IND 012678

WRITTEN REQUEST – AMENDMENT #2

Novartis Pharmaceuticals Corporation
Attention: Kristine Ogozalek, MS
Global Regulatory Team Lead
One Health Plaza
East Hanover, NJ 07936

Dear Kristine Ogozalek:

Please refer to your correspondence dated September 19, 2025, requesting changes to FDA's September 17, 2025, Written Request for pediatric studies for secukinumab.

We have reviewed your proposed changes and are amending the Written Request. All other terms stated in our Written Request issued on July 18, 2025, and as amended on September 17, 2025, remain the same. (Text added is underlined. Text deleted is strikethrough.)

I. Juvenile Ankylosing Spondylitis (JAS)

JAS is a descriptive term for the clinical presentation of ankylosing spondylitis (AS) occurring before the age of 16. JAS is diagnosed using the established criteria for diagnosing AS in adults[1] based on persistent low back pain and stiffness for more than three months and/or limitation of motion of the lumbar spine and/or limitation of chest expansion plus X-ray radiologic evidence of sacroiliitis (grade ≥2 bilaterally or grade 3-4 unilaterally). The true incidence of JAS is unknown; however, it is estimated that 10-20% of patients diagnosed with AS present before 16 years of age, and that most of these cases occur in patients who are at least 8 years of age.[2] The overall prevalence of JAS is estimated to be fewer than 1 per 1000 children. A number of treatments are approved for adult AS, including TNF inhibitors, IL-23 inhibitors and IL-17 inhibitors (including Cosentyx), however no treatments are approved for JAS.

II. Axial Juvenile Spondyloarthritis (AxJSpA)

AxJSpA is a descriptive term for the clinical presentation of non-radiographic axial spondyloarthritis (nr-axSpA) occurring before the age of 16. There are established

[1] Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: a proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8

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criteria for diagnosing adults with nr-axSpA[3], including inflammatory back pain without X-ray radiologic evidence of sacroiliitis but with either MRI evidence of sacroiliitis and one additional spondyloarthritis (SpA) feature or HLA-B27+ and at least two SpA features. Previously, it has been recognized that a significant number of children with juvenile idiopathic arthritis (JIA) can have spondyloarthritis and present with clinical symptoms of inflammatory back pain (e.g., enthesitis related arthritis [ERA] and juvenile psoriatic arthritis [JPsA]) and may have evidence of sacroiliitis on MRI.[4] However, it is only recently that criteria to define axial involvement in children with non-radiographic spondyloarthritis have become available.[5] The AxJSpA criteria incorporate genetic, clinical, and imaging domains. Imaging evidence of sacroiliitis (active inflammation and/or structural lesions) is necessary but not sufficient for classification. A threshold score of ≥ 55 out of 100 is required for AxJSpA classification. Notably, ~50% of the pediatric cohort of over 400 children used to derive the AxJSpA criteria had a history of enthesitis and may have fulfilled criteria for a diagnosis of ERA, however the new AxJSpA criteria would capture a population of children with axial disease. This represents the first pediatric-specific axial spondyloarthritis classification criteria and addresses an important unmet need in facilitating the development of treatments for this patient population. The true incidence of AxJSpA is unknown. The prevalence of AxJSpA is estimated to be approximately 1 in 1000 children. There are no treatments approved for AxJSpA.

Cosentyx (secukinumab) has been approved for use in pediatric patients as young as 2 years of age for several conditions, including plaque psoriasis (PsO), psoriatic arthritis (JPsA), and enthesitis-related arthritis (ERA). For pediatric PsO, the primary study supporting approval was a 52-week, multicenter, randomized, double-blind, placebo and active-controlled trial that enrolled 162 pediatric patients 6 years of age and older, with severe PsO who were candidates for systemic therapy. For JPsA and ERA, the primary study supporting approval was a 3-part, double-blind, placebo controlled, event-driven, randomized, phase 3 study in 86 pediatric patients (aged 2 to less than 18 years) with active JPsA or ERA. The trial consisted of an open-label portion (up to week 12) followed by randomized withdrawal and open-label treatment (up to week 104), with an additional open-label extension study providing long-term safety and efficacy data for up to 4 years in patients who completed the core study. These studies are not included in this WR because they have previously been submitted and the indications approved for

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pediatric patients. Additionally, public health benefit also exists for treatments for pediatric hidradenitis suppurativa (HS). Studies for HS in patients 12-17 years of age have been conducted and have already been submitted. Therefore, studies in HS are also not included in this WR. The studies outlined in this Written Request are designed to evaluate the safety and efficacy of secukinumab in the treatment of JAS and AxJSpA.

The efficacy of secukinumab in patients with JAS aged 12 to < 18 may be wholly extrapolated from efficacy data in adults with AS because the classification criteria are identical to those used for adult AS (Assessment of Spondyloarthritis International Society [ASAS] criteria), and the same enrollment criteria would be expected to yield similar efficacy results between adult and juvenile AS populations. Safety for this population can be leveraged from existing studies of pediatric patients with ERA, JPsA, and psoriasis (PsO), as well as from adult AS patients. No studies are requested in patients less than 12 years of age, including neonates, because AS is extremely rare in this age group as it requires time for the inflammatory processes and structural changes that are characteristic of the disease to develop.

The efficacy of secukinumab in treating AxJSpA in patients 6 to < 18 years of age can be evaluated based on assessment of the subset of AxJSpA subjects within pediatric data in related diseases (i.e., ERA and JPsA) and may also be partially extrapolated from efficacy data in adults with nr-axSpA. Therefore, this WR must include a retrospective analysis of data from a completed phase 3, randomized, double-blind, placebo-controlled, treatment withdrawal trial and its associated extension trial in patients with ERA and JPsA to evaluate efficacy in the subset of pediatric subjects who fulfill the criteria for AxJSpA. Safety can be based on assessment of data from the completed phase 3 ERA/JPsA study in the subset of pediatric subjects who fulfill the criteria for AxJSpA. Additionally, safety for this population can be leveraged from existing studies of pediatric patients with ERA, JPsA, and PsO, as well as from adult patients with nr-axSpA. Studies are not requested in patients younger than 6 years of age, including neonates, because AxJSpA is rare in this age group.

To obtain needed pediatric information on secukinumab, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Food and Drug Administration Amendments Act of 2007, that you submit information from the studies described below.

- ***Nonclinical study(ies)*:**

  Based on review of the available nonclinical toxicology, no additional animal studies are required at this time to support the clinical studies described in this Written Request.

- ***Clinical studies:***

Study 1: A retrospective analysis to evaluate the safety and efficacy of secukinumab in patients meeting criteria[6] for AxJSpA, using data from a phase 3, randomized, double-blind, placebo-controlled, treatment withdrawal trial that studied patients with ERA and JPsA. The analysis, including selection criteria for patients with AxJSpA must be agreed upon with the Agency.

Study 2: Long-term safety and tolerability of secukinumab in patients meeting criteria[7] for AxJSpA, and comparison to patients with ERA and JPsA who do not meet such criteria in an extension trial. The selection criteria for patients with AxJSpA must be agreed upon with the Agency.

- ***Study Objectives:***

Study 1 – The primary objective is to evaluate the safety and efficacy of secukinumab in a subset of patients meeting to be agreed upon criteria for AxJSpA using data from a phase 3, randomized, double-blind, placebo-controlled treatment withdrawal trial.

Study 2 – The primary objective is to assess the long-term safety and tolerability of secukinumab in a subset of patients meeting to be agreed upon criteria for AxJSpA in an extension trial. A secondary objective is to compare the long-term safety and tolerability of secukinumab between this patient subset and those with ERA and JPsA patients who do not meet such criteria.

- ***Patients to be Studied:***

Study 1 must include at least 6 patients meeting agreed upon criteria for AxJSpA in a phase 3 trial, which enrolled a total of 86 ERA and JPsA patients 2 to < 18 years of age.

Study 2 must include at least 6 patients meeting agreed upon criteria for AxJSpA in an extension trial followed while on continuous treatment with secukinumab for a minimum of 104 weeks.

- ***Study endpoints:***

[6] Weiss PF, Brandon TG, Aggarwal A, Burgos-Vargas R, Colbert RA, Horneff G, Laxer RM, Minden K, Ravelli A, Ruperto N, Smith JA, Stoll ML, Tse SM, Van den Bosch F, Maksymowych WP, Lambert RG, Biko DM, Chauvin NA, Francavilla ML, Jaremko JL, Herregods N, Kasapcopur O, Yildiz M, Srinivasalu H, Lovell DJ, Nigrovic PA, Foeldvari I, Klein-Gitelman MS, Ozen S, Naden R, Hendry AM, Joos R. Classification Criteria for Axial Disease in Youth With Juvenile Spondyloarthritis. Arthritis & Rheumatology. 2024;76(12):1797-1808.

[7] See footnote 6

- ☐ Primary efficacy endpoint(s):
    - ☐ BASDAI at Week 12 (or cJADAS/JADAS with justification)
- ☐ Key secondary efficacy endpoints should include (using an agreed upon statistical hierarchy):
    - ☐ BASDAI during the randomized withdrawal period (or cJADAS/JADAS with justification)
    - ☐ Physician's Global Assessment of disease activity (VAS)
    - ☐ Parent's/subject's Global Assessment of subject's overall well-being (VAS included within CHAQ)
    - ☐ Overall back pain (VAS)
    - ☐ Nocturnal back pain score (VAS)
    - ☐ Modified Schober's test
    - ☐ JSpADA index
    - ☐ JIA ACR30/50/70/90

- *Safety Endpoints/Monitoring: The protocol must include a plan for monitoring of the following safety endpoints:*
    - ☐ Adverse events, tolerability assessments, vital signs (e.g., blood pressure, heart rate, respiratory rate, temperature, weight), and laboratory parameters including CBC, CMP; screening for HIV, Hepatitis B, Hepatitis C, and tuberculosis
    - ☐ Known adverse events of special interest including infection, hypersensitivity reactions, inflammatory bowel disease, and eczematous eruptions

  The protocol must include a plan for appropriate monitoring of all adverse events.

- *Statistical information, including power of study(ies) and statistical assessments:*
    - For Study 1 – The incidence of treatment emergent adverse events must be summarized by relationship to the study drug and overall. In addition, laboratory values and vital signs must be summarized. Provide a descriptive summary of the efficacy outcomes.

- For Study 2 - The incidence of treatment emergent adverse events must be summarized by relationship to the study drug and overall. In addition, laboratory values and vital signs must be summarized. Provide a descriptive summary of the efficacy outcomes.

The following information pertains to all clinical studies in the Written Request:

- *Extraordinary results:* In the course of conducting these studies, you may discover evidence to indicate that there are unexpected safety concerns, unexpected findings of benefit in a smaller sample size, or other unexpected results. In the event of such findings, there may be a need to deviate from the requirements of this Written Request. If you believe this is the case, you must contact the Agency to seek an amendment. It is solely within the Agency's discretion to decide whether it is appropriate to issue an amendment.

- *Biological product information:*

  - *dosage form: pre-filled syringe (PFS)*
  - *route of administration: subcutaneous injection*
  - *regimen: As agreed upon in the protocol*

  Use an age-appropriate formulation in the study(ies) described above. If an age-appropriate formulation is not currently available, you must develop and test an age-appropriate formulation and, if it is found safe and effective in the studied pediatric population(s), you must seek marketing approval for that age-appropriate formulation.

  In accordance with section 505A(e)(2), if

  (1) you develop an age-appropriate formulation that is found to be safe and effective in the pediatric population(s) studied (i.e., receives approval);
  (2) the Agency grants pediatric exclusivity, including publishing the exclusivity determination notice required under section 505A(e)(1) of the Act; and
  (3) you have not marketed the formulation within one year after the Agency publishes such notice,

  the Agency will publish a second notice indicating you have not marketed the new pediatric formulation.

  If you demonstrate that reasonable attempts to develop a commercially marketable formulation have failed, you must develop and test an age-

appropriate formulation that can be prepared by a licensed pharmacist, in a licensed pharmacy, from commercially available ingredients. Under these circumstances, you must provide the Agency with documentation of your attempts to develop such a formulation and the reasons such attempts failed. If we agree that you have valid reasons for not developing a commercially marketable, age-appropriate formulation, then you must submit instructions for preparing an age-appropriate formulation from commercially available ingredients that are acceptable to the Agency. If you conduct the requested studies using such a formulation, the following information must be provided for inclusion in the product labeling upon approval: active ingredients, diluents, suspending and sweetening agents; detailed step-by-step preparation instructions; packaging and storage requirements; and formulation stability information.

Bioavailability of any formulation used in the studies must be characterized, and as needed, a relative bioavailability study comparing the approved drug to the age appropriate formulation may be conducted in adults.

- *Labeling that may result from the study(ies)*: You must submit proposed pediatric labeling to incorporate the findings of the study(ies). Under section 505A(j) of the FD&C Act, regardless of whether the study(ies) demonstrate that secukinumab is safe and effective, or whether such study results are inconclusive in the studied pediatric population(s) or subpopulation(s), the labeling must include information about the results of the study(ies). Under section 505A(k)(2) of the FD&C Act, you must distribute to physicians and other health care providers at least annually (or more frequently if FDA determines that it would be beneficial to the public health), information regarding such labeling changes that are approved as a result of the study(ies).

- *Format and types of reports to be submitted*: You must submit full study reports (which have not been previously submitted to the Agency) that address the issues outlined in this request, with full analysis, assessment, and interpretation. In addition, the reports must include information on the representation of pediatric patients of ethnic and racial minorities. All pediatric patients enrolled in the study(ies) should be categorized using one of the following designations for race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander or White. For ethnicity, you should use one of the following designations: Hispanic/Latino or Not Hispanic/Latino. If you choose to use other categories, you should obtain agency agreement.

  Under section 505A(d)(2)(B) of the FD&C Act, when you submit the study reports, you must submit all postmarketing adverse event reports regarding this drug that are available to you at that time. All post-market reports that would be reportable under section 21 CFR 600.80 should include adverse events occurring in an adult or a pediatric patient. In general, the format of the post-market

adverse event report should follow the model for a periodic safety update report described in the guidance for industry *E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs* and the guidance addendum.[8] You are encouraged to contact the reviewing Division for further guidance.

For studies started after December 17, 2017 , study data must be submitted electronically according to the Study Data Tabulation (SDTM) standard published by the Clinical Data Interchange Standards Consortium (CDISC) provided in the document "Study Data Specifications," which is posted on FDA.gov[9] and referenced in the guidance for industry *Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*.

- *Timeframe for submitting reports of the study(ies):* Reports of the above studies must be submitted to the Agency on or before (10~~09~~/21~~30~~/25). Please keep in mind that pediatric exclusivity attaches only to existing exclusivity, patent protection or exclusivity that would otherwise expire nine (9) months or more after pediatric exclusivity is granted, and FDA has 180 days from the date that the study reports are submitted to make a pediatric exclusivity determination. Therefore, to ensure that a particular patent or exclusivity is eligible for pediatric exclusivity to attach, you are advised to submit the reports of the studies at least 15 months (9 months plus 6 months/180 days for determination) before such patent or exclusivity is otherwise due to expire.

  If FDA has not determined whether secukinumab is eligible for reference product exclusivity under section 351(k)(7) of the PHS Act, you may submit a request for reference product exclusivity with supporting data and information to the Agency. Note that neither the issuance of this formal pediatric Written Request, nor any request for exclusivity made by you confers or otherwise implies that you are eligible for reference product exclusivity under section 351(k)(7) of the PHS Act.

- *Response to Written Request:* Under section 505A(d)(2)(A)(i), within 180 days of receipt of this Written Request you must notify the Agency whether or not you agree to the Written Request. If you agree to the request, you must indicate when the pediatric studies will be initiated. If you do not agree to the request, you must indicate why you are declining to conduct the study(ies). If you decline on

[8] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[9] https://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM312964.pdf

the grounds that it is not possible to develop the appropriate pediatric formulation, you must submit to us the reasons it cannot be developed.

Furthermore, if you agree to conduct the study(ies), but have not submitted the study reports on or before the date specified in the Written Request, the Agency may utilize the process discussed in section 505A(n) of the Act.

For ease of reference, a complete copy of the Written Request, as amended, is attached to this letter.

Reports of the studies that meet the terms of the Written Request dated July 18, 2025, as amended by this letter and by previous amendment(s) dated September 17, 2025, must be submitted to the Agency on or before October 21, 2025, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

Submit reports of the studies as a supplement to an approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, clearly mark your submission **"SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter.

In accordance with section 505A(k)(1) of the Act, FDA must make available to the public the medical, statistical, and clinical pharmacology reviews of the pediatric studies conducted in response to this Written Request within 210 days of submission of your study report(s). These reviews will be posted regardless of the following:

- the type of response to the Written Request (i.e., complete or partial response);
- the status of the application (i.e., withdrawn after the supplement has been filed or pending);
- the action taken (i.e., approval, complete response); or
- the exclusivity determination (i.e., granted or denied).

FDA will post the medical, statistical, and clinical pharmacology reviews on the FDA website.[10]

If you wish to discuss any amendments to this Written Request, submit proposed changes and the reasons for the proposed changes to your application. Clearly mark submissions of proposed changes to this request **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. We will notify you in writing if we agree to any changes to this Written Request.

[10] https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm316937.htm

If you have any questions, contact Javonna Stevens, Regulatory Project Manager, at (301) 796-4240 or Javonna.stevens@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Raj Nair, MD
Director
Office of Rheumatology and Transplant Medicine
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE:

- Complete Copy of Written Request as Amended

IND 012678

WRITTEN REQUEST

Novartis Pharmaceuticals Corporation
Attention: Kristine Ogozalek, MS
Global Regulatory Team Lead
One Health Plaza
East Hanover, NJ 07936

Dear Kristine Ogozalek:

Reference is made to your July 18, 2024, Proposed Pediatric Study Request for secukimumab. Further reference is made to the FDA Inadequate Study Request Letter dated November 5, 2024.

On May 22, 2025, FDA requested a teleconference to discuss the possibility to assess and identify patients for juvenile ankylosing spondylitis (JAS) and Axial Juvenile Spondyloarthritis (AxJSpA) in study CAIN457F2304.

I. Juvenile Ankylosing Spondylitis (JAS)

JAS is a descriptive term for the clinical presentation of ankylosing spondylitis (AS) occurring before the age of 16. JAS is diagnosed using the established criteria for diagnosing AS in adults[1] based on persistent low back pain and stiffness for more than three months and/or limitation of motion of the lumbar spine and/or limitation of chest expansion plus X-ray radiologic evidence of sacroiliitis (grade ≥2 bilaterally or grade 3-4 unilaterally). The true incidence of JAS is unknown; however, it is estimated that 10-20% of patients diagnosed with AS present before 16 years of age, and that most of these cases occur in patients who are at least 8 years of age.[2] The overall prevalence of JAS is estimated to be fewer than 1 per 1000 children. A number of treatments are approved for adult AS, including TNF inhibitors, IL-23 inhibitors and IL-17 inhibitors (including Cosentyx), however no treatments are approved for JAS.

II. Axial Juvenile Spondyloarthritis (AxJSpA)

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criteria for diagnosing adults with nr-axSpA[3], including inflammatory back pain without X-ray radiologic evidence of sacroiliitis but with either MRI evidence of sacroiliitis and one additional spondyloarthritis (SpA) feature or HLA-B27+ and at least two SpA features. Previously, it has been recognized that a significant number of children with juvenile idiopathic arthritis (JIA) can have spondyloarthritis and present with clinical symptoms of inflammatory back pain (e.g., enthesitis related arthritis [ERA] and juvenile psoriatic arthritis [JPsA]) and may have evidence of sacroiliitis on MRI.[4] However, it is only recently that criteria to define axial involvement in children with non-radiographic spondyloarthritis have become available.[5] The AxJSpA criteria incorporate genetic, clinical, and imaging domains. Imaging evidence of sacroiliitis (active inflammation and/or structural lesions) is necessary but not sufficient for classification. A threshold score of ≥ 55 out of 100 is required for AxJSpA classification. Notably, ~50% of the pediatric cohort of over 400 children used to derive the AxJSpA criteria had a history of enthesitis and may have fulfilled criteria for a diagnosis of ERA, however the new AxJSpA criteria would capture a population of children with axial disease. This represents the first pediatric-specific axial spondyloarthritis classification criteria and addresses an important unmet need in facilitating the development of treatments for this patient population. The true incidence of AxJSpA is unknown. The prevalence of AxJSpA is estimated to be approximately 1 in 1000 children. There are no treatments approved for AxJSpA.

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- ***Clinical studies:***

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Study 2: Long-term safety and tolerability of secukinumab in patients meeting criteria for AxJSpA, and comparison to patients with ERA and JPsA who do not meet such criteria in an extension trial. The selection criteria for patients with AxJSpA must be agreed upon with the Agency.

- ***Study Objectives:***

  Study 1 – The primary objective is to evaluate the safety and efficacy of secukinumab in a subset of patients meeting to be agreed upon criteria for AxJSpA using data from a phase 3, randomized, double-blind, placebo-controlled treatment withdrawal trial.

  Study 2 – The primary objective is to assess the long-term safety and tolerability of secukinumab in a subset of patients meeting to be agreed upon criteria for AxJSpA in an extension trial. A secondary objective is to compare the long-term safety and tolerability of secukinumab between this patient subset and those with ERA and JPsA patients who do not meet such criteria.

- ***Patients to be Studied:***

  Study 1 must include at least 6 patients meeting agreed upon criteria for AxJSpA in a phase 3 trial, which enrolled a total of 86 ERA and JPsA patients 2 to < 18 years of age.

  Study 2 must include at least 6 patients meeting agreed upon criteria for AxJSpA in an extension trial followed while on continuous treatment with secukinumab for a minimum of 104 weeks.

- ***Study endpoints:***

  ☐ Primary efficacy endpoint(s):

  ☐ BASDAI at Week 12 (or cJADAS/JADAS with justification)

  ☐ Key secondary efficacy endpoints should include (using an agreed upon statistical hierarchy):

- ☐ BASDAI during the randomized withdrawal period (or cJADAS/JADAS with justification)
- ☐ Physician's Global Assessment of disease activity (VAS)
- ☐ Parent's/subject's Global Assessment of subject's overall well-being (VAS included within CHAQ)
- ☐ Overall back pain (VAS)
- ☐ Nocturnal back pain score (VAS)
- ☐ Modified Schober's test
- ☐ JSpADA index
- ☐ JIA ACR30/50/70/90

- *Safety Endpoints/Monitoring: The protocol must include a plan for monitoring of the following safety endpoints:*

  - ☐ Adverse events, tolerability assessments, vital signs (e.g., blood pressure, heart rate, respiratory rate, temperature, weight), and laboratory parameters including CBC, CMP; screening for HIV, Hepatitis B, Hepatitis C, and tuberculosis
  - ☐ Known adverse events of special interest including infection, hypersensitivity reactions, inflammatory bowel disease, and eczematous eruptions

  The protocol must include a plan for appropriate monitoring of all adverse events.

- *Statistical information, including power of study(ies) and statistical assessments:*

  - For Study 1 – The incidence of treatment emergent adverse events must be summarized by relationship to the study drug and overall. In addition, laboratory values and vital signs must be summarized. Provide a descriptive summary of the efficacy outcomes.

  - For Study 2 - The incidence of treatment emergent adverse events must be summarized by relationship to the study drug and overall. In addition, laboratory values and vital signs must be summarized. Provide a descriptive summary of the efficacy outcomes.

The following information pertains to all clinical studies in the Written Request:

- *Extraordinary results:* In the course of conducting these studies, you may discover evidence to indicate that there are unexpected safety concerns, unexpected findings of benefit in a smaller sample size, or other unexpected results. In the event of such findings, there may be a need to deviate from the requirements of this Written Request. If you believe this is the case, you must contact the Agency to seek an amendment. It is solely within the Agency's discretion to decide whether it is appropriate to issue an amendment.

- *Biological product information:*

  - *dosage form: pre-filled syringe (PFS)*
  - *route of administration: subcutaneous injection*
  - *regimen: As agreed upon in the protocol*

  Use an age-appropriate formulation in the study(ies) described above. If an age-appropriate formulation is not currently available, you must develop and test an age-appropriate formulation and, if it is found safe and effective in the studied pediatric population(s), you must seek marketing approval for that age-appropriate formulation.

  In accordance with section 505A(e)(2), if

  (1) you develop an age-appropriate formulation that is found to be safe and effective in the pediatric population(s) studied (i.e., receives approval);
  (2) the Agency grants pediatric exclusivity, including publishing the exclusivity determination notice required under section 505A(e)(1) of the Act; and
  (3) you have not marketed the formulation within one year after the Agency publishes such notice,

  the Agency will publish a second notice indicating you have not marketed the new pediatric formulation.

  If you demonstrate that reasonable attempts to develop a commercially marketable formulation have failed, you must develop and test an age-appropriate formulation that can be prepared by a licensed pharmacist, in a licensed pharmacy, from commercially available ingredients. Under these circumstances, you must provide the Agency with documentation of your attempts to develop such a formulation and the reasons such attempts failed. If we agree that you have valid reasons for not developing a commercially marketable, age-appropriate formulation, then you must submit instructions

for preparing an age-appropriate formulation from commercially available ingredients that are acceptable to the Agency. If you conduct the requested studies using such a formulation, the following information must be provided for inclusion in the product labeling upon approval: active ingredients, diluents, suspending and sweetening agents; detailed step-by-step preparation instructions; packaging and storage requirements; and formulation stability information.

Bioavailability of any formulation used in the studies must be characterized, and as needed, a relative bioavailability study comparing the approved drug to the age appropriate formulation may be conducted in adults.

- *Labeling that may result from the study(ies)*: You must submit proposed pediatric labeling to incorporate the findings of the study(ies). Under section 505A(j) of the FD&C Act, regardless of whether the study(ies) demonstrate that secukinumab is safe and effective, or whether such study results are inconclusive in the studied pediatric population(s) or subpopulation(s), the labeling must include information about the results of the study(ies). Under section 505A(k)(2) of the FD&C Act, you must distribute to physicians and other health care providers at least annually (or more frequently if FDA determines that it would be beneficial to the public health), information regarding such labeling changes that are approved as a result of the study(ies).

- *Format and types of reports to be submitted*: You must submit full study reports (which have not been previously submitted to the Agency) that address the issues outlined in this request, with full analysis, assessment, and interpretation. In addition, the reports must include information on the representation of pediatric patients of ethnic and racial minorities. All pediatric patients enrolled in the study(ies) should be categorized using one of the following designations for race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander or White. For ethnicity, you should use one of the following designations: Hispanic/Latino or Not Hispanic/Latino. If you choose to use other categories, you should obtain agency agreement.

  Under section 505A(d)(2)(B) of the FD&C Act, when you submit the study reports, you must submit all postmarketing adverse event reports regarding this drug that are available to you at that time. All post-market reports that would be reportable under section 21 CFR 600.80 should include adverse events occurring in an adult or a pediatric patient. In general, the format of the post-market adverse event report should follow the model for a periodic safety update report described in the guidance for industry *E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs* and the guidance

addendum.[6] You are encouraged to contact the reviewing Division for further guidance.

For studies started after December 17, 2017 , study data must be submitted electronically according to the Study Data Tabulation (SDTM) standard published by the Clinical Data Interchange Standards Consortium (CDISC) provided in the document "Study Data Specifications," which is posted on FDA.gov[7] and referenced in the guidance for industry *Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*.

- *Timeframe for submitting reports of the study(ies):* Reports of the above studies must be submitted to the Agency on or before (10/21/25). Please keep in mind that pediatric exclusivity attaches only to existing exclusivity, patent protection or exclusivity that would otherwise expire nine (9) months or more after pediatric exclusivity is granted, and FDA has 180 days from the date that the study reports are submitted to make a pediatric exclusivity determination. Therefore, to ensure that a particular patent or exclusivity is eligible for pediatric exclusivity to attach, you are advised to submit the reports of the studies at least 15 months (9 months plus 6 months/180 days for determination) before such patent or exclusivity is otherwise due to expire.

  If FDA has not determined whether secukinumab is eligible for reference product exclusivity under section 351(k)(7) of the PHS Act, you may submit a request for reference product exclusivity with supporting data and information to the Agency. Note that neither the issuance of this formal pediatric Written Request, nor any request for exclusivity made by you confers or otherwise implies that you are eligible for reference product exclusivity under section 351(k)(7) of the PHS Act.

- *Response to Written Request:* Under section 505A(d)(2)(A)(i), within 180 days of receipt of this Written Request you must notify the Agency whether or not you agree to the Written Request. If you agree to the request, you must indicate when the pediatric studies will be initiated. If you do not agree to the request, you must indicate why you are declining to conduct the study(ies). If you decline on the grounds that it is not possible to develop the appropriate pediatric formulation, you must submit to us the reasons it cannot be developed.

  Furthermore, if you agree to conduct the study(ies), but have not submitted the study reports on or before the date specified in the Written Request, the Agency may utilize the process discussed in section 505A(n) of the Act.

[6] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.
[7] https://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM312964.pdf

Appendix

The following table shows the criteria for AxJSpA proposed by Weiss P., et al.

(b) (4)

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/

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