Post-Expo West Update

Substantiating Product Claims, Managing Marketing Risk, and Upcoming Cosmetic Regulations | April 27, 2023

Todd A. Harrison
Co-Chair and Partner | 202.344.4724 | taharrison@Venable.com

Claudia A. Lewis
Co-Chair and Partner | 202.344.4359 | calewis@Venable.com

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Agenda

- Melatonin JAMA Letter
- FTC Notice of Penalty Offenses
- FTC Health Products Compliance Guidance
- Back to Basics: What Does Substantiation Mean?
- Cosmetics Regulatory Update
- Brief Notes on Plaintiffs Bar and Warning Letters

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Recent JAMA Melatonin Letter

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JAMA "Research Letter" on Quantity of Melatonin and CBD in Gummies

- Published April 25, 2023 in JAMA (Journal of the American Medical Association)
- The 25 products analyzed were chosen by looking an NIH's Dietary Supplement Label Database for products labeled as containing melatonin (narrowed from 30 products purchased by reviewing labels after purchase to confirm melatonin was on the label)
  - Only one sample per brand evaluated
  - One product did not contain melatonin, only CBD.
  - Of the 24 products containing melatonin, actual levels ranged between 74% and 347% of the labeled quantity; only three of the 25 products were within 10% of the labeled quantity.
  - Authors point out these are similar results to a Canadian study.
- "Administration of as little as 0.1 mg to 0.3 mg of melatonin to young adults can increase plasma concentrations into the normal nighttime range."
  - But "Consuming melatonin gummies as directed could expose children to between 40 and 130 times higher quantities of melatonin. Unintentional ingestions could lead to consumption that greatly exceeds these dosages of melatonin."

FTC Notice of Penalty Offenses

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FTC Notices of Penalty Offenses

- On April 13, FTC sent out nearly 700 letters to various companies attempting to put those companies on notice that "they should avoid deceiving consumers with advertisements that make product claims that cannot be backed up or substantiated."

- There is **no finding of fault at this time**: FTC is saying you should evaluate your claims and substantiation to make sure you are in compliance. It is not limited to health claims, though.

- FTC states that it sent letters outlining notice of "specific unlawful acts and practices, including failing to have:
  1) A reasonable basis consisting of competent and reliable evidence for objective product claims;
  2) Competent and reliable scientific evidence to support health or safety claims; and
  3) At least one well-controlled **human clinical trial** to support claims that a product is effective in curing, mitigating, or treating a serious disease."

- "The unlawful acts or practices also include:
  1) Misrepresenting the level or type of substantiation for a claim, and
  2) Misrepresenting that a product claim has been **scientifically or clinically proven**."

FTC Notices of Penalty Offenses (cont.)

- This Notice is in part a result of the *AMG* litigation wherein the Supreme Court limited the FTC's authority to seek equitable monetary relief on grounds that the FTCA does not expressly authorize equitable monetary relief under section 13(b).
- However, FTC is now using an old administrative order procedure: if a company is on notice of a violation, and then a later investigation determines there *was* a violation, monetary penalties are still possible.
- FTC has taken similar actions before, but not on dietary supplements/health products specifically.
  - In fact, there have been approximately 1,900 recipients of the three previous rounds of notices of penalty offenses: 1,100 for the money-making ventures; 700 on endorsements; 70 for-profit education companies. Investigations and settlements may still be ongoing for those previous notice sweeps.
- A generalized letter is unlikely to qualify as legal "notice."
- FTC's action could spur private litigation attention.

FTC Notices of Penalty Offenses (cont.)

Next steps

1) Evaluate flagship products
   i. The types of claims being made *everywhere* they are made
   ii. Review substantiation dossiers considering the connection between the claims and the science

2) Evaluate otherwise high-profile products in the same manner

3) Evaluate website to ensure separation between scientific data and product listings to reduce risk

4) Consider advantages to litigating defensible claims in light of FTC notices

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FTC Regulatory Authority and the Health Products Compliance Guidance

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Federal Trade Commission Basics

- FTC enforces Sections 5 and 12 of the FTC Act, along with the FTC's policy statements on deception and advertising substantiation.
- FTC also issues Policy Statements and "Guides" for specific industries and advertising practices.
  - These are not official regulations.
- The 2022 Health Products Guidance sets out the basic advertising principles for a broad range of "health products." This is an update to the 1998 guidance.
  - This affects all parties that participate directly in marketing and promotion, or have authority to control those practices, have responsibility.
- FTC can issue a wide array of remedies: civil penalties, injunctions, restitution, corrective advertising.

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Basics of 1998 Guidance (*Dietary Supplements: An Advertising Guide for Industry*)

- Informed the status quo of claim substantiation for dietary supplements for the last 25 years
- Sought to allow for "sufficient" flexibility in achieving substantiation (no rigid or fixed formula)
- Focused on dietary supplements, in light of the recent passage of DSHEA
- Outlined FTC expectations regarding identifying claims, when disclosures and qualifications may be needed, how claims may be substantiated, and what kind of evidence is required

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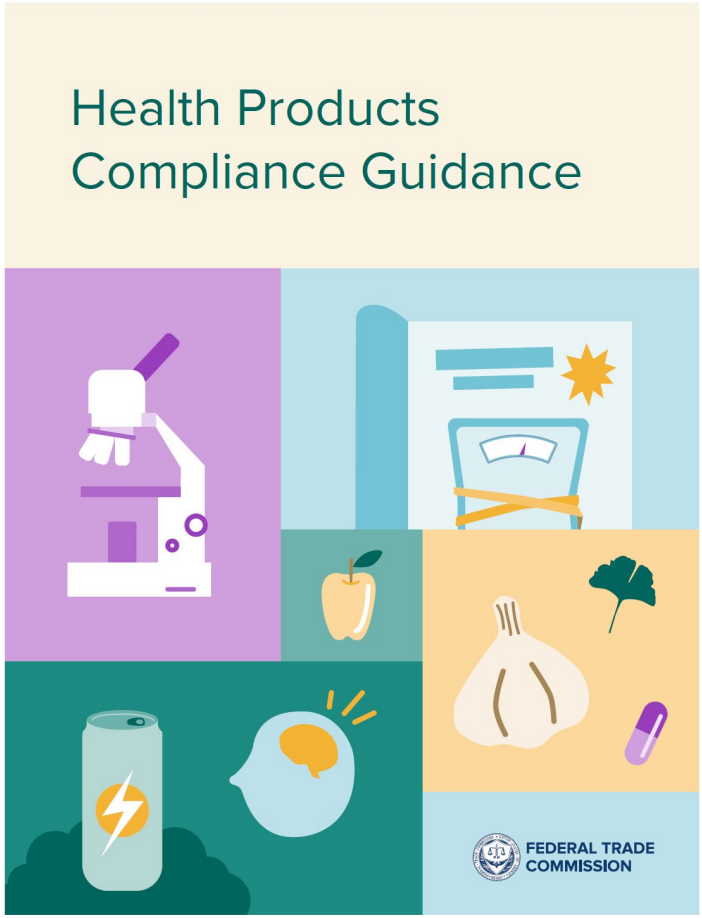
Basics of 2022 Guidance



- Covers "any health-related product," not just dietary supplements (foods, cosmetics, devices, supplements, etc.)
- Represents a broadening of FTC focus and potential private litigation challenges
- Several topics are updated:
  - Substantiation standard
    - Adequacy of clinical studies
    - Interpretation of results
  - Consumer testimonials and expert endorsements (clear disclosures of material connections)
  - Disclosures and qualifying language ("Vague qualifying terms are inadequate")

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Notable Changes

- **Substantiation standard** (discussed later)
- "**Clinically tested ingredient**" can imply not just that the ingredient was tested, but also that the test results prove a benefit.
- **Disclosures** must be "*clear and conspicuous*"; visual *and* audible for videos; social media disclosures cannot simply use hyperlinks
- **Qualifying terms** like "promising," "preliminary," "initial," or "pilot" are considered positive, and thus do not operate as disclaimers about the state of the science behind a claim.
- Citing to **third party literature**, even several clicks away, may not prevent FTC (or litigators) from holding the marketer accountable for substantiating any implied claims made.
- Claiming a product has been **traditionally used** for some purpose could trigger several disclosure/qualification requirements (including that that there is no scientific basis for the traditional use), and FTC has even suggested conducting consumer copy tests to demonstrate understanding of the claim.

What Does Substantiation Mean?

2023 and Beyond

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FTC's Update to the Substantiation Standard

- Competent and Reliable Scientific Evidence (**CARSE**)
  - Historically, the CARSE standard permits full and careful consideration of a wide range of relevant scientific evidence.
  - Double-blind, randomized, placebo-controlled studies have not been explicitly required for dietary supplement advertising.
- FTC **now** explains that generally, "substantiation of health-related benefits will need to be in the form of randomized, controlled human clinical testing to meet the competent and reliable scientific standard."
- The **quality of studies relied upon** is also now a focus of the agency:
  - Will evaluate based on control group, randomization, double blinding, statistically significant results, and clinically meaningful results.
  - To determine if clinically meaningful, will consider clarity of the protocol, submission of protocol to an IRB, registration of the clinical trial in a public database, duration of the study, dropout rates, noncompliance, dose-response relationship, and more.

Substantiating Your Claims

The general substantiation rules still apply, such that an advertiser must have a "reasonable basis" for any verifiable claim that is not puffing (whether express or implied) – i.e., advertiser must have objective evidence that supports the claim.

FTC considers the following in determining what level of support is reasonable:

- Type of claim
- The product
- The consequences of a false claim
- The benefits of a truthful claim
- Ease and cost of developing substantiation for the claim
- The amount of substantiation experts in the field believe is reasonable

However, FTC will likely place greater emphasis in its evaluation of a company's substantiation on the **quality**, **type**, and **amount** of substantiation, as well as the extent to which that substantiation **relates to the claims** being made.

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What Are the Key Factors in Determining the Type and Amount of Substantiation Required?

- RCTs are generally the type of substantiation that experts would require for health benefit claims.
  - No requirement for the number – replication adds to the weight
  - Quality is more important than quantity
- Epidemiological/observation studies can substantiate a claim where RCTs aren't otherwise feasible or experts in the field consider it acceptable, but otherwise don't prove a causal link.
- Animal and *in vitro* studies not sufficient to substantiate health-related claims.
- Anecdotal evidence of consumer experience and surveys are never sufficient (same with HCP's observation of the effect of a health product on patients).
- Public health recommendations are not sufficient for establishing a causal link or to support a claim.

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What Are the Key Quality Factors?

Study quality will generally be evaluated by considering:

- Control group
- Randomization
- Double blinding
- Statistically significant results
- Clinically meaningful results

To determine if **clinically meaningful**, consider:

- Clarity of the protocol
- Submission of protocol to an IRB
- Registration of the clinical trial in a public database
- Inclusion/exclusion criteria
- Duration of the study
- Dropout rates
- Noncompliance
- Dose-response relationship
- Quality of written report

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Other Quality Factors

- Validation
- Temporal nature of effect
- Number of subjects
- Health of subjects (all healthy or have disease/condition)
- Statistical significance is more critically evaluated – FTC is concerned about post-hoc analysis and "p-hacking"
- Application of the study results to the claimed benefit
- Absence of contrary evidence, if substantiation is weak, will not help

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Totality of the Evidence and Relevance to the Claim

Totality of the Evidence

- Cannot discount research that does not support a claimed effect
- Consistency with surrounding body of evidence
- Explanation for inconsistencies
  - E.g., differences in dosage for route of administration, populations tested, or methodology

Relevance to the Claim

- Similarity of dosage and formulation studied to advertised product
- Similar route of administration
- Study outcomes v. benefits advertised
- Representation of research results
- Emerging science as basis for a claim: qualifications are important

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Substantiation Dossier

- Retaining substantiation often involves maintaining some type of file or dossier dedicated to claims substantiation.
- A substantiation dossier will look different depending on what information you need to keep on file to support your advertising claims, but examples could include:
  - A digital folder where the organization can organize and store any communications, certifications, etc. that support the organization's advertising claims;
  - A substantiation sheet listing information relevant to substantiation, potentially including relevant links if it is stored online;
  - A substantiation chart summarizing relevant sources (particularly common for companies that need to support advertising claims with a variety of clinical studies); or
  - Any other format that makes sense contextually and is easy to reference.
- **The form in which substantiation is stored is less important than the fact that it exists and can be found when it is needed.**

Substantiation Dossier (cont.)

- The documentation that is necessary to substantiate a claim varies depending upon the claim that is being made.
- FTC does not have specific requirements for which documents are required to support every possible type of claim, but at a minimum, when a claim is express (e.g., "tests prove," "doctors recommend," and "studies show"), Essential Formulas should have **at least the advertised level of substantiation.**
- Keep in mind that some claims, such as claims involving statistical estimates, are more difficult to substantiate than others.

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Disclosures

When is a disclosure required?

- If an ad makes express or implied claims that are likely to be misleading without certain qualifying information, the information must be disclosed.
- A disclosure cannot cure a false claim; it can only qualify or limit a claim to avoid a misleading impression.
- Preference for disclosure in primary text; alternatively, provide clear and conspicuous disclosure.

What is "Clear and Conspicuous"?

- There is no set formula; it depends on the information that must be provided and the nature of advertisement.
- **P**lacement, **P**roximity, **P**rominence, **P**resentation

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Modernization of Cosmetics Regulation Act "MOCRA"

A New Age of Cosmetics Regulation

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Consolidated Appropriations Act 2023

- Signed by President Biden on December 29, 2022
- Includes several updates to FDA authority through the Food and Drug Omnibus Reform Act (FDORA), including for cosmetics, devices, and more
- Generally, MOCRA sets new requirements for cosmetic manufacturers, to make sure that they meet Good Manufacturing Practice (GMP) standards, register and list their products with FDA, report on adverse events and maintain adverse event records, substantiate the safety of their products, and label fragrance allergens.

Modernization of Cosmetics Regulation Act of 2022 (MOCRA)

- Good Manufacturing Practice (GMP) standards (NPRM will be required)
- Registration and listing requirements
  - FDA now will have the authority to suspend the registration of a facility
- Adverse event reports and records
- Mandatory recall authority
- Some new labeling requirements
  - Each product must include a domestic address and other contact information through which adverse events can be received. In addition, fragrance allergens must be identified on the label of a product.
- Requires the Secretary of Health and Human Services to assess the use of perfluoroalkyl and polyfluoroalkyl substances in cosmetic products regarding the safety of their use in cosmetics and submit a report no later than 3 years after enactment of MOCRA

Facility Registration Requirements

- Facility registration requirements will apply to any facility that, on the date of enactment, engages in the manufacturing or processing of a cosmetic for distribution in the US.
- Registration is required no later than one year after the enactment of MOCRA.
- New facilities must register within 60 days of engaging in manufacturing or processing.
- FDA excludes from the definition of "facility" establishments that "solely perform" either labeling, relabeling, packaging, repackaging, holding, or distributing.
- FDA "stopped accepting and processing submissions to the voluntary registration program for cosmetics establishments and products" and is "developing a program for submission of the facility registrations and product listings mandated by MOCRA and will provide further updates on its forthcoming availability."

Cosmetic Product Listings

- Product listings are required no later than one year after the enactment of MOCRA, and new products must be listed within 120 days of marketing.
- Must include a list of ingredients, including fragrances, flavors, colors, and the applicable cosmetic category, but submission of a label is not required.
- Authority to suspend the registration of a facility if it determines that a cosmetic product manufacturer who distributes a product in the US that has a "reasonable probability of causing serious adverse health consequences or death to humans and … has a reasonable belief that other products manufactured … may be similarly affected because of a failure that cannot be isolated to a product … or is sufficiently pervasive …"

Safety Substantiation

- Within one year of enactment, cosmetic manufacturers must also have "adequate substantiation of safety" for products marketed.
  - "Tests or studies, research, analyses, or other evidence or information that is considered, among experts, qualified by scientific training and experience to evaluate the safety of cosmetic products and their ingredients, sufficient to support a reasonable certainty that a cosmetic product is safe."

- "Safe" is defined as "not injurious to users under the conditions of use prescribed" or responses that are customary or usual.
  - Minor and transient reactions or skin irritations in some users do not rise to this "injurious" standard.
  - FDA may consider the cumulative or other relevant exposure to the product, including any of its ingredients, in coming to this determination. Failure to meet these requirements will result in the cosmetic product being considered adulterated.

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GMP Standards

- NPRM (notice of proposed rulemaking) by December 29, 2024
- Final Rule by December 29, 2025
- Opportunity to consult with FDA on the development of these standards.
  - Exclusions from GMP requirements: businesses that only engage in, for example, labeling, packaging, holding, or distributing

Other Labeling Requirements

- Each product must include a domestic address and other contact information through which adverse events can be received, effective two years after enactment (December 29, 2024).
- Labeling requirements that will apply to cosmetics products intended for use only by professionals effective one year after enactment (December 29, 2023).
- Fragrance allergens must now be identified on the label of a product. Fragrance allergens are to be determined by regulation. FDA is required to publish an NPRM no later than 18 months after enactment of MOCRA (June 29, 2024), and a final rule requiring their disclosure on labels 180 days after public comment closes (December 29, 2024).
- FDA is required to issue a rulemaking within one year regarding the testing and specification methods for testing for asbestos in talc-containing cosmetic products.

What To Do Now

- Some requirements will apply as early as December 29, 2023.
- Evaluate whether you are required to register with FDA by that date and be compiling the necessary safety substantiation.
- Due to the new GMP requirements, audit manufacturing processes, product safety testing and the methods used, warning statements provided on product labels, and other advertising and marketing statements made about the products.
- Evaluate how consumer complaints are handled, along with record keeping and adverse event reporting to FDA. These new rules necessarily require additional standard operating procedure (SOP) development and training.
- Review insurance policies for additional recall and safety-related coverage.

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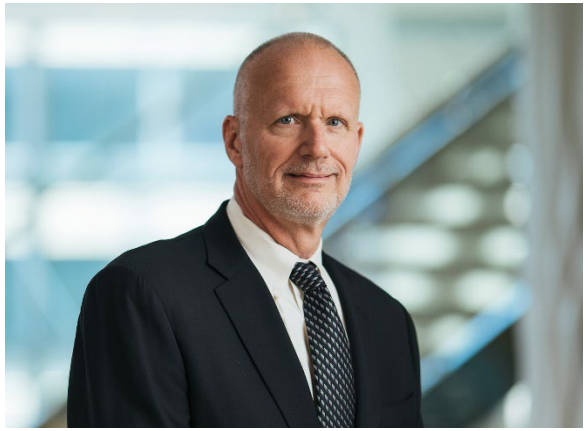
Questions? Contact Us



Todd A. Harrison
Partner and Co-Chair
+1 202.344.4724
taharrison@Venable.com

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calewis@Venable.com

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