SPECIAL REPORT

AACC Guidance Document on Biotin Interference in Laboratory Tests

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Background: Laboratory tests that use streptavidin–biotin binding mechanisms have the potential to be affected by high circulating biotin concentrations, which would produce positive and negative interference in biotinylated competitive and noncompetitive (sandwich) immunoassays, respectively. Consumption of high-dose biotin supplements for cosmetic or health-related reasons has drawn attention to biotin interference in clinical laboratory tests. Case reports and in vivo studies show that ingestion of supplemental biotin can cause clinically significant errors in select biotinylated immunoassays.

Content: This AACC Academy document is intended to provide guidance to laboratorians and clinicians for preventing, identifying, and dealing with biotin interference. In vivo and in vitro spiking studies have demonstrated that biotin concentrations required to cause interference vary by test and by manufacturer. This document includes discussion of biotin's mechanisms for interference in immunoassays, pharmacokinetics, and results of in vitro and in vivo studies and cites examples of assays known to be affected by high biotin concentrations. This document also provides guidance recommendations intended to assist laboratories and clinicians in identifying and addressing biotin interference in laboratory testing.

Summary: The recent increase in the use of high-dose biotin supplements requires laboratorians and clinicians to be mindful of the potential for biotin interference in biotinylated immunoassay-based laboratory tests. Laboratories, clinicians, regulators, and patients should work together to ensure accurate laboratory results. Laboratories have several options for identifying suspected biotin interference in specimens. Alternatively, the relatively fast elimination of biotin allows the potential for rapid follow-up specimen analysis if necessary.

Biotin (vitamin B7) is a coenzyme involved in multiple metabolic processes, including carbohydrate metabolism, fatty acid synthesis, amino acid catabolism, and gluconeogenesis *(1)*. The Institute of Medicine recommends a daily biotin intake of 30 μg *(2)*. Although the inclusion of biotin in over-the-counter multivitamins is common, biotin supplementation is not usually necessary because biotin is found in numerous foods (e.g., meat, fish, nuts, grains, eggs, and dairy products). High doses of biotin (up to 3333 times the recommended daily dose [i.e., 100 000 μg or 100 mg]) are available over-the-counter and have been used for a variety of medical conditions, including diabetes,

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Received August 2, 2019; accepted on October 28, 2019
DOI: 10.1093/jalm/jfz010

lipid disorders, biotinidase deficiency, carboxylase deficiencies, and peripheral neuropathy (3–5), as well as for hair, nail, and skin health (6, 7). Although no clinical evidence supports the use of high-dose biotin for beauty concerns, ongoing clinical trials have highlighted the potential therapeutic role of daily 300 mg biotin in slowing the morbidity associated with progressive and relapsing multiple sclerosis (8–12) .

Biotin is also an essential reagent in biochemical applications. Its binding with avidin (e.g., streptavidin), one of the strongest noncovalent bonds, has been exploited in biochemical studies since the 1970s (13). Many laboratory tests that have been approved or cleared by the US Food and Drug Administration (FDA) are immunoassays that utilize biotin and streptavidin binding in the assay design (i.e., biotinylated immunoassays). Their strong binding is particularly useful for amplifying and isolating the assay readout, which increases the ability of the assay to detect lower quantities or concentrations of the analyte, decreases the number of steps required for analyte measurement, and allows for more rapid measurement of biomolecules of interest (14).

Normal circulating concentrations of biotin derived from the diet and normal metabolism are too low to interfere with biotinylated immunoassays. Biotin in over-the-counter multivitamins (doses up to 1 mg) has not been reported to cause immunoassay interference. However, ingestion of high-dose biotin supplements (e.g., ≥5 mg) results in significantly elevated blood concentrations that can interfere with commonly used biotinylated immunoassays. Evidence of interference has been described in case reports, in vivo studies (with study participants), and in vitro studies (biotin addition to mimic high blood concentrations), as described herein. In November 2017, the FDA released a Safety Communication warning the public that biotin supplementation may interfere with laboratory tests (15). The potential for biotin interference in some assays may be substantial, as one study determined that approximately 7% of emergency room patients exhibited circulating biotin concentrations >10 ng/mL (>40.9 nmol/L) (16).

MECHANISMS OF BIOTIN INTERFERENCE

The mechanisms of biotin interference with biotinylated immunoassays can be explained in the context of how biotin and streptavidin binding is used in biotinylated assays. Immunoassays are generally categorized as either competitive or noncompetitive (sandwich). In general, streptavidin–biotin binding is used during assay incubation to couple biotinylated antibodies in sandwich immunoassays, or biotinylated antigens in competitive immunoassays, to streptavidin-coated magnetic surfaces (e.g., beads). When a biological specimen contains excess biotin, the biotin competes with the biotinylated antibodies or antigens for binding to the streptavidin-coated magnetic surfaces, resulting in reduced capture of the biotinylated antibodies or antigens. Excess biotin produces falsely low results in sandwich immunoassays because the assay signal is directly proportional to the analyte concentration. In competitive immunoassays, excess biotin causes falsely elevated results because the assay signal is inversely proportional to the analyte concentration. Specific details of biotin interference have been described extensively in other publications (17–27). Of note, excessive biotin in a blood sample is not likely to interfere with immunoassays that do not utilize biotin and streptavidin binding in the assay design or that utilize a streptavidin–biotin complex bound in reagents before incubation with blood samples.

BIOTIN PHARMACOKINETICS

Normal circulating concentrations of biotin typically range from 0.1 to 0.8 ng/mL in individuals

consuming the recommended daily dose of 30 μg *(28)*. Biotin is rapidly absorbed after ingestion and exhibits peak plasma concentrations within 1 to 2 hours *(29, 30)*. Oral doses of 10 mg, equivalent to some of the highest doses in over-the-counter products, resulted in peak plasma concentrations ranging from 55 to 140 ng/mL (225–573 nmol/L) *(29)*, whereas oral doses of 100 mg resulted in peak plasma concentrations ranging from 375 to 450 ng/mL (1535–1842 nmol/L) *(11)*. The accumulation of biotin does occur, and sequential daily dosing revealed circulating concentrations twice as high on Day 7 compared with the same time point on Day 1 *(29)*. Data analysis revealed that steady-state concentrations are reached after 3 days of constant biotin intake *(29)*. Low concentrations of biotin are cleared quickly from the circulation of healthy individuals, with an elimination half-life of approximately 2 hours *(30)*, whereas experiments with high doses indicate a half-life up to 18.8 hours *(11)*. A pharmacokinetics study of apparently healthy individuals determined that blood concentrations can be expected to drop below 20 ng/mL (81.9 nmol/L) in 1, 5.5, 20, 108, and 146 hours after oral biotin doses of 1, 5, 10, 100, and 300 mg, respectively *(29)*. However, delayed clearance and/or higher circulating concentrations of biotin may be observed in those with impaired renal function.

SUMMARY OF CASE REPORTS

Case reports involving biotin interference in laboratory tests (Table 1) *(19–27, 31–41)* have been reported worldwide (United States, China, Europe, South America, Australia, New Zealand, and Middle Eastern countries) and may involve all ages (newborns to older adults) and genders. Treatments for multiple sclerosis and inborn errors of metabolism are the 2 most cited reasons for biotin ingestion in these published cases of interference. The majority of these cases involved biotin interference with thyroid-stimulating hormone (TSH) and other thyroid-function tests; the rest involved other endocrine tests, such as parathyroid hormone (PTH), adrenocorticotropic hormone, prolactin, testosterone, and cortisol. In many of these case studies, biotin interference was confirmed by significant changes in the affected laboratory results when the patient stopped consuming biotin.

SUMMARY OF IN VIVO STUDIES

A common strategy to investigate biotin interference with laboratory tests is to perform in vivo studies using a crossover study design in which blood specimens are collected from study participants before (baseline) and after biotin ingestion. Using this study design, Wijeratne et al. *(34)*, Trambas et al. *(42)*, Lim et al. *(39)*, and Biscolla et al. *(43)* demonstrated that a single dose of biotin ingestion (e.g., 10–300 mg) in healthy volunteers can interfere with selected laboratory tests (e.g., free thyroxine [T_4], free triiodothyronine [T_3], thyroglobulin, dehydroepiandrosterone sulfate [DHEAS], estradiol, testosterone, ferritin, progesterone, vitamin B12, prostate-specific antigen [PSA], parathyroid hormone [PTH], luteinizing hormone, and follicle-stimulating hormone [FSH]). Li et al. *(18)* demonstrated that, among 6 healthy volunteers who took 10 mg of biotin per day for 7 days, biotin-associated interference was found in 9 of 23 biotinylated immunoassays by 3 manufacturers (Roche, Ortho Clinical Diagnostics, Siemens), including TSH, total T_3, free T_4, free T_3, PTH, NT-proBNP, and 25-hydroxyvitamin D. The assays exhibited varying degrees of biotin interference among manufacturers.

Biotin is predominately eliminated in the urine, so the potential for interference in urine immunoassay tests is also of concern. To this end, Williams et al. *(44)* examined biotin interference in 7 different urine human chorionic gonadotropin pregnancy

Table 1. Case reports involving biotin interference in laboratory tests.

Author	Country	No. of cases	Age	Sex	History/diagnosis	Dose/ day, mg	Reason for biotin use	Misdiagnosis
Henry et al. *(32)*	Saudi Arabia	1	1 day	F[a]	NR	10	Organic acidemia	Graves disease
Meany et al. *(31)*	USA	1	64 years	F	CKD	5	Restless leg syndrome	Hypoparathyroidism
Kwok et al. *(33)*	China	1	3 years	F	Propionic acidemia	10	Metabolic disorder	Graves disease
Wijeratne et al. *(34)*	Australia	1	1 week	NR	Metabolic disorder	30	Lactic acidosis, liver failure	Graves disease
Waghray et al. *(27)*	USA	2	60–62 years	F	CKD	1.5–5.0	Hair growth and neuropathy	Hyperparathyroidism
Barbesino *(20)*	USA	1	55 years	M	MS	300	MS	Graves disease
Elston et al. *(35)*	New Zealand	1	63 years	F	MS	300	MS	Graves disease
Kummer et al. *(37)*	Germany	6	<18 years	NR	Metabolic disorder	2–5[b]	Metabolic disorder	Graves disease
Minkovsky et al. *(25)*	USA	1	74 years	F	MS	300	Multiple sclerosis	Graves disease
Bülow Pedersen and Laurberg *(21)*	Denmark	1	1 day	F	Newborn failure to thrive	5	Biotinidase deficiency, family history	Graves disease
Al-Salameh et al. *(19)*	France	1	32 years	M	X-linked adrenomyeloneuropathy	100	X-linked adrenomyeloneuropathy	Graves disease
Batista et al. *(36)*	Brazil	1	NR	NR	NR	5–300	Hair and nail growth	Graves disease, hyperestrogenism
Cusini et al. *(38)*	Italy	1	69 years	F	MS	300	MS	Graves disease
Lim et al. *(39)*	France	2	NR	NR	MS	300	MS	Graves disease
Sharma et al. *(41)*	USA	1	60 years	NR	NR	10	NR	Graves disease
Willeman et al. *(40)*	France	1	39 years	M	MS	>0.05	MS	Graves disease
De Roeck et al. *(22)*	Belgium	1	NR	NR	MS	300	MS	Graves disease
Evans et al. *(23)*	Australia	1	15 months	M	Mitochondrial disorder	15	Mitochondrial disorder	Graves disease
Koehler et al. *(24)*	Germany	1	47 years	M	MS	300	MS	Graves disease
Stieglitz et al. *(26)*	USA	1	48 years	F	Palpitations, inability to lose weight	5	Hair and nail growth	Graves disease, testosterone-secreting tumor

Most cases involved interference with TSH and other thyroid-function tests. Biotin consumption indicated as total amount ingested per day.
[a] F, female; NR, not reported; CKD, chronic kidney disease; M, male; MS, multiple sclerosis.
[b] Dose in mg/kg.

tests and demonstrated that one test failed to develop a control line when tested with nonpregnant volunteers' urine collected 2 to 4 hours after 10 mg biotin ingestion. This result was likely caused by interference with the process in which immobilized streptavidin binds to a biotinylated dye to display the control line.

SUMMARY OF IN VITRO (SPIKING) STUDIES

Although in vivo studies work well for analytes that are normally present in patient specimens, they are not effective for evaluating interference for analytes that are normally absent or are present only during certain physiologic conditions (e.g., human chorionic gonadotropin during pregnancy) or pathologic conditions (e.g., tumor markers during cancer). For these latter analytes, in vitro studies are more practical. In vitro studies have been performed to investigate biotin interference by measuring patient samples with known analyte concentrations after spiking with known quantities of biotin. Three general findings have been observed from these studies. First, the degree of biotin interference is directly related to the amount of biotin added to the specimen—that is, the higher the biotin concentration over the interference threshold, the more severe the interference. Second, a test may exhibit different degrees of biotin interference from one manufacturer to another, and this is consistent with in vivo studies *(18)*. With biotin at 6 and 15 ng/mL (24.6 and 61.4 nmol/L), for example, in vitro studies of TSH immunoassays exhibited biotin-mediated negative interference of approximately 7% and 10% in Vitros 5600 *(45)* and Roche Elecsys *(46)*, respectively, whereas 300 ng/mL (1228 nmol/L) biotin was required to produce a comparable effect in the Siemens Vista LOCI TSH immunoassay *(47)*. Similarly, at 400 ng/mL biotin, the competitive Siemens LOCI and Roche Elecsys free T_4 assays exhibited biotin-mediated positive biases of 26% and 1146%, respectively *(46, 47)*. Third, the degree of biotin interference varies from one assay to the next within a particular manufacturer's immunoassay platform. Willeman et al. demonstrated that a biotin concentration of 400 ng/mL (1637 nmol/L) resulted in positive biases with the Siemens Vista LOCI competitive estradiol and free T_3 immunoassays of 52% and 866%, respectively *(47)*.

Literature findings on the effects of analyte concentrations on the magnitude of biotin interference are inconsistent. Meany et al. *(31)* demonstrated, for example, that the magnitude of biotin interference when present in concentrations between 5 and 160 ng/mL was independent of Roche Elecsys PTH levels (i.e., 33 and 487 ng/L). In contrast, Trambas et al. *(46)* demonstrated that 500 ng/mL biotin produced variable amounts of positive interference in the Roche Elecsys competitive estradiol immunoassay that ranged from 3428% down to 292% as the estradiol concentration was increased from 18 to 499 pmol/L. However, these results should be interpreted with caution because this study examined biotin at only a single concentration of 500 ng/mL (equivalent to blood concentrations observed 1–2 hours after ingestion of 100–300 mg biotin). Consequently, more comprehensive studies may be needed to investigate the effects of analyte concentration on the degree of biotin interference.

RECOMMENDATIONS FROM THE FDA AND IN VITRO DIAGNOSTIC TEST MANUFACTURERS

FDA Recommendations

In its 2017 Safety Communication, the FDA issued comprehensive recommendations to consumers, healthcare providers, laboratory personnel, and lab-test manufacturers regarding biotin interference *(15)*. These recommendations

echoed those issued previously from manufacturers advocating increased communication among all parties about the ingestion of biotin and biotin-containing supplements before laboratory testing. The FDA reported an increased number of adverse events associated with biotin interference but, because of incomplete data, did not recommend a time frame to avoid biotin before specimen collection for laboratory tests. Given the wide variety and number of laboratory assays in use, the FDA recommended that clinical laboratories should contact assay manufacturers if they have questions about biotin interference. It was recommended that manufacturers use a minimum of 1200 ng/mL biotin to investigate potential interference and to determine the lowest concentrations of biotin that could cause clinically significant interference in their assays. The FDA did not provide specific guidance on interference thresholds deemed significant, but most manufacturers assign a ±10% deviation as the threshold for analytic significance.

Ideally, manufacturers will reformulate assays that are sensitive to biotin and will continue to offer customer support on this issue. This may involve the use of precomplexed antibodies or other mechanistic solutions. One manufacturer recently reformulated its TSH and troponin assays in direct response to concerns about biotin interference. Given that the timeline from initial assay design to reformulation and governmental approval requires months to years, laboratorians and clinicians will have to remain mindful of this issue for some time to come.

Manufacturer Recommendations

Diagnostic manufacturers have increased communications (e.g., informative bulletins, field safety notifications, package inserts, webinars, and websites) to laboratory personnel about the potential for biotin interference. For example, an informational bulletin published by Ortho Clinical Diagnostics indicated the possibility of biotin interference in some Vitros assays in specimens with biotin concentrations >2.4 ng/mL (>9.8 nmol/L) or those from individuals ingesting 300 μg/day. The company did not recommend a retrospective review of patient results to evaluate past interference from biotin. Instead, Ortho Clinical Diagnostics emphasized open communication between laboratories and clinicians to identify patients whose results may have been affected by biotin interference. Beckman Coulter issued a field safety notification to its customers that warned of biotin interference in only 4 assays (Access Total T3, Access Thyroglobulin, Access Free T4, and Access GI Monitor) at concentrations of >100 ng/mL (>409 nmol/L). Roche Diagnostics performed a pharmacokinetics study (n = 54) involving doses of 5 and 10 mg biotin and found that circulating concentrations dropped below 30 ng/mL (122.8 nmol/L) in all participants after 3.5 and 8 hours, respectively *(29)*. Based on these findings, Roche Diagnostics recommended that patients wait 8 hours before undergoing laboratory testing after consuming 5–10 mg doses of biotin *(29)*. Siemens also informed its customers about the potential for biotin interference with select assays on the ADVIA Centaur, Immulite, Dimension EXL, and Dimension Vista. Table 2 summarizes biotin interference thresholds or degrees of biotin-mediated interference, as obtained from manufacturers' package inserts, for many (but not all) immunoassay-based laboratory tests. The table is limited to the most common high-volume immunoassay platforms because it would be too time-consuming to evaluate all assays from all companies. Users should refer to manufacturers' most recent package inserts because assay formulations may be updated and changed.

Recommendations to Laboratories and Clinicians

Laboratories, clinicians, and patients should increase communication regarding biotin interference

Table 2. Interference thresholds for biotin-mediated interference as obtained from manufacturers' assay package inserts.

Manufacturer	Assay, instrument	Direction of error	Interference threshold, ng/mL
Beckman Coulter Inc.			
	GI Monitor (CA 19-9), Access	Decrease	>25
	Thyroglobulin, Access	Decrease	>10
	Thyroglobulin Antibody II, Access	Decrease	>100
	Total Thyroxine (T4), Access	Increase	>10
	Free Triiodothyronine (T3), Access	Increase	>10
	Total T3, Access	Increase	>1.0
Ortho Clinical Diagnostics			
	AFP, Vitros	Decrease	>10
	Anti-HAV IgM, Vitros	Decrease	>10
	Anti-HAV Total, Vitros	Increase	>10
	bHCG, Total II, Vitros	Decrease	>10
	Cancer Antigen 125, Vitros	Decrease	>10
	Cancer Antigen 15-3, Vitros	Decrease	>10
	Cancer Antigen 19-9, Vitros	Decrease	>10
	Carcinoembryonic Antigen (CEA), Vitros	Decrease	>10
	CK-MB, Vitros	Decrease	>10
	Cortisol, Vitros	Increase	>10
	Estradiol, Vitros	Increase	>5
	Ferritin, Vitros	Decrease	>10
	Folate, Vitros	Increase	>10
	Follicle Stimulating Hormone, Vitros	Decrease	>10
	Insulin, Vitros	Decrease	>160
	Luteinizing Hormone, Vitros	Decrease	>5
	Myoglobin, Vitros	Decrease	>20
	NT-proBNP, Vitros	Decrease	>20
	Parathyroid Hormone, Intact, Vitros	Decrease	>5
	Progesterone, Vitros	Increase	>20
	Prolactin, Vitros	Decrease	>10
	Prostate Specific Antigen (PSA), Vitros	Decrease	>10
	Testosterone, Vitros	Increase	>10
	Troponin I ES, Vitros	Decrease	>10
	Vitamin B12, Vitros	Increase	>20
	25-Hydroxyvitamin D, Vitros	Increase	>15
Roche Diagnostics			
	AFP α1-fetoprotein	Decrease	>60
	ACTH, Elecsys	Decrease	>70
	Anti-HAV IgM	Decrease	>50

Continued

Table 2. (continued)

Manufacturer	Assay, instrument	Direction of error	Interference threshold, ng/mL
	Anti-TPO	Increase	>10
	Anti-Thyroglobulin, Elecsys	Increase	>60
	Anti-TSH Receptor, Elecsys	Increase	>10
	Anti-HBc IgM	Decrease	>100
	Anti-HCV	Decrease	>50
	C-Peptide	Decrease	>60
	Cancer Antigen 125 II	Decrease	>35
	Cancer Antigen 15-3 II	Decrease	>320
	Carbohydrate Antigen 19-9	Decrease	>100
	Calcitonin, Elecsys	Decrease	>40
	Carcinoembryonic Antigen (CEA)	Decrease	>120
	Cortisol II	Increase	>30
	Creatine Kinase MB	Decrease	>30
	Anti-CCP	Decrease	>70
	DHEA-S	Increase	>70
	Estradiol III, Elecsys	Increase	>36
	Folate III	Increase	>21
	Free T4 II, Elecsys	Increase	>20
	Free T3 III, Elecsys	Increase	>70
	FSH, Elecsys	Decrease	>60
	HCG STAT	Decrease	>40
	HCG+B, Elecsys	Decrease	>80
	Hepatitis B Antigen, Elecsys	Decrease	>40
	Hepatitis B Core Antibody, Elecsys	Increase	>30
	Hepatitis B Surface Antigen	Decrease	>44
	Human Epididymal Protein 4	Decrease	>50
	Human Growth Hormone	Decrease	>30
	IGF-1, Elecsys	Decrease	>50
	Immunoglobulin E	Decrease	>100
	Insulin, Elecsys	Decrease	>60
	Luteinizing Hormone, Elecsys	Decrease	>50
	Myoglobin	Decrease	>50
	Myoglobin STAT	Decrease	>50
	N-MID Osteocalcin, Elecsys	Decrease	>50
	Parathyroid Hormone, Elecsys	Decrease	>50
	Parathyroid Hormone STAT, Elecsys	Decrease	>50
	NT-proBNP II	Decrease	>30
	NT-proBNP II STAT	Decrease	>30
	Procalcitonin, BRAHMS Elecsys	Decrease	>30
	Progesterone III, Elecsys	Increase	>30

Continued

Table 2. (continued)

Manufacturer	Assay, instrument	Direction of error	Interference threshold, ng/mL
	Prolactin II, Elecsys	Decrease	>40
	PSA Total, Elecsys	Decrease	>60
	Sex Hormone Binding Globulin, Elecsys	Decrease	>70
	Triiodothyronine (T3), Elecsys	Increase	>10
	Testosterone II, Elecsys	Increase	>30
	Thyroid Stimulating Hormone, Elecsys	Decrease	>1200
	Thyroxine (T4), Elecsys	Increase	>100
	Troponin I, Elecsys	Decrease	>30
	Troponin T	Decrease	>50
	Troponin T STAT	Decrease	>50
	Troponin T STAT Gen.5 (reformulated)	Decrease	>1200
	Vitamin B12, Elecsys	Increase	>50
	25-Hydroxyvitamin D	Increase	>70
	Vitamin D Total II, Elecsys	Increase	>30
Siemens			
	B-type Natriuretic Peptide, Centaur	Decrease	>250
	Cyclosporine, Centaur	Increase	>75
	DHEAS, Centaur	Increase	>25
	Folate, Centaur	Increase	>50
	HAV IgM, Centaur	Decrease	>500
	HAVT, Centaur	Increase	>25
	HBc IgM, Centaur	Decrease	>150
	Sex Hormone Binding Globulin, Centaur	Decrease	>250
	Testosterone II, Centar	Increase	>50
	Troponin I Ultra, Centaur	Decrease	>20
	B-type Natriuretic Peptide, Dimension EXL	Decrease	>250
	Folate, Dimension EXL	Increase	>250
	Free T3, Dimension EXL	Increase	>100
	Free T4L, Dimension EXL	Increase	>100
	Troponin I, Dimension EXL	Decrease	>100
	TSHL, Dimension EXL	Decrease	>250
	Vitamin B12, Dimension EXL	Increase	>100
	Vitamin D, Dimension EXL	Increase	>500
	AFP, Dimension Vista	Decrease	>1000
	CA125, Dimension Vista	Decrease	>500
	CA19-9, Dimension Vista	Decrease	>500
	CEA, Dimension Vista	Decrease	>500
	CTNI, Dimension Vista	Decrease	>100
	Digoxin, Dimension Vista	Increase	>500
	Estradiol (E2), Dimension Vista	Increase	>250

Continued

Table 2. (continued)

Manufacturer	Assay, instrument	Direction of error	Interference threshold, ng/mL
	Ferritin, Dimension Vista	Decrease	>500
	Folate, Dimension Vista	Increase	>250
	FSH, Dimension Vista	Decrease	>500
	Free T3, Dimension Vista	Increase	>50
	Free T4, Dimension Vista	Increase	>250
	Luteinizing Hormone, Dimension Vista	Decrease	>1200
	MMB, Dimension Vista	Decrease	>250
	PBNP, Dimension Vista	Decrease	>250
	Progesterone, Dimension Vista	Increase	>100
	Prolactin, Dimension Vista	Decrease	>500
	SIRO, Dimension	Decrease	>500
	Troponin I, Dimension Vista	Decrease	>100
	TSH, Dimension Vista	Decrease	>100
	Vitamin B12, Dimension Vista	Increase	>100
	BR-MA (CA 15-3), Immulite 1000	Decrease	>100
	CEA, Immulite 1000	Increase	>9
	CKMB, Immulite 1000	Decrease	>2
	EPO, Immulite 1000	Decrease	>5
	Gastrin, Immulite 1000	Decrease	>2
	OM-MA (CA125), Immulite 1000	Increase	>2
	Thyroglobulin, Immulite 1000	Decrease	>5
	Vitamin B12, Immulite 1000	Increase	>250
	Allergen specific IgG4, Immulite 2000	Decrease	>250
	BR-MA (CA 15-3), Immulite 2000	Decrease	>100
	3gAllergy Specific IgE, Immulite 2000	Decrease	>5
	Anti HBc, Immulite 2000	Decrease	>5
	CEA, Immulite 2000	Increase	>2
	CKMB, Immulite 2000	Decrease	>5
	EPO, Immulite 2000	Decrease	>2
	Folic Acid, Immulite 2000	Increase	>1000
	Gastrin, Immulite 2000	Decrease	>2
	OM-MA (CA125), Immulite 2000	Increase	>5
	Thyroglobulin, Immulite 2000	Decrease	>5

Data are not all inclusive and do not contain information on all laboratory tests. The data are presented as reported by individual manufacturers at the time of this writing. To convert ng/mL to nmol/L, multiply ng/mL by 4.093.

with biotinylated immunoassay–based laboratory tests. Laboratories should determine which of their immunoassays may be affected by biotin interference and educate clinicians about the findings. Communication may be accomplished several ways, including the use of formal memos and laboratory bulletins and participation in conferences and clinical rounds. Laboratories should also seek to inform patients of the potential for biotin interference with laboratory test results. Methods could involve the

use of placards in outpatient phlebotomy centers, with information on biotin use. Healthcare systems could include questions about the use of biotin and nutritional supplements during the inpatient/outpatient registration process. Clinicians could query patients about their use of food supplements and explain the relevance. Electronic health records could be updated to display an alert to clinicians at the time of test order whenever tests with known biotin interference are ordered. Clinicians should contact the laboratory when laboratory results do not fit the patient's clinical picture or if the patient is known to have consumed a dose of biotin >5 mg *(48, 49)*. Because hundreds or thousands of specimens may pass through a laboratory each day, laboratory personnel often rely on clinician feedback to help identify issues with test results.

Laboratories may use various methods to verify suspected biotin interference, including use of a specimen diluent for the assay *(50)*, removal of excess biotin via streptavidin-coated beads *(51)*, and biotin quantification via chromatography (LC-MS/MS) or other procedure. Ideally, a specimen suspected of biotin interference should be analyzed with a different assay that does not use biotin in its format *(49, 50)*. Alternatively, the laboratory may request a new specimen after the patient has abstained from biotin for a time. It is recommended that patients who have consumed 5–10 mg biotin wait a minimum of 8 hours before having blood collected for laboratory tests *(29, 40, 49)*. Longer washout periods, up to 72 hours, may be required to prevent interference in assays with interference thresholds <30 ng/mL (<122.8 nmol/L) *(29)*. Unless medically contraindicated, patients being prescribed a high-dose biotin therapy (≥100 mg/day) should abstain from biotin for a minimum of 72 hours before blood collection *(9, 47, 52)*. Keep in mind that those with renal impairment may exhibit higher circulating biotin concentrations and prolonged elimination rates. Reporting patient results after dilution or biotin removal is not recommended unless the procedure has been validated by the laboratory *(49, 52, 53)*.

SUMMARY

The recent increase in the use of high-dose biotin supplements requires that laboratorians and clinicians be mindful of the potential for biotin interference in biotinylated immunoassay–based laboratory tests. Laboratories, clinicians, and patients should work together to ensure accurate laboratory results. Laboratories have several options for identifying suspected biotin interference in specimens. Alternatively, the relatively fast elimination of biotin allows for rapid follow-up specimen analysis.

Nonstandard abbreviations: TSH, thyroid-stimulating hormone; PTH, parathyroid hormone; T_4, thyroxine; T_3, triiodothyronine

Author Contributions: *All authors confirmed they have contributed to the intellectual content of this paper and have met the following 4 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; (c) final approval of the published article; and (d) agreement to be accountable for all aspects of the article thus ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.*

D. Li, financial support, provision of study material or patients.

Authors' Disclosures or Potential Conflicts of Interest: *Upon manuscript submission, all authors completed the author disclosure form. Disclosures and/or potential conflicts of interest:* **Employment or Leadership:** P.B. Kyle, AACC Academy Council. **Consultant or Advisory Role:** None declared. **Stock Ownership:** None declared. **Honoraria:** D. Li, Abbott Diagnostics, Diasorin; P.B. Kyle, AACC. **Research Funding:** None declared. **Expert Testimony:** None declared. **Patents:** None declared. **Other Remuneration:** D. Li, Abbott Diagnostics, Diasorin.

Role of Sponsor: No sponsor was declared.

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