CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761086Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 122136

MEETING MINUTES

Amgen Inc.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

Attention: Renee Martin, PhD
Senior Manager, Global Regulatory Affairs, Biosimilars

Dear Dr. Martin:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for ABP710.

We also refer to the meeting between representatives of your firm and the FDA on October 31, 2018. The purpose of the meeting was to discuss the proposed format and content of the ABP710 BLA.

A copy of the official minutes of the meeting is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-3420.

Sincerely,

{See appended electronic signature page}

Christine Ford, MS, RPh
CAPT, U.S. Public Health Service
Program Coordinator
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type:	Biosimilar
Meeting Category:	BPD Type 4
Meeting Date and Time:	October 31, 2018 3:00 – 4:00 PM (ET)
Meeting Location:	White Oak Building 22, Conference Room: 1419
Application Number:	IND 122136
Product Name:	ABP710
Indication:	The same indications as approved for US-licensed Remicade (infliximab)
Sponsor/Applicant Name:	Amgen Inc.
Meeting Chair:	Dr. Nikolay Nikolov, Associate Director, Rheumatology
Meeting Recorder:	Christine Ford, Regulatory Project Manager

FDA ATTENDEES (‡denotes participation by phone):

Nikolay Nikolov, MD, Associate Director, Rheumatology, Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
Rachel Glaser, MD, Clinical Team Leader, DPARP
Keith Hull, MD, PhD, Clinical Reviewer, DPARP
Christine Ford, MS, RPh, Regulatory Project Manager, DPARP
Yongman Kim, PhD, Biometrics Team Leader, Division of Biometrics II (DBII)
Ginto Pottackal, PhD, Biometrics Reviewer, DBII
Anshu Marathe, PhD, Team Leader, Division of Clinical Pharmacology II (DCPII)
Tao Liu, PhD, Clinical Pharmacology Reviewer, DCPII
Ping Ji, PhD, Clinical Pharmacology Reviewer, DCPII
William Hallett, PhD, Team Leader, Division of Biotechnology Review & Research II (DBRRII)
Yetao Jin, PhD, Product Quality Reviewer, DBRRII
Kathleen Jones, PhD, Microbiologist, Microbiology Assessment Branch IV (MABIV)
Chao Wang, PhD, CMC Statistics Reviewer, Division of Biometrics VI (DBVI)‡
Sue Lim, MD, Director of the Scientific Review Staff, Therapeutic Biologics & Biosimilars Staff (TBBS)
Michele Dougherty, PhD, TBBS Reviewer
Cristina Ausin, PhD, TBBS Reviewer
Tyree Newman, Sr. Regulatory Health Project Manager, TBBS
David Kettl, MD, Division of Dermatology and Dental Products (DDDP)‡
Gary Chiang, MD, Clinical Reviewer, DDDP‡
Ingrid Chapman, PharmD, Risk Management Analyst, Office of Surveillance and Epidemiology (OSE)

Saharat Patanavanich, PharmD, Safety Regulatory Project Manager, OSE‡
Tony Tran, Pharmacy Student

EASTERN RESEARCH GROUP ATTENDEES:

Christopher Sese
Hannah Busey

SPONSOR ATTENDEES:

Maje Babatola, MS, Senior Manager, Global Regulatory Affairs, Biosimilars CMC
Gary Fanjiang, MD, MBA, MS, Executive Medical Director
Diana Landa, MS, Executive Director, Global Regulatory Affairs, Biosimilars
Renee Martin, PhD, Senior Manager, Global Regulatory Affairs, Biosimilars
Shin Oh, PhD, Senior Manager, Biostatistics, Biosimilars Development
Jean Pan, PhD, Director, Biostatistics, Biosimilars Development
Joe Portilla Arias, PhD, Manager, Global Regulatory Affairs, Biosimilars, CMC
Barbara Rellahan, MS, PhD, Director, Product Quality

BACKGROUND:

Amgen is developing ABP710 as a proposed biosimilar to US-licensed Remicade (infliximab) and plans to submit the BLA sometime during the fourth quarter of the 2018 calendar year. They requested this Type 4 meeting to discuss the proposed structure, format, and content of the application. FDA issued meeting preliminary comments on October 26, 2018.

In an email sent October 30, 2018, Amgen requested further discussion on responses to Question 3.

The content of FDA's October 26, 2018, meeting preliminary comments is included below in its entirety, with the sponsor's questions from the briefing package in *italics;* FDA's responses in normal font; and the sponsor's October 30, 2018, emailed responses also noted in *italics* (slides provided as an Attachment at the end of the minutes). A summary of meeting discussions of points not already captured in the meeting preliminary comments, and if any, are found in **bold normal font** following the specific area of discussion.

QUESTIONS and RESPONSES:

FDA may provide further clarifications of, or refinements and/or changes to the responses and the advice provided at the meeting based on further information provided by the sponsor and as the Agency's thinking evolves on certain statutory provisions regarding applications submitted under section 351(k) of the Public Health Service Act (PHS Act).

Question 1

Does FDA agree that Amgen is not required to include a Risk Evaluation and Mitigation Strategy (REMS) with the BLA and instead a Medication Guide, similar to Remicade, as part of the approved labeling is adequate in this BLA?

FDA response:
Remicade Lyophilized Concentrate for intravenous injection was released from its previously approved REMS (refer to the letter posted under the approval history for US-

licensed Remicade at Drugs@FDA with the action date August 1, 2011). We have also determined that "maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21CFR 208.1." Accordingly, at this time, developing a Medication Guide for patients would be appropriate for your proposed biosimilar product. Based on the information currently available, we do not believe that a REMS will be necessary. We will make a final determination for the need for a REMS and/or Medication Guide during the review of your application.

Question 2

Does the Agency agree that the proposed content, structure, and format of Module 3 will facilitate review of the BLA?

FDA response:

Your proposed structure and format of Module 3 appears appropriate to facilitate review of the BLA. The adequacy of the content of Module 3 will be a review issue. Please note, the sterilization validation of all product contact equipment should be submitted in section 3.2.P.3.5. See FDA Additional CMC Microbiology comments below. Regarding the proposed drug substance (DS) and drug product (DP) specifications, we have the following recommendations:

a. In the Drug Substance Specification Tests in Table 4 on Page 20 of the meeting package, you indicate only SEC to test for purity and impurities. This proposed testing strategy does not provide sufficient control of charge-based impurities or glycosylation variants. Additionally, there is no proposed control strategy for ADCC activity. Update the DS and DP control strategy to include ADCC activity.

b. In the Drug Product Specification Tests in Table 7 on Page 26 of the meeting package, you do not include the test for uniformity of dosage units in the DP specification. This test should be included for this lyophilized product in the DP specification in accordance with USP <905>.

Question 3

Does the Agency have any comments or additional points to consider regarding the results from Study 20140111 in the RA population in order to support ABP 710 biosimilarity to the Remicade reference product?

FDA response:

Your primary analysis shows an estimated difference between the ACR20 response probabilities at week 22 of over 9% with an upper bound of the 90% CI that exceeds the upper similarity margin of +15%. In your application, justify that your data support there are no clinically meaningful differences between ABP 710 and US-licensed Remicade despite the primary efficacy analysis findings in your comparative clinical study. The assessment of whether you have adequately supported a demonstration of no clinically meaningful differences will be a review issue and will be based on the totality of the data and information submitted in the application.

Sponsor's emailed response:
Refer to Amgen's slides attached at the end of the minutes. Amgen presented the content of their slides, particularly slide 8, entitled "Study 20140111: Phase 3 Efficacy and Safety study of ABP710 compared with infliximab in subjects with moderate to severe Rheumatoid Arthritis." Their conclusions listed as follows:

- *"The statistical results for ACR20 at week 22 confirmed non-inferiority but were unable to confirm non-superiority.*
- *The overall results of the Phase 3 study support no clinically meaningful difference between ABP 710 and infliximab.*
  - *Adjustment for imbalances in baseline characteristics reduced the observed differences of ACR20 at week 22.*
  - *The observed difference of the ACR20 components at week 22 are not clinically meaningful when interpreted in context of MCII.*
  - *Continuous variables, DAS28-CRP and Hybrid ACR, demonstrated comparable efficacy profiles throughout the study.*
  - *ACR20, ACR50 and ACR70 also demonstrated comparable efficacy profiles throughout the study.*
  - *The observed ACR20 results are within the range of infliximab historical data.*
- *The totality of evidence support the conclusion that ABP 710 is highly similar to infliximab with no clinically meaningful differences."*

Discussion:
Amgen emphasized that through various analyses ABP710 demonstrated comparable efficacy for all the parameters tested at the specified timepoints except for the primary endpoint, ACR20 at week 22, which the sponsor attributed to chance.

FDA reiterated that a determination of biosimilarity will be based on the totality of the data submitted in the application, including analytical data, PK similarity data, and the comparative clinical study, and that the justification for the observed differences in the primary endpoint will be a review issue. In exploring reasons for the difference noted in the primary endpoint, FDA asked Amgen if they powered the study appropriately (a sample size calculation required 620 subjects based on previous trials) and accounted for study dropouts. FDA also asked whether the sponsor had calculated the p-value using a two-one-sided test (TOST) for similarity.

Amgen replied that the TOST procedure was used, resulting in a p-value slightly greater than 0.05.

FDA indicated that Amgen will have to provide a justification for the assumptions used when calculating the study size.

In response to FDA questions of whether differences in immunogenicity that could have impacted clinical results, Amgen responded that observed ADA binding and neutralizing antibodies were similar between ABP710 and US-licensed Remicade. Amgen also observed a decrease in efficacy over time, but this was similar between arms as well. In addition, trough concentrations were similarly impacted by ADA status between treatment groups.

In the BLA submission, FDA recommended that the sponsor submit a root cause analysis evaluating different factors that might impact exposure, immunogenicity, etc., that may have contributed to the difference noted in the clinical response. Then, as applicable, Amgen should include justifications for any uncertainties or why the difference(s) noted do not preclude a determination that there are no clinically meaningful differences between APB710 and US-licensed Remicade.

Amgen asked if FDA preferred the use of DAS28 as an endpoint over ACR20.

FDA responded that the DAS28 could be considered, however there may be insufficient data in the public domain to inform robust margin selection. FDA further explained that use of the proposed change in DAS28 of 0.6 is not adequate as a margin because that difference reflects patient level response. In response to inquiry about use of the ACR hybrid, FDA replied that it would measure the same components as the ACR response. The key point is that the sponsor must justify the differences observed based on the above considerations.

FDA reminded the sponsor to submit PK datasets as well as the bioanalytical method validation reports. Refer to Post-Meeting Clinical Pharmacology Comments provided in the section below for information on the format for the submission.

Post-Meeting Clinical Pharmacology Comments:

For your application, complete the bioanalytical method performance summary tables below, using one method per analyte per table. Do not delete any rows or columns from the tables. State "not applicable" if certain rows or columns are not applicable. Include any additional bioanalytical data that may be relevant to the submission. Include this information in Module 5.3.1.4 along with the method validation reports and any amendments in your BLA submission.

Table 1. Summary method performance of a bioanalytical method to measure [analyte] in [matrix]

Bioanalytical method validation report name, amendments, and hyperlinks		
Method description		
Materials used for calibration curve & concentration		
Validated assay range		
Material used for QCs & concentration		
Minimum required dilutions (MRDs)		
Source & lot of reagents (LBA)		
Regression model & weighting		
Validation parameters	**Method validation summary**	**Source location**

Calibration curve performance during accuracy & precision	Number of standard calibrators from LLOQ to ULOQ	x	
	Cumulative accuracy (%bias) from LLOQ to ULOQ Product A Product B	 x to y% x to y%	
	Cumulative precision (%CV) from LLOQ to ULOQ Product A Product B	 ≤ x% ≤ x%	
QCs performance during accuracy & precision	**<u>Cumulative accuracy (%bias) in 5 QCs</u>** QCs: Product A Product B	 x to y% x to y%	
	<u>Inter-batch %CV</u> QCs: Product A Product B	 ≤ x% ≤ x%	
	<u>Total error</u> QCs: Product A Product B	 ≤ x% ≤ x%	
Selectivity & matrix effect	Number of total lots tested. Range of observed bias. State any issue		
Interference & specificity	Number of total lots tested. Range of observed bias. State any issue		
Hemolysis effect	Number of total lots tested. Range of observed bias. State any issue		
Lipemic effect	Number of total lots tested. Range of observed bias. State any issue		
Dilution linearity & hook effect	Describe data here		
Bench-top/process stability	Describe data here Product A Product B		
Freeze-Thaw stability	Describe data here Product A Product B		
Long-term storage	Describe data here Product A Product B		
Parallelism	Describe data here		
Carry over	Describe data here		
Method performance in study number (In addition to the report name, also provide hyperlink to the report)			
Assay passing rate	(including incurred sample reanalysis (ISR))		
Standard curve performance	• Cumulative bias range: x to y% • Cumulative precision: ≤ x% CV		
QC performance	• Cumulative bias range: x to y% • Cumulative precision: ≤ x% CV • TE: ≤ x% (LBA only)		
Method reproducibility	Incurred sample reanalysis was performed in x% of study samples		

	and x % of samples met the pre-specified criteria	
Study sample analysis/ stability	Describe storage stability coverage for standard/QC and samples	

If the method above was modified, describe the modification(s) and cross-validation results, with any additional information in Table 2 below.

Table 2. Summary of method [x] modification(s) and cross-validation results

Bioanalytical method validation report name and hyperlink			
Changes in method			
New validated assay range if any			
Validation parameters	**Cross-validation performance**		**Source location**
Calibration curve performance during accuracy & precision	Cumulative accuracy (%bias) in standard calibrators from LLOQ to ULOQ	x to y%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤ x%	
QCs performance during accuracy & precision	Cumulative accuracy (%bias) in 5 QCs	x to y%	
	Inter-batch %CV	≤ x%	
	Percent total error (TE)	≤ x%	
Cross-validation	Numbers of spiked or incurred samples analyzed and result		
List other parameters			

Complete and submit Table 3 with the BLA submission to provide the information regarding the bioanalytical methods used in pivotal clinical pharmacology studies and its life-cycle information pertaining to the submission. We recommend that this table be placed in eCTD 2.7.1 along with summary biopharmaceutics. Also include any additional bioanalytical information that might be relevant.

Table 3. Summary life cycle information of bioanalytical method(s) used in submission of BLA/NDA # to measure analyte X in matrix (including Ligand Binding Assay-based biomarker)

	Method validation #1	**Method validation #2**	**Clinical Study x**	**Clinical Studies y-z**
Analyte	Drug name	Drug x, Drug y	Drug x, and Drug y	Drug x, Drug z
Validation type	Full	Partial validation of method xx	NA	NA
• CTD ref #	Ref # in eCTD	x0000.0xxxxxxx	x0000.0xxxxxxx	x0000.0xxxxxxx

• method ID • BA site	Method ID xx (version)	SOP xxxx or Method xxx (v 1.0)	SOP xxxx or Method xxx (v 1.0)	SOP xxxx or Method xxx (v 1.0)
	Name of BA test facility	US Lab 1	US lab 1	Other lab
• Matrix	Serum/ Plasma/Urine/ whole blood			
• Platform	LC/MS, ELISA, ECL			
• Format	A validated sandwich format using x as capture and y as detection, a bridging format using z as both capture and detection, competitive assay using x as a capture and b as a competitor			
Stock reference & lot (expiry)	Drug 1, lot 1	Drug 1, lot 2 Drug 2, lot 1		
Calibration range (LLOQ - ULOQ) and levels validated	x- x000 ng/mL (eg. 2, 5, 50, 250, 1000, 1500, 2000 ng/mL)	x- x000 ng/mL	x- x000 ng/mL	x- x000 ng/mL
Matrix/ study population	Normal or x diseased serum	Normal serum	Normal serum	x Diseased population
Relevant reference and applicable report amendment (s) and links -Amendment 1 -Amendment 2				
Amendment history				

FDA Additional CMC Microbiology comments:

We are providing additional product quality microbiology comments for you to consider during development of your commercial manufacturing process and preparation of your 351(k) BLA submission.

1. All facilities should be registered with the FDA at the time of the 351(k) BLA submission and ready for inspection in accordance with 21 CFR 600.21 and 601.20(b)(2). Include in the BLA submission a complete list of the manufacturing and testing sites with their corresponding FEI numbers. A preliminary manufacturing schedule for the drug substance and drug product should be provided in the BLA submission to facilitate the planning of pre-license inspections during the review cycle. Manufacturing facilities should be in operation and manufacturing the product under review during the inspection.

2. Information and data for CMC product quality microbiology should be submitted in the specified sections indicated below.

(b) (4)

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(b) (4)

DISCUSSION OF THE CONTENT OF A COMPLETE APPLICATION

The original 351(k) application will be subject to "the Program" under BsUFA II. Therefore, at this meeting be prepared to discuss and reach agreement with FDA on the content of a complete application, including preliminary discussions regarding the approach to developing the content for risk evaluation and mitigation strategies (REMS), where applicable, patient labeling (e.g., Medication Guide and Instructions For Use) and, where applicable, the development of a Formal Communication Plan. You and FDA may also reach agreement on submission of a limited number of minor application components to be submitted not later than 30 days after the submission of the original application. These submissions must be of a type that would not be expected to materially impact the ability of the review team to begin its review. All major components of the application are expected to be included in the original application and are not subject to agreement for late submission.

Discussions and agreements will be summarized at the conclusion of the meeting and reflected in FDA's meeting minutes. If you decide to cancel this meeting and do not have agreement with FDA on the content of a complete application or late submission of any minor application components, your application is expected to be complete at the time of original submission.

In addition, we remind you that the application is expected to include a comprehensive and readily located list of all clinical sites and manufacturing facilities.

Finally, in accordance with the BsUFA II agreement, FDA has contracted with an independent contractor, Eastern Research Group, Inc. (ERG), to conduct an assessment of the Program. ERG will be in attendance at this meeting as silent observers to evaluate the meeting and will not participate in the discussion. Please note that ERG has signed a non-disclosure agreement.

Information on the Program is available at
https://www.fda.gov/forindustry/userfees/biosimilaruserfeeactbsufa/default.htm

PREA REQUIREMENTS

Under the Pediatric Research Equity Act [section 505B of the Federal Food, Drug and Cosmetic Act (FD&C Act) (21 U.S.C. 355c)], all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain a pediatric assessment to support dosing, safety, and effectiveness of the product for the claimed indication unless this requirement is waived, deferred, or inapplicable.

Section 505B(l) of the FD&C Act, added by section 7002(d)(2) of the Affordable Care Act, provides that a biosimilar product that has not been determined to be interchangeable with the reference product is considered to have a new "active ingredient" for purposes of PREA, and a pediatric assessment is required unless waived or deferred.

FDA encourages prospective biosimilar applicants to submit an initial pediatric study plan (PSP) as early as practicable during product development. FDA recommends that you allow adequate time to reach agreement with FDA on the proposed PSP prior to initiating your comparative clinical study (see additional comments below regarding expected review timelines).

Sections 505B(e)(2)(C) and 505B(e)(3) of the FD&C Act set forth a process lasting up to 210 days for reaching agreement with FDA on an initial PSP. FDA encourages the sponsor to meet with FDA to discuss the details of the planned development program before submission of the initial PSP. The initial PSP must include an outline of the pediatric study or studies that a sponsor plans to conduct (including, to the extent practicable, study objectives and design, age groups, relevant endpoints, and statistical approach); and any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation. You must address PREA for every indication for which you seek licensure, and we encourage you to submit a comprehensive initial PSP that addresses each indication. For indications for which the labeling for the reference product contains adequate pediatric information, you may be able to fulfill PREA requirements by satisfying the statutory requirements for biosimilarity and providing an adequate scientific justification for extrapolating the pediatric information from the reference product to your proposed product (see question and answer I.11 in FDA's guidance for industry on Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009). For conditions of use for which the reference product does not have adequate pediatric information in its labeling, a waiver (full or partial), or a deferral, may be appropriate if certain criteria are met.

After the initial PSP is submitted, a sponsor must work with FDA to reach timely agreement on the plan, as required by FDASIA (see section 505B(e) of the FD&C Act and FDA's Guidance for Industry on Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidaces/UCM360507.pdf). It should be noted that requested deferrals or waivers in the initial PSP will not be formally granted or denied until the product is licensed.

PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57 including the Pregnancy and Lactation Labeling Rule (PLLR) (for applications submitted on or after June 30, 2015). As you develop your proposed PI, we encourage you to review the labeling review resources on the *PLR Requirements for Prescribing Information* and *Pregnancy and Lactation Labeling Final Rule* websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products.
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information related to pregnancy, lactation, and females and males of reproductive potential.
- Regulations and related guidance documents.
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

Pursuant to the PLLR, you should include the following information with your application to support the changes in the Pregnancy, Lactation, and Females and Males of Reproductive Potential subsections of labeling. The application should include a review and summary of the available published literature regarding the drug's use in pregnant and lactating women and the effects of the drug on male and female fertility (include search parameters and a copy of each reference publication), a cumulative review and summary of relevant cases reported in your pharmacovigilance database (from the time of product development to present), a summary of drug utilization rates amongst females of reproductive potential (e.g., aged 15 to 44 years) calculated cumulatively since initial approval, and an interim report of an ongoing pregnancy registry or a final report on a closed pregnancy registry. If you believe the information is not applicable, provide justification. Otherwise, this information should be located in Module 1. Refer to the draft guidance for industry – *Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format* (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM425398.pdf).

In addition, you should review the draft FDA Guidance for Industry, "Labeling for Biosimilar Products," March 2016 at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM493439.pdf.

Prior to submission of your proposed PI, use the SRPI checklist to ensure conformance with the format items in regulations and guidances.

NONPROPRIETARY NAME

On January 13, 2017, FDA issued a final guidance for industry entitled *Nonproprietary Naming of Biological Products*, available at: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm459987.pdf, stating that, for certain biological products, the Agency intends to designate a proper name that includes a four-letter distinguishing suffix that is devoid of meaning.

Please note that certain provisions of this guidance describe a collection of information and are under review by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (PRA). These provisions of the guidance describe the submission of proposed suffixes to the FDA, and a sponsor's related analysis of proposed suffixes, which are considered a "collection of information" under the PRA. FDA is not currently implementing provisions of the guidance that describe this collection of information.

However, provisions of the final guidance that do not describe the collection of information should be considered final and represent FDA's current thinking on the nonproprietary naming of biological products. These include, generally, the description of the naming convention (including its format for originator, related, and biosimilar biological products) and the considerations that support the convention.

Your proposed 351(k) BLA would be within the scope of this guidance. As such, FDA intends to assign a four-letter suffix for inclusion in the proper name designated in the license at such time as FDA approves the BLA.

Office of Scientific Investigations (OSI) Requests

The Office of Scientific Investigations (OSI) requests that the items described in the draft Guidance for Industry Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions (February 2018) and the associated Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications be provided to facilitate development of clinical investigator and sponsor/monitor/CRO inspection assignments, and the background packages that are sent with those assignments to the FDA ORA investigators who conduct those inspections. This information is requested for all major trials used to support safety and efficacy in the application (i.e., phase 2/3 pivotal trials). Please note that if the requested items are provided elsewhere in submission in the format described, the Applicant can describe location or provide a link to the requested information.

Please refer to the draft Guidance for Industry Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions (February 2018) and the associated Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications:

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/UCM332466.pdf

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/UCM332468.pdf.

DISCUSSION OF THE CONTENT OF A COMPLETE APPLICATION – POST MEETING

- All applications are expected to include a comprehensive and readily located list of all clinical sites and manufacturing facilities included or referenced in the application.

- Major components of the application are expected to be submitted with the original application and are not subject to agreement for late submission. You intend to submit a complete application and therefore, there are no agreements for late submission of application components.

MANUFACTURING FACILITIES

To facilitate our inspectional process, we request that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

ISSUES REQUIRING FURTHER DISCUSSION:

There were no issues requiring further discussion.

ATTACHMENTS AND HANDOUTS:

Amgen's slides emailed October 30, 2018, begin on the next page.

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CHRISTINE H FORD
11/20/2018