

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
125289

OTHER REVIEW(S)



3/11/09

DEPARTMENT OF HEALTH AND HUMAN SERVICES MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

Division of Anesthesiology, General Hospital, Infection Control and Dental Devices
General Hospital Device Branch HFZ-480

Date: March 11, 2009

Consultation for: BLA 125289 Simponi (golimumab) Injection
Consultation To: Sharon Turner-Rinehardt Regulatory Health Project Manager
Division of AARP/ODE II/CDER/HFD-170

Consultation From: Pandu R. Soprey Ph.D.
THROUGH: Anthony Watson Branch Chief GHDB/DAGID/CDRH/ HFZ-480
Applicant / Sponsor: Centocor Research and Development

INDICATION FOR USE:

SIMPONI, is a tumor necrosis factor (TNF) blocker indicated for the treatment of:
Rheumatoid Arthritis (RA) (1.1) in combination with methotrexate.
SIMPONI (Golimumab) is delivered by using Centocor Autoinjector (autoinjector) or the **b(4)**
_____ device.

CROSS REFERENCES (LIST RELATED LICENSE APPLICATION, INDS, NDAS, PMAS, 510(K)S, IDES, BMFS, AND DMFS REFERENCED IN THE CURRENT APPLICATION)

Letter of Authorization Safety Syringe _____
Letter of Authorization Safety Syringe _____
Syringe barrel with fixed needle Drug Master File (DMF) and Master File for Devices (MAF), **b(4)**
for the (_____),
_____ needle shield (_____)
Plunger stopper / _____) Letters of Authorization to access the Master Files
are provided in Module 1.4.1

INTENT THIS REVIEW:

To review the manufacturing, process control, process validation, performance and stability of the delivery devices. The sponsor uses the Centocor Autoinjector and _____
_____ devices to deliver the drug product.

REVIEW:

1. DRUG SUBSTANCE and DRUG PRODUCT:

Golimumab formulated bulk (FB) is manufactured by _____
_____ at Centocor B.V, located in Leiden, The Netherlands.

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A summary description of the drug substance manufacturing process, including process controls, process validation, process development, analytical controls and stability is presented in Module 3.2.S.2.2, Description of Manufacturing Process and Process Controls, Overview.

The golimumab _____

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syringe. Two golimumab PFS presentations are manufactured from the FB, a 50 mg/syringe dose (0.5 mL nominal fill volume) and a 100 mg/syringe dose (1.0 mL nominal fill volume).

The golimumab PFS (Pre-filled Syringe) manufacturing process is made of the following separate procedures: _____

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_____ Manufacturing of the drug product is performed according to the process described in Module 3.2.P.3.3, Description of Manufacturing Process and Process Controls, PFS (Pre-filled syringe).

2.0 DEVICES

The golimumab PFS (pre-filled syringe) is shipped to Cilag AG, located in Schaffhausen, Switzerland, for assembly into either the Centocor Autoinjector (autoinjector) or _____

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Centocor uses two drug delivery devices to be assembled with the golimumab PFS _____, long syringe with a fixed, 27G half-inch stainless steel needle). The purpose of these devices is to aid in drug delivery and provide for protection against accidental needlesticks. The final presentations of golimumab include: 1) a pre-filled, disposable autoinjector that automatically delivers the labeled dose contained in the PFS, and 2) a needle guard externally attached to the PFS that automatically extends and locks over the PFS needle following complete manual injection.

2.1 Pre-filled Syringe:

The container closure system utilized for CNTO 148 final product is a pre-filled syringe (PFS) consisting of the following components:

1. _____

2. _____

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2.3 Centocor Autoinjector:

The Centocor Autoinjector (autoinjector) components and their materials of construction are summarized in Table 1 (Module 3.2.P.7). The autoinjector uses the pre-filled syringe (PFS) equipped with the non-rigid needle shield. Detailed technical information about the autoinjector is reported to FDA in a Master File for Devices (MAF) for the autoinjector. Information about autoinjector suitability and performance is provided in 3.2.P.2.4, Container Closure System.

The autoinjector is assembled from two main subassemblies, termed Subassembly A and Subassembly B. During final assembly of a 1.0 mL volume autoinjector, the PFS is inserted into Subassembly A in an assembly fixture under controlled force, and an additional component, the Latch Actuator, is snapped into place. For autoinjector designed to contain 0.5 mL of drug volume, a longer 0.5 mL latch actuator and a 0.5 mL spacer is used to accommodate the stopper position of the 0.5 mL PFS. Subassembly B is then snapped onto Subassembly A to complete the assembly of the product.

Device assembly validation was performed to qualify assembly and secondary packaging of the golimumab PFS into either an autoinjector or [REDACTED]. All validation results supporting the autoinjector semi-automated and the [REDACTED] assembly processes are included in Module 3.2.P.3.5, Process Validation and/or Evaluation, Description of Manufacturing Process and Process Controls, Autoinjector or [REDACTED].

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All results for all golimumab Autoinjector (100 mg and 50 mg) and Placebo Autoinjector (0.5 mL) held at the recommended storage conditions of 2 to 8°C met the acceptance criteria for all functional stability tests at all time points up to 9 months. The golimumab Autoinjector (50 and 100 mg) functionality data and additional supporting studies presented in this section support a shelf life claim of 24 months (from the date of manufacture of the golimumab PFS) when stored at the recommended temperature of 2 to 8°C and protected from light. The data presented for the accelerated aging tests of the component parts in the design-verification test program demonstrated that the subassemblies and components remain functional beyond the proposed golimumab PFS shelf life.

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3.0 AUTO INJECTOR:

Centocor autoinjector is a delivery device for delivery of drug products filled in prefilled in glass syringes. The autoinjector is intended for use in the subcutaneous administration of drugs by healthcare providers, caregivers, and patients, including those with moderate to severe hand

impairment, in the home or clinical environment. The development of the autoinjector was guided by FDA Design Control Regulations (21 CFR 820.30), international regulatory requirements for devices (e.g., ISO 11608 Pen injectors for medical use – Part 1) and by International Conference on Harmonization (ICH) guidelines for drug delivery devices.

Centocor has performed design verification tests of the autoinjector using two representative liquid monoclonal antibodies and demonstrated that the autoinjector meets predetermined acceptance criteria for expelled volume, delivery time, force to actuate, cap/needle shield removal force, needle protrusion, drop test survival, component shelf life, and biocompatibility of patient contact materials.

The autoinjector needlestick prevention feature was evaluated in a simulated use study conforming to FDA's *Guidance for Industry and FDA Staff Medical Devices with Sharps Injury Prevention Features* (FDA, August 2005). This study, and an additional tolerability study and a self-administration study, confirmed that the autoinjector, when used with its instructions for use and with patient training, is suitable for drug administration by the intended patient populations.

Centocor has included a comparison of its autoinjector to other marketed prefilled and reusable auto-injectors and demonstrated that its autoinjector has the same or very similar technological characteristics, intended uses, principles of operation, and performance as the marketed products.

3.1 Overview of Autoinjector Description and Operation

The subject autoinjector is very similar to marketed auto injectors that have been cleared as Class II devices by CDRH FDA as a "Syringe Needle Introducer" under FDA Product Code KZH. The autoinjector 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.

3.2 Marketing History:

The subject autoinjector has not been approved for marketing in the U.S. or in any international markets when this MAF was submitted. However, the injector has been used in three investigational trials in the U.S. to date as follows:

CNTO 148 (golimumab) (BB-IND 9925, Ser. No. 0161): A Phase 1, Randomized Cross-Over Study to Evaluate the Safety and Tolerability of Placebo Subcutaneously Administered at 3 Different Injection Sites Using an Investigational Autoinjector Device or a PFS (Protocol C0999D01).

CNTO 148 (golimumab) (BB-IND 9925, Ser. No. 0173): A Phase 1, Randomized, Open-label, Parallel-design, Inpatient/Outpatient Study to Assess the Bioequivalence of a Single-dose Subcutaneous Administration of Golimumab Delivered by the Centocor Autoinjector or a Needle and Syringe in Healthy Subjects (Protocol C0524T24).

CNTO 148 (golimumab) (BB-IND 9925, Ser. No. 0283): An Open-Label, Randomized, Validation Study to Establish That the Design, Functionality, and Ergonomic Features of the Autoinjector Conform to Defined User Needs and Intended Use for Self-Administration by Subjects With Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, or Psoriasis (Protocol C0999D02).

Currently marketed similar autoinjectors are: Autoject 2 ([redacted]) and Autoject Mini ([redacted]), Confidose IM and SC ([redacted]) and the SHL Medical Disposable Auto-injector ([redacted]). **b(4)**

FDA CDER has licensed other pre-filled biological drug autoinjector dosage forms (Aranesp® SureClick™, Enbrel® SureClick™, Humira® Pen injector).

3.3 APPLICABLE STANDARDS:

The Pen Injector (device) is designed to conform to the current ISO 11608:2000, Pen-injectors for medical use, Part 1: Requirements and test methods standard. Patient contacting materials are to be tested in accordance with guidelines outlined in ISO 10993-1 Biological Evaluation of Medical Devices for skin contacting device materials having limited contact duration (≤ 24 hours). Tests performed included Cytotoxicity, Sensitization, and Irritation/Intracutaneous Reactivity. Results materials biocompatibility tests are summarized in Section 10.4 of this MAF **b(4)**

3.4 DESIGN CONTROLS:

Centocor has summarized the design objectives and the corresponding performance requirements for the autoinjector in relation to the design controls:

The firm has provided information and specifications for the following:

- i) **Physical Characteristics Nominal Specification/Description:** Weight, Length, Activation button, Inspection window.
- ii) **Functional Characteristics:** Single use, Dose Delivery, Fill volume, Delivery Mechanism, and needle retraction, Audible “clicks” upon actuation and needle retraction, piston visible window after delivery, Cap removal Cap designed for pull and/or twist removal.
- iii) **Safety Characteristics:** Sharps Injury Prevention Passive Interlock System, Button Lock prevents inadvertent depression of the Button, Cap must be removed and the SIS disengaged by pressing the autoinjector against the skin before the actuation Button can be depressed. Needle resides inside device before and after injection, Needle automatically retracts following dose delivery, Drug Product Inspection window provided to check for visible particles and Counterfeit Prevention.
- iv) **Performance Characteristics:** Cap Removal Force [redacted] Interlock Sleeve Disengagement Force [redacted] **b(4)**

Force to overcome Button Lock (Safety) _____, Drug Delivery Time 1.0 mL and 0.5 mL configurations _____ Drug flow rate _____ Drug Delivery Depth _____ Needle Insertion Force _____ Needle Retraction Force > _____ (Secondary Spring).

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3.4.1 Design Validation

Centocor has completed a Simulated Use Study (SUS) with health care professionals and patients who routinely administer subcutaneous medications. Centocor followed the FDA's Guidance for Industry and FDA Staff Medical Devices with Sharps Injury Prevention Features (FDA, August 2005) in the preparation and execution of its protocol.

The objectives of the study were as follows:

- To confirm bench test performance results that the autoinjector operates reliably when used by health care professional and patients.
- To confirm that the design meets end users expectations
- To assess the usefulness of the proposed IFU during simulated use
- To evaluate whether or what type of training may be needed. After reviewing the autoinjector IFUs and practicing on training autoinjector(s), 65 evaluators were each instructed to actuate eight devices into an injection training pad. A total of 520 consecutive actuations were completed, simulating important clinical variables. Subject evaluators included physicians, nurses who routinely performed subcutaneous injection, patients trained for self-injection, and patients who currently self administer subcutaneous drugs including those with significant hand impairment (i.e., RA patients). There were no failures (defined as either a needlestick injury or a significant problem with the safety feature(s) that may lead to an injury) among the 520 actuations and therefore, there is a greater than 97.5% confidence that the true autoinjector failure rate that potentially could lead to a needlestick injury is less than or equal to _____. The study included uniform technique with proper precautions, consistent observations during use, scoring and usability evaluation of certain features, completes data collection, and reporting. The clinical study report for the SUS is provided (Section 12). The study tested the 1.0 mL version of the autoinjector, which is identical to the 0.5 mL version except for a longer Latch Actuator and Spacer as described (Section 5.3.).

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The safety features under testing in the SUS operate in an equivalent manner between the two variants of the device. Centocor also completed a Tolerability Study (Protocol C0999D01) submitted in IND amendment (BB-IND 9925, Serial No. 0161). The objective of the study was to evaluate the safety and tolerability of a single 1 mL subcutaneous dose of placebo delivered from the autoinjector and a single 1 mL subcutaneous dose of placebo delivered manually from a PFS to different anatomical regions of the body (upper arm, abdomen, and upper thigh), as administered by a healthcare provider. Since this study used placebo to assess the tolerability of the injection, the study is relevant to the device contribution to tolerability.

There were no serious adverse events. The clinical study report for the Tolerability Study is provided (Section 13).

Following the SUS and Tolerability Study, Centocor performed a Self Injection Study that was submitted as an IND amendment for CNTO 148 (BB-IND 9925, Serial No.0283). This

was a validation study of the Centocor autoinjector in the expected target population. There were 68 subjects enrolled (35 with RA, psoriatic arthritis (PsA), or ankylosing spondylitis [AS], and 33 with psoriasis). At least 15 subjects with RA or PsA were required to have impaired hand function (impairment is defined as HAQ-DI total score >0) and at least 15 of the total 30 subjects were required to have had prior or current experience with SC self-administration. The objectives were to validate the ability of patients, with training and use of the IFU, to perform self-administration with the device as assessed through observation of their attempts and through an IFU questionnaire that tested their knowledge of the device. Each subject self-administered a total of two SC injections of placebo with the Centocor autoinjector as single SC injections in each of two injection sites (one each for abdomen and thigh).

CONCLUSION:

The results of the study indicated that 100% of subjects were able to complete the injections with the first or second attempt in at least one of the injection sites regardless of diagnostic group or subgroup strata. Skin pinching techniques were advantageous in some subjects. The self-administration study results and the IFU assessment demonstrated that the device is suitable for intended target population (Section 14).

3.5 Device Labeling:

Labeling and IFU are provided in the drug product section of the BLA that references this (b)(4). An example of the label is shown (Figure 19). An example of the IFU included with the autoinjector is shown. Final labeling of the combination product will be approved with the drug product package insert by CDER.

3.6 Device Risk Analysis:

Centocor has prepared summary Risk Analysis Tables for design, user, and process related risks based on comprehensive FMEA activities and reviews conducted throughout the development process. These tables include the hazard, the cause of the hazard, and risk categories based on the severity (S) and probability (P) of these events. The included the mitigation and controls that were implemented to reduce these risks to acceptable levels and an assessment of how these controls and mitigation reduced these hazards or risks. The se summary tables are based on individual FMEAs for specific hazards and provide an overall assessment of the risks associated with the autoinjector and how the multiple approaches to their mitigation have addressed those risks includes the design-related and general risks. These risks have been mitigated in multiple approaches in the design phase, including selection of materials, design tolerances, component performance assessments, as well as design verification testing to demonstrate robustness and safety of the design. User-specific risks are identified that are mitigated by effective labeling or training or particular design features. The risks that are related to the assembly of the device and provide an assessment of autoinjector risk, including detectability (D) of faults related to assembly are described.

The scoring system used is consistent with ISO 14971:2000/Amd.1:2003, *Medical Devices – Application of Risk Management to Medical Devices*, and provided a general tool for assessing the relative risks before and after mitigation. The scoring system is described in key tables following the risk tables.

CONCLUSION:

Centocor prepared and implemented a Risk Management Plan for the design and development of the autoinjector for use with biological drugs. The scope of the plan includes development activities performed at [redacted] and the activities performed by its contractors and suppliers, including the development of design specifications, component and subassembly manufacturing and testing, and final assembly with the PFS. The plan has been developed in line with ISO 14971, *Medical devices – Application of risk management to medical devices*, and ISO 13485, *Medical Devices Quality Management Systems - Requirements for regulatory purposes*.

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3.7 Autoinjector Assembly:

The Cilag receives, accepts, and stores incoming autoinjector parts, subassemblies, and PFSs from the suppliers and performs the final assembly operation. The assembly process is performed using a [redacted] steps. The basic steps for the process are depicted in the flowchart (MAF Figure 21).

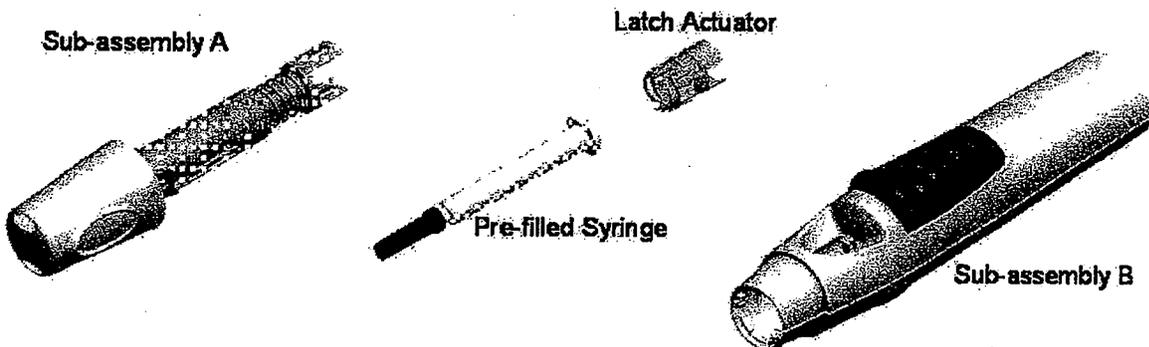
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3.7.1 Device Components:

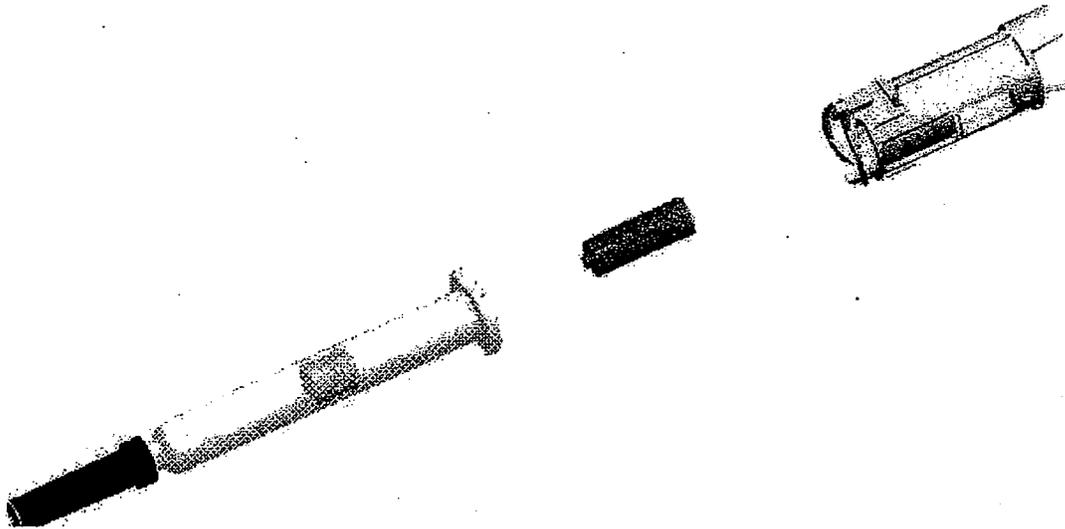
The Centocor autoinjector is composed of several plastic and metal parts (e.g., springs) and an [redacted] assembled into subassemblies for final assembly with the PFS. The autoinjector is assembled from two main subassemblies, termed Subassembly A and Subassembly B (Figure).

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During final assembly of a 1.0 mL volume autoinjector, the PFS is inserted into Subassembly A in an assembly fixture under controlled force, and an additional component, the Latch Actuator, is snapped into place. Subassembly B is then snapped onto Subassembly A to complete the assembly of the product.



For autoinjector designed to contain 0.5 mL of drug volume, a longer 0.5 mL latch actuator and a 0.5 mL spacer is used to accommodate the stopper position of the 0.5 mL PFS. The relevant parts for the 0.5 mL configuration are illustrated in Figure 4.



The 1.0 mL injector device incorporates [REDACTED] (Metal Retainer, Main Spring, and Return Spring), two adhesive labels (Product Label and Tamper Evidence Label), and a [REDACTED]. As noted above, the 0.5 mL device uses an additional polymer component (the 0.5 mL Spacer) and requires an alternative design of the Latch Actuator. All of these components are shown in, and the list of the molded component parts for the autoinjector is provided.

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3.7.2 In-process Controls

In addition to automated in-line checks performed during the assembly process, IPCs (in process controls) be performed on the fully assembled autoinjector prior to secondary packaging. The IPC tests (described below) and the Release Tests, encompass full functional performance testing of the autoinjector as a finished medical device and ensure compliance with specifications. Finished autoinjectors are sampled from the assembly line at the beginning of batch production, at defined time intervals throughout the assembly run, and at the end of the batch. Samples are tested for the IPC parameters. Information about these tests is also provided to CDER reviewers in the drug product section of the BLA (Module 2.3.P.8. Page 121).

COMMENTS:

The following tests were conducted: i) Expelled volume test - reported in mL and must meet the minimal labeled dose as per PFS specifications, ii) Cap removal test - performed by removing the cap of the autoinjector and visually verifying that the tamper evident label is torn and that the PFS needle shield is retained in the cap, iii) Delivery time test - The delivery time test is performed by measuring the time between actuation of the autoinjector resulting in an audible noise (click), to when the dose is delivered and syringe retraction begins resulting in a second audible click. The results are reported in seconds and meet the delivery time (<15 seconds), iv) Visual inspection defects (before and after firing) and v) Force to activate.

3.7.2.1 Tests Performed Before Actuation:

The autoinjector is visually inspected for any defects in appearance. The inspection checks that the assemblies are complete and fit together correctly, the cap is assembled in the correct

position, and no specks/spots are present in the window. The results are reported as pass/fail (attribute test). The following tests were performed: i) Button lock check, ii) Sliding Interlock, iii) Sleeve check.

3.7.2.2 Tests Performed After Actuation:

The following tests were performed: Needle retraction check, Plunger check, Post-use Button lock check.

3.7.3 Release Testing Specifications:

The release testing for the combination product includes a review of the IPC test results for the autoinjector functionality. For release of the drug product, the following functional specifications must be met for the autoinjector.

In-process tests and Specifications:

Test	Acceptance criteria
Appearance	Assemblies are complete and fit together correctly, cap is assembled in the correct position and no specks/spots are present in the window.
Button lock check	Device cannot be actuated with the button without engagement of the SIS
Sliding Interlock Sleeve check	SIS can be pressed and returns to its initial position. Device cannot be actuated with the button after SIS manipulation
Needle retraction check	Needle has been retracted after actuation
Plunger Rod check	The yellow indicator appears in the window and no liquid is observed through window
Post-use Button lock check	Button locks in down position
Expelled volume test	0.5-0.6mL; 1.0mL-1.1mL
Cap removal test	Tamper evident label torn. Needle shield retained in the cap
Delivery time test	
Force to activate test	

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Validation information regarding the assembly of the autoinjector is provided in the drug product section of the BLA that references this MAF. This summary information is provided for completeness in support of the MAF for the autoinjector.

3.7.4 Summary of Assembly process

The process validation of the final assembly of autoinjector with PFS consisted of the production and evaluation of three batches each of 1.0 mL and 0.5 mL autoinjectors (Pg. 99, Table 13). Three model drug liquids (two liquid monoclonal antibodies and a placebo) were used in the validation study.

The objective of the process validation testing was to demonstrate the consistency of assembling the _____ long glass syringe with 27 G, half-inch fixed needle and needle shield together with the autoinjector device. The process validation included syringes prefilled with

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three liquid drug products (CNTO 148, _____, and CNTO 148 placebo) to effectively challenge the overall assembly process using a broader range of PFS characteristics. The autoinjector assembly process is the same for all products in that it is dependent upon the physical characteristics of the autoinjector, the _____ (PFS), and the fill volume.

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Process validation testing consisted of five tests: Expelled Volume, Delivery Time, Force to Actuate, Cap Removal, and Visual Appearance and Defects. Three of these autoinjector tests, the Force to Actuate, Cap Removal, and Visual Appearance and Defects tests, are independent of the liquid in the syringe. The tests for Expelled Volume and Delivery Time are dependent on the liquid in the PFS, but the results, regardless of the drug product used, must meet autoinjector release specifications. The process validation program demonstrated that the autoinjector assembly met predetermined acceptance criteria.

3.7.4.1 Results Assembly Process Validation

The autoinjector assembly process validation results provided in BLA submissions and in MAF. All autoinjectors were assembled with the PFS in a semi-automated process described above using qualified/specified components and subassemblies. Process parameters were set and controlled within the ranges established during equipment qualification.

To demonstrate that the assembled autoinjectors consistently meet the specifications for critical quality attributes applicable to Centocor's final drug products, routine IPC tests and validation tests were performed. Container closure integrity after assembly of PFS (1.0 mL and 0.5 mL) with the autoinjector was demonstrated. The validation test results for the batches (six batches) in Table 14, Table 15, Table 16 and in Table 17 (MAF).

CONCLUSION:

All batches of autoinjectors (0.5 mL and 1.0 mL) met the acceptance criteria for all tests and the process was successfully validated.

For Visual Appearance and Defects and Cap Removal, for visual defects was performed on a representative sample of assembled autoinjectors before and after actuation. The results of these tests for the six autoinjector batches demonstrate that the acceptance criteria for the process validation study were met.

3.7.5 Container Closure Integrity

As part of the assembly equipment qualification at Cilag, container closure integrity tests were performed on the _____ autoinjector combination to assure that the assembly process did not affect container closure integrity (CCI). The assembly process includes inserting the PFS into the front assembly and cap of the autoinjector, which functions to grip the needle shield allowing for easy removal. To confirm that this step does not impact the CCI of the needle shield on the needle tip, a blue dye intrusion test, using CNTO 148 placebo PFS as a model drug product, was performed.

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To assess the overall integrity of the _____ following the complete autoinjector assembly process, a standard microbial ingress test was performed. These tests confirm that

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assembly with the autoinjector does not affect the drug product. The autoinjector does not directly contact the drug product or the fluid pathway during injection.

The results of this test confirmed that CNTO 148 PFS CCI was not compromised during assembly of the PFS with the autoinjector below the established operating parameters. The results of the CCIT also demonstrate that shipping of the PFS. The semi-automated assembly process of the autoinjector with 1.0 mL and 0.5 mL PFS has been successfully validated.

3.8 Biocompatibility

The autoinjector is constructed of suitable polymers that are the same or similar to those used in other marketed autoinjectors. During use of the device, healthcare providers, patients, or caregivers will likely contact the outer surfaces of the autoinjector.

Accordingly, medical device regulations require assessment of the biocompatibility of the patient-contacting materials in accordance with the FDA Blue Book Memorandum #G95-1 and the guidelines outlined in ISO 10993-1, Biological Evaluation of Medical Devices, to demonstrate the biological safety of the autoinjector and its component materials.

Based on the FDA/ISO definitions, the autoinjector component is categorized as a skin contacting surface device having limited contact duration (≤ 24 hours).

Samples of the patient-contact materials () were tested. The following components were tested: Case Nose, Button, Top Case, Bottom Case, SIS, Cap. **b(4)**

The following test was conducted:

- Cytotoxicity (ISO 10993-5), L929 Minimum Essential Medium (MEM) Elution Test:
- Systematic Injection Test: Acute systemic toxicity (ISO 10993-11)
- Sensitization (ISO 10993-10) Kligman Maximization Test:
- Irritation/Intracutaneous Reactivity (ISO 10993-10)

The tests and results are described the test results demonstrated that the materials selected for the autoinjector are biocompatible.

In addition, the autoinjector uses a standard () 1 mL long syringe with a fixed, **b(4)**
27 G, half-inch stainless steel needle. The syringe uses a ()
coated stopper. This syringe is currently marketed in the USA and a Letter of Authorization
permitting FDA to access the relevant Drug Master Files is provided. The needle shield used
contains dry natural rubber components, and is so noted in the labeling.

RECOMMENDATIONS:

Considering the information provided regarding the proposed autoinjector (device) performance, technological characteristics and safety, the autoinjector is safe for use in delivery of Simponi drug (golimuab).


Reviewer: Pandu R. Soprey March 11, 2009

BC/GHDB/DAGID/CDRH: 



Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research

Office of Biotechnology Products
Silver Spring, MD
Tel. 301-796-4242

Memorandum

PROJECT MANAGER'S REVIEW

Application Number: STN 125289/0/25

Name of Drug: Simponi®

Sponsor: Centocor Inc.

Material Reviewed: Simponi® (golimumab) Carton and Container Labels

OBP Receipt Date: December 3, 2008

Amendment Reviewed: April 10, 2009

Background:

Centocor Inc. has submitted a Biologic License Application (BLA) supplement for Simponi® (golimumab), a human IgG1_K monoclonal antibody supplied in a sterile solution in either an autoinjector or a prefilled Type I glass syringe containing 50 mg/5 mL. The product is administered by subcutaneous injection.

Labels Reviewed:

Simponi® (golimumab) Container Label
Prefilled Syringe
Autoinjector Physician Sample
Autoinjector

Simponi® (golimumab) Carton Label
Prefilled Syringe
Autoinjector Physician Sample
Autoinjector

8 Page(s) Withheld

 Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

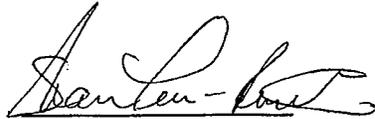
 Draft Labeling (b5)

 Deliberative Process (b5)

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Recommendations

Labeling revisions, deficiencies, and issues should be communicated to the Sponsor with a request that updated labeling be submitted to the application. This updated version of labeling will be used for further labeling discussions.

 8/5/08

Sharon Turner-Rinehardt
Regulatory Health Project Manager

Supervisory Comment/Concurrence:

 3/31/09

Parinda Jani
Chief, Project Management Staff

Drafted: STR/010708

Revised/Initialed:

Finalized:

Filename: CSO Labeling Review Template (updated 1-16-07).doc

CSO LABELING REVIEW OF PLR FORMAT