DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125476/0

BLA APPROVAL

Takeda Pharmaceuticals U.S.A., Inc.
Attention: Colleen Costello, Ph.D.
Senior Director, Regulatory Affairs
Millennium Pharmaceuticals, Inc.
40 Landsdowne Street
Cambridge, MA 02139

Dear Dr. Costello:

Please refer to your Biologics License Application (BLA) dated and received June 20, 2013, submitted under section 351(a) of the Public Health Service Act for Entyvio (vedolizumab).

We acknowledge receipt of your amendments dated March 27, 2013, April 08, 2013, July 03, 08, 24, 25, 30, 2013, August 08, 21(2), 23, 28, 2013, September 09(3), 6, 18(2), 20, 25, 2013, October 03, 04, 07, 11, 15, 18, 21, 22, 23, 30(2), 2013, November 04, 06, 08, 11(2), 14, 15(2), 18, 19, 20, 26(2), 27(2), 2013, December 02, 05, 06(3), 11, 2013, January 14, 15, 16(2), 20, 22, 24, 27, 31(2), 2014, February 10, 20, 25, 27, 28, 2014, March 10, 11, 20, 26, 31, 2014, April 02, 03, 07, 10(2), 14(2), 17, 23, 28, 30, 2014, May 02, 05, 07, 08, 09(2), and May 16, 2014.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 1898 to Takeda Pharmaceuticals U.S.A., Inc., Deerfield, IL, under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product Entyvio (vedolizumab).

ENTYVIO (vedolizumab) is indicated for:

- inducing and maintaining clinical response,
- inducing and maintaining clinical remission,
- improving the endoscopic appearance of the mucosa, and
- achieving corticosteroid-free remission

in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

and,

ENTYVIO (vedolizumab) is indicated for:

- achieving clinical response,
- achieving clinical remission, and
- achieving corticosteroid-free remission

in adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture vedolizumab drug substance at (b) (4) (b) (4). The drug product will be manufactured at (b) (4) (b) (4). Drug product will be labeled and packaged at (b) (4) (b) (4) You may label your product with the proprietary name, Entyvio, and will market it as a single use vial containing 300 mg vedolizumab lyophilized powder for Injection.

DATING PERIOD

The dating period for Entyvio (vedolizumab) shall be 36 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the (b) (4) (b) (4) The dating period for your drug substance shall be (b) (4) (b) (4)

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Entyvio (vedolizumab) to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Entyvio (vedolizumab), or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your December 06, 2013, submission containing final printed carton and container labels.

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 indications in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric studies requirement for patients ages 0 to 4 years with moderately to severely active ulcerative colitis because necessary studies are impossible or highly impracticable. This is because there is a low incidence of the disease in this age group. We are waiving the pediatric studies requirement for patients ages 0 to 5 years with moderately to severely active Crohn's disease because necessary studies are impossible or highly impracticable. This is because there is a low incidence of the disease in this age group.

We are deferring submission of your pediatric studies for ages 5 to 17 years (moderately to severely active ulcerative colitis) and for ages 6 to 17 years (moderately to severely active Crohn's disease) for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing

studies must be reported annually according to 21 CFR 601.28 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

1. Conduct a juvenile animal toxicology study of 3 months duration in an appropriate species before initiation of the pediatric studies in patients 5 to 17 years of age.

   Final Protocol Submission: February 2015
   Study Completion: August 2015
   Final Report Submission: February 2016

2. Conduct a dose-ranging study to determine the pharmacokinetics/ pharmacodynamics, safety, and tolerability of Entyvio (vedolizumab) in pediatric patients 5 to 17 years of age with moderately to severely active ulcerative colitis or Crohn's disease who have failed conventional therapy.

   Final Protocol Submission: March 2016
   Study Completion: July 2019
   Final Report Submission: July 2020

3. Conduct a randomized, placebo-controlled, blinded, multicenter study of the induction and maintenance of clinical response and remission by Entyvio (vedolizumab) in pediatric patients 6 to 17 years of age with moderately to severely active Crohn's disease who have failed conventional therapy.

   Final Protocol Submission: August 2020
   Study Completion: May 2026
   Final Report Submission: May 2027

4. Conduct a randomized, placebo-controlled, blinded, multicenter study of the induction and maintenance of clinical response and remission by Entyvio (vedolizumab) in pediatric patients 5 to 17 years of age with moderately to severely active ulcerative colitis who have failed conventional therapy.

   Final Protocol Submission: August 2020
   Study Completion: June 2027
   Final Report Submission: June 2028

Submit the protocols to your IND 009125 with a cross-reference letter to this BLA.

Reports of these required pediatric postmarketing studies must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark

your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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.

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 assess a signal of a serious risk of serious infections (such as respiratory and gastrointestinal infections) or to identify the unexpected serious risks of progressive multifocal leukoencephalopathy (PML) and malignancies related to the use of Entyvio (vedolizumab).

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 these serious risks.

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

5. A postmarketing, prospective, observational, cohort study of vedolizumab versus other agents for inflammatory bowel disease. The study's primary outcome is serious infections. Secondary outcomes include, but are not limited to, progressive multifocal leukoencephalopathy (PML), malignancy, and specific infections including gastrointestinal and upper respiratory infections. Specify concise case definitions and validation algorithms for both primary and secondary outcomes. Justify the choice of appropriate comparator population(s) and estimated background rate(s) relative to vedolizumab-exposed patients; clearly define the primary comparator population for the primary objective. Design the study around a testable hypothesis to assess, with sufficient sample size and power, a clinically meaningful increase in serious infection risk above the comparator background rate, with a pre-specified statistical analysis method. For the vedolizumab-exposed and comparator(s), the study drug initiation period should be clearly defined, including any exclusion and inclusion criteria. Ensure adequate number of patients with at least 24 months of vedolizumab exposure at the end of the study.

The timetable you submitted on April 14, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	November 2014
Interim Report Submission:	July 2018
Study Completion:	June 2021
Final Report Submission:	June 2022

Submit the protocol to your IND 009125 with a cross-reference letter to this BLA. Submit the final report to your BLA. 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 601.70 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 601.70 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 601.70. 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

6. Complete Clinical Trial C13008, an open-label trial to determine the long-term safety of Entyvio (vedolizumab) in patients with ulcerative colitis and Crohn's disease. Safety evaluations include but are not limited to the occurrence of serious infections including progressive multifocal leukoencephalopathy (PML) and malignancies.

The timetable you submitted on April 03, 2014, states that you will conduct this trial according to the following schedule:

Trial Completion:	March 2016
Final Report Submission:	March 2017

7. Conduct a prospective, observational pregnancy exposure registry study in the United States that compares the pregnancy and fetal outcomes of women exposed to Entyvio (vedolizumab) during pregnancy to an unexposed control population or collect Entyvio (vedolizumab) pregnancy exposure data by collaborating with an existing disease-based pregnancy registry.

The timetable you submitted on April 15, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	May 2015
Study Completion:	May 2021
Final Report Submission:	May 2022

8. Conduct a milk-only lactation study in lactating women receiving vedolizumab therapeutically to assess concentrations of vedolizumab in breast milk using a validated assay in order to appropriately inform the Nursing Mother's subsection of labeling.

The timetable you submitted on April 15, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	March 2015
Study Completion:	March 2018
Final Report Submission:	March 2019

9. A study to reanalyze banked immunogenicity serum samples from ulcerative colitis trial C13006 and Crohn's disease trial C13007 to determine the presence of anti-drug antibodies (ADA) using an improved ADA assay format with reduced sensitivity to product interference.

The timetable you submitted on April 03, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	April 2015
Study Completion:	March 2016
Final Report Submission:	March 2017

10. Evaluate in a step-wise approach the disease-drug-drug interaction (Disease-DDI) potential for vedolizumab to indirectly affect the exposure of CYP substrate drugs by modulating pro-inflammatory cytokines in patients with ulcerative colitis and Crohn's disease who are treated with vedolizumab.

The timetable you submitted on April 03, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	March 2015
Study Completion:	September 2019
Final Report Submission:	September 2020

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

11. To perform additional testing to confirm the monoclonality of the master cell bank.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: December 2014

12. To add osmolality testing to the vedolizumab drug product lot release specifications. The analytical procedure, qualification report, proposed acceptance criterion, and data used to set the proposed acceptance criterion will be submitted as a CBE-30.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: September 2014

13. To add polysorbate 80 testing to the vedolizumab drug product lot release specifications. The analytical procedure, qualification report, proposed acceptance criterion, and data used to set the proposed acceptance criterion will be submitted as a CBE-30.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: December 2014

14. To develop a non-reducing SDS-based assay that is capable of providing quantitative data for the evaluation of size-related impurities and to implement this assay in the release and stability programs for vedolizumab drug substance and drug product after sufficient data have been acquired to set appropriate acceptance criteria. The analytical procedure, validation report, proposed acceptance criterion, and data used to set the proposed acceptance criterion will be submitted as a CBE-30.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: February 2016

15. To develop a validated, sensitive, and accurate assay for the detection of binding antibodies to vedolizumab, including procedures for accurate detection of binding antibodies to vedolizumab in the presence of vedolizumab levels that are expected to be present in the serum or plasma at the time of patient sampling.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: December 2014

16. To develop a validated, sensitive, and accurate assay for the detection of neutralizing antibodies to vedolizumab, including procedures for accurate detection of neutralizing antibodies to vedolizumab in the presence of vedolizumab levels that are expected to be present in the serum or plasma at the time of patient sampling.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: December 2014

17. To develop and validate a product-specific host cell protein (HCP) assay that has improved sensitivity and capability to detect a greater range of potential HCPs compared to the current assay and to implement this assay in the vedolizumab drug substance release program. The analytical procedure, validation report, proposed acceptance criterion, and data used to set the proposed acceptance criterion will be submitted as a CBE-30.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: December 2017

18. To re-evaluate vedolizumab drug substance lot release and stability specifications after 30 lots have been manufactured at the commercial scale. The corresponding data, the analysis and statistical plan used to evaluate the specifications, and any proposed changes to the specifications will be provided in the final study report.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: December 2016

19. To re-evaluate vedolizumab drug product lot release and stability specifications after 30 lots have been manufactured at the commercial scale. The corresponding data, the analysis and statistical plan used to evaluate the specifications, and any proposed changes to the specifications will be provided in the final study report.

The timetable you submitted on May 05, 2014, states that you will conduct this study according to the following schedule:

Final Study Report Submission: December 2018

20. To conduct a maximum hold time study for the formulated drug substance using representative containers. If low endotoxin recovery is found in the formulated drug substance during the maximum hold time study, either hold times will be reevaluated or an alternative method to measure endotoxin in formulated drug substance will be developed and validated.

The timetable you submitted on April 03, 2014, states that you will conduct this study according to the following schedule:

Final Report Submission: December 2014

21. To verify the endotoxin recovery results for the (b) (4) (b) (4) and establish action limits for this solution once the results are confirmed by a validated method. If low endotoxin recovery is found, maximum hold times (b) (4)

The timetable you submitted on April 03, 2014, states that you will conduct this study according to the following schedule:

Final Report Submission: December 2014

22. To assess the sensitivity of the current dye and microbial ingress assays for container closure integrity testing. The studies will be conducted by perforating the container closure system with needles and capillaries that vary in internal diameter down to an internal size of (b) (4). If it is determined that the current methods are not sensitive to perforations of (b) (4), the methods will be optimized as necessary for the detection of breaches (b) (4).

The timetable you submitted on April 28, 2014, states that you will conduct this study according to the following schedule:

Final Report Submission: December 2014

23. To conduct studies to qualify the endotoxin kinetic turbidometric LAL assay for testing vedolizumab bulk drug product and finished drug product. Qualification studies will be conducted on three lots of endotoxin-spiked undiluted bulk drug product and finished drug product held under worst case hold conditions in the relevant containers. These studies should demonstrate acceptable endotoxin recoveries of spiked endotoxin initially and after worse case hold conditions. In the event kinetic turbidometric qualification studies demonstrate that acceptable endotoxin recoveries from the spiking studies are not achieved, the USP <151> rabbit pyrogen method will be used to release the finished drug product.

The timetable you submitted on April 28, 2014, states that you will conduct this study according to the following schedule:

Final Report Submission: December 2014

24. To conduct studies to qualify an endotoxin assay for Vedolizumab Drug Product [redacted]. Validation will be conducted with [redacted] held under worst case conditions in the relevant containers. The qualified methods will be implemented for routine testing of the drug product [redacted]

The timetable you submitted on April 28, 2014, states that you will conduct this study according to the following schedule:

Final Report Submission: September 2014

Submit clinical protocols to your IND 009125 for this product. Submit chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For

more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). You should submit postmarketing adverse experience reports to:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

We request that for a period of two years, you submit all cases of serious infections, possible cases of progressive multifocal leukoencephalopathy (PML), liver injury, and malignancies reported with Entyvio (vedolizumab) as 15-day alert reports, and that you provide detailed analyses of clinical study and post-marketing reports of serious infections, possible cases of PML, liver injury, and malignancy as adverse events of special interest in your Periodic Benefit-Risk Evaluation Report (PBRER). These analyses should show cumulative data relative to the date of approval of Entyvio (vedolizumab) as well as relative to the prior PBRER. Medical literature reviews for case reports/case series of serious infections, possible cases of PML, liver injury, and malignancy reported with Entyvio (vedolizumab) should also be provided in the PBRER.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA-3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4206
Silver Spring, MD 20903

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

PDUFA V APPLICANT INTERVIEW

FDA has contracted with Eastern Research Group, Inc. (ERG) to conduct an independent interim and final assessment of the Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs under PDUFA V ('the Program'). The PDUFA V Commitment Letter states that these assessments will include interviews with applicants following FDA action on applications reviewed in the Program. For this purpose, first-cycle actions include approvals, complete responses, and withdrawals after filing. The purpose of the interview is to better understand applicant experiences with the Program and its ability to improve transparency and communication during FDA review.

ERG will contact you to schedule a PDUFA V applicant interview and provide specifics about the interview process. Your responses during the interview will be confidential with respect to the FDA review team. ERG has signed a non-disclosure agreement and will not disclose any identifying information to anyone outside their project team. They will report only anonymized results and findings in the interim and final assessments. Members of the FDA review team will be interviewed by ERG separately. While your participation in the interview is voluntary, your feedback will be helpful to these assessments.

If you have any questions, call Kevin Bugin, Regulatory Project Manager, at (301) 796-2302.

Sincerely,

{See appended electronic signature page}

Amy G. Egan, M.D., M.P.H.
Deputy Director (acting)
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

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

/s/

AMY G EGAN
05/20/2014