</td>
<td>These are micropore filters specifically designed to prevent passage of <em>Legionella</em> bacteria and other specific microorganisms in potable water systems. They are typically fitted to water outlets (e.g., faucets, shower heads) or installed in water supply lines proximal to equipment (e.g., ice machines, drinking fountains)</td>
</tr>
<tr>
<td>Pontiac fever</td>
<td>A mild respiratory infection caused by <em>Legionella</em> bacteria, typically includes fever, chills and malaise but not pneumonia; rarely lab diagnosed, resolves without medical treatment</td>
</tr>
<tr>
<td>Potable water</td>
<td>Finished water, after treatment, that is safe and satisfactory for drinking and cooking; a building water distribution system that provides hot or cold water intended for human consumption (e.g., drinking, bathing, showering, cooking, dishwashing, maintaining oral hygiene)</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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</tr>
<tr>
<td>Presumptive treatment</td>
<td>Treatment based on best clinical judgment of the cause, in the absence of or prior to results of laboratory testing (see also “empiric treatment”)</td>
</tr>
<tr>
<td>Primary prevention</td>
<td>Approaches and measures taken to prevent the first case of a disease or condition from occurring, e.g., for LD, routine monitoring and maintenance of water sources to ensure absent or sufficiently low levels of Legionella contamination (see also secondary prevention)</td>
</tr>
<tr>
<td>Public Water System (PWS)</td>
<td>As defined in the Safe Drinking Water Act, a system for the provision to the public of water for human consumption through pipes or other constructed conveyances, if such a system has at least fifteen service connections or regularly serves at least twenty-five individuals; “human consumption” is defined to include drinking, bathing, showering, cooking, dishwashing, and maintaining oral hygiene but not hand washing or swimming; “constructed conveyance” is broadly interpreted to refer to any manmade conduit such as ditches, culverts, waterways, flumes, mine drains, or canals</td>
</tr>
<tr>
<td>Quinolones</td>
<td>A group of bactericidal antibiotics (see “fluoroquinolones”) that includes ciprofloxacin, levofloxacin, moxifloxacin</td>
</tr>
<tr>
<td>Risk</td>
<td>Refers to the likelihood and severity of negative consequences; for legionellosis, reflects the likelihood and degree of contamination of a source (e.g., water source) that can make someone sick, and the likelihood and consequences of an exposed person developing Legionella infection, especially LD</td>
</tr>
<tr>
<td>Risk factors</td>
<td>An epidemiological term reflecting variables that are associated with an elevated risk of disease or infection; some risk factors for legionellosis are older age, a history of smoking, chronic lung disease, and exposure to a specific contaminated water source</td>
</tr>
<tr>
<td>Safe Drinking Water Act (SDWA)</td>
<td>The main federal law that ensures the quality of American’s drinking water; SWDA requires EPA to determine the level of contaminants in drinking water at which no adverse health effects are likely to occur</td>
</tr>
<tr>
<td>Secondary prevention</td>
<td>Approaches or measures taken to prevent additional cases of a disease or condition from occurring, once one or more initial cases are identified; measures taken to limit further transmission of an outbreak are examples of secondary prevention, e.g., for LD, measures to decontaminate a water source/system implicated in an outbreak (see also primary prevention)</td>
</tr>
<tr>
<td>Selective media</td>
<td>Refers to the substance used to culture a specific organism; whereas some organisms grow on routinely used culture media, selective media are non-routine media that must be used in order for the organism to grow; Legionella only grow on very specific, “selective” (i.e., non-routine) media</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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</tr>
<tr>
<td>Sensitivity</td>
<td>One measure of the accuracy of a diagnostic test, expressed as a percentage; indicates the percentage of “true positives” that are detected by the test (e.g., of 100 persons known to be positive, the percentage that the test detects as positive); perfect sensitivity means no false negative results</td>
</tr>
<tr>
<td>Serogroup</td>
<td>A distinctly different but related organism within a given genus and species, e.g., <em>Legionella pneumophila</em> serogroup 1</td>
</tr>
<tr>
<td>(Water) Source</td>
<td>A water system, used here to refer to a system that can harbor <em>Legionella</em>, such as a potable water system, hot tub or spa, decorative water fountain, or nebulizer</td>
</tr>
<tr>
<td>Specificity</td>
<td>One measure of the accuracy of a diagnostic test, expressed as a percentage; indicates the percentage of “true negatives” identified as negative by the test (e.g., of 100 persons known to be negative, the percentage that the test identifies as negative); perfect specificity means no false positive results</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Clinical features as reported by the patient (e.g., nausea is a symptom and vomiting is a sign; feeling hot is a symptom and a measured temperature above 98.6 °F is a sign)</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>Rapid breathing (e.g., respiratory rate of more than 20 breaths/minute in an adult)</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>A group of broad-spectrum bacteriostatic antibiotics whose use has become less because of drug resistance</td>
</tr>
<tr>
<td>Transient water system</td>
<td>If the noncommunity water system is not a nontransient system, it is considered to be a transient system; examples are restaurants, churches, and campgrounds</td>
</tr>
<tr>
<td>Travel-associated LD</td>
<td>LD that is suspected or statistically proven to be associated with exposure to <em>Legionella</em> away from one’s residence, e.g., in a hotel, convention center, or cruise ship, within ten days prior to becoming ill</td>
</tr>
<tr>
<td>Treatment Technique (TT)</td>
<td>Used in lieu of a <strong>Maximum Contaminant Level (MCL)</strong> to reduce the level of a contaminant in drinking water when it is not economically or technically feasible to determine the level of that contaminant at particularly low concentrations; TT is an enforceable procedure</td>
</tr>
<tr>
<td>UAT: Urinary antigen test</td>
<td>A test for a specific protein found in <em>Legionella pneumophila</em> serogroups 1, which accounts for nearly all (but not 100%) of LD cases; highly accurate, but may miss LD infections due to other serogroups or other <em>Legionella</em> species</td>
</tr>
<tr>
<td>VA</td>
<td>Federal Department of Veterans Affairs</td>
</tr>
<tr>
<td>VHA</td>
<td>Veterans Health Administration (within the VA)</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Appendix 4. Pathophysiology and clinical diagnosis of LD

Pathophysiology

The “pathophysiology” of LD refers to what happens in the body of someone who is infected with *Legionella*. The *Legionella* bacteria are either inhaled or choked (“aspirated”) deep into the lungs. There, they infect certain types of white blood cells (macrophages and monocytes) in the small air sacs (alveoli) where oxygenation of the blood takes place. Extensive infection means that full oxygenation does not occur, resulting in lower levels of oxygen in the blood (“hypoxia”). Hypoxia leaves a person feeling short of breath; often people breathe faster as a result of this (“tachypnea”), which then further distorts the balance of key chemicals within the blood. Although the body does develop measurable antibodies to help fight the infection (through “B cells,” or “humoral immunity”), the most important immune response is via activation of another kind of cell, “T cells”, or “cell-mediated immunity.” The fact that this is the most important way the body fights *Legionella* infection explains why people with weakened immune systems due to disease or therapy are especially susceptible to LD once infected with *Legionella* bacteria.

Clinical diagnosis

Clinical diagnosis refers to all the information the clinician can glean from talking to and examining a patient with regard to the possible causes and best treatment of a patient’s illness. Diagnostic testing provides additional information, as described in the next section. A clinical visit typically begins with taking a patient’s vital signs (temperature, blood pressure, heart rate, respiratory rate) and asking a number of important questions—the patient history. The clinician then examines the patient and determines what additional testing might be necessary to help establish the diagnosis with more certainty, and the best treatment.

**Vital signs.** Patients with pneumonia, including LD, typically have an elevated temperature (fever in LD patients may reach 38.8-40° C, or roughly 102-104° F) and breathing that is faster than normal (“tachypnea”, e.g., above 20 breaths per minute for adults) because of infection and/or fever. They also may have heart rates slower than expected (“relative bradycardia”) in the presence of fever or fast breathing.

**Patient history.** The clinician will ask about when the patient became ill, the full range of symptoms and when they evolved. The relevant past medical history includes a history of smoking, any disease or treatment associated with a weakened immune system, and a full listing of current medications (some medications can cause slower heartbeat or faster breathing, and others could interfere with potential treatments). Exposure history includes asking about travel within the past 2-14 days (e.g., hotel, cruise ship) and recent exposure at any facility with fountain, spa, mist or other potentially contaminated water source, including residential facilities with such systems. Note that the incubation period is typically 2-10 days, but asking about exposures up to 14 days prior to onset of symptoms allows for uncertainty in the actual date a person became ill.
Physical examination. The clinician will typically examine the patient’s entire body, since clinical clues may come from various sources to indicate which diagnoses are more likely or less likely, in conjunction with the patient’s history and vital signs.

Differential diagnosis. Based on the patient history, vital signs and physical examination, the clinician will form hypotheses about the range of possible causes of the patient’s illness. This is called the “differential diagnosis.” The purpose of the differential diagnosis is to help the clinician determine the most appropriate diagnostic tests (if any) to perform to help identify the precise cause of the illness, and also to inform the most appropriate initial treatment if the patient is too severely ill to await diagnostic test results. For example, various different causes of pneumonia may need to be considered initially—and tested for, especially in severely ill patients—before a definitive diagnosis is made and the most specifically appropriate treatment is initiated. It is important to note that a definitive diagnosis of any condition is much more likely if the condition is included in the differential diagnosis, and conversely, specific diagnosis is highly unlikely if it is not initially considered. This is especially important for making a diagnosis of LD since there are specialized tests that are important for LD, but they are not undertaken for all cases of pneumonia and clearly would not be undertaken unless the clinician suspects LD and orders those specific tests.

A tool to facilitate clinical diagnosis of LD. Certain features of LD may make this the more likely among several possible diagnoses associated with a clinical picture of pneumonia. For example, pneumonia together with symptoms and signs beyond the respiratory system (“extrapulmonary”), such as nausea, vomiting, abdominal pain, headache, and confusion, may suggest LD over other causes of pneumonia. A different constellation of signs and symptoms may make LD less likely. The table below is an example of a tool to help with the clinical diagnosis of LD in adults, based on a weighted point scale of different clinical features that are more likely or less likely to be present in LD patients.
### Modified Winthrop-University Hospital Infection Disease Division’s Point System for Diagnosing Legionnaire’s Disease in Adults: Assessment

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Qualifying Conditions</th>
<th>Point Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature &gt;102°F*</td>
<td>With relative bradycardia</td>
<td>+5</td>
</tr>
<tr>
<td>Headache</td>
<td>Acute onset</td>
<td>+2</td>
</tr>
<tr>
<td>Mental confusion/lethargy*</td>
<td>Not drug induced</td>
<td>+4</td>
</tr>
<tr>
<td>Ear pain</td>
<td>Acute onset</td>
<td>-3</td>
</tr>
<tr>
<td>Non-exudative pharyngitis</td>
<td>Acute onset</td>
<td>-3</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>Acute, not chronic</td>
<td>-3</td>
</tr>
<tr>
<td>Sputum (purulent)</td>
<td>Excluding chronic bronchitis</td>
<td>-3</td>
</tr>
<tr>
<td>Hemoptyis*</td>
<td>Mild/moderate</td>
<td>-3</td>
</tr>
<tr>
<td>Chest pain (pleuritic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loose stools/watery diarrhea*</td>
<td>Not drug induced</td>
<td>+3</td>
</tr>
<tr>
<td>Abdominal pain*</td>
<td>With or without diarrhea</td>
<td>+1</td>
</tr>
<tr>
<td>Renal failure*</td>
<td>Acute, not chronic</td>
<td>+3</td>
</tr>
<tr>
<td>Shock/hypotension*</td>
<td>Excluding acute cardiac or pulmonary causes</td>
<td>-5</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>Excluding non-CAP causes</td>
<td>-5</td>
</tr>
<tr>
<td>Lack of response to beta lactams</td>
<td>After 72 h (excluding viral pneumonias)</td>
<td>+5</td>
</tr>
</tbody>
</table>

**Laboratory Features**

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Qualifying Conditions</th>
<th>Point Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest radiograph</td>
<td>Rapidly progressive asymmetrical infiltrates* (excluding severe influenza /SARS)</td>
<td>+3</td>
</tr>
<tr>
<td>Decreased arterial oxygen and increased alveolar-arterial oxygen gradient (&gt;35)*</td>
<td>Acute onset</td>
<td>-5</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>Acute onset</td>
<td>+1</td>
</tr>
<tr>
<td>Hypophosphatemia*</td>
<td>Acute onset</td>
<td>+5</td>
</tr>
<tr>
<td>Increased SGOT/SGPT*</td>
<td>Acute onset</td>
<td>+2</td>
</tr>
<tr>
<td>Increased total bilirubin</td>
<td>Otherwise unexplained</td>
<td>+1</td>
</tr>
<tr>
<td>Increased LDH (&gt;400 U/L)*</td>
<td>Excluding HIV/PCP</td>
<td>-5</td>
</tr>
<tr>
<td>Increased CPK</td>
<td>Acute onset</td>
<td>+4</td>
</tr>
<tr>
<td>Increased CRP (&gt;30 mg/L)</td>
<td>Acute onset</td>
<td>+5</td>
</tr>
<tr>
<td>Increased cold agglutinins (≥ 1:64)</td>
<td>Acute onset</td>
<td>-5</td>
</tr>
<tr>
<td>Severe relative lymphopenia (&lt;10%)</td>
<td></td>
<td>+5</td>
</tr>
<tr>
<td>Increased ferritin (&gt; 2xn)</td>
<td></td>
<td>+5</td>
</tr>
<tr>
<td>Microscopic hematuria*</td>
<td>Excluding trauma, BPH, Foley catheter, urological neoplasms</td>
<td>+2</td>
</tr>
</tbody>
</table>

*Otherwise unexplained (acute and associated with pneumonia)

**Scoring: Likelihood of Legionella infection**

<table>
<thead>
<tr>
<th>Total point score</th>
<th>Likelihood of Legionella infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;15</td>
<td>Very likely</td>
</tr>
<tr>
<td>5-15</td>
<td>Likely</td>
</tr>
<tr>
<td>≤ 5</td>
<td>Unlikely</td>
</tr>
</tbody>
</table>

Appendix 5. Diagnostic testing for *Legionella* infection

The determination of whether and how to test for the pathogen in cases of pneumonia is based on several factors, including the likely source of infection (e.g., health care facility or community) the severity of illness, and patient risk factors including age ≥ 65 years. The clinician should order specific diagnostic testing for patients suspected of having LD, e.g., those for whom LD is in the differential diagnosis, who score 5 or above using the clinical diagnostic tool described in Appendix 4 (if the clinician chooses to use it), for patients who:

- Have failed outpatient antibiotic therapy (typically beta-lactam drugs such as penicillins or cephalosporins)
- Have severe pneumonia, especially those requiring intensive hospital care
- Are immunocompromised and have clinical pneumonia
- Have pneumonia in the setting of a legionellosis outbreak
- Have a relevant travel or exposure history and clinical findings consistent with *Legionella*
- Are suspected of having healthcare-associated pneumonia (i.e., acquired in a healthcare setting such as a hospital)

A chest x-ray is almost always taken in patients with clinical pneumonia, to help point to the type of pneumonia and inform treatment. In the case of LD, the chest x-ray indicates abnormalities but not a distinctive pattern that points specifically to LD. Some chest x-ray patterns will suggest a different cause for the patient’s pneumonia, or a diagnosis other than pneumonia.

The various laboratory diagnostic tests are based on what happens to the body upon infection with *Legionella*. Some diagnostic tests look for the *Legionella* bacteria, for example looking at sputum (or another respiratory sample) under a microscope, but this is rarely diagnostic for LD. Other testing involves culturing such respiratory secretions, which typically takes days. Yet other tests look for bacterial breakdown products such as a specific *Legionella* antigen (a protein specifically from *Legionella*), which is detectable in the urine beginning very early during illness. The body produces antibodies within about two or three weeks of a first *Legionella* infection, but this timing is too late for practical purposes of treating a patient. Testing for antibody is more important for determining, after the fact, which persons were infected in a population, for example if an epidemiologic investigation is conducted.

Several laboratory tests can be used to detect *Legionella* in the body. Most of these are specific to this organism and different from tests used to detect other causes of pneumonia. Therefore, it is especially important to collect the right kind of specimen and order the appropriate testing for LD. The different diagnostic tests for *Legionella* and their key characteristics are noted in the table below, including the source of the specimen, test, timing, accuracy (sensitivity and specificity), advantages and disadvantages. Each of these is described in more detail below.

---

52 Mandell 2007, WHO 2007
### Characteristics of diagnostic laboratory tests for Legionella*

<table>
<thead>
<tr>
<th>Test</th>
<th>Timing</th>
<th>Detectable Results</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPUTUM or OTHER RESPIRATORY SPECIMEN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture</td>
<td>Any time before treatment  &gt;5 days (up to 14 days)</td>
<td>20-80</td>
<td>100</td>
<td></td>
<td>Advantages: Detects all serogroups (in persons or environment) Disadvantages: Technically difficult, slow, sensitivity highly dependent on laboratory’s technical skill, may be negative if specimen is collected after antibiotic therapy is started</td>
</tr>
<tr>
<td>DFA</td>
<td>Negative after 4-6 days  2-4 hr</td>
<td>25-75</td>
<td>≥ 95</td>
<td></td>
<td>Disadvantages: Usually only for <em>L. pneumophila</em>; despite high test specificity, false positives possible due to cross-reactions with other bacteria; not relevant to environmental samples</td>
</tr>
<tr>
<td>PCR</td>
<td>Rapid: Same day</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
<td>Advantages: Potentially can detect all serogroups Disadvantages: Assays vary by laboratory and are not approved by FDA; test sensitivity and specificity not well established; not first-line test for environmental samples, but potentially relevant to identify false negatives reflecting viable pathogen that cannot be cultured (e.g., in outbreak investigation)</td>
</tr>
<tr>
<td><strong>URINE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary antigen test (UAT)</td>
<td>From Day 1-3 of illness  15 minutes</td>
<td>70-100</td>
<td>100</td>
<td></td>
<td>Advantages: Accurate, detectable early, rapid results Disadvantages: test is only for <em>L. pneumophila</em> serogroup 1 (which may cause 80-95% of community-acquired LD cases)</td>
</tr>
<tr>
<td><strong>BLOOD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paired serology</td>
<td>≥ 2-3 wks</td>
<td>80-90</td>
<td>&gt; 99</td>
<td></td>
<td>Advantages: Not affected by antibiotic treatment, stays positive for months Disadvantages: Timing not useful for clinical management purposes, 5-10% of the population has titer &gt; 1:256</td>
</tr>
</tbody>
</table>

* Adapted from CDC (at [http://www.cdc.gov/legionella/diagnostic-testing.html](http://www.cdc.gov/legionella/diagnostic-testing.html))

** Examples of specimens include sputum, respiratory secretions collected through bronchoscopy, lung tissue, pleural effusion
The recommended tests for definitive diagnosis of LD (in bold font below) include the urine antigen test and culture of respiratory secretions on the specific (“selective”) media appropriate for *Legionella*. These and other diagnostic tests are described below.

**Urinary antigen test (UAT).** This test requires a sample of urine. It is easy to perform using one of several different commercial test kits and produces highly accurate results (up to 40 percent false negatives, few to no false positives). However, it is designed to detect only *Legionella pneumophila* serogroup 1, which causes most but not all cases of LD.

**Selective media culturing.** This test requires a respiratory sample, such as sputum; collection of a good sputum sample may require the assistance of a respiratory therapist. Specific growth media are required to grow *Legionella* bacteria. One example is an agar medium containing L-cysteine such as buffered charcoal yeast extract (BCYE) agar. The World Health Organization recommends using both selective and non-selective agar media, in case a supplement in the selective medium inhibits *Legionella* growth. Cultures are incubated for up to fourteen days and are examined every two or three days. The bacterial yield is highly dependent on the skill of the laboratory, especially in preparing the growth media. When feasible, it is important to collect the respiratory specimen for culturing before antibiotic treatment is started, since antibiotics may render laboratory cultures negative.

**Direct fluorescent antibody (DFA) test.** This tests for *Legionella* antigen in a respiratory specimen, using a known *Legionella* antibody that has been tagged with a marker that lights up (fluoresces). If *Legionella* is present, the tagged antibody attaches to it, and it becomes detectable using the appropriate lab equipment. If *Legionella* is not present, the antibody has nothing to attach to and is washed out, leaving nothing detectable by the equipment. Most DFA tests are for *Legionella pneumophila*.

**Polymerase chain reaction (PCR) tests.** These tests are used to detect *Legionella pneumophila* DNA in clinical specimens, which are typically from the respiratory tract (sputum, etc.). PCR basically involves stimulating multiplication of the organism’s DNA and then testing for its presence. This allows for very small specimens to be used and only becomes “positive” if the organism (i.e., its DNA) is present in the specimen. However, the FDA has not yet approved PCR tests for clinical use because data remain insufficient to document their accuracy.

**Paired serology.** This test requires drawing a blood specimen early during illness (the baseline, or “S1”, specimen) and then again at least two or three weeks later (the “S2” specimen). The laboratory then tests for the level of *Legionella* antibodies in both specimens. Typically, at least a fourfold rise in the amount (“titer”) of antibody in S2 compared to S1 indicates recent *Legionella* infection. A single high titer may reflect acute infection, but may also reflect past infection. Paired serology is not practical for clinical diagnostic purposes, since results are not available in time to treat a patient with pneumonia.
Appendix 6. Surveillance case definition for legionellosis

In 2005, CSTE updated the case definition and diagnostic criteria for legionellosis, mainly to enhance timely detection of outbreaks associated with travel.\(^{53}\)

- Legionellosis comprises two clinically and epidemiologically distinct illnesses: Legionnaires' disease, which is characterized by fever, myalgia, cough, and clinical or radiographic pneumonia; and Pontiac fever, a milder illness without pneumonia.

- **Laboratory criteria for diagnosis**
  - **Confirmed**
    - By culture: isolation of any *Legionella* organism from respiratory secretions, lung tissue, pleural fluid, or other normally sterile fluid.
    - By detection of specific *Legionella pneumophila* serogroup 1 antigen in urine using validated reagents.
    - By seroconversion: fourfold or greater rise in specific serum antibody titer to *Legionella pneumophila* serogroup 1 using validated reagents.
  - **Suspect**
    - By seroconversion: fourfold or greater rise in antibody titer to specific species or serogroups of *Legionella* other than *L. pneumophila* serogroup 1 (e.g. *L. mediasi*, *L. pneumophila* serogroup 6).
    - By seroconversion: fourfold or greater rise in antibody titer to multiple species of *Legionella* using pooled antigen and validated reagents.
    - By the detection of specific *Legionella* antigen or staining of the organism in respiratory secretions, lung tissue, or pleural fluid by direct fluorescent antibody (DFA) staining, immunohistochemistry (IHC), or other similar method, using validated reagents.

- **Case classification**
  - **Confirmed case**: a clinically compatible case that meets at least one of the confirmatory laboratory criteria
    - Travel-associated: a case that has a history of spending at least one night away from home, either in the same country of residence or abroad, in the ten days before onset of illness.
  - **Suspect case**: a clinically compatible case that meets at least one of the suspect laboratory criteria
    - Travel-associated: a case that has a history of spending at least one night away from home, either in the same country of residence or abroad, in the ten days before onset of illness.

- **Nosocomial or healthcare-associated case**: A patient with laboratory-confirmed legionellosis who was hospitalized continuously for \(\geq 10\) days prior to onset of illness is considered a “definite” nosocomial, or healthcare-associated, case; a laboratory-confirmed infection that occurs 2-9 days after hospitalization is considered a “probable” nosocomial case.\(^{54}\) The 2005 CSTE update further stipulates that, within seven days of notification of an LD case, a health department should try to ascertain travel history (the person spent \(\geq 1\) night away from home in the ten days prior to illness) and report the travel destination (city and state or country) to CDC. If there is no travel history, the health department should complete the case report and send it to CDC within 30 days.

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\(^{53}\) CSTE 2005 (both references)

\(^{54}\) CDC 1997
Appendix 7. Legionellosis surveillance trends

CDC publishes periodic surveillance summaries for specific diseases, including legionellosis. A report reflecting legionellosis case reports in the United States from 2000 through 2009 indicates that the 50 states and District of Columbia reported a total of 22,418 cases, including 99.5 percent that were classified as LD and 0.5 percent classified as Pontiac fever.\textsuperscript{55} Thus, routine surveillance functionally reflects LD rather than the full spectrum of legionellosis. Cases were confirmed mostly by the UAT (97 percent of the cases reported between 2005 and 2009), and by culture in only 5 percent of those cases. CDC notes that disease surveillance reporting is passive, meaning that it is dependent on clinicians diagnosing and reporting cases; also, the UAT only detects \textit{Legionella pneumophila} serogroup 1. Therefore, the actual number of cases occurring each year is considerably greater than the number officially reported. CDC cites a more comprehensive study that estimated 8,000-18,000 annual cases.\textsuperscript{56}

The number of reported cases increased from 1,110 cases in 2000 to 3,522 in 2009. These numbers also reflected an increase in age-adjusted disease incidence rates per 100,000 population. Geographically, the Middle Atlantic region (New Jersey, New York and Pennsylvania) consistently had the highest population-based incidence rate compared to the eight other U.S. regions, as shown in the table below (from CDC MMWR August 19, 2011. 60(32), page 2084).

<table>
<thead>
<tr>
<th>U.S. Census division</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>New England</td>
<td>0.38</td>
<td>0.48</td>
<td>0.81</td>
<td>0.79</td>
<td>0.71</td>
<td>1.00</td>
<td>1.20</td>
<td>1.04</td>
<td>1.43</td>
<td>1.21</td>
</tr>
<tr>
<td>Middle Atlantic</td>
<td>0.73</td>
<td>0.67</td>
<td>0.88</td>
<td>1.41</td>
<td>1.25</td>
<td>1.74</td>
<td>2.21</td>
<td>1.86</td>
<td>2.33</td>
<td>2.60</td>
</tr>
<tr>
<td>East North Central</td>
<td>0.64</td>
<td>0.58</td>
<td>0.64</td>
<td>0.67</td>
<td>1.03</td>
<td>0.96</td>
<td>1.26</td>
<td>1.24</td>
<td>1.34</td>
<td>1.45</td>
</tr>
<tr>
<td>West North Central</td>
<td>0.35</td>
<td>0.27</td>
<td>0.33</td>
<td>0.37</td>
<td>0.38</td>
<td>0.49</td>
<td>0.40</td>
<td>0.54</td>
<td>0.66</td>
<td>0.60</td>
</tr>
<tr>
<td>South Atlantic</td>
<td>0.40</td>
<td>0.42</td>
<td>0.42</td>
<td>0.97</td>
<td>0.72</td>
<td>0.73</td>
<td>0.81</td>
<td>0.74</td>
<td>0.79</td>
<td>0.73</td>
</tr>
<tr>
<td>East South Central</td>
<td>0.25</td>
<td>0.21</td>
<td>0.26</td>
<td>0.57</td>
<td>0.53</td>
<td>0.47</td>
<td>0.59</td>
<td>0.53</td>
<td>0.61</td>
<td>0.73</td>
</tr>
<tr>
<td>West South Central</td>
<td>0.09</td>
<td>0.11</td>
<td>0.12</td>
<td>0.27</td>
<td>0.55</td>
<td>0.24</td>
<td>0.29</td>
<td>0.46</td>
<td>0.34</td>
<td>0.44</td>
</tr>
<tr>
<td>Mountain</td>
<td>0.24</td>
<td>0.31</td>
<td>0.31</td>
<td>0.49</td>
<td>0.49</td>
<td>0.49</td>
<td>0.62</td>
<td>0.52</td>
<td>0.46</td>
<td>0.68</td>
</tr>
<tr>
<td>Pacific</td>
<td>0.18</td>
<td>0.16</td>
<td>0.17</td>
<td>0.24</td>
<td>0.19</td>
<td>0.26</td>
<td>0.28</td>
<td>0.32</td>
<td>0.40</td>
<td>0.43</td>
</tr>
<tr>
<td>Total</td>
<td>0.40</td>
<td>0.41</td>
<td>0.45</td>
<td>0.74</td>
<td>0.70</td>
<td>0.75</td>
<td>0.91</td>
<td>0.86</td>
<td>0.99</td>
<td>1.08</td>
</tr>
</tbody>
</table>

* New England: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; Middle Atlantic: New Jersey, New York, and Pennsylvania; East North Central: Illinois, Indiana, Michigan, Wisconsin, and Ohio; West North Central: Iowa, Kansas, Minnesota, Nebraska, North Dakota, and South Dakota; South Atlantic: Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, and West Virginia; East South Central: Alabama, Kentucky, Mississippi, and Tennessee; West South Central: Arkansas, Louisiana, Oklahoma, and Texas; Mountain: Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, and Wyoming; Pacific: Alaska, California, Hawaii, Oregon, and Washington.

Peak disease occurrence was in the summer months, with cases occurring from June to October accounting for 62 percent of all cases. Nearly one-fourth (24 percent) of reported cases occurring in U.S. residents were associated with travel (81 percent of these with domestic travel only; five percent with cruise ship travel). However, CDC notes that disproportionate reporting by some states of mainly or only travel-associated legionellosis may represent a bias against reporting cases that are not travel-associated. Thus, the actual proportions of travel-associated and non-travel-associated legionellosis are not known, based strictly on surveillance reporting. Nor is the precise proportion of nosocomial infections (acquired in health care facilities) known, but clearly this is not the

\textsuperscript{55} CDC \textit{MMWR} surveillance summary 2011 (Vol 60, No. 12)

\textsuperscript{56} Marston 1997
sole source of *Legionella* infection and therefore also not the sole opportunity for prevention and control.

CDC conducts surveillance for waterborne disease outbreaks, considering recreational water and drinking water sources separately. *Legionella* is associated with both of these. An extensive 2011 review described the characteristics of 134 recreational water-associated outbreaks and 48 drinking-water-associated outbreaks from 2007-2008 plus an additional 70 previously unreported waterborne outbreaks from 1973-2002. Among these were 91 *Legionella* outbreaks. The most recent reports from this surveillance system, for outbreaks occurring during 2009-2010, describe 81 outbreaks associated with recreational water and 45 outbreaks associated with drinking water and other non-recreational water sources; among these were 26 *Legionella* outbreaks. All *Legionella* outbreaks were associated with acute respiratory infection (most others were associated with gastrointestinal or skin diseases); all but one respiratory outbreak was associated with *Legionella*. A range of water sources was implicated in outbreaks in which *Legionella* was implicated. These are discussed in more detail under “Managing the Environment.”

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57 CDC 2011 (*MMWR* 60[12])
Appendix 8. Steps in an epidemiologic/environmental investigation

When a suspected outbreak of legionellosis occurs (two or more cases associated with the same source within the preceding six months), the health department may decide to undertake an epidemiologic investigation to identify the source of the infection and recommend measures to limit further transmission. While not intended to serve as a detailed handbook for the epidemiologists who will undertake the investigation, the steps below provide an idea of how such an investigation unfolds. This helps the involved persons, such as facility managers and residents, understand some of the questions they may be asked.

1. Define and find cases
   - Examine the clinical (e.g., hospital, nursing home) records of suspected cases and note the key features of illness, and use these features to develop a case definition for purposes of outbreak investigation (alternatively, use the CSTE case definition, with addition of parameters to define milder clinical disease [Pontiac fever] and delimit the time period in question)
   - Look for additional cases (initiate “active surveillance,” e.g., at the hospital or residential facility where the case/cases occurred)
   - Record information about cases: Obtain and list information about each case (the CDC Legionellosis Case Report Form may be used)\(^59\)
     - Person – Who: age, gender, any other relevant specific characteristics
     - Place – Where: where cases live, traveled, convened
     - Time – When: Date of onset of all identified cases, presented as a graph known as an epidemic (“epi”) curve. The pattern of the epi curve offers insights about disease source and transmission.

2. Generate hypotheses about likely sources of transmission
   - Looking at the records, the epidemiologic information (person-place-time) and talking with early cases can shed light on where and how they may have become infected: Do they reside in the same long-term care facility? Were they patients or visitors to the same community hospital? Were they exposed to a given water source at the same facility or event? CDC has also created a “hypothesis-generating questionnaire” to help guide this process.\(^60\) Based on all the information, the epidemiologist will generate hypotheses about potential source of contamination, e.g., a specific water source and mode of exposure.

3. Test the hypotheses
   - The epidemiologist will develop and administer a questionnaire that asks about different characteristics of ill and non-ill persons studied and their exposure to various potential sources of LD infection, including intensity of exposure. Comparison of ill and non-ill persons is key to the investigation. This explains

\(^{60}\) CDC: [http://www.cdc.gov/legionella/downloads/hypothesis-generating-questionnaire.pdf](http://www.cdc.gov/legionella/downloads/hypothesis-generating-questionnaire.pdf)
why not just sick persons, but also well ones, will be asked to provide key information that in turn may provide clues about the source of an LD outbreak.

- The analytic approach basically determines, through statistical methods, differences between ill/affected persons and otherwise comparable non-ill/non-affected persons in terms of their different exposures to specific water sources. Statistical analysis can point to the likely source of the outbreak.

4. Find the point of contamination and source of the outbreak (which water source)

- The epidemiological analyses should help point to the source of the outbreak. Culturing of different water sources will help indicate the existence, type and extent of *Legionella* contamination and thus inform potential remedial actions.

5. Control the outbreak

- The purpose of an outbreak investigation is to determine the source and take the necessary measures to limit further exposure. For LD, this usually means decontaminating and reducing the exposure of vulnerable people to the implicated water source.

- It is also important to communicate with local stakeholders (e.g., the affected facility and its residents) and even the broader public about the source of the outbreak, how people can avoid exposure, and measures being undertaken to decontaminate the water source.

6. Decide the outbreak is over

- An outbreak ends when the number of new illnesses reported drops back to the number normally expected (for LD, presumably zero new LD cases and documented drop or absence of *Legionella* contamination in the implicated water source).
Appendix 9. Drinking water regulation and monitoring at federal and state levels

Facilities must monitor public water systems (PWS) as defined by the Environmental Protection Agency (EPA) and regulated by state authorities such as the Pennsylvania DEP. Other sources that can be monitored are those known to be, or even possibly, conducive to Legionella growth and dispersion, such as spas, misters, sprays, fountains, and, as an example of more recently identified sources, ice machines.

Public Water System Regulations

Federal level

According to the federal SDWA, a public water system (PWS) is a system for the provision to the public of water for human consumption through pipes or other constructed conveyances, if such a system has at least fifteen service connections or regularly serves at least twenty-five individuals. “Human consumption” is defined to include drinking, bathing, showering, cooking, dishwashing, and maintaining oral hygiene, but not hand washing or swimming. “Constructed conveyance” is broadly interpreted to refer to any manmade conduit such as ditches, culverts, waterways, flumes, mine drains, or canals.61

PWSs are categorized as either community or noncommunity water systems. Noncommunity water systems are categorized as either transient or nontransient.

- **Community Water System (CWS):** a PWS that serves at least 15 service connections that are used by year-round residents or regularly serves at least 25 year-round residents. PA DEP defines three sizes of CWS: Large (serving > 50,000 people), medium (serving 3,301-50,000 people), and small (serving ≤ 3,300 people). Most facilities relevant to these guidelines likely have small community water systems.62
- **Noncommunity Water System:** any PWS that is not a CWS is considered to be a noncommunity water system
- **Nontransient water system:** a noncommunity water system that serves at least 25 of the same people for at least 6 months of the year; examples of nontransient noncommunity water systems are schools, hospitals, commercial establishments, and industrial parks
- **Transient water system:** if the noncommunity water system is not a nontransient system, it is considered to be a transient system; examples of transient community water systems are restaurants, churches, and campgrounds

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61 EPA: [http://water.epa.gov/infrastructure/drinkingwater/pws/pwsdef2.cfm](http://water.epa.gov/infrastructure/drinkingwater/pws/pwsdef2.cfm)
All PWSs that propose a construction, operation or substantial modification activity must apply for a permit from the Pennsylvania DEP.\textsuperscript{63} Moreover, Pennsylvania Safe Drinking Water Regulations define a consecutive water system as “A public water system which obtains all of its water from another public water system and resells the water to a person, provides treatment to meet a primary MCL or provides drinking water to an interstate carrier. The term does not include bottled water and bulk water systems.”\textsuperscript{64} The Pennsylvania DEP conducts routine inspections and monitoring of permitted PWSs.

The obligations of facilities whose drinking water system requires a DEP permit may include:

- Obtaining a permit to construct and operate the system prior to any construction or operation.
- Employing an appropriately certified operator.
- Completing and submitting appropriate monitoring plans.
- Conducting routine compliance monitoring in accordance with the monitoring plans and the SDWA.
- Providing notification to consumers when violations occur.

Community water systems are required to have an Operation and Maintenance Plan and an Emergency Response Plan.\textsuperscript{65} An Operation and Maintenance Plan contains the following information:

- Description of facilities
- Safety, including identification and description of hazards
- Start-up and operations, including overall controls of water source, normal operating conditions, standard operating procedure for disinfection, emergency operating conditions, emergency operating procedure
- Procedures for repairing and replacing water mains
- Maintenance
- Records and reporting
- Laboratory sampling and compliance reporting
- Public notification quick reference guide

\textsuperscript{63} For more information on the permitting process, see: http://www.elibrary.dep.state.pa.us/dsweb/Get/Document-47493/383-2100-108.pdf.

\textsuperscript{64} See http://www.elibrary.dep.state.pa.us/dsweb/Get/Document-76320/Safe%20Drinking%20Water%20Act.pdf

\textsuperscript{65} A template for an Operation and Maintenance Plan for Public Water Systems can be found at: http://www.elibrary.dep.state.pa.us/dsweb/View/Collection-8798. A template for an Emergency Response Plan can be found at: http://www.elibrary.dep.state.pa.us/dsweb/View/Collection-8776
An Emergency Response Plan contains the following information:

- Emergency reference table including emergency situation, contacts, and phone numbers
- Means of communication including lines of communication and emergency communications equipment
- Summary description of the system including location of pertinent operational information, source information, treatment information, description of surrounding area, finished water storage, system demand, other pertinent system information
- Assessment of available resources including mutual aid agreements, procedures for providing reserve capacity or an approved alternative water supply, power supply equipment, inventory of repair equipment, vehicles and construction equipment, spare equipment for water source, spare parts for treatment, miscellaneous equipment for system
- Corrective actions for probably emergencies including list of probable emergencies and description of corrective actions

Safe Drinking Water Act

Federal level

The Safe Drinking Water Act (SDWA) is the main federal law that ensures the quality of American’s drinking water. SWDA requires EPA to determine the level of contaminants in drinking water at which no adverse health effects are likely to occur. These non-enforceable health goals, based solely on possible health risks and exposure over a lifetime, with an adequate margin of safety, are called maximum contaminant level goals (MCLG). Contaminants are any physical, chemical, biological or radiological substances or matter in water. EPA sets MCLGs based on the best available science to prevent potential health problems.

For most contaminants, EPA sets an enforceable regulation called a maximum contaminant level (MCL) based on the MCLG. MCLs are set as close to the MCLGs as possible, considering cost, benefits and the ability of public water systems to detect and remove contaminants using suitable treatment technologies. When there is no reliable method that is economically and technically feasible to measure a contaminant at particularly low concentrations, a treatment technique is set as a standard, rather than an MCL. A treatment technique is an enforceable procedure or level of technological performance that public water systems must follow to ensure control of a contaminant.

State level

States are charged with further regulation and enforcement of national policy under the SDWA. For example, states may set a more stringent MCL or treatment technique level than EPA for pathogens and indicators in drinking water. For a list of MCLs from the Pennsylvania DEP, see: http://files.dep.state.pa.us/Water/BSDW/DrinkingWaterManagement/RegsStandardsResources/pa-mcls_06.pdf
Monitoring requirements

According to EPA standards, all community and non-transient non-community water systems that use disinfection measures, except for UV, must monitor for disinfection byproducts in the distribution system. Monitoring requirements are included in Table 2. Samples should be collected at a frequency specified by DEP for water systems that fall under government regulation, or a frequency appropriate to the risk management plan or circumstances for water systems not under such regulation, for example quarterly or annually. Consecutive Water Systems carry monitoring requirements that are more relevant to buildings than to source water treated and provided to the building by, for example, a municipal supplier. Consecutive water systems must monitor the water in their distribution system for disinfection byproducts, lead, copper, total coliforms and any specific treatments the building has added.

Facilities should determine the relevant water sources to monitor and frequency of sampling based on facility-generated and DEP-approved Operation and Maintenance Plans. Additional monitoring may be required by permit, including monitoring for Legionella if the facility has experienced a waterborne disease outbreak. The permit will specify the frequency and location of any additional monitoring requirements. Samples should be analyzed by laboratory certified by CDC’s ELITE program. Public notification is required if public water systems exceed the MCL/MRDL, fail to comply with TT requirement, or other violations such as failure to monitor.

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67 For further information about public notification, see [http://www.portal.state.pa.us/portal/server.pt/community/public_drinking_water/21162/public_notification/1258843#OMTemplates](http://www.portal.state.pa.us/portal/server.pt/community/public_drinking_water/21162/public_notification/1258843#OMTemplates)
Appendix 10. Technical resources: Where to call for more information

Health: clinical, public health

- Allegheny County Health Department (ACHD; 955 Rivermont Dr., Pittsburgh 15207; 412-687-ACHD (2243), FAX: 412-578-8325, [http://www.achd.net/newweb/contactForm.html](http://www.achd.net/newweb/contactForm.html); information at: [http://www.achd.net/mainstart.html](http://www.achd.net/mainstart.html)
  - Epidemiology & Biostatistics: 412-687-2243; [http://www.achd.net/biostats/index.html](http://www.achd.net/biostats/index.html)
  - Infectious Disease Program: 412-578-8062; [http://www.achd.net/infectd/index.html](http://www.achd.net/infectd/index.html)
  - Public Health Laboratory: 412-578-8070; [http://www.achd.net/admin/healthlab.html](http://www.achd.net/admin/healthlab.html)
- Technical consultation: Special Pathogens Laboratory, Pittsburgh (Phone: 877-775-7284 or 412-281-5335; Fax (412) 281-7445); [http://www.specialpathogenslab.com/](http://www.specialpathogenslab.com/)
- CDC: 1600 Clifton Rd, Atlanta, GA 30333; Tel 800-CDC-INFO (800-232-4636) TTY: (888) 232-6348
  - Laboratory testing and certification: [http://www.cdc.gov/legionella/elite.html](http://www.cdc.gov/legionella/elite.html)

Drinking water systems

- Pennsylvania Department of Environmental Protection, main website: [http://www.depweb.state.pa.us/portal/server.pt/community/dep_home/5968](http://www.depweb.state.pa.us/portal/server.pt/community/dep_home/5968) ; email: RA-epcontactus@pa.gov . Permitting and 24-hour services are handled by the relevant PA DEP regional office:
  - North-central Regional Office (serving Bradford, Cameron, Centre, Clearfield, Clinton, Columbia, Lycoming, Montour, Northumberland, Potter, Sullivan, Tioga): 208 West Third Street, Suite 101, Williamsport, PA 17701-6448; Main Number / Emergency Response: (570) 327-3636; Fax: (570) 327-3565 or (570) 327-3420
  - Northwest Regional Office (serving Butler, Clarion, Crawford, Elk, Erie, Forest, Jefferson, Lawrence, McKean, Mercer, Venango, Warren): 230 Chestnut Street, Meadville, PA 16335; Business Hours: (814) 332-6945 / After Hours: (800) 373-3398
  - Southeast Regional Office (serving: Bucks, Chester, Delaware, Montgomery, Philadelphia): 2 East Main Street, Norristown, PA 19401; Main and 24-hour emergency number: (484) 250-5900
  - South-central Regional Office (serving: Adams, Bedford, Berks, Blair, Cumberland, Dauphin, Franklin, Fulton, Huntingdon, Juniata, Lancaster, Lebanon, Mifflin, Perry, York): 909 Elmerton Avenue, Harrisburg, PA 17110; Business Hours: (717) 705-4700 / Emergency Response (24 hours): (877) 333-1904
Southwest Regional Office (serving: Allegheny, Armstrong, Beaver, Cambria, Fayette, Greene, Indiana, Somerset, Washington, Westmoreland): 400 Waterfront Drive, Pittsburgh, PA 15222-4745; Emergency Notification Number: (412) 442-4000

- PA DEP Bureau of Safe Drinking Water: 717-787-9633; [http://www.depweb.state.pa.us/](http://www.depweb.state.pa.us/)
- Allegheny County Health Department, Public Drinking Water Program; Phone: 412-578-8047

**Legionella testing laboratories certified by CDC ELITE program**

- CDC laboratory testing and certification: [http://www.cdc.gov/legionella/elite.html](http://www.cdc.gov/legionella/elite.html)

**ELITE-certified laboratories in Pennsylvania**

- PA Department of health, Bureau of Labs. 110 Pickering Way, Exton, PA 19341. Phone: 484-870-6398. [http://www.health.state.pa.us/labs](http://www.health.state.pa.us/labs).
- Pennsylvania DEP; 575 Interstate Drive, mailing- P.O. Box 1467, Harrisburg, PA 17110. Phone: 717-346-8670; [http://www.dep@pa.gov](http://www.dep@pa.gov)
- Criterion Laboratories, Inc. 3370 Progress Drive, Suite J, Bensalem, PA 19020. Phone: 215-244-1300. [http://www.criterionlabs.com](http://www.criterionlabs.com)
- U.S. Micro-Solutions, Inc., 475C Willow Crossing Road, Greensburg 15601; Phone: 724-853-4047

**Allegheny County**

- Pittsburgh VA Med Center. University Drive C, Pittsburgh, PA 15240. Phone: 412-360-6558.
- Special Pathogens Laboratory, 1401 Forbes Ave, suite 209, Pittsburgh 15219; Phone: (877) 775-7284 or (412) 281-5335; Fax (412) 281-7445; [http://www.specialpathogenslab.com/](http://www.specialpathogenslab.com/)
- West Penn Allegheny Health System – Core Lab. 1307 Federal Street, Pittsburgh, PA 15212. Phone: 412-359-6090.