GEORGIA SUPERIOR COURT
CLERKS' COOPERATIVE AUTHORITY

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2. This public document
has been signed by **PRENCINA GREENE**

3. acting in the capacity of **NOTARY PUBLIC, STATE OF GEORGIA**

4. bears the seal/stamp of **PRENCINA GREENE**
NOTARY PUBLIC
BARROW COUNTY, GEORGIA

CERTIFIED

5. at **ATLANTA, GEORGIA** 6. the **12TH DAY OF FEBRUARY, 2018**

7. by **GEORGIA SUPERIOR COURT CLERKS' COOPERATIVE AUTHORITY**

8. No. **I-519468**

9. Seal/Stamp

10. Signature:

JOHN E. EARLE
EXECUTIVE DIRECTOR

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STATE OF GEORGIA
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ssen Pharmaceuticals, Inc.
40 Olympic Drive
thens, GA 30601-1645
+1 (706) 425-3804

janssen
PHARMACEUTICAL COMPANIES
OF Johnson & Johnson

The attached document is intended for submission in Chile.

J. E. Johnson 29-JAN-2018

Timothy E. Johnson, P.E.
Senior Director of Quality
Janssen Pharmaceuticals, Inc.
1440 Olympic Drive
Athens, Georgia 30601
Office: +1 (706) 425-3804

Sworn and subscribed to before me this 29th day of January 2018.

Prencina Greene
Notary Signature

PRENCINA GREENE
Notary Public, Georgia
Barrow County
My Commission Expires
July 20, 2019

ChiCo 152318

U.S. FOOD & DRUG ADMINISTRATION

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Atlanta District

10/04/2017

Janssen Pharmaceutical Inc
1440 Olympic Dr
Athens, GA 30601-1645, US

Reference: Inspection Date(s): 07/11/2017 - 07/14/2017

Location: Janssen Pharmaceutical Inc
1440 Olympic Dr
Athens, GA 30601-1645, US

Dear Mr. Timothy E. Johnson, Senior Director of Quality

We are enclosing a copy of the establishment inspection report (EIR) for the inspection that the U.S. Food and Drug Administration (FDA) conducted at your premises on the referenced locale and date(s). When the Agency concludes that an inspection is "closed" under 21 CFR 20.64(d)(3), it will release a copy of the EIR to the inspected establishment. This procedure is applicable to EIRs for inspections completed on or after April 1, 1997.

The Agency continually works to make its regulatory process and activities more transparent to the regulated industry. Releasing this EIR to you is part of this effort. The copy being provided to you comprises the narrative portion of the report; it may reflect redactions made by the Agency in accordance with the Freedom of Information Act (FOIA) and 21 CFR Part 20. This, however, does not preclude you from requesting additional information under FOIA.

If there is any question about the released information, feel free to contact me at 404-669-4566.

For more information on the U.S. FDA, please visit our website at www.fda.gov.

Sincerely,

Lareese K. Thomas -S

Digitally signed by Lareese K. Thomas -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2000359724, cn=Lareese K. Thomas -S
Date: 2017.10.04 16:45:44 -04'00'

FEI: 1033845

Enclosure: Establishment Inspection Report (EIR)

Establishment Inspection Report	FEI:	**1033845**
Janssen Pharmaceutical Inc	EI Start:	7/11/2017
Athens, GA 30601-1645	EI End:	7/14/2017

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SUMMARY

The current inspection (cNSpect Operation ID 61061) was conducted pursuant to CP 7346.832, Pre-approval Inspections per assignment from Division Pre-approval Manager for the following applications:

- N019813/S-72, Duragesic® (fentanyl citrate) Controlled Release Film
- N209155/ORIG-1, Oxycodone HCl Capsules
- A209385/ORIG-1, Oxycodone HCl/Acetaminophen Tablets
- A209897/ORIG-1, Oxycodone HCl Solution
- A209958/ORIG-1, Hydrocodone Bitartrate and Acetaminophen Tablets
- A209069-ORIG-1-resub-3, Buprenorphine HCl and Naloxone HCl Dihydrate Tablets
- N209653-ORIG-1, Rexista® (oxycodone HCl) Extended-Release Tablets
- N207975/S-003, Vantrela ER® (hydrocodone bitartrate) Tablets

A GMP inspection was also conducted pursuant to CP 7356.002F, Active Pharmaceutical Ingredients, and CP 7356.002, Drug Process Inspections. This inspection covered the following systems: Quality, Facilities and Equipment, Laboratory Controls, and Packaging and Labeling. Other systems were covered, but not in detail. I also reviewed the firm's corrective actions from the previous inspection including CAPAs, current procedures, and practices. The firm continues to operate as an API manufacturer. All corrections have been made.

An FDA-483 was not issued at the conclusion of the inspection. Several items were discussed with the firm as described below. There were no samples collected.

Previous inspection of this active pharmaceutical ingredient manufacturer (API) was conducted from 02/10 – 20/2014, and was classified NAI.

During the current inspection, my credentials were displayed and the Form FDA-482, Notice of Inspection, was issued to Timothy E. Johnson, Senior Director of Quality, whom identified himself as the most responsible Quality Unit person on site **(Attachment 1)**. All regulatory correspondence should be addressed to him at the firm's address.

Daily wrap-up meetings were held with those individuals involved in the inspection. During these discussions, I pointed out any concerns that had surfaced during the day's activities. Management was afforded the opportunity to respond to or clarify any of the concerns raised.

ADMINISTRATIVE DATA

Inspected firm:	Janssen Pharmaceutical Inc
Location:	1440 Olympic Dr Athens, GA 30601-1645
Phone:	706-425-3695
FAX:	706-353-3205
Mailing address:	1440 Olympic Dr Athens, GA 30601-1645
Dates of inspection:	7/11/2017-7/14/2017
Days in the facility:	4
Participants:	**Johnetta F Walters, Investigator**

MANUFACTURING/DESIGN OPERATIONS

The firm has recently undergone divestiture from Noramco, Inc. The Toll Manufacturing and Supply Agreement is submitted as **Exhibit 1**. Organizational charts are submitted as **Exhibit 2**. The firm's overview presentation is submitted as **Exhibit 3**. An example of the letter submitted to customers is submitted as **Exhibit 4**. The Quality Unit remains largely unchanged.

Significant personnel changes include the following:

1. Niamh Hunt has assumed responsibilities of General Manager of the firm. The Quality and Manufacturing groups operate independently of one another with independent goals.
2. Susan O. Daniel has assumed the role of Microbiology Manager, and no longer works as the QA Manager.
3. Iris Y. Moore has assumed the role of Senior QA Manager.
4. Kristi M. Longmire has assumed to role of Manufacturing Manager.
5. The firm no longer employs on-site regulatory personnel. The firm instead uses Global Regulatory for support.

The firm has reported one major facility change regarding API operations since the last inspection. Building 6 is now annexed to Noramco, Inc., and is no longer part of the Janssen campus. The construction which had been previously initiated on the medical device site (Ethicon) is now complete.

JPI continues to operate as a manufacturer of active pharmaceutical ingredients. Products which will continue to be manufactured and/or tested at the Janssen Pharmaceuticals, Inc. facility are outlined in **Exhibit 5**.

JPI has transferred manufacturing and/or testing responsibilities for a number of Drug Master Files (DMF) to Noramco – Wilmington. Specifically, the divestment includes all opioid-based controlled substances. The firm does, however, still manufacture Methylphenidate. Significant production changes include the following:

Product	Testing Responsibilities	Manufacturing Responsibilities
Codeine Phosphate DMF 006413	Noramco – Wilmington	-
Codeine Phosphate DMF 025856	Noramco - Wilmington	Noramco - Wilmington
Morphine Sulfate DMF 006967	Noramco – Wilmington	-
Oxycodone Hydrochloride DMF 020875	Noramco – Wilmington	Noramco – Wilmington
Oxymorphone Hydrochloride DMF 022816	Noramco – Wilmington	-

Purified Oxycodone Base DMF 021353	Noramco – Wilmington	-
Amphetamines DMF 029601 – 029604	Noramco – Wilmington	Noramco – Wilmington
Fentanyl Base DMF 028037	Noramco – Athens	-

JPI transferred full rights and ownership of the above DMFs. JPI still operates as a contract manufacturing and/testing facility on the following DMFs:

- Hydrocodone Bitartrate (DMF 021158) – manufacturing and testing
- Hydromorphone Hydrochloride (DMF 019561) – manufacturing and testing
- Methylphenidate Hydrochloride (DMF 022244) – manufacturing and testing
- Tapentadol Hydrochloride (DMF 021084) – manufacturing and testing
- Buprenorphine Hydrochloride (DMF 023683) – manufacturing and testing
- Buprenorphine Base (DMF 023684) – manufacturing and testing
- Fentanyl Base (DMF 028037) testing only until 07/01/17

JPI retains the rights and ownership of the following DMFs:

- Topiramate (DMF 010919)
- Methylphenidate Hydrochloride (DMF030510)
- Terconazole (DMF005925)
- Miconazole Nitrate (010913)

Major equipment changes since the last inspection include installation of a new R004 reactor at the end of 2015 with the first batch being run December 2015. Reactor System 008-R004 is a multi-function reactor system used for the production of multiple active pharmaceutical ingredients manufactured in Building 8 located on JPI's Athens site. I reviewed the associated IQ/OQ/PQ report 008-R004 and 008-R004-A001 (Agitator). No deficiencies were noted. Of note, R007 is scheduled for replacement during 2017.

During the previous inspection, a verbal observation was noted concerning glass integrity in the reactor lining. At the conclusion of the inspection, the firm was advised of reactor age and that some may require replacement. During the current inspection, Mr. Johnson provided a summary overview of the firm's efforts to prevent glass contamination in the product (**Exhibit 6**). In summary, the

product is dissolved, filtered and examined for insoluble matter. There is currently no technology to detect breakage above the liquid line in the reactor. Issues typically occur the line in the upper head. Rinses are used when clean; nozzles are checked manually at every cleaning. Vendor recommends spark testing. Glass is inert to essentially all chemistry. There is yet to be determined a method to specifically detect glass fractures in this equipment. Benjamin R. King presented the firm's current thinking in Quality Improvements Around Glass-Lined Equipment (**Exhibit 7**). The firm's efforts have concluded in the following:

- Glass monitoring alternatives explored and one unit purchased
- Alternatives determined to incur more risk than mitigated and were not implemented
- Site has completed several risk mitigation efforts based on FMEA's that have been successful in eliminating glass failures vs merely detecting failures after they have occurred

After witnessing a demonstration of the equipment and reviewing the reactor diagrams, I agree with the firm's assessment.

Pre-Approval Inspection

- My review of data for all of the below applications included review of Annual Product Reviews (APR), stability data, process validation, and executed batch records. No deficiencies were revealed.A209958/ORIG-1, Hydrocodone Bitartrate and Acetaminophen Tablets
- Topiramate (DMF 010919)
    - I reviewed the executed batch record for 15HN111. I also reviewed the associated APR. No deficiencies were noted.
- Methylphenidate Hydrochloride (DMF030510)
    - I reviewed the executed batch record for batch 16GN856. I also reviewed the associated APR. There were no returns or recalls associated with this time period (04/01/2015 – 03/31/2016). Two complaints (291606 and 367311) were reviewed. The APR was conducted as outlined in DS-SOP-2830.

My review of the data concludes that the firm (1) is ready for commercial manufacturing, (2) has conformed to the submitted DMFs, and (3) has submitted true data.

Management's responses to discussion items covered during the inspection and voluntary corrective actions are briefly addressed below:

During my review of the firm's complaint data, I noted a trend involving the Malvern Particle Sizer. It was revealed that the firm was not following its own SOP for equipment calibration. Specifically, section 5.10 of DS-SOP-10605 (Particle Sizer – Malvern – Mastersizer 2000, **Exhibit 8**) states the following: "*A Performance Verification should be performed by the manufacturer annually, or after the instrument have been moved or has non-routine maintenance.*" The most recent Malvern Qualification was documented as February 2014 (**Exhibit 9**). Prior to the closeout of the inspection, the firm scheduled qualification with the vendor (**Exhibit 10**). Qualification should be verified during the next inspection.

There have been no recalls since the last inspection.

No samples were collected.

X Johnetta F Walters
Investigator
Signed By: Johnetta F. Walters -S
Date Signed: 8/15/2017