DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 201739/S-006

SUPPLEMENT APPROVAL
NEW POSTMARKETING REQUIREMENTS

Kaleo, Inc.
111 Virginia Street, Suite 300
Richmond, VA 23219

Attention: Glen Kelley
Director, Regulatory Affairs

Dear Mr. Kelley:

Please refer to your Supplemental New Drug Application (sNDA) dated and received August 19, 2016, and your amendments, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Auvi-Q (epinephrine injection, USP) Auto-Injector.

This "Changes Being Effected in 30 days" supplemental new drug application provides for a new drug cartridge assembly line (b) (4)

We have completed our review of this supplemental new drug application, as amended. This supplement is approved.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

Since Auvi-Q (epinephrine injection, USP) was approved on August 10, 2012, we have become aware of the voluntary recall of Auvi-Q (epinephrine injection, USP) Auto-Injector due to the potential for device failure, inaccurate dose delivery, and failure to deliver drug. Device failure may result in the serious risk of untreated anaphylaxis and subsequent loss (i.e. failure) of the

expected pharmacologic action of Auvi-Q (epinephrine injection, USP). We consider this information to be "new safety information" as defined in section 505-1(b)(3) of the FDCA.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify the unexpected serious risk of untreated anaphylaxis that may result from device failure when using Auvi-Q (epinephrine injection, USP) Auto-Injector.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

3172-1 Develop a reliability requirement and specification, complete adequate testing to verify the reliability specification, and control the reliability of Auvi-Q (epinephrine injection, USP) Auto-Injector through manufacturing and future modifications.

The timetable you submitted on February 16, 2017 states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	May	2017
Final Protocol Submission:	September	2017
Study Completion:	April	2018
Final Report Submission:	June	2018

Submit the reliability specification, test protocol, and manufacturing control plan for PMR 3172-1 in your protocol submission for review by the Agency. The study protocol must be finalized with FDA concurrence prior to initiating testing.

3172-2 Conduct a case study analysis of all reports of failure of Auvi-Q (epinephrine injection, USP) Auto-Injector to activate, or failure of Auvi-Q (epinephrine injection, USP) Auto-Injector to deliver the full-labeled dose, or other device malfunctions. Perform detailed analyses of reported device failures (including reported malfunctions that did, as well as did not result in patient harm), full event narratives of the failure and any subsequent adverse events, and the results of root cause analysis performed for the reported failure.

The timetable you submitted on February 16, 2017 states that you will conduct this study according to the following schedule:

Final Protocol Submission:	June	2017
Interim Report Submission:	October	2018
Interim Report Submission:	October	2019
Final Report Submission:	October	2020

Interim analysis reports for PMR 3172-2 should also include a description of your procedures for monitoring and analyzing the adverse event reports. Additionally, include in your interim reports an analysis of the reporting period data as well as an overall analysis of the cumulative data.

Submit the protocols to your IND 119686 with a cross - reference letter to this NDA. Submit all final reports to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: "**Required Postmarketing Protocol Under 505(o)**", "**Required Postmarketing Final Report Under 505(o)**", "**Required Postmarketing Correspondence Under 505(o)**".

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80).

If you have any questions, call Carol F. Hill, Senior Regulatory Health Project Manager for Safety, at 301-796-1226.

Sincerely,

{See appended electronic signature page}

Sally Seymour, MD
Deputy Director for Safety
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SALLY M SEYMOUR
02/17/2017