



May 1, 2018

Re: BIOTIN TESTING UPDATE

Dear Client:

Clinical Labs of Hawaii, together with other professional societies, has distributed biotin interference notices to all its providers and patients. Our recommendation is to withhold biotin administration (when clinically feasible) for at least 8 hours before laboratory testing. In mega doses (>150 mg biotin), the supplement should be held for at least 2-3 days.

In the following pages, we have references from our manufacturer, Roche Diagnostics, that may be helpful.

If you have any questions, please contact our Client Services Department:

808.677.7998.....	Oahu
808.935.4814 (option 1).....	East Hawaii
866.281.6816.....	West Hawaii
866.281.6816.....	Kauai
808.244.5567.....	Maui

Thank you,

Clinical Labs of Hawaii

Biotin supplement and influence on results of immunoassays

ABOUT BIOTIN

Biotin (vitamin B7, vitamin H) is a water-soluble vitamin of the B complex that is used as supplementation and for medical treatment. While no recommended daily intake (RDI) for biotin supplementation exists, because biotin deficiency is extremely rare, suggested daily intake for adults in the U.S. is 30–100 mcg.¹ The effective half-life of biotin varies between 8 and 18 hours.²

BIOTIN AND LABORATORY RESULTS

Streptavidin and biotin naturally form a strong, highly specific and stable bond. This system has been used for many years and allows the development of sensitive, specific and accurate immunoassays. There are different types of interference and sources of error that can affect the accuracy of immunoassays.^{3–5} While the intake of high doses of biotin can lead to interference with immunoassays, there is no risk for such assay interference associated with the intake of biotin as part of a standard multivitamin.⁶

BIOTIN USE: THREE PATIENT POPULATIONS

Because biotin deficiency is considered extremely rare, no RDI exists. Suggested biotin intake for adults ranges from 30–100 mcg per day.¹ When considering biotin use as a supplement, keep in mind three specific populations:

- **Daily multivitamin use**
- **Medical high-dose biotin therapy**
- **OTC lifestyle high-dose biotin supplementation**

Daily multivitamin use:

Many consumers take biotin as an ingredient within a standard daily multivitamin. This dose is typically 30–40 mcg.

Medical high-dose biotin therapy:

High-dose biotin is used as a therapy for inherited conditions such as biotinidase deficiency⁷ biotin-thiamin-responsive basal ganglia disease⁸ and holocarboxylase synthetase deficiency.⁷ High-dose biotin is also currently being used in clinical trial settings as a potential treatment for patients with multiple sclerosis.⁹

OTC lifestyle high-dose biotin supplementation:

Some consumers take high-concentration biotin supplements (5,000–10,000 mcg) currently packaged to promote hair, skin and nail beauty.

BIOTIN INTERFERENCE IN ROCHE ELECSYS® IMMUNOASSAYS

To mitigate potential interference, patients taking biotin doses >5,000 mcg should wait at least 8 hours after the last biotin administration before a sample is taken as stated in all Roche immunoassay package inserts.

IDENTIFICATION OF PATIENTS UNDER BIOTIN TREATMENT

To ensure testing accuracy, it is important to ask patients about their use of all supplements, including biotin, before any laboratory tests are run. Patients may not know the exact doses of biotin that they are taking, but the following flow chart will help guide conversations with your patient.

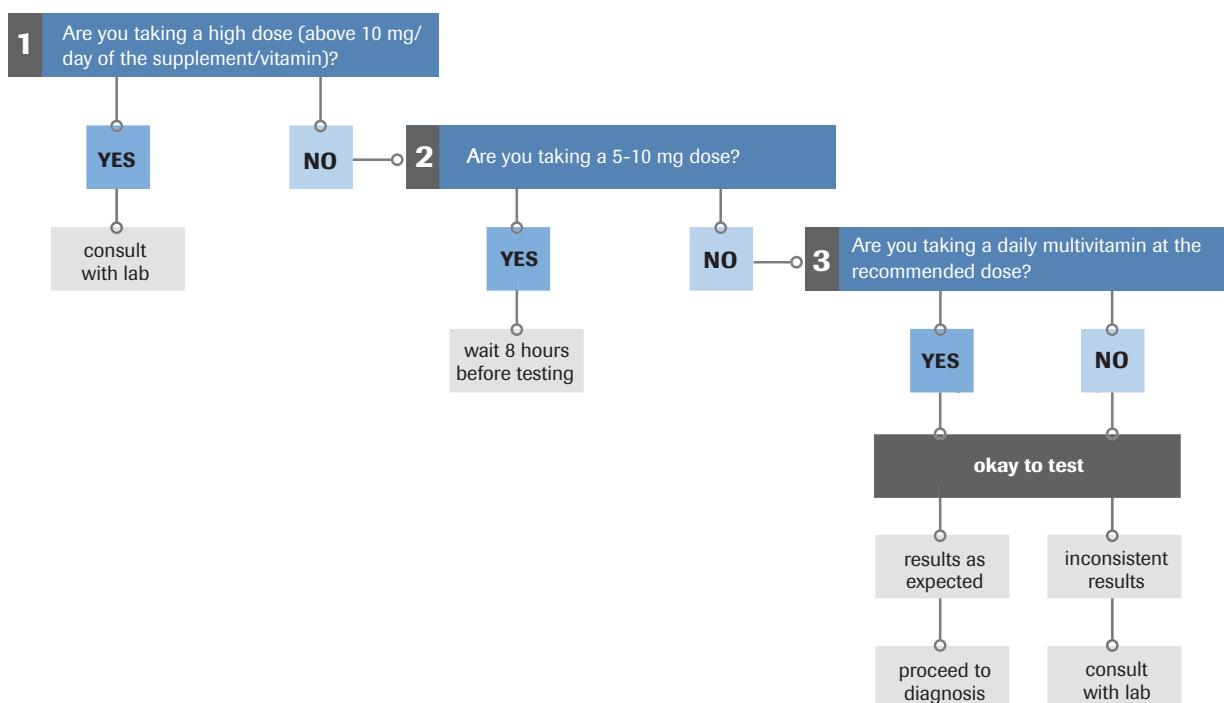
PATIENT TESTING

In both normal and emergency settings, it is important to ask patients the right questions ahead of testing. By asking patients about their biotin intake levels, you can be aware of potential interference from the outset and factor this into your diagnostic evaluation, alongside other key parameters. Diagnosis and a decision of treatment should be evaluated with regard to the clinical picture.

In an emergency setting, we recommend proceeding with testing, taking into account the full patient profile and undergoing re-testing if you suspect interference. The impact of the biotin interference results depends on specific aspects of the assay design. For further guidance and detail, contact your laboratory.

PHYSICIAN FLOW CHART

Establish high dose



1. <http://www.mayoclinic.org/drugs-supplements/biotin-oral-route/description/drg-20062359>, accessed on 5/26/2017.
2. Peyro Saint Paul et al, Expert Opin. Drug Metab-Txicol. 2016, 12: 327-344.
3. Boscato et al, Clin Chem 1998, 34(1): 27-33.
4. Kroll et al, Clin Chem 1994, 40(11 Pt 1): 1996-2005.
5. Kricka, Clin Chem 1999, 45(7): 942-956.
6. Internal data, manuscript in preparation.
7. Wolf B. Biotinidase Deficiency. 2000 Mar 24 [Updated 2016 Jun 9]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017.
8. Kassem et al, AJNR 2014, 35 (10): 1990-1995.
9. Sedel et al, Mult. Scler. Relat. Disord. 2015, 4: 159-169.

FACTS ABOUT BIOTIN

ROCHE PHARMACOKINETIC STUDY

By the numbers

While suggested daily intake of biotin for adults ranges from 30 to 100 mcg (US)¹, higher doses of biotin are sold as hair and nail beauty supplements.

Roche completed a pharmacokinetic study (n=54) to test the biotin thresholds in our immunoassay package inserts. You may see the conclusions below, segmented by dose. We also re-measured the biotin thresholds of our assays, which both confirmed the tolerance thresholds listed in the package inserts, and demonstrated that several assays have an even more robust tolerance than current package insert claims.

PK STUDY CONCLUSIONS, BY DOSE

MULTI-VITAMIN	30-60 mcg PER DAY	No RDI exists because deficiencies are very rare	No impact on immunoassays
HAIR & NAIL SUPPLEMENTS	5-10 mg PER DAY	More than 125x recommended daily intake	Tolerance threshold of 30ng/mL 5 mg dose: 100% of subjects are below threshold within 3.5 hours 10 mg dose: 100% of subjects are below threshold within 8 hours
EXPERIMENTAL THERAPEUTIC REGIMEN	>10 mg PER DAY	Doctor-directed for specific patient populations, like multiple sclerosis	Patients are receiving this dose while being monitored by physicians

CONCLUSIONS

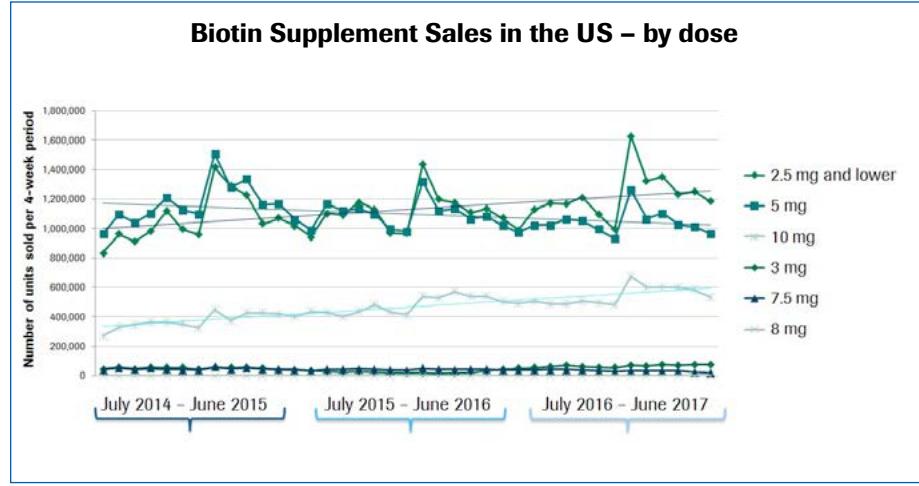
As part of testing best-practices, patients should be asked to report all medications they are taking, both Rx and OTC supplements prior to a blood draw. We encourage lab partners to continue to use our assays according to the package inserts as a critical insight into the full clinical picture. If a result looks suspicious, redraw the sample.

NIELSEN DATA OBSERVATIONS

SUPPLEMENT SALES – LOWER DOSES MAKE UP MAJORITY OF SALES

INSIGHTS

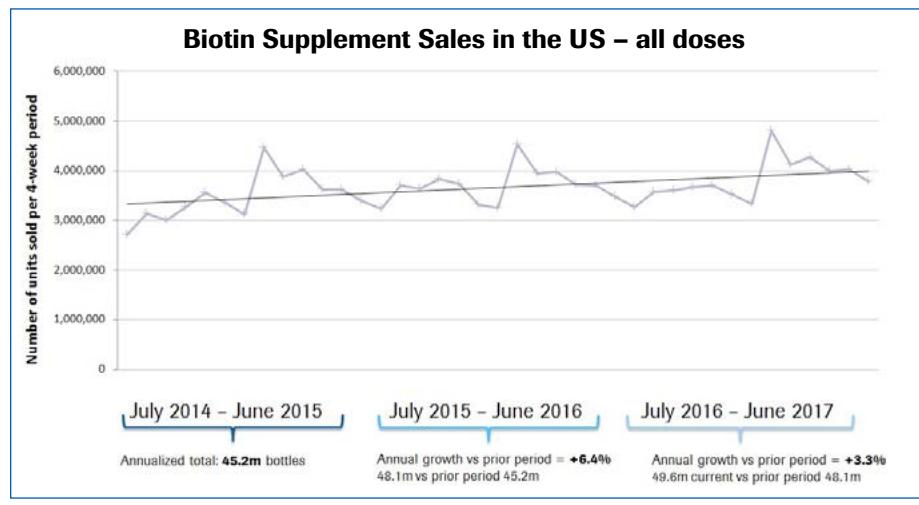
- The majority of biotin sales are in doses of ≤ 2.5 mg.
- Sales of 5 mg doses have actually declined over the past three years.
- Sales of 10 mg doses are significantly less than 5 mg and lower doses.



GROWTH RATE HAS SLOWED IN RECENT MONTHS

INSIGHTS

- Biotin sales have been trending slightly upwards in the US over a three-year period from July 2014-June 2017.
- From July 2015 to June 2016, sales of all doses increased 6.4% over the previous 12 month period.
- Total biotin sales growth is slowing in recent periods. The growth rate slowed to 3.3% from July 2016 to June 2017.



CONCLUSIONS

An increase in overall biotin sales does not necessarily correlate to an increased risk of test interference. Lower doses (2.5 mg and under) make up the majority of biotin sales.

There has been market noise about high growth rates of biotin supplement sales. At a growth rate of 3.3%, as seen from July 2016 to June 2017, it would take 22 years for purchase volumes to double.

QUESTIONS? Indianapolis.msa@roche.com