



Food and Drug Administration
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Document Control Room W-066-0609
Silver Spring, MD 20993-0002

Ms. Debera Brown
Vice President, Regulatory Affairs
Asthmatx, Incorporated
888 Ross Drive, First Floor
Sunnyvale, California 94089

APR 27 2010

Re: P080032
Alair Bronchial Thermoplasty System: Alair Catheter and Alair RF Controller
Filed: December 30, 2008
Amended: January 6, February 4, February 17, June 9, June 11, June 25, October 1,
October 9, 2009, December 11, 2009, and December 14, 2009
Procode: OOO

Dear Ms. Brown:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Alair Bronchial Thermoplasty System. This device is indicated for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long acting beta agonists. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at one year.

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for the Alair Catheter and Alair RF Controller, the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you have agreed to provide the following data in post-approval study (PAS) reports. Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.

1. The first post-approval study is to evaluate durability of effectiveness of the Alair System in patients with severe persistent asthma. The study population will consist of Alair-group subjects who are currently in the follow-up phase of the AIR2 Trial (Protocol #04-02).

The primary endpoint of the PAS is the proportion of subjects experiencing severe exacerbations during the first year after the Alair treatment compared to subsequent 12-month periods out to 5 years. The study hypothesis to be evaluated is that the upper 95% confidence limit of the difference in proportions of subjects experiencing severe exacerbations (i.e., the subsequent 12-month proportion minus the first 12-month proportion) is less than 20%.

The secondary endpoints will include the following additional safety endpoints for which data are currently being collected in the AIR2 Trial:

- Severe exacerbation rates (exacerbations / subject / year)
- Respiratory adverse events (rates of respiratory adverse events, and proportion of subjects with respiratory adverse events)
- Emergency room visits for respiratory symptoms (rates of emergency room visits, and proportion of subjects with emergency room visits for respiratory symptoms)
- Hospitalizations for respiratory symptoms (rates of hospitalizations, and proportion of subjects with hospitalizations for respiratory symptoms)
- Respiratory Serious Adverse Events (detailed narratives will be provided for each event)
- Forced Expiratory Volume in 1 second (FEV₁)

For primary effectiveness endpoint, the primary analysis will test the hypothesis whether the upper 95% confidence limit of the difference in proportions of subjects experiencing severe exacerbations (i.e., the subsequent 12-month proportion minus the first 12-month proportion) is less than 20%. The proportions of patients with severe exacerbations at each year will be calculated with the denominator as the number of patients who complete follow-up visits for that particular year. Patients who are lost to follow-up will be excluded from the analysis.

In addition to the primary analyses, a sensitivity analysis will be conducted at 5 years.

Secondary effectiveness endpoints will be evaluated with descriptive statistics with 95% CI. All adverse events (AE) will be summarized by the number of the subjects reporting the adverse events, system organ class, preferred term, severity, relationship to procedure, and the duration of the AEs.

You have also agreed to make every reasonable effort to limit the cumulative loss-to-follow-up to be less than 20% at the 5 year follow-up (with an average yearly loss <5%). Beginning with the subjects entering the study at Year 2, and assuming a 20% dropout, approximately 140 subjects are expected to be evaluable for the 5-year endpoint.

2. The second PAS study will be a prospective, open-label, single arm, multi-center study conducted in the United States. The study objective is to demonstrate durability of treatment effect and to evaluate the short-term and longer-term safety profile of the Alair System in the United States in the intended use population. The sponsor will enroll up to 300 subjects (a minimum of 250 subjects) to achieve 200 evaluable study subjects at the end of 5 years post-treatment; this is based on a 20% lost-to-follow-up over 5 years.

The primary endpoint will be the proportion of subjects experiencing severe exacerbations during the subsequent 12-month periods (for Years 2, 3, 4, and 5) compared to the first 12-month proportion after the Alair treatment. The study hypothesis is to demonstrate that the proportion of subjects who experience severe exacerbations in the subsequent 12-month follow-up [for Year 2, Year 3, Year 4 and Year 5 (in 12-month periods)] is not statistically worse when compared with the first 12-month proportion, which begins 6-weeks after the last Alair treatment. This objective will be met if the upper 95% confidence limit of the difference in proportions (i.e., the subsequent 12-month proportion minus the first 12-month proportion) is less than 20%.

The secondary endpoints will include the following additional safety endpoints which will be evaluated annually through Year 5 following treatment with the Alair System:

- Rates of Severe exacerbations (exacerbations / subject / year)
- Respiratory adverse events (rates of respiratory adverse events, and proportion of subjects with respiratory adverse events)
- Emergency room visits for asthma symptoms (rates of emergency room visits and proportion of subjects with emergency room visits for asthma symptoms)
- Hospitalizations for asthma symptoms (hospitalizations/ subject/ year, and proportion of subjects with hospitalizations for respiratory symptoms)
- Respiratory Serious Adverse Events (detailed narratives will be provided for each event)
- Pre- and post-bronchodilator FEV₁

The analysis plan for the primary and secondary effectiveness endpoints, and the AEs will be the same as described for the first PAS in this order.

You have also agreed to make every reasonable effort to limit the cumulative loss-to-follow-up to less than 20% at the 5 year follow-up (with an average yearly loss <5%). If the follow-up rate is unacceptably low during the 5 year follow-up, FDA will consider other options to limit loss-to-follow-up, including requiring you to recruit more subjects.

You must also update your patient and physician labeling (via PMA supplement) to reflect the results of the post-approval study at 5 years, as soon as these data are available, as well as any other time points deemed necessary by FDA if significant new information from the study becomes available.

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval studies. Your PMA supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order"

(www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process"

(www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise become aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can

process, review and archive (general information:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm>; clinical and statistical data:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm>)

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Michael J. Ryan at 301-796-6283.

Sincerely yours,

Handwritten signature of Christy Foreman in black ink.

Christy Foreman
Acting Director
Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration

4/27/2010