

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT OFFICE ADDRESS AND PHONE NUMBER United States Food and Drug Administration 12420 Parklawn Drive, Room 2032 Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 10/08-11,15&16/2018
	FEI NUMBER 3011566408

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: Mr. Jaime del Campo, Site Head Director

FIRM NAME Gadea Biopharma S.L.	STREET ADDRESS Parque Tecnológico de León, C/Nicostrato Vela S/N
CITY, STATE AND ZIP CODE León 24009, Spain	TYPE OF ESTABLISHMENT INSPECTED Contract sterile injectable drug products manufacturer

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:


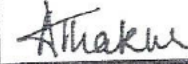
Preapproval Inspection (PAI):

(b) (4) (b) (4) (b) (4) mg/ml Inj. (b) (4)
 (b) (4) (b) (4) (b) (4) mg/ml Inj. (b) (4)
 (b) (4) (b) (4) Inj. (b) (4) mg (b) (4) ml

OBSERVATION 1
 The information stated in the submitted drug application is not exactly as is on site. Specifically, drug application (b) (4) states that the firm is ready for inspection and identified as having functions, responsibilities, and operations including primary packaging and vial labeling. On site observation revealed no labeling equipment and currently site has no capability to perform labeling operations for vials.

OBSERVATION 2
 Labeling equipment is not qualified in preparation for commercialization of drug product. Specifically, one of the responsible functions described in the drug application (b) (4) is labeling and labeling machine is in placed to perform labeling operation for (b) (4) but is not currently qualified.

OBSERVATION 3
 There are no established written procedures for handling labeling and packing operations. For examples,
 A. Procedures describing in sufficient detail the controls employed for the issuance of labeling are not written.
 B. Written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination and testing of labeling and packaging materials.
 C. Procedures designed to assure that correct labels, labeling and packaging materials are used for drug products are not written.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE  	EMPLOYEE(S) NAME AND TITLE (Print or Type) Kham Phommachanh, Consumer Safety Officer Aditi S. Thakur, Chemist Reviewer	DATE ISSUED 10/16/2018
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OBSERVATION 4



The Certificate of Analysis from the drug application does not match the raw data from the analytical test records and specification sheet. Specifically, drug application (b) (4) the related substance impurities results provided in the COA approved on 10/21/2016 for the batches (b) (4) submitted to the agency does not match the reported results on raw data on the specification sheet for all the corresponding batches.

- a) For batch (b) (4) the related substance HPLC (%w/w) COA submitted in the application did not match the Analytical Development Specification
- b) For batch (b) (4) the related substance HPLC (%w/w) COA submitted in the application did not match the Analytical Development Specification
- c) For batch (b) (4) the related substance HPLC (%w/w) COA submitted in the application did not match the Analytical Development Specification

OBSERVATION 5

Original records of analysis submitted in the drug application was not available. Specifically, the original COA record for (b) (4) for batches (b) (4) were not available. Specifically,

- a) The original copy of the COA record approved on 10/21/2016 submitted in the application for the batches (b) (4) was not available.
- b) The original copy of the COA record approved on 10/21/2016 submitted in the application for the batches (b) (4) was not available.
- c) The original copy of the COA record approved on 10/21/2016 submitted in the application for the batches (b) (4) was not available.

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OBSERVATION 6

There is no established written procedure in the event of change in the version of the Certificate of Analysis.

Specifically, controls and procedures to track change history for the certificates of analysis (CoA), which document whether a drug meets specifications, to prevent unauthorized changes to a CoA after quality unit approval is deficient. For example,
 A. ^{(b) (4)} Batch ^{(b) (4)} three version of COA approved on 10/21/2016, 03/31/2017, 10/15/2018 were found without providing any unique identification number on the document.
 B. ^{(b) (4)} Batch ^{(b) (4)} three version of COA approved on 10/21/2016, 03/31/2017, 10/15/2018 were found without providing any unique identification number on the document.
 C. ^{(b) (4)} Batch ^{(b) (4)} three version of COA approved on 10/21/2016, 03/31/2017, 10/15/2018 were found without providing any unique identification number on the document.

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