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United States Department of Health and Human Services
Food and Drug Administration
Docket No. FDA 2013-S-0610

Date: August 27, 2026

The undersigned submits this petition under 21 U.S.C. § 201(g) (section 201(g) of the Federal Food, Drug, and Cosmetic Act), 42 U.S.C. § 262(i)(1) (section 351 of the Public Health Service Act), and 21 C.F.R. § 10.30 to request the Commissioner of Food and Drugs to take the actions requested below.

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A. Actions Requested

The undersigned requests that the U.S. Food and Drug Administration ("*FDA*" or the "*Agency*"):

(1) Revoke FDA's determination that animal-derived thyroid ("*ADT*") products are "biological product[s]" under section 351(i) of the Public Health Service Act;
(2) Announce that FDA will classify ADT products as a drug, as defined in section 201(g) of the Federal Food, Drug, and Cosmetic Act; and
(3) Withdraw the September 16, 2022 letter to the National Association of Boards of Pharmacy ("*NABP*") and the August 6, 2025 letter to manufacturers, importers, and distributors of animal-derived thyroid products, and any other publication in which FDA describes ADT as being subject to the "biological product" definition.

B. Statement Of Grounds

I. Summary.

Approximately 1.5 million patients in the United States depend on ADT products to treat hypothyroidism. This includes patients who have had their thyroid removed, destroyed by Hashimoto's disease, or irradiated during cancer treatment, and they suffer from debilitating symptoms: chronic and intense fatigue, cognitive impairment, weight gain, hair loss, autoimmune complications, and inflammation, among many others. Many of these patients have attempted to treat their condition with FDA-approved synthetic thyroid medications, but their symptoms persisted or deteriorated. The common refrain from these patients is that ADT is the only medication that restores their quality of life and allows them to feel like their normal selves again. Indeed, ADT is often the difference between severe illness and a functional, thriving life. FDA is now threatening to take away these patients' ability to lead a normal life simply because it (wrongly) determined that ADT meets the statutory definition of "biological product" and therefore should not be regulated as a "drug." This formalistic decision is not only divorced from the real impacts that it will have on patients; it is also incorrect as a matter of law.

To start, FDA is wrong that the product meets the statutory definition of a "biological product." FDA's determination that ADT meets this definition relied solely on the fact a component of ADT, the thyroglobulin, is a "protein" or is "analogous" to a protein. But the definition requires more than just identifying these components. The statute, controlling case law, and even FDA's own guidance make clear that the protein or analogous protein must be an active pharmaceutical ingredient ("*API*"). Thyroglobulin is not an API. Rather, the scientific evidence demonstrates that the thyroglobulin is a carrier protein, which helps control the release of the drugs that are bound to it, but does not play a role in treating the condition. This is not unusual. A number of products contain proteins that play a pharmacokinetic role but do not furnish the pharmacological activity, and the Agency regulates these products as drugs.

Moreover, FDA's determination violated the Administrative Procedure Act. FDA failed to follow rulemaking procedures by not seeking public comment before imposing such an impactful rule. The determination is also arbitrary and capricious because FDA:

(1) misapplied the definition of "biological product";

(2) ignored its own policy that requires the biological component to be an API;

(3) entirely failed to provide an explanation as to why the thyroglobulin is an API;

(4) failed to explain why it classifies products with similar traits as drugs but refuses to classify ADT as a drug; and

(5) failed to consider the reliance interests of the physicians who prescribe compounded ADT products, the pharmacies that compound the ADT products, and the patients who require the continued availability of compounded ADT products to maintain quality of life.

Finally, public policy reasons should compel the Agency to reconsider its stance. ADT is a well-researched product with over a hundred years of documented efficacy in patients who rely on it as the only available means to treat their thyroid condition. ADT is essential to these patients, and denying them access is not only unnecessary; it is harmful. For these reasons we ask that the Agency (1) revoke its decision to classify ADT as a biological product, (2) announce that ADT will be classified as a drug, and (3) withdraw all previous statements in which FDA describes ADT as being subject to requirements of "biological products" under the Public Health Service Act.

II. Background.

a. Animal-Derived Thyroid Products Are Critical to Treating Certain Patients with Hypothyroidism.

Hypothyroidism, a condition of decreased thyroid hormone production, affects approximately 2% of the U.S. adult population, and millions of Americans take thyroid hormone replacement therapy to maintain normal circulating thyroid hormone levels and to prevent or improve symptoms such as fatigue, weight gain, cold intolerance, and depressed mood.[1] Two categories of thyroid hormone replacement therapy are marketed in the United States: synthetic products containing either levothyroxine ("*LT4*") or liothyronine ("*LT3*"), and ADT products, which are commonly described as desiccated thyroid extract.[2] ADT products are composed of thyroglobulin, an alpha amino acid polymer that acts as a carrier of the thyroid hormones thyroxine ("*T4*") and triiodothyronine ("*T3*")[3] and are marketed under names including Armour Thyroid, NP Thyroid, Nature-Throid, and Natural Thyroid.[4]

ADT is the oldest pharmacological treatment for hypothyroidism, becoming the dominant therapy in the early 1900s.[5] As of 1965, approximately four of every five prescriptions for thyroid

[1] FDA, *FDA's Actions to Address Unapproved Thyroid Medications*, https://www.fda.gov/drugs/enforcement-activities-fda/fdas-actions-address-unapproved-thyroid-medications (*last visited* June 15, 2026) (hereinafter "*FDA Actions*"); Letter from Shannon Glueck, U.S. FDA, to Lemrey "Al" Carter, National Association of Boards of Pharmacy 1-2 (September 16, 2022) (hereinafter "*2022 Pharmacist Letter*"), enclosed herein as Exhibit 1 (Notice from FDA determining that ADT is a biologic and not eligible for compounding).

[2] FDA Actions; 2022 Pharmacist Letter at 2.

[3] Letter from FDA to Manufacturers, Importers, and Distributors of Animal-Derived Thyroid Products at 3 (Aug. 6, 2025), https://www.fda.gov/media/188081/download, (hereinafter "*2025 Notice to Industry*"), enclosed herein as Exhibit 2.

[4] 2022 Pharmacist Letter at 2.

[5] Mohamed K.M. Shakir et al., *Comparative Effectiveness of Levothyroxine, Desiccated Thyroid Extract, and Levothyroxine+Liothyronine in Hypothyroidism*, 106 J. Clin. Endocrinol. & Metab. e4400, e4401 (2021); Matthew D. Ettleson & Antonio C. Bianco, *Individualized Therapy for Hypothyroidism: Is T4 Enough for Everyone?*, 105 J. Clin. Endocrinol. & Metab. e3090, e3090–91 (2020).

hormone in the United States were for ADT.[6] Today, these products remain a common form of treatment even after the introduction of synthetic products containing LT4 and LT3, as an estimated 1.5 million patients receiving thyroid hormone replacement are prescribed ADT products.[7] Further, many of these patients are prescribed and rely on a compounded ADT formulation, prepared by pharmacies pursuant to Section 503A of the Federal Food, Drug, and Cosmetic Act ("*FD&C Act*")[8] and consistent with the Thyroid U.S. Pharmacopeia ("*USP*") drug monograph.[9]

The option to use ADT is particularly impactful for autoimmune or immunologically sensitive patients who cannot tolerate the dyes and filler ingredients prevalent in FDA-approved medications like Synthroid, Tirosint, Levoxyl, and Unithroid, all of which contain LT4 as the only active ingredient.[10] FDA-approved LT4 products can also be ineffective in patients whose thyroids cannot convert T4 to the needed T3 hormone, or patients who have had their thyroid removed, destroyed by Hashimoto's disease, or irradiated. These patients need a combination of LT4 and LT3 to restore thyroid function—a combination that does not exist in any single FDA-approved medication—but does in ADT.

Moreover, thyroid treatment is specific to the patient and there is no single dose or medication that fits every patient. With respect to dosing, precision is necessary in thyroid management but the FDA-approved products come in limited dosage strengths that make precise treatment difficult. Additionally, as previously stated, there is no FDA-approved medication that contains both LT4 and LT3 that many of those with hypothyroidism need. Yet, ADT combines both of these active ingredients and ADT is the only medication that makes it possible to replace what a patient without a thyroid has lost. Further, ADT, rather than pure T3 or pure T4, is better suited for compounding. As explained in more detail below, achieving the microgram-level precision patients require using only the pure T3 or pure T4, is difficult and inevitably introduces some imprecision, whereas ADT comes with a USP drug monograph that makes it straightforward and safe to compound.[11]

The clinical record reflects meaningful patient benefit from ADT. A large online survey of hypothyroid patients reported higher median treatment satisfaction among respondents taking

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[6] Adrian H. Heald et al., *Natural Desiccated Thyroid for the Treatment of Hypothyroidism*?, 14 Frontiers Endocrinol. 1309159, at 1–2 (2024).
[7] 2025 Notice to Industry at 2; FDA Actions.
[8] 21 U.S.C. § 301 *et seq.*
[9] 2022 Pharmacist Letter at 2; USP Monograph for Thyroid, United States Pharmacopeia (May 2016); 21 U.S.C. § 353a(b)(1)(A)(i)(I); 21 U.S.C.A. § 353a(b)(1)(A)(i)(I) ("A drug product may be compounded under [Section 503A] if the licensed pharmacist . . . compounds the drug product using bulk drug substances . . . that comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding").
[10] *See* Synthroid (Levothyroxine Sodium Tablets) Label, FDA, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021402s017lbl.pdf; *see also* Tirosint (Levothyroxine Sodium Capsules) Label, FDA, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2007/021924s002lbl.pdf; Levoxyl (Levothyroxine Sodium Tablets) Label, FDA, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021301s026lbl.pdf; Unithroid (Levothyroxine Sodium Tablets) Label, FDA, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2000/21210lbl.pdf.
[11] Peter Koshland, PharmD, Statement of Support, at p. 2 (hereinafter "*Koshland Statement*"), enclosed herein as Exhibit 9.

ADT than among respondents taking LT4 alone or LT4+LT3.[12] In a prospective, randomized, double-blind, crossover study, outcomes for the overall group were similar across LT4, LT4+LT3, and ADT, while a subgroup of the most symptomatic participants on LT4 preferred and showed improvement on T3-containing therapy, including ADT.[13] A 2024 review likewise identified a role for ADT in carefully selected patients who remain symptomatic despite treatment with an FDA-approved LT4 therapy.[14]

The consequences of inadequate thyroid management are profound and far-reaching, as the thyroid affects virtually every system in the body. Patients may experience energy loss, cognitive impairment and brain fog, weight gain leading to other chronic illnesses, systemic inflammation, and autoimmune reactions—symptoms that greatly impact patients' day-to-day functioning and can render patients bedridden.[15] However, when dosed appropriately, ADT products can mimic normal thyroid function and restore clinical euthyroidism. As such, ADT is not just a convenience for the patients that use it—it is essential to their overall wellbeing.[16] It is therefore critical that these patients continue to have access to these products.[17]

b. FDA's Regulation of Protein Products as Biologics Instead of Drugs.

FDA regulates medications under two parallel statutory regimes: the FD&C Act,[18] which governs drugs approved through new drug applications ("*NDAs*"),[19] and the Public Health Service Act ("*PHS Act*"),[20] which governs "biological products" licensed through biologics license applications ("*BLAs*").[21] In March of 2010, Congress passed the Biologics Price Competition and Innovation Act of 2009 ("*BPCI Act*"),[22] which, among other things, amended the statutory definition of "biological product" (sometimes referred to herein as "*biologics*") in the PHS Act to add the category "protein."[23] As amended, the statute defines a "biological product" as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings."[24] The BPCI Act adopted a ten-year waiting period before products newly incorporated into the definition of "biological product" with NDA approvals under

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[12] Sarah J. Peterson et al., *An Online Survey of Hypothyroid Patients Demonstrates Prominent Dissatisfaction*, 28 Thyroid 707, 716 (2018).
[13] Shakir et al., *supr*a note 5, at e4400–01, e4413.
[14] A. A. Patel, M. K. Shakir, F. Tuamokumo, A. C. Bianco & T. D. Hoang, *The Effect of Combination Thyroid Hormone Therapies on Symptoms in Patients with a Suboptimal Response to Levothyroxine: A Post-Hoc Analysis*, 8 J. Endocrine Soc'y (Supp. 1) bvae163.2084 (2024), DOI: 10.1210/jendso/bvae163.2084.
[15] Dawn Ipsen, PharmD, FACP, FACA, FAVCP, Statement of Support, p. 2 (hereinafter "*Ipsen Statement*"), enclosed herein as Exhibit 10.
[16] Brittany Bohinc Henderson, MD, ECNU, Statement of Support, p. 2 (hereinafter "*Henderson Statement*"), enclosed herein as Exhibit 7.
[17] Heald et al., *supra* note 6, at 1, 3.
[18] 21 U.S.C. § 301 *et seq.*
[19] FD&C Act § 505 (21 U.S.C. § 355).
[20] 42 U.S.C. § 201 *et seq.*
[21] PHS Act § 351 (42 U.S.C. § 262).
[22] Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, § 7002, 124 Stat. 119, 804 (2010).
[23] BPCI Act § 7002(b) & (e), 124 Stat. 814 & 817 (the BPCI originally amended the definition to exempt "any chemically synthesized polypeptide" from the definition of the "protein" but this exception was removed by the Further Consolidated Appropriations Act, 2020, Pub. L. No. 116-94, § 605, 133 Stat. 2534, 2758 (2019)).
[24] PHS Act § 351(i)(1).

section 505 of the FD&C Act would be deemed to be a license under the PHS Act.[25] This transition date was March 23, 2020.[26]

Congress did not define "protein," and the term lacks a scientific consensus on how to define it, so FDA took to notice-and-comment rulemaking to issue a definition. FDA defined "protein" to mean "any alpha amino acid polymer with a specific, defined sequence that is greater than 40 amino acids in size."[27] Although FDA referred to this as a "bright-line" approach, FDA further clarified its thinking in March 2020, when it issued the guidance titled "The 'Deemed To Be a License' Provision of the BPCI Act, Questions and Answers" (herein "*Deemed QA Guidance*" or "*Guidance*").[28] Of particular importance, the Guidance clarified that not all products containing proteins are regulated as biologics. Rather "a drug product that contains a protein only as an inactive ingredient (e.g., a drug product formulated with human serum albumin as an inactive ingredient) is not considered to be a 'protein' for purposes of the statutory definition of 'biological product' and the transition provision of the BPCI Act."[29] In other words, the protein component of the product must be an API of the product for the product to fall within the PHS Act.

The distinction between drug and biologic is not merely one of form—rather, there are impactful differences. Importantly, one consequence of being classified as a biologic is that such products are not eligible for compounding by pharmacies under section 503A of the FD&C Act.[30]

c. FDA's Determination That ADT Is a Biological Product.

Soon after the BPCI Act's ten-year transition period ended, FDA began referring to ADT as a biological product.[31] For example, in 2020, FDA issued two warning letters to manufacturers of ADT products, alleging that the products are biological products because they contain thyroglobulin, an alpha amino acid polymer with a specific defined sequence consisting of 2770 amino acids, which meets the definition of "protein."[32] In the alternative, the warning letters also stated that the products are biological products because they are "'analogous' to a protein because the identified biological product (i.e., protein) component in these naturally derived mixtures is necessary for the activity of the product and contributes to achieving the intended therapeutic effect."[33]

In 2022, FDA issued a letter to the National Association of Boards of Pharmacy (hereinafter "*2022 Pharmacist Letter*") to advise that FDA intends to regulate ADT as a biological product. Again, FDA took the position that ADT was a biological product because the

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[25] BPCI Act § 7002(e)(4).
[26] Deemed QA Guidance at 1.
[27] Biological Product Proposed Rule at 63,817; FDA, Final Rule, *Definition of the Term "Biological Product,"* 85 Fed. Reg. 10,057 (Feb. 21, 2020) (hereinafter "*Biological Product Final Rule*") (codifying definition at 21 C.F.R. § 600.3(h)(6)).
[28] FDA, *The "Deemed To Be a License" Provision of the BPCI Act, Questions and Answers, Guidance for* Industry, Mar. 2020, https://www.fda.gov/media/135838/download.
[29] Deemed QA Guidance at 5.
[30] 2022 Pharmacist Letter.
[31] *See, e.g.*, Warning Letter to Acella Pharmaceuticals, LLC, CMS No. 604438 (Aug. 14, 2020), enclosed herein as Exhibit 3; Warning Letter to RLC Labs, CMS No. 607596 (Oct. 9, 2020), enclosed herein as Exhibit 4; 2022 Pharmacist Letter; August 2025 Notice to Industry at 1.
[32] Warning Letter to Acella Pharmaceuticals, LLC, CMS No. 604438 (Aug. 14, 2020).
[33] *Id.*; *see also* Warning Letter to RLC Labs, CMS No. 607596 (Oct. 9, 2020) (same).

thyroglobulin in the ADT exceeded the size threshold of amino acids in FDA's definition of "protein."[34] FDA added that, because they are biological products, ADT products are not eligible for the compounding exemptions afforded under sections 503A and 503B of the FD&C Act.[35]

On August 6, 2025, FDA expanded on its classification rationale in its notice to manufacturers, importers, and distributors of ADT (hereinafter "*2025 Notice to Industry*" or "*Notice*"). The Notice announced that FDA "intends to take action against marketed unapproved" ADT products, asserting that such products "require an approved [BLA] under section 351 of the [PHS] Act in order to be legally marketed," and that "[t]here are no FDA-approved BLAs for the ADT products currently on the market."[36] FDA specified that its Notice was intended to "promote compliance with FDA's premarket approval requirements" and as of August 2026, the Agency intends to "initiat[e] action against manufacturers, distributors, and importers of ADT and unapproved ADT products intended for commercial distribution."[37]

Like the warning letters and the 2022 Notice, the 2025 Notice to Industry offered two alternative grounds for treating ADT as a "biological product." First, FDA reasoned that ADT is a "protein" because it "necessarily contains thyroglobulin, an alpha amino acid polymer with a specific defined sequence consisting of 2,770 amino acids," and that a product "composed primarily of protein components (e.g., thyroglobulin)" falls within the Agency's size-based interpretation of the statutory term "protein."[38] Second, and in the alternative, FDA reasoned that ADT is "analogous" to a protein, and thus a biological product, because it "includes an identified biological product component (i.e., thyroglobulin) that is necessary for the activity of the product and contributes to achieving the intended therapeutic effect," while also potentially including non-biological components such as free T3 and free T4.[39] Finally, the Letter announced a risk-based patient transition period of up to twelve months before the Agency would initiate action against manufacturers.[40]

FDA has reiterated this position in other communications. On the same day it issued the 2025 Notice to Industry, FDA also responded to a citizen petition from AbbVie confirming that "a marketed unapproved ADT product requires a license under section 351 of the [PHS] Act in order to be legally commercially distributed."[41] In a February 2, 2026, response to a bipartisan congressional letter urging that ADT be classified as a drug rather than a biologic, FDA repeated that ADT meets the definition of a biological product and reaffirmed its intent to review and approve such products through the BLA process.[42] On March 11, 2026, FDA issued a further notice to industry reiterating its risk-based enforcement approach and announcing that it plans to issue draft guidance before August 2026, describing both its compliance priorities and conditions of

[34] 2022 Pharmacist Letter.
[35] 2022 Pharmacist Letter.
[36] August 2025 Notice to Industry at 1.
[37] August 2025 Notice to Industry at 5.
[38] August 2025 Notice to Industry at 2-3.
[39] August 2025 Notice to Industry at 3.
[40] August 2025 Notice to Industry at 4-5.
[41] Letter from FDA to Neal Parker & Raymond C. Votzmeyer, AbbVie Inc., Dkt. No. FDA-2024-P-1715, at 3 (Aug. 6, 2025) (hereinafter "*AbbVie Petition Response*").
[42] Letter from Martin A. Makary, Comm'r of FDA, to Hon. Diana Harshbarger 1 (Feb. 2, 2026) (hereinafter "*Harshbarger Response*").

continued enforcement discretion for marketed unapproved ADT products, as well as draft guidance on the development of ADT products to support marketing applications.[43]

Notably, in all of these public statements, FDA's rationale rests entirely on the fact that the thyroglobulin is a "protein" component of ADT or that it is the "necessary" activity-contributing component of an "analogous" product.[44] At no point has FDA articulated why it believes that the thyroglobulin is an API. As set forth in the argument that follows, that rationale is in tension with FDA's own interpretation of this term in guidance and in litigation, and with the undisputed physiology of the product, under which thyroglobulin functions only as a carrier that is enzymatically degraded before absorption while the small-molecule hormones T3 and T4 serve as the only APIs in this medication.

The practical consequence of FDA's classification is significant: because biological products subject to licensure under the PHS Act are not eligible for the compounding exemptions of the FD&C Act, FDA's position would render ADT products ineligible for compounding and, absent an approved BLA, subject to enforcement action. This interpretation has shut off supplies of ADT products to the millions of patients that rely on it, including those suffering from Hashimoto's disease, or have had their thyroid removed or irradiated, many of whom only respond to ADT therapy after synthetic therapies have failed them.

III. Argument.

a. ADT's Protein Component Is Not an Active Pharmaceutical Ingredient.

The scientific evidence demonstrates that FDA's classification of ADT as a biological product cannot withstand scrutiny under the statutory definition, controlling case law, and FDA's own guidance. FDA interprets products containing proteins or "analogous" proteins to be biological products only if the component is an API. As discussed below, evidence demonstrates that the protein component of ADT is not an API. Instead, the active ingredients in ADT are the T3 and T4 small molecules that do not meet the definition of a protein and are appropriately regulated as drugs. The protein component of ADT, the thyroglobulin, merely acts as a carrier of the active ingredients (T3 and T4) and does not furnish any pharmacological activity. Indeed, FDA regulates products with similar proteinaceous or animal-derived components as drugs products. Accordingly, classifying ADT as a biologic is contrary to the law and FDA's own practices. ADT must therefore be classified, and regulated, as a drug.

i. Legal Standard.

1. FDA's Statutes, Regulations, and Guidance Make Clear That the Protein Component Must Be the API to Meet the Definition of Biological Product.

The statute defines "biological product" as a "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product

[43] Letter from FDA to Mfrs., Imps. & Distribs. of Animal-Derived Thyroid (ADT) Prods. (Mar. 11, 2026) (hereinafter "*March 2026 Notice to Industry*"), enclosed herein as Exhibit 5.
[44] August 2025 Notice to Industry.

… ***applicable to the prevention, treatment, or cure of a disease or condition of human beings***."[45] The qualifying phrase "applicable to the prevention, treatment, or cure of a disease" modifies each enumerated category, including "protein" and "analogous product." The protein or protein analogous component itself must therefore be the component that treats the disease.

To account for this statutory limitation, as discussed in Part B.II.b above, FDA's Deemed QA Guidance clarified that if a product contains a protein that functions only as an inactive ingredient, then the protein is not cause to regulate the product as a biologic. Specifically, the guidance states that "a drug product that contains a protein only as ***an inactive ingredient*** (e.g., a drug product formulated with human serum albumin as an inactive ingredient) is not considered to be a 'protein' for purposes of the statutory definition of 'biological product.'"[46]

FDA's regulation defines "inactive ingredients" as "any component other than an active ingredient."[47] The same regulation defines "active ingredient" as any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease."[48] Thus, as FDA recognizes in the Deemed QA Guidance, for a drug with proteins to be regulated as a biologic the protein must furnish pharmacological activity.[49] FDA also has applied this principle in practice: for example, in albumin-bound paclitaxel, paclitaxel is the active ingredient and human albumin—a large plasma protein—is considered an inactive ingredient, and therefore FDA classifies the product as a drug.[50]

2. Finished Dosage Form Is Not Relevant when Determining the Pharmacologically Active Component.

The API of a product is determined by how the product furthers the therapeutic purpose and is not determined by how the product is composed in its finished dosage form.[51] In *Ipsen Biopharmaceuticals Inc. v. Becerra*, Ipsen, the sponsor of the product Somatuline Depot, argued that the product's API was a protein and therefore FDA should classify the product as a biologic. While both the manufacturer and FDA agreed that the proper question is whether a protein was the API, they disagreed as to when the determination should be made.[52] Ipsen argued that the determination should be made when the product was in its finished dosage form. Somatuline Depot's API is lanreotide acetate, which is a molecule containing eight amino acids (referred to as an octapeptide).[53] In finished dosage form, the octapeptide is linked together to form nanotubes to allow for extended release of the lanreotide acetate octapeptides.[54] The nanotubes' total amino acids far exceeds the forty amino acids needed to meet the definition of "protein."

[45] 42 U.S.C. § 262(i)(1) (emphasis added).
[46] Deemed QA Guidance at 5 (emphasis added).
[47] 21 C.F.R. § 314.3(b).
[48] *Id.*
[49] *Ipsen Biopharmaceuticals v. Becerra*, 108 F.4th 836, 841 (D.C. Cir. 2024); *see also Ipsen Biopharmaceuticals Inc. v. Becerra,* 678 F.Supp.3d 20 (D.D.C. 2023).
[50] *See, e.g.*, FDA, Labeling, Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound), NDA No. 216338 (2023), https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216338s000lbl.pdf.
[51] *Ipsen*, 678 F. Supp. 3d at 37–38, *aff'd*, 108 F.4th 836 (D.C. Cir. 2024).
[52] *Ipsen*, 108 F.4th at 841.
[53] *Ipsen*, 678 F. Supp.3d at 36.
[54] *Ipsen*, 678 F.Supp.3d at 27.

However, to FDA, the finished dosage form was irrelevant. Rather, the relevant inquiry was how the lanreotide acetate behaved to effectuate the therapeutic purpose.[55] For Somatuline Depot, once the therapy is administered, the lanreotide acetate octapeptides individually separated from the nanotube to bind to somatostatin receptors to exercise the drug's functions. Because the octapeptides contain less than forty amino acids when they bind to receptors, they did not meet the definition of a protein. In contrast, the nanotubes acted to control the release rate of the octapeptides, which FDA recognized as "'alter[ing] the pharmacokinetics' – movement of the drug, including distribution and absorption – 'but does not change the active ingredient that is intended to furnish pharmacological activity."[56] Thus, according to FDA, the important inquiry is not the form in which the product is administered, ***including design features to affect dosing***, rather, the inquiry is what is the specific component of the product that "confers the pharmacological activity" upon administration of the therapy.[57]

The D.C. District Court agreed that, based on the language in the definition of "biological product" that the protein must be "applicable to the prevention, treatment, or cure of a disease," FDA was correct to examine what specific molecule furnished the therapeutic purpose, notwithstanding the form upon which it was initially administered.[58] The D.C. Circuit affirmed, confirming that FDA must focus on a product's active ingredient, rather than its finished dosage form, when determining whether the product falls within the statutory "protein" category.

Taken together, the statute, the rulemaking, FDA's guidance, and the *Ipsen* precedent support an analytical focus on the active ingredient and the component or components that actually furnish pharmacological activity, rather than on the finished dosage form or structural complexity. *Ipsen* further supports the narrower proposition that ***a structural or formulation feature affecting drug release is not the active ingredient*** when it has not been shown to confer pharmacological activity. As discussed below, ADT's APIs are the T3 and T4 molecules, whereas the thyroglobulin does not confer any pharmaceutical therapeutic purpose, rather it serves as a carrier protein. Therefore, the product should be classified as a drug.

3. Products Analogous to Proteins Must Meet the API Standard.

The PHS Act's definition of "biological products" also includes products that are "analogous" to proteins and the other enumerated categories of products. FDA has declined to define "analogous" protein product. In its final rule issuing the definition of a protein, FDA merely stated it is not a product that is "specifically excluded from this final rule."[59] In litigation, FDA has stated that a product is analogous to a protein when it shares a "critical characteristic" such as the size of the amino acid polymer and specific defined sequence.[60] An example FDA provided is "naturally derived mixtures that include one or more identified biological product component(s) (e.g., protein), as well as one or more non-biological product component(s) (e.g., lipids) that can contribute to the product's activity."[61] In other non-binding communications, it has stated that ADT is analogous to a protein product because the thyroglobulin is a "biological component" that

[55] *Id.* at 38.
[56] *Id.* at 39.
[57] *Id.* at 36.
[58] *Id.* at 37.
[59] 85 Fed. Reg. at 10061.
[60] *Ipsen*, 108 F.4th at 839, 844.
[61] *Id.* at 844.

is "necessary for the activity of the product and contributes to achieving the intended therapeutic effect."[62]

At bottom, however, remains the PHS Act's definitional provision that requires the "analogous" protein to be "applicable to the prevention, treatment, or cure of a disease."[63] The reasoning of *Ipsen* thus still holds true that for a product to be "analogous" to a protein product, the analogous feature must be an API regardless of the finished dosage form.[64]

ii. The T3 and T4 Molecules, Not the Protein, are the Active Pharmaceutical Ingredients of ADT, and Therefore ADT Is a Drug.

The scientific record establishes that the protein component of ADT (thyroglobulin) is a carrier for the drug components (T3 and T4), which functions by delivering the drugs to the body and controlling the release. Importantly, thyroglobulin has no independent receptor-mediated pharmacological activity and thus there is no identified pathway in which the thyroglobulin could further the therapeutic purpose. Understanding the distinction between carrier and API requires examining thyroglobulin's molecular structure, its role in thyroid hormonogenesis, the mechanism by which it releases thyroid hormones during digestion, and the pharmacological activity of the released hormones.

The published scientific literature characterizes thyroglobulin as a carrier for thyroid hormones, while identifying T3 and T4 as the molecules responsible for the downstream thyroid-hormone effects.[65] Thyroglobulin specifically serves as the macromolecular carrier on which thyroid hormones are synthesized and stored.[66] Select tyrosine residues within the thyroglobulin polypeptide chain undergo iodination by thyroid peroxidase in the presence of hydrogen peroxide to form monoiodotyrosine (MIT) and diiodotyrosine (DIT).[67] Coupling of two DIT residues yields thyroxine (T4), while coupling of one MIT and one DIT yields triiodothyronine (T3).[68] These iodinated residues remain covalently incorporated within the thyroglobulin polypeptide until released by proteolysis.[69] Thyroglobulin thus functions as a biosynthetic precursor and intracellular storage reservoir for thyroid hormones. [70]

The fate of thyroglobulin after oral administration further confirms its carrier roles, as opposed to serving any therapeutic purpose. Following oral administration, the thyroglobulin component of ADT, a large protein containing covalently incorporated iodothyronine residues, is

[62] 2025 Letter to Industry at 3; *see also* Warning Letter to Acella Pharmaceuticals, LLC, CMS No. 604438 (Aug. 14, 2020); *see also* Warning Letter to RLC Labs, CMS No. 607596 (Oct. 9, 2020) (same).
[63] PHS Act § 351(i)(1).
[64] *See supra* Part B.III.a.ii.
[65] *See* Bruno Di Jeso & Peter Arvan, *Thyroglobulin From Molecular and Cellular Biology to Clinical Endocrinology*, 37 Endocr. Rev. 2 (2016); Francesca Coscia et al., *The Structure of Human Thyroglobuli*n, 578 Nature 627 (2020); Bassett et al. at 1-3.
[66] Cintia E. Citterio et al., *The Role of Thyroglobulin in Thyroid Hormonogenesis*, 15 Nat. Rev. Endocrinol. 323, 323-24 (2019).
[67] *Id.* at 324.
[68] *Id.* at 323.
[69] *Id.* at 324.
[70] *Id.* at 323-24.

subjected to gastrointestinal proteolysis.[71] This process releases the protein-bound iodothyronines, including T3 and T4.[72] The resulting hormones, together with T3 and T4 already present in free form, become bioavailable after oral administration.[73] Following release of the hormones, hydrolysis breaks the thyroglobulin into oligopeptides and amino acids, which are further broken down in the body. [74] Although limited absorption of larger intact proteins cannot be excluded, there is no identified independent catalytic or receptor-mediated therapeutic activity for thyroglobulin.[75] Rather the evidence demonstrates that it remains a storage protein for T3 and T4, whereas T3 is the primary endogenous ligand that mediates thyroid hormone receptor activation.[76] The 2025 Letter to Industry appears to acknowledge this process, where it states that following oral administration, "proteolytic enzymes of the gastrointestinal tract release iodothyronines and iodotyrosines (including T3 and T4) from the thyroglobulin."[77] Importantly, the 2025 Letter to Industry identifies no therapeutic activity that is attributed to the thyroglobulin.

In contrast to thyroglobulin, bioavailable T3 and T4, whether released from thyroglobulin or already present in free form, are the pharmacologically active moieties responsible for the therapeutic effect of ADT.[78] In their free form, T3 and T4 contain no peptide bonds and are not amino acid polymers.[79] Rather, they are iodinated diphenyl ether derivatives.[80] They therefore do not, and cannot, satisfy FDA's regulatory definition of a "protein." T3 and T4 are the same thyroid hormone molecules that provide the pharmacological activity of the synthetic levothyroxine ("*LT4*") and liothyronine ("*LT3*") that FDA regulates as drugs. Indeed, FDA has approved multiple NDAs for synthetic LT3 and LT4 products,[81] confirming that T3 and T4 are drug substances, not biological products. FDA has never suggested that these molecules are proteins or analogous to proteins, consistent with treating these hormones as small-molecule drug substances rather than proteins.

The pharmacological mechanism through which T3 and T4 treat hypothyroidism is well established. T3 and T4 released during digestion, together with hormones already present in free form, are absorbed through the intestinal epithelium into the portal circulation.[82] T4 serves predominantly as a circulating prohormone that is converted to T3 by type 1 and type 2

[71] Hugh James Freeman, *Clinical Relevance of Intestinal Peptide Uptak*e, 6 World J. Gastrointest. Pharmacol. & Ther. 22, 23 (2015) ("Protein digestion and absorption in humans depends on initial enzymatic hydrolysis in the stomach and proximal small intestine. The hydrolytic products include oligopeptides and amino acids that ultimately undergo small intestinal uptake into the portal vein.").
[72] LeBoff MS et al., *Bioavailability of thyroid hormones from oral replacement preparations*, Metabolism 31(9): 900-905 (1982).
[73] *Id.*
[74] Freeman, *supr*a note 71, at 23; Warren M. Miner-Williams, Bruce R. Stevens & Paul J. Mough*an, Are Intact Peptides Absorbed from the Healthy Gut in the Adult Hum*an?, 27 Nutrition Res. Revs. 308, 308, 311 (2014).
[75] Citterio et al., *supr*a note 66, at 323-24; Gregory A. Brent*, Mechanisms of Thyroid Hormone Acti*on, 122 J. Clin. Investigation 3035, 3035–36 (2012); Amy Schroeder et al.*, The Ability of Thyroid Hormone Receptors to Sense T4 as an Agonist Depends on Receptor Isoform and on Cellular Cofactor*s, 28 Molecular Endocrinology 745, 745–46 (2014).
[76] *Id.*
[77] 2025 Letter to Industry at 3 (citing LeBoff, *supr*a note 72).
[78] Mahmoud Nassar et al., *Evaluating the Effectiveness of Combined T4 and T3 Therapy or Desiccated Thyroid Versus T4 Monotherapy in Hypothyroidism: A Systematic Review and Meta-Analysi*s, 24 BMC Endocr. Disorders 90, at 2, 10 (2024).
[79] Mary B. Dratman & Joseph V. Martin, *The Many Faces of Thyroxin*e, 7 AIMS Neuroscience 17, 27 (2020).
[80] *Id.* at 17.
[81] FDA Actions; 2022 Pharmacist Letter at 2.
[82] Josef Kohrle, *The Colorful Diversity of Thyroid Hormone Metabolite*s, 8 Eur. Thyroid J. 115, 124 (2019).

iodothyronine deiodinases (D1 and D2). T3 has substantially higher affinity for thyroid hormone receptors and is the principal receptor-active thyroid hormone.[83] It enters target cells, binds to nuclear thyroid hormone receptors, and modulates the transcription of genes governing basal metabolic rate, thermogenesis, cardiac output,[84] lipid metabolism, bone turnover, and neurocognitive function.[85]

No comparable downstream role has been established for intact thyroglobulin after oral ADT administration.[86] This reality is exemplified by the fact that the therapeutic endpoints monitored in patients receiving ADT do not measure an independent pharmacological effect of thyroglobulin, rather they measure serum thyrotropin, free T3, and free T4 concentrations, circulating thyroid hormone concentrations and pituitary feedback.[87]

Regulatory, pharmacopeial, labeling, and clinical standards support the conclusion that ADT dosing and clinical monitoring are based on T3 and T4 content and effects rather than measured thyroglobulin content. Since 1985, the USP standard has been keyed to thyroid hormone content rather than iodine content, making T3 and T4 content the compendial measure of product potency. Marketed ADT products such as Armour Thyroid and NP Thyroid are labeled by the mass of thyroid in grains or milligrams and specify the corresponding T3 and T4 content in micrograms; they are not labeled by thyroglobulin quantity. Clinical dosing and monitoring use labeled product strength and serum TSH, free T4, and free T3 rather than measured thyroglobulin content. Indeed, in a citizen petition submitted by the manufacturer of Amour Thyroid, the manufacturer explained that the thyroglobulin in their product is hydrolyzed in the body to yield T4 and T3, and states that those hormones provide the therapeutic effect.[88]

Applying the regulatory framework to the available scientific evidence, the relevant scientific question is whether intact thyroglobulin furnishes an independent pharmacological activity, rather than whether it is simply present in the product or participates upstream in hormone storage and release.[89] As demonstrated above, the molecules that mediate the established pharmacological effects of ADT are bioavailable T3 and T4, which are small-molecule hormones that bind thyroid hormone receptors and mediate the thyroid hormone replacement effect. There is no evidence that Thyroglobulin furnishes an independent receptor-mediated pharmacological effect; instead, the evidence demonstrates that it serves as a carrier and storage protein from which iodothyronines are released during digestion.

Therefore, the controlling precedent in *Ipsen* is on all fours. FDA's explanations for why ADT is a biologic rest entirely on the fact that the product contains a protein that exceeds the forty amino acid requirement in the definition of protein. But FDA makes the same mistake that Ipsen made when arguing that Somatuline Depot was a biological product. Both analyses rest on the finished dosage form of the product rather than on how the product confers the pharmacological

[83] Citterio et al., *supra* note 66, at 323, 326.
[84] *Id.* at 323.
[85] Angela D. Mazza, *Personalized Approaches to Hypothyroidism: The Role of Triiodothyronine (T3) in Thyroid Hormone Replacemen*t, 17 Cureus e90685, at 2, 5 (2025).
[86] Citterio et al., *supr*a note 66, at 324, 327; Bassett et al., *sup*ra note 65, at 1-3.
[87] Nassar et al., *supr*a note 78, at 3-5, tbl.1, tbl.2.
[88] Heald et al., *supr*a note 6, at 2; USP Monographs, Thyroid Tablets, *supr*a note 9; Citizen Petition from AbbVie Inc., Docket No. FDA-2024-P-1715 (Apr. 2024), https://www.regulations.gov/document/FDA-2024-P-1715-0001.
[89] 21 C.F.R. § 314.3(b).

activity upon administration of the therapy. FDA has identified no pharmacological activity attributable to the thyroglobulin in any of the various notices describing its position (because there is none). Much like Somatuline Depot, the protein element of ADT acts to control the release rate of the T3 and T4, which may "alter the pharmacokinetics . . . but does not change the active ingredient that is intended to furnish pharmacological activity."[90] FDA cannot have it both ways. Short of providing sound evidence that adequately trumps the evidence described above that thyroglobulin does not confer pharmacological activity, FDA must classify ADT as a drug.

iii. ADT Is Not "Analogous" to a Protein and Therefore Is Not a Biological Product under the PHS Act.

FDA's alternative theory that ADT is "analogous" to a protein is equally flawed. FDA contends that ADT is "analogous" to a protein because thyroglobulin is "necessary for the activity of the product and contributes to achieving the intended therapeutic effect."[91] This argument fails for several reasons.

FDA's alternative theory cannot rest on the mere presence of substances that are analogous to a protein in the finished dosage form. As discussed in Part B.III.a.i.3, to satisfy the definition of biological product, the protein analogous feature must be an API.[92] The only "analogous" feature that FDA has identified in its various notices is the thyroglobulin.[93] As discussed in Part B.III, the thyroglobulin portion of ADT provides no pharmacological activity, and therefore ADT cannot be considered analogous to a protein such that it would cause it to meet the definition of a biological product.

Additionally, to the extent FDA considers other portions of the ADT to be "analogous" to a protein, as recognized by the D.C. Circuit, a product "analogous" to a protein must share the "critical characteristics" of proteins.[94] The APIs, T3 and T4, are iodinated diphenyl ether derivatives with molecular weights below 800 daltons and share none of the defining characteristics of proteins.

Finally, FDA's argument is illogical. The thyroglobulin portion of ADT is a protein,[95] as it meets the amino acid size threshold in the definition of a protein in FDA's regulation.[96] The same component cannot also be "analogous" to a protein because it *is* a protein. Analogous means having "similar function but different structure and origin."[97] Here, there are no substances that have similar function to a protein but different structure or origin. Rather, the only component that has a protein function is the protein thyroglobulin, which is an inactive ingredient in the ADT.

Accordingly, FDA cannot rely on the "analogous product" clause to force ADT into the PHS Act's jurisdiction.

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[90] *Ipse*n, 678 F. Supp. 3d at 36.
[91] August 2025 Notice to Industry at 3.
[92] *See supra* Part B.III.a.iii.
[93] *See* 2025 Letter to Industry at 3.
[94] *Ipsen*, 678 F. Supp. 3d at 41; *Ipsen*, 108 F.4th at 840.
[95] But it is "not considered to be a 'protein' for purposes of the statutory definition of 'biological product.'" Deemed QA Guidance at 5.
[96] 21 C.F.R. § 600.3(h)(6).
[97] *See* Merriam Webster, https://www.merriam-webster.com/dictionary/analogous#medicalDictionary.

iv. FDA's Treatment of Comparable Products Supports Regulating ADT as a Drug.

FDA's treatment of other products containing proteinaceous or animal-derived components supports regulating ADT as a drug. Across these products, FDA has focused on the identity and pharmacological function of the active ingredient rather than treating animal origin, molecular complexity, or the presence of a protein as determinative. For example:

- **Somatuline Depot:** As discussed in Part B.III.a.i.3, FDA regulates Somatuline Depot under an NDA. Its active ingredient, lanreotide acetate, is an eight-amino-acid peptide that self-assembles into nanotube structures in the finished dosage form to provide extended release. These nanotube structures far exceed the required amino acid count to meet FDA's definition of a protein. FDA nevertheless determined, and the D.C. Circuit upheld, that the relevant active ingredient is the individual lanreotide acetate molecule that furnishes the pharmacological activity, rather than the larger self-assembled nanotube structure. Somatuline Depot therefore supports focusing on the component that furnishes pharmacological activity rather than on the size or structural complexity of the finished dosage form.
- **Paclitaxel protein-bound particles for injectable suspension (albumin-bound)**: FDA regulates this product under an NDA, identifying paclitaxel as the active ingredient and human albumin, a large plasma protein, as an inactive ingredient. The product demonstrates that a large protein may be integral to a formulation without becoming the active ingredient or requiring regulation of the product as a biologic.[98]
- **DefenCath**: FDA approved DefenCath under an NDA with taurolidine and heparin sodium as active ingredients. FDA-approved labeling describes heparin as a heterogeneous group of straight-chain anionic mucopolysaccharides, called glycosaminoglycans, derived from porcine intestinal mucosa. DefenCath therefore demonstrates that an animal-derived, structurally complex polymer may be regulated under the drug framework.[99]
- **Conjugated Estrogens**: Similarly, FDA regulates conjugated estrogens (e.g., Premarin), a naturally derived hormone mixture purified from pregnant mares' urine, under the drug framework.[100] The product demonstrates that a naturally derived, heterogeneous mixture of small-molecule hormones remains subject to the drug framework. This example is relevant to the product's animal origin and mixture complexity.

Taken together, these products support focusing on the components that furnish pharmacological activity, not merely the presence of a protein, animal origin, or molecular complexity. Somatuline Depot and albumin-bound paclitaxel confirm that FDA may distinguish a protein formulation component from the drug active ingredient. DefenCath and conjugated estrogens further confirm that complex and naturally derived products remain subject to the drug framework when their pharmacologically active components are not proteins. In ADT, bioavailable T3 and T4 furnish the established receptor-mediated effects, while no independent

[98] FDA, Labeling, Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound), NDA No. 216338 (2023), https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216338s000lbl.pdf.

[99] FDA, Labeling DefenCath (Taurolidine and Heparin) Catheter Lock Solution, NDA No. 214520 (2023). https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/214520s003lbl.pdf

[100] FDA, Product-Specific Guidance for Conjugated Estrogens (Naturally Sourced); *see* FDA, Labeling, Premarin (conjugated estrogens tablets, USP), https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/004782s142lbl.pdf.

catalytic or receptor-mediated therapeutic activity has been established for intact thyroglobulin. These comparators therefore support regulating ADT as a drug.

b. FDA's Classification Violates the Administrative Procedure Act.

Beyond the substantive classification errors described above, FDA's decision is independently defective under the Administrative Procedure Act ("*APA*").[101] FDA's decision to utilize the incorrect standard when assessing whether to regulate ADT under the PHS Act meant that it relied on factors Congress did not intend for FDA to consider. FDA also ignored its own guidance without providing a rational justification. Moreover, FDA did not consider important factors such as reliance interests of patients, physicians and other health care providers, and pharmacies that reasonably relied on FDA's Deemed QA Guidance indicating that FDA would regulate ADT as a drug and therefore ADT would remain available for compounding. Finally, FDA's determination was a legislative rule requiring notice-and-comment rulemaking pursuant to section 505(b) of the APA. FDA's actions therefore are not legally supportable and any planned enforcement must be stayed until these defects are cured.

i. FDA's Determination That ADT Is a Biologic Is Arbitrary and Capricious Because It Is Inconsistent with the Statute and FDA's Own Guidance, and Failed to Consider Important Factors Impacting Patients and Providers.

An agency rule is arbitrary and capricious if the agency "failed to consider an important aspect of the problem," "relied on factors which Congress has not intended it to consider," produced a decision that is "unreasoned," or "is so implausible that it could not be ascribed to a difference in view or the product of agency expertise."[102] The requirement of a reasoned decision also means the agency cannot contradict its prior rules or existing policy sub silentio and, importantly, that it must meaningfully consider any reliance interests that may be at stake if it consciously decides to change its position.[103]

FDA's decision failed to consider factors that Congress intended it to consider by misinterpreting the statutory definition. By classifying ADT as a biologic based upon its finished dosage form, instead of the API, FDA ignored the statutory requirement that the protein or analogous product must be "applicable to the prevention, treatment, or cure of a disease or condition of human beings."[104] As discussed in Part B.III.a.i., this language required FDA to classify products based upon their API, rather than their finished dosage form.[105] By misapplying

[101] 5 U.S.C. §§ 551-559, 701-706.
[102] *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983); *U.S. Sugar Corp. v. Env't Protection Agency*, 830 F.3d 579, 606 (D.C. Cir. 2016).
[103] *See FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 515 (2009) (citing *Smiley v. Citibank (South Dakota), N.A.*, 517 U.S. 735, 742 (1996)); *see also Encino Motorcars, LLC v. Navarro*, 579 U.S. 211, 221 (2016) ("Agencies are free to change their existing policies as long as they provide a reasoned explanation for the change. . . . In explaining its changed position, an agency must also be cognizant that longstanding policies may have engendered serious reliance interests that must be taken into account.") (citation modified).
[104] PHS Act § 351(i)(a).
[105] *See supra* Part B.III; *Ipsen*, 108 F.4th at 841.

the statute, FDA failed to consider the key question that Congress intended, which caused the decision to be arbitrary and capricious.[106]

FDA's classification decision also ignored its own policy outlined in the Deemed QA Guidance that proteins must be the API to cause a product to be classified as a biologic. At no point in the various notices and letters has FDA explained why it believes that the thyroglobulin is the API. By ignoring its own guidance, FDA fails to provide reasoned decision making or justify why it is departing from its policy—the epitome of arbitrary decision making.[107]

Moreover, even if FDA was of the position that the thyroglobulin was an API, FDA never attempted to justify this position. In all of the various notices FDA has provided, the Agency only addresses whether thyroglobulin is a protein or analogous to a protein. It never addresses whether the protein plays any role outside of pharmacokinetics. The APA requires reasoned decision making, and the complete lack of an explanation provides no basis upon which to conclude that the Agency's determination was reasonable.[108]

FDA's decision is also inconsistent with FDA's practices of regulating like-products as drugs. As discussed in Part B.III.a.i.3, FDA has treated Somatuline Depot, albumin-bound paclitaxel, conjugated estrogens, and DefenCath—all of which contain proteinaceous, animal-derived, or naturally derived components—as drugs. Yet FDA classifies ADT as a biologic without articulating a principled basis for the disparate treatment. An agency that treats like cases differently must provide a reasoned explanation; failure to do so renders the action arbitrary.[109]

Finally, when an agency changes course, it must "be cognizant that longstanding policies may have engendered serious reliance interests that must be taken into account."[110] Here, the reliance interests are substantial: approximately 1.5 million patients currently use ADT, and prescribers, pharmacists, and compounders have relied on its availability under the drug framework for over a century.

For patients, ADT is a lifetime medication; it is not a "band-aid" product that improves a patient's condition until such a point that the patient can ease off. Rather, patients will perpetually require this medication in order for their thyroids to function at optimal levels. Dr. Sarah Zielsdorf, a board-certified internal medicine physician and Institute for Functional Medicine Certified Practitioner (FMCP-M), explained that she:

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[106] *See Genus Med. Techs., LLC v. FDA*, 427 F. Supp. 3d 74, 87 (D.D.C. 2019), *aff'd*, 994 F.3d 631 (D.C. Cir. 2021) (holding that FDA's decision was arbitrary where it chose to regulate contrast agent as a drug instead of a device because it violates the statutory definitions).

[107] *See FDA v. Wages and White Lion Invests., L.L.C.*, 604 U.S. 542, 568 (2025) ("Agencies are free to change their existing policies as long as they provide a reasoned explanation for the change, display awareness that they are changing position, and consider serious reliance interests.") (citation modified).

[108] *See State Farm*, 463 U.S. at 43 ("the agency must examine the relevant data and articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made") (quotation marks omitted).

[109] *See Burlington N. & Santa Fe Ry. Co. v. Surface Transp. Bd.*, 403 F.3d 771, 776–77 (D.C. Cir. 2005) (citations and quotation marks omitted); *see Prairie Band Potawatomi Nation v. Yellen*, 63 F.4th 42, 47 (D.C. Cir. 2023) (finding that Agency's decision was arbitrary and capricious because it treated similar cases differently without providing a legitimate reason for doing so).

[110] *Dep't of Homeland Sec. v. Regents of the Univ. of Cal.*, 140 S. Ct. 1891, 1913 (2020) (quoting *Encino Motorcar*s, 579 U.S. at 222).

> fear[s] for the lives of some of [her] patients if they cannot get access to ADT. Some of [her] patients may be forced back onto therapies they cannot tolerate or cannot use effectively. For others with severe hypothyroid symptoms that need ADT to maintain daily basic functioning, loss of access will not be a mere inconvenience; ***it will be a profound medical crisis***.[111]

Dr. Brittany Bohinc Henderson, MD, ECNU, who has dedicated her career to advancing the diagnosis and treatment of thyroid disease, has also relied on the availability of ADT so that she can prescribe compounded versions of the medication that fit the individual needs of her patients. To her, "uninterrupted access to compounded ADT is critical. Compounded ADT allows [her] to prescribe slight variations in LT3 and LT4 that create meaningful differences for [her] patients."[112]

Compounding pharmacies have also relied on the availability of ADT so that they can fill the many prescriptions issued by providers like Dr. Henderson and Dr. Zielsdorf. These pharmacies traditionally have filled hundreds of compounded ADT prescriptions for patients each year.[113] FDA's classification—which forecloses compounding under section 503A—directly disrupts those interests without acknowledgment.

When FDA acknowledged in the Deemed QA Guidance that the protein elements of product must be the API for it to be regulated as a biological product, it implicitly acknowledged that ADT would continue to be regulated as a drug. FDA violated the APA by reversing course without acknowledging and responding to the interests of those who relied on the continued availability of these products under the drug pathway. These interests demanded consideration, and the failure to do so resulted in an arbitrary decision.

ii. The Classification Required Notice-and-Comment Rulemaking.

FDA's classification is also procedurally invalid. FDA's determination that ADT products are biological products constitutes a legislative rule that was required to undergo notice-and-comment rulemaking under 5 U.S.C. § 553. Although section 553(b)(A) exempts "interpretative rules, general statements of policy, or rules of agency organization, procedure, or practice" from notice-and-comment requirements, FDA's classification does not fall within any of these exemptions. The classification imposes new, binding legal obligations on regulated parties: it requires manufacturers to obtain BLA approval under section 351 of the PHS Act, and it forecloses compounding under FD&C Act sections 503A and 503B, eliminating a legal pathway on which pharmacies, prescribers, and patients have relied for decades. A rule that changes the legal obligations of regulated parties, restricts the availability of an established drug product, and alters the conditions under which that product may be manufactured or dispensed is substantive in nature, not merely interpretive.[114] An interpretive rule merely "advises the public of the agency's

[111] Sarah J. Zielsdorf, MD, MS, Statement of Support, p. 2 (hereinafter "*Zielsdorf Statement*") (emphasis added), enclosed herein as Exhibit 6.
[112] Henderson Statement, at p. 2.
[113] *See, e.g.*, Ipsen Statement at p. 2.
[114] *See City of Billings v. Transportation Sec. Admin.*, 153 F.4th 46, 52 (D.C. Cir. 2025); *N.H. Hosp. Ass'n v. Azar*, 887 F.3d 62, 74 (1st Cir. 2018).

construction of the statutes and rules which it administers" without creating new rights or obligations.[115]

By contrast, the August 2025 Notice creates new obligations (BLA requirement), extinguishes existing rights (compounding eligibility), and prescribes enforcement consequences. It is therefore a legislative rule, and FDA's failure to provide notice and an opportunity for public comment before issuing it renders the classification procedurally invalid under the APA.[116] The absence of any notice-and-comment process is particularly significant here because the classification implicates the health and welfare of approximately 1.5 million patients and raises complex scientific questions that would have benefited from public input by affected stakeholders, including physicians, pharmacists, compounders, patient advocacy organizations, and scientific experts.

c. Patient Access to Life-Altering Medications Must Be Protected.

"*The first dose of ADT felt like going from a world in black and white to a world of color*."[117]

This is the kind of life-altering impact ADT has had on the lives of countless patients across the United States. FDA's classification of ADT as a biological product threatens to cause significant harm to the many patients that have relied on this vital medication for years. It is therefore in the best interest of the public that FDA ensure the availability of ADT by revoking its classification of ADT as a biological product and regulate ADT as a drug.

As discussed in Part B.II., hypothyroidism is associated with a wide range of symptoms that can profoundly affect nearly every aspect of daily life. Common manifestations include persistent fatigue and energy depletion, cold intolerance, unexplained weight gain, hair loss, dry skin, brittle nails, gastrointestinal dysfunction, cardiovascular complications, musculoskeletal pain, joint inflammation and myxedema, fibromyalgia and reproductive harm, not to mention the cognitive symptoms such as intense brain fog, depression, and anxiety. When thyroid function is poorly managed through suboptimal treatment, patients often continue to suffer diminished quality of life, feeling unheard by medical professionals and inadequately treated. Poorly controlled hypothyroidism can also serve as a gateway to additional autoimmune conditions, including celiac disease, rheumatoid arthritis, and Type 1 Diabetes, compounding the already heavy burden on patients' physical and emotional health. Ultimately, effective thyroid management requires attentive, patient-centered care that prioritizes symptom resolution and overall well-being, and this care can only be offered when providers have access to all viable treatment options. This must include ADT.

i. Physicians That Specialize in Hypothyroidism Rely on Compounded ADT Products.

In support of this petition, two prominent physicians known for their practice of treating patients with thyroid conditions provided statements explaining the critically important nature of

[115] *City of Billings*, 153 F.4th at 52 (*quoting Shalala v. Guernsey Mem'l Hosp.*, 514 U.S. 87, 99 (1995)).
[116] *See N.H. Hosp. Ass'n*, 887 F.3d at 70-74; *Am. Acad. of Pediatrics v. Food & Drug Admin.*, 379 F. Supp. 3d 461, 497 (D. Md. 2019) (FDA's enforcement discretion guidance was a legislative rule requiring notice and comment rulemaking).
[117] Zielsdorf Statement, at p. 1.

ADT.[118] One, Dr. Brittany Bohinc Henderson, MD, ECNU, has dedicated her career to advancing the diagnosis and treatment of thyroid disease.[119] She developed an interest in ADT when she realized that the FDA-approved thyroid medications (i.e., Synthroid, Tirosint, Levoxyl, and Unithroid, all of which contain Levothyroxine as the only active ingredient) were insufficient to fully control thyroid disease in many of her patients. And although many of these patients could tolerate the manufactured ADT products (e.g., NP Thyroid and Armour Thyroid), some could not tolerate the fillers or the pharmacodynamics of an instant release, manufactured product, and they required a compounded ADT formulation that is slower release. The ability to have various medication formulations available is essential to quality of life and resolution of thyroid symptoms in this patient population. When dosed appropriately, ADT products can mimic normal thyroid function and restore clinical euthyroidism. For these patients, there is often no adequate FDA-approved or commercially manufactured substitute.

To Dr. Henderson, FDA's classification of ADT as a biologic product "has become a human rights issue." She has patients who have had their thyroid removed due to cancer, multinodular goiter, Graves' Disease or due to other reasons and require lifelong thyroid replacement medicine. Many of these patients also have autoimmune thyroiditis, the most common reason for thyroid disease in the developed world, and thus have sensitivities to many of the FDA-approved drug excipients. Many of the ADT products have no dyes and fewer excipients, allowing for improved tolerability. Importantly, many patients report substantially improved well-being and markedly fewer side effects on ADT products. Because the science of why some patients do better on one formulation vs. another is still evolving, Dr. Henderson believes it is ***imperative*** that individual clinical judgement be respected and preserved.

The second provider, Dr. Sarah J. Zielsdorf, MD, MS, is a board-certified internal medicine physician and Institute for Functional Medicine Certified Practitioner (FMCP-M) with over ten years of experience in functional and internal medicine.[120] Her experience with ADT is both professional and personal. On a professional level, her practice actively treats around 2,000 patients, the strong majority of whom are being treated for thyroid management. But on a personal level, Dr. Zielsdorf is also intimately familiar with thyroid management. She was diagnosed with hypothyroidism at age 19. Despite being prescribed FDA-approved Synthroid, her condition continued to deteriorate because her body was not converting T4 to T3. Dr. Zielsdorf was eventually bedbound, gained 50 pounds, lost her menstrual cycle, developed severe liver problems, was told she could never have children, and, at the worst, had difficulty speaking her own name. Upon being treated with ADT, she "felt like going from a world in black and white to a world of

[118] Zielsdorf Statement, at p. 1-2; Henderson Statement, at p. 1-3.

[119] Henderson Statement, at p. 1. Dr. Henderson currently serves as Chief Medical Officer and owner of the Charleston Thyroid Center and as Chief Medical Officer of MyThyroidDoctor.com, a telemedicine thyroid practice. She has held faculty and medical director roles in endocrinology at Duke University and Wake Forest Baptist Health, where she directed the Thyroid & Endocrine Neoplasia Clinic and the Fellows Thyroid Ultrasound and Biopsy Clinic, and is the author of 20 peer-reviewed publications on thyroid-related topics. At any given time, her practice has 20,000 active patients from across the U.S. who are seeking treatment for thyroid management, and approximately 15% of these patients are being successfully treated with ADT medications.

[120] Zielsdorf Statement, at p. 1. Dr. Zielsdorf is the owner and medical director of Motivated Medicine, PLLC, a functional and translational/internal medicine practice in Illinois, which focuses on complex chronic and autoimmune-driven illnesses, including thyroid disease, sex hormone management, and adrenal disorders. Dr. Zielsdorf has specifically addressed thyroid conditions in her clinical and educational work and has authored numerous publications on thyroid disease management and presented on the topic at many professional conferences.

color." Within just months her health improved, her menstrual cycle returned, and she became pregnant. Dr. Zielsdorf fights for the availability of ADT because this particular medication has the ability to be the difference between profound, debilitating illness and a vibrant, thriving life.

ii. Compounding Pharmacies Safely Produce Customized ADT Therapies.

Many compounding pharmacies dispense prescriptions for ADT, and several pharmacists were eager to contribute to the statements of support for this petition. It is the shared hope of these pharmacists to preserve the practice of compounding ADT to ensure that those patients who rely on these medications are able to get the treatment they need. In response to growing prescription volume and patient demand, these pharmacies have each dispensed hundreds of, and in some cases more than 1,000, ADT prescriptions in a given year. These statistics reflect a fraction of the pharmacies in the U.S. that serve thyroid patients, but they demonstrate a clear and sustained clinical need for compounded ADT.

The pharmacies recognize FDA's concerns with ADT's potency, content uniformity, labeling, impurity, and manufacturing quality in the 2025 Notice to Industry. The pharmacies do not seek to dismiss those concerns—thyroid medications require careful dosing and monitoring and appropriate quality controls, and FDA is right to consider them. However, the Agency's concerns do not support a categorical conclusion that ADT products are unsuitable for continued patient access through compounding. Instead, the quality system concerns identified by FDA in the 2025 Notice are already adequately addressed through targeted, risk-based measures.

Specifically, pharmacies already employ rigorous quality and safety controls to ensure the safety of compounded medications. Their processes include vendor qualification to ensure that API manufacturers are registered with and inspected by FDA, Certificate of Analysis review, and verification of acceptance criteria and internal specifications for the USP monograph for thyroid, among many others. For example, VLS Pharmacy performs weighted calculations for every capsule and maintains a method of validation from lowest to highest dose, with all compounding performed in strict accordance with USP standards.[121] As part of the quality assurance practice for Clark's Compounding Pharmacy and Kusler's Compounding Pharmacy, the pharmacies screen for allergies, drug interactions, and recalls, source exclusively from FDA-registered manufacturers and state-licensed wholesalers, and screen Certificates of Analysis for microbial growth, residual solvents, mold, and yeast as part of the USP monograph process.[122] Notably, none of these pharmacies has ever received a patient or provider complaint related to the quality of a compounded ADT product, and has never received a report of a serious adverse event related to compounded ADT.

Moreover, it is safer to compound with ADT as an API than with pure T4 or T3 on its own. From a potency standpoint, pure T3 and pure T4 are each extremely potent and are dosed in micrograms (i.e., one one-thousandth of a single milligram). Even with the most diligent processes, there is still a far greater risk of inconsistent potencies in individual capsules of T3 or T4 than there is in compounding with ADT, which is dosed in milligrams. Further, ADT also has a monograph,

[121] Gopesh Patel, R.Ph., Statement of Support, at p. 1-2 (hereinafter "*Patel Statement*"), enclosed herein as Exhibit 12.
[122] Ipsen Statement, at p. 2; *see also* Steve Hoffart, PharmD, FAAMM, ABAAHP, Statement of Support, p. 1-2, enclosed herein as Exhibit 11; Koshland Statement, at p. 1-2.

which makes it more straightforward and easier to compound with than pure T3 or T4.[123] Accordingly, classification of ADT as a biologic causes more problems than it solves by failing to provide a reasonable alternative for patients who will be harmed by the lack of access.[124]

These pharmacists demand access to ADT because they share a common interest—they want what is best for their patients. And, what is best for their patients is the ability to dispense the medication that is the best fit for the patient. In many cases, this best fit is compounded ADT.

iii. Patients Will Suffer Without Compounded ADT.

Classifying ADT as a biological product will result in clinically meaningful deterioration for patients who cannot tolerate FDA-approved alternatives or for whom these alternatives simply do not work. The classification removes a vital treatment option that is genuinely life-altering for the patients who depend on it; patients who have likely already exhausted all FDA-approved alternatives and only arrive at a compounding pharmacy when nothing else on the market has worked for them. Those who cannot access proper thyroid treatment cannot live normal lives—they experience energy loss, cognitive impairment and brain fog, weight gain leading to other chronic illnesses, systemic inflammation, and autoimmune reactions, which can render patients bedridden.[125] One pharmacist believes that this classification will cause "one hundred percent of affected patients [to] seek these medications from unregulated overseas pharmacies or from the black market," thereby profoundly harming patients whose quality of life will diminish significantly without proper dosing from a licensed pharmacy under physician supervision.[126]

For example, one patient reported that, despite working in the fitness industry for 15 years, she experienced complete lethargy, unexplained and unexpected weight gain, inflammation, and brain fog. She felt like she lost control of her life. When she was diagnosed with a thyroid issue, however, she was prescribed a combination of FDA-approved synthetic levothyroxine and Armour Thyroid, which she took for eight years. Unfortunately, her symptoms prevailed and she did not get better. However, everything changed when she was prescribed a compounded ADT medication. Thanks to the compounded formulation, her thyroid levels stabilized and she only has to get bloodwork done every six months rather than every three months (which was the frequency when she was on synthetic levothyroxine and Armour Thyroid). Importantly, her brain fog vanished, her energy returned, and her weight gain resolved.[127]

Another patient was living with Hashimoto's disease for almost 20 years and was initially prescribed FDA-approved Synthroid. He took Synthroid for nine to ten years but continued to feel worse. Synthroid was not working for him because of its rapid release nature once it is ingested. By contrast, when he was eventually prescribed a compounded ADT medication, it was formulated to be slow-release and better mimic his body's natural thyroid pattern. This medication "genuinely gave [him his] life back." He transitioned from an obese, inactive individual to an athlete and his ability to function day to day was restored. Now, he is more physically active than ever before, and he participates in competitive events like triathlons and ultra marathons.[128] This is not a minor

[123] Koshland Statement, at p. 2.
[124] Jerry Beamer, R.Ph., Statement of Support, p. 2, enclosed herein as Exhibit 8.
[125] Ipsen Statement, at p. 2-3.
[126] Patel Statement, at p. 2.
[127] Amanda Murdock, Statement of Support, p. 1, enclosed herein as Exhibit 13.
[128] Ashley Neboschick, Statement of Support, p. 1, enclosed herein as Exhibit 14.

difference—in his words, "it is literally the difference between me taking a medication that simply keeps me alive and a medication that allows me to function and thrive on a daily basis."[129]

A third patient shared these experiences. When she was first diagnosed, she was prescribed Synthroid, but this medication did not help her. She experienced brain fog, fatigue, weight gain, puffy eyes, cold hands and feet, dry hair, constipation, and bloating. When she was finally switched to an ADT medication, her condition significantly improved. Her weight returned to normal, her digestion improved, she experienced relief from chronic fatigue, and her energy levels stabilized. She had been on some form of thyroid medication for over 15 years, and ADT is the only medication that has worked for her. As a Certified Physician Assistant with over 11 years of experience in thoracic surgery and functional medicine, she often sees these same results in her patients.[130]

Classifying ADT as a biologic and thus revoking access to compounded ADT formulations will cause serious, tangible harm to patients who have no viable alternative. In many cases, these patients have already endured years on FDA-approved synthetic medications that failed them, yet FDA seems inclined to effectively force patients back on these drugs that will certainly diminish these patients' quality of life. ADT is a life-changing medication, and it is in the best interest of the public that FDA revoke its classification of ADT as a biological product and regulate ADT as a drug.

IV. Conclusion.

For the reasons stated above, we ask that FDA revoke the Agency's determination that ADT products are classified as biological products; announce that FDA will classify ADT as a drug; and withdraw the September 16, 2022 letter to NABP and the August 6, 2025 letter to manufacturers, importers, and distributors of animal-derived thyroid products, and any other publication in which FDA describes ADT as being subject to the "biological product" definition. FDA's decision to classify ADT as a biologic is defective because it is inconsistent with the statutory requirements for a biological product, it was determined in an arbitrary and capricious manner and failed to use the required notice-and-comment process, and puts consumers into harm's way by providing no other pathway to address their critical needs.

C. Environmental Impact

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.30.

[129] *Id.*
[130] Larisa Baldwin, PA-C, Statement of Support, p. 1-2, enclosed herein as Exhibit 15.

Docusign Envelope ID: E0F4EE6C-56AE-8C96-829A-3FA09FC5DCE6

BLANKROME

D. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.



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EXHIBIT 1

2022 Pharmacist Letter

U.S. FOOD & DRUG ADMINISTRATION

September 16, 2022

Lemrey "Al" Carter, MS, PharmD, RPh
Executive Director/Secretary
National Association of Boards of Pharmacy
1600 Feehanville Dr
Mount Prospect, IL 60056
acarter@NABP.pharmacy

Dear Dr. Carter:

The purpose of this letter is to bring to the attention of the National Association of Boards of Pharmacy (NABP) that the Food and Drug Administration (FDA) is aware of desiccated thyroid extract (DTE) that appears to have been prepared by state-licensed pharmacies being offered to patients. These products can put patients at harm. We encourage you to share this information with your members.

There are two types of thyroid replacement therapies: (1) synthetic therapies containing only levothyroxine or liothyronine; and (2) therapies made from DTE, which is produced from dried ground animal thyroid glands. DTE is sold in the United States as Armour Thyroid, NP Thyroid, Nature-Throid, and Natural Thyroid, among other names.

While synthetic thyroid replacement therapies containing only levothyroxine or liothyronine are drugs subject to approval under the Federal Food, Drug, and Cosmetic Act (FD&C Act), therapies containing DTE are biological products subject to licensure under section 351 of the Public Health Service Act (PHS Act).

DTE products meet the definition of a "biological product" under section 351(i) of the PHS Act (21 U.S.C. § 262(i)). Under that definition, a "biological product" is "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, *protein, or analogous product*, . . . applicable to the prevention, treatment, or cure of a disease or condition in human beings." 21 U.S.C. § 262(i)(1) (emphasis added). FDA's regulations define the term "protein" in the statutory definition of "biological product" to mean "any alpha amino acid polymer with a specific, defined sequence that is *greater* than 40 amino acids in size" (see 21 CFR 600.3(h)(6); see also 85 FR 10057). DTE meets the definition of a biological product because it is a "protein" or "analogous" to a protein. DTE is derived from animal thyroid glands (usually porcine, meaning from a pig) and necessarily contains thyroglobulin, an alpha amino acid polymer with a specific defined sequence, consisting of 2,770 amino acids.

Section 351(a)(1) of the PHS Act prohibits the introduction into interstate commerce of any biological product unless "a biologics license . . . is in effect for the biological product." Biological products subject to licensure under section 351 of the PHS Act are not eligible for the exemptions for compounded drug products under sections 503A and 503B of the FD&C Act.

FDA has not approved any biologics license applications (BLAs) for DTE products. Some biological products, including thyroglobulin products, had historically been approved under section 505 of the FD&C Act (21 U.S.C. § 355). However, the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) required that as of March 23, 2020, all sponsors seeking approval of a biological product that previously could have been submitted under section 505 of the FD&C Act (21 U.S.C. § 355) must submit a BLA under section 351 of the PHS Act (42 U.S.C. § 262).

In addition, unlicensed DTE products have not been reviewed by the FDA to ensure safety, purity, and potency, and therefore may present issues with respect to quality and dosing, among other things. For example, tablets made from the same batches may not always have the same hormone levels. Inconsistent dosage can have serious consequences for patients; too much medication can cause bad side effects, and too little can be ineffective. As a reminder, FDA does not interact with the vast majority of licensed pharmacists and licensed physicians who compound drug products, because these compounders are not licensed by FDA and generally do not register their facilities with FDA. Therefore, FDA is often not aware of potential problems with their compounded drug products or compounding practices unless it receives a complaint. Recently, FDA has received complaints related to the safety, purity, and potency of unlicensed DTE products that appear to have been prepared by state-licensed pharmacies.

We advise that you encourage state boards of pharmacy to submit to FDA any concerns or questions involving the preparation of biological products, including DTE, outside the scope of an approved BLA. States that wish to provide this information to FDA should submit the information by email to the following mailbox: compounding@fda.hhs.gov.

We are also sending this letter to the Federation of State Medical Boards to facilitate communication among associations with shared goals regarding these matters.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

We look forward to continuing to work with you on matters related to human drug compounding. If you have additional questions, please contact the Office of Compounding Quality and Compliance at compounding@fda.hhs.gov.

Sincerely,

Shannon Glueck, PharmD
Branch Chief
Branch 4
Division of Compounding II
Office of Compounding Quality and Compliance
Office of Compliance
Center for Drug Evaluation and Research

EXHIBIT 2

2025 Notice to Industry

VIA EMAIL

August 6, 2025

NAME
FIRM
ADDRESS
EMAIL

RE: _____

Dear Manufacturers, Importers, and Distributors of Animal-Derived Thyroid Products:

The Food and Drug Administration (FDA or we) intends to take action against marketed unapproved animal-derived thyroid (ADT) products (sometimes described as desiccated thyroid extract (DTE) products). ADT products require an approved biologics license application (BLA) under section 351 of the Public Health Service (PHS) Act in order to be legally marketed in the U.S. (42 U.S.C. 262(a)(1)). There are no FDA-approved BLAs for the ADT products currently on the market.

As described in more detail below, FDA intends to take action against marketed unapproved ADT products. To provide notice to manufacturers, importers, and distributors, we are issuing this letter. This notice also serves to promote compliance with FDA's premarket approval requirements. In addition, the timing further discussed below is intended to provide patients currently using these products sufficient time to work with their healthcare providers to transition to an FDA-approved thyroid hormone replacement product.

BACKGROUND

Overt hypothyroidism, a condition of decreased thyroid hormone production from the thyroid gland, affects approximately 2% of the adult population in the U.S.[1] Thyroid hormone replacement products treat hypothyroidism by replacing the hormones that patients need to

[1] Wyne KL et al, 2022, Hypothyroidism Prevalence in the United States: A Retrospective Study Combining National Health and Nutrition Examination Survey and Claims Data, 2009–2019, J Endocr Soc, 7(1): bvac172.

maintain normal circulating thyroid hormone levels and thereby prevent or improve symptoms of hypothyroidism, such as fatigue, weight gain, constipation, cold intolerance, or depressed mood, among others. In general, thyroid hormone replacement products have a narrow therapeutic index, meaning that tight dose regulation is needed to maintain circulating thyroid hormone levels within a narrow therapeutic range.[2]

ADT products were the first pharmacological treatments developed for replacement or supplemental therapy in patients with hypothyroidism and have been in use for this purpose since the late 19th century.[3,4] ADT is a naturally derived mixture from animal thyroid glands. Initially, these products were derived from bovine (cow), ovine (sheep), or porcine (pig) thyroid glands, but currently most ADT products are porcine-derived thyroid extracts.

ADTs are no longer the predominant source of thyroid hormone replacement. Synthetic liothyronine sodium (LT3 or synthetic liothyronine) and synthetic levothyroxine sodium (LT4 or synthetic levothyroxine) became commercially available following FDA approval in 1956 and 2002, respectively.[5,6] These synthetic products provide an approved safe and effective alternative to ADT products for treatment of hypothyroidism. In 2024, approximately 94% of the 24 million patients receiving thyroid hormone replacement were prescribed synthetic levothyroxine sodium, while only 6% (1.5 million patients) received unapproved ADT products.[7] FDA is unaware of any studies demonstrating the safety and effectiveness of ADT products, meaning the benefits and risks of treatment with ADT products have not been adequately assessed.

Certain safety and effectiveness concerns about unapproved ADT products guided current recommendations by professional medical societies and shifted prescribing practices. These concerns include inconsistent potencies from batch to batch of the unapproved ADT products, the

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[2] FDA, Guidance for Industry: Levothyroxine Sodium Tablets – In Vivo Pharmacokinetic and Bioavailability Studies and In Vitro Dissolution Testing (December 2000). FDA guidances are available on the FDA guidance web page. FDA updates guidances periodically. To make sure you have the most recent version of a guidance, check the guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[3] FDA, Older Therapies Aren't Necessarily Better for Thyroid Hormone Replacement, https://www.fda.gov/consumers/consumer-updates/older-therapies-arent-necessarily-better-thyroid-hormone-replacement.

[4] Connelly KJ, Park JJ, and LaFranchi SH, 2022, History of the Thyroid, Horm Res Paediatr, 95(6): 546-556.

[5] NDA 010379. Drugs@FDA: FDA-Approved Drugs; https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=010379.

[6] NDA 021402. Drugs@FDA: FDA-Approved Drugs; https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=021402.

[7] Symphony Health. Metys. Data extracted February 2025. Percentages shares may sum to more than 100 percent due to patients who may have received more than one product category in a calendar year.

potential for viral contamination due to the animal source, and supraphysiological levels of the thyroid hormone triiodothyronine (T3) provided by the ADT products, which may result in symptoms of hyperthyroidism.[8,9,10,11,12,3,13]

LEGAL AND REGULATORY HISTORY

ADT products meet the definition of a "biological product" in section 351(i)(1) of the PHS Act (42 U.S.C. 262(i)(1)) because ADT (the drug substance) is a "protein" or because it is "analogous" to a protein. FDA's regulations define "protein" to mean "any alpha amino acid polymer with a specific, defined sequence that is greater than 40 amino acids in size" (21 C.F.R. 600.3(h)(6)). ADT is derived from animal (usually porcine) thyroid glands and is a naturally derived mixture that necessarily contains thyroglobulin, an alpha amino acid polymer with a specific defined sequence consisting of 2,770 amino acids. In animal thyroid preparations such as porcine-derived ADT, the thyroid hormones T3 and thyroxine (T4) are incorporated into the thyroglobulin by peptide bonds, and ADT also may contain free T3 and free T4.[14] Following oral administration of an ADT tablet, for example, the proteolytic enzymes of the gastrointestinal tract release iodothyronines and iodotyrosines (including T3 and T4) from the thyroglobulin.[10] ADT that is composed primarily of protein components (e.g., thyroglobulin) is a "biological product" because it falls within the Agency's interpretation of the statutory term "protein" (see 21 C.F.R. 600.3(h)(6)).

Alternately, ADT is "analogous" to a protein, and, thus, a "biological product" because it includes an identified biological product component (i.e., thyroglobulin) that is necessary for the activity of the product and contributes to achieving the intended therapeutic effect and also may include identified non-biological product components (e.g., free T3 and free T4) that can contribute to the product's activity.

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[8] Jackson IM and Cobb WE, Why does anyone still use desiccated thyroid USP?, 1978 Am J Med 64(2): 284-288.
[9] Penny R and Frasier SD, 1980, Elevated serum concentrations of triiodothyronine in hypothyroid patients. Values for patients receiving USP thyroid, Am J Dis Child. 134(1): 16-18.
[10] LeBoff MS et al, 1982, Bioavailability of thyroid hormones from oral replacement preparations, Metabolism 31(9): 900-905.
[11] Lev-Ran A, 1983, Part-of-the-day hypertriiodothyroninemia caused by desiccated thyroid, JAMA 250(20): 2790-2791.
[12] MI Surks et al, 1972, A new radioimmunoassay for plasma L-triiodothyronine: measurements in thyroid disease and in patients maintained on hormonal replacement, J Clin Invest. 51(12): 3104-3113.
[13] Jonklaas J et al, 2014, Guidelines for the Treatment of Hypothyroidism: Prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement, Thyroid 24(12): 1670-1751.
[14] Idrees T et al, 2020, Liothyronine and Desiccated Thyroid Extract in the Treatment of Hypothyroidism, Thyroid 30(10): 1399-1413.

Although the majority of therapeutic biological products have been licensed under the PHS Act, some protein products historically had been approved under section 505 of the Federal Food, Drug, and Cosmetic (FD&C) Act. On March 23, 2010, the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) clarified the statutory authority under which certain products would be regulated by amending the definition of a "biological product" in section 351(i) of the PHS Act to include a "protein" (and products "analogous" to a protein) and describing procedures for submission of a marketing application for certain biological products. As of March 23, 2020, all sponsors seeking approval of a biological product that previously could have been submitted under section 505 of the FD&C Act, including ADT products, must submit a marketing application (i.e., a BLA) under section 351 of the PHS Act.

ADT products marketed without a biologics license under the PHS Act are unapproved biological products. This includes ADT products that are prepared by a licensed pharmacist in a state-licensed pharmacy or a federal facility, a licensed physician, or an outsourcing facility. Biological products subject to licensure under section 351 of the PHS Act are not eligible for the exemptions for compounded drugs under sections 503A and 503B of the FD&C Act, nor is there an exemption under section 351 of the PHS Act from the requirement to have an approved BLA.[15]

SAFETY, EFFECTIVENESS, AND QUALITY CONCERNS WITH UNAPPROVED ADT PRODUCTS

Unlike approved biological products, unapproved ADT products currently on the market have not undergone FDA's premarket evaluation, which involves, among other things, an assessment of manufacturing processes and controls, evaluation of labeling, and examination of ADT supplier suitability. Unapproved ADT products have presented issues with potency, content uniformity, labeling, and impurities identified through inspections, sampling, and patient complaints. These products pose unique risks compared to synthetic thyroid drug products because they are derived from animal thyroid glands, potentially containing process-related impurities, elemental impurities, and ADT-unique impurities (e.g., organic iodine and inorganic iodide) and contaminants (e.g.,

[15] For additional discussion of FDA policies pertaining to the mixing, diluting, and repackaging of approved biological products, see FDA's Guidance for Industry: Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application (January 2018). This guidance is currently available at https://www.fda.gov/media/90986/download. FDA updates guidances periodically. To make sure you have the most recent version of a guidance, check the guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents

viruses and other objectionable microbes). The potency and bioavailability of unapproved ADT products can be highly variable both between batches and within batches, creating uncertainty about the quantity of active hormones delivered, which is particularly concerning given the narrow therapeutic index for thyroid replacement therapies where minor dose changes can lead to serious adverse effects.

Since late 2017, FDA inspections of ADT manufacturers, ADT product manufacturers, and ADT product distributors have identified significant current good manufacturing practice (CGMP) violations, resulting in warning letters, an import alert, and recalls due to issues including, but not limited to: inadequate quality unit oversight, lack of stability data to support labeled expiration dates, failure to investigate out-of-specification results, and manufacturing processes not operating in a state of control. FDA is aware of over 500 adverse event reports associated with ADT products from 1968 through February 2025, with a substantial increase between 2019-2020 that may have been related to several voluntary recalls of subpotent or superpotent ADT products.

Additionally, unapproved ADT products have inconsistent labeling that does not comply with regulatory standards, with some products including the non-metric unit of measurement of “grain” and using different measurements for one "grain" (ranging from 60 mg to 65 mg), creating confusion and potential dosing errors that FDA premarket review could prevent.

RISK-BASED PATIENT TRANSITION PERIOD

FDA understands that a significant number of patients currently take unapproved ADT products. We believe it will require up to 12 months to safely transition patients to an FDA-approved thyroid hormone replacement product. FDA intends to provide adequate time to transition patients to an FDA-approved thyroid hormone replacement product before initiating action against manufacturers, distributors, and importers of ADT and unapproved ADT products intended for commercial distribution. During this time, FDA will continue to apply a risk-based enforcement policy.[16]

It is your responsibility to ensure that your firm complies with all applicable requirements of

[16] See 85 FR 75331 (Nov. 25, 2020) and 86 FR 28605, 28608 (May 27, 2021) (“FDA will continue to exercise its existing general approach to prioritizing regulatory and enforcement action [for marketed unapproved new drugs], which involves risk-based prioritization in light of all the facts of a given circumstance.”).

federal law and FDA regulations. Within 30 working days from the date of receipt, please acknowledge receipt of this letter by emailing FDAADVISORY@fda.hhs.gov. Please include your firm name and the unique identifier "_____" in the subject line of the email.

Sincerely,

U.S. Food and Drug Administration

U.S. Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993
www.fda.gov

EXHIBIT 3

Warning Letter to Acella Pharmaceuticals, LLC

WARNING LETTER

Acella Pharmaceuticals, LLC

MARCS-CMS 604438 — AUGUST 14, 2020

More Warning Letters (/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters)

Delivery Method:

VIA Electronic Mail

Product:

Drugs

Recipient:

Harold A. Deas, Jr.

Chief Executive Officer

Acella Pharmaceuticals, LLC

1880 McFarland Parkway
Suite 110-B
Alpharetta, GA 30005-1794
United States

Issuing Office:

Office of Pharmaceutical Quality Operations, Division II

United States

Mr. Deas:

The U.S. Food and Drug Administration (FDA) inspected your facility, Acella Pharmaceuticals, LLC, FEI 3006691461, at 1880 McFarland Parkway, Suite 110-B, Alpharetta, Georgia, from December 17, 2019, to January 7, 2020.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug product is adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

Additionally, your NP Thyroid drug products are adulterated under section 501(b) of the FD&C Act, 21 U.S.C. 351(b), for failure to conform to compendial standards for strength, quality, or purity.

Feedback

Information and records gathered during the course of the inspection and information available on your website, www.acellapharma.com, reflect that your products are intended to treat a disease or condition. Therefore, your NP Thyroid products are drugs as defined in section 201(g) of the FD&C Act, 21 U.S.C. 321(g). Your products, which contain thyroglobulin (an alpha amino acid polymer with a specific defined sequence consisting of 2770 amino acids), are also biological products as defined in section 351(i)(1) of the Public Health Service Act (PHS Act), 42 U.S.C. 262(i)(1) because they are a “protein” as defined in 21 C.F.R. 600.3(h)(6), or are “analogous” to a protein because the identified biological product (i.e., protein) component in these naturally derived mixtures is necessary for the activity of the product and contributes to achieving the intended therapeutic effect.

We reviewed your January 28, 2020, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence on February 28, 2020, on March 31, 2020 and on April 17, 2020.

During our inspection, our investigators observed specific violations including, but not limited to, the following.

1. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity (21 CFR 211.160(b)).

In your quality agreement with your contract manufacturer (CMO), **(b)(4)**, both you and your CMO are responsible for determining adequate drug specifications. The active ingredient assay specification you developed with your CMO for levothyroxine and liothyronine in your NP Thyroid products were not appropriate. The active ingredient assay specifications you established with your CMO for levothyroxine and liothyronine was **(b)(4)**. However, the United States Pharmacopeia (USP) monograph for Thyroid Tablets, USP has levothyroxine and liothyronine assay acceptance criteria of **(b)(4)**. Thyroid Tablets outside of the USP acceptance criteria are adulterated within the meaning of 501(b) of the FD&C Act, 21 U.S.C. 351(b), in that their strength, quality, or purity falls below the standards set forth in an official compendium recognized in the FD&C Act.

We acknowledge that you updated the NP Thyroid active ingredient assay specification as committed in your April 17, 2020, letter. This communication also indicated that there were no lots released exceeding 110.0% made with your current active pharmaceutical ingredient (API) supplier and current process. However, FDA inspected your CMO from May 5 to 15, 2020, and found 13 lots within expiry made with your previous API supplier that exceeded 110.0% USP specification during release or stability testing. We acknowledge that your firm subsequently agreed to voluntarily recall these 13 lots. However, these lots should have been identified in your earlier investigation and communication.

In response to this letter, provide:

• A review of all other products that you are the product owner or own-label distributor to determine whether or not their specifications are appropriate and justifiable. Conduct a risk assessment for any products and corresponding lots lacking appropriate and justifiable specifications. If any products are found to be outside of compendial standards or other appropriate specifications, indicate the corrective actions you will take, including notifying customers and initiating recalls.

• Updated procedures to ensure that product specifications undergo a routine review to ensure they remain appropriate.

2. Your firm failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products (21 CFR 211.22(a)).

Your quality control unit failed to provide adequate oversight of your CMO to ensure that expiration dating claims were supported by adequate stability data. Per the quality agreement with your CMO, both you and your CMO are responsible for all label claims for the product, including any expiration dating claims.

FDA inspected your CMO May 5 to 15, 2020, and found there was no long-term stability data to support the batches that had been manufactured with your new API supplier. The validation batches manufactured by your CMO using the new API supplier were made in May and June 2019, yet were not placed into a long-term stability study until May 1, 2020.

Furthermore, your firm was responsible for auditing your CMO to ensure a stability program was appropriately implemented and followed. Stability data is critical for ensuring that products maintain their identity, strength, quality, purity, and safety throughout their labeled shelf-lives.

In response to this letter, provide:

• An action plan with timelines and a summary of results from testing retain samples of all NP Thyroid batches within expiry. You should test all appropriate quality attributes including, but not limited to, identity and strength of active ingredients of each batch. If testing yields an OOS result, indicate the corrective actions you will take, including notifying customers and initiating recalls.

• A comprehensive assessment and remediation plan to ensure your QU is given the authority and resources to effectively function. The assessment should also include, but not be limited to:
o A determination of whether procedures used by your firm are robust and appropriate;
o Provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices;
o Oversight and approval of investigations and discharging of all other QU duties to ensure identity, strength, quality, and purity of all products; and,

• A description of improvements to your procedures and processes for conducting audits of your contract manufacturers to ensure that they operate in compliance with CGMP.

FDA Sample Results of Thyroid Tablets

FDA sampled NP Thyroid (Thyroid Tablets, USP), 120mg strength lot M328J19-8 from your facility and found low, out-of-specification results for both active ingredients. Because of the narrow therapeutic range of this product, content uniformity is critical and it is especially important to prevent patients with hypothyroidism from receiving insufficient or excessive doses. We acknowledge that your firm did not distribute this lot from your contract warehouse and agreed to voluntarily destroy it.

Use of Contract Manufacturers

Drugs must be manufactured in conformance with CGMP. FDA is aware that many drug manufacturers use independent contractors such as production facilities, testing laboratories, packagers, and labelers. FDA regards contractors as extensions of the manufacturer.

You are responsible for the quality of your drugs regardless of agreements in place with your contract facilities. You are required to ensure that drugs are made in accordance with section 501(a)(2)(B) of the FD&C Act to ensure safety, identity, strength, quality, and purity. See FDA's guidance document *Contract Manufacturing Arrangements for Drugs: Quality Agreements* at https://www.fda.gov/media/86193/download (/media/86193/download).

Unapproved New Drugs

Based on the information your firm submitted to FDA's electronic Drug Registration and Listing System and the information collected during the December 17, 2019 – January 7, 2020 inspection, FDA has determined that your firm is distributing NP Thyroid, a biological product, without FDA approval or a valid biologics license.

We encourage you to contact FDA's unapproved drugs coordinator, Dr. Sally Loewke, at 301-796-0710 for assistance in communicating with the FDA on the application process for your unapproved biological product.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive list of violations that exist in connection with your product(s). You are responsible for investigating and determining the causes of these violations and for preventing their recurrence or the occurrence of other violations.

If you are considering an action that is likely to lead to a disruption in the supply of drugs produced on your behalf, FDA requests that you contact CDER's Drug Shortages Staff immediately, at drugshortages@fda.hhs.gov (mailto:drugshortages@fda.hhs.gov), so that FDA can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Staff also allows you to meet any obligations you may have to report discontinuances or interruptions in your drug supply under 21 U.S.C. 356C(b). This also allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on your products.

Correct the violations cited in this letter promptly. Failure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction. Unresolved violations in this warning letter may also prevent other Federal agencies from awarding contracts.

FDA may also withhold approval of requests for export certificates and approval of pending new drug applications or supplements listing your facility as a supplier or manufacturer until the above violations are corrected. We may re-inspect to verify that you have completed your corrective actions.

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your violations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Please identify your response with FEI 3006691461. Send your electronic reply to Dr. Shawn Larson – Compliance Officer at Shawn.Larson@fda.hhs.gov (mailto:Shawn.Larson@fda.hhs.gov) and ORAPHARM2_Responses@fda.hhs.gov (mailto:ORAPHARM2_Responses@fda.hhs.gov).

If you have questions regarding the contents of this letter, please contact Dr. Larson at 214-253-5216.

Sincerely,
/S/
Tamala Bogan
Acting Program Division Director
Office of Pharmaceutical Quality Operations,
Division II

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EXHIBIT 4

Warning Letter to RLC Labs

WARNING LETTER

RLC Labs Inc.

MARCS-CMS 607596 — OCTOBER 09, 2020

More Warning Letters (/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters)

Delivery Method:

VIA SIGNATURE CONFIRMED DELIVE

Product:

Drugs

Recipient:

Mr. Ricky L. Cox

President and CEO

RLC Labs Inc.

1850 E Riverview Dr

Phoenix, AZ 85034-6703

United States

Issuing Office:

Division of Pharmaceutical Quality Operations IV

United States

WARNING LETTER

October 9, 2020

Dear Mr. Cox:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, RLC Labs Inc., FEI 3002523846, at 1850 E Riverview Drive, Phoenix, Arizona, from February 20 to March 5, 2020.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

Feedback

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Our inspection also revealed that your firm failed to fulfill its registration and listing obligations under section 510(j) of the FD&C Act, which is prohibited under section 301(p), 21 U.S.C. 360 and 331(p). As a result, your drugs are misbranded under section 502(o) of the FD&C Act, 21 U.S.C. 352(o).

Additionally, your WP Thyroid® and Nature-Throid® drug products are adulterated under section 501(b) of the FD&C Act, 21 U.S.C. 351(b), for failure to conform to compendial standards for strength, quality, or purity.

Information and records gathered during the course of the inspection, and information available on your website, www.getrealthyroid.com, reflect that your products are intended to treat a disease or condition. Therefore, your products are drugs as defined in section 201(g) of the FD&C Act [21 U.S.C. 321(g)]. Your products, which contain thyroglobulin (an alpha amino acid polymer with a specific defined sequence consisting of 2770 amino acids), are also biological products as defined in section 351(i)(1) of the Public Health Service Act (PHS Act) [42 U.S.C. 262(i)(1)] because they are a “protein” as defined in 21 C.F.R. 600.3(h)(6) or are “analogous” to a protein because the identified biological product (i.e., protein) component in these naturally derived mixtures is necessary for the activity of the product and contributes to achieving the intended therapeutic effect.

Please be advised that to lawfully market a drug that is a biological product, a valid biologics license must be in effect [42 U.S.C. 262(a)]. Such licenses are issued only after the sponsor shows that the product is safe, pure, and potent. While in the development stage, such products may be distributed for clinical use in humans only if the sponsor has an investigational new drug application (IND) in effect as specified by FDA regulations [21 U.S.C. 355(i); 42 U.S.C. 262(a)(3); 21 CFR Part 312]. None of your products are the subject of an approved biologics license application (BLA), nor is there an IND in effect for any of them. Based on this information, we have determined that your actions have violated the FD&C Act and the PHS Act.

We reviewed your March 26, 2020, response to our Form FDA 483 in detail.

During our inspection, our investigators observed specific violations including, but not limited to, the following.

CGMP Violations

1. Your firm’s quality control unit did not review and approve written procedures for production and process control, including any changes to them, designed to ensure that the drug products you manufacture have the identity, strength, quality, and/or purity they purport or are represented to possess (21 CFR 211.100(a)).

Your firm failed to provide data to demonstrate that your manufacturing processes, including the blending of active pharmaceutical ingredients (API) lots for your WP Thyroid and Nature-Throid drug products, have been validated. During the inspection you could not locate the process validation data to present to the investigators. In addition, critical equipment used to manufacture these drug products were not qualified.

Your response is inadequate. You did not provide the validation data requested at inspection. You proposed to re-initiate the process validation for your drug products. However, you failed to provide interim measures to ensure that your manufacturing processes are in a state of control. Regarding equipment qualifications, you stated that you have initiated qualification activities on some equipment and that you will correct deficient qualification on all drug production equipment. You failed to provide a Master Validation Plan, validation/qualification protocols, and specific timelines for completion.

FDA collected ten samples during the inspection, covering several different strengths of WP Thyroid and Nature-Throid. Six samples were found to be sub-potent for at least one of the two active ingredients. Thyroid Tablets outside of the USP acceptance criteria are adulterated within the meaning of 501(b) of the FD&C Act, 21 U.S.C. 351(b), in that their strength, quality, or purity falls below the standards set forth in an official compendium recognized in the FD&C Act.

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Because of the narrow therapeutic range of this drug product, it is especially important to prevent patients with hypothyroidism from receiving insufficient or excessive doses. Appropriate controls and understanding of your manufacturing process is essential to ensuring a safe and effective drug product. We acknowledge that your firm agreed to voluntarily recall all lots of WP Thyroid and Nature-Throid with current expiry due to sub-potency.

Process validation evaluates the soundness of design and state of control of a process throughout its lifecycle. Each significant stage of a manufacturing process must be designed robustly, controlled appropriately, and assure the ongoing quality of raw material inputs, in-process materials, and finished drugs.

Failure to implement adequate process validation can result in insufficient understanding of process variables or failure to detect a drift in capability, which increases the risk of drug quality defects.

See FDA's guidance document Process Validation: General Principles and Practices for general principles and approaches that FDA considers to be appropriate elements of process validation at https://www.fda.gov/media/71021/download.

In response to this letter, provide:

- A detailed summary of your validation program for ensuring a state of control throughout the product lifecycle, along with associated procedures. Describe your program for process performance qualification, and ongoing monitoring of both intra-batch and inter-batch variation to ensure a continuing state of control.
- A timeline for performing appropriate process performance qualification (PPQ) for each of your marketed drug products.
- Include your process performance protocol(s), and written procedures for qualification of equipment and facilities.
- Provide a detailed program for designing, validating, maintaining, controlling and monitoring each of your manufacturing processes that includes vigilant monitoring of intra-batch and inter-batch variation to ensure an ongoing state of control. Also, include your program for qualification of your equipment and facility.An assessment of each drug product process to ensure that there is a data-driven and scientifically sound program that identifies and controls all sources of variability, such that your production processes will consistently meet appropriate specifications and manufacturing standards. This includes, but is not limited to, evaluating suitability of equipment for its intended use, sufficiency of detectability in your monitoring and testing systems, quality of input materials, and reliability of each manufacturing process step and control.

2. Your firm failed to follow a written testing program designed to assess the stability characteristics of drug products and to use results of stability testing to determine appropriate storage conditions and expiration dates (21 CFR 211.166(a)).

You lack an adequate stability program for your WP Thyroid and Nature-Throid drug products, labeled with two- and three-year expiry periods respectively. During the inspection you provided stability data for drug product manufactured in your previous facility and with an API manufactured by a different supplier. No stability studies have been conducted for these drug products manufactured at your current facility with API from your current supplier.

In response to this observation, you acknowledged expiry dating was based on stability data from 2012 and from drug products manufactured at your previous facility. You proposed to engage a third-party laboratory to perform accelerated and real time stability studies for your drug products. In addition, you committed to test random retain samples of batches.

Your response is inadequate because it lacks stability protocols.

In response to this letter, provide:

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- A comprehensive, independent assessment and corrective action and preventive action (CAPA) plan to ensure the adequacy of your stability program. Your remediated program should include, but not be limited to:

o Stability indicating methods
o Stability studies for each drug product in its marketed container-closure system before distribution is permitted
o an ongoing program in which representative batches of each product are added each year to the program to determine if the shelf-life claim remains valid
o detailed definition of the specific attributes to be tested at each station (timepoint)

- All procedures that describe these and other elements of your remediated stability program.

3. Your firm failed to test samples of each component for conformity with all appropriate written specifications for purity, strength, and quality (21 CFR 211.84(d)(2)).

There is no assurance that the incoming API used to manufacture WP Thyroid and Nature-Throid drug products conforms with appropriate specifications to ensure that it meets the purported purity, strength, and quality. The inspection documented the use of at least **(b)(4)** different assay specifications for Liothyronine (T3) and Levothyroxine (T4). Individual API lots are received and mixed to produce a master blend that is then used to formulate your drug products.

Thyroid hormone drug products have a narrow therapeutic index and require a well-controlled API blend to ensure that finished drug products match their labeled strength. Without adequately established specifications for the API there is a lack of assurance that you can consistently manufacture drug product that meets quality attributes.

In your response, your firm committed to establishing specifications. However, you failed to include a timeline for when specifications would be established or adequate interim measures.

In response to this letter, provide:

- A description of how you will test each component lot for conformity with all appropriate specifications for identity, strength, quality, and purity. If you intend to accept any results from your supplier's Certificates of Analysis (COA) instead of testing each component lot for strength, quality, and purity, specify how you will robustly establish the reliability of your supplier's results through initial validation as well as periodic re-validation. In addition, include a commitment to always conduct at least one specific identity test for each incoming component lot.
- The chemical and microbiological quality control specifications you use to test and release each incoming lot of component for use in manufacturing. Provide the justification for any specification established.
- A summary of results obtained from testing all components to evaluate the reliability of the COA from each component manufacturer. Include your SOP that describes this COA validation program.

4. Failure to establish an adequate quality control unit and the responsibilities and procedures applicable to the quality control unit are not in writing and fully followed. (21 CFR 211.22(a) and 211.22(d)).

Your quality unit (QU) failed to ensure that you have adequate procedures and did not provide adequate oversight of your manufacturing activities. For example:

- You lacked adequate systems to ensure proper documentation of manufacturing activities and for change management.
- Cleaning validation was not performed to demonstrate that cleaning agents are able to safely remove all drug product residues after manufacturing higher dosage products to lower dosage products.
- You lacked a CGMP training program for your employees engaged in CGMP operations.
- You failed to perform and establish procedures for annual product reviews and supplier qualification.

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- You failed to establish appropriate procedures for the handling of rejected materials.

In addition, your quality personnel were unaware of complaint spreadsheets being maintained outside of the quality unit and these complaints were not investigated by the quality unit. Complaints documented in your spreadsheets involving WP Thyroid and Nature-Throid drug products noted many concerns about drug product potency, which were reflected by the failing samples mentioned earlier.

In your response you promised to establish and expand your quality unit, hiring qualified individuals and establishing SOPs. However, you failed to provide sufficient detail or adequate supporting documentation to support your CAPA. No interim measures or procedures were provided.

Significant findings in this letter indicate that your quality unit is not able to fully exercise its authority and/or responsibilities. Your firm must provide the quality unit with the appropriate authority and sufficient resources to carry out its responsibilities and consistently ensure drug quality.

In response to this letter, provide:

- A comprehensive assessment and remediation plan to ensure your QU is given the authority and resources to effectively function. The assessment should also include, but not be limited to:

o A determination of whether procedures used by your firm are robust and appropriate
o Provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices
o A complete and final review of each batch and its related information before the QU disposition decision
o Oversight and approval of investigations and discharging all other QU duties to ensure identity, strength, quality, and purity of all products

Also describe how top management supports quality assurance and reliable operations, including but not limited to timely provision of resources to proactively address emerging manufacturing/quality issues and to assure a continuing state of control.

- A comprehensive, independent assessment of your change management system. This assessment should include, but not be limited to, your procedure(s) to ensure changes are justified, reviewed, and approved by your quality unit. Your change management program should also include provisions for determining change effectiveness.
- Appropriate improvements to your cleaning validation program, with special emphasis on incorporating conditions identified as worst case in your drug manufacturing operation. This should include but not be limited to identification and evaluation of all worst-case:

o drugs with higher toxicities
o drugs with higher drug potencies
o drugs of lower solubility in their cleaning solvents
o drugs with characteristics that make them difficult to clean
o swabbing locations for areas that are most difficult to clean
o maximum hold times before cleaning

In addition, describe the steps that must be taken in your change management system before introduction of new manufacturing equipment or a new product.

- A summary of updated SOPs that ensure an appropriate program is in place for verification and validation of cleaning procedures for products, processes, and equipment.

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See FDA's guidance document Quality Systems Approach to Pharmaceutical CGMP Regulations for help implementing quality systems and risk management approaches to meet the requirements of CGMP regulations 21 CFR, parts 210 and 211 at https://www.fda.gov/downloads/Drugs/Guidances/UCM070337.pdf (https://www.fda.gov/downloads/Drugs/Guidances/UCM070337.pdf).

Unapproved Biological Product Violations

Please be advised that to lawfully market a drug that is a biological product, a valid biologics license must be in effect [42 U.S.C. 262(a)]. Such licenses are issued only after the sponsor shows that the product is safe, pure, and potent. While in the development stage, such products may be distributed for clinical use in humans only if the sponsor has an IND in effect as specified by FDA regulations [21 U.S.C. 355(i); 42 U.S.C. 262(a)(3); 21 CFR Part 312]. None of your products are the subject of an approved BLA, nor is there an IND in effect for any of them. Based on this information, we have determined that your actions have violated the FD&C Act and the PHS Act.

Misbranding Violations

FDA's inspection dated February 20 to March 5, 2020, revealed that RLC Labs Inc. at 1850 E Riverview Dr, Phoenix, Arizona manufactures, labels and distributes porcine-derived thyroid drug tablets for human use under the brand names of WP Thyroid and Nature-Throid.

Section 510(j) of the FD&C Act and 21 Code of Federal Regulations (CFR) Part 207 outline the requirements for establishment registration and listing of drug products. Your firm has failed to maintain its establishment registration and submit drug listing information to the FDA for the drugs manufactured at the above facility, including WP Thyroid and Nature-Throid.

Under section 510(j) of the FD&C Act, your firm failed to fulfill its listing obligations, which is a prohibited act under section 301(p), [21 U.S.C. 360(j) and 331(p)]. In addition, your firm's failure to fulfill its registration obligations misbrands the product(s) you manufacture at this facility under section 502(a) of the FD&C Act, and your firm's failure to fulfill its drug listing obligations misbrands the product(s) under section 502(o) of the FD&C Act. Introduction or delivery for introduction into interstate commerce of a misbranded product is a prohibited act under section 301(a) (21 U.S.C. 352(o) and 331(a)).

CGMP Consultant Recommended

Based upon the nature of the violations we identified at your firm, we strongly recommend engaging a consultant qualified as set forth in 21 CFR 211.34 to assist your firm in meeting CGMP requirements.

Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive list of violations that exist at your facility. You are responsible for investigating and determining the causes of these violations and for preventing their recurrence or the occurrence of other violations.

Correct the violations cited in this letter promptly. Failure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction. Unresolved violations in this warning letter may also prevent other Federal agencies from awarding contracts.

FDA may also withhold approval of requests for export certificates and approval of pending new drug applications or supplements listing your facility as a supplier or manufacturer until the above violations are corrected. We may re-inspect to verify that you have completed your corrective actions.

Top ()

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your violations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion. If you believe that your products are not in violation of the FD&C Act or you have complied with FDA regulations, include your reasoning and any supporting information for our consideration.

Please send your electronic reply to ORAPharm4_Responses@fda.hhs.gov or mail your reply to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
19701 Fairchild Road
Irvine, CA 92612-2506

Please identify your response with unique identifier CMS 607596.

If you have questions regarding any issues in this letter, please contact William V. Millar, Compliance Officer via email at william.millar@fda.hhs.gov or by phone at (503) 671-9711 Ext. 30.

Sincerely,
/S/

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV

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EXHIBIT 5

March 2026 Notice to Industry

VIA EMAIL

March 11, 2026

Dear Manufacturers, Importers, and Distributors of Animal-Derived Thyroid (ADT) Products:

As stated in the Agency's August 6, 2025 letter, "FDA intends to provide adequate time to transition patients to an FDA-approved thyroid hormone replacement product before initiating action against manufacturers, distributors, and importers of ADT and unapproved ADT products intended for commercial distribution. During this time, FDA will continue to apply a risk-based enforcement policy."

Under FDA's current policy, FDA is applying its general, risk-based enforcement approach to unapproved ADT products, giving enforcement priority to drugs that pose the highest risk to public health.

FDA plans to issue draft guidance before August 2026 that describes the Agency's compliance priorities and conditions of continued enforcement discretion for marketed unapproved ADT products. This draft guidance will be issued consistent with good guidance practices. FDA also intends to simultaneously publish a draft guidance regarding the development of ADT products to support submission of marketing applications.

FDA is committed to ensuring patient safety for those patients currently using unapproved ADT products while firms seek approval of marketing applications for ADT products.

If you have any questions related to this notice, please contact FDAADVISORY@fda.hhs.gov, and include your firm name and the unique identifier "XXXXXX" in the subject line of the email.

Sincerely,

U.S. Food and Drug Administration

EXHIBIT 6

Zielsdorf Statement

M O T I V A T E D
M E D I C I N E

480 E. ROOSEVELT RD, SUITE 105
WEST CHICAGO, IL 60185

Statement of Support by Dr. Sarah Zielsdorf

Qualifications

My name is Sarah J. Zielsdorf, MD, MS, and I am a board-certified internal medicine physician and Institute for Functional Medicine Certified Practitioner (FMCP-M) with over ten years of experience in functional and internal medicine. Since 2019, I have been the owner and medical director of Motivated Medicine, PLLC, a functional and translational/internal medicine practice in Illinois. My clinical focus centers on complex chronic and autoimmune-driven illnesses, including thyroid disease, sex hormone management, and adrenal disorders, and I have specifically addressed thyroid conditions in my clinical and educational work. I am also a microbiologist with a unique background treating the relationship between the microbiome and the immune system, which often drives the development of autoimmunity.

I have authored numerous publications on thyroid disease management and presented on the topic at many professional conferences. I also teach compounding pharmacists thyroid hormone replacement formulations and the nuances of prescribing ADT. In addition to my thyroid-focused practice, I maintain active partnerships with compounding pharmacies as an advocate for precision, patient-centered medicine and compounded therapies.

Experience with Treatment of Desiccated Thyroid Medications

Desiccated thyroid ("*ADT*") has been an effective treatment for thyroid hormone replacement since the 1800s, and it remains a clinically necessary treatment today. My experience with ADT is both professional and personal. On a professional level, at any given time my Illinois practice is actively treating 2,000 patients, the strong majority of which are being treated for thyroid management.
On a personal level, I was diagnosed with hypothyroidism at age 19. Despite being prescribed FDA-approved Synthroid, I became sicker and sicker as my body was not converting T4 to T3. I was eventually bedbound, gained 50 pounds, lost my menstrual cycle, developed severe liver problems, was told I could never have children, and, at the worst, had difficulty speaking my own name. My first dose of ADT felt like going from a world in black and white to a world of color. Within just months my health improved, my menstrual cycle returned, and I became pregnant. This is why ADT must remain available to patients—it has the ability to be the difference between profound, debilitating illness and a vibrant, thriving life.

Why is ADT generally preferred over FDA-approved drugs containing Levothyroxine or Liothyronine?

To be clear, I will prescribe whatever my patient needs, whether that be synthetic thyroid medications like Synthroid (Levothyroxine) or Cytomel (Liothyronine), manufactured ADT such as Armour Thyroid or NP Thyroid, or compounded ADT. However, in many instances, such as patients with no thyroid function because their thyroid has been removed, destroyed by Hashimoto's disease, or irradiated, ADT is simply the best option because it is the only medication that makes it possible to fully replace what a patient without a thyroid has lost.

The FDA-approved formulations are often unsuitable for my patients because these products have a variety of excipients, allergens, and antigens that my autoimmune or

immunologically sensitive patients cannot tolerate. Reactions range from joint pain or rash to anaphylaxis and risk of sudden death due to shock and airway collapse. The most common reason for hypothyroidism in the United States is due to Hashimoto's disease, an autoimmune disease which can destroy the thyroid gland and cause loss of function. Autoimmune disease patients make antibodies against proteins, and food colorings/dyes are proteins found in these products. Many of our patients can tolerate very few foods, let alone medication fillers or allergens. I even have some patients so sensitive that they can no longer eat regular food and require amino acid-based nutrition by mouth, or must be tube fed. Other patients, due to extreme gastrointestinal malabsorption from chronic illness (and sometimes specific autoimmune diseases such as atrophic gastritis or pernicious anemia), lose the ability to absorb the regular medications with their fillers. For all of these reasons, these patients need an alternative that provides hypoallergenic or otherwise tolerable filler and individualized dosing. ADT provides this alternative.

The symptoms my patients experience when they are undertreated or unable to tolerate available alternatives can be devastating, including: anaphylaxis, rashes, hives, angioedema, heart palpitations, extreme fatigue, being bedbound, joint pain, fibromyalgia, malabsorption, gastritis, anemia, bacterial overgrowth, painful sores, abnormal blood levels, severe lipid abnormalities, miscarriages, constipation requiring hospitalization, brain fog, and swelling from myxedema. Low T3 is also associated with cardiac side effects, such as arrhythmias and risk of myocardial infarction, which are concerns for patients who are either overmedicated or poorly monitored, or treated with thyroid medication when they do not have hypothyroidism. Indeed, a 2003 cardiac study showed that low T3 was significantly associated with mortality in patients with heart disease.[1] ADT has proven time and time again to be the most medically appropriate treatment for these patients.

I have had several cases of patients with treatment-resistant arrhythmias including bradyarrhythmias (slow heart rate) requiring high doses of T3 to maintain normal rate and rhythm. I had one case where my patient was undergoing cardiac bypass and the in-hospital endocrinologist refused to give my patient her T3 medication. Her heart rate and blood pressure would not normalize even with continuous drips of medications. The patient was so upset and sick that she self-discontinued her own IV and refused further care until she was given her medication that she had been stable on for years prior to surgery. Subsequently, her blood pressure, pulse, heart rhythm, and labs all normalized. We have had innumerable cases of patients treated with ADT or T4/T3 combinations with immediate improvement in all cardiac markers including heart failure parameters, lipids, blood pressure, insulin sensitivity, hemoglobin A1c, resolution of fatty liver, and more.

Beyond these clinical challenges, patients and their prescribers are at the mercy of changes to the formularies of FDA-approved products. As such, we work with each patient to formulate their medication with a variety of fillers, including probiotics and inert fillers that are more easily absorbed by chronically ill patients, especially for ADT. We also formulate troches (special lozenges) of T3, which bypass the gut and liver and start to absorb via the oral mucosa under the tongue and go directly into circulation. These are critically important and life-saving therapies for patients who have no other option if they are unable to acquire these formulae.

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MEDICINE

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WEST CHICAGO, IL 60185

I do not say this lightly: I fear for the lives of some of my patients if they cannot get access to ADT. Some of my patients may be forced back onto therapies they cannot tolerate or cannot use effectively. For others with severe hypothyroid symptoms that need ADT to maintain daily basic functioning, loss of access will not be a mere inconvenience; it will be a profound medical crisis. For these reasons, I strongly urge FDA to revoke its determination that ADT is a biological product and continue to allow patients access to this life-saving medication.

Thank you,

/s/ Sarah Zielsdorf

Dr. Sarah Zielsdorf
August 19, 2026

EXHIBIT 7

Henderson Statement



Statement of Support by Dr. Brittany Bohinc Henderson

Qualifications

I am Dr. Brittany Bohinc Henderson, MD, ECNU, and I have dedicated my career to advancing the diagnosis and treatment of thyroid disease. I currently serve as Chief Medical Officer and owner of the Charleston Thyroid Center and as Chief Medical Officer of MyThyroidDoctor.com, a telemedicine thyroid practice. I have also held faculty and medical director roles in endocrinology at Duke University and Wake Forest Baptist Health, where I directed the Thyroid & Endocrine Neoplasia Clinic and the Fellows Thyroid Ultrasound and Biopsy Clinic. I hold an Endocrine Certification in Neck Ultrasound (ECNU) for thyroid and parathyroid ultrasound and FNA biopsy, along with board certifications in Endocrinology, Diabetes, and Metabolism and in Internal Medicine from the American Board of Internal Medicine.

My research portfolio spans precision medicine in differentiated thyroid cancer, LGR5 as a marker of papillary thyroid cancer aggressiveness (which was funded by the American Thyroid Association Clinical Investigator Grant), thyroid hormone metabolism in liver fibrogenesis, and hedgehog signaling in human medullary thyroid cancer. I have served as clinical investigator or co-principal investigator on multiple thyroid cancer trials, including a study of selumetinib in advanced differentiated thyroid cancer with AstraZeneca and Duke University and an examination of the association between environmental exposures to Polybrominated Diphenyl Ethers and papillary thyroid carcinoma.

I am the author of twenty peer-reviewed publications on thyroid-related topics, ranging from resistance to thyroid hormone beta to the utility of liquid thyroxine in hypothyroid patients with small intestinal bacterial overgrowth syndrome, and I co-authored the book "What You Must Know About Hashimoto's Disease: Restoring Thyroid Health Through Traditional and Complementary Medicine." I have also served as the founding member and co-president of the American College of Thyroidology and have lectured nationally and internationally on thyroid nodules, Hashimoto's disease, thyroid eye disease, and starting a thyroid practice.

Experience with Treatment of Desiccated Thyroid Medications

My experience with desiccated thyroid extract (also referred to as "*animal-derived thyroid*" or "*ADT*") medications began when I realized that the FDA-approved thyroid medications (i.e., Synthroid, Tirosint, Levoxyl, and Unithroid, all of which contain Levothyroxine (LT4) as the only active ingredient) were insufficient to fully control thyroid disease in many of my patients. My practice has 20,000 active patients from all across the United States who are seeking treatment for thyroid management, and approximately 15% are being successfully treated with ADT medications. Many of these patients can tolerate the manufactured ADT products (e.g., NP Thyroid, Armour Thyroid), but some cannot tolerate the fillers or the pharmacodynamics of an instant release product, and they require a compounded ADT formulation that is slower release. Although patients who require compounded ADT comprise a minority of my patient population

(approximately 1%), the ability to have various medication formulations available is essential to quality of life and resolution of thyroid symptoms in this patient population. For these patients, there is often no adequate FDA-approved or commercially manufactured substitute.

Why is ADT generally preferred over FDA-approved drugs containing Levothyroxine or Liothyronine?

Many of my patients require full thyroid replacement, which, I find, is best treated through a combination of Levothyroxine (LT4) *and* Liothyronine (LT3). While I acknowledge that there are FDA-approved medications containing LT4 and LT3, these drugs are available in only a few fixed dosage strengths and there is not a single FDA-approved drug on the market that combines both LT4 and LT3. The drug that *does* combine these active ingredients is ADT. Additionally, the dyes and fillers prevalent in the FDA-approved LT4 and LT3 products pose an issue for autoimmune thyroid patients with multiple chemical and additive sensitivities; ADT, on the other hand, is dye-free and free of many fillers and additives. Despite being bioidentical to human T4 and T3, ADT products are formulated from a porcine source and, for reasons not yet understood, some patients who cannot tolerate FDA-approved LT4 and LT3 dosed separately (many times due to side effects) ***can*** tolerate and achieve excellent clinical outcomes on ADT products.

When dosed appropriately, ADT products can mimic normal thyroid function and restore clinical euthyroidism. Moreover, thyroid treatment is specific to the patient and there is no single dose, and no single medication, that fits every patient. As such, uninterrupted access to compounded ADT is critical. Compounded ADT allows me to prescribe slight variations in LT3 and LT4 that create meaningful differences for my patients. Because it is compounded, the Thyroid USP compounded strengths are unique to the patient. They can range from 10 mg to 300 mg depending on whether the desired formulation is slow release or instant release. For example, I may prescribe ***slow release*** Thyroid USP 220 mg 55% Methocel once daily or ***slow release*** Thyroid USP 50 mg capsules PO twice daily. Compounding also allows me to prescribe formulations that do not contain allergenic fillers or dyes that many patients (especially those with hyperthyroidism and other autoimmune disorders) cannot tolerate. Every compounded prescription is unique to the patient (including weight, whether the patient has any residual endogenous thyroid function, and whether there are comorbidities that affect thyroid hormone peripheral metabolism).

In my clinical experience, this has become a human rights issue. I have patients who have had their thyroid removed due to cancer, multinodular goiter, Graves' Disease or due to other reasons and require lifelong thyroid replacement medicine. Many of these patients also have autoimmune thyroiditis, the most common reason for thyroid disease in the developed world, and, therefore, have sensitivities to many of the FDA-approved LT4 and LT3 drug excipients. Many of the ADT products have no dyes and fewer excipients, allowing for improved tolerability. Additionally, many patients report substantially improved well-being and markedly fewer side effects on ADT products. Because studies have not yet been performed examining why some

patients do better on one formulation vs. another, it is imperative that individual clinical judgement be respected and preserved. Many of these patients have tried FDA-approved synthetic medications with side effects or without improvement in their quality of life. For these patients, ADT is frequently the only therapy that relieves their symptoms and restores their quality of life.

The option to compound ADT products is imperative as well; many of these patients cannot tolerate any of the manufactured products like NP Thyroid or Armour Thyroid. Many of my postmenopausal, thin female patients cannot tolerate the FDA-approved LT4 or LT3 products or manufactured ADT products, primarily due to a loss of thyroid binding proteins in menopause and with the aging process. They have tried and failed many of the FDA-approved and manufactured products and have regained their quality of life on compounded Thyroid USP using ADT. This option needs to remain available for these patients. Accordingly, reclassifying ADT as a biologic would abruptly strip thousands of patients of a therapy on which they depend, with no equivalent FDA-approved alternative to take its place.

For these reasons, I respectfully but strongly urge FDA to revoke its scientifically unsupported determination that ADT is a biological product and continue to allow patients uninterrupted access to this safe, effective, and medically necessary medication.

Sincerely,



Dr. Brittany Bohinc Henderson, MD, ECNU

August 12, 2026

EXHIBIT 8

Beamer Statement



Andrews APOTHECARY

custom compounded Rxs, wellness solutions & gifts for you & your pets
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PCAB ACCREDITED Compounding Pharmacy

Statement of Support by Jerry Beamer, R.Ph.

Qualifications

My name is Jerry Beamer and I am a registered pharmacist and compounding specialist at Andrews Apothecary in Winston-Salem, North Carolina. I have been actively compounding since 1984, when I graduated from UNC-Chapel Hill with a Bachelor of Science in Pharmacy. Over the course of more than four decades in pharmacy practice, I have developed extensive expertise in compounding, with a particular focus on bioidentical hormone replacement therapy, clinical hormone consultations, and clinical consulting.

As owner and operator of Andrews Apothecary since 2009, I collaborate closely with physicians and other medical providers to support hormone therapy decision-making. My clinical focus areas include interpretation of saliva and laboratory testing in hormone therapy, non-sterile and sterile compounding of customized dosage forms, and pharmacist-provider collaboration. I am also a recognized speaker and educator, having presented at PCCA International Seminars and the ACT legislative conference in Washington, D.C., on compounding pharmacy and hormone therapy topics.

Desiccated Thyroid Medications

There is an unmet clinical need among patients whose thyroid conditions are not adequately managed by commercially available fixed-dose products. Patients treated with compounded ADT are not patients who casually selected this therapy. In virtually every case, these patients first attempted treatment with Synthroid or another FDA-approved synthetic levothyroxine (T4) product, then progressed to commercial ADT products such as Armour Thyroid or NP Thyroid when they failed to adequately convert T4 to T3. Thyroid hormones operate within a narrow therapeutic index, meaning that small dosage variations can produce significant clinical differences. Between the fixed strengths offered by commercial manufacturers, there are patients who require precise intermediate doses that only compounding can provide.

Quality and Safety Controls

It is industry standard for compounding pharmacies to rely on Certificates of Analysis for the active pharmaceutical ingredients ("*API*") received. The Certificates allow us to verify the identity, purity, and potency of API. Our API vendors are FDA-registered and inspected facilities, providing a critical layer of regulatory oversight.

Andrews Apothecary has never received a patient or provider complaint related to the quality of a compounded ADT product, and we have never received a report of a serious adverse



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PCAB ACCREDITED Compounding Pharmacy

event related to compounded ADT. Our safety record reflects the diligence with which we approach every aspect of the compounding process.

Impact of Biologic Classification on Patients

Classifying ADT as a biological product will prove to have profound impacts on patients. As I have explained, patients do not arrive at ADT as a first choice—they arrive after suffering through other therapies that have failed them. These are patients for whom commercially available fixed-dose products are clinically inadequate. Without access to compounded ADT, these patients will suffer. They will lack the precise dosing they require, and there is no reasonable alternative available for them on the market.

Classification of ADT as a biologic causes more problems than it solves. In particular, FDA is not providing a reasonable alternative for the patients who will be harmed by the lack of access to the one product that adequately treats their conditions (manufactured ADT or compounded ADT). For these reasons, I respectfully but strongly urge FDA to revoke its determination that ADT is a biological product and continue to allow patients uninterrupted access to this vital medication.

Sincerely,

Jerry Beamer

Jerry Beamer, R.Ph.
August 12, 2026

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EXHIBIT 9

Koshland Statement

Koshland Pharm
Custom Compounding Pharmacy

301 Folsom Street, Suite B San Francisco, CA 94105
KOSHLANDPHARM.COM • 415.344.0600

Statement of Support by Peter Koshland, PharmD

Qualifications

My name is Peter Koshland, I am the founder and CEO of Koshland Pharm: Custom Compounding Pharmacy, a PCAB-accredited compounding pharmacy in San Francisco, California. I earned my Doctor of Pharmacy degree from the University of California, San Francisco ("*UCSF*") School of Pharmacy in 2000 and have been a licensed California pharmacist for over 25 years. I have owned and operated Koshland Pharm for 17 years, during which time our practice has specialized in sterile and non-sterile compounding, with a particular focus on hormone replacement therapy and thyroid treatments. I also serve as an Adjunct Clinical Professor of Pharmacy at UCSF, where I teach non-sterile compounding and clinical applications within the Pharm.D. curriculum.

I currently serve as a Board Member and Chair-Elect of the Alliance for Pharmacy Compounding, where I also chair the California Initiative leading statewide legislative and regulatory advocacy to protect patient access to critical compounded medications. I was named Compounding Pharmacist of the Year by the Professional Compounding Centers of America in 2025, received the Champion of Naturopathic Medicine Award from the California Naturopathic Doctors Association in 2023, and earned the Steven C. Feldman Compounding Award from the California Pharmacists Association in 2013. In 2019, I was invited to testify before the National Academies of Sciences, Engineering, and Medicine on the clinical utility of compounded bioidentical hormone therapy. My career has been dedicated to ensuring patients have access to safe, effective, and individualized compounded medications.

Desiccated Thyroid Medications

Animal derived thyroid ("*ADT*") is a unique thyroid product that is more effective for certain patients than anything else available. For these patients, ADT is life-changing. This cannot be overstated: thyroid function is the foundation for hormone health.

By the time patients reach a compounding pharmacy, it typically means they have tried and failed on commercial synthetic thyroid products like Synthroid (levothyroxine). For example, many postmenopausal patients can no longer adequately convert T4 into T3 as confirmed by their ongoing blood tests. These patients have likely tried the synthetic options that only contain levothyroxine as an active ingredient and saw little benefit (i.e., no improvement in hypothyroid symptoms like constipation, cognitive issues, dysthymia, or cold extremities). Often, and thankfully, when these patients try ADT, many feel significant improvement in their symptoms. For these patients, ADT is the only drug that addresses their hypothyroidism. This may be explained in part by the fact that ADT contains both T4 and T3 in a natural ratio.

Quality and Safety

It is safe to compound ADT pursuant to the United States Pharmacopeia ("*USP*") drug monograph for Thyroid. The monograph defines the quality, identity, strength, purity, and testing methods for Thyroid and acts as a scientific "rulebook" to ensure drugs are safe and consistently

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prepared. Additionally, vendors, like the active pharmaceutical ingredient ("*API*") wholesalers, are qualified according to vendor qualification guidelines, and when API arrives, it is accompanied by a Certificate of Analysis from the API manufacturer. The Certificate shows batch-specific test results, acceptance criteria, and product identity. It is industry standard to rely on the information provided in the Certificate, and if anything on the Certificate is not aligned with the USP monograph, or if we question the product whatsoever, it is not used in compounding.

Also, it is much safer to compound with ADT as an API than it is to compound with pure T3 or pure T4 on their own. You see, ADT is dosed in milligrams, but T4 and T3 are each dosed in ***micrograms*** (i.e., one one-thousandth of a single milligram). ADT comes with a USP drug monograph, which makes it straightforward and safe to compound. If ADT is classified as a biologic and removed from compounders' formularies, pharmacies will be forced to compound with pure synthetic T3 and T4 instead, which increases risks to patients given the strength of T3 and T4 and their relative high potencies. Even with the most diligent processes, there is still a far greater risk of inconsistent potencies in individual capsules of pure T3 and pure T4 than there is working with ADT dosed in milligrams.

Impact to Patients if ADT is Classified as a Biologic

If compounded ADT is no longer available for patients, the consequences will be devastating. The patients have already exhausted commercial alternatives—they only arrive at a compounding pharmacy when nothing else on the market has worked for them and they need something custom-made specific for their bodies. These patients will lose the one medication that has restored their quality of life after years, or even decades, of suffering. Some patients may be forced to seek ADT through unregulated sources, such as the black market and overseas suppliers, where there is no quality oversight, no testing, and no pharmacist ensuring safety. Other patients will be left with no effective treatment at all, returning to lives diminished by untreated or poorly managed hypothyroidism.

Patients deserve continued access to this safe, effective, and well-regulated medication. For these reasons, I urge FDA to keep ADT available to patients as a drug and to revoke FDA's determination that ADT is a biological product.

Sincerely,

Peter Koshland

Peter Koshland, PharmD

August 12, 2026

EXHIBIT 10

Ipsen Statement

Kusler's COMPOUNDING PHARMACY Clark's COMPOUNDING PHARMACY

Statement of Support by Dawn M. Ipsen, PharmD, FACP, FACA, FAVCP

Qualifications

I am Dawn M. Ipsen, PharmD, FACP, FACA, FAVCP, a compounding pharmacist with over 25 years of professional experience and a Doctor of Pharmacy from the University of Washington. I am a Full Fellow of the American College of Apothecaries and of the American College of Veterinary Pharmacists. I currently serve on the Alliance for Pharmacy Compounding Board of Directors for District 7 and am a member of the Washington State Pharmacy Association and serve as Chairman Emeritus of the Compounding Special Interest Group a position I have held since 2018. I also have a clinical faculty role at the University of Washington School of Pharmacy and am affiliate faculty at Bastyr University, where I instruct in Clinical Pharmacology and Dermatology.

I have been recognized for my contributions to the pharmacy profession, including receiving the L. David Sparks Compounding Advocacy Award (2025), the University of Washington Pharmacy Alumni Association Distinguished Alumni Award (2021), the PCCA Pharmacist of the Month Award (2015), and the Washington State Pharmacy Association Distinguished Young Pharmacist of the Year Award (2011). I am a Fellow of the Alliance for Pharmacy Compounding (2024) and have been a member of the Professional Compounding Centers of America since 2014, serving on their Advisory Council from 2019 to 2022. I have presented extensively at local, state, and national professional conferences on topics including thyroid health, compounding regulatory trends, autoimmunity, pain management, and low dose naltrexone therapy.

For the past 12 years, I have served as the owner and operator of two nonsterile compounding pharmacies: Clark's Compounding Pharmacy in Bellevue, Washington, and Kusler's Compounding Pharmacy in Snohomish, Washington. My pharmacies possess expert knowledge in compounding for bioidentical hormone replacement therapy, women's health, men's health, pain management, thyroid health, autoimmune conditions, dermatology, and veterinary medicine. We work with approximately 800 to 1,000 healthcare providers and provide medication consultations for patients and doctors on hormone replacement therapy, pain management, medication review and optimization, and nutritional support.

Quality and Safety Controls

Our pharmacies operate under the most stringent quality standards in the profession. In Washington State, United States Pharmacopeia ("*USP*") standards are written into law, and we

are inspected against and held to full compliance with USP General Chapters <795> *Pharmaceutical Compounding – Nonsterile Preparations* and <800> *Hazardous Drugs—Handling in Healthcare Settings*. Both Clark's Compounding Pharmacy and Kusler's Compounding Pharmacy have passed regulatory inspections with zero deficiencies.

We maintain a comprehensive quality assurance and quality control process that includes staff training, thorough documentation, multiple verification checkpoints from the time a prescription is received through the compounding and dispensing of the final product, and our method validation establishes set procedures and guidelines for weighing product. We screen for allergies, drug interactions, and recalls, and our systems allow us to trace any product down to the individual patient level.

As other compounding pharmacies do, we collect and assess a Certificate of Analysis for every batch of active pharmaceutical ingredient ("*API*") we receive, and we source exclusively from FDA-registered manufacturers and state-licensed wholesalers. This ensures that the raw materials entering our compounding process meet rigorous federal quality standards before we begin any preparation. When we review the Certificate, we screen for microbial growth, residual solvents, mold, and yeast as part of the USP monograph process.

Neither of our pharmacies has ever had a quality or safety issue raised during a regulatory inspection. We have never received a patient or provider complaint related to the quality of a compounded desiccated thyroid extract medication, also known as animal derived thyroid ("*ADT*"), and we have never received a report of a serious adverse event related to compounded ADT.

Impact of Biologic Classification on Patients

Clark's Compounding Pharmacy and Kusler's Compounding Pharmacy have witnessed a growing interest in ADT. The increasing number of patients and prescribing clinicians year after year demonstrates the continued and growing clinical need for individualized compounded ADT therapies.

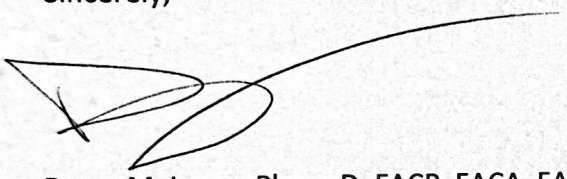
Classifying ADT as a biological product and removing the ability to compound with such products will prove to be incredibly harmful to patients. The clinical consequences of inadequate thyroid management are profound and far-reaching. Patients will experience energy loss, cognitive impairment and brain fog, weight gain leading to other chronic illnesses, systemic inflammation, and autoimmune reactions. These symptoms impact patients' day-to-day functioning and can render patients bedridden. The thyroid affects virtually every system in

the body, and when patients cannot access the individualized therapy they require, the downstream health consequences are severe.

Patients who lose access to compounded DTE may seek medications from overseas or unregulated sources. Alternatively, they may return to synthetic thyroid medications or manufactured ADT medications, which are the very medications that they have already tried and on which they have failed.

For these reasons, I respectfully but strongly urge FDA to revoke its unsupported determination that ADT is a biological product and to allow patients access to this critical medication.

Sincerely,



Dawn M. Ipsen, PharmD, FACP, FACA, FAVCP

August 5, 2026

EXHIBIT 11

Hoffart Statement

EST. 2002

Magnolia Pharmacy

CUSTOM CREATIONS

HOMETOWN VALUES

Statement of Support by Steve Hoffart, PharmD, FAAMM, ABAAHP

Qualifications

I am Steve Hoffart, PharmD, FAAMM, ABAAHP, a pharmacist, healthcare entrepreneur, and national advocate with over three decades of experience in pharmacy practice. I hold a Doctor of Pharmacy and a Bachelor of Science in Pharmacy (Highest Honors) from the University of Texas at Austin, a Fellowship from the American Academy of Anti-Aging Medicine ("*FAAMM*"), and Board Certification from the American Board of Anti-Aging Health Practitioners ("*ABAAHP*"). I have completed advanced fellowship training in functional medicine, personalized medicine, longevity, regenerative medicine, metabolic health, and disease prevention.

In 2002, I founded Magnolia Pharmacy in Magnolia, Texas, and have built it into a forty-person healthcare organization serving tens of thousands of patients and partnering with thousands of healthcare providers. I expanded the practice beyond traditional pharmacy into compounding, functional medicine, hormone optimization, weight management, wellness testing, pharmacist consultations, longevity, and nutrition. When it comes to thyroid management, our practice model is built on the conviction that treatment must be individualized: patients present with different conversion profiles, different sensitivities to excipients, and different dosing requirements that only compounded formulations can address.

I currently serve as Chairman of American Pharmacies, where I help represent independent community pharmacies at the national level, with advocacy centered on fair patient access and the continued ability of locally owned pharmacies to care for their communities. I am also professionally engaged with the National Community Pharmacists Association, Professional Compounding Centers of America, the Alliance for Pharmacy Compounding, the Texas Pharmacy Association, and the American Academy of Anti-Aging Medicine.

Desiccated Thyroid Medications

The rationale for compounding desiccated thyroid extract, also known as animal derived thyroid ("*ADT*") is straightforward: while there are quality commercial thyroid products on the market, those products do not work for every patient. Commercially available ADT is offered in only a limited range of fixed strengths (for example, Armour Thyroid is available in dosage strengths of 15, 30, 60, 90, 120, 180, 240, and 300 milligrams). However, many patients present with diverse gut issues, nutrient depletions, and physiological differences that means they fall between these fixed doses and require precise intermediate strengths to achieve optimal thyroid function.

Additionally, some patients are allergic to the inactive ingredients found in commercial thyroid products. Synthroid, for example, contains acacia, confectioner's sugar (contains corn starch), lactose monohydrate, magnesium stearate, povidone, and talc, while Armour Thyroid contains calcium stearate, dextrose, microcrystalline cellulose, sodium starch glycolate and opadry white. Patients with allergies to cornstarch or microcrystalline cellulose cannot take either of these products. Compounding allows these patients to receive custom, hypoallergenic formulations of ADT that commercial manufacturers simply cannot provide.

People need individualized medicine; they need acknowledgment from health care providers that sometimes n=1. This is especially true in the idiosyncratic thyroid hormone space, where patients are presenting with intense fatigue and an inability to function on a daily basis. What works for one patient will not necessarily work for the other.

Quality and Safety Controls

Magnolia Pharmacy maintains rigorous quality and safety controls for all compounded preparations. We purchase active pharmaceutical ingredients ("*API*") exclusively from state-licensed wholesalers that source from

FDA-registered and inspected manufactures. Each shipment of API arrives with a Certificate of Analysis, and the material must be standardized to meet United States Pharmacopeia ("*USP*") requirements before we will accept it and compound into patient-specific medications.

We have never had an ADT quality issue raised during any regulatory inspection. We have never received a patient or provider complaint related to the quality of a compounded ADT product, and we have never received a report of a serious adverse event related to compounded ADT.

Impact of Biologic Classification on Patients

The classification of ADT as a biological product removes a vital treatment option that is genuinely life-altering for the patients who depend on it. Without access to compounded ADT, patients will lose the ability to receive personalized thyroid therapy. While commercial options will remain available for many patients, those with allergies to commercial excipients or who require personalized dosing will have their options completely eliminated. There will be no ability to help these patients achieve optimal thyroid function.

I must stress that patients who cannot access proper thyroid treatment cannot live normal lives. They are fatigued, run down, have difficulty performing their jobs and showing up in their roles as parents or caretakers. Proper thyroid function is foundational to daily functioning, and for patients who require individualized therapy, compounded ADT is the only path to that outcome.

For these reasons, I urge FDA to revoke its determination that ADT is a biological product and continue to allow patients uninterrupted access to this safe, effective, and medically necessary medication.

Sincerely,

Steve Hoffart, PharmD, FAAMM, ABAAHP
August 5, 2026

EXHIBIT 12

Patel Statement

VLS PHARMACY INC.

Statement of Support by Gopesh Patel, R.Ph.

Qualifications

My name is Gopesh Patel, and I am the pharmacist-in-charge and owner at VLS Pharmacy and New Drug Loft. I have spent my career focusing on providing high quality prescriptions and compounded medications, as well as overseeing the state-of-the-art sterile compounding facilities at VLS Pharmacy, which is accredited by the Pharmacy Compounding Accreditation Board through the Accreditation Commission for Health Care. I am a graduate of MS University in Baroda, India, and I have extensive clinical knowledge in hormone replacement therapy, dermatology, urology and IV therapy—knowledge that I willingly share with fellow compounders during frequent lectures at educational seminars.

My philosophy is patient-centered. I take great pride in the quality of the compounded medications that I prepare and I work closely with all my staff to instill this same mindset and commitment to excellence.

Desiccated Thyroid Medications

VLS Pharmacy has compounded desiccated thyroid extract (also referred to as *"animal derived thyroid"* or *"ADT"*) medications for many patients. It is my belief that thyroid treatment cannot be a one-size-fits-all approach, and often requires custom formulations for individual patients.

In practice, many patients present with individualized hormonal deficiencies that require precise adjustments. Every patient's physiology is different, and the clinical outcomes I observe confirm that customized compounding produces superior results for patients who cannot be adequately served by commercial fixed-dose products. For example, some patients have low triiodothyronine (T3) levels and require more thyroxine (T4) to assist with faster T3 conversion. To treat these patients, a compounded ADT formulation can achieve the exact hormonal profile each patient requires. Additionally, some patients are allergic to the inactive ingredients found in commercial thyroid products. Synthroid, for example, contains the following inactive ingredients: acacia, confectioner's sugar (contains corn starch), lactose monohydrate, magnesium stearate, povidone, and talc. Armour Thyroid's inactive ingredients are calcium stearate, dextrose, microcrystalline cellulose, sodium starch glycolate and opadry white. Patients with allergies to cornstarch or microcrystalline cellulose cannot take either of these products, but can take, and do well on, compounded allergen-free formulations that eliminate the offending excipients while still being able to deliver the precise therapeutic dose.

Quality and Safety Controls

VLS Pharmacy maintains rigorous quality and safety controls for all compounded preparations. For example, we obtain a Certificate of Analysis with every shipment of active pharmaceutical ingredients (*"API"*), and it is from the Certificate that we determine what needs to be compounded and verify that specifications are met. We then perform weight calculations for every capsule and maintain a method of validation from lowest to highest dose. All compounding is performed in our hazardous room in strict accordance with USP standards.

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www.vlspharmacy.com

VLS Pharmacy has never had a quality or safety issue raised during any regulatory inspection. We have never received a patient or provider complaint related to the quality of a compounded ADT product, and we have never received a report of a serious adverse event related to compounded ADT.

Impact of Biologic Classification on Patients

Classifying ADT as a biological product will result in severe consequences for patients. The physicians who prescribe these medications perform bloodwork and thorough testing to determine precisely what each patient needs. Most prescribing physicians understand that fixed commercial dosing does not adequately serve all patients, which is exactly why they turn to compounding pharmacies.

Without compounded ADT, I expect that one hundred percent of affected patients will seek these medications from unregulated overseas pharmacies or from the black market, which will profoundly harm patients. If patients cannot obtain ADT in the proper manner and at the proper dosing from a licensed pharmacy under physician supervision, their quality of life will deteriorate significantly.

The thyroid controls virtually every system in the human body. When thyroid function is inadequately managed, patients face serious and potentially life-threatening consequences, including cardiac complications that could result in hospitalization or death. Compounded ADT often is the only means to adequately manage these issues. For these reasons, I respectfully but strongly urge FDA to revoke its scientifically unsupported determination that ADT is a biological product and allow patients access to this safe, effective, and medically necessary medication.

Sincerely,

Gopesh Patel, R.Ph.
August 18, 2026

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EXHIBIT 13

Murdock Statement

Statement of Support by Amanda Murdock

My name is Amanda Murdock, and I want to share my experience with thyroid disease and explain why access to compounded desiccated thyroid medication (also referred to as "*animal-derived thyroid medication*" or "*ADT*") is not merely a preference for me—it is a medical necessity.

To start, I have worked in the fitness industry for over 15 years. I am incredibly active and proud that I maintain a very healthy and clean lifestyle. However, despite this, I began experiencing complete lethargy, unexplained and unexpected weight gain, inflammation, and brain fog. I had no energy and felt like I was losing control over my life. These symptoms felt devastating for me.

Eventually, my thyroid issues were finally diagnosed and I was prescribed a combination of synthetic levothyroxine and Armour Thyroid, which I was on for eight years. Unfortunately, I never felt completely like myself on this medication, no matter how much the dosages were increased or tweaked. I continued to feel like I had no energy and continued gaining weight, despite feeling like I was doing everything right.

Everything changes for me when I was prescribed a compounded ADT medication. Thanks to compounding, my dose could be precisely customized in a way that was not possible with the FDA-approved synthetic products or the commercial Armour Thyroid product. For example, the amount of ADT in the compounded medication was able to be adjusted by as little as two milligrams at a time—the kind of fine-tuning that is only possible in a compounding pharmacy. Thanks to the compounded formulation, my thyroid levels have been stable and I only have to get bloodwork done every six months rather than every three months (which was the cadence when I was on synthetic levothyroxine and Armour Thyroid). Importantly, my brain fog has resolved, my energy has returned, and my weight gain has resolved.

If I lose access to compounded ADT I genuinely do not know what I will do. The other treatments I have tried over the years simply do not work for me, and going back to those medications would mean returning to unstable thyroid levels, debilitating fatigue, brain fog, weight gain, and overall hormonal imbalance. It feels extremely unfair to deny access to such a vital medication without considering the extreme impact it will have on patient's lives, especially when this medication has the ability to restore quality of life to me and so many other patients.

Sincerely,

/s/ Amanda Murdock

August 5, 2026

EXHIBIT 14

Neboschick Statement

Statement of Support by Ashley Neboschick

My name is Ashley Neboschick, and I have been living with Hashimoto's disease for almost 20 years. Hashimoto's is an autoimmune disorder where the immune system attacks the thyroid gland, typically leading to an underactive thyroid (i.e., hypothyroidism), fatigue, and weight gain. Desiccated thyroid ("*ADT*") medication has been the only treatment I have received that has improved my quality of life and allows me to function every day.

However, I was not always treated with ADT. Initially, my doctors prescribed me Synthroid, an FDA-approved medication containing synthetic levothyroxine. I took Synthroid for nine to ten years but continued to feel worse and worse. I felt like someone had let the air out of me—I felt lazy, I did not feel like moving, I simply had no energy to do anything but sleep.

Around 2016, my providers switched me to an ADT medication and, eventually, I was prescribed a compounded ADT formulation. This medication genuinely gave me my life back—I transitioned from an obese, inactive individual to an athlete. My ability to function day to day was restored, I had enough energy to get through the day, and, most importantly, I felt like myself again. Now, I am more physically active than ever before, and I participate in competitive events like triathlons, ultra marathons, and various other running events. These activities were not possible for me before I was prescribed ADT.

Synthroid did not work for me because my thyroid produces T3 and T4 hormones at steady levels, but Synthroid releases and fades rapidly once it is ingested. By contrast, my compounded ADT medication was able to be formulated to be slow-release and mimic my body's natural thyroid pattern. This is not a minor difference—it is literally the difference between me taking a medication that simply keeps me alive and a medication that allows me to function and thrive on a daily basis.

ADT is a lifetime medication for me. It does not matter how well I eat or how much I exercise; my body will still require this medication for the rest of my life in order for my thyroid to function at optimal levels. Without compounded ADT, I am forced to look for this medication elsewhere because I will not return to taking Synthroid or any other synthetic thyroid medication. I have already lived through nearly a decade on Synthroid and am well-acquainted with its effects, and I do not intend to go back to that reduced quality of my life. Compounded ADT is not just a convenience for me—it is the foundation of my ability to function, to work, and to live life as myself.

Sincerely,

Ashley Neboschick
August 5, 2026

EXHIBIT 15

Baldwin Statement

Statement of Support by Larisa Baldwin, PA-C

Qualifications

My name is Larisa Baldwin, and I am a Certified Physician Assistant with over 11 years of experience. My clinical background includes thoracic surgery and functional medicine, including inpatient and outpatient care, cancer surveillance, multidisciplinary coordination of care, and root-cause-oriented internal medicine. I have extensive experience treating and diagnosing patients with hormone imbalances and have focused on treating thyroid conditions in my patients. I treat many patients with thyroid conditions and have seen firsthand, both as a provider and as a patient, how critical proper thyroid management is to a person's overall health and quality of life.

Experience with Treatment of Desiccated Thyroid Medications

I have a vested interest in treating hypothyroidism because it is a condition I live with every day. When I was first diagnosed, I was prescribed FDA-approved Synthroid. However, this medication did not help me at all. I experienced brain fog, fatigue, weight gain, puffy eyes, cold hands and feet, dry hair, constipation, and bloating. When I was finally switched to a desiccated thyroid medication (also referred to as "*animal derived thyroid*" or "*ADT*") by my provider, my condition significantly improved. My provider prescribed me a compounded ADT formulation, and my weight returned to normal, my digestion improved, I experienced relief from my chronic fatigue, and my energy levels stabilized. I have been on some form of thyroid medication for over 15 years, and compounded ADT is the only medication that has worked for me.

Professionally, I see these same results in my patients. That is, before treatment, they commonly report fatigue, brain fog, weight gain (even while on a GLP-1 medication), hair loss and thinning, bloating and constipation, an inability to regulate body temperature (feeling cold all the time), dry skin and nails, joint pain, poor concentration, and depression. Many of my patients failed to improve on synthetic thyroid medications, but after treatment with an ADT medication, my patients feel significant relief from those symptoms.

Why is ADT generally preferred over FDA-approved drugs containing Levothyroxine or Liothyronine?

While I will prescribe any medication that is best for my patients, ADT, and specifically compounded ADT, is generally a better fit for my patients over FDA-approved drugs containing Levothyroxine or Liothyronine. One aspect of compounded ADT that significantly helps both my patients and me is that the pharmacy can add a fiber to the capsule, which allows for slow release of the thyroid hormones, thereby more naturally mimicking how the thyroid works in the body. The FDA-approved synthetic medications do not replicate the slow-release mechanism that can be achieved by compounded ADT. Without the slow-release element, patients often experience a peak in T3 followed by a sharp fall, which can require dosing multiple times a day just to manage this fluctuation. Furthermore, only with compounded forms can you achieve a patient-specific dose, whereas alternatives such as Armour Thyroid and NP Thyroid are very limited in dosing options.

Compounded ADT is also essential during conditions like pregnancy. During my own pregnancy I was monitored extremely closely because I had to remain on my thyroid medication. Small adjustments were made to the strength of my compounded ADT to maintain my health as well as the safety of the fetus and support healthy fetal development.

Without ADT as an option for patients, patients may be forced to take the synthetic thyroid medications, which will likely lead to less optimal thyroid lab values. Even when lab values appear optimal, patients may not feel well, which is ultimately what matters—quality of life. **We cannot just treat a lab, we have to treat the patient**. Improperly managed thyroid function can also contribute to infertility. And, for patients who have had their thyroid removed or who suffer from autoimmune diseases, the lack of access to ADT would have devastating results. ADT has been safely used for far longer than the synthetic thyroid medications. Removing ADT would not just be a disservice to patients like me, it would be harmful.

Aside from compounded ADT, there is no good alternative medication for me on the market. The FDA-approved synthetic medications simply do not work for me. Losing access to this medication will significantly alter my quality of life. It is not a preference—this is the only medication that allows me to live my life and function normally.

As such, I strongly urge FDA to revoke its determination that ADT is a biological product and continue to allow patients access to this critical medication.

Sincerely,



Larisa Baldwin, PA-C

August 11, 2026