DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

May 26, 2015

Firm name
Address

Re: PMA Number(s)

Dear X,

The Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) previously requested information from your firm to evaluate a postmarket safety issue associated with the use of soft tissue filler (dermal filler) implants approved by FDA and identified with product code LMH (Implant, Dermal, for Aesthetic Use). The safety concern is related to serious clinical consequences when the soft tissue filler implant is inadvertently injected into blood vessels. Rare but serious adverse events that are associated with intravascular injection of soft tissue filler material in the face include (acute or permanent) vision impairment, blindness, cerebral ischemia or cerebral hemorrhage, leading to stroke, skin necrosis, and damage to underlying facial structures. This issue was brought to our attention through Medical Device Reports (MDRs), publications in peer-reviewed journals[1], and clinician experts. As discussed below, additional information can be included in the labeling regarding this issue to assist health care practitioners and patients understand the risks associated with intravascular injection of soft tissue filler implants, and reduce the likelihood and/or severity of these serious adverse events. Therefore, CDRH requests that all manufacturers who currently market soft tissue filler implants review their most-recently approved health care practitioner and patient labeling, and consider including the following:

Health Care Practitioner Labeling Modifications:

- The following Warning: "Introduction of product into the vasculature may lead to embolization, occlusion of the vessels, ischemia, or infarction. Take extra care when injecting soft tissue fillers, for example inject the product slowly and apply the least amount of pressure necessary. Rare but serious adverse events associated with the intravascular injection of soft tissue fillers in the face have been reported and include temporary or permanent vision impairment, blindness, cerebral ischemia or cerebral

[1] Several literature articles were reviewed including:
Curruthers JD, Fagien S, Rohrich RJ, Weinkle S, Curruthers A. Blindness Caused by Cosmetic Filler Injection: A Review of Cause and Therapy. *Plastic and Reconstructive Surgery*, 2014; 134(6): 1197-1201.

Ozturk CN, Li Y, Tung R, Parker L, Piliang MP, Zins JE, Complications Following Injection of Soft-Tissue Fillers. *Aesthetic Surgery Journal*, 2013; 33(6): 862-877.

hemorrhage, leading to stroke, skin necrosis, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following symptoms, including changes in vision, signs of a stroke, blanching of the skin, or unusual pain during or shortly after the procedure. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner specialist should an intravascular injection occur."

- The following Precaution: "In order to minimize the risks of potential complications, this product should only be used by health care practitioners who have appropriate training, experience, and who are knowledgeable about the anatomy at and around the site of injection."

- The following Precaution: "Health care practitioners are encouraged to discuss all potential risks of soft tissue injection with their patients prior to treatment and ensure that patients are aware of signs and symptoms of potential complications."

- In addition, consider inclusion of available safety information that has been collected through surveillance of post-market use of your device(s), including adverse reactions to intravascular injection of soft tissue fillers into the Post-Market Surveillance section of your health care practitioner labeling. Please contact Mark Trumbore (Mark.Trumbore@fda.hhs.gov or by phone 301-796-6970) in the Office of Device Evaluation prior to submitting a PMA Supplement for further information on appropriate information to include under the Post-Market Surveillance section of the health care practitioner labeling.

Patient Labeling Modifications:

- The following information to any form of instructions for use, and brochures distributed to patients: "Warning: One of the risks with using this product is unintentional injection into a blood vessel. The chances of this happening are very small, but if it does happen, the complications can be serious, and may be permanent. These complications, which have been reported for facial injections, can include vision abnormalities, blindness, stroke, temporary scabs, or permanent scarring of the skin. If you have changes in your vision, signs of a stroke (including sudden difficulty speaking, numbness or weakness in your face, arms, or legs, difficulty walking, face drooping, severe headache, dizziness, or confusion), white appearance of the skin, or unusual pain during or shortly after treatment, you should notify your health care practitioner immediately."

Submitting the Requested Label Changes to FDA

Modification to PMA labeling requires the submission of a PMA Supplement to FDA. A *Special PMA Supplement – Changes Being Effected* is an appropriate Supplement to submit for the labeling changes described above. Please note that this type of Supplement does not require the submission of a user fee. Refer to FDA's guidance "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision" (Section IV, Part E) for guidance on submitting PMA supplements for changes to an existing PMA device.

If you choose to modify your labeling, please submit a PMA Supplement within 45 days from the date of this letter. To facilitate review of your submission, please provide a red-lined copy and a clean copy.

Please note. If you choose to modify your labeling to address this issue but plan to deviate from the suggested language above, we are providing you the opportunity to receive FDA feedback on your language prior to your implementation and submission of a new PMA Supplement. Please contact Kathleen White at CDRHSignalManagement@fda.hhs.gov if you choose to pursue this option. Additionally, please keep in mind FDA's Guidance on Medical Device Patient Labeling, issued on April 19, 2001 when modifying your patient labeling. This guidance document outlines the recommended sequence for important information, as well as how to present that information in ways that are appropriate and comprehensible for lay readers.

If you modify your device labeling, submit three (3) copies of the PMA supplement and reference the PMA number above to facilitate processing. Clearly mark the Supplement as a *Special PMA Supplement- Changes Being Effected*. Send PMA supplements to the following address:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center - W066-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Supplements should be submitted in accordance with FDA's guidance, "eCopy Program for Medical Device Submissions."

Please acknowledge receipt of this letter via email within 3 business days by replying to CDRHSignalManagement@fda.hhs.gov. Please include your manufacturer and device name in the subject line of the email. If you have questions about this request, please contact Kathleen White at the same email address or by telephone at 301-796-5832.

Sincerely,

Aron Yustein, M.D.
Clinical Deputy Director and Chief Medical Officer
Office of Surveillance and Biometrics
Center for Devices and Radiological Health
U.S. Food and Drug Administration