Micronutrient Testing

Policy Number: AHS – G2099 – Micronutrient Testing	Effective Date: 11/01/2026

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I. Policy Description

Micronutrients are dietary components, often referred to as vitamins and minerals, which although only required by the body in small amounts, are vital to development, disease prevention, and wellbeing.[1,2] Micronutrients are not produced in the body and must be derived from the diet. Micronutrients include essential trace elements such as boron, iron, zinc, selenium, manganese, iodine, copper, molybdenum, cobalt, and chromium,[3,4] and essential vitamins such as vitamins A, B, C, D, and K (organic).[5]

For guidance on testing for micronutrients vitamin D, vitamin B, and folic acid, please refer to AHS-G2005-Vitamin D Testing, AHS-G2014-Vitamin B12 and Methylmalonic Acid Testing, and AHS-G2154-Folate Testing, respectively.

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

1) Serum micronutrient testing as a general screen for nutritional disorders **DOES NOT MEET COVERAGE CRITERIA.**

2) Intracellular micronutrient panel testing (e.g., SpectraCell, Cell Science Systems cell micronutrient assay, ExaTest) **DOES NOT MEET COVERAGE CRITERIA**.

III. Table of Terminology

Term	Definition
ASEM	Analytical scanning electron microscopy
CDC	The Centers for Disease Control
CLIA	Clinical Laboratories Improvement Amendments
CLIA '88	Clinical Laboratory Improvement Amendments of 1988
CMA	Cellular micronutrient assay
CMS	Centers for Medicare and Medicaid

CSS	Cell Science Systems
EXA	Energy dispersive x-ray analysis
FDA	Food and Drug Administration
HPLC	High-performance liquid chromatography
LDT	Laboratory-developed test
SI	Stimulation index
WHO	World Health Organization

IV. Scientific Background

Micronutrients, such as zinc, selenium, and copper, are involved in metabolic processes, either as catalysts or facilitators for various enzymatic functions. Micronutrient deficiency can result from general malnutrition, a current illness, or side effects of medications or procedures. Nutritional loss may exacerbate severe illness and side effects of medications as the inflammatory response draws micronutrients to the damaged organs, causing an increase in oxidative stress, and normal defense mechanisms to fail.[6] For example, oxidative damage in copper deficiency results in muscle weakness and edema, and impaired oxidative status in iodine deficiency leads to a decrease in thyroid hormone synthesis and mental retardation.[7,8]

The measurement of serum vitamin and mineral levels is widely available from numerous commercial testing companies. Normal serum nutrient concentration varies based on its function in the body. Serum concentrations of nutrients involved in regulatory mechanisms, such as calcium and zinc, are maintained within narrow ranges regardless of body stores and any changes only occur with severe nutrient deficiency. Other nutrients, such as carotenoids, vary in the body depending on recent intake or half-life length. Environmental factors, such as infections or stress, can also influence serum nutrient concentrations. Vitamin C, Vitamin B, selenium, and magnesium play a role in reducing the levels of cortisol and adrenalin in the body.[9] Nutrient concentrations may also vary based on the tissue. Nutrient concentrations in cell membranes or bone fluctuate less, but these measurements are more difficult to obtain.[10] Serum nutrient testing is promoted to the public as a nutrient deficiency screening and supplement personalization, but these tests are usually unwarranted. There is not enough information available regarding the optimal blood levels of vitamins. Moreover, there is a lack of evidence that vitamin supplements prevent disease in healthy adults with low blood levels of vitamins, apart from those with specific diets or conditions. Vitamin deficiencies typically occur in special populations such as the elderly or those with gastric bypass surgery, and not the general public.[11]

Another possible method of measuring nutrient deficiency is to assess the intracellular concentration (as opposed to the typical serum measurement). Intracellular micronutrient lymphocyte analysis was developed based on the premise that a peripheral blood lymphocyte reflects the genetic and biochemical state of the person at the time it was formed.[12]

Proprietary Testing

Lymphocyte measurement is the basis of SpectraCell's micronutrient testing procedure. Lymphocytes are isolated from the blood sample and placed in a culture medium containing the optimal levels of nutrients for sustained growth. A given micronutrient is removed, and then growth is measured and compared against the 100% level of growth. For example, Vitamin B6 may be removed from the medium. The growth rate of the cell is theoretically only dependent on vitamin B6 as all other micronutrients are at optimal levels; therefore, any deficiency in cell growth would be caused by issues with intracellular

Vitamin B6. This is done for all 31 micronutrients in the panel and results are reported. The micronutrients included in SpectraCell's panels are as follows: Vitamins A, B1, B2, B3, B6, B12, C, D, E, and K, as well as biotin, folate, pantothenate, calcium, magnesium, manganese, zinc, copper, asparagine, glutamine, serine, oleic acid, alpha-lipoic acid, coenzyme Q10, cysteine, glutathione, selenium, chromium, choline, inositol, and carnitine. SpectraCell also provides an assessment of "Total Antioxidant Function," an "Immune Response Score," and measures of fructose sensitivity and glucose-insulin metabolism.[13]

Another test analyzing intracellular concentration is ExaTest by IntraCellular Diagnostics. From their laboratory website, this test uses "rapidly metabolizing sublingual epithelial cells under Analytical Scanning Electron Microscopy, (ASEM) an Energy Dispersive X-Ray Analysis, (Exatest) to reflect fast tissue changes of vital mineral electrolytes." This test is primarily for aid with the management of heart disease and provides tissue evaluations of magnesium, sodium, calcium, phosphorus, potassium, and chloride. ExaTest proclaims its ability to follow a patient's metabolic status and assess electrolyte imbalance easily. First, the buccal, epithelial cells are swabbed from the patient. Then the sample is analyzed by the proprietary energy dispersive x-ray analysis and bombarded with X-Rays. Energy is released by wavelengths (unique to each element), and the element composition is analyzed and reported. ExaTest states that the serum or urine of some minerals do not correlate with intracellular levels and that these deficiencies are common in patients with various health issues, particularly heart disease. Buccal cells are used as they are easily accessible and have an easily analyzed structure for electrolytes.[14]

Vibrant America has also developed a test that gives both extracellular and intracellular information on approximately 40 vitamins, minerals, amino acids, fatty acids and antioxidants in the body.[15] Vibrant America states that the benefits of intracellular testing include the identification of potential functional deficiencies in the cellular nutrient absorption process (which may increase the risk of certain diseases), and the identification of an individual's nutritional status in the previous four to six months.[15]

Another possible method of analyzing nutrient deficiency is by measuring lymphocyte proliferation in response to micronutrient concentration. Cell Science Systems (CSS) released a cellular micronutrient assay (CMA) which measures the effect of micronutrients on lymphocyte proliferation when stimulated with a mitogen. According to their protocol, lymphocytes are primarily separated from the patient's whole blood and the patient's own serum is added back to the lymphocytes. The cells are stimulated with a mitogen and baseline lymphocyte proliferation rates (without the addition of micronutrients) are recorded. Next, micronutrients are added to the lymphocyte culture and proliferation rates are compared to the baseline rate. If the addition of micronutrients to the lymphocyte culture enhances lymphocyte proliferation, a nutrient insufficiency is reported. If the lymphocyte proliferation rate with the addition of micronutrients does not exceed the baseline rate, it likely indicates sufficient stores of that nutrient. The CMA measures vitamins, amino acids, minerals, and other nutrients such as carnitine, alpha-ketoglutarate, choline, glutathione, and inositol. By measuring intracellular levels of micronutrients, the test is intended to provide insight into the long-term nutritional status (6 months) versus the short term variability of serum nutrient levels, which is prone to daily fluctuations.[16]

Genova Diagnostics released NutrEval FMV® a comprehensive blood and urine test that evaluates over 125 biomarkers and 40 antioxidants, vitamins, minerals, essential fatty acids, and amino acids in patients 2 years and older. These levels provide insight into digestive function, toxic exposure, mitochondrial function, and oxidative stress. According to their website, NutrEval is not meant to be a substitute for other conventional nutritional panels (complete blood count, comprehensive metabolic panel), but

rather a complement by providing additional information.[17]

Analytical Validity

In a randomized observational analysis, the CSS CMA was used to examine nutritional status in 845 American individuals aged 13 years and older. Results were expressed as the stimulation index (SI), which is the percentage of lymphocyte stimulation in response to the mitogen. All subjects were divided into two groups based on their diet. The first group had a healthy diet, consisting of whole fresh foods including fruits, vegetables, nuts, while the poor diet group reported high consumption of sweets, fried, frozen, and starchy foods. CMA analysis indicated that the "mean values for micronutrient deficiency were significantly higher in the poor diet group as compared to the healthy diet group with p-values of 0.0017 and 0.0395, respectively." According to the authors, "the adequate functioning of this defensive system is critically impacted by intracellular nutritional status, and its interaction with the host' cells. Lacking adequate nutrition, the immune system is clearly deprived of the components needed to generate an effective immune response."[18]

Clinical Utility and Validity

While limited research has been completed regarding intracellular micronutrient lymphocyte analysis, Yamada, et al. (2004) did complete a study with 41 type 2 diabetes patients and 50 healthy controls. No participants were taking vitamin supplements at the time of the study. Blood samples were taken from all participants during a fasting state; the researchers determined that the lymphocyte vitamin C level was significantly lower in the type 2 diabetes patients than in controls.[19] This study may support the above theory that lymphocytes can be used as an indicator of an individual's nutrient state.

Houston (2010) published a small study stating that treating the intracellular micronutrient deficiencies in combination with optimal diet, exercise and other weight management resulted in reaching blood pressure goals for 62% of a hypertensive population.[20] Another small study of ten patients found that both genders showed overall improvement in their vitamin and mineral cellular storage balance after being tested with SpectraCell's assessment.[21] However, the authors of each of the aforementioned studies (Houston, Bucci, Frye, and Shive) are associated with SpectraCell Laboratories. SpectraCell has listed several studies on their website discussing serum versus intracellular deficiencies; from discussing the effect of the inflammatory response on serum micronutrient levels to Vitamin B12's difficult serum profile to micronutrient deficiencies in special populations.[22] However, none of these studies reported use SpectraCell's actual method as of 2018, nor did the studies cover the healthy population for which the test is marketed. Most of these studies listed used other methods such as HPLC to measure micronutrient levels instead of the proprietary method provided by SpectraCell. Few other studies listed on SpectraCell's website used lymphocytes as the analyte as well.

In a case report, Ye, et al. (2024) illustrated that micronutrient testing is of significant clinical value in chronic pain management. A 58-year-old woman with two years of progressively painful, treatment-refractory peripheral neuropathy was evaluated after requesting a permanently implanted spinal cord stimulator. The medical history included leiomyomatosis, prior exploratory laparotomy with incidental granulosa cell tumor (with no further evidence of disease), and newly diagnosed Type 2 diabetes, although the clinical timeline was inconsistent with primary diabetic neuropathy. The individual underwent intracellular micronutrient and metabolic testing using a validated lymphocyte-based assay (SpectraCell™), which measures 33 analytes in addition to two proprietary markers (Immunidex™ and Spectrox™). Results revealed multiple significant deficiencies, including oleic acid, zinc, manganese,

vitamin A, coenzyme Q-10, copper, and fructose, with borderline low levels of glutamine, alpha-lipoic acid, and vitamin C; both proprietary markers were also low. This case illustrates the diagnostic challenge posed by micronutrient deficiencies and highlights the underutilization of micronutrient testing despite its noninvasive nature. Following targeted supplementation, the patient experienced complete resolution of neuropathic symptoms, suggesting that biomarker-guided identification of deficiencies may reveal reversible contributors to chronic pain. However, given limited regulatory oversight of supplements and evolving evidence in nutritional science, careful clinical judgment remains essential when integrating such testing into patient care.

In an observational study, Coelho, et al. (2020) studied the association between serum and dietary antioxidant micronutrients and advanced liver fibrosis in non-alcoholic fatty liver disease (NAFLD). 72 NAFLD patients were evaluated for levels of retinol, alpha-tocopherol, ascorbic acid, beta-carotene, serum zinc, and selenium. "A high proportion of inadequate serum retinol (20.8%), vitamin C (27%), and selenium (73.6%) was observed in the patients with NAFLD, in addition to a significant inadequacy of vitamin A (98.3%) and vitamin E (100%) intake." Those with advanced liver fibrosis had reduced levels of serum retinol. Overall, "NAFLD patients showed an important serum deficiency and insufficient dietary intake of the evaluated micronutrients."[24]

V. Guidelines and Recommendations

No studies evaluating the accuracy or clinical utility of intracellular micronutrient testing compared to standard testing for vitamin or mineral levels were identified. In addition, no controlled studies that evaluated changes to patient management or health impact of intracellular micronutrient testing were identified. Limited data are available on correlations between serum and intracellular micronutrient levels. Intracellular micronutrient analysis was not included in reviews on micronutrient analysis.[10,25]

No recommendations or practice guidelines recommending intracellular micronutrient testing were identified in a literature search. While measurement of serum levels of several vitamins is widely available, testing for deficiencies is usually unwarranted.[11]

VI. Applicable State and Federal Regulations

Food and Drug Administration (FDA)

Intracellular micronutrient testing is offered by companies SpectraCell, IntraCellular Diagnostics, and CSS Corporation which have Clinical Laboratories Improvement Amendments (CLIA) accredited laboratories. SpectraCell's micronutrient panel test, the IntraCellular Diagnostics ExaTest, Genova Diagnostic's NutrEval FMV, and the CSS CMA have not been through the FDA approval process.

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

VII. Applicable CPT/HCPCS Procedure Codes

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all inclusive and is subject to updates. In addition, codes listed are not a guarantee of payment.

CPT	Code Description
82128	Amino acids; multiple, qualitative, each specimen
82136	Amino acids, 2 to 5 amino acids, quantitative, each specimen
82180	Ascorbic acid (vitamin c), blood
82310	Calcium; total
82379	Carnitine (total and free), quantitative each specimen
82495	Chromium
82525	Copper
82978	Glutathione
83735	Magnesium
83785	Manganese
84207	Pyridoxal phosphate (vitamin b-6)
84252	Riboflavin (vitamin b-2)
84255	Selenium
84425	Thiamine (vitamin b-1)
84446	Tocopherol alpha (Vitamin E)
84590	Vitamin A
84591	Vitamin, not otherwise specified
84597	Vitamin K
84630	Zinc

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VIII. Evidence-based Scientific References

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IX. Revision History

Revision Date	Summary of Changes
01/01/2022	Initial Effective Date
07/19/2022	Updated background and evidence-based scientific references. Literature

	review did not necessitate modification to coverage criteria. Removal of code 84999 Revised code disclaimer statement
06/28/2023	Annual Review: Literature review did not necessitate changes to coverage criteria. Policy edited for clarity and consistency. Committee approved: 06/28/2023
05/14/2024	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria. Committee approved: 05/14/2024
05/21/2025	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria. Committee approved: 05/21/2025
06/17/2026	CAB Review Q2 2026: Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria. The following changes were made for clarity and consistency: Title changed from “Intracellular Micronutrient Analysis” to “Micronutrient Testing” New CC1 to align with enforcement of micronutrient codes within policy: “1) Serum micronutrient testing as a general screen for nutritional disorders DOES NOT MEET COVERAGE CRITERIA.” Removed CPT code 82607, 82652, 82725, 82746, 84999, 86353, 88348 Committee Approved: 06/17/2026