At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare.

Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

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Frequently asked questions

Biotin Interference

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All immunoassays, regardless of manufacturer, can be affected by interfering substances. The prevalence of immunoassay interference is variable and depends on the type of interferent present. Some common interferences include icterus, hemolysis, lipemia, human anti-mouse antibodies (HAMA), and biotin. Biotin interference was the topic of a recent FDA safety alert, which highlights the need for clinicians to be aware of laboratory results that may be affected by a variety of interfering substances.

What is biotin?

Biotin, or vitamin B7, is an essential nutrient that is naturally present in foods including meat, fish, eggs, seeds, nuts, and certain vegetables, such as sweet potatoes, spinach, and broccoli. This vitamin is involved in a variety of metabolic processes, including gluconeogenesis, fatty acid synthesis, and carbohydrate utilization.

The U.S. Food and Nutritional Board established a daily reference intake (DRI) of biotin of approximately 30 µg/day for healthy adults, assumed to ensure nutritional adequacy. While the majority of individuals obtain sufficient biotin from food sources, biotin deficiency can occur in pregnant and breastfeeding women,[1,2] individuals with chronic alcohol exposure[3] or those with biotinidase deficiency.[4,5]

Biotin is available in over-the-counter dietary supplements offered as biotin alone, or in B-complex and multi-vitamins. Although not supported by clinical evidence, biotin has also become a popular supplement packaged to enhance hair, skin, and nail health. In some of these products, biotin may be present at greater than 10 times the established DRI. In recent years, high dose biotin levels (300,000 µg/day) have been explored as a therapy to treat conditions such as multiple sclerosis, chronic kidney disease, and certain inborn errors of metabolism.[6]

Why is there so much concern about biotin interference?

The increased use of biotin by the general public as a lifestyle supplement, in addition to new experimental pharmacologic therapies, has led to an increasing number of reports of analytical interference in assays that use a biotin-streptavidin architecture.

Why do manufacturers use streptavidin-biotin in the design of some of their assays?

Streptavidin-biotin technology is commonly used by many manufacturers in assay design because it is a very efficient and effective tagging/bonding agent. Biotin binds streptavidin with high affinity, forming one of the strongest known noncovalent bonds.

How does assay design affect biotin interference?

The susceptibility of an assay to biotin interference largely depends on the assay design employed when using the streptavidin-biotin architecture. Assays using streptavidin-biotin technology are designed in one of two basic formats: preformed or nonpreformed.

Preformed assays are less susceptible to interference from biotin in patient samples. They utilize streptavidin-coated beads that are prebound to biotinylated antibody during the manufacturing process. This complexed biotinylated antibody is bound prior to the introduction of the patient sample in the assay reaction. The biotinylated bond is not easily broken, therefore, excess serum biotin will not prevent the binding capture antibody or antigen to its target.

In the nonpreformed assay design, the complexed biotinylated antibody formation occurs after the addition of the patient sample, exposing the interaction to excess biotin present in the sample. Serum biotin can bind to the streptavidin on the bead and prevent the biotin capture antibody/antigen target analyte from binding to the substrate, yielding a false result.

Biotin interference may be associated with either a positive or negative bias. In sandwich-formatted assays, lower-than-expected results or a negative bias are typically observed. In competitive formatted assays, a higher or positive bias is typically observed. In either case, the resulting bias may have a significant impact on clinical interpretation.

What is the prevalence of biotin supplementation in the general population?

Limited studies are available regarding the prevalence of biotin use in the general population.

In In one study 490 serum samples from emergency department (ED) patients were collected for biotin measurement. The results of this study showed that only 8 of the 490 samples had biotin levels >2 ng/mL. The highest concentration of biotin observed was 45 ng/mL. Of 490 ED samples assessed, 482 (98%) contained biotin concentrations <1 ng/mL.[7]

In a second independent study biotin consumption was observed among 1,944 outpatients presenting for scheduled blood collection at a primary phlebotomy center. 7.7% of the respondents (149 persons) reported use of biotin supplementation. The second part of this study involved the quantitation of biotin levels in samples from 1,442 ED patients. Biotin concentrations measured in this population ranged from ≤ 5 ng/mL to 280 ng/mL. Approximately 51.1% of the samples had biotin concentrations ≤ 5 ng/mL while approximately 7.4% of samples had biotin levels ≥10 ng/mL.[8]

How is Siemens Healthineers managing the risk of biotin interference?

Many of Siemens Healthineers' immunoassays do not use the streptavidin-biotin design; therefore, these assays are not susceptible to biotin interference. Streptavidin-biotin technology has been used in a subset of the immunoassays to optimize performance. Most of these assays are preformed, with the streptavidin-biotin complex formed during the manufacturing process, prior to the introduction of the patient sample. For these assays, susceptibility to biotin interference is unlikely or exhibits a bias of less than 10%, which is generally considered to be within acceptable limits.

The remaining few immunoassays that use streptavidin-biotin technology in a nonpreformed design with the streptavidin-biotin reaction taking place during assay incubation after the introduction of the patient sample are more susceptible to biotin interference from excess biotin in the patient sample.

With the growing awareness regarding the evolving use of biotin and the potential for biotin interference, Siemens Healthineers is working to identify and more clearly report potential interference in assays utilizing the streptavidin-biotin architecture. For individuals ingesting mega-doses of biotin up to 300 mg/day, serum concentrations as high as 1160 ng/mL have been observed.[6] Acridinium ester immunoassays that utilize the streptavidin-biotin design and have no effect with biotin up to 1200 ng/mL have been reassessed for risk of biotin interference up to a level of 3500 ng/mL of biotin.

Siemens Healthineers is committed to designing future assays to limit the use of the streptavidin-biotin technology. In cases where a streptavidin-biotin bond is necessary for optimal assay performance, our internal verification protocol will proactively include interference testing of biotin to assess potential risk of biotin interference on sample recovery.

How can laboratorians and clinicians manage potential risk?

Raising awareness and evolving communication among clinicians, patients and laboratorians is essential to manage the potential influence of biotin interference. Siemens Healthineers encourages laboratories to discuss potential biotin interference with their associated healthcare providers.

- **Clinicians**
  Clinicians should initiate open communication with your patients on the use of over the counter biotin supplementation. Consider the entire clinical picture when interpreting laboratory results. If a lab test result is unexpected and does not align with the clinical presentation of your patient, consider biotin interference as a possible source of error and discuss with the laboratory director.

- **Laboratorians**
  Laboratorians should understand the assays that you offer. Check the instructions for use (IFU) to determine the biotin tolerance limits. In addition, be aware of other proteins or exogenous substances that may interfere with interpretation of test results. By understanding the differing susceptibilities between assay architectures, clinical laboratories can initiate and continue educational efforts to help clinicians better manage the potential impact of biotin on test results within their patient populations.

For further information about interferences refer to the assay-specific instructions for use (IFU)