CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
BLA 125289/S103

Trade Name: SIMPONI® SmartJect® autoinjector

Generic Name: golimumab

Sponsor: Janssen Biotech, Inc.

Approval Date: 12/27/2013

Indication: The Simponi® SmartJect® auto injector is a single-use, disposable, drug delivery device that allows users to administer a dose of Simponi into subcutaneous tissue (abdomen, thigh, or outer area of upper arm) in the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and ulcerative colitis. This autoinjector is intended for use by healthcare professionals, caregivers, or patients for self-administration in the home environment.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 125289/S103

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 125289/S103

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125289/103

SUPPLEMENT APPROVAL

Janssen Biotech, Inc.
Welsh & McKean Roads
Spring House, PA 19477

Attention: Salvatore Morello, Director
Global Regulatory Affairs, Immunology

Dear Mr. Morello:

Please refer to your Supplemental Biologics License Application (sBLA), dated and received June 28, 2013, submitted under section 351(a) of the Public Health Service Act for Simponi (golimumab).

We acknowledge receipt of your amendments received October 10, November 5, and December 13, 17, and 20, 2013.

This "Prior Approval" supplemental biologics application provides for a minor design modification (the addition of a "flange" feature to safety interlock sleeve [SIS], and a change in color of the SIS) to the SmartJect Autoinjector and labeling changes to the Instructions for Use (IFU).

APPROVAL & LABELING

We have completed our review of this supplemental 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 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the Instructions for Use) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

REQUIRED PEDIATRIC ASSESSMENTS

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

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

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Christine Chung, R.Ph., Regulatory Project Manager, at (301) 796-3420.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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

/s/

BADRUL A CHOWDHURY
12/27/2013

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 125289/S103

LABELING

INSTRUCTIONS FOR USE

SIMPONI® (SIM-po-nee)
(golimumab)
SmartJect® autoinjector

If your doctor decides that you or a caregiver may be able to give your injections of SIMPONI at home, you should receive training on the right way to prepare and inject SIMPONI.

Do not try to inject SIMPONI yourself until you have been shown the right way to give the injections by your doctor or nurse.

It is important to read, understand, and follow these instructions before using the SIMPONI SmartJect autoinjector so you inject the right way. Call your doctor if you or your caregiver has any questions about the right way to inject SIMPONI.

Read this information before you start

Important things to know about your SmartJect autoinjector

When you are ready to inject SIMPONI, position the autoinjector straight onto your skin (90 degrees), then push firmly. **Do not press the button until you have pushed the autoinjector firmly against your skin, allowing the green safety sleeve to slide into the clear cover.**

The green safety sleeve (see Figure A) helps prevent accidental injections. The sleeve must slide into the clear cover before you will be able to press the button.

When the button is pressed you will hear a **loud first 'click' sound**. **Do not lift the autoinjector away from your skin. Hold and wait for the second 'click'.** It is very important to practice injecting SIMPONI with your doctor or nurse so you become comfortable with this 'click' sound.

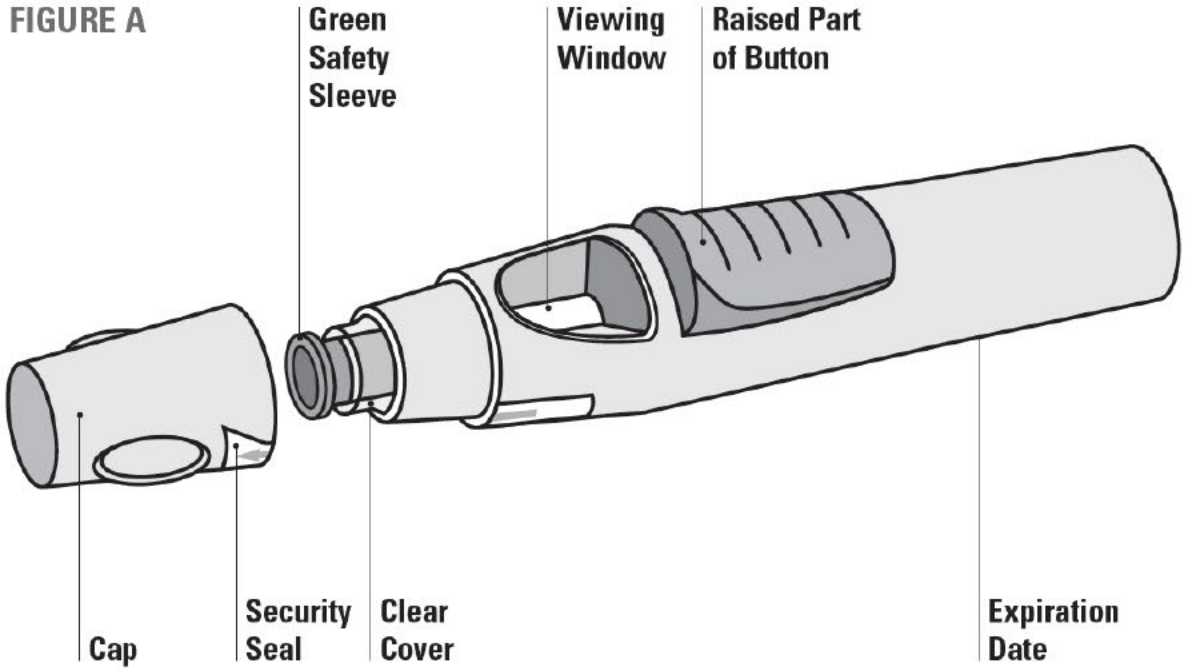
Keep holding the autoinjector firmly against your skin until you hear a second 'click' sound (may take 3-15 seconds), **then lift the autoinjector. The injection is complete when you hear the second 'click'.** If you lift the autoinjector before hearing the **second 'click',** you may not get the full dose of medicine.

Important things to remember
- **Do not** remove the cap until you get to Step 3.1.
- **Do not** press the button until you get to Step 3.3.
- **Do not** shake the SmartJect autoinjector at any time.

Read <u>all</u> instructions below before using SmartJect autoinjector

Figure A below shows what the SmartJect autoinjector looks like.

FIGURE A

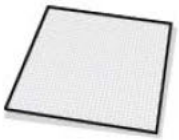


STEP 1. Gather and inspect the supplies for your injection

You will need these supplies for an injection of SIMPONI. See Figure B.

- 1 alcohol swab
- 1 cotton ball or gauze
- 1 SIMPONI prefilled SmartJect autoinjector from the refrigerator (stored at 36ºF to 46ºF (2ºC to 8ºC))
- 1 sharps disposal container for throwing away the used SmartJect autoinjector. See Step 4.2 for disposal instructions.

FIGURE B



1 alcohol swab

1 cotton ball or gauze

1 SIMPONI single use SmartJect autoinjector

Sharps container for autoinjector disposal

1.1 Check expiration date

- Check the expiration date ("EXP") on the SmartJect autoinjector.
- You can also check the expiration date printed on the back panel of the SIMPONI carton, to the left of the SIMPONI logo.
- If the expiration date has passed, **do not** use the SmartJect autoinjector. Call your doctor or pharmacist, or call 1-800-JANSSEN (1-800-526-7736) for help.

1.2 Check security seal

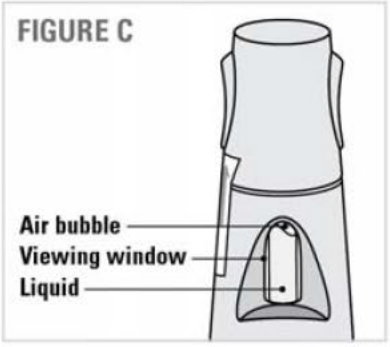
- Check the security seal around the cap of the SmartJect autoinjector. If the security seal is broken, **do not** use the SmartJect autoinjector.

1.3 Wait 30 minutes

- To ensure proper injection, allow the autoinjector to sit at room temperature outside the carton for 30 minutes and out of the reach of children.
- **Do not** warm the SmartJect autoinjector in any other way (for example, **do not** warm it in a microwave or in hot water).
- **Do not** remove the SmartJect autoinjector cap while allowing it to reach room temperature.

1.4 Check the liquid in the SmartJect autoinjector

FIGURE C

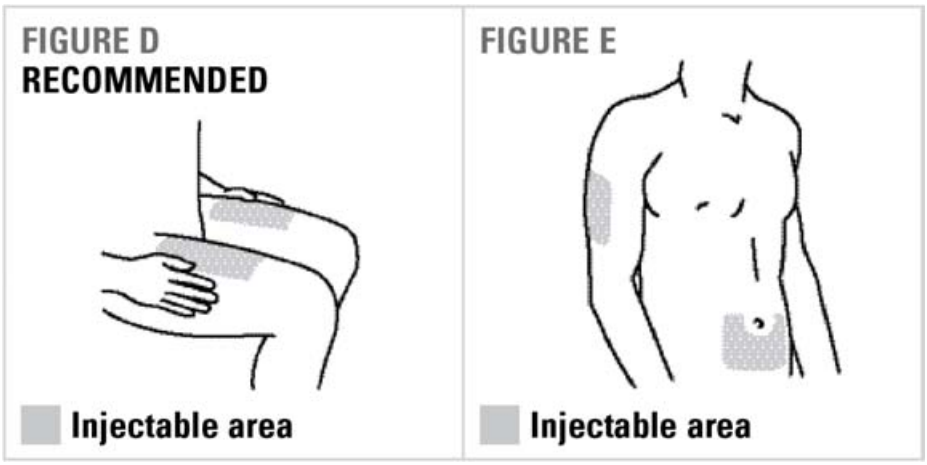


- Look through the viewing window of the SmartJect autoinjector. See Figure C.
- Make sure that the liquid in the prefilled syringe is clear and colorless to slightly yellow in color. You may see a small amount of tiny particles that are white, or that you can see through.
- **Do not** inject the liquid if it is cloudy or discolored, or has large particles in it.
- You may also notice an air bubble. This is normal. See Figure C.

STEP 2. Choose and prepare the injection site

2.1 Choose the injection site

- The recommended injection site is the front of your middle thighs. See Figure D.
- You can also use the lower part of the abdomen below the navel (belly button), except for the two-inch area directly around the navel. See Figure E.
- If a caregiver is giving you the injection, the outer area of the upper arms may also be used. See Figure E.



- If more than one injection is needed for a dose of SIMPONI, each injection should be given at different sites on the body.
- Choose a different injection area each time you give your injection. See Figures D and E.
- **Do not** inject into areas where the skin is tender, bruised, red, scaly, or hard. Avoid areas with scars or stretch marks.

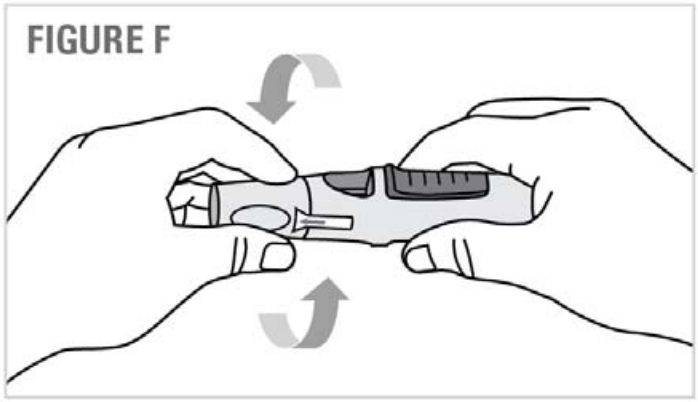
2.2 Prepare the injection site

- Wash your hands well with soap and warm water.
- Wipe the injection site with an alcohol swab.
- **Do not** touch this area again before giving the injection. Allow the skin to dry before injecting.
- **Do not** fan or blow on the clean area.

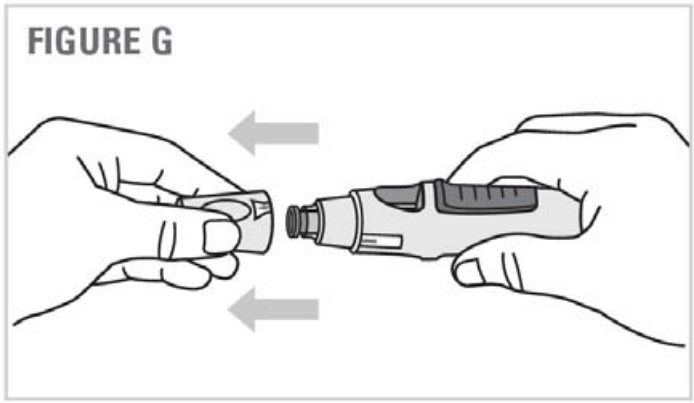
STEP 3. Inject SIMPONI using the single dose SmartJect autoinjector

3.1 Remove cap

- **Do not remove the cap until you are ready to inject SIMPONI.** Inject SIMPONI within 5 minutes after the cap has been removed.
- When you are ready to inject, twist the cap slightly to break the security seal. See Figure F.



- Pull the cap off and throw it in the trash right away. See Figure G.



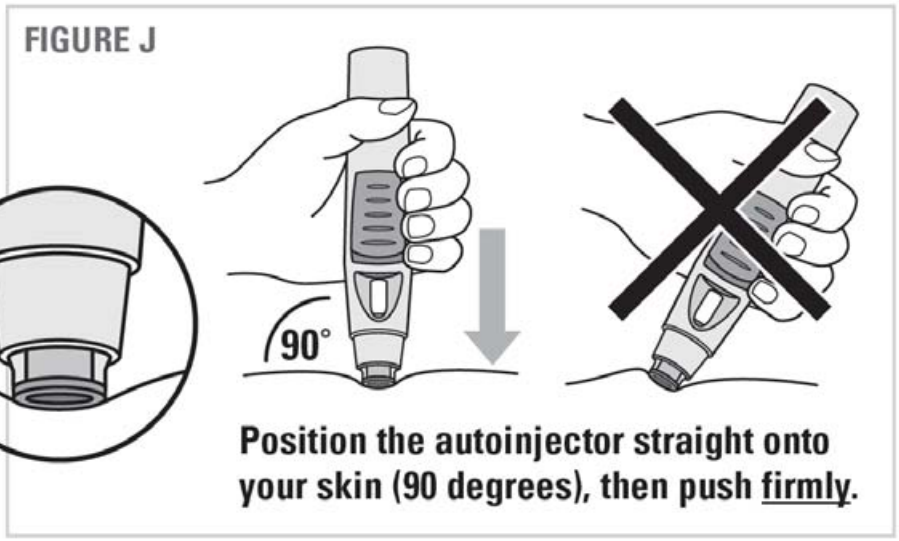
- **Do not** put the cap back on because it may damage the needle inside the SmartJect autoinjector.
- **Do not** use your SmartJect autoinjector if it is dropped without the cap in place.

3.2 Push autoinjector firmly against skin

- Hold the SmartJect autoinjector comfortably in your hand. **DO NOT PRESS THE BUTTON AT THIS TIME.**
- Choose from 2 injection methods:
    - You should inject the medicine without pinching the skin.
      See Figure H.

- If you prefer, you may pinch the skin to create a firmer surface for your injection.
  See Figure I.

- Position the **open end** of the SmartJect autoinjector **straight onto your skin** (90 degrees) and **push <u>firmly</u>** until the green safety sleeve slides into the clear cover. See Figure J.

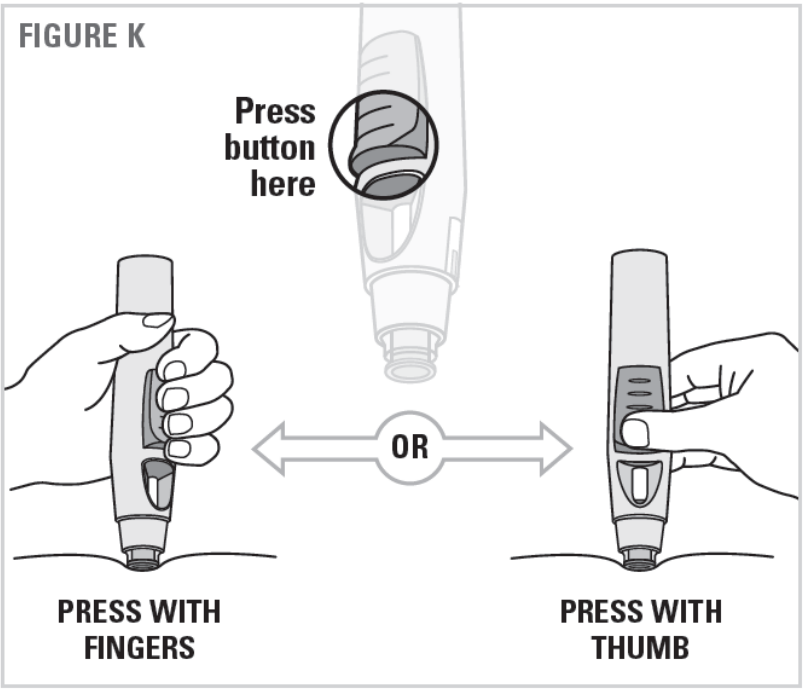


3.3 Press button to inject. Hold and wait!

- **Continue to hold the SmartJect autoinjector firmly against the skin, and press the raised part of the button with your fingers or thumb.** See Figure K.

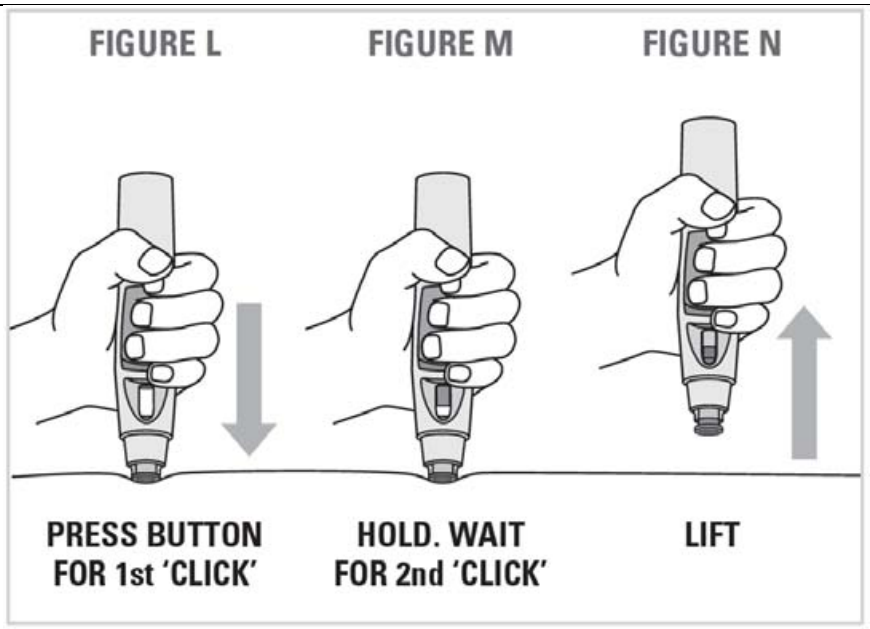
  NOTE: You will not be able to press the button unless the autoinjector is pushed firmly against your skin and the green safety sleeve slides into the clear cover.

FIGURE K



- After the button is pressed, it will stay pressed in so you do not need to keep pressure on it.
- **You will hear a loud first 'click' sound, do not be alarmed.** This is normal. This 'click' means that the needle has been inserted and the injection has started. You may or may not feel a needle prick at this time. See Figure L.
- **Do not lift the SmartJect autoinjector away from your skin until you hear the second loud 'click'. If you lift the autoinjector before the second 'click', you may not get your full dose of medicine.** See Figure M.

3.4 Wait for second 'click' (3-15 seconds)



- **Keep holding the SmartJect autoinjector against your skin until you hear the second 'click' sound. It usually takes about 3 to 6 seconds, but may take up to 15 seconds before you hear the second 'click' sound.** See Figure M**.**

- The **second 'click'** sound means that the injection is finished and the needle has pulled back (retracted) into the SmartJect autoinjector.

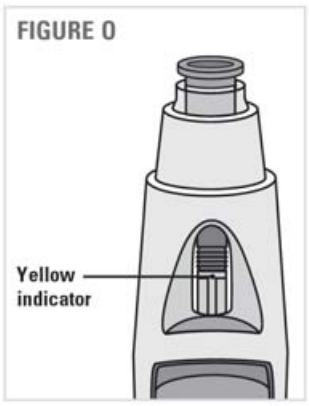
- Lift the SmartJect autoinjector from the injection site. See Figure N.

- If you have a problem hearing the 'clicks', count for 15 seconds from the time you pressed the button and then lift the SmartJect autoinjector from the injection site.

STEP 4. After the injection

4.1 Check the viewing window

- After you finish injecting, check the viewing window to see the yellow indicator. See Figure O. This means the SmartJect autoinjector has worked the right way.
- The yellow indicator will fill about half of the viewing window. This is normal.
- If you do not think you received your injection, check the yellow indicator again to confirm that the dose was delivered.



- If you do not see the yellow indicator in the viewing window, call 1-800-JANSSEN (1-800-526-7736) for help. **Do not** administer a second dose without speaking to your doctor.

4.2 Dispose of the used SmartJect autoinjector

- Put your used SmartJect autoinjector in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of) the SmartJect autoinjector in your household trash.** See Figure P.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
    - made of a heavy-duty plastic,
    - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
    - upright and stable during use,
    - leak-resistant, and
    - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- **Do not** dispose of your used sharps disposal container in your household trash unless your community guidelines permit this.
- **Do not** recycle your used sharps disposal container.

4.3 Use Cotton Ball or Gauze

- There may be a small amount of blood or liquid at the injection site, which is normal.
- You can press a cotton ball or gauze over the injection site for 10 seconds. **Do not** rub the injection site.
- You may cover the injection site with a small adhesive bandage, if needed.

Need more help with your injection?

Quick Reminders

Do not press the button until you are ready to inject SIMPONI.

Position the autoinjector straight onto your skin (90 degrees), then push firmly.

Press the raised part of the button to start the injection and listen for the **first 'click'**. **Do not** lift the SmartJect autoinjector away from your skin yet.

Keep holding the autoinjector firmly against your skin until you hear the **second 'click',** or you can count to 15 after pressing the button.

Lift and check the viewing window to confirm that you see the yellow indicator.

If you're having difficulty injecting:

- Make sure you removed and disposed of the cap.
- Make sure you **do not** press the button while positioning and pushing the autoinjector firmly against your skin.
- Try pushing the autoinjector against your skin more firmly.
- Try using two hands to inject. Use your other hand to steady the autoinjector.
- Make sure you press the raised part of the button. See Figure K.
- Try pressing the button with a little more force.
- Make sure your injection site is flat. If you are using the "pinching technique," try pinching less skin.
- Try a different injection site. See Figures D and E.

For additional questions or assistance, or to share your feedback, call 1-800-JANSSEN (1-800-526-7736).

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by:
Janssen Biotech, Inc.
Horsham, PA 19044
US License No. 1864

Revised: 12/2013

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 125289/S103

MEDICAL REVIEW(S)

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY PRODUCTS
10903 New Hampshire Avenue; Building 22
Silver Spring MD 20993-0002

Medical Officer Review

BLA:	125289/103
Drug name:	Simponi® (Golimumab)
Sponsor:	Janssen Biotech, Inc
Approved indications:	Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, and Ulcerative Colitis
Type of Submissions:	Prior Approval Supplement
Date of Submission:	28 June 2013
Date of Receipt:	28 June 2013
Review Date:	27 November 2013
Reviewer:	Janet W. Maynard, M.D.
Dep Dir for Safety:	Sally Seymour, M.D.

1. Introduction and Executive Summary

This is a medical officer review of prior approval supplement proposing modifications to the golimumab SmartJect Autoinjector device and labeling. These modifications were made to minimize medication errors and enhance usability of the autoinjector. The sponsor conducted a human factors study of the proposed device and labeling changes. In addition, the sponsor submitted physical and engineering information and test data related to the performance, mechanical stability, and safety and effectiveness of the modified device.

This review will summarize the changes made to the device and labeling and recommendations of the various consulting divisions. The submitted data suggest that the proposed device and labeling modifications are reasonable. The recommend regulatory action is approval.

1A. Recommendations for Regulatory Action

Our overall recommendation is approval of this Prior Approval Supplement.

2. Product Background and Regulatory History

Simponi® (golimumab) is a human immunoglobulin (Ig) G1κ monoclonal antibody that belongs to the class of tumor necrosis factor (TNF) blocking drugs. Simponi binds with high affinity to both soluble and transmembrane forms of TNFα. Simponi was approved for the treatment of rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis in solution for subcutaneous injection as a single-use pre-filled pen or as a single-use prefilled syringe on April 24, 2009.

In December 20, 2012, the sponsor indicated that they planned to make several modifications to the Simponi SmartJect Autoinjector and the Instructions for Use (IFU). In February 2013, FDA reviewed and provided general advice to the Sponsor regarding a proposed human factors study protocol intended to support the proposed changes. In general, the human factors study protocol was found to be acceptable.

The labeling and device modifications were based on historical customer feedback, human factors expert's reviews of the IFU, FDA feedback on the IFU, and the human factors study results.

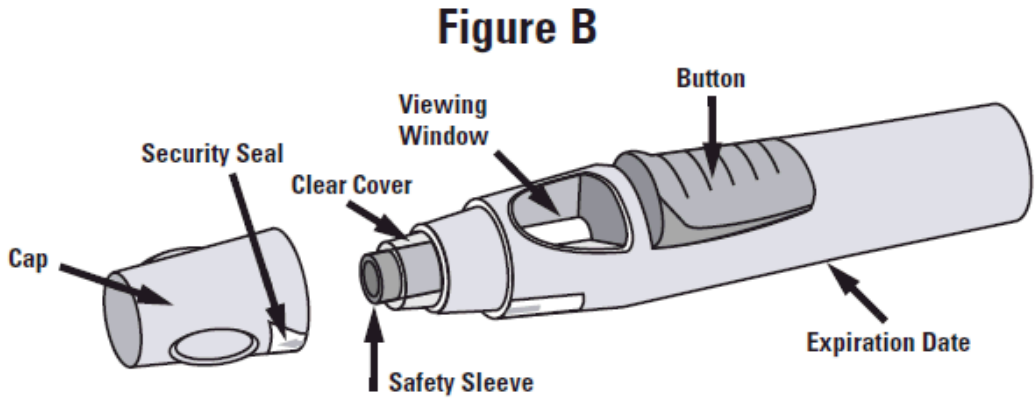
3. Overview of Changes Proposed in this Prior Approval Supplement

This prior approval supplement was submitted in an effort to enhance usability of the Simponi SmartJect. The SmartJect device design has been modified to include a small flange feature (ledge) on the skin contacting end of the Safety Interlock Sleeve (SIS) that interfaces with the patient. The flange was incorporated into the SIS design to provide more contact surface area against injection sites and thereby reduce skin depression and pressure sensation during use. In addition to the SIS, (b) (4) These changes were made as a result of current user input and focus group studies on the current product. A

human factors validation study was performed to support all of the changes. The validation study incopororated FDA feedback on the human factors study protocol.

3A. Currently Approved Simponi SmartJect Autoinjector
The currently approved golimumab drug product presentations are 50mg/0.5mL single dose pre-filled syringe (PFS), a 50mg/0.5mL single dose prefilled SmartJect Autoinjector, 100mg/1mL single dose prefilled prefilled syringe, and a 100mg/1mL single dose prefilled SmartJect Autoinjector. The currently approved Simponi SmartJect Autoinjector is shown in Figure 1.

Figure 1. Currently Approved Simponi SmartJect Autoinjector



Source: Patient Instruction's for Use

3B. Proposed Changes to the Simponi SmartJect Device
The proposed changes to the Simponi SmartJect Device include a small ledge (flange) at the distal end of the Safety Interlock Sleeve to provide more contact surface area against the injection sites, which should reduce skin depression and pressure sensation during use (Figure 2).

In order to support these changes, the Sponsor submitted physical and engineering information and tests data related to the performance, mechanical stability, and safety and effectiveness of the modified device. The CDRH-device review team assessed these data and felt the results from the testing were acceptable. The design modifications do not appear to have affected the safety and effectiveness of the device. In addition, CDRH-Office of Compliance reviewed the submitted data and noted that it appeared to be approvable from the perspective of the Medical Device Regulations.

The submitted data were also reviewed by CDER/OBP. It was noted that because the biochemistry and other product quality attributes beyond the device have not changed, CDER/OBP did not have any quality issues arising from the proposed device changes.

3C. Labeling changes

The Sponsor submitted changes to the IFU to attempt to decrease medication errors associated with use of the SmartJect Autoinjector. These changes were reviewed by DPARP and the Division of Medical Policy Programs (DMPP). DMPP recommended changes to simplify the wording and clarify concepts when possible, ensure that the IFU is consistent with the prescribing information, remove unnecessary or redundant information, and ensure that the IFU meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information. DMPP felt that the IFU was acceptable with these proposed changes.

Reviewer's comments: This reviewer agreed with DMPP's recommendations to modify the IFU.

3D. Human Factors Testing to Support Proposed Changes to Simponi SmartJect Autoinjector

The Sponsor conducted one human factors study to evaluate the proposed labeling and device modifications. This study was reviewed by CDRH and DMEPA.

The human factors study included 46 participants, including experienced SmartJect Users (untrained), potential SmartJect Users (untrained), and potential SmartJect users (trained). The training consisted of one-on-one patient training, which included a review of how to use the autoinjector, and a supervised injection where the moderator remained in the

room to assist as needed. The participants returned one week later for a validation session, and they performed two unsupervised injections, which is representative of their actual use of the device at home.

In the study, there were no failures or use errors across all critical and essential components or Instructions for Use knowledge probe tasks. There were five "close calls" observed where the participants lifted the autoinjector before the injection was complete (prior to hearing the second click). However, all of these participants were determined to have received the full dose. All participants, except one, learned from the first close call and waited for the second click on their second injection trial. All participants demonstrated that they know to wait until the second click before removing the device.

The CDRH-human factors review team and DMEPA noted that the human factors study report was acceptable. They felt the human factors validation study confirms the safe and effective use of the device and the associated IFU and the incremental improvements may help users to better operate the device.

Reviewer's comments: The submitted data support the conclusion that the proposed modifications do not impact the safe and effective use of the device and may provide incremental improvements to help users better operate the device.

4. Summary of Changes and Recommendations

The Applicant proposes modifications to the Simponi SmartJect Autoinjector device and labeling to enhance use of the Simponi Autoinjector. Specifically, the Sponsor proposes to modify the SmartJect device design through addition of a small flange feature (ledge) on the skin contacting end of the Safety Interlock Sleeve (SIS) that interfaces with the patient. In addition, modifications are proposed to the IFU. The Sponsor has performed stability testing and a human factors study to support the proposed changes. The data suggest that the modifications maintain the safety and effectiveness of the product and may provide incremental improvements to help users to better operate the device.

4.1 Recommended Regulatory Action

The recommended regulatory action is Approval of this prior approval supplement.

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

/s/

JANET W MAYNARD
12/20/2013

SALLY M SEYMOUR
12/20/2013

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 125289/S103

CHEMISTRY REVIEW(S)

sBLA STN 125289-103

Golimumab

Janssen Biotech, Inc

Erik Read, Ph.D., Product Quality Reviewer, LCB, DMA
Kurt Brorson, Ph.D., Principal Investigator, LCB, DMA

Division of Monoclonal Antibodies

OBP CMC Review Data Sheet

1. **sBLA#:** STN 125289-103

2. **REVIEW DATE:** December 9, 2013

3. **PRIMARY REVIEW TEAM:**
Product Quality Team: Erik K. Read
RPM: Christine Chung

4. **MAJOR GRMP DEADLINES**
Final Action Date: December 29, 2013

5. **COMMUNICATIONS WITH SPONSOR AND OND:**

Communication/Document	Date
Simponi s103 IR cdrhdoe.pdf	October 29, 2013

6. **SUBMISSION(S) REVIEWED:**

Submission	Date Received	Review Completed (Yes/No)
125289-103 [sBLA, PAS]	June 28, 2013	Yes

7. **DRUG PRODUCT NAME/CODE/TYPE:**
   a. **Proprietary Name:** CNTO 148
   b. **Trade Name:** Simponi
   c. **Non-Proprietary/USAN:** golimumab
   d. **CAS name:** 476181-74-5
   e. **OBP systematic name:** MAB HUMAN (IGG1) ANTI CAA26669 (TNF-alpha_HUMAN) [CNTO 148]

PHARMACOLOGICAL CATEGORY:

8. **DOSAGE FORM:** pre-filled syringe, autoinjector
9. **STRENGTH/POTENCY:** 100 mg/mL
10. **ROUTE OF ADMINISTRATION:** subcutaneous
11. **REFERENCED MASTER FILES:**

DMF #	HOLDER	ITEM REFERENCED	Letter of Cross Reference	COMMENTS (STATUS)
1556	CDRH	Centocor Autoinjector		

12. **INSPECTIONAL ACTIVITIES.** N/A

14. **CONSULTS REQUESTED BY** CDER/OND/ODE II RPM Christine Chung on

August 1, 2013 for Patient Labeling Review Consultation by CDER-DMPP-Patient Labeling Team

August 1, 2013 for Patient Labeling Review Consultation by CDER-OSE-DMEPA

August 1, 2013 for intercenter consult (ICC 1300425) by Center of Devices and Radiological Health (CDRH)

October 29, 2013 for intercenter consult by Center of Devices and Radiological Health (CDRH) – Office of Compliance

17. **ADMINISTRATIVE**

Erik K. Read, Ph.D. Primary Reviewer Division of Monoclonal Antibodies	
Kurt Brorson, Ph.D., Research Biologist, Division of Monoclonal Antibodies	

B. CC Block

Recipient	Date
Christine Chung	
David Frucht	
Kathleen Clouse	

REVIEW SUMMARY

The shape and color of Sliding Interlock Sleeve (SIS) of the Centocor Autoinjector has been modified. Because the biochemistry and other product quality attributes beyond the device have not changed, CDER/OBP has no quality issues arising from this change and the recommendations of the consult reviewers should determine approval the SIS modifications.

The Sponsor has conducted human factor studies (HFS) for patient use and accelerated stability studies for mechanical performance in support of the SIS modifications. Consult reviews have been requested by the OND RPM on August 1, 2013 to assess mechanical stability of the modified SIS, the impact of this change as measured by HFS, and the resulting revision in patient instructions for use (IFU), and labeling supplement.

The assigned consult reviewers have followed-up on issues raised.

R REGIONAL

A DMEPA consult request (OSE RCM# 2013-1780 was sent on August 1, 2013 by Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) RPM Christine Chung to evaluate the proposed IFU for Simponi (Golimumab) Smartject Autoinjector review Human Factors Study (HFS) results that tested the minor design modification to the Smartject Autoinjector.

On November 13, 2013, Teresa McMillan, the assigned DMEPA reviewer completed the human factor, label, and labeling review (DARRTS documentId=090140af803003cf) which concluded,

> DMEPA concludes that the Human Factors Validation Study confirms safe and effective use of the device and the associated IFU and the incremental improvements may help users to better operate the device.

Reviewers Note: *The reviewer concurs with the sense of the DMEPA consult review that there are no issues or concerns arising from changes to the IFU or the results of the human factor studies.*

On November 25, 2013, Twanda Scales, the assigned DMPP Patient Labeling Reviewer completed a review (DARRTS documentId=090140af80303d25) of the revised IFU which concluded.

> The IFU is acceptable with our recommended changes.

Reviewers Note: *The reviewer concurs with the sense of the DMPP consult review that the IFU are acceptable and DMPP will follow up on the recommended changes.*

P DRUG PRODUCT

3.2.P.2.4 Container Closure System

The shape and color of Sliding Interlock Sleeve (SIS) of the Centocor Autoinjector has changed. This is one component of the entire device, the rest of which is unchanged. Reference is made to Master File for Devices, MAF-1556 and a Letter of Authorization that was provided as part of module 1.4.1

The Sponsor asserts that a bridging human factors study to compare the modified design with the currently marketed device showed no negative impact of this change upon the performance, safety, assembly, and functional stability relative to the FDA approved SIMPONI drug product. This assertion will be reviewed by CDRH.

Reviewers note: *The autoinjector is considered secondary packaging and the approved pre-filled syringe component of this system has not been changed. Because this is a device change, a CDRH consult review has been requested, and the assigned CDRH reviewer will follow-up on any issues raised.*

On October 23, 2013, QuynhNhu Nguyen, Biomedical Engineer/Human Factors Reviewer (CDRH/ODE/DAGID) completed a HFS validation report review (DARRTS documentId=090140af80301179) and concluded,

> This consultant finds the human factors study report acceptable and has no further questions.

Reviewers Note: *The reviewer concurs with the sense of the CDRH/ODE/DAGID consult review that the HFS report is acceptable.*

On October 24, 2013, William M. Burdick, Biomedical Engineer/Physicist CDRH/ODE/DAGRID, General Hospital Device Branch completed a review (DARRTS documentId=090140af8030117c) of the physical and engineering information and test data related to the performance, mechanical stability, and safety and effectiveness of the modified device, and concluded,

> It appears that the sponsor conducted a thorough and valid assessment of the modified SIMPONI Smartject® Autoinjector. From the results cited in BLA 125289 AND MAF 1556, it appears that the modified autoinjector is as safe and effective as the original autoinjector. I have no issues with the subject device.

On October 29, 2013, CDER/OND/ODEII RPM Christine Chung conveyed the following information request to the Sponsor on behalf of CDRH-Office of Compliance reviewer Isabel Tejero,

> We refer to supplemental BLA 125289/103 for Simponi (golimumab) which proposes changes to the Instructions for Use (IFU) and a minor design modification to the SmartJect Autoinjector. We have the following request for information.

1. Provide documentary evidence that the implemented design change in the device constituent part of the Simponi combination product was done in compliance with 21 CFR 820.30, particularly with section (i), design changes, which applies to any changes made to the Simponi combination product.
2. Provide documentary evidence that any changes made to the manufacturing process (assembly, packaging) of the Simponi combination product to accommodate the design change in the device constituent part were verified and validated.

On November 5, 2013 the Sponsor (JBI) uploaded amendment to supplement STN 125289/103.2 which included a response addressing the IR questions/requirements.

Reviewers note: *The proposed change to the SIS is acceptable from a CDER standpoint and the CDRH consult reviewer finds that the proposed container closure system change to the SIS is acceptable.*

3.2.P.7 Container Closure Description

The final presentation of SIMPONI is comprised of a Pre-filled Syringe (PFS) within a Centocor Autoinjector assembly (see exploded diagram below). Each PFS includes CNTO 148 (golimumab) Drug Product (DP) with (b) (4) sterile clean fill 1-mL syringe with a affixed 27 guage half-inch stainless steel needle, and needle shield. Autoinjector components are described within MAF-1556. Both the PFS and the autoinjector assembly were reviewed and approved under the original BLA (STN125289) in 2009.

In this sBLA, the color/colorant column entry of the SIS row in Table 1 of Module 3.2.P.7 was modified from "Dusk (OM77013) " to "Green" to reflect the SIS color change.

(b) (4)

Reviewers note: *The proposed change in description is acceptable from a CDER standpoint and the CDRH consult reviewer finds that the proposed container closure system change to the SIS is acceptable.*

3.2.P.8.1 Stability Summary and Conclusion

The Sponsor added a new subsection entitled, "*9.2 Accelerated Aging Study of the Modified Centocor (SmartJect®) Autoinjector*". It summarizes mechanical performance studies evaluating effects of the design change in the shape and color of the Sliding Interlock Sleeve (SIS) autoinjector component. Briefly, unassembled modified autoinjector components were aged at 50 +/- 3°C for up to 60 days then assembled with SIMPONI PFS then tested for performance

stability. Release tests for key device performance measures of modified assemblies with SIMPONI PFS (50 mg / 0.5 mL, and 100 mg / 1.0 mL) include: cap removal, dose delivery time, expelled volume, and visual appearance. Additionally, SIMPONI PFS (50 mg / 0.5 mL) samples were tested by force to actuate.

Reviewers Note: *As the drug substance and pre-filled syringe drug product release tests have not changed, additional stability studies evaluating the antibody product biochemistary are unnecessary.*

Additional text summarizing this study was added to the "*11 Conclusions*" section wherein the Sponsor asserts that the accelerated stability testing results "confirm reliable mechanical operation" of the modified SIS that is "equivalent to a device age of 36 months".

Reviewers note: *The stability study did not evaluate antibody biochemistry. However, as the golimumab antibody solution contact surface has not changed, no differences in antibody stability are expected. A CDRH consult review has been performed and raised no issues.*

3.2.R Regional Information
3.2.R.4 Medical Device – Centocor Autoinjector

Sponsor updated module to include the amendment date of Master Device File MAF-1556 that includes the modified SIS components.

Reviewers note: *A CDRH consult review has completed, and the assigned CDRH reviewer has not raised any issues.*

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/s/

ERIK K READ
12/09/2013

KURT A BRORSON
12/09/2013

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 125289/S103

OTHER REVIEW(S)

Division of Pulmonary, Allergy, and Rheumatology Products

REGULATORY PROJECT MANAGER LABELING REVIEW

Application: BLA 125289/103

Name of Drug: Simponi (golimumab) SmartJect Autoinjector

Applicant: Janssen Biotech, Inc. (JBI)

Submission Date: June 28, 2013

Receipt Date: June 28, 2013

Background and Summary Description:

JBI submitted this prior approval labeling supplement to revise the SIMPONI SmartJect Autoinjector Instructions for Use (IFU) to reflect a minor design modification (the addition of a "flange" feature to safety interlock sleeve [SIS], and a change in color of the SIS).

Review:

The following were consulted to review the labeling and data to support the proposed changes.

- CDRH-Human Factors (HF) and OSE/Division of Medication Error and Prevention Analysis (DMEPA) were consulted to review the results of Human Factors validation study conducted by Janssen to test the minor design modification.
- CDRH/Office of Device Evaluation (ODE)/General Hospital Device Branch was consulted to review the physical and engineering information and test data related to the performance, mechanical stability, and safety and effectiveness of the modified device.
- CDRH/ Office of Compliance (OC)/Division of Manufacturing & Quality was consulted to review changes to device manufacturing with the proposed design modification to SmartJect.
- Division of Medical Policy Programs (DMPP)/Patient Labeling Team (PLT) was consulted for review of the proposed labeling changes to the IFU.

Labeling comments were issued by DPARP to the sponsor on December 4, 2013, as recommended by PLT's review dated November 26, 2013, and then on December 19, 2013. Janssen submitted final labeling revisions in an amendment to the supplement received December 20, 2013, which were acceptable to the clinical and PLT review teams.

I compared the IFU received on December 20, 2013, with the last approved IFU dated May 15, 2013, for efficacy supplements S-077,078, 079 – DGIEP approval of Simponi for ulcerative colitis. There were no other changes than those provided for in this Prior approval supplement and as indicated in the Review section above.

Recommendations:

Clinical review team's review dated December 20, 2013, recommend approval of this supplement. CMC/OBP's review dated December 9, 2013, stated that no quality concerns were raised with the proposed minor device modification and referred to the recommendations of the

consult reviews. CDRH/OC's review dated December 20, 2013, stated that there are "no apparent deficiencies that would indicate that the safety and effectiveness of the device constituent part are compromised." CDRH/ODE's review dated October 25, 2013, stated, "The results from the testing are acceptable. The design modifications have not appeared to affect the safety and effectiveness of the device." CDRH/HF's (October 24, 2013) and DMEPA's (November 13, 2013) reviews concluded that results of the HF validation study confirm safe and effective use of the modified device. PLT found Janssen's December 20, 2013, labeling amendment to be acceptable.

Pending review by the Director of DPARP, this PAS labeling supplement for the SmartJect IFU should be approved.

Christine Chung, R.Ph.	December 26, 2013
Regulatory Project Manager	Date
Colette Jackson for Sandy Barnes	December 26, 2013
Chief, Project Management Staff	Date

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/s/

CHRISTINE H CHUNG
12/26/2013

COLETTE C JACKSON
12/26/2013
Signed for S. Barnes

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy Initiatives
Division of Medical Policy Programs

PATIENT LABELING REVIEW

Date:	**November 25, 2013**
To:	Badrul A. Chowdhury, MD, PhD Director **Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Melissa Hulett, MSBA, BSN, RN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Twanda Scales, RN, BSN, MSN/Ed. Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
Subject:	Patient Labeling Review: Instructions for Use (IFU)
Drug Name (established name):	Simponi (golimumab)
Dosage Form and Route:	50mg/0.5ml Injection
Application Type/Number:	BLA 125289
Supplement Number:	S-103
Applicant:	Janssen Biotech, Inc.

1 INTRODUCTION

On June 28, 2013, Janssen Biotech, Inc. (JBI) submitted for the Agency's review and approval a Prior Approval Supplement (PAS) for SIMPONI (golimumab) Smartject Autoinjector. SIMPONI (golimumab) injection was originally approved on April 24, 2009, for the treatment of:

- Rheumatoid Arthritis in adults in combination with methotrexate
- Psoriatic Arthritis in adults alone or in combination with methotrexate
- Active Ankylosing Spondylitis in adults

Further reference is also made to the Human Factors Study Protocol submitted on December 20, 2012 and FDA feedback received on February 27, 2013. This PAS (S-103) was submitted to propose revisions to the SIMPONI (golimumab) Smartject Autoinjector IFU based on several inputs including; historical customer feedback, human factors experts' reviews of the IFU, FDA feedback on the IFU received February 27, 2013 (related to the FDA's review of the Human Factors Study protocol and IFU to be tested), the results of Human Factors Studies (HFS), and internal JBI reviews involving the commercial, device design, quality, and Johnson & Johnson (J&J) design stakeholders. In addition, JBI proposes a minor design modification to the SmartJect® Autoinjector due to updates to several figures in the IFU.

This review is written by the Division of Medical Policy Programs (DMPP) in response to a request by the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) on August 5, 2013 for DMPP to review the Applicant's proposed IFU for SIMPONI (golimumab) Smartject Autoinjector.

2 MATERIAL REVIEWED

- Draft SIMPONI (golimumab) Smartject Autoinjector (IFU) received on June 28, 2013, and received by DMPP on November 20, 2013.
- Approved SIMPONI (golimumab) injection Prescribing Information (PI) dated November 13, 2013.

3 REVIEW METHODS

In our focused review of the IFU we have:

- simplified wording and clarified concepts where possible
- ensured that the IFU is consistent with the prescribing information (PI)
- removed unnecessary or redundant information
- ensured that the IFU meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

4 CONCLUSIONS

The IFU is acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP on the correspondence.

- Our review of the IFU is appended to this memo. Consult DMPP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the IFU.

Please let us know if you have any questions.

24 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

TWANDA D SCALES
11/25/2013

MELISSA I HULETT
11/26/2013

LASHAWN M GRIFFITHS
11/26/2013

C O N S U L T R E V I E W

Date: October 24, 2013

From: William M. Burdick, Biomedical Engineer/Physicist
CDRH/ODE/DAGRID, General Hospital Device Branch

To: Ms. Christine Chung, Regulatory Project Manager
CDER/OND/ODEII
Division of Pulmonary, Allergy, and Rheumatology Products, HFD-570

Through: Richard Chapman, Branch Chief
ODE/DAGRID, General Hospital Devices Branch

Subject: **ICC1300425 – BLA 125289/103: Janssen Biotech SIMPONI SmartJect® Autoinjector -Engineering Consult to Assess Delivery Performance and Mechanical Stability of modifications to Subject Autoinjector, which includes modified flange on Sliding Interlock Sleeve and change in color of Sleeve**

Information I reviewed
I reviewed the physical and engineering information and test data related to the performance, mechanical stability, and safety and effectiveness of the modified device. Documents I reviewed were MAF 1556 and BLA 125289/103, Modules 3.2.P.7, 3.2.P.2.4, 3.2.P.8.1, and 3.2.R.4.

Information I did not Review
Information which I did not review included the following:

- Biocompatibility
- Sterility
- Compatibility between the Material Comprising the Device and Contacting Drug
- Stability of the Drug in the Device
- Human Factors

PURPOSE OF DEVICE

The SIMPONI SmartJect® autoinjector is a single-use, disposable, drug delivery device that allows users to administer a dose of SIMPONI into subcutaneous tissue (abdomen, thigh, or outer area of upper arm) in the treatment of Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, and Ulcerative Colitis. The autoinjector is intended for use by healthcare professionals, caregivers, or patients for self-administration in the home environment.

DEVICE DESCRIPTION

The SIMPONI SmartJect® Autoinjector is very similar to marketed autoinjectors that have been cleared as Class 2 devices by CDRH as a "Syringe Needle Introducer" (FDA Product Code KZH). Like other marketed autoinjectors, the SmartJect® uses a spring-powered mechanism to insert a hypodermic needle attached to a syringe through the skin and to inject the drug at a predetermined depth in subcutaneous tissue. Following injection, the autoinjector automatically retracts the needle and syringe into the case. The autoinjector performs all three phases of the injection process with a single push-button operation: needle insertion, complete drug injection, and needle withdrawal. A safety interlock sleeve prevents actuation until the autoinjector is pressed against the skin with moderate force. The injection depth is approximately 7.5 mm. The autoinjector delivers either a 0.5 mL or 1.0 mL dose, depending on the fill volume of the syringe. The time from button actuation to needle retraction is less than or equal to 15 seconds. These parameters are similar to those used for manual injection for this same route of administration. The features of the autoinjector are illustrated in Figure 1.

Figure 1 Illustration of autoinjector and features

Figure 2 shows an annotated, exploded view of the autoinjector for CNTO 148 PFS.

Additional information is provided in the MAF. (See Module 3.2.R, Medical Devices, Autoinjector.)

Figure 2

The autoinjector itself is not a sterile device; however, it is designed for, and pre-assembled with, a standard (b) (4) syringe with a fixed, 27G, half-inch stainless steel needle. These syringes are (b) (4) filled with either 0.5 mL or 1.0 mL of drug product and then assembled with the autoinjector and labeled for the drug product dosage.

The autoinjector is intended for use by healthcare professionals, caregivers, or patients for self-administration. The operation of the device is straightforward, requiring only three steps:

1. Pull cap (using slight rotation if necessary to break the tamper-evident label) to remove the needle shield from the syringe.
2. Position device at injection site and press against skin to release the safety interlock feature.
3. Press button to actuate while maintaining contact with skin.

The SmartJect® device design has been modified to include a small ledge (flange) at the distal end of the Safety Sleeve to provide more contact surface area against the injection sites, which should reduce skin depression and

pressure sensation during use.

ASSESSMENT OF PERFORMANCE, MECHANICAL STABILITY, AND SAFETY & EFFECTIVENESS OF MODIFIED SIMPONI SMARTJECT® AUTOINJECTOR

The shelf life of the SmartJect® SIMPONI Autoinjector combination product is determined primarily by the shelf life of the SIMPONI drug product (DP) in the pre-filled syringe (PFS). The autoinjector materials include polymer plastics, metal, and (b) (4) compounds, which are generally more stable than the SIMPONI DP and do not require storage at 2 to 8 °C or protection from light to extend device shelf life to practical expiration dates. Information on the SIMPONI PFS stability is provided in Module 3.2.P.8.1, Stability Summary and Conclusion, SIMPONI Pre-filled Syringe.

However, International Conference on Harmonisation (ICH) Topic Q1A (R2) *Stability Testing of New Drug Substances* (2003) states that stability studies should include testing of those attributes of the DP that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy, including functionality tests (e.g., for a dose-delivery system). Therefore, in addition to stability studies on the SIMPONI PFS, the sponsor initiated an ongoing functional stability study of the autoinjector.

The stability data provided in the submission are supplemented with additional design- verification data on the environmental aging effects on the autoinjector subassemblies and components. Tests are performed following assembly of the autoinjector using the aged subassemblies and parts, and the tests performed are a subset of the same functionality tests that are conducted for batch release for the SIMPONI SmartJect® Autoinjector.

A description of the testing along with the results is provided below.

Functional Stability Testing

The autoinjector functional stability program includes samples from one process validation batch (lot 7DS51) containing SIMPONI PFS (100 mg, 1.0 mL), and one stability batch (lot 7ISUF00) containing SIMPONI PFS (50 mg, 0.5 mL) evaluated under real time (2 to 8°C) and accelerated (25°C/60% RH) storage conditions. While the 1.0 mL and 0.5 mL PFS are representative for the autoinjector's functionality with drug product, the sponsor has also entered autoinjectors with SIMPONI placebo (0.5 mL) from process validation lot 7CSVG00 into its stability-monitoring program to better assess autoinjector functionality at the 0.5 mL volume and autoinjector performance attributes independent of the drug product. A description of the batches can be found in Table 1 below. The sponsor also commits to enter one batch of autoinjectors assembled with SIMPONI PFS (50 mg) into an annual functional

stability program at the recommended 2 to 8°C storage temperature condition under the same testing protocol to complement the program. (See Module 3.2.P.8.2, Stability Commitment, Autoinjector.)

Table 1 SIMPONI Autoinjector batches in stability program

Batch	Strength (mg)	Autoinjector Designation	PFS batch	Age of SIMPONI PFS at time of assembly[a]
7DS51	100 mg (1 mL)	Validation	07D012	3 months
7ISUF00	50 mg (0.5 mL)	Stability	07H021[b]	4 months
7CSVG00	Placebo (0.5 mL)	Validation	07B161	6 months

[a] SIMPONI PFS stored at 2 to 8°C prior to assembly

[b] SIMPONI PFS batch 07H021 (50 mg/syringe) is a clinical batch manufactured after the PFS validation campaigns. The batch is not included in Module 3.2.P.8.3, Stability Data, PFS, or Module 3.2.P.8.1, Stability Summary and Conclusions, PFS.

The analytical procedures used in the functional stability program for process validation batches of SIMPONI SmartJect® Autoinjectors (50 and 100 mg) and Placebo Autoinjectors (0.5 mL) are shown in Table 2. The same procedures are conducted for batch release as described in Module 3.2.P.5.2, Analytical Procedures, Autoinjector and Module 3.2.P.5.4, Batch Analyses. The applicable stability specifications and acceptance criteria for these tests are provided in Module 3.2.P.5.6, Justification of Specifications, Autoinjector.

Table 2 Analytical procedures used for SIMPONI Autoinjector functional stability program at the recommended 2 to 8°C storage condition and the accelerated 25°C/60% RH storage conditions

Attribute	Analytical Procedure[a]
Appearance	Visual Appearance and Defects[b]
Before Actuation:	• Button lock check • Sliding interlock sleeve (SIS) check
After Actuation:	• Needle retraction check • Plunger rod check • Post use button lock check
Performance	Cap Removal Force to Actuate Delivery Time Expelled Volume

[a] A detailed description of analytical procedures are presented in Module 3.2.P.5.2, Analytical Procedures (Autoinjector) and Module 3.2.P.5.3, Validation of Analytical Procedures (Autoinjector). The specifications for each analytical procedure are presented in Module 3.2.P.5.6, Justification of Specifications, Autoinjector. The release specifications for SIMPONI Autoinjector (100 and 50 mg) are the same as those used for stability specifications (2 to 8°C). All samples are held at room temperature for at least 30 minutes prior to testing.

[b] As part of the procedure, autoinjectors are visually inspected for proper assembly and appearance at every time point.

All functional stability tests for the autoinjectors with syringes filled with regular (stored at 2 to 8 °C) are performed at 3 month intervals up to the total life of three years/36

months (ICH). All functional stability tests for the autoinjectors with syringes filled with aged batches (stored at stored at 25°C/60% RH) are performed at 3 month intervals up to the total of 12 months.

RESULTS

The results of the stability testing are provided in the following table.

Table 8 Functional stability data for process validation SIMPONI Autoinjector batch 7DS51, 100 mg at 2 to 8°C

Months Stored		Visual Appearance and Defects	Cap Removal	Force to Actuate	Delivery Time	Expelled Volume [c]
Stability Specification at 2 to 8°C		*No visual defects before and after firing*	*Needle shield remains in cap. Tamper-evident label separates at the perforations*	(b) (4) *Newton (N) Minimum to Maximum*	(b) (4) *sec Minimum to Maximum*	(b) (4) *mL Minimum to Maximum*
Timepoint	Drug product (PFS) Age[b]					
0[a]	4	Complied	Complied	3.9 to 7.7	6 to 7	1.03 to 1.05
3	7	Complied	Complied	3.8 to 5.8	7 to 8	1.03 to 1.05
6	10	Complied	Complied	3.6 to 5.6	7 to 9	1.03 to 1.05
9	13	Complied	Complied	4.1 to 5.7	6 to 8	1.04 to 1.05
12	16	Complied	Complied	3.2 to 7.8	6 to 7	1.02 to 1.05
18	22	Complied	Complied	3.9 to 7.6	6 to 8	1.03 to 1.05
21[d]	25	Complied	Complied	3.7 to 7.3	6 to 9	1.03 to 1.05
24	28	Complied	Complied	4.1 to 9.2	6 to 8	1.03 to 1.04
30	34	Complied	Complied	4.4 to 9.0	7 to 9	1.03 to 1.05
36	40					

[a] Initial time point (t=0) corresponds to testing date after autoinjector assembly.
[b] SIMPONI Autoinjector lot 7DS51 was assembled using SIMPONI PFS process validation lot 07D012 (see Table 1). The stability studies are designed to extend beyond the proposed shelf life of the SIMPONI PFS (Module 3.2.P.8.1, Stability Summary and Conclusion, PFS) to gather additional information on the Autoinjector components.
[c] For trending purposes data is presented to nearest 0.01 mL
[d] Stability protocol amended to include 21 month time point to coincide approximately with end of shelf life for SIMPONI PFS (24 months).

Table 9 Functional stability data for SIMPONI Autoinjector batch 7DS51, (100 mg) at 25°C/60% RH

Months Stored		Visual Appearance and Defects	Cap Removal	Force to Actuate	Delivery Time	Expelled Volume [g]
Evaluation Criteria [a]		*No visual defects before and after firing*	*Needle shield remains in cap. Label separates at the perforations.*	(b) (4) *Newtons (N) Minimum to Maximum*	(b) (4) *sec Minimum to Maximum*	(b) (4) *mL Minimum to Maximum*
Timepoint	Drug Product (PFS) Age					
0[b]	4	Complied	Complied	3.9 to 7.7	6 to 7	1.03 to 1.05
3	7	Complied	Complied	3.8 to 7.2	7 to 10	1.03 to 1.05
6	10	Did not comply[c]	Complied	3.1 to 8.2	8 to 21[d]	1.02 to 1.05
9	13	Did not comply[c]	Complied	3.5 to 5.7	13 to 49[e]	1.03 to 1.04
12[f]	16					

[a] Test results will be evaluated against stability specifications at 2 to 8°C for information purposes only in comparison.
[b] Initial time point (t=0) corresponds to testing date after autoinjector assembly.
[c] It was observed that the piston stopper did not reach completion of travel - no liquid was present (6 month). Yellow indicator is not visible and no liquid remains in barrel after (b) (4) seconds (9 months). It was noted that some of the autoinjectors with visual defects also showed prolonged delivery time (footnote d and e). (See Section 10.5 for discussion of these results.)
[d] Five of 40 autoinjectors exceeded the stability specification for the 2 to 8°C condition.
[e] Sixteen of 20 autoinjectors exceeded stability specification for the 2 to 8°C condition.
[f] This portion of the stability program was discontinued after two consecutive "did not comply" results per the protocol.
[g] For trending purposes data is presented to nearest 0.01 mL

Table 10 Functional stability data for SIMPONI Autoinjector (50 mg) batch 7ISUF00 at 2 to 8°C

Months Stored		Visual Appearance and Defects	Cap Removal	Force to Actuate	Delivery Time	Expelled Volume[c]
Stability Specification at 2 to 8°C		*No visual defects before and after firing*	*Needle shield remains in cap. Tamper-evident label separates at the perforations*	(b) (4) *Newton (N) Minimum to Maximum*	(b) (4) *sec Minimum to Maximum*	(b) (4) *mL Minimum to Maximum*
Timepoint	Drug product (PFS) Age[b]					
0[a]	4	Complied	Complied	3.8 to 4.7	2 to 3	0.51 to 0.57
3	7	Complied	Complied	3.6 to 4.8	3 to 4	0.51 to 0.57
6	10	Complied	Complied	3.2 to 4.7	3 to 4	0.51 to 0.56
9	13	Complied	Complied	3.1 to 6.2	3 to 4	0.51 to 0.56
12	16	Complied	Complied	4.3 to 7.7	3 to 4	0.52 to 0.57
18	22	Complied	Complied	3.8 to 6.1	2 to 3	0.50 to 0.58
20[d]	24	Complied	Complied	4.2 to 10.0	3 to 4[e]	0.52 to 0.55[e]
24	28					
30	34					
36	40					

[a] Initial time point (t=0) corresponds to testing date after autoinjector assembly.
[b] SIMPONI Autoinjector lot 7ISUF00 was assembled using SIMPONI PFS process validation lot 07H021 (see Table 1). The stability studies are designed to extend beyond the proposed shelf life of the SIMPONI PFS (Module 3.2.P.8.1, Stability Summary and Conclusion, PFS) to gather additional information on the Autoinjector components.
[c] For trending purposes data is presented to nearest 0.01 mL
[d] The protocol for this lot was revised to add a 20 month time point to correspond to a 24 month shelf life for the product based on the PFS age.
[e] 1 out of 20 devices failed (needle failed ot retract and did not expel complete volume) and therefore no values were reported for this device. The investigation confirmed an assembly error. The spacer was not in the correct position. the spacer misalignemtn was blocking the spring cartridge movement.

Table 11 Functional stability data for SIMPONI Autoinjector (50 mg) batch 7ISUF00 at 25°C/60% RH

Months Stored		Visual Appearance and Defects	Cap Removal	Force to Actuate	Delivery Time	Expelled Volume[c]
Evaluation Criteria[a]		*No visual defects before and after firing*	*Needle shield remains in cap. Tamper evident label separates at the perforations.*	(b) (4) *Newton(N) Minimum to Maximum*	(b) (4) *sec Minimum to Maximum*	(b) (4) *mL Minimum to Maximum*
Timepoint	Drug Product (PFS) Age					
0[b]	4	Complied	Complied	3.8 to 4.7	2 to 3	0.51 to 0.57
3	7	Complied	Complied	3.3 to 4.3	3 to 4	0.51 to 0.57
6	10	Complied	Complied	2.9 to 4.1	3 to 6	0.52 to 0.55
9	13	Did not comply[d]	Complied	3.7 to 5.5	3 to 7	0.51 to 0.56
12[f]	16	Did not comply[d]	Complied	3.4 to 6.0	4 to 180[e]	0.49[g] to 0.55

[a] Test results will be evaluated against stability specifications at 2 to 8°C for information purposes only in comparison.
[b] Initial time point (t=0) corresponds to testing date after autoinjector assembly.
[c] For trending purposes data is presented to nearest 0.01 mL
[d] In 4 of 20 units, the yellow indicator was not completely visible in the observation window but no liquid remained in barrel after needle retraction ((b) (4) seconds). (See Section 10.5 for discussion of this result.)
[e] One sample had a delivery time > 180 seconds Remaining 19 samples had a range of 4 – 11 This unit was one of the 4 units mentioned in footnote d.
[f] This portion of the stability program will be discontinued due to the two consecutive "did not comply" results.
[g] The 0.49 value is considered a passing result since the final product specification is (b) (4)

Functional stability studies with Placebo Autoinjector

Placebo for SIMPONI SmartJect® Autoinjector process validation batch 7CSVG00, assembled with Placebo for SIMPONI PFS (0.5 ml) was also placed on a functional stability-monitoring program at the recommended 2 to 8°C storage temperature and the accelerated 25°C/60% RH storage temperature conditions. The functional stability data for the Placebo Autoinjector (0.5 mL) at the recommended storage condition and the accelerated storage condition are presented in Table 12 and Table 13, respectively. The Placebo Autoinjectors remain essentially unchanged for all attributes including delivery time and expelled volume through 24 months of storage at the recommended 2 to 8°C temperature condition and 12 months at the accelerated 25°C/60% RH temperature condition. No visual defects were observed before or after actuation for any of the samples tested at both storage temperature conditions.

ASSESSMENT OF THE RESULTS

The results from the testing are acceptable. The design modifications have not appeared to affect the safety and effectiveness of the device.

Design Verification Testing

As part of the autoinjector design verification, the sponsor has assessed the aging characteristics of the autoinjector subassemblies and components stored under real time warehouse conditions ((b)(4)°C) and accelerated ((b)(4)°C) conditions by performing functionality tests of the autoinjector using those parts, as reported in the Master File (MAF) for the original autoinjector, MAF 1556. The schedule and key applicable tests for this program are presented in Table 5 and Table 6.

Table 5 **Device design verification functionality testing schedule following real time aging of subassemblies at warehouse conditions and assembly with SIMPONI (100 mg and 50 mg) PFS. Scheduled time points for corresponding procedure**

	Pull point in Months[a]										
Design Requirement[b]	0	1	3	6	9	12	18	24	36	48[c]	60[c]
Delivery Time	√	√	√	√	√	√	√	√	√	√	√
Appearance and Defects Test (Functionality) and Cap Removal Force to Actuate	√	√	√	√	√	√	√	√	√	√	√

[a] The subassemblies are pulled at each time point and assembled with SIMPONI PFS (100 mg/syringe) batch 905160 or SIMPONI PFS (50 mg/syringe) batches made available for each test time point. The functionality of the autoinjectors is measured after assembly. Note: 48 and 60 month pull points have been added to the program.

[b] The design requirements are measured using similar procedures as those used in the functional stability monitoring program for SIMPONI Autoinjectors and referenced in the Module 3.2.R, Medical Device, Autoinjector.

[c] The protocol was revised to remove the 39 month time point and add 48 and 60 month timepoints.

Table 6 **Device design verification functionality testing schedule following accelerated aging of subassemblies at (b)(4)°C and assembly with SIMPONI (100 mg and 50 mg) PFS. Scheduled time points for corresponding procedure**

	Pull Point in Days[a]								
Design Requirement[b]	0	5	10	15	20	30	40	50	60
Delivery Time	√	√	√	√	√	√	√	√	√
Appearance and Defects Test (Functionality) and Cap Removal Force to Actuate	√	√	√	√	√	√	√	√	√

[a] The subassemblies are pulled at each time point and assembled with SIMPONI PFS (100 mg/syringe) or SIMPONI PFS (50 mg/syringe) batches made available for each test time point. The functionality of the autoinjectors are measured after assembly.

[b] The design requirements are measured using similar procedures as those used in the functional stability monitoring program for SIMPONI Autoinjectors and referenced in the Module 3.2.R, Medical Device, Autoinjector.

The device design verification test program included a study to assess the effects of elevated temperature conditions (accelerated aging) on autoinjector sub-assemblies and components in support of the shelf life of the fully assembled SIMPONI Autoinjector. In this study, autoinjector subassemblies and components were

conditioned at [redacted]C, pulled from the environmental storage chamber at defined time points according to a predefined testing schedule described in Table 6, then assembled with SIMPONI PFS (50 mg/0.5 mL or 100 mg/1.0 mL) and tested for autoinjector functionality. Test results, for both accelerated and real time aging tests are provided in Module 3.2.P.8.3, Stability Data, Autoinjector (See also Module 3.2.R, Medical Device, Autoinjector). The functionality results for accelerated aging ([redacted]°C) tests are summarized in Table 15 and Table 16 for SIMPONI Autoinjectors 50 mg and 100 mg, respectively. Mean delivery time and force to actuate data, and the attribute test for functionality (autoinjector delivery cycle and needle retraction) over the time periods specified are reported. These tests verify the overall functional performance of the SIMPONI Autoinjector.

Table 15 Design verification tests at the accelerated ([redacted]°C) condition. SIMPONI Autoinjector (50 mg) assembled at each pull point with SIMPONI PFS (50 mg).

	Pull Point in Days[a]								
Design Verification Requirement [b]	0	5	10	15	20	30	40	50	60
Delivery (Cycle) Time (Acceptance criteria: [redacted] seconds)									
Mean (seconds)	2.9	3.7[c]	3.6	3.8	3.8	3.1	4.7	3.9	3.8
Functionality (delivery and needle retraction) and Cap removal (Acceptance criteria: Pass)									
Accepted	20	20	20	20	20	20	20	20	20
Rejected	0	0	0	0	0	0	0	0	0
Force to actuate (Acceptance criteria: [redacted] Newtons)									
Mean (Newtons)	4.99	4.21	4.31	3.97	3.84	3.95	6.22	5.23	3.70

[a] The subassemblies were pulled at each time point and assembled with SIMPONI PFS (50 mg/syringe) batch 905159. The functionality of the autoinjectors was measured after assembly. SIMPONI PFS were stored at 2 to 8°C until time of assembly.

[b] The methodology and acceptance criteria used in design verification studies are similar to those used in the functional stability program for SIMPONI Autoinjectors (see Section 3, of this Module) and the testing is done for design verification purposes.

[c] Data is from [redacted] samples at each pull point except for delivery time for the 5-day pull point where data on 19 samples were evaluable.

Accelerated Aging Study of the Modified Janssen (SmartJect®) Autoinjector

A minor design change to the shape and color of the Sliding Interlock Sleeve (SIS) autoinjector component [redacted] has been made to the approved autoinjector for SIMPONI (CNTO 148).

An accelerated aging study was conducted to assess the effects of aging on the modified autoinjector subassemblies and components that could potentially impact the overall performance of the autoinjector when assembled with SIMPONI PFS. This modification is described in detail in MAF 1556, Amendment 2 for the Centocor (now Janssen) Autoinejctor (SmartJect® Autoinjector).

To conduct the study, modified autoinjector subassemblies and components were conditioned (aged) at [redacted] C for up to 60 days, then assembled with SIMPONI PFS, and tested for key performance measures that may have been impacted by the modification. Cap Removal, including force to remove, Dose Delivery Time, Expelled Volume, Force to Actuate and Visual Appearance were the tests performed on the modified SmartJect® Autoinjector with the aged components.

Time intervals for the stability pulls were 0, 30, and 60 days and represent an equivalent age of 36 months at the 60-day point based on Arrhenius modeling of polymer component materials stored at [redacted] °C. A total of 200 device subassemblies and components were tested in the study. The product configurations assembled with the aged SmartJect® parts and tested were SIMPONI PFS 50 mg/0.5 mL and 100 mg/1.0 mL.

The tables of results below include the test results for each of the above SIMPONI SmartJect® presentations using aged components. The tables provided are as follows:

- **Table 20:** Release test results using aged SmartJect components assembled with SIMPONI PFS (50 mg / 0.5 mL)
- **Table 21:** Release test results using aged SmartJect components assembled with SIMPONI PFS (100 mg/ 1.0 mL)

Table 21: Release test results using aged SmartJect components assembled with Simponi PFS (100 mg/ 1.0 mL)

Test [a]	Acceptance Criteria	Component Pull Point for Assembly with PFS in Days 0	30	60
Cap removal	Needle shield removal	Pass	Pass	Pass
Dose delivery time (sec)	(b) (4) seconds			
Mean		5.4	5.1	5.5
Minimum		4.9	4.8	5.0
Maximum		5.9	6.0	6.2
Expelled volume (mL)	(b) (4) mL			
Mean		1.03	1.03	1.03
Minimum		1.02	1.01	1.01
Maximum		1.04	1.03	1.03
Force to Actuate (N)	(b) (4) N			
Mean		5.4	3.7	3.8
Minimum		4.3	3.3	3.4
Maximum		6.4	4.4	4.3
Visual Appearance (mechanical function)	Free of visual defect and confirmed needle retraction	Pass	Pass	Pass

[a] Data are from (b) (4) samples at each pull point.

Table 21: Release test results using aged SmartJect components assembled with Simponi PFS (100 mg/ 1.0 mL)

Test [a]	Acceptance Criteria	Component Pull Point for Assembly with PFS in Days 0	30	60
Cap removal	Needle shield removal	Pass	Pass	Pass
Dose delivery time (sec)	(b) (4) seconds			
Mean		5.4	5.1	5.5
Minimum		4.9	4.8	5.0
Maximum		5.9	6.0	6.2
Expelled volume (mL)	(b) (4) mL			
Mean		1.03	1.03	1.03
Minimum		1.02	1.01	1.01
Maximum		1.04	1.03	1.03
Force to Actuate (N)	(b) (4) N			
Mean		5.4	3.7	3.8
Minimum		4.3	3.3	3.4
Maximum		6.4	4.4	4.3
Visual Appearance (mechanical function)	Free of visual defect and confirmed needle retraction	Pass	Pass	Pass

[a] Data are from (b) (4) samples at each pull point.

ASSESSMENT OF THE RESULTS

The results from the testing are acceptable. The design modifications have not appeared to affect the safety and effectiveness of the device.

CONCLUSION

It appears that the sponsor conducted a thorough and valid assessment of the modified SIMPONI Smartject® Autoinjector. From the results cited in BLA 125289 AND MAF 1556, it appears that the modified autoinjector is as safe and effective as the original autoinjector. I have no issues with the subject device.

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Digital Signature Concurrence Table	
Reviewer Sign-Off William M. Burdick	
Branch Chief Sign-Off Richard Chapman	

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/s/

CHRISTINE H CHUNG
11/15/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES **M E M O R A N D U M**

Food and Drug Administration
Office of Device Evaluation
10903 New Hampshire Avenue
Silver Spring, MD 20993

CDRH Human Factors Review

DATE: October 23, 2013

FROM: QuynhNhu Nguyen, Biomedical Engineer/Human Factors Reviewer, CDRH/ODE/DAGID

THROUGH: Ron Kaye, MA, Human Factors and Device Use-Safety Team Leader, CDRH/ODE/DAGID

TO: Christine Chung, Senior Regulatory Project Manager, OND/ODEII/DPARP

SUBJECT: **NDA 125289/103**
Applicant: Janssen Biotech, Inc.
Device Constituent: Simponi SmartJet Autoinjector
Drug Constituent: Golinumab
Intended Treatment: Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis

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QuynhNhu Nguyen, Combination Products Human Factors Specialist

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Ron Kaye, Human Factors and Device Use-Safety Team Leader

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CDRH Human Factors Review

Overview and Conclusion

The Division of Pulmonary , Allergy, and Rheumatoid Products, Office of New Drugs, requested a Human Factors consultative review of the BLA 125289/103 submitted by Janssen Biotech for their modified Simponi SmartJect Autoinjector. This review provides CDRH Human Factors team's review on the Human Factors validation study report.

The human factors validation study was conducted with 46 participants across three patient user groups, where one of the naïve user groups received training. The study was designed to evaluate critical and essential tasks associated with the use of the autoinjector. The study showed no failures or use errors across all tasks and Instructions for Use knowledge probe tasks. There were five "close calls" but resulted in delivery of complete dose.

Conclusion: This consultant finds the human factors study report acceptable and has no further questions.

Background: In a cover letter dated December 20, 2012, Janssen Biotech, Inc. indicated that they have made several modifications to the Simponi SmartJect Autoinjector as well as updates to the Instructions for Use. The SmartJect device design has been modified to include a small flange feature (ledge) on the skin contacting end of the Safety Interlock Sleeve (SIS) that interfaces with the patient. The flange was incorporated into the SIS design to provide more contact surface area against injection sites and thereby reduce skin depression and pressure sensation during use. In addition to the SIS, (b) (4) no other components of the device have been changed. These changes were made as a result of current user input and focus group studies on the current product. As a result, CDRH was consulted to review the human factors study protocol to validate that the proposed design changes. During the development of the SmartJect autoinjector several HFSs were conducted in support of the SIMPONI SmartJect BLA approval. In addition, JBI conducted a study of SmartJect autoinjector usage that involved a series of customer focus groups in six major US cities. A formative usability study using the to-be-marketed (modified) SmartJect autoinjector was conducted in December, 2012 with 10 participants [diagnosed with rheumatoid arthritis (RA) or psoriatic arthritis (PsA)].

In a cover letter date June 28, 2013 (sequence 284), Janssen Biotech indicates that additional revisions to the IFU in addition to the previously reported changes. Jassen has performed a human factors validation study to validate all of the changes. The validation study incorporated FDA's feedback on the human factors study protocol. As a result, the Master File for Devices (MAF 1556) includes additional information on the human factors validation study of the revised IFU and of the modified device. The human factors validation study can also be found in sequence 288 of the BLA.

CDRH Human Factors Review

Combination Product Device Information

Submission Number: BLA 125289/103
Applicant: Janssen Biotech, Inc.
Drug Constituent: Golimumab
Device Constituent: Simponi SmartJect Autoinjector
Intended treatment: Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis

CDRH Human Factors Involvement History

- 9-JAN-2013: CDRH HF was requested to provide a review of a protocol for Human Factors (HF) validation study
- 8-FEB-2013: CDRH HF indicated that the protocol was found acceptable, and had one general advice for the Applicant regarding the report.
- 23-OCT-2013: CDRH HF was requested to provide a review of a Human Factors validation study report

Review of Human Factors Related Information

Review Materials

The human factors study report is dated May 2013 (prepared by (b) (4)). The study was conducted with 46 participants. Table 1 provides a breakdown of the three user groups and the level of training that each user group received during the study.

User Group	N	Mean Age
Experienced SmartJect Users (Untrained)	N=16	49 years
Potential SmartJect Users (Untrained)	N=15	49 years
Potential SmartJect Users (Trained)	N=15	49 years
TOTAL	**N=46**	

Table 1: Breakdown of User Groups

The training consists of a one-on-one patient training session, which includes a review of how to use the autoinjector, and a supervised injection where the moderator remained in the room to assist where needed. The participants returned one week later for a validation session, and they performed two unsupervised injections, which is representative of their actual use of the device at home. The naïve participants were randomly assigned an injection site (either abdomen or thigh).

The study showed no failures or use errors across all critical and essential, and Instructions for Use knowledge probe tasks. There were five "close calls" observed where the participants lifted the autoinjector before injection was complete (i.e. prior to hearing the second click). All these participants were determined to have delivered a full dose. All except one participant learned from their close calls, and waited for the second click on their second injection trial. When asked about these injections, all the participants demonstrated that they know to wait until the second click before removing the device.

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Appendix 2: Description of the SmartJect autoinjector

The SmartJect autoinjector is a prefilled, spring-powered, single use, disposable device for the subcutaneous (SC) administration of a single dose of a liquid biologic drug product. It was designed as a platform delivery device for several liquid biologic drug products filled in standard glass syringes and has a simple, universal design that is suitable for use by clinicians, caregivers, and patients, including those with hand impairment and pain in the hands and wrists resulting from diseases such as RA, and PsA.

The SmartJect autoinjector performs all 3 phases of the SC injection process with a single push button operation; needle insertion, drug injection of the fixed dose, and needle withdrawal. During use, the device automatically extends the syringe needle approximately 7.5 mm into tissue and delivers up to a 1.0 mL dose of product. The time from button actuation to needle retraction is no greater than 15 seconds and is typically 3 to 6 seconds. Following use, the syringe and needle are automatically retracted within the device to reduce the risk of inadvertent needle sticks.

The SmartJect autoinjector was approved by the FDA for SIMPONI in April 2009 for selfadministration in the RA, PsA and AS patient populations, (b) (4)

Additional technical information regarding the SmartJect autoinjector was filed with CDRH in 2009 as a Master File for Devices (MAF 1556), including extensive test data on the technology's suitability, design, manufacturing, performance and its Design and User FMEAs (Hazard Analyses).

The modification involves a slight change in shape of the injection molded sliding interlock sleeve (Safety Sleeve) (b) (4) These changes have no impact on any other mechanical performance or safety function of the device. The modification of the sliding interlock sleeve is depicted in Figure below.

(b) (4)

(b) (4)

The design intent of the Sliding Interlock Sleeve (SIS) is to prevent accidental misfiring of the autoinjector; the user must push the autoinjector against the injection site, moving the sleeve inward, in order to release the push button's "action" allowing the autoinjector to actuate when the user intentionally presses the button. In this modified Smartject design, the end of the SIS that comes in to contact with the skin has been modified by incorporating a small flange feature. The intent of this modification is to reduce the pressure sensed by the patient during compression of the sleeve, reduce the potential for skin interference between the SIS and clear outer sleeve (Clear Cover), and to provide a positive stop of the SIS against the clear outer sleeve (Clear Cover) while pressing the device against the skin for the injection.

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/s/

CHRISTINE H CHUNG
11/15/2013

HUMAN FACTOR, LABEL, AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Application Type and Number:	BLA 125289
	(b) (4)
Date of Submission:	June 28, 2013
Established Name and Strength:	(Golimumab)
	Injection
	50 mg/0.5 mL
	(b) (4)
	Injection
Product Type:	Single ingredient
Marketing Category:	Prescription
Applicant Name:	Jansen Biotech, Inc
OSE RCM #:	2013-1780
Date of This Review:	November 12, 2013
Primary Reviewer:	Teresa McMillan, PharmD
Team Leader:	Lubna Merchant, PharmD, M.S.
Acting Division Director:	Kellie Taylor, PharmD, MPH

1. REASON FOR REVIEW

This review responds to a request from Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) to evaluate the proposed Instructions for Use (IFU) for Simponi (Golimumab) Smartject Autoinjector, BLA 125289 for areas of vulnerability that could lead to medication errors. In addition, DPARP requested we review Human Factors Study (HFS) results that tested the minor design modification to the Smartject Autoinjector for golimumab and (b) (4) *** [an investigational new drug application] because the applicant tested both products in the same study.

2. CONCLUSION AND RECOMMENDATIONS

DMEPA concludes that the Human Factors Validation Study confirms safe and effective use of the device and the associated IFU and the incremental improvements may help users to better operate the device.

If you have further questions or need clarifications, please contact Nichelle Rashid, OSE Project Manager, at 301-796-3904.

3. MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. A summary or the image of the materials reviewed can be found in Section 5, Appendices. In addition, a FDA Adverse Event Reporting System (FAERS) search was not conducted for this supplement because medication errors with this product were evaluated in OSE Review #2013-188 and 2013-281, dated February 14, 2013. There have been reports of difficulty actuating the device, incomplete injection and accidental firing associated with the Simponi Smartject. The intent of the proposed device modifications and IFU is to prevent accidental misfiring of the autoinjector.

Table 1. Materials considered for review of the Applicant's Human Factors Validation Study and Instructions for Use

Section	Materials Reviewed
5.1	Product Prescribing Information/proposed modification to device
5.2	Human Factors Validation Study Design and Results
5.3	Instructions for Use

4. OVERALL FINDINGS AND ASSESSMENT OF MATERIALS REVIEWED

All forty-six participants successfully performed the critical tasks and delivered a full dose of golimumab or [redacted] (b) (4) ***. There were five close calls that involved participants lifting up the device prior to the second click. In all cases, the participants received a full dose and no solution was noted at the injection site indicating any partial dose. The participants cited the following reasons for removing the device prematurely: heard the sound or hissing of the liquid moving through the device just prior to the second click or realized they received the full dose but did not wait for the second click.

The issue of removing the device prior to the end of injection or prior to the second click is not a new risk associated with the Smartject device and is seen with the currently marketed device. Since all of the solution went into the injection pad (i.e. no solution was observed at the injection site) thus confirming a full dose was delivered, we have no concerns with the five close calls reported for the device because no new risks were identified.

5. APPENDICES

5.1 Product Prescribing Information

Table 2. Relevant Product Information for Golimumab	
Active Ingredient	Golimumab
Indication	Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis
Route of Administration	Subcutaneous injection
Dosage Form	Solution for injection
Strength	50 mg/0.5 mL
Dose and Frequency	50 mg subcutaneously once monthly
How Supplied	Packs of one single-use Simponi Smartject Autoinjector and one single-use prefilled syringe (both are glass syringes with 27 gauge ½ inch needles)
Storage	Refrigerate at 36°F to 46° F (2° C to 8° C)
Proposed modification to the Autoinjector	The proposed modifications to the device include: a small flange feature (ledge) on the skin contacting end of the Safety Interlock Sleeve which will provide more contact surface area against the skin and help to reduce skin depression and pressure sensation during use and the Cap and the external case or nose of the autoinjector have been modified to accommodate the safety sleeve change.

5.2 Human Factors Validation Study Design:

DMEPA reviewed the protocol in OSE Review #2013-188 and 2013-281, dated February 14, 2013. All of DMEPA's human factors protocol recommendations from the previous review were implemented. The tables 3 and 4 below summarize the study design and results.

Table 3. Study Design

	User Group 1	**User Group 2**	**User Group 3**
Number of subjects	N=16	N=15	N=15
User Type	RA, PsA & AS	RA, PsA & AS	RA, PsA & AS
Device Experience	SmartJect Experienced	SmartJect Naive	SmartJect Naive
Training Group	Untrained	Untrained	Trained (By Moderator as HCP)
Injection Sites	Abdomen or Thigh – Patient's current site	Abdomen or Thigh – Counterbalanced order	Abdomen or Thigh – Counterbalanced order
Supervised Drug/Injection	N/A	N/A	Counterbalanced Test Order; SIMPONI vs. Sirukumab
1st Drug/Injection	SIMPONI	Counterbalanced Test Order: SIMPONI vs. Sirukumab	Counterbalanced Test Order: SIMPONI vs. Sirukumab
2nd Drug/Injection	Sirukumab	Counterbalanced Test Order: SIMPONI vs. Sirukumab	Counterbalanced Test Order: SIMPONI vs. Sirukumab
# of Sessions	1 Session	1 Session	2 Sessions (with 1 Week Training Decay)

TOTAL = 46 Participants; 107 Total Injections (15 supervised, 92 unaided)

Table 4: Study results: All forty-six participants successfully performed the critical tasks.

Observation/Task	Risk Level	SmartJect Users - Untrained	SmartJect Naïve - Untrained	SmartJect Naïve - Trained	Overall
First Injection Performed					
Failure to remove cap?	Low	0/16	0/15	0/15	0/46 (0%)
Failure to inject within 5 minutes of cap removal?	N/A	0/16	0/15	0/15	0/46 (0%)
Failure to activate injection?	High	0/16	0/15	0/15	0/46 (0%)
Failure to inject at proper angle?	Medium	0/16	0/15	0/15	0/46 (0%)
Failure to deliver full dose?	High	0/16	0/15	0/15	0/46 (0%)
Second Injection Performed					
Failure to remove cap?	Low	0/16	0/15	0/15	0/46 (0%)
Failure to inject within 5 minutes of cap removal?	N/A	0/16	0/15	0/15	0/46 (0%)
Failure to activate injection?	High	0/16	0/15	0/15	0/46 (0%)
Failure to inject at proper angle?	Medium	0/16	0/15	0/15	0/46 (0%)
Failure to deliver full dose?	High	0/16	0/15	0/15	0/46 (0%)
All Injections					
Failure to remove cap?	Low	0/32	0/30	0/30	0/92 (0%)
Failure to inject within 5 minutes of cap removal?	N/A	0/32	0/30	0/30	0/92 (0%)
Failure to activate injection?	High	0/32	0/30	0/30	0/92 (0%)
Failure to inject at proper angle?	Medium	0/32	0/30	0/30	0/92 (0%)
Failure to deliver full dose?	High	0/32	0/30	0/30	0/92 (0%)

5.3 Instructions for Use

Using the principles of human factors and Failure Mode and Effects Analysis,[1] along with postmarketing medication error data, we evaluated the following materials that the Applicant submitted on June 28, 2013:

[1] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI: 2004.

10 Page(s) of Draft Labeling has been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

TERESA S MCMILLAN
11/12/2013

LUBNA A MERCHANT
11/12/2013

KELLIE A TAYLOR
11/13/2013

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

BLA 125289/S103

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

ELECTRONIC CORRESPONDENCE

Date: December 19, 2013

To: Salvatore Morello, Director Global Regulatory Affairs	**From:** Christine Chung, R.Ph. Regulatory Project Manager
Company: Janssen Biotech, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Phone: (215) 986-1210	**Fax number:** 301-796-9728
Email: smorell@its.jnj.com	**Phone number:** 301-796-3420

Subject: Simponi supplemental BLA 125289/103
Additional FDA labeling comments for Instructions for Use (IFU)

Total no. of pages including cover: **17**

Comments: Please call or send an email to confirm receipt at christine.chung@fda.hhs.gov

RESPONSE REQUESTED BY: COB December 20, 2013

Document to be mailed: YES ☑ NO

We refer to Simponi SmartJect supplemental BLA 125289/103 and have the following labeling comments. Additional labeling changes may be forthcoming. Submit revised labeling incorporating changes in the attached marked up label.

Send your response to me via secure email at christine.chung@fda.hhs.gov no later than close of business Friday, December 20, 2013. Your response will subsequently need to be submitted officially to the BLA.

If you have any questions, please contact me at 301-796-3420.

Drafted by: DMPP/ 12.16.2013
JMaynard/ 12.16.2013
cchung/ 12.18.2013

Cleared by: SBarnes/ 12.19.2013

Finalized: cchung/ 12.19.2013

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/s/

CHRISTINE H CHUNG
12/19/2013

MANDATORY: Send a copy of the consult request form to the Office of Combination Products (OCP) as follows:
--Originating Center: When the consult request is initiated.
--Consulting Center: When the consult is completed.
Email: combination@fda.gov or FAX: 301-847-8619

For additional information: Contact OCP by email or by telephone (301-796-8930) or refer to OCP's intranet page http://inside.fda.gov:9003/ProgramsInitiatives/CombinationProducts/ReviewerTools/default.htm.

For Consulting Center Use Only:

Date Received: _____
Assigned to: _____
Date Assigned: _____
Assigned by: _____

Completed date: _____
Reviewer Initials: _____
Supervisory Concurrence: _____

Intercenter Request for Consultative or Collaborative Review Form

To (Consulting Center):
Center: CDRH/OC/DOE-A
Division: Compliance/Div of Enforcement A
Mail Code: HF
Consulting Reviewer Name: Carl Fischer, PhD
Building/Room #: WO 66 Room 3526
Phone #: 301-796-5489
Fax #:
Email Address: carl.fischer@fda.hhs.gov
RPM/CSO Name and Mail Code:

From (Originating Center):
Center: CDER/OND/ODEII
Division: Division of Pulmonary, Allergy, and Rheumatology Products
Mail Code: HFD-570
Requesting Reviewer Name: Christine Chung
Building/Room #: WO22/3306
Phone#: 301-796-3420
Fax #: 301-796-9728
Email Address: christine.chung@fda.hhs.gov
RPM/CSO Name and Mail Code: Christine Chung HFD-570
Requesting Reviewer's Concurring Supervisor's Name: Sandy Barnes, CPMS

Receiving Division: If you have received this request in error, you must contact the request originator by phone immediately to alert the request originator to the error.

Date of Request: 10/29/2013
Requested Completion Date: 12/13/2013

Submission/Application Number: BLA 125289/103
(Not Barcode Number)
Submission Type: sBLA 103
(510(k), PMA, NDA, BLA, IND, IDE, etc.)

Type of Product: ☐ Drug-device combination ☐ Drug-biologic combination ☑ Device-biologic combination ☐ Drug-device-biologic combination ☐ Not a combination product

Submission Receipt Date: 6/28/2013
Official Submission Due Date: PDUFA 12/28/13

Name of Product: Simponi SmartJect
Name of Firm: Janssen Biotech

Intended Use: treatment of Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, and Ulcerative Colitis.

Brief Description of Documents Being Provided (e.g., clinical data -- include submission dates if appropriate):

EDR link to submission http://cberedrweb.fda.gov:8080/esp/cberedr.jsp?folderObjId=0bbcaea681268602
Cover: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\cover.pdf
device: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m3\32-body-data\32r-reg-info\32r4-medical-device-autoinjector.pdf
ccs: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m3\32-body-data\32p-drug-prod\active-pfs\32p7-cont-closure-sys\32p7-container-closure-system-ai.pdf

Documents to be returned to Requesting Reviewer? ☐ Yes ☑ No

Complete description of the request. Include history and specific issues, (e.g., risks, concerns), if any, and specific question(s) to be answered by the consulted reviewer. The consulted reviewer should contact the request originator if questions/concerns are not clear. Attach extra sheet(s) if necessary:

Type of Request: ☑ Consultative Review ☐ Collaborative Review

Please assign perform CDRH OC review of changes to device manufacturing due to minor design modification to the autoinjector. "At this time, JBI is hereby submitting additional revisions to the SIMPONI® SmartJect® Autoinjector IFU. In addition, a minor design modification to the SmartJect® Autoinjector (the addition of a "flange" feature to safety interlock sleeve [SIS], and a change in color of the SIS), necessitated updates to several figures in the IFU."
Please contact me if you have any questions or cannot access the edr links.

Reference ID: 3398817

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/s/

CHRISTINE H CHUNG
10/30/2013

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

ELECTRONIC CORRESPONDENCE

Date: December 4, 2013

To: Salvatore Morello, Director Global Regulatory Affairs	**From:** Christine Chung, R.Ph. Regulatory Project Manager
Company: Janssen Biotech, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Phone: (215) 986-1210	**Fax number:** 301-796-9728
Email: smorell@its.jnj.com	**Phone number:** 301-796-3420

Subject: Simponi supplemental BLA 125289/103
FDA labeling comments for Instructions for Use (IFU)

Total no. of pages including cover: **26**

Comments: Please call or send an email to confirm receipt at christine.chung@fda.hhs.gov

RESPONSE REQUESTED BY: COB December 10, 2013

Document to be mailed: YES ☑ NO

We refer to Simponi SmartJect supplemental BLA 125289/103 and have the following labeling comments. Additional labeling changes may be forthcoming. Submit revised labeling incorporating changes in the attached marked up label.

Send your response to me via secure email at christine.chung@fda.hhs.gov no later than close of business Tuesday, December 10, 2013. Your response will subsequently need to be submitted officially to the BLA.

If you have any questions, please contact me at 301-796-3420.

Drafted by: DMPP/ 11.26.2013
cchung/ 11.29.2013

Cleared by: SBarnes/ 12.3.2013

Finalized: cchung/ 12.4.2013

24 Page(s) of Draft Labeling has been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

CHRISTINE H CHUNG
12/04/2013

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

ELECTRONIC CORRESPONDENCE

Date: October 29, 2013

To: Salvatore Morello, Director Global Regulatory Affairs	**From:** Christine Chung, R.Ph. Regulatory Project Manager
Company: Janssen Biotech, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Phone: 215-986-1210	**Fax number:** 301-796-9728
Email: smorell@its.jnj.com	**Phone number:** 301-796-3420

Subject: BLA 125289/103 – Simponi SmartJect
FDA request for information: combination product manufacturing information

Total no. of pages including cover: **3**

Comments: ***Response requested no later than Wednesday November 6, 2013***

Please call or send an email to confirm receipt at christine.chung@fda.hhs.gov

Document to be mailed: YES ☑ NO

We refer to supplemental BLA 125289/103 for Simponi (golimumab) which proposes changes to the Instructions for Use (IFU) and a minor design modification to the SmartJect Autoinjector. We have the following request for information.

1. Provide documentary evidence that the implemented design change in the device constituent part of the Simponi combination product was done in compliance with 21 CFR 820.30, particularly with section (i), design changes, which applies to any changes made to the Simponi combination product.
2. Provide documentary evidence that any changes made to the manufacturing process (assembly, packaging) of the Simponi combination product to accommodate the design change in the device constituent part were verified and validated.

Submit your response to me via secure email at christine.chung@fda.hhs.gov no later than COB November 6, 2013. Your response will subsequently need to be submitted officially to the BLA. If you have any questions, please contact me at 301-796-3420.

Drafted by: CDRH/DOEA – Isabel Tejero, Carl Fischer/ 10.29.2013
cchung/ 10.29.2013

Initialed by: SBarnes/ 10.29.2013

Finalized: cchung/ 10.29.2013

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/s/

CHRISTINE H CHUNG
10/29/2013

MANDATORY: Send a copy of the consult request form to the Office of Combination Products (OCP) as follows:
--Originating Center: When the consult request is initiated.
--Consulting Center: When the consult is completed.
Email: combination@fda.gov or FAX: 301-847-8619

For additional information: Contact OCP by email or by telephone (301-796-8930) or refer to OCP's intranet page http://inside.fda.gov:9003/ProgramsInitiatives/CombinationProducts/ReviewerTools/default.htm.

For Consulting Center Use Only:

Date Received: _____
Assigned to: _____
Date Assigned: _____
Assigned by: _____

Completed date: _____
Reviewer Initials: _____
Supervisory Concurrence: _____

Intercenter Request for Consultative or Collaborative Review Form

To (Consulting Center):
Center: CDRH/ODE/DAGID
Division: General Hospital Branch Device
Mail Code: HF
Consulting Reviewer Name: Jacqueline Ryan
Building/Room #: WO 66 Room 1257
Phone #: 301-796-9599
Fax #: 301-847-8115
Email Address: jacqueline ryan@fda hhs.gov
RPM/CSO Name and Mail Code:

From (Originating Center):
Center: CDER/OND/ODEII
Division: Division of Pulmonary, Allergy, and Rheumatology Products
Mail Code: HFD-570
Requesting Reviewer Name: Christine Chung
Building/Room #: WO22/3210
Phone#: 301-796-3420
Fax #: 301-796-9728
Email Address: christine.chung@fda hhs.gov
RPM/CSO Name and Mail Code: Christine Chung HFD-570
Requesting Reviewer's Concurring Supervisor's Name: Sandy Barnes, CPMS

Receiving Division: If you have received this request in error, you must contact the request originator by phone immediately to alert the request originator to the error.

Date of Request: 8/1/2013

Requested Completion Date: 10/28/2013

Submission/Application Number: BLA 125289/103
(Not Barcode Number)

Submission Type: sBLA 103
(510(k), PMA, NDA, BLA, IND, IDE, etc.)

Type of Product: ☑ Drug-device combination ☐ Drug-biologic combination ☐ Device-biologic combination ☐ Drug-device-biologic combination ☐ Not a combination product

Submission Receipt Date: 6/28/2013

Official Submission Due Date: 12/28/13

Name of Product: Simponi SmartJect

Name of Firm: Janssen Biotech

Intended Use: treatment of Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, and Ulcerative Colitis.

Brief Description of Documents Being Provided (e.g., clinical data -- include submission dates if appropriate):

EDR link to submission http://cberedrweb fda.gov:8080/esp/cberedr.jsp?folderObjId=0bbcaea681268602
Cover: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\cover.pdf
IFU clean: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\simponi-patient-instruct-smartject-clean.pdf
IFU tracked: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\simponi-patient-instruct-smartject-annotated.doc
CDRH-Human Factors will also be consulted.

Documents to be returned to Requesting Reviewer? ☐ Yes ☑ No

Complete description of the request. Include history and specific issues, (e.g., risks, concerns), if any, and specific question(s) to be answered by the consulted reviewer. The consulted reviewer should contact the request originator if questions/concerns are not clear. Attach extra sheet(s) if necessary:

Type of Request: ☑ Consultative Review ☐ Collaborative Review

Please assign CDRH reviewer(s) to prior approval sBLA 125289/103 - a minor design modification to the autoinjector
"At this time, JBI is hereby submitting additional revisions to the SIMPONI® SmartJect® Autoinjector IFU. The proposed changes to the SIMPONI® SmartJect® Autoinjector IFU are based on several inputs including historical customer feedback, human factors experts' reviews of the IFU, FDA feedback on the IFU received 27 February 2013 related to the FDA's review of the Human Factors Study protocol and IFU to be tested, the results of Human Factors Studies (HFS), and internal JBI reviews involving the commercial, device design, quality, and Johnson & Johnson (J&J) design stakeholders. In addition, a minor design modification to the SmartJect® Autoinjector (the addition of a "flange" feature to safety interlock sleeve [SIS], and a change in color of the SIS), necessitated updates to several pages in the IFU."

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/s/

CHRISTINE H CHUNG
08/01/2013

MANDATORY: Send a copy of the consult request form to the Office of Combination Products (OCP) as follows:

--Originating Center: When the consult request is initiated.

--Consulting Center: When the consult is completed.

Email: combination@fda.gov or FAX: 301-847-8619

For additional information: Contact OCP by email or by telephone (301-796-8930) or refer to OCP's intranet page http://inside.fda.gov:9003/ProgramsInitiatives/CombinationProducts/ReviewerTools/default.htm**.**

For Consulting Center Use Only:

Date Received: _____
Assigned to: _____
Date Assigned: _____
Assigned by: _____

Completed date: _____
Reviewer Initials: _____
Supervisory Concurrence: _____

Intercenter Request for Consultative or Collaborative Review Form

To (Consulting Center):
Center: CDRH
Division: ODE/DAGRID
Mail Code: HF
Consulting Reviewer Name: Quynh Nhu Nguyen
Building/Room #: WO 66 Room 2531
Phone #: 301-796-6273
Fax #:
Email Address: quynht nguyen@fda hhs.gov
RPM/CSO Name and Mail Code:

From (Originating Center):
Center: CDER/OND/ODEII
Division: Division of Pulmonary, Allergy, and Rheumatology Products
Mail Code: HFD-570
Requesting Reviewer Name: Christine Chung
Building/Room #: WO22 3306
Phone#: 301-796-3420
Fax #: 301-796-9728
Email Address: christine.chung@fda hhs.gov
RPM/CSO Name and Mail Code: Christine Chung HFD-570
Requesting Reviewer's Concurring Supervisor's Name: Sandy Barnes, CPMS

Receiving Division: If you have received this request in error, you must contact the request originator by phone immediately to alert the request originator to the error.

Date of Request: 8/1/13

Requested Completion Date: 10/28/13

Submission/Application Number: BLA 125289/103
(Not Barcode Number)

Submission Type: prior approval labeling supplement
(510(k), PMA, NDA, BLA, IND, IDE, etc.)

Type of Product: ☑ Drug-device combination ☐ Drug-biologic combination ☐ Device-biologic combination ☐ Drug-device-biologic combination ☐ Not a combination product

Submission Receipt Date: 6/28/13

Official Submission Due Date: 12/28/13

Name of Product: Simponi SmartJect

Name of Firm: Janssen Biotech

Intended Use: treatment of Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, and Ulcerative Colitis.

Brief Description of Documents Being Provided (e.g., clinical data -- include submission dates if appropriate):

EDR link to submission http://cberedrweb fda.gov:8080/esp/cberedr.jsp?folderObjId=0bbcaea681268602
Cover: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\cover.pdf
IFU clean: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\simponi-patient-instruct-smartject-clean.pdf
IFU tracked: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\simponi-patient-instruct-smartject-annotated.doc
CDRH will also be consulted regarding design modification.

Documents to be returned to Requesting Reviewer? ☐ Yes ☑ No

Complete description of the request. Include history and specific issues, (e.g., risks, concerns), if any, and specific question(s) to be answered by the consulted reviewer. The consulted reviewer should contact the request originator if questions/concerns are not clear. Attach extra sheet(s) if necessary:

Type of Request: ☑ Consultative Review ☐ Collaborative Review

Please provide Human Factors review of prior approval sBLA 125289/103 - "At this time, JBI is hereby submitting additional revisions to the SIMPONI® SmartJect® Autoinjector IFU. The proposed changes to the SIMPONI® SmartJect® Autoinjector IFU are based on several inputs including historical customer feedback, human factors experts' reviews of the IFU, FDA feedback on the IFU received 27 February 2013 related to the FDA's review of the Human Factors Study protocol and IFU to be tested, the results of Human Factors Studies (HFS), and internal JBI reviews involving the commercial, device design, quality, and Johnson & Johnson (J&J) design stakeholders. In addition, a minor design modification to the SmartJect® Autoinjector (the addition of a "flange" feature to safety interlock sleeve [SIS], and a change in color of the SIS), necessitated updates to several figures in the IFU." Please contact me if you need cannot access links

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/s/

CHRISTINE H CHUNG
08/01/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125289/103

**PRIOR APPROVAL SUPPLEMENT -
ACKNOWLEDGEMENT & FILING**

Janssen Biotech, Inc.
Welsh & McKean Roads
P.O. Box 776
Spring House, PA 19477

Attention: Salvatore Morello
Director, Global Regulatory Affairs

Dear Mr. Morello:

We have received your Supplemental Biologics License Application (sBLA) submitted under section 351(a) of the Public Health Service Act for the following:

BLA SUPPLEMENT NUMBER: 125289/103

PRODUCT NAME: SIMPONI (golimumab)

DATE OF SUBMISSION: June 28, 2013

DATE OF RECEIPT: June 28, 2013

This supplemental application proposes changes to the SIMPONI SmartJect Autoinjector IFU and a minor design modification to the SmartJect Autoinjector.

The supplemental application was filed on August 27, 2013, in accordance with 21 CFR 601.2(a). The goal date is December 28, 2013.

CONTENT OF LABELING

If you have not already done so, promptly submit the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action.

SUBMISSION REQUIREMENTS

Cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary, Allergy, and Rheumatology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

You are also responsible for complying with the applicable provisions of sections 402(i) and (j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

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

Sincerely,

{See appended electronic signature page}

Christine Chung, R.Ph.
CDR, 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

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/s/

CHRISTINE H CHUNG
10/11/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADM NISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:			FROM:	
Mail: OSE			Christine Chung, RPM, DPARP, 796-3420	
DATE 8/1/13	IND NO.	BLA NO. 125289/103	TYPE OF DOCUMENT sBLA	DATE OF DOCUMENT 6/28/13
NAME OF DRUG Simponi (golimumab) SmartJect	PRIORITY CONSIDERATION Standard		CLASSIFICATION OF DRUG DPARP	DESIRED COMPLETION DATE 10/28/13

NAME OF FIRM: Janssen Biotech, Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☑ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: PDUFA Date: 12/28/13

This is a consult for review of revised (IFU) for prior approval labeling supplement and human factors aspects. "The proposed changes to the SIMPONI® SmartJect® Autoinjector IFU are based on several inputs including historical customer feedback, human factors experts' reviews of the IFU, FDA feedback on the IFU received 27 February 2013 related to the FDA's review of the Human Factors Study protocol and IFU to be tested, the results of Human Factors Studies (HFS), and internal JBI reviews involving the commercial, device design, quality, and Johnson & Johnson (J&J) design stakeholders. In addition, a minor design modification to the SmartJect® Autoinjector (the addition of a "flange" feature to safety interlock sleeve [SIS], and a change in color of the SIS), necessitated updates to several figures in the IFU."
The entire application including labeling is electronic and is accessible in RMS/BLA or at
<http://cberedrweb.fda.gov:8080/esp/cberedr.jsp?folderObjId=0bbcaea681268602>
Cover: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\cover.pdf
IFU clean: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\simponi-patient-instruct-smartject-clean.pdf
IFU tracked: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\simponi-patient-instruct-smartject-annotated.doc

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☑ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

CHRISTINE H CHUNG
08/01/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADM NISTRATION

REQUEST FOR PATIENT LABELING REVIEW CONSULTATION

TO:
CDER-DMPP-PatientLabelingTeam

FROM: (Name/Title, Office/Division/Phone number of requestor)
Christine Chung, RPM, DPARP, x-63420

REQUEST DATE:
8/1/2013

NDA/BLA NO.:
sBLA
125289/103

TYPE OF DOCUMENTS:
(PLEASE CHECK OFF BELOW)

NAME OF DRUG:
Simponi (golimumab)
SmartJect

PRIORITY CONSIDERATION:
Standard

CLASSIFICATION OF DRUG:
DPARP

DESIRED COMPLETION DATE
(Generally 2 Weeks after receiving substantially complete labeling)
11/28/13

SPONSOR:
Janssen Biotech, Inc

PDUFA Date: 12/28/2013

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:
(Check all that apply)
☐ PATIENT PACKAGE INSERT (PPI)
☐ MEDICATION GUIDE
☒ INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION
☐ ORIGINAL NDA/BLA
☐ EFFICACY SUPPLEMENT
☐ SAFETY SUPPLEMENT
☒ LABELING SUPPLEMENT
☐ MANUFACTURING (CMC) SUPPLEMENT
☐ PLR CONVERSION

REASON FOR LABELING CONSULT
☐ INITIAL PROPOSED LABELING
☒ LABELING REVISION

EDR link to submission:
http://cberedrweb fda.gov:8080/esp/cberedr.jsp?folderObjId=0bbcaea681268602

Please Note: DMPP uses substantially complete labeling, which has already been marked up by the CDER Review Team, when reviewing MedGuides, IFUs, and PPIs. Once the substantially complete labeling is received, DMPP will complete its review within 14 calendar days. Please provide a copy of the sponsor's proposed patient labeling in Word format.

COMMENTS/SPECIAL INSTRUCTIONS:
Prior approval labeling supplement BLA 125289/103.
This is a consult for evaluation and review of patient labeling (Instructions for Use) for Simponi (golimumab) SmartJect.
Cover: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\cover.pdf
IFU clean: \\cdsesub1\bla\ectd_submissions\stn125289\0284\m1\us\simponi-patient-instruct-smartject-clean.pdf
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PDUFA Date: 12/28/2013

SIGNATURE OF REQUESTER

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/s/

CHRISTINE H CHUNG
08/01/2013