CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205054Orig1s000

OTHER REVIEW(S)

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: June 10, 2018

TO: Julia Beaver, M.D.
Director
Division of Oncology Products (DOP1)
Office of Hematology and Oncology Products
Office of New Drugs

William Chong, M.D.
Director (Acting)
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Office of New Drugs

Atiqur Rahman, Ph.D.
Director
Division of Clinical Pharmacology V
Office of Clinical Pharmacology
Office of Translational Sciences

FROM: Gajendiran Mahadevan, Ph.D.
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Arindam Dasgupta, Ph.D.
Deputy Director
DNDBE
OSIS

SUBJECT: Surveillance inspection of (b) (4)

Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) conducted an inspection of the analytical portion of studies NON-RESPONSIVE GP-C-05-PRO (NDA 205054) conducted at (b) (4)

Form FDA 483 was issued at the inspection close-out. The final inspection classification is Voluntary Action Indicated (VAI).

Significant objectionable conditions were observed during this inspection that impacted the reliability of a portion of data

(b) (4)

The inspectional finding mentioned above is isolated in nature and did not affect the data from study NON-RESPONSIVE Therefore, I conclude that the data from study NON-RESPONSIVE and data from other bioanalytical studies using similar methods conducted by the site are reliable for further Agency review.

Inspected Studies:

NON-RESPONSIVE

Bioanalytical Study Conduct Dates: NON-RESPONSIVE

NDA 205054

Study Number: GP-C-05-PRO
Study Title: "Efficacy and safety of a new leuprolide acetate 22.5 mg depot formulation in the treatment of prostate cancer."
Bioanalytical Study Conduct Dates: March 2-May 10, 2016

Analytical site: (b) (4)

(b) (4)

OSIS scientist Gajendiran Mahadevan, Ph.D. audited the analytical portion of the above studies at (b) (4)

The inspection included a thorough examination of study records, facility, laboratory equipment, method validation, sample analyses, and interviews with the site's staff and management. As a part of surveillance approach, I selected and audited several key in vivo study components across multiple studies that best represent (b) (4) bioanalytical operations at (b) (4)

At the conclusion of the inspection, I observed objectionable conditions and issued a one-item Form FDA 483 to the analytical site. The Form FDA 483 observation (**Attachment-2**), the firm's response dated (b) (4) (**Attachment-3**), and my evaluation are presented below.

(b) (4)

(b) (4)

Conclusion:

Significant objectionable conditions were observed during this inspection and Form FDA 483 was issued. The final inspection classification is Voluntary Action Indicated (VAI).

(b) (4)

The inspectional finding is isolated in nature and did not affect the reliability of data from study NON-RESPONSIVE and other bioanalytical studies using similar methods conducted by the site (**Attachment-1**). Thus, the analytical data from studies using similar methods conducted between the previous inspection NON-RESPONSIVE and the end of the current surveillance interval should be reliable for review by the Agency without an inspection.

Gajendiran Mahadevan, Ph.D.
Pharmacologist
DNDBE, OSIS

Final Classification:

Analytical Site

VAI- b(4)
FEI#

cc:
OTS/OSIS/Kassim/Choe/Kadavil/Fenty-Stewart/Nkah/CDER-OSIS-BEQ@fda.hhs.gov
OTS/OSIS/DNDBE/Bonapace/Dasgupta/Ayala/Biswas/Mahadevan
OTS/OSIS/DGDBE/Cho/Jang/Choi/Skelly/Au

OND/OHOP/DOP1/Beaver
OND/ODEII/DEMP/Chong
OTS/OCP/Rahman/Song/Hamed

Draft: 07/05/2018; 07/10/2018
Edit: RCA 07/09/2018; 07/10/2018; AD 07/10/2018

ECMS: b(4)

OSIS File #: NON-RESPONSIVE (NDA 205054)

FACTS: b(4)

Attachment-1

Studies in support of Pending Applications

Application #	Study #	Study Type (in vitro)	Drug Name	Dates of conduct
NON-RESPONSIVE				
NDA 205054	GP-C-05-PRO	In Vivo	Leuprolide Acetate	March 2-May 10, 2016

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

/s/

GAJENDIRAN MAHADEVAN
07/10/2018

RUBEN C AYALA
07/10/2018

ARINDAM DASGUPTA
07/10/2018

M E M O R A N D U M **DEPARTMENT OF HEALTH AND HUMAN SERVICES**
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: June 5, 2015

TO: Geoffrey Kim,, M.D.
Director, Division of Oncology Products (DOP1)
Office of Hematology and Oncology Products
Office of New Drugs

Hylton V. Joffe, M.D., M.M.Sc
Director, Division of Bone, Reproductive and Urology Products (DBRUP)
Office of Drug Evaluation III
Office of New Drugs

John Peters, M.D.
Director (Acting)
Office of Bioequivalence
Office of Generic Drugs

FROM: Arindam Dasgupta, Ph.D.
Lead Pharmacologist
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Charles Bonapace, Pharm.D.
Director (Acting)
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Addendum to review of the Surveillance and "For Cause" Inspection of (b) (4) covering NDA 205054 (LUTRATE DEPOT, sponsored by GP Pharm S.A.); NON-RESPONSIVE

Summary:

At the request of the Division of Oncology Products 1 (DOP1) and the Division of Bone, Reproductive and Urology Products (DBRUP), the Office of Study Integrity and Surveillance (OSIS) conducted

an inspection of the analytical portion of the following bioequivalence studies conducted by [redacted] (b) (4) An additional study from a recently submitted [redacted] NON-RESPONSIVE was also selected as part of a surveillance approach to assess the firm's overall bioanalytical operations and capability to conduct bioequivalence studies.

[redacted] (b) (4)

Study Number: GP/C/05/PRO
Study Title: "Efficacy and safety of a new Leuprolide acetate 22.5 mg depot formulation, in prostate cancer"

NON-RESPONSIVE

[redacted]

OSIS provided an initial review of inspectional findings for the surveillance inspection at [redacted] (b) (4) (**Attachment A**). This addendum provides our evaluation of the response for observation #1:

Analytical site: [redacted] (b) (4)

NON-RESPONSIVE

[redacted]

[redacted] (b) (4) **Response:**

NON-RESPONSIVE

OSIS evaluation:

NON-RESPONSIVE

Recommendations:

Following the review and evaluation of the Form FDA 483 observation and the response from [redacted] (b) (4), the analytical data generated for NON-RESPONSIVE was not affected by the cited observation. Therefore, I recommend that the data for the analytical portion of NON-RESPONSIVE be accepted for agency review. My prior recommendation to accept the data for the analytical portion of studies [redacted] (b) (4) GP/C/05/PRO (NDA 205054) NON-RESPONSIVE remains the same.

Arindam Dasgupta, Ph.D.
Lead Pharmacologist
DNDBE, OSIS

Final Classification:

VAI – (b) (4)
(FEI# (b) (4)

DARRTS CC:

OSIS/Taylor/Haidar/Bonapace/Skelly/Choi/
OSIS/Dejernett/Nkah/Fenty-Stewart/Johnson
OSIS/DNDBE/Bonapace/Dasgupta/Cho
CDER/OND/ODEIII/DBRUP/Joffe/ Eufrecina P. Deguia
CDER/OND/OHOP/DOPI/Kim/ Charlene N Wheeler
OTS/OCP/DCPV/Song
OGD/Peters

Draft: AD 06/03/2015
Edits: CB 6/4/2015
OSI file#s: NDA 205054 NON-RESPONSIVE
ECMS: Cabinets/CDER_OC/OSI/Division of Bioequivalence & Good Laboratory Practice Compliance/INSPECTIONS/BE Program/Analytical Sites/ (b) (4)
FACTS: (b) (4)

Attachment A

M E M O R A N D U M **DEPARTMENT OF HEALTH AND HUMAN SERVICES**
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: April 15, 2015

TO: Geoffrey Kim,, M.D.
Director, Division of Oncology Products (DOP1)
Office of Hematology and Oncology Products
Office of New Drugs

Hylton V. Joffe, M.D., M.M.Sc
Director, Division of Bone, Reproductive and Urology Products (DBRUP)
Office of Drug Evaluation III
Office of New Drugs

John Peters, M.D.
Director (Acting)
Office of Bioequivalence
Office of Generic Drugs

FROM: Arindam Dasgupta, Ph.D.
Lead Pharmacologist
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Charles Bonapace, Pharm.D.
Director (Acting)
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Surveillance and "For Cause" Inspection of (b) (4) covering NDA 205054 (LUTRATE DEPOT, sponsored by GP Pharm S.A.); NON-RESPONSIVE

Summary:

At the request of the Division of Oncology Products 1 (DOP1) and the Division of Bone, Reproductive and Urology Products (DBRUP), the Office of Study Integrity and Surveillance (OSIS) conducted an inspection of the analytical portion of the following

bioequivalence studies conducted by (b) (4) An additional study from a recently submitted NON-RESPONSIVE was also selected as part of a surveillance approach to assess the firm's overall bioanalytical operations and capability to conduct bioequivalence studies. **Additional details including study conduct dates can be found in Attachment 1.**

(b) (4)

Study Number: GP/C/05/PRO
Study Title: "Efficacy and safety of a new Leuprolide acetate 22.5 mg depot formulation, in prostate cancer"

NON-RESPONSIVE

The inspection of the analytical portion of these studies was conducted by Arindam Dasgupta Ph.D.(Lead Pharmacologist, DNDBE/OSIS) at (b) (4) The audit included a thorough examination of facilities and equipment, review of study records and correspondence, and interviews and discussions with (b) (4) management and staff. As part of global assessment of the firm's bioanalytical operations, several key study components that best represent the firm's bioanalytical operations were selected and audited across the studies. Recent or ongoing studies were also selected for audit to gain a better perspective of (b) (4) current bioanalytical operations. OSIS audited the studies requested by DBRUP and DOP1 using the above surveillance approach.

(b) (4)

Following the inspection of (b) (4) Form FDA 483 was issued (**Attachment 2**). OSIS received a written response to the inspectional finding from (b) (4) on (b) (4) (**Attachment 3**). (b) (4) also indicated that they intend to provide a second response containing additional data by end of (b) (4) The Form FDA 483 observations, (b) (4) response, and our evaluation of the observations follow.

NON-RESPONSIVE

Firm's Response: NON-RESPONSIVE

NON-RESPONSIVE

OSIS Evaluation: (b) (4)

[redacted]

[redacted]

Conclusion:

Following the review and evaluation of the Form FDA 483 observations and the response from [redacted] the analytical data generated for studies [redacted] **GP/C/05/PRO,** [redacted] were not affected by the cited deficiency. Therefore, I recommend that the data for the analytical portions of studies [redacted] **GP/C/05/PRO (NDA 205054),** [redacted] be accepted for further agency review. The analytical data generated for the study [redacted] can be accepted for agency review following the submission of [redacted]

Arindam Dasgupta, Ph.D.
Lead Pharmacologist
DNDBE, OSIS

Final Classification:

VAI – (b) (4)
(FEI# (b) (4)

DARRTS CC:

OSIS/Taylor/Haidar/Bonapace/Skelly/Choi/
OSIS/Dejernett/Nkah/Fenty-Stewart/Johnson
OSIS/DNDBE/Bonapace/Dasgupta/Cho
CDER/OND/ODEIII/DBRUP/Joffe/ Eufrecina P. Deguia
CDER/OND/OHOP/DOPI/Kim/ Charlene N Wheeler
OTS/OCP/DCPV/Song
OGD/Peters

Draft: AD 04/15/2015
Edits: CB 04/15/2015
OSI file#s: NDA 205054 NON-RESPONSIVE
NON-RESPONSIVE
ECMS: Cabinets/CDER_OC/OSI/Division of Bioequivalence & Good Laboratory Practice Compliance/INSPECTIONS/BE Program/Analytical Sites/ (b) (4)
FACTS: (b) (4)

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

/s/

ARINDAM DASGUPTA
04/15/2015

CHARLES R BONAPACE
04/16/2015

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

CLINICAL INSPECTION SUMMARY

DATE: March 11, 2015

TO: Charlene Wheeler, Regulatory Project Manager
YangMin (Max) Ning, M.D., Ph.D., Medical Reviewer
Division of Oncology Products 1

FROM: Lauren Iacono-Connors, Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

THROUGH**:** Susan Thompson, M.D.
Team Leader
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

Kassa Ayalew, M.D., M.P.H.
Branch Chief
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections

NDA: 205054

APPLICANT: GP-Pharm S.A.

DRUG: Lutrate Depot (leuprolide acetate for depot suspension: (b) (4) 22.5 mg)

NME: No

THERAPEUTIC CLASSIFICATION: Standard

INDICATION: For the palliative treatment of advanced prostate cancer.

CONSULTATION REQUEST DATE: October 8, 2014
INSPECTION SUMMARY GOAL DATE: March 31, 2015
DIVISION ACTION GOAL DATE: May 31, 2015
PDUFA DATE: May 31, 2015

I. BACKGROUND:

This 505 (b)(2) NDA seeks marketing approval of (b) (4) leuprolide depot (b) (4) (Lutrate Depot (b) (4) 22.5 mg every three months) for palliative treatment of advanced prostate cancer. (b) (4) the sponsor conducted a single arm trial in patients with prostate cancer. (b) (4) indication (treatment of prostate cancer) (b) (4) dosing regimen (b) (4) one injection every three months). The primary endpoint was achievement and maintenance of castration (defined as testosterone levels of ≤0.5 ng/mL) from Day 28 through Day 168.

The application for marketing in the U.S. is submitted as a 505 (b)(2), because leuprolide depot (b) (4) 22.5 mg are formulated under the same pharmaceutical form, are intended for the same indications, and have similar efficacy and safety profiles to that of the respective Lupron® Depot formulations authorized and marketed in the U.S.

Administration of leuprolide acetate results in an initial increase in circulating levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH), leading to a transient increase in levels of gonadal steroids. However, continuous administration of leuprolide acetate results in decreased levels of LH and FSH. As a result, testosterone is reduced in males to levels associated with castration (≤ 0.5 ng/mL in serum). According to the sponsor, these decreases are observed within two to four weeks after the start of treatment and are maintained as long as treatment continues. Castrate levels of testosterone in prostate cancer patients have been demonstrated for periods of up to seven years, and the effect is reversible upon discontinuation of drug therapy.

The application is supported by safety and efficacy results of (b) (4) GP/C/05/PRO, "Efficacy and Safety of a New Leuprolide Acetate 22.5 mg Depot Formulation in the Treatment of Prostate Cancer."

(b) (4) Study GP/C/05/PRO was conducted at 25 enrolling clinical centers in the U.S. Planned enrollment was 150 subjects. A total of 213 subjects were screened, and 163 subjects were enrolled into the study.

The clinical development (b) (4) is covered in IND 72790.

(b) (4) clinical sites were chosen for inspection. For Study GP/C/05/PRO Site 1 (Dr. Neal Shore, Myrtle Beach, SC) and Site 24 (Dr. Laurence Belkoff, Bala Cynwyd, PA) were inspected. (b) (4) These sites were selected for inspection based on enrollment of large numbers of study subjects and significant primary efficacy results pertinent to decision making.

II. RESULTS (by Site):

Name of CI or Sponsor/CRO, Location	Protocol #, Site #, and # of Subjects	Inspection Date	Final Classification
(b) (4)			
CI#3: Dr. Laurence Belkoff Urologic Consultants at SE PA 1 Presidential Blvd, Suite 100 Bala Cynwyd, PA 19004	Protocol: GP/C/05/PRO Site Number: 24 Number of Subjects: 27	February 5-12, 2015	VAI

Key to Classifications

NAI = No deviation from regulations.
VAI = Deviation(s) from regulations.
OAI = Significant deviations from regulations. Data unreliable.
Pending = Preliminary classification based on information in 483 or preliminary communication with the field; EIR has not been received from the field, and complete review of EIR is pending.

1. **CI#1: Dr. Neal Shore (b) (4) Study GP/C/05/PRO, Site 1)**

a. **What was inspected:** (b) (4) With respect to Study GP/C/05/PRO, the site screened twenty seven subjects, twenty four subjects were enrolled, and twenty four completed the study. All subjects' informed consent documents were reviewed. The record audit was in accordance with the clinical investigator compliance program, CP 7348.811. Most importantly, the testosterone levels generated by the local laboratory at this site, per protocol, were compared with the testosterone levels generated by (b) (4) used to generate testosterone level data for overall study and submission to NDA 205054) for determination of chemical castration and durability of this response. The record audit included comparison of source documentation to CRFs and data listings, with particular attention paid to inclusion/exclusion criteria compliance, adverse events, treatment regimens, and reporting of AEs in accordance with the protocol. The FDA investigator also assessed test article accountability, monitoring reports and financial disclosure records.

b. **General observations/commentary:** Generally, the investigator's execution of the protocol was found to be adequate. Records and procedures were clear, and generally well organized. The inspection revealed no significant deficiencies. The primary efficacy endpoint of chemical castration (testosterone level) generated by the local laboratory was consistent with that generated by the central laboratory and submitted to application for both studies. Review of source documentation for eligibility, treatment regimens, study drug administration cycles, and drug accountability found no discrepancies. A Form FDA 483 was not issued.

c. **Assessment of data integrity:** The data for Dr. Shore's site, associated with (b) (4) GP/C/05/PRO submitted to the Agency in support of NDA 205054, appear reliable based on available information.

Note: The general observations and actions on inspection are based on preliminary communications with the FDA field investigator. An inspection summary addendum will be generated if conclusions change upon receipt and review of the final EIR.

(b) (4)

(b) (4)

3. **CI#3: Dr. Laurence Belkoff (Study GP/C/05/PRO, Site 24)**

a. **What was inspected:** The site screened thirty seven subjects, and twenty seven subjects were enrolled. Twenty six subjects completed the study. Informed consent documents were verified for all enrolled subjects. The study records of fifteen subjects were comprehensively audited to verify data listings submitted to NDA 205054. The record audit was in accordance with the clinical investigator compliance program, CP 7348.811. Most importantly, the testosterone levels generated by the local laboratory at this site, per protocol, were compared with the testosterone levels generated by (b) (4) used to generate testosterone level data for overall study and submission to NDA 205054) for determination of chemical castration and durability of this response. The record audit included comparison of source documentation to CRFs and data listings, with particular attention paid to inclusion/exclusion criteria compliance, adverse events, treatment regimens, and

reporting of AEs in accordance with the protocol. Test article accountability, monitoring reports and financial disclosure records were also assessed.

b. General observations/commentary: Generally, the investigator's execution of the protocol was found to be adequate. The inspection revealed no significant deficiencies. Records and procedures were clear, and generally well organized. The primary efficacy endpoint of chemical castration (testosterone level) generated by the local laboratory was consistent with that generated by the central laboratory and submitted to application, with 3 exceptions. Per protocol the site used the central clinical laboratory for testosterone analyses at Visits 1, 5, 7, 9, and 10. The site also had their local clinical laboratory generated testosterone levels for the same time points but not the central laboratory results. The FDA field investigator verified that testosterone testing was performed per protocol. Dr. Belkoff stated that the local testosterone results should be similar between the local clinical laboratory and the central laboratory at the same time points. For three subjects (b) (6) the local laboratory had corresponding testosterone levels that were slightly greater than that reported by the central laboratory.

	Visit	Approx. Day	Local Laboratory Testosterone (ng/mL)	Central Laboratory Testosterone (ng/mL) [Listing 7]
Subject (b) (6)	1	-14 to -1	5.11	
	2	0		6.26
	3	2		8.21
	4	14		0.784
	5	**28**	**0.55**	**0.238**
	6	56		0.1
	7	84	0.6	0.141
	8	86		0.112
	9	112	0.4	0.119
	10	168	0.4	0.116
Subject (b) (6)	1	-14 to -1	5.61	
	2	0		5.95
	3	2		8.16
	4	14		2.95
	5	**28**	**0.54**	**0.341**
	6	56		0.129
	7	84	0.3	<0.100
	8	86		0.121
	9	112	0.26	<0.100
	10	168	0.37	<0.100

	Visit	Approx. Day	Local Laboratory Testosterone (ng/mL)	Central Laboratory Testosterone (ng/mL) [Listing 7]
Subject (b) (6)	1	-14 to -1	3.26	
	2	0		4.43
	3	2		4.54
	4	14		0.639
	5	**28**	**0.71**	**0.192**
	6	56		0.117
	7	84	0.46	0.147
	8	86		0.119
	9	112	0.45	0.139
	10	168	0.41	0.114

OSI Reviewer notes: OSI shared these findings with DOP1 Medical Reviewer Dr. YangMin (Max) Ning on (b) (6) Dr. Ning verified that the determination of castration for these studies relied on the testosterone levels measured by the central laboratory and not the individual site local laboratories. In addition, Dr. Ning clarified that since those discrepancies occurred on Day 28, the listed patients above would be considered "successful" for chemical castration. OSI and DOP1 are in agreement that the testosterone level discrepancies noted above between the local and central laboratories will have no impact on study outcome.

Review of source documentation for eligibility, treatment regimens, study drug administration cycles and drug accountability found no discrepancies. The inspection found a number of minor record keeping issues but nothing that would impact study safety and efficacy outcomes or subject safety. There was no evidence of underreporting of serious adverse events, however, there were several instances noted where adverse events were either not reported to the sponsor or misreported. A Form FDA 483 was issued citing one inspectional observation.

Observation 1: Failure to prepare or maintain adequate and accurate case histories with respect to observations and data pertinent to the investigation.

Specifically,

a. An injection site reaction described in Patient Diary 4 for Subject (b) (6) after the second administration of the test article was not reported to the sponsor in the eCRF.
b. A hot flash adverse event starting (b) (6) for Subject (b) (6) was evaluated as probably/likely relate icle, but was reported to the sponsor in the eCRF as not related.

c. The following adverse events for Subject (b) (6) were reported to the sponsor in the eCRF as recovered/resolved, when the adverse event worksheets did not indicate an outcome.
   A) Stomach pain starting (b) (6)
   B) Tremors starting (b) (6)

OSI Reviewer notes: For this study the Safety endpoints include the evaluation of the safety of the new formulation based on AEs, local tolerability, vital signs, World Health Organization (WHO)/Eastern Cooperative Oncologic Group (ECOG) performance status, bone pain, urinary pain, and urinary symptoms and after administration, occurrence of hot flushes and clinical laboratory and electrocardiogram (ECG) results.

The misreported AEs found during this inspection represent a small proportion of all AEs reported for this site. These observations appear to be isolated and non-systemic for this site and should not importantly impact overall study outcome for safety.

c. **Assessment of data integrity**: The data for Dr. Belkoff's site, associated with Study GP/C/05/PRO submitted to the Agency in support of NDA 205054, appear reliable based on available information.

III. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Based on the review of inspectional findings for clinical investigators Dr. Shore (b) (4) Study GP/C/05/PRO, Site 1), (b) (4) and Dr. Belkoff (Study GP/C/05/PRO, Site 24), the data for (b) (4) GP/C/05/PRO appear reliable.

The classification for clinical investigators Dr. Karlin and Dr. Shore (preliminary) is No Action Indicated (NAI). The classification for clinical investigator Dr. Belkoff is Voluntary Action Indicated (VAI).

With respect to the inspectional findings at Dr. Belkoff's site, the inspection found a number of minor record keeping issues but nothing that would impact study safety and efficacy outcomes or subject safety. There were several instances noted where adverse events were either not reported to the sponsor or misreported. The misreported AEs found during this inspection represent a small proportion of all AEs reported for this site. These observations appear to be isolated and non-systemic for this site and should not importantly impact overall study outcome for safety.

Based upon available information the overall data for (b) (4) GP/C/05/PRO in support of this application may be considered reliable based on available information.

Note: The observations noted above for Dr. Shore (b) (4) Study GP/C/05/PRO, Site 1) are based on the preliminary communications provided by the FDA field investigators. An inspection summary addendum will be generated if conclusions change significantly upon receipt and complete review of the EIRs.

{See appended electronic signature page}

Lauren Iacono-Connors, Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Susan D. Thompson, M.D.
Team Leader
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Kassa Ayalew, M.D., M.P.H.
Branch Chief
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

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

/s/

LAUREN C IACONO-CONNORS
03/11/2015

SUSAN D THOMPSON
03/11/2015

KASSA AYALEW
03/11/2015

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: November 6, 2014

TO: Amna Ibrahim, M.D.
Director (Acting)
Division of Oncology Products 1
Office of New Drugs

FROM: Charles Bonapace, Pharm.D.
Chief, Good Laboratory Practice Branch
Division of Bioequivalence and GLP Compliance (DBGLPC)
Office of Scientific Investigations (OSI)

SUBJECT: **FY 2015, CDER PDUFA, High Priority Directed Pre-Approval Data Validation Inspection, Bioresearch Monitoring, Human Drugs, CP 7348.001**

RE: NDA 205054
DRUG: Leuprolide acetate for depot suspension (LUTRATE DEPOT)
SPONSOR: GP Pharm S.A., Sant Quinti De Mediona Barcelona, Spain

This memo acknowledges receipt of your request for an inspection of the analytical portion of the following bioequivalence (BE) studies.

(b) (4)

[redacted]

Study #2: GP/C/05/PRO
Study Title: "Efficacy and safety of a new Leuprolide acetate 22.5 mg depot formulation, in prostate cancer"

The Office of Scientific Investigations (OSI) will conduct the inspection of the analytical portion of the above studies.

OSI requests that OND not reveal detailed information regarding the inspection to the applicant or to the study site prior to the start of the inspection. The site will receive this information during the inspection opening meeting. The inspection will be conducted under Bioresearch Monitoring Compliance Program CP 7348.001, not under CP 7348.811 (Clinical Investigators).

DBGLPC POC: Arindam Dasgupta, Ph.D.
Pharmacologist
Office of Scientific Investigations
Tel: 1-301-796-3326
Fax: 1-301-847-8748
E-mail: arindam.dasgupta@fda.hhs.gov

DARRTS cc:
OSI/DBGLPC/Taylor/Bonapace/Haidar/Choi/Dasgupta/Skelly/Gupta
OSI/DBGLPC/Fenty-Stewart/Nkah/Dejernett/Johnson
CDER/OND/PM/Wheeler/Ibrahim

Draft: HG 10/30/2014
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