



Provocation Considerations

Provoked testing, also known as challenge testing, involves the use of a detoxification support and/or chelating agent prior to urine collection to determine the level of toxic burden in the body.

Provoking agents work by pulling toxins from an individual's tissues so higher levels are present in the urine—thus leading to more “moderate” or “high” test results.

Some providers use provoking agents because they believe they are necessary to release toxins stored in the tissues, while others choose not to because the mobilization of toxins stored in the body can create oxidative stress and damage, particularly among patients with impaired biotransformation and detoxification pathways.

Provocation isn't one-size-fits-all—nor is it safe for all patients. **The decision to provoke depends on the individual patient's health status and what the ordering provider hopes to learn.**

Does Vibrant Wellness provide guidance for provocation?

No, we do not offer guidance or advice regarding a specific provoking agent, dose, or timing of provocation before testing.

Why not?

- Provoking agents mobilize toxins stored in body tissues/fat cells, moving them into circulation.
- Toxins stored in tissues can be largely unreactive, whereas circulating toxins tend to create more oxidative stress and damage.
- Only the ordering provider, who knows the patient's clinical history, can determine whether the patient can handle increased toxin circulation secondary to provocation.

It is up to the ordering provider's clinical discretion whether to recommend a provoked test for their patient and determine the provoking agent, dose, and timing of provocation before testing.

What reference ranges does Vibrant Wellness use?

The reference ranges on the Heavy Metals, Environmental Toxins, Mycotoxins, and PFAS Chemicals tests are based either on Vibrant's internal validation study or results from the National Health and Nutrition Examination Survey (NHANES).

NHANES

NHANES conducts urine and blood biomonitoring in a nationally representative sample of Americans. NHANES measures several heavy metals and several environmental toxins. Using NHANES data for reference ranges allows ordering providers and patients to compare heavy metal and environmental toxin exposure results to the general population.

NHANES does not conduct biomonitoring for mycotoxins, so all reference ranges on the Mycotoxin test are derived from the Vibrant Wellness internal validation study of 1,000 adults. The PFAS Chemicals test was internally validated and does not use NHANES reference ranges.

The tests on the table in the next page use NHANES data for reference ranges.



Panel	Test Name	Panel	Test Name
Heavy Metals	Antimony	Environmental Toxins	Atrazine mercapturate
Heavy Metals	Arsenic	Environmental Toxins	3-Phenoxybenzoic Acid (3PBA)
Heavy Metals	Barium	Environmental Toxins	mono-2-ethylhexyl phthalate (MEHP)
Heavy Metals	Beryllium	Environmental Toxins	mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)
Heavy Metals	Cadmium	Environmental Toxins	mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)
Heavy Metals	Cesium	Environmental Toxins	Mono-ethyl phthalate (MEtP)
Heavy Metals	Lead	Environmental Toxins	Methylparaben
Heavy Metals	Mercury	Environmental Toxins	Propylparaben
Heavy Metals	Platinum	Environmental Toxins	Butylparaben
Heavy Metals	Thallium	Environmental Toxins	Ethylparaben
Heavy Metals	Tin	Environmental Toxins	N-acetyl-S-(2-carbamoyl-ethyl)-cysteine (NAE)
Heavy Metals	Tungsten	Environmental Toxins	N-Acetyl (2-Cyanoethyl) Cysteine (NACE)
Heavy Metals	Uranium	Environmental Toxins	N-Acetyl (2-Hydroxypropyl) Cysteine (NAHP)
Environmental Toxins	2,4-Dichlorophenoxyacetic Acid (2,4-D)	Environmental Toxins	N-Acetyl (3,4-Dihydroxybutyl) Cysteine (NADB)
Environmental Toxins	Perchlorate	Environmental Toxins	2-Hydroxyethyl Mercapturic Acid (HEMA)
Environmental Toxins	Diethyldithiophosphate (DEDTP)	Environmental Toxins	N-Acetyl Propyl Cysteine (NAPR)
Environmental Toxins	Dimethyldithiophosphate (DMDTP)	Environmental Toxins	Bisphenol A (BPA)
Environmental Toxins	Diethylthiophosphate (DETP)	Environmental Toxins	Triclosan
Environmental Toxins	Dimethylphosphate (DMP)	Environmental Toxins	2-Methylhippuric Acid (2MHA)
Environmental Toxins	Diethylphosphate (DEP)	Environmental Toxins	Phenylglyoxylic Acid (PGO)
Environmental Toxins	Dimethylthiophosphate (DMTP)	Environmental Toxins	N-acetyl phenyl cysteine (NAP)
Environmental Toxins	Atrazine		

Internal Validation Study

All other tests in the Heavy Metals, Environmental Toxins, Mycotoxins, and PFAS Chemicals reports use the Vibrant Wellness internal validation study of 1,000 adults. Specifically, the analyte levels of 1,000 healthy individuals were measured and plotted on a Gaussian curve.

- **In Control:** Levels that are less than the 75th percentile.
- **Moderate:** Levels between the 75th and 95th percentile.
- **High:** Levels greater than the 95th percentile.

Vibrant Wellness's Heavy Metals, Mycotoxins, Environmental Toxins, and PFAS Chemicals reference ranges apply to non-provoked conditions.

Do well-established provoked reference ranges exist?

No, there are no standardized reference ranges for provoked tests, likely related to the numerous variations in the types of provocation agents used, variations of dosages, and variations in routes of administration, as well as variability associated with each specific analyte.

What are the limitations of using non-provoked reference ranges to interpret provoked test results?

- When using provocation before testing, levels may appear falsely elevated when interpreted using non-provoked reference ranges.
- Additionally, the clinical utility of post-provocation urine testing is an area of controversy in environmental medicine. For example, in heavy metal testing, scientific studies demonstrate that administering chelating agents leads to increased excretion of various metals into the urine, even in healthy individuals without metal-related diseases.^{1,2} Ultimately, it is up to the provider to decide whether to use a provocation agent before Heavy Metals, Mycotoxins, Environmental Toxins, and PFAS Chemicals testing.

Can Vibrant provide any guidance for 6-hour or 24-hour urine collection?

Vibrant does not require a 6-hour or 24-hour urine collection for the Mycotoxins, Heavy Metals, Environmental Toxins, or PFAS Chemicals test. Vibrant requires only the first-morning urine.

If a 6-hour or 24-hour urine collection is preferred, follow the below guidelines:

- 6-hour and 24-hour urine collection containers are not provided.
- The collection container should be sterile and metal-free (e.g., Medline 24-Hour Urine Collection Bottle).
- Collect every urine specimen using the abovementioned collection container over the specified time period.
- Shake to homogenize.
- Pipette urine from the collection container into the 15 mL specimen tube provided.

References:

1. Marchese, M. Heavy Metal Testing Controversies: The Post-Provocative Urine Test. Townsend Letters (January 2016), pages 90-92.
2. Ruha AM. Recommendations for the provoked challenge urine testing. J Metal Toxicology. 2013 Dec; 9(4): 318-325.