

Investigating Health Claims Allegedly Associated With Biosolids

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This protocol is based on an amalgamation of methods from existing federal programs as an attempt to put biosolids health claims investigations on the same basis that the Agency for Toxic Substances and Disease Registry (ATSDR) uses to investigate potential chemical exposures at hazardous waste sites and the Centers for Disease Control and Prevention (CDC) use to evaluate outbreaks of communicable diseases. In general, investigations should be carried out by agencies with environmental health capabilities such as CDC, ATSDR, state or local health departments or academic institutions with public health departments. Individuals carrying out the investigations should be qualified in fields such as medicine, epidemiology, environmental health, medical microbiology, analytical chemistry. Any study should be of a level of quality consistent with existing EPA guidelines¹. The protocol contains 3 categories of investigations: clinical, environmental, and health investigations. The protocol also discusses the use of information obtained from investigations in determining causation.

Clinical Investigations

A report of a disease must be verified by a licensed physician or equivalent health care provider. Diseases should be classified according to International Classification of Diseases—Clinical Modification (ICD-9-CM)². The physician should follow a standard process in establishing an environmental diagnosis³:

- Establish the clinical characteristics of the medical condition
- Characterize exposure (to microbial pathogen or chemical)
- Demonstrate correlation between exposure and clinical manifestation
- Establish diagnosis of environmental medical condition.

The physician should consider clinical toxicology in the case of potential chemical exposure, alternative etiologies, temporal relations, and the effect of removal from exposure.

If chemical exposure is alleged, the exact identities of the chemical agents should be established using standard chemical measurement techniques⁴. If exposure to a microbial pathogen is alleged, the identities of the species should be established using standard

¹ See: A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information or Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the EPA.

² www.cdc.gov/nchs/about/otheract/icd9/abtcd9.htm

³ Brooks, S. 1995. Environmental Medicine. Mosby-Year Book, Inc. St. Louis, MO.

⁴ For example, EPA's TO series for air or SW-846 for solid or liquid media.

clinical laboratory tests⁵. All notifiable diseases should be reported to the appropriate authorities. CDC has developed a powerful tool for foodborne disease known as the Outbreak Investigation Toolkit which could be readily adapted for use with biosolids associated outbreaks.

A wide variety of tests exists for clinical investigation of putative odor impacts⁶. Tests and tools have been investigated for symptoms including eye irritation, headache, nasal congestion, nasal irritation, throat irritation, hoarseness, palpitations, sensory alterations, shortness of breath, and stress. For example, eye irritation may be investigated using slit lamp examination, blink rate, tear film stability, lissamine green staining of conjunctiva, and corneal carbon dioxide threshold. If multiple chemical sensitivity (MCS) is a potential diagnosis, the clinical investigation should be expanded to include immunologic, respiratory, cardiovascular, neurological, psychological and social function tests⁷. The Environmental Exposure and Sensitivity Inventory (EESI) is a clinical instrument developed for evaluating MCS following a well-defined exposure. Use of the EESI can help to make perceptions more objective, especially if administered over time or if the exposure has stopped.

Environmental Investigations to Demonstrate Exposure

Standard methods should be used for sampling and analysis of environmental media for chemical or microbiological agents. Sources of methods include: APHA/AWWA/WEF *Standard Methods for the Examination of Water and Wastewater*. EPA's SW-846 for chemicals in soils and biosolids, EPA's Microbiological Methods for Monitoring the Environment: Water and Wastes, EPA's POTW Sludge Sampling and Analysis Guidance document. FDA's Bacteriological Analytical Manual and publications of ASTM. All quality assurance and quality control guidelines should be adhered to. If a standard method is not available, methods published in the peer reviewed literature may be used with proper QA/QC.

Health Studies

Agency for Toxic Substances and Disease Registry (ATSDR) differentiates between Type 1 (exploratory) and Type 2 (application of rigorous scientific methods to evaluate specific exposure-outcome relationships)⁸. Type 1 studies include disease prevalence surveys, pilot investigations, cluster investigations, surveillance activities, health statistics reviews, exposure registries and exposure investigations. The following are needed for a type 1 study:

- Reasonable ability to document and characterize exposure in the target area

⁵ For example, see Mahon & Manuselis, 2000. *Textbook of Diagnostic Microbiology*, 2nd ed. Saunders, Philadelphia.

⁶ See Table 1 in Schiffman, S.S. et al. 2000. Potential health effects of odor from animal operations, wastewater treatment, and recycling of byproducts. *Jour Agromedicine* 7:7-81.

⁷ Ashford, N. & Miller, C. 1998. *Chemical Exposures* 2nd Ed. Van Nostrand Reinhold.

⁸ Guidance for ATSDR Health Studies. www.atsdr.cdc.gov/HS/gd1.html

- Adequate study size for the type of study recommended
- Ability to identify and locate subjects and records
- Appropriate comparisons for rates of occurrence
- Ability to control confounding factors and biases

If the results of a type 1 study show the potential for an association between exposure and disease, then a type 2 (what is normally thought of as an epidemiologic study) may be conducted. Type 2 studies include case-control and cohort studies. The following are needed for a type 2 study:

- Ability to reasonably estimate or document individual exposure
- Ability to document or validate health outcomes
- Adequate study size and statistical power
- Ability to locate subjects and records
- Availability of an appropriate control or comparison population
- Ability to control confounding factors and minimize biases
- Ability to determine influence of environmental behavioral or other factors.

Any health study must be quality assured through documentation that standard practices have been followed. Federally funded studies normally require peer review of the study protocol and the report of results.

Epidemiologic Causation

A critical element in evaluating claims associated with alleged exposure to biosolids is whether the exposure caused the disease. Causation may be thought of as a chain of events that links an injury to toxic substance or pathogen exposure. This chain must not be broken for causation to be demonstrated. In evaluating a chain of causation for a specific injury or illness, analysts usually start by evaluating the illness and then determining whether the subject was actually exposed to the agent of concern. The exposure analysis is based on biomonitoring, dosimetry, environmental monitoring, mathematical modeling, questionnaires, or a combination of these methods. Once it has been determined that exposure has occurred, a toxicology/microbiology/epidemiology review is conducted to determine if a health hazard exists. The existence of a health hazard is then linked to the exposure through risk assessment concepts such as dose-response quantification. Finally, confounding causes of the illness are investigated. Only when exposure has occurred at a level sufficient to elicit an adverse health effect that is not explainable by other causes can the exposure be causally linked to the disease.

The scientific literature presents several general principles for assessing causation in individuals⁹:

⁹ Lillienfeld, D.E. & Stolley, P.D. 1994. *Foundations of Epidemiology*. Oxford University Press.

- **Hazard identified/qualitative toxicology.** Is the chemical (or microorganism) capable of causing the alleged disease in the person claiming damage?
- **Exposure and Dose Response.** Did the person claiming the disease contact the hazardous chemical (or pathogenic microorganism) at a sufficient level (duration, frequency, intensity) to result in an injury?
- **Time course of disease.** Was exposure temporally related to the injury given appropriate considerations of disease latency?
- **Confounders/differential diagnosis.** Are there possible alternative causes for the disease?
- **Analysis of scientific plausibility.** Do toxicologic, epidemiologic, microbiological, chemical, and clinical data present an internally consistent and coherent view of the disease?

Microbiological Causation

The subject of microbial causation of disease was first addressed by Robert Koch in 1884. Koch's Postulates, which are still used today:

- The microorganism should be found in all cases of the disease and its distribution in the body should be consistent with the observed lesions;
- The microorganism should be grown in pure culture for several generations;
- When the pure culture is inoculated into susceptible animal species, the typical illness must result; and
- The microorganism must be capable of being isolated from the experimentally produced disease.

More recent interpretations of Koch's Postulates involve DNA identification of microorganisms.

There are several keys to the application of Koch's Postulates to claims of illness. First, the illness must have an infectious etiology. Claims of cancer, cardiovascular disease, and reproductive effects are not likely to be of microbiological origin whereas claims of gastroenteritis and upper respiratory illness may well have an infectious source. Second, an actual microorganism species must be identified using standard protocols. Normally this involves obtaining a sample from the patient, which is cultured and tested. At a minimum, testing should involve morphological and biochemical testing. To avoid ambiguity, most contemporary forensic investigators rely on DNA testing. The identification of the correct species of microorganism is critical not only for causation but for treatment of a potentially exposed individual. The key factor in determining if biosolids cause infectious disease is to identify the pathogen in the subject, the source, and along the exposure pathway.