

Appendix 1: Case Definition for Pesticide-Related Illness and Injury Reportable to the National Public Health Surveillance System

Frequently Asked Questions (FAQs)

Q1. The terms signs and symptoms are used throughout the case definition. What is the difference between the two?

A1. Signs are objective findings that can be observed and described by a licensed health care professional. Typically, this is the information one would find in the "physical exam" or "physical findings" section of a medical record, or acute poisoning reporting form. These findings do not rely on the subjective reporting of sensations by the affected individual. An objective knowledgeable observer includes all licensed health care professionals (e.g. MD, DO, PA, RN, EMT etc.).

Symptoms are any subjective evidence of a disease or a condition as perceived and reported by the patient. This includes reported changes from normal function, sensation, or appearance. You would find this information in the "History" section of a medical record.

Q2. How should we classify the exposure when an affected individual, their coworker or family member indicates that they were "drenched" by pesticide spray?

A2. If there is no other corroborating evidence presented by an objective observer then the information meets criteria "A2". If there is documentation by medical personnel, emergency responders (police, Emergency Medical Technician, etc.), an employer, agency representative, or investigators that the individual was observed to be drenched at the scene or treatment facility this would be classified as meeting criteria "A1b". However, it must be remembered that these observers must be *objective and independent*, and therefore they can not be the affected individual.

Q3. How should an exposure be classified when an individual has a dermal exposure that is difficult to document as a direct exposure?

For example: A person handles an object contaminated with pesticides then touches another part of the body with their possibly contaminated hand. The individual then develops a dermal response at the site of hand contact.

A3. If the individual is confident that contact with the pesticide product definitely occurred, and the hand to body part contact occurred shortly afterward, and the dermal response is documented by a licensed health care professional, code the exposure as "A1d" (documentation by a licensed health care professional of a characteristic eye injury or dermatologic effects at the site of direct exposure to a

pesticide product known to produce such effects). Code as "A2" (evidence of exposure based solely upon written or verbal report) if the dermal response is not documented by a licensed health care professional. If the history is vague, or contact may have been with a plant or product other than a pesticide, code as "A4" (insufficient data).

Q4. How do we interpret cholinesterase results when performing case classification?

A4. Each state may choose to develop their own internal guidelines. The following very cursory discussion is provided to assist states in this process. Cholinesterase depression is defined as one (or more) of the following:

- 1) 30% depression from baseline (pre-exposure or 60-90 days post exposure) RBC cholinesterase level
- 2) 40% depression from baseline plasma cholinesterase level
- 3) Cholinesterase level below laboratory normal range.

The level of depression may be determined by serial post-exposure testing if a baseline test is not available. (For example - testing 2 weeks and 4 weeks post exposure show a gradual increase in cholinesterase by percentages in 1 and 2 above, over the levels at initial testing.) A test that shows significant depression as described above should be considered evidence of exposure, and ranked as meeting criteria "A1c". It should also be considered evidence for a new post-exposure health effect and helps to meet the criteria for "B1" (an additional post-exposure sign or test/laboratory finding would be needed to fully meet the criteria for "B1"). A test result which does not indicate depression should not be considered an indication that substantial exposure has not occurred. The timing of testing, laboratory variation, the wide normal range, and administration of praloxidime chloride (2PAM) prior to testing can all lead to negative results.

Q5. Can the applicator who is directly affected by exposure, or has performed the application that is associated with health effects supply information that can be considered "evaluation by a trained professional" specified in criteria "A1b"?

A5 No. Individuals who are considered professional observers should be objective. An applicator who is the 'case' can not be considered an objective observer. Nor can an applicator be an objective observer when there are allegations or observations suggesting a misapplication may have occurred. A trained, licensed applicator not directly involved with the case could be an observer under "A1b". For example, a second applicator is called in to help evaluate damage to plants on the property, or to help alleviate odors in an office from an application by another applicator. This second individual's observation can meet the requirements of a trained professional observer as specified in "A1b".

Q6. What is the definition of antidote that should be used to evaluate exposure (A1c)?

A6. By antidote, we mean an agent that counteracts the effects of the pesticide. There are two types of antidotes that satisfy this definition: pharmacological antidotes and specific antidotes. Pharmacological antidotes counteract the pharmacological effects of the absorbed pesticide. Often, individuals poisoned with pesticides have a high tolerance to repeated doses of pharmacological antidotes. For example, those poisoned with anticholinesterase pesticides have a high tolerance to atropine. As such, very high doses of atropine are often required to treat individuals poisoned with anticholinesterase pesticides. Another pharmacological antidote is phenobarbital.

Specific antidotes interact directly with absorbed pesticide or some product of it to block the biochemical effect of the pesticide. Examples include pralidoxime chloride (2-PAM), vitamin K, and pesticide-specific monoclonal antibodies that are under development.

Antidotes are not the same as adjunct treatment that may help relieve symptoms or effects of the exposure in a less direct manner. This also does not include agents that prevent absorption of the ingested pesticide (e.g. activated charcoal).

Q7. How can we end up with a classification that is different from the clinical diagnosis in the medical record? Isn't that "second guessing" the physician's evaluation of the patient?

A7. The case classification scheme and the clinical diagnosis serve different purposes. The purpose of the case classification scheme is to serve surveillance and epidemiologic-related functions. The classification scheme provides objective guidelines for assessing the certainty of the evidence regarding exposure and health effects. In contrast, the purpose of the clinical diagnosis is to guide the immediate treatment course for the individual. In addition, the clinician may use more intuitive and subjective criteria when making a diagnosis. Therefore, it is possible that the classification category may differ from the clinical diagnosis.

Q8. The classification scheme seems too stringent. By excluding individuals who report only one symptom, we may be missing important cases. For example, a child with seizures after DEET exposure would be excluded. How can we address this?

A8. The classification scheme does require the presence of at least two post-exposure symptoms for a report to be considered a case. This may result in the

exclusion of a very small number of actual pesticide-related illnesses or injuries. Most concerns about excluding cases due to this criterion can be alleviated by using structured protocols for obtaining medical histories from the individual and/or health care professional. If a single sign or symptom is reported, requesting more details will usually elicit additional signs or symptoms. Asking about commonly related symptoms as part of an interview is an acceptable practice. For example, it is appropriate to ask about symptoms of nausea if an individual reports vomiting; stomach cramping if diarrhea is reported, or loss of consciousness with seizure. This approach should help resolve concerns about the classification system resulting in false negatives.

Q9. How do we assess signs and symptoms when an individual has a pre-existing condition that may influence their physiologic response to an exposure?

A9. Few studies have examined the effect of pre-existing disease on the toxicity of pesticides. We are not aware of any studies that found differences in signs and symptoms among pesticide-poisoned individuals with pre-existing conditions. Therefore, if someone presents with an atypical set of symptoms for a particular pesticide, a score of C2 should be strongly considered under "evidence supporting a causal relationship between pesticide exposure and health effects".

However, it is possible that those with some pre-existing conditions will have reduced physiologic reserve. Therefore, these individuals may manifest symptoms at a lower pesticide dose compared to a young, healthy individual. Nonetheless, in these individuals, the signs and symptoms should be characteristic of the particular pesticide, and the temporal relationship should be appropriate.

It is possible that pesticide exposure may exacerbate a pre-existing condition (e.g., organophosphate exposure can cause increased shortness of breath in exposed individuals, including individuals with chronic lung disease). However, the signs and symptoms that are present should be consistent with poisoning from the pesticide in question.

Q10. How do we address a situation when the underlying condition may create a set of symptoms that are similar to the symptoms caused by the pesticide?

A10. As has been stated previously, pesticide exposure may exacerbate a pre-existing condition. However, keep in mind that the signs and symptoms that are present should be consistent with poisoning from the pesticide in question. In addition, there should be an appropriate temporal relationship (i.e. exposure preceded the health effect and the latency between exposure and effect is appropriate), and the pesticide exposure should be of sufficient dose.

Q11. How do we determine whether the evidence for an exposure-health effect relationship is insufficient versus inconsistent?

A11. When there is little literature on the health effects associated with a particular pesticide and none of it describes the health effects of interest, then the evidence for an exposure-health effect relationship is considered "insufficient" and a score of "C4" is appropriate. However, if there are many references on the health effects associated with a particular pesticide, and none describe the health effects of interest, then the evidence for an exposure-health effect relationship is considered "inconsistent" and a score of "C2" is appropriate.

Q12. The term "exposure dose" is used in section C (Evidence supporting a causal relationship between pesticide exposure and health effects). Often little information is available on dose. How should we interpret "dose"?

A12. The use of this term refers to whether the dose was sufficient to produce the observed health effects. Unfortunately, there is a paucity of data available on the minimum dose of a pesticide needed to produce health effects in humans. In addition, reaction to a pesticide exposure can vary across individuals. It should be remembered that some individuals may be much more sensitive to a pesticide and manifest health effects at a much lower dose compared to other individuals. Other factors such as duration of exposure, use of protective equipment, amount of time between exposure and collection of the environmental sample, and the effect of intervening weather conditions on environmental samples and observations must be factored in when evaluating the actual "exposure dose" likely experienced by the individual. When available, the peer-reviewed literature should be examined for guidance. The judgment of colleagues in the State Department of Agriculture may also be helpful

When dealing with self-reports, qualitative information on exposure dose can be obtained. For example, information can be obtained about proximity to the source of exposure, duration of exposure, did health effects manifest in others who were exposed, etc. Assessing this information may require experience and the assistance of other knowledgeable colleagues.

Q13. Often we learn that an individual was exposed to a particular functional class of pesticides (e.g. insecticide, herbicide, etc.), but we can't determine the name of the product or the active ingredient. Should an exposure score of "A2=written or verbal report" or "A4=insufficient data" be assigned?

A13. When only the pesticide class is known, a score of "A4=insufficient data" must be assigned. This is because the pesticides within a particular class can vary widely in toxicity. Therefore, it would be impossible to determine if any observed health

effects are consistent and or characteristic with the pesticide exposure. However, if the chemical class of the pesticide is known (e.g. organophosphate, or carbamate), but the specific pesticide product or active ingredient is unknown, a score of "A1" or "A2" can be considered. This is because pesticides within a specific chemical class can produce similar health effects (see Appendix 2).

Q14. Can documentation or a clinical description "by a licensed health care professional" as specified in criteria "A1d", "A1e" and "B1", be provided by the licensed health care professional who is directly affected by exposure (please note that this is similar to question Q5)?

A14 No. Individuals who are considered professional observers should be objective. A health care professional who is the 'case' cannot be considered an objective observer. A licensed health care professional not directly involved in the exposure event would meet the criteria under "A1d", "A1e" and "B1".