

**Definition of Manifest and Manifestation from Federal Regulations Implementing  
GINA Requirements for Group Health Insurance**

**45 CFR § 146.122(a)(6)**

(6)(i) Manifestation or manifested means, with respect to a disease, disorder, or pathological condition, that an individual has been or could reasonably be diagnosed with the disease, disorder, or pathological condition by a health care professional with appropriate training and expertise in the field of medicine involved. For purposes of this section, a disease, disorder, or pathological condition is not manifested if a diagnosis is based principally on genetic information.

(ii) The rules of this paragraph (a)(6) are illustrated by the following examples:

Example 1. (i) Facts. Individual A has a family medical history of diabetes. A begins to experience excessive sweating, thirst, and fatigue. A's physician examines A and orders blood glucose testing (which is not a genetic test). Based on the physician's examination, A's symptoms, and test results that show elevated levels of blood glucose, A's physician diagnoses A as having adult onset diabetes mellitus (Type 2 diabetes).

(ii) Conclusion. In this Example 1, A has been diagnosed by a health care professional with appropriate training and expertise in the field of medicine involved. The diagnosis is not based principally on genetic information. Thus, Type 2 diabetes is manifested with respect to A.

Example 2. (i) Facts. Individual B has several family members with colon cancer. One of them underwent genetic testing which detected a mutation in the MSH2 gene associated with hereditary nonpolyposis colorectal cancer (HNPCC). B's physician, a health care professional with appropriate training and expertise in the field of medicine involved, recommends that B undergo a targeted genetic test to look for the specific mutation found in B's relative to determine if B has an elevated risk for cancer. The genetic test with respect to B showed that B also carries the mutation and is at increased risk to develop colorectal and other cancers associated with HNPCC. B has a colonoscopy which indicates no signs of disease, and B has no symptoms.

(ii) Conclusion. In this Example 2, because B has no signs or symptoms of colorectal cancer, B has not been and could not reasonably be diagnosed with HNPCC. Thus, HNPCC is not manifested with respect to B.

Example 3. (i) Facts. Same facts as Example 2, except that B's colonoscopy and subsequent tests indicate the presence of HNPCC. Based on the colonoscopy and subsequent test results, B's physician makes a diagnosis of HNPCC.

(ii) Conclusion. In this Example 3, HNPCC is manifested with respect to B because a health care professional with appropriate training and expertise in the field of medicine involved has made a diagnosis that is not based principally on genetic information.

Example 4. (i) Facts. Individual C has a family member that has been diagnosed with Huntington's Disease. A genetic test indicates that C has the Huntington's Disease gene variant. At age 42, C begins suffering from occasional moodiness and disorientation, symptoms which are associated with Huntington's Disease. C is examined by a neurologist (a physician with appropriate training and

expertise for diagnosing Huntington's Disease). The examination includes a clinical neurological exam. The results of the examination do not support a diagnosis of Huntington's Disease.

(ii) Conclusion. In this Example 4, C is not and could not reasonably be diagnosed with Huntington's Disease by a health care professional with appropriate training and expertise. Therefore, Huntington's Disease is not manifested with respect to C.

Example 5. (i) Facts. Same facts as Example 4, except that C exhibits additional neurological and behavioral symptoms, and the results of the examination support a diagnosis of Huntington's Disease with respect to C.

(ii) Conclusion. In this Example 5, C could reasonably be diagnosed with Huntington's Disease by a health care professional with appropriate training and expertise. Therefore, Huntington's Disease is manifested with respect to C.