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Client Alert

FDA and Life Sciences

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2022 Year in Review: FDA Drug and Device Advertising and Promotion Enforcement

In 2022, the U.S. Food and Drug Administration (FDA or the Agency) issued a total of nine enforcement letters targeting advertising and promotion violations for prescription drugs and devices. A summary of the noteworthy trends and issues spotted in these letters is outlined below.

NOTABLE PRESCRIPTION DRUG ENFORCEMENT TRENDS IN 2022

Of the nine total advertising and promotion letters in 2022, four were issued by FDA's Office of Prescription Drug Promotion (OPDP). Of these four, one was a Warning Letter and three were Untitled Letters. The OPDP letters mark the lowest number seen since 2010, continuing the more than decade-long decline in volume of enforcement letters.

- **Most Commonly Cited Violations:** Of the four letters, one cited misbranding of an investigational new drug, while the remaining three letters all cited violations of false or misleading risk presentation and false or misleading benefit presentation.
  - **Misbranding of an Investigational Drug (Pre-approval Promotion) –** In its only Warning Letter of the year, OPDP continued its focus on and enforcement against misbranding and pre-approval promotion of investigational drugs. *See* Leronlimab Warning Letter. In this instance, FDA had previously cautioned in a public statement that CytoDyn's data on leronlimab, an investigational drug, did not support the clinical benefit of the drug for the treatment COVID-19. Yet, four months later, the company's CEO was featured in a video interview mischaracterizing clinical data and making claims that promoted leronlimab as safe and effective for COVID-19, thus prompting OPDP's Warning Letter.
  - **False or Misleading Risk Presentations –** The following summarizes the range of OPDP objections for false or misleading risk presentations:

- **Lack of fair balance** – Lack of fair balance was cited in across a variety of promotional materials, including print pieces, websites, and social media posts. In particular, OPDP routinely flags when promotional materials fail to present information relating to risks with a prominence and readability reasonably comparable with the presentation of benefits. *See e.g.*, Roszet Untitled Letter. In two letters, a lack of fair balance was exacerbated by the simultaneous presentation of risk and benefit information in video formats, creating competing and distracting sets of information that limited viewer comprehension. *See, e.g.,* Duobrii and Trulicity Untitled Letters. Notably, this issue has come up in recent years in the context of direct-to-consumer television ads and social media or website videos, signaling OPDP's increasing focus on fair balance in video formats.
- **Omission of material risk information** – Two letters challenged promotional materials for failing to disclose important risks associated with the use of the advertised product. For example, a social media post for Trulicity failed to include a warning about increased risks of hypoglycemia when the product is used concomitantly with insulin. *See* Trulicity Untitled Letter.
- **Misleading imagery in patient videos** – In the Duobrii Untitled Letter, the failure to include information about serious risks to the fetus and for photosensitivity/sunburn was made worse with imagery showing a female patient of child-bearing age (alongside two young children) and wearing clothing that exposes her shoulders and arms. *See e.g.*, Duobrii Untitled Letter.

— **False or Misleading Benefit Presentations –** The following summarizes the range of OPDP objections for false or misleading benefit presentations:

- **Unsubstantiated efficacy claims** – In two letters, OPDP challenged claims based on studies that were not designed to support conclusions about product efficacy. For example, efficacy claims for Roszet were based on retrospective calculations of pooled data from two unrelated studies that did not even evaluate Roszet. Further, study limitations precluded efficacy conclusions due to potential for a Type I error and lack of control for multiplicity testing, among others. *See* Roszet Untitled Letter; *see also* Duobrii Untitled Letter (challenging efficacy claims and conclusions based on a post hoc analysis for which there was no prespecified statistical procedure controlling for type 1 error rate).
- **Misleading superiority claims** – In one letter, OPDP cited as misleading express claims of "superior efficacy" and additional claims made by a patient spokesperson suggesting that the product is clinically superior to other products. In both instances, the Agency noted the lack of available data to support such claims. *See* Duobrii Untitled Letter.
- **Omission of material fact** – In two letters, OPDP challenged as misleading product claims that failed to adequately communicate the indication and/or limitations of use associated with the product. *See e.g.,* Trulicity and Roszet Untitled Letters.

NOTABLE DEVICE ENFORCEMENT TRENDS IN 2022

Of the nine total letters issued in 2022, five were related to medical device advertising and promotion violations. These were sent by FDA's Office of Product Evaluation and Quality (OPEQ), within the Agency's Center for Devices and Radiological Health (CDRH), usually in conjunction with FDA's Office of Medical Device and Radiological Health Operations, which coordinates device inspections within the Office of Regulatory Affairs (ORA). In addition to these traditional Warning Letters, CDRH issued an additional four Warning Letters related to the marketing and sale of COVID-19 products, such as diagnostic tests, masks, and gloves, without FDA emergency use authorization, clearance, or approval. This is a substantial decrease compared to the COVID-19-related letters issued in 2021, which tallied at a whopping forty-six and which came on the heels of 21 letters issued in 2020 for COVID-19-related

marketing. Worth noting, the number of advertising and promotion letters in 2022 appears to remain relatively consistent with recent years, as there were six in 2020 and five in 2021.

All five of the non-COVID-19 Warning Letters issued in 2022 addressed the promotion of unapproved new devices or unapproved new indications of already marketed devices. Notably, three of the five letters were for aesthetic devices; this continues last year's trend, where aesthetic devices were overrepresented in the device Warning Letters issued by the Agency. Thus, these devices appear to remain high among FDA's enforcement priorities. In one letter, FDA expressly noted that the letter was preceded by a non-public "It has come to our attention" letter and other private outreaches to the company, thus serving as a reminder that CDRH continues to relay compliance concerns in ways other than Warning Letters. Digital promotion remains an area rife for scrutiny; all of the device letters expressing concerns about device promotion cited promotional activity that occurred, at least in part, on company websites as well as, in one case, non-company websites owned and controlled by a company executive. Additionally, this is also the first time since 2018 where the number of advertising and promotion Warning Letters related to devices outnumbered those related to prescription drugs.

SUMMARY OF ENFORCEMENT LETTERS

For your reference, we have prepared a chart that lists the nine letters issued to pharmaceutical drug and device manufacturers for promotional violations in 2022, including summaries of the promotional violations alleged in each letter and hyperlinks to each letter and related promotional materials. The chart follows this client alert.

WEBINAR: Year in Review for Drug and Device Advertising and Promotion

Join us on January 24 for a review of key takeaways from the FDA's 2022 drug and device advertising and promotion enforcement letters and a discussion of other noteworthy developments relevant to drug and medical device marketing. Our experienced panel will discuss:

- Lessons learned from 2022 drug and device advertising and promotion enforcement and trends related to social media, patient videos and online interviews, misleading efficacy claims, presentation of risk information, and pre-approval promotion
- Other relevant developments, including recent device-related Lanham Act litigation, FTC activities related to endorsements and consumer reviews, and OPDP research initiatives
- Predictions for what may be expected in 2023

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2022 PRESCRIPTION DRUG AND DEVICE ADVERTISING & PROMOTION ENFORCEMENT LETTERS

DRUGS

Date (Hyperlink to Letter)	Drug Indications (As Referenced in Letter)	Letter Type	Boxed Warning	Form of Communication	Summary of Alleged Violations
06-02-2022	**ROSZET® (rosuvastatin and ezetimibe) tablets, for oral use** Roszet is indicated in adults (1) as an adjunct to diet in patients with primary non-familial hyperlipidemia to reduce low-density lipoprotein cholesterol (LDL-C) and (2) alone or as an adjunct to other LDL-C-lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.	UL	No	Doctor Info Letter	• **False or Misleading Claims about Efficacy** Unsubstantiated Efficacy Claims ○ OPDP challenged efficacy claims made in a "Roszet Doctor Info Letter." OPDP emphasized that cited claims were based on studies that were not designed to support conclusions about product efficacy. As outlined in more detail below, efficacy claims were based on retrospective calculations of pooled data from two unrelated studies, neither of which evaluated Roszet. Further, study limitations precluded efficacy conclusions due to potential for a Type I error and lack of control for multiplicity testing. ○ The info letter makes the following claims, which misleadingly attribute specific levels of LDL-C reductions to the drug product at various dosages and are based on a "scientifically unsound analysis." ▪ *"**TOTAL* LDL-C REDUCTIONS*** • *Roszet 10 mg/10 mg **64%*** • *Roszet 20 mg/10 mg **66%*** • *Roszet 40 mg/10 mg **72%**"* ▪ *"Roszet 5 mg/10 mg total LDL-C reduction is 59%*."* ○ OPDP found that the LDL-C reduction claims "depict numbers that were retrospectively calculated by combining the results of [] two unrelated studies, neither of which evaluated the specific combination of rosuvastatin and ezetimibe (i.e., Roszet)." Further, the studies at issue differ with respect to patient population, statin type and dose, and duration, thus limiting any cross-study comparisons and combination of results. ▪ Notably, OPDP pointed out that "FDA is not aware of a scientific basis for combining study results in this manner." ○ OPDP also took issue with the following claims and presentations, as they "create a misleading impression regarding the efficacy of Roszet in achieving specific levels of LDL-C reduction over specific periods of time" (emphasis original and references omitted): ▪ *"**Patients Can Get Below 70 mg/dL with <u>One</u> Pill Daily**"* ▪ *"Mean LDL-C Reductions Achieved in Clinical Trials"* • *"**GRAVITY Study*** ○ *Baseline LDL-C **163** mg/dl → Final LDL-C **65** mg/dl after 12 weeks (Dose: rosuvastatin/ezetimibe 10 mg/10 mg)*

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					○ *Baseline LDL-C **165** mg/dl → Final LDL-C **59** mg/dl after 12 weeks (Dose: rosuvastatin/ezetimibe 20 mg/10 mg)"* • *"**EXPLORER Study*** ○ *Baseline LDL-C **189** mg/dl → Final LDL-C **57** mg/dl after 6 weeks (Dose: rosuvastatin/ezetimibe 40 mg/10 mg)"* ○ OPDP explained that there are multiple limitations to the cited studies that ultimately preclude such claims: ▪ LOCF and mITT introduce bias and increase the chance of committing a Type I error; ▪ No control for multiplicity testing of secondary endpoints, including LDL-C <70 mg/dL; and ▪ Misleadingly implies that the GRAVITY study represents 12 weeks of treatment with Roszet. Omission of Material Information from the Approved Indication ○ Additionally, OPDP found that the info letter does not sufficiently communicate that one of the drug's indications is as an *adjunct* to diet to reduce select patients' LDL-C. The drug's full indication is listed in "much smaller font size and with minimal white space at the bottom of the page," compared to more attention-grabbing claims, such as *"Patients Can Get Below 70 mg/dL with One Pill Daily,"* which "misleadingly suggests that Roszet alone, in the absence of diet, provides these benefits." • **False or Misleading Risk Presentation** Lack of Fair Balance ○ OPDP concluded that the communication is misleading as it fails "to present information relating to the contraindications and warnings and precautions for Roszet with a prominence and readability reasonably comparable with the presentation of information relating to the benefits of Roszet." ▪ Specifically, benefit claims for the drug are "presented in conjunction with colorful graphics and large bolded headlines, with significant white space" while risk information is "relegated to the bottom of the first page" and subsequent page, in small font and in paragraph format.
03-31-22	**DUOBRII™ (halobetasol propionate and tazarotene) lotion, for topical use** DUOBRII™ is indicated for the topical treatment of plaque psoriasis in adults.	UL	No	Direct-to-Consumer Video/ Storyboard Webpage	• **False or Misleading Risk Presentation** Omission of Risk Information and Misleading Patient Testimonial ○ OPDP concluded that a direct-to-consumer video for Duobrii lotion is misleading because it "includes efficacy claims for Duobrii but fails to include important risk information associated with the drug." OPDP noted that "[b]y omitting serious risks associated with Duobrii and material facts pertaining to serious risks, the video misleadingly suggests that Duobrii is safer than has been demonstrated." ○ Notably, OPDP was concerned that material facts regarding the warning and precaution of embryofetal risk are omitted. OPDP found that this omission "especially concerning" as the patient in the video, who appears to be of child-bearing age and is shown with two young children, states (emphasis added), *"I've been using DUOBRII for 2 years, it works into my routine. I have cleared my plaque psoriasis on my elbows. I didn't have flaky skin, it wasn't sore, it wasn't red. When I have a flare up, I apply it."* ▪ OPDP concluded that this implies that "a female of reproductive potential can initiate Duobrii or use it whenever she has a psoriasis flare up without regard to the measures needed to mitigate the risk of birth defects associated with Duobrii."

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					○ OPDP further explained that the video also "fails to include any information regarding the warning and precaution for photosensitivity and the risk for sunburn. This omission is further exacerbated by claims and presentations of a Duobrii-treated patient depicted outside, with exposed shoulders and arms. In earlier scenes, before Duobrii is introduced, the same patient states, *'Coworkers, my husband, my kids, even my students would notice my elbow. So, I would wear a lot of three-quarter length even when it was warm outside . . . .'"* ▪ OPDP concluded that these claims and this presentation "suggest that a patient does not need to take measures to avoid exposure to sunlight after treatment with Duobrii when this is not the case." ○ Lack of Fair Balance - OPDP also objected to how the video presents information related to warnings and precautions "in text-only format in small font relegated to the bottom of the screen. At the same time, benefit claims for Duobrii are prominently presented on the screen in large print while also simultaneously announced verbally by the narrator in the audio portion of the video." OPDP found that this minimized the risks of the drug. • **False or Misleading Claims about Efficacy** Misleading and Unsubstantiated Superiority Claims ○ OPDP noted that the video shows a physician spokesperson making the following claim regarding the efficacy of Duobrii (emphasis added): ▪ *"Adults with plaque psoriasis now have another topical treatment option. Approved by the FDA in 2019, DUOBRII is the first and only topical that combines two active ingredients, both with anti-inflammatory benefits that limit plaque growth."* ○ OPDP pointed out that, in reality, "[t]here are other FDA-approved topical combination products (e.g., betamethasone and calcipotriene) marketed prior to Duobrii for the treatment of plaque psoriasis." ○ OPDP was also concerned with the following superiority claims made by the video's patient spokesperson (emphasis added): ▪ *"I have seen many doctors over the last 11 years for my psoriasis. The creams I was prescribed were thick, and greasy, and they had an odor and they did not work for me."* ▪ *"When I first started using DUOBRII, I noticed how light and non-greasy it was. Within days, I started to see results."* ▪ *"I've been using DUOBRII for 2 years, it works into my routine. I have cleared my plaque psoriasis on my elbows. I didn't have flaky skin, it wasn't sore, it wasn't red."* ○ OPDP concluded that these claims misleadingly suggest that (1) "Duobrii is clinically superior to or more effective than other treatments for plaque psoriasis when this has not been demonstrated," and (2) "Duobrii has been shown to be effective in patients who failed to respond to other plaque psoriasis treatments, when this is not the case." ▪ OPDP noted that although such claims may accurately reflect an individual spokesperson's own experience with a drug, a personal experience alone cannot support the suggestion that a drug is superior to others on the market. The inclusion of superimposed text in the video stating that *"People with psoriasis may respond to treatments differently and at different times. Individual results may vary"* does not effectively mitigate this misleading impression.

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					Unsubstantiated efficacy claims ○ On the webpage, OPDP also highlighted the following efficacy-related misleading claims and presentations (bolded emphasis original, underlined emphasis added, references omitted): ▪ ***"Demonstrated synergy: superior efficacy vs the aggregated results of two monotherapies"*** ▪ A graph entitled, *"Treatment success at 8 weeks with the effect of the vehicle removed"* • A bar graph that depicts *"treatment success"* as 42.8% for Duobrii Lotion and 32.5% for the monotherapies aggregated, after the vehicle results are removed. ▪ ***"More patients experienced treatment success with DUOBRII Lotion than the aggregated success rates of both monotherapies"*** ▪ *"DUOBRII Lotion exceeded the clinical definition of synergy by 31.7% at 8 weeks"* ○ OPDP stated that these claims regarding efficacy and mechanism of action are misleading as they draw conclusions based on inadequate data. Specifically, claims "are based on data derived from post hoc analyses of a single phase 2 trial, of limited sample size." The claims describing treatment success at 8 weeks overstate efficacy because they "present[] a much larger difference in efficacy between treatment arms than was actually demonstrated.".
02-11-22	**Leronlimab (IND)** Leronlimab is an investigational new drug for which there is no emergency use authorization or marketing approval in the United States.	**WL**	**N/A**	**CEO Video Interview**	• **Misbranding of an Investigational New Drug** ○ OPDP issued this Warning Letter after reviewing a video interview dated September 22, 2021, featuring the company's CEO discussing leronlimab, an investigational new drug being studied for the treatment of COVID-19. The video was made available on the corporate website via hyperlink to Proactive Media's YouTube page. Proactive Media is a publishing service, compensated to publish content. ○ Approximately four months before this video was released, FDA issued a public statement addressing the development of leronlimab and noting that "[w]ith the conclusion of both the CD10 and CD12 clinical trials, it has become clear that the data currently available do not support the clinical benefit of leronlimab for the treatment of COVID-19."[1] ○ OPDP found that the CEO video interview mischaracterized data and made promotional statements regarding efficacy of investigational leronlimab as a treatment for COVID-19. In reality, the study failed its primary and secondary endpoints. Some examples include (underlined emphasis added): ▪ *"In the United States, we did a trial of 394 patients which included severe and critically ill population. In the critically-ill population, our results were really strong. . ."* ▪ *"Our critically-ill population that we did in the United States when we gave a dose of leronlimab, the survival rate was 78%. Once we gave them another dose, the survival rate went up to 82%."* ▪ *"Imagine, if 78% went to 82, the next one would be maybe 88, and then 95. I am making up numbers, but if it goes to that kind of numbers, if it just follows the same pattern what we learned, this is going to be the most fantastic results anybody could ever imagined to have. Now I'm not saying that's what we're going to get, but I'm saying that's what the results are showing."*

[1] FDA Statement on Leronlimab (May 17, 2021), available at https://www.fda.gov/drugs/drug-safety-and-availability/statement-leronlimab.

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					▪ *"The primary endpoint…is the discharge, the rate of patients who get on ventilator and get discharged. That endpoint was 166% better in our trial that we did in the United States versus placebo…166%."* ○ OPDP concluded that the video "significantly mischaracterizes" the drug's clinical trial data, and "create[s] a misleading impression regarding the safety and efficacy of the product." ▪ To OPDP, this video is particularly concerning from a public health perspective as it suggests that the drug provided a clinical benefit to those with COVID-19, which can result in respiratory failure and death.
01-19-2022	**TRULICITY® (dulaglutide) injection, for subcutaneous use** Trulicity is indicated (1) as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus and (2) to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.	UL	Yes	Social Media Post (Instagram Ad)	• **False or Misleading Benefit Presentation** ○ OPDP issued an Untitled Letter for an Instagram post for the type 2 diabetes drug, Trulicity. The Untitled Letter indicated that FDA received a Bad Ad Program complaint regarding this Instagram post and other posts with similar claims and presentations. Omission of Material Information from the Approved Indication ○ OPDP found the Instagram post to be misleading because "the video portion of the post prominently communicates that Trulicity can help *'lower A1C along with diet and exercise,'* but it fails to adequately communicate Trulicity's FDA-approved indication and the limitations of use." Namely, OPDP noted that the drug's Medication Guide contains the following (underlined emphasis added): ▪ *TRULICITY is an injectable prescription medicine that is used:* • *along with diet and exercise to improve blood sugar (glucose) in adults with type 2 diabetes mellitus.* ▪ *It is not known if TRULICITY can be used in people who have had pancreatitis.* ▪ *TRULICITY is not a substitute for insulin and is not for use in people with type 1 diabetes or people with diabetic ketoacidosis.* ▪ *TRULICITY is not recommended for use in people with severe stomach or intestinal problems.* ○ OPDP concluded that the post's communication of the scope of the drug's FDA-approved indication is misleading as it has not been demonstrated that Trulicity will help *"lower A1C"* in all patients. ○ OPDP also noted that "the indication and the limitations of use are presented only in small, fast-paced scrolling font in a small window below the video, relegated to the bottom of the post, competing for the consumer's attention with several distracting video elements . . . that detract from the communication of the indication and limitations of use." Ultimately, this caused OPDP to find that this presentation does not mitigate the post's misleading impression. • **False or Misleading Risk Presentation** Lack of Fair Balance ○ OPDP found the post to be misleading as it fails to "present information relating to risks associated with the drug with a prominence and readability reasonably comparable with the presentation of information relating to the benefits of the drug." ▪ Specifically, the post prominently displays benefits claims about the drug, emphasized by "colorful, compelling, and attention-grabbing fast-paced visuals that take up the majority of the post in a video with frequent scene changes, busy scenes, and large-moving superimposed text along with other competing modalities such as the strong, fast-moving musical beat," but it

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					confines risk information to "a small window" in the bottom of the post and presents it "using fast-paced, scrolling, small font that is difficult to read and cannot be adequately processed or comprehended by consumers." <u>Omission of Material Information</u> ○ Additionally, OPDP noted that the post does not include material information from the warning and precaution for hypoglycemia with concomitant use of insulin secretagogues or insulin.

DEVICES

Date (Hyperlink to Letter)	Device Indications (As Referenced in Letter)	Letter Type	Form of Communication	Summary of Alleged Violations
11-18-2022	**CellQuicken Analyzer (Smart-Watch, and Software)** **RoyalVibe Ultrasound Generator** **Envirovibe Water Restructuring Pad** **Brainvibe Neuroplasticity Visual Program** **RoyalVibe Therapy Balls** **RoyalVibe Application** These devices are marketed as a kit and as individual devices, intended for the diagnosis and treatment of several diseases including but not limited to cancer, Alzheimer's, ischemic stroke, arthritis, and type 1 diabetes.	WL	**Website – RoyalVibe** **Website – CellQuicken**	• **Promotion of Unapproved New Device** ○ For each of these six products, OPEQ listed multiple claims and/or IFU quotes that revealed that the products are devices intended to cure, mitigate, treat, or prevent disease, or they are intended to affect the structure or any function of the body, yet the company did not have clearance or approval for the devices. The following are select examples: ▪ CellQuicken Analyzer claim: • *"'CellQuicken Analyzer' is the tool that helps detect the root cause of your condition. It helps you understand why the disease formed in the first place."* ▪ RoyalVibe Ultrasound Generator claim: • *"RoyalVibe Health uses 'Bioresonance Focused Ultrasound' technology and our therapy protocol help heal from different condition diagnoses, like Alzheimer's, Diabetes, Stroke, Cancer, and many others."* ▪ Envirovibe Water Restructuring Pad IFU: • *"According to feedback from our clients, in addition to restructuring your water, the EnviroVibe has proven to be incredibly effective for treating pain; inflammation; wounds; broken bones; stomach ailments such as diarrhea or constipation, etc."* ▪ BrainVibe Neuroplasticity Program IFU: • Screenshot of companion app includes an Audio *"Treatment List"* for *"Addiction Reduction"* ▪ Therapy Balls Spine Alignment claim: • *"Not only is it effective for general health, immune system, and such conditions as severe scoliosis, but it also has shown some major pain relief for people with Parkinson's disease, depression, Glaucoma, headache, Migraine, joint pain, and other mild and severe health conditions."* ▪ RoyalVibe Application IFU: • *"9. On your RoyalVibe application, log into your Health Advice Hub account on the application. Find your treatment under the correct dependent and run the program."* ○ In the Warning Letter, OPEQ stated that because the company has not fulfilled annual registration and device listing requirements for fiscal year 2022, all of the company's devices are deemed misbranded. Further, because there is no approved application for premarket approval (PMA), approved investigational device exemption, or cleared 510(k) exemption for any of the devices, they are also deemed adulterated and misbranded. ○ Additionally, OPEQ noted that "an FDA investigator provided you [the company] with a Notice of Inspection on June 17, 2022, but you did not permit FDA's inspection of your establishment," and "you did not respond to the investigator's subsequent requests to inspect your establishment." OPEQ stated that the company indicated that it "uses this establishment as an address for customers in the United States to return their products for repair or replacement."

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				▪ Accordingly, this amounted to denying and/or limiting an inspection of the company's establishment where the devices are processed, packed, and/or held, which is a violation of the Federal Food, Drug, and Cosmetic Act ("FDCA" or "the Act"), resulting in further adulteration of the devices.
09-15-22	**Plasma MD** **Plasma +** These are devices intended to improve the appearance of skin by stimulating the production of collagen and other proteins.	**WL**	Website	• **Promotion of Unapproved New Device** ○ FDA found, and the company acknowledged in an FDA-483 response, that the products at issue are devices as they were intended to affect the structure or any function of the body (e.g., tightening and smoothing skin; lessening the appearance of lines or wrinkles). This was evidenced by claims on the company's website, such as: ▪ *"This handheld device looks like a pen, but it's actually a state-of-the-art tool that uses plasma, a naturally occurring ionized gas, to combat wrinkles and tighten sagging skin on the face and body."* ▪ *"PlasmaMD works to improve skin by stimulating the production of collagen and elastin, the proteins that keep skin firm and supple."* ○ In this Warning Letter, OPEQ concluded that the products are adulterated because the company does not have an approved PMA or an approved application for an investigational device exemption for any of these devices. ○ OPEQ also found that the devices are misbranded on three fronts: ▪ The company did not timely notify FDA of its intent to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of the devices, as required by section 510(k) of the Act, ▪ The labels of the devices did not bear a unique device identifier, as required for every medical device, and ▪ The company, as a labeler of a device, failed to submit required information electronically to FDA's Global Unique Device Identification Database (GUDID). ○ The Warning Letter also detailed seven unique instances in which the company failed to comply with current good manufacturing practice requirements; thus, on these grounds too, the products are adulterated.
08-05-22	**Relumins Premium Derma Pen** **Relumins Premium Derma Pen Plus** **MESOpower pen and needle modules** **Relumins Branded 35 needle Dermastamper** **Relumins Branded 80 needle Dermastamper**	**WL**	Website	• **Promotion of Unapproved New Device** ○ OPEQ determined that the products at issue are devices as they "are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body." Specifically, the products are intended to affect the structure or function of the body because they use technology/features that "indicate penetration or some effect beyond the stratum corneum into living layers of skin" or "provide[] micro current to 'stimulate the body's tissue[s]' that will 'target' various areas on the face and neck." The following select claims from the company's website support this finding: ▪ Relumins Premium Derma Pen & Relumins Premium Derma Pen Plus • *"Can help to lighten the appearance of hyper-pigmentation."* • *"Use the pen on your face or body to reduce the appearance of acne scars, fine lines, wrinkles and stretch marks."* • *"You can even use it on your scalp to stimulate hair growth."*

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	Relumins branded 1200 needle Dermaroller 1.0 mm **Relumins branded 1200 needle Dermaroller 2.0 mm** **Relumins Intense Glow Beauty Care Tool** These are devices intended to improve the appearance of skin through the use of needles or electrical current that affect the structure or function of the body.			▪ MESOpower Pen and Needle Modules • *"More than 50% of stretch marks and acne scar improvement"* ▪ Relumins Branded 35 Needle Titanium Needle Dermastamper and Relumins Branded 80 Needle Dermastamper • *"Improves skin texture and reduces the appearance of wrinkles"* • *"0.05mm (click for Relumins Roller in this size!)- Fine lines, Light Wrinkles, Open Pores, Pigmentation Marks, Acne Scars, Mild Ice Pick Scars, Face Rejuvenation"* ▪ Relumins Branded 1200 Needle Dermaroller 1.0 mm and Relumins Branded 1200 Needle Dermaroller 2.0 mm • *"Lighten Acne Scar Hyper-pigmentation to Reduce the Appearance of Indented Acne Scars, Wrinkles and Lines"* ▪ Relumins Intense Glow Beauty Care Tool • *"Target areas include under-eye pouches, crow's feet, wrinkles around the nose and mouth, chin skin, frown lines and improving the appearance of neck wrinkles"* • *"Solar panel provides microcurrent to stimulate the body's tissue"* ○ Based on FDA's review of "evidence collected during [an] inspection, including product packaging and labels, user manuals, brochures, and product labeling on your firm's website," the Agency determined that the products are both adulterated and misbranded. ▪ The devices are adulterated because for each product, there is no approved application for PMA or approved investigational device exemption. ▪ The devices are also misbranded because the company does not have a cleared 510(k) for any of the devices and has not fulfilled annual registration and device listing requirements for fiscal year 2022. ○ Although the company attempted to claim in its FDA-483 response that the investigator indicated that the company did not distribute devices, this was inconsistent with the investigator's documented findings on the FDA-483.
02-28-22	**NeuroField X3000/X3000 Plus (device)** **NeuroField Q21 (device)** NeuroField X3000 and NeuroField Q21 were registered and listed as biofeedback devices, which are "instrument[s] that provide[] a visual or auditory signal corresponding to the status of one or more of a patient's physiological parameters (e.g., brain alpha wave activity, muscle activity, skin	**WL**	Website	• **Promotion of Unapproved New Device** ○ OPEQ acknowledged that NeuroField X3000 and NeuroField Q21 were registered and listed as biofeedback devices, which is a device type that is exempted from premarket notification procedures "when it is a prescription battery powered device that is indicated for relaxation training and muscle reeducation and prescription use." ○ Yet, after reviewing the company's website and materials, OPEQ found that the devices are being intended for uses that "exceed or otherwise differ from the [biofeedback device] classification." Because of this difference, premarket 510(k) notification would be required before introducing the devices into commerce for commercial distribution. The company, however, failed to fulfill this requirement, so the products are misbranded. ○ In addition to claims found in the products' manuals, the following are select examples of claims from the company's website:

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	temperature, etc.) so that the patient can control voluntarily these physiological parameters." **NeuroField64 and NeuroField EEG (software products)** These software products accompany the company's other products.			▪ NeuroField X3000/X3000 Plus website claim, indicating that it is "intended for stimulation-based treatment use, which is an intended use beyond the scope of the biofeedback device classification" • *"The X3000 Plus is a low intensity 4 channel pEMF (pulsed electromagnetic field) generator using four 400-wind coil packs for precision placement anywhere on the body."* • *"[T]he X3000 Plus is the first pEMF system in the world to combine stimulation with z-score, norm referenced operant conditioning methods."* ▪ NeuroField64 Q21 website claim, indicating that it is "intended for use as an electroencephalograph (EEG), which is a device use that . . . is not exempt from premarket notification requirements." • *"The Q21 is a 19+1 channel Electroencephalogram with a low noise floor of 0.25 µV peak to peak from 0.1 to 10.0Hz, meaning that you can record EEG without worrying about noise contamination."* • *"The Q21 is a Quantitative Electroencephalograph . . . ."* o Additionally, the firm's website and materials that accompany its devices refer to the NeuroField64 and NeuroField EEG software products. The descriptions of the use and functions of these products cause them to appear to meet the definition of device under the FDCA. For example, the website makes claims such as the following: • *"NeuroField64 is a 64-bit program that brings together all of NeuroField's hardware products and features into one platform!"* • *"The X3000 Plus is a software-controlled system which is fully customizable all the way down to the easy-to-use patient database."* The specifications for X3000 Plus identify NeuroField64 as the compatible software. • *"NeuroField EEG is a 64-bit program module, used in conjunction with NeuroField's Q21 Amplifier that marks the beginning of our journey into EEG recording and analysis."* • *"Record EEG in a pristine 24-bit resolution with a frequency range of 0.5 - 70 Hz range."* o OPEQ also found that the company promoted its products on other websites, including seemingly independent websites that were actually under ownership or the control of the company's CEO, and social media for uses that are beyond the scope of biofeedback device classification, "such as recording QEEG data, neurostimulation, and treatment of various medical conditions." o Additionally, OPEQ found that the products are also adulterated as there is no approved application for PMA or approved investigational device exemption for any of these devices, and there are six unique instances in which the company failed to comply with current good manufacturing practice requirements.
01-28-2022	**CLEAR** This device is a "Needle-type epilator." **ERASE**	**WL**	Website	• **Promotion of Unapproved New Device** o After reviewing the company's website, OPEQ determined that these products are devices as they "are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body." o Accordingly, because the company does not have an approved PMA, an approved application for an investigational device exemption, or a cleared 510(k) notification for any of these devices, and, for

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	This device appears to be classified under the regulation pertaining to electrosurgical cutting and coagulation device and accessories. **LIFT** This device appears to be classified under the regulation pertaining to focused ultrasound stimulator system for aesthetic use. **SILK** This device appears to be classified under the regulation pertaining to laser surgical instrument for use in general and plastic surgery and in dermatology.			the CLEAR device appears to exceed the limits of an applicable 510(k)-exemption, these devices are deemed adulterated and misbranded. Specifically: ▪ CLEAR: needle-type epilators are only "intended to destroy the dermal papilla of a hair," and these devices are ordinarily exempt from a premarket notification requirement, but this product is marketed for different intended uses that exceed the exemption and thus trigger the 510(k) requirement. For instance, the device is marketed to address, among other issues: • "Telangiectasia (capillaries)" • "Clogged Pores" • "Skin Tags" • "Fibromas" ▪ ERASE: electrosurgical cutting and coagulation devices and accessories are not 510(k)-exempt, but the company does not hold a 510(k) for the device. Additionally, generic devices of type are "intended to remove tissue and control bleeding by use of high-frequency electrical current." Yet, the company markets this product with claims such as the following: *"[t]he combination of microneedles and radio frequency heats the underlying layers, causing constriction and tightening of the skin, as well as the stimulation of collagen and elastin production."* ▪ LIFT: ultrasound stimulator systems for aesthetic are not 510(k)-exempt, but the company does not hold a 510(k) for the device. Additionally, generic devices of this type use "focused ultrasound to produce localized, mechanical motion within tissues and cells for the purpose of producing either localized heating for tissue coagulation or for mechanical cellular membrane disruption" and are intended for "noninvasive aesthetic use." Notably, the company's website claims that this device's mechanism of action is *"High Intensity Focused Ultrasound (HIFU)"* that *"directly delivers heat energy to skin and subcutaneous tissue."* Additional listed benefits include *"Lifts & Tightens Cheeks"* and *"Improve the Jawline."* ▪ SILK: laser surgical instruments for use in general and plastic surgery and in dermatology are not 510(k)-exempt, but the company does not hold a 510(k) for the device. Additionally, generic devices of this type are "laser device[s] intended to cut, destroy, or remove tissue by light energy emitted by carbon dioxide." Yet, the company's website states that *"[t]he 'SILK 810 nm Diode Laser by Skin Sheek makes permanent hair removal affordable for your clients."* ○ Prior to issuing the Warning Letter, FDA made numerous attempts to contact the company by phone and email to resolve these issues to no avail. In a phone conversation, the company stated that the SILK device received 510(k) clearance, but it failed to provide FDA with the clearance or approval submission number.