AMA
AMERICAN MEDICAL ASSOCIATION

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Victoria Marshall
Senior Advisor
Office of the Assistant Secretary for Health
U.S. Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Re: Docket No. HHS-OASH-2026-0496: Enforcement Discretion Policy Regarding 503A Compounding Using Certain Peptide Bulk Drug Substances

Dear Ms. Marshall:

On behalf of the physician and medical student members of the American Medical Association (AMA), I am writing regarding the U.S. Department of Health and Human Services (HHS) draft "Enforcement Discretion Policy Regarding 503A Compounding Using Certain Peptide Bulk Drug Substances." For the reasons detailed below, **the AMA opposes the HHS non-enforcement compounding policy regarding non-FDA-approved substances BPC-157, KPV, TB-500, MOTS-c, Semax, and Epitalon.** At a threshold level, these substances should not be made more available because of the potential harm they pose to patients. These potential harms will exist whether patients access them through the gray market or a small-scale compounder under the non-enforcement policy.

The AMA provided extensive comments urging that the U.S. Food and Drug Administration (FDA) not include these substances on the 503A Bulks List and we commend the FDA for its focus on science and patient safety in excluding these substances from the list. The AMA continues to steadfastly support the rigorous FDA drug approval process to help ensure efficacy and safety for every drug. None of the substances included in the HHS non-enforcement policy have received FDA approval, nor are any of them currently undergoing review under an active Investigational New Drug (IND) application. Allowing these substances to be compounded without sufficient guardrails and oversight threatens public safety.

The AMA wants to emphasize several concerns we previously provided to the FDA. These concerns were raised following the FDA's July 2026 Pharmacy Compounding Advisory Committee meeting and take on added significance given that these are the substances HHS proposes to make more widely available without evidence of safe and effective use in humans. Patients will not truly know what they are injecting. Unlike the compounding of substances approved by the FDA for the 503A Bulks List, the six proposed non-enforcement peptides may refer to numerous different products with varying compositions, formulations, or salt forms. Similarly, several of the synthetic peptides are known by multiple names, increasing the risk that patients will receive and inject a substance that is different than what they, or their physician or pharmacist, intended. Without standardized nomenclature and pharmacological structure, it is difficult to determine precisely what substance is being compounded, prescribed, studied, or administered to patients. Said differently, the AMA does not support federal policy that allows public access to questionable substances given the harm that may occur.

The AMA opposes the rushed nature of the HHS decision because it has the potential to cause serious harm and has adverse implications for patients. The fact that these peptides were deemed not fit to be included on the 503A Bulks Substances List by the FDA scientific staff underscores the concerns surrounding these peptides. Adoption of a non-enforcement policy would leave physicians and pharmacists unable to reasonably know the properties and characteristics of the products supplied to patients as well as the clinically appropriate uses, dosing, and monitoring of these substances. Beyond a lack of nomenclature consistency and clarity, foundational elements of drug development, clinical utilization, and safety remain incomplete for these synthetic peptides. These missing elements include characterized formulations, validated pharmacokinetics, toxicology and safety profiles, established dosing parameters including routes of administration, and quality specifications and manufacturing controls necessary to ensure the identity, purity, and consistency of the substance. This is the information that physicians rely upon when determining whether prescribing such products is consistent with accepted standards of medical practice. Currently compounded products, such as hormone replacement therapy and GLP-1 medications, are supported by FDA-reviewed manufacturing information, preclinical data, and clinical trials demonstrating their clinical use and safety in patients. The HHS-proposed peptides have not undergone comparable review. Social media influencers cannot serve as reliable substitutes for FDA review or well-designed clinical trials.

The AMA appreciates that the proposed HHS framework is an attempt to address some of the patient safety concerns that are being raised regarding accessing substances for human use outside of the traditional healthcare pathways. We note, however, that the proposed framework elements are voluntary, not standardized, and lack any rigorous oversight to ensure compliance and accountability. The AMA recognizes that many patients already obtain these products through unregulated channels, often referred to as "gray markets," creating significant concerns regarding identity, potency, purity, labeling accuracy, contamination, and product consistency. A non-enforcement policy, however, provides no confidence that there will be any increase in product accuracy, sterility, or consistency. Rather, if the non-enforcement policy proceeds, HHS will be effectively endorsing non-FDA-approved substances for injection without providing patients with any assurance of safety or quality. The proposed non-enforcement policy does not eliminate the so-called gray market—it simply gives it federal permission to grow.

The AMA also is concerned that the scientific role of the FDA Center for Drug Evaluation and Research (CDER) is being circumvented because this HHS draft policy implies that there now is evidence demonstrating the safety and efficacy of these substances. If there is new evidence that would enhance the ability of CDER to evaluate these substances, the AMA urges that this new evidence becomes part of the official record and be evaluated by CDER for scientific authenticity, efficacy, and safety. With the scientific review by CDER, an FDA decision to approve a new drug, to withdraw a drug's approval, or to change the indications for use of a drug is based on sound scientific and medical evidence derived from controlled trials and real-world data fit for the regulatory purpose. Bypassing CDER sets a dangerous precedent that untested and potentially unsafe substances can be authorized through government fiat. That is not how our nation's drug safety framework is built. The AMA emphasizes again that science must be the guide for determining whether substances may be used safely and effectively.

The AMA also has concerns regarding the justifications HHS uses to bypass the role of CDER and FDA to ensure drug safety and efficacy. Historical use and "multiple human studies" are not reliable substitutes for well-designed clinical trials that are essential to ensure an adequate "human safety record." Just because a pharmacy can compound these peptides does not mean that consumers can or should trust the safety of such compounded substances, particularly without verified sources of active pharmaceutical ingredients for compounding.

Furthermore, consistency and standardization in naming should not be compromised. In the traditional drug development pathway, sponsors seek a United States Adopted Name (USAN) while products are undergoing clinical development. The intent of a USAN is to establish standardized, unique, and informative nonproprietary names for specific active ingredients and therapeutic substances marketed in the United States. A USAN is recognized by the FDA as the legal name for the active drug ingredient and is used for the United States Pharmacopeia monograph that defines the standards, properties, and characteristics of drugs. This is required for drugs to be marketed in the U.S. and provides numerous benefits: a USAN promotes clear communication among clinicians, researchers, regulators, pharmacists, and patients, further ensuring that the contents of a medication bottle or vial are accurate and understood by all, reducing medication errors, helping to identify and track safety concerns, and supporting the accurate interpretation of scientific literature. If HHS allows this proposed policy to go into effect, the AMA is concerned that it will effectively endorse increased confusion and risk for patients.

Allowing these substances to be used in compounded formulations exposes patients to unnecessary risks and undermines confidence in the evidence-based standards that guide drug evaluation and approval. **The AMA opposes the HHS non-enforcement policy and urges HHS to rescind the policy in favor of having the substances' efficacy and safety undergo the full FDA review process.** If the substances meet the FDA's requirements for safe use, and the evidence supports inclusion on the 503A Bulks List, then let the evidence demonstrate that.

Please reach out to me directly at 312-464-5288 or John.Whyte@ama-assn.org if you have questions or need further information.

Sincerely,



John Whyte, MD, MPH.