WAC 296-849-60020 Medical guidelines for benzene. (1) You must include an explanation of the contents of this section to employees as required in Training, WAC 296-849-11050.

(2) You must provide a copy of this section to the licensed health care professional (LHCP) as required in Step 4 of the medical evaluation process found in Medical evaluations, WAC 296-849-12030.

Table 8
Medical Guidelines For Evaluating Employees Exposed to Benzene

Part 1: Becoming familiar with medical requirements in this chapter
In addition to requiring employers to train employees and protect them from exposure to benzene, this chapter (the Benzene rule) requires employers to monitor their employees' health with assistance from licensed health care professionals (LHCPs). • For employees who will use respirators, the LHCP will also need to provide the employer with a written medical opinion clearing the employee for workplace respirator use. These guidelines were designed to support an informed partnership between the LHCP and the employer when monitoring the health of employees exposed to benzene. The employer initiates this partnership by providing the LHCP with a copy of the chapter and other supporting information about the employee and job conditions. The LHCP can then become familiar with the medical monitoring requirements found in WAC 296-849-12030 through 296-849-12080, which address: • Frequency and content for routine (initial and periodic) medical examinations and consultations; • Emergency and other unplanned medical follow-up; • Medical opinions; • Employee medical removal; • Medical records retention and content.
Part 2: Benzene toxicology
Benzene is primarily an inhalation hazard. Systematic absorption may cause depression of the hematopoietic system, pancytopenia, aplastic anemia, and leukemia. Clinical evidence of leukopenia, anemia, and thrombocytopenia, singly or in combination, has been frequently reported among the first signs. **Health information about benzene, WAC 296-848-50010,** provides **basic information** about the health effects and symptoms associated with benzene exposure. **Reference:** • Other sources for toxicology information include: – ToxFAQs™ and the Toxicological Profile for Benzene. This free document is available from the Agency for Toxic Substances and Disease Registry (ATSDR) and can be obtained by: ■ Visiting http://www.atsdr.cdc.gov/toxprofiles OR ■ Calling 1-888-422-8737

- A variety of technical resources on benzene from the National Institutes for Occupational Safety and Health (NIOSH) by visiting http://www.cdc.niosh/topics/chemicals.html

Part 3: Treatment of acute toxic effects

When providing assistance to someone contaminated with benzene, make sure **you** are adequately protected and do not risk being overcome by benzene vapor.

Remove the patient from exposure immediately.

Give oxygen or artificial resuscitation, if indicated.

Flush eyes, wash skin if contaminated and remove all contaminated clothing.

Recovery from mild exposures is usually rapid and complete. Symptoms of intoxication may persist following severe exposures.

Part 4: Preventive considerations

The principal effects of benzene exposure which form the basis for the requirements in this chapter are pathological changes in the hematopoietic system, reflected by changes in the peripheral blood and manifesting clinically as pancytopenia, aplastic anemia, and leukemia.

Consequently, the medical monitoring program is designed to observe, on a regular basis, blood indices for early signs of these effects, and although early signs of leukemia are not usually available, emerging diagnostic technology and innovative regimes make consistent surveillance for leukemia, as well as other hematopoietic effects, essential.

Symptoms and signs of benzene toxicity can be nonspecific. Only a detailed history and appropriate investigative procedure will enable a physician to rule out or confirm conditions that place the employee at increased risk.

Bone marrow may appear normal, aplastic, or hyperplastic, and may not, in all situations, correlate with peripheral blood forming tissues. Because of variations in the susceptibility to benzene morbidity, there is no "typical" blood picture.

The onset of effects of prolonged benzene exposure may be delayed for many months or years after the actual exposure has ceased and identification or correlation with benzene exposure must be sought out in the occupational history.

There are special provisions for medical tests in the event of hematologic abnormalities or for emergency situations.

- This chapter specifies that blood abnormalities that persist must be referred "unless the physician has good reason to believe such referral is unnecessary." Examples of conditions that could make a referral unnecessary despite abnormal blood limits are iron or folate deficiency, menorrhagia, or blood loss due to some unrelated medical abnormality.
- Blood values that require referral to a hematologist or internist are noted under Part 5: Hematology guidelines.

Part 5: Hematology guidelines

The following guidelines are established to assist the examining LHCP with regard to which laboratory tests are necessary and when to refer an employee to the specialist. A minimum battery of tests is to be performed using strictly standardized methods.

Basic tests

- The following must be determined by an accredited laboratory:
  - Red and white cell counts;
  - Platelet counts;
  - White blood cell differential;
  - Hematocrit;
  - Red cell indices.
- The normal ranges for the red cell and white cell counts are influenced by altitude, race, and sex, and therefore should be determined by the accredited laboratory in the specific area where the tests are performed.
- Either a decline from an absolute normal or an individual's baseline to a subnormal value or a rise to a supra-normal value, are indicative of potential toxicity, particularly if all blood parameters decline.
  - The normal total white blood count is approximately 7,200/mm^3 plus or minus 3,000;
  - For cigarette smokers the white count may be higher and the upper range may be 2,000 cells higher than normal for the laboratory;
  - In addition, infection, allergies and some drugs may raise the white cell count;
  - The normal platelet count is approximately 250,000 with a range of 140,000 to 400,000. Counts outside this range should be regarded as possible evidence of benzene toxicity.
- Certain abnormalities found through routine screening are of greater significance in the benzene-exposed worker and **require prompt consultation with a specialist,** namely:
  - Thrombocytopenia;
  - A trend of decreasing white cell, red cell, or platelet indices in an individual over time is more worrisome than an isolated abnormal finding at one test time. The importance of trend highlights the need to compare an individual's test results to baseline and/or previous periodic tests;
  - A constellation or pattern of abnormalities in the different blood indices is of more significance than a single abnormality. A low white count not associated with any abnormalities in other cell indices may be a normal statistical variation, whereas if the low white count is accompanied by decreases in the platelet and/or red cell indices, such a pattern is more likely to be associated with benzene toxicity and merits thorough investigation;

- Anemia, leukopenia, macrocytosis or an abnormal differential white blood cell count should alert the physician to further investigate and/or refer the patient if repeat tests confirm the abnormalities. If routine screening detects an abnormality, follow-up tests which may be helpful in establishing the etiology of the abnormality are the peripheral blood smear and the reticulocyte count;
- The extreme range of normal for reticulocytes is 0.4 to 2.5 percent of the red cells, the usual range being 0.5 to 1.2 percent of the red cells, but the typical value is in the range of 0.8 to 1.0 percent;
- A decline in reticulocytes to levels of less than 0.4 percent is to be regarded as possible evidence (unless another specific cause is found) of benzene toxicity requiring accelerated surveillance. An increase in reticulocyte levels to about 2.5 percent may also be consistent with (but is not as characteristic of) benzene toxicity.

Additional tests

1. Peripheral blood smears:

- Collecting the sample: As with reticulocyte count, the smear should be with fresh uncoagulated blood obtained from a needle tip following venipuncture or from a drop of earlobe blood (capillary blood). If necessary, the smear may, under certain limited conditions, be made from a blood sample anticoagulated with EDTA (but never with oxalate or heparin).
- Prepping the smear: When the smear is to be prepared from a specimen of venous blood which has been collected by a commercial Vacutainer type tube containing neutral EDTA, the smear should be made as soon as possible after the venesection. A delay of up to twelve hours is permissible between the drawing of the blood specimen into EDTA and the preparation of the smear if the blood is stored at refrigerator (not freezing) temperature.
- Minimum mandatory observations:
  - The differential white blood cell count;
  - Description of abnormalities in the appearance of red cells;
  - Description of any abnormalities in the platelets;
  - A careful search must be made throughout of every blood smear for immature white cells such as band forms (in more than normal proportion, i.e., over 10 percent of the total differential count), any number of metamyelocytes, myelocytes, or myeloblasts. Any nucleate or multinucleated red blood cells should be reported. Large "giant" platelets or fragments of megakaryocytes must be recognized;

- An increase in the proportion of band forms among the neutrophilic granulocytes is an abnormality deserving special mention, for it may represent a change which should be considered as an early warning of benzene toxicity in the absence of other causative factors (most commonly infection). Likewise, the appearance of metamyelocytes, in the absence of another probable cause, is to be considered a possible indication of benzene-induced toxicity;
- An upward trend in the number of basophils, which normally do not exceed about 2.0 percent of the total white cells, is to be regarded as possible evidence of benzene toxicity. A rise in the eosinophil count is less specific but also may be suspicious of toxicity if it rises above 6.0 percent of the total white count;
- The normal range of monocytes is from 2.0 to 8.0 percent of the total white count with an average of about 5.0 percent. About 20 percent of individuals reported to have mild but persisting abnormalities caused by exposure to benzene show a persistent monocytosis. The findings of a monocyte count which persists at more than 10 to 12 percent of the normal white cell count (when the total count is normal) or persistence of an absolute monocyte count in excess of $800/mm^3$ should be regarded as a possible sign of benzene-induced toxicity;
- A less frequent but more serious indication of benzene toxicity is the finding in the peripheral blood of the so-called "pseudo" (or acquired) Pelger-Huet anomaly. In this anomaly many, or sometimes the majority, of the neutrophilic granulocytes possess two round nuclear segments - less often one or three round segments - rather than three normally elongated segments. When this anomaly is not hereditary, it is often but not invariably predictive of subsequent leukemia. However, only about two percent of patients who ultimately develop acute myelogenous leukemia show the acquired Pelger-Huet anomaly. Other tests that can be administered to investigate blood abnormalities are discussed below; however, such procedures should be undertaken by the hematologist.

2. Sucrose water test and Ham test:

- An uncommon sign, which cannot be detected from the smear, but can be elicited by a "sucrose water test" of peripheral blood, is transient paroxysmal nocturnal hemoglobinuria (PNH), which may first occur insidiously during a period of established aplastic anemia, and may be followed within one to a few years by the appearance of rapidly fatal acute myelogenous leukemia. Clinical detection of PNH, which occurs in only one or two percent of those destined to have acute myelogenous leukemia, may be difficult; if the "sucrose water test" is positive, the somewhat more definitive Ham test, also known as the acid-serum hemolysis test, may provide confirmation.

Important clinical findings

1. Individuals documented to have developed acute myelogenous leukemia years after initial exposure to benzene may have progressed through a preliminary phase of hematologic abnormality. In some instances pancytopenia (i.e., a lowering in the counts of all circulating blood cells of bone marrow origin, but not to the extent implied by the term "aplastic anemia") preceded leukemia for many years.

- Depression of a single blood cell type or platelets may represent a harbinger of aplasia or leukemia. The finding of two or more cytopenias, or pancytopenia in a benzene-exposed individual, must be regarded as highly suspicious of more advanced although still reversible, toxicity.
- "Pancytopenia" coupled with the appearance of immature cells (myelocytes, myeloblasts, erythroblasts, etc.), with abnormal cells (pseudo Pelger-Huet anomaly, atypical nuclear heterochromatin, etc.), or unexplained elevations of white blood cells must be regarded as evidence of benzene overexposure unless proved otherwise.
- Many severely aplastic patients manifested the ominous findings of:
  - 5 to 10 % myeloblasts in the marrow;
  - Occasional myeloblasts and myelocytes in the blood;
  - 20 to 30 monocytes.
- It is evident that isolated cytopenias, pancytopenias, and even aplastic anemias induced by benzene may be reversible and complete recovery has been reported on cessation of exposure. However, since any of these abnormalities is serious, the employee must immediately be removed from any possible exposure to benzene vapor.
  - Certain tests may substantiate the employee's prospects for progression or regression. One such test would be an examination of the bone marrow, but the decision to perform a bone marrow aspiration or needle biopsy is made by the hematologist.

2. The findings of basophilic stippling in circulating red blood cells (usually found in one to five percent of red cells following marrow injury), and detection in the bone marrow of what are termed "ringed sideroblasts" must be taken seriously, as they have been noted in recent years to be premonitory signs of subsequent leukemia.

3. Recently peroxidase-staining of circulating or marrow neutrophil granulocytes, employing benzidine dihydrochloride, have revealed the disappearance of, or diminution in, peroxidase in a sizable proportion of the granulocytes, and this has been reported as an early sign of leukemia. However, relatively few patients have been studied to date. Granulocyte granules are normally strongly peroxidase positive. A steady decline in leukocyte alkaline phosphatase has also been reported as suggestive of early acute leukemia.

- Peroxidase and alkaline phosphatase staining are usually undertaken when the index of suspicion for leukemia is high.

4. Exposure to benzene may cause an early rise in serum iron, often but not always associated with a fall in the reticulocyte count. Thus, serial measurements of serum iron levels may provide a means of determining whether or not there is a trend representing sustained suppression of erythropoiesis.

5. Measurement of serum iron, determination of peroxidase and of alkaline phosphatase activity in peripheral granulocytes can be performed in most pathology laboratories.

[Statutory Authority: RCW 49.17.010, 49.17.040, 49.17.050, and 49.17.060. WSR 18-22-116, § 296-849-60020, filed 11/6/18, effective 12/7/18; WSR 07-03-153, § 296-849-60020, filed 1/23/07, effective 6/1/07.]