

Prenatal Vitamins

GOALS

The goals of this project were to:

- Evaluate the overall quality and safety of prenatal vitamins
- Test prenatal vitamins for nutrients and heavy metals
- Assess compliance with tolerable upper intake levels (UL) and USP tolerances

TEST APPROACH AND METHODS

Eighteen products of prenatal vitamins were evaluated. Three samples, representing one to three lots, plus two duplicates were tested for heavy metals; vitamins A, B2, B9, C, D2, D3, and E; and the minerals calcium, iron, and zinc at an accredited laboratory.

Ten pills/gummies were used to determine the average pill weight for each lot of each product. A composite of each lot was prepared from at least 10 pills/gummies for all analyses.

The prenatal vitamins were prepared and analyzed in accordance with the following methods:

- Vitamin A (AOAC 2012.10) retinyl acetate and retinyl palmitate by HPLC-FLD and beta-carotene by HPLC-DAD
- Vitamins B2 (AOAC 2015.14) and B9 (AOAC 2022.002) by LC-MS/MS
- Vitamin C (AOAC 2012.22) by HPLC-VWD
- Vitamins D2 and D3 (AOAC 2016.05mod.) by LC-MS/MS
- Vitamin E retinyl acetate and retinyl palmitate (AOAC 2012.10) by HPLC-FLD and retinyl succinate (USP 551) by HPLC-DAD
- Calcium, iron, and zinc (AOAC 2011.14) by ICP-OES
- Arsenic, cadmium, lead, and mercury (AOAC 2012.007) by ICP-MS

We reviewed all the test results and quality control data provided by the contract labs for accuracy and clarity, and checked for errors.

DATA ANALYSIS

To estimate the average concentration of a heavy-metal contaminant (arsenic, cadmium, lead, and mercury) in a supplement, we applied a method used by many risk assessors,¹ including the Environmental Protection Agency.² If a contaminant was detected or measurable in any of the samples of the product, the samples that had test results below the method detection limit, or MDL, were assumed to have a concentration of half the MDL for that contaminant. If the contaminant was not detected in any of the samples tested of the product, we assumed a concentration of zero for all the samples of that product for the contaminant. This approach to risk assessment appropriately considered important uncertainties about potential levels of undetected risk in samples with test results below the MDL. For vitamins and minerals, the amounts found during testing were compared with amounts listed on the product labels.

RISK ASSESSMENT

We estimated a pregnant person's daily intake (based on the manufacturer's recommended daily servings), at 19 to 30 years old (with an average weight of 61 kg, or 134 pounds),³ of the tested arsenic; cadmium; lead; mercury; vitamins A, B2, B9, C, D2, D3, and E; and the minerals calcium, iron, and zinc for each product and, where appropriate and applicable, compared the intake estimates with the exposure limits in the table on the following page. In addition, tested vitamins and minerals were compared with USP tolerance ranges, where applicable. Note that vitamin A tested values were compared with the specific forms of vitamin A listed on the label (r. palmitate, r. acetate, or beta-carotene). Vitamin A values from testing were compared with the values in the formulation (r. acetate, r. palmitate, b-carotene, or RAE units) listed on the label. Total vitamin A values in RAE units were calculated as follows: $0.55 \times \text{retinyl palmitate} + 0.87 \times \text{retinyl acetate} + 0.5 \times \text{beta-carotene}$.⁴ Vitamin B9 values from testing were compared with those in the formulation (folic acid, mTHF, or DFE (folate)). Total vitamin B9 values in DFE (folate) units were calculated as follows: $1.7 \times \text{folic acid} + 1.7 \times \text{mTHF}$.⁵ Vitamin E values from testing were compared with the values in the formulation (α-tocopherol, α-tocopherol acetate, or α-tocopherol succinate) listed on the label.

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¹Xue, J.; Zartarian, V.; Wang, S.; et al., "Probabilistic Modeling of Dietary Arsenic Exposure and Dose and Evaluation with 2003-2004 NHANES Data," *Environmental Health Perspectives*, 118, no. 3 (2010): 345-50. ²"Regional Guidance on Handling Chemical Concentration Data Near the Detection Limit in Risk Assessments," Environmental Protection Agency, www.epa.gov/risk/regional-guidance-handling-chemical-concentration-data-near-detection-limit-risk-assessments. ³<https://www.ncbi.nlm.nih.gov/books/NBK45193>. ⁴AOAC 2012.10. ⁵<https://www.fda.gov/media/129863/download>.

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Health-Based Exposure Limits Selected for Risk Assessments for Select Heavy Metals, Vitamins, and Minerals				
Chemical	EPA RfD ug/kg bw/d	OEHHA MADL (NSRL) ug/day	NIH UL (mg/day)	USP Tolerance Range % of Label Value
Arsenic	0.06 ⁶	10 ¹⁴	ND	NA
Cadmium	NA	4.1 ⁷	ND	NA
Lead	NA	0.5 ⁸	ND	NA
Mercury	0.1 ⁹	NA	ND	NA
Vitamin A	NA	NA	3 ¹⁰	90-170 (chewable gels) 90-165 (tablets/capsules) ¹¹
Vitamin B2	NA	NA	ND ¹⁰	90-150 (chewable gels) ¹²
Vitamin B9 (as folate)	NA	NA	1.0 ¹⁰	90-150 (tablets/capsules) 90-245 (chewable gels) ¹¹
Vitamin C	NA	NA	2,000 ¹⁰	90-250 (chewable gels) 90-150 (tablets/capsules) ¹¹
Vitamin D	NA	NA	0.1 ¹⁰	90-165 (tablets/capsules) 90-170 (chewable gels) ¹¹
Vitamin E	NA	NA	1,000 ¹⁰	90-165 (tablets/capsules) 90-170 (chewable gels) ¹¹
Calcium	NA	NA	2,500 ¹³	90-125 (tablets/capsules) 90-130 (chewable gels) ¹¹
Iron	NA	NA	45 ¹³	90-125 (tablets/capsules) ¹²
Zinc	NA	NA	40 ¹³	90-125 (tablets/capsules) 90-130 (chewable gels) ¹¹

EPA=Environmental Protection Agency

NIH=National Institutes of Health

OEHHA=California's Office of Environmental Health Hazard Assessment

UL=tolerable upper intake level

USP=United States Pharmacopeia

ug/day=micrograms per day

ND=Not determined

NA=Not available

⁶ https://iris.epa.gov/static/pdfs/0278_summary.pdf. ⁷ <https://oehha.ca.gov/media/downloads/cnr/cadmium20madl.pdf>. ⁸ <https://oehha.ca.gov/proposition-65/chemicals/lead>. ⁹ <https://www.ncbi.nlm.nih.gov/books/NBK225764>. ¹⁰ <https://www.ncbi.nlm.nih.gov/books/NBK56068/table/summarytables.t7?report=objectonly>. ¹¹ https://cersi.umd.edu/sites/cersi.umd.edu/files/Session_1-1_NataliaDavydovaCandy-Like_Oct30_2023.pdf. ¹² <https://www.uspnf.com/errata/oil-and-water-soluble-vitamins-minerals-chewable-gels-2021-05-01>. ¹³ https://www.ncbi.nlm.nih.gov/books/NBK545442/table/appJ_tab9/?report=objectonly. ¹⁴ <https://oehha.ca.gov/proposition-65/chemicals/arsenic-inorganic-arsenic-compounds>