### DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION DISTRICT ADDRESS AND PHONE NUMBER 09/19/2019-09/27/2019\* ORA OPQO HQ, Room #2032 3007373532 12420 Parklawn Drive, Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry Mr. Madan Mohan Reddy, Director FIRM NAME Aurobindo Pharma Limited Unit VII, Formulation Plant, Plot S-1, Survey 411, 425, 434-435, 458, TSIIC, Green Industrial Park CITY, STATE, ZIP CODE, COUNTRY TYPE ESTABLISHMENT INSPECTED Polepally, Mahaboob Nagar, Finished Product Manufacturer Telangana, 509302, India

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

# DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

#### OBSERVATION 1

There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically, your firm's investigations were found to be deficient in that the Out of Specification (OOS) results have been invalidated for various tests without identifying scientifically sound and justifiable root causes. Human errors and instruments error have been attributed as major potential root causes and passing retest results have been reported. Our review of your OOS Investigations during the period beginning January 2017 until September 2019 revealed the following for U.S. marketed products:

| Category                   | Total OOS | Total Invalided | % Invalidated* |
|----------------------------|-----------|-----------------|----------------|
| Raw Material               | 112       | 102             | 91%            |
| In-Process                 | 85        | 65              | 76%            |
| Hold Time Study            | 16        | 15              | 94%            |
| Process Validation         | 42        | 18              | 43%            |
| Finished Product Testing   | 172       | 112             | 65%            |
| Finished Product Stability | 72**      | 72              | 100%           |

\*rounded, \*\*excludes exhibit batches

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE

Tamil Arasu, Investigator

Jogy George, Investigator

Emmanuel J. Ramos, Investigator

FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 1 OF 14 PAGES

|  | DEPARTMENT OF HEALT<br>FOOD AND DRUG   |   |   |   |
|--|--|---|---|---|
| DISTRICT ADDRESS AND PHO   |  | ADMINISTRATIO                                     | DATE(S) OF INSPECTION   | VM 22 20  |
| ORA OPQO HQ,   | Room #2032   |   | 09/19/2019-09/27,<br>FEINUMBER  | /2019*  |
| 12420 Parkla   | awn Drive, Rockville, MD 20857   |   | 3007373532  |   |
| ORAPHARMInte   | rnational483responses@fda.hhs  | s.gov   |   |   |
| Industry Information   | n: www.fda.gov/oc/industry   |   |   |   |
|  | han Reddy, Director  |   |   |   |
| FIRM NAME  |  | STREET ADDRESS                                    |   |   |
| Aurobindo Ph   | arma Limited   |   | Formulation Plan  |   |
|  |  |   | 11, 425, 434-435,<br>dustrial Park  | 456, ISIIC,   |
| CITY, STATE, ZIP CODE, COUN  |  | TYPE ESTABLISHM                                   |   |   |
|  | Mahaboob Nagar,<br>509302, India   | Finished  | Product Manufacti   | ırer  |
| retailgalla,   | 309302, Illata   |   |   |   |
| Examples includ  | e, but are not limited to, the following   | ing investiga                                     | ations:   |   |
| (A) OOS Invest   | tigation FUSTOOS190024 for (b) (   | 4)  |   | Tablets (b) mg  |
| batches (b) (4)  | inguitor 1 001 0 001 7 002 4 101 (-7)  | ,   | was initi   | ated on 04/29/2019  |
|  | say failures during the 3M stability   | testing (25°                                      |   |   |
| incorrect sonicat  | ion time as the probable root cause.   | Based on the                                      | nis assumption, 5 hypo  | othesis studies were  |
| initiated using (b)  |  |   | without intermittent si   |   |
|  | for (b) mins sonication with intermi   |   |   |   |
| failing results an   | d hypothesis results are as follows:   |   | O Comment Production and American   |   |
|  |  |   |   |   |
|  |  | I Company   |   |   |
|  | Batch No.  |   | Assay (%)   |   |
| -(b) (4)   | Batch No.  | [5  | Assay (%) Specification: (b) (4) to   | b) (4) %]   |
| -(b) (4)   | Batch No.  | [5  | Assay (%) Specification: (b) (4) (b) (4)                                    | b) (4) ½]   |
| -(b) (4)   | Batch No.  | [5  | Assay (%) Specification: (b) (4) (b) (4)                                    | b) (4) ½]   |
| -(b) (4)<br>-<br>-   | Batch No.  | [5  | Assay (%) Specification: (b) (4) (b) (4)                                    | b) (4) %]   |
| -(b) (4)<br>-<br>-   |  | [8  | Assay (%) Specification: (b) (4) (b) (4)                                    | b) (4) ½]   |
| -(b) (4)<br>-<br>-<br>-  | Hypothesis Study   | [5  | (b) (4)   | b) (4) ½]   |
| -(b) (4)<br>-<br>-<br>-  | Hypothesis Study Hypotheis-1A(b) mins  | [5  | Assay (%) Specification: (b) (4) (b) (4)                                    | b) (4) ½]   |
| -(b) (4)<br>-<br>-<br>-  | Hypothesis Study Hypothesis-1A(b) mins Hypothesis-1B,  | [5  | (b) (4)   | b) (4) ½]   |
| -(b) (4)   | Hypothesis Study Hypotheis-1A(b) mins Hypothesis-1B, Hypotheis-1C, mins  | [5  | (b) (4)   | b) (4) ½]   |
| -(b) (4)   | Hypothesis Study Hypotheis-1A(b) mins Hypothesis-1B, Hypotheis-1C, Hypothesis-1D, mins   |   | (b) (4)   | b) (4) ½o]  |
| -(b) (4)   | Hypothesis Study Hypotheis-1A(b) mins Hypothesis-1B, Hypotheis-1C, mins  | [5  | (b) (4)   | b) (4) ½ ]  |
|  | Hypothesis Study Hypotheis-1A(b) mins Hypothesis-1B, Hypothesis-1C, Hypothesis-1D, mins Hypothesis-2, (b) mins (per STP)   |   | (b) (4)   |   |
| We were unable   | Hypothesis Study Hypotheis-1A(b) mins Hypothesis-1B, Hypotheis-1C, Hypothesis-1D, mins Hypothesis-2, (b) mins (per STP)  to determine if the hypothesis studi  | ies were act                                      | (b) (4)   | ifically, our review  |
| We were unable indicated that all                                    | Hypothesis Study Hypotheis-1A(b) mins Hypothesis-1B, Hypotheis-1C, Hypothesis-1D, mins Hypothesis-2, (b) mins (per STP)  to determine if the hypothesis studil associated analytical worksheets  | es were act                                       | (b) (4)  ually conducted. Speciported hypothesis stud                       | ifically, our review  |
| We were unable indicated that all sonication time of                 | Hypothesis Study  Hypothesis-1A(b) mins Hypothesis-1B, mins Hypothesis-1C, mins Hypothesis-1D, mins Hypothesis-2, (b) mins (per STP)  to determine if the hypothesis studil associated analytical worksheets of (b) minutes. The analytical worksheets   | ies were act for the purposheets were             | (b) (4)  ually conducted. Speciported hypothesis stude reviewed and approve | ifically, our review lies have the same wed by the QC and                             |
| We were unable indicated that all sonication time of                 | Hypothesis Study Hypotheis-1A(b) mins Hypothesis-1B, Hypotheis-1C, Hypothesis-1D, mins Hypothesis-2, (b) mins (per STP)  to determine if the hypothesis studil associated analytical worksheets  | ies were act for the purposheets were             | (b) (4)  ually conducted. Speciported hypothesis stude reviewed and approve | ifically, our review lies have the same wed by the QC and                             |
| We were unable indicated that all sonication time of                 | Hypothesis Study  Hypothesis-1A(b) mins Hypothesis-1B, mins Hypothesis-1C, mins Hypothesis-1D, mins Hypothesis-2, (b) mins (per STP)  to determine if the hypothesis studil associated analytical worksheets of (b) minutes. The analytical worksheets   | ies were act for the purposheets were             | (b) (4)  ually conducted. Speciported hypothesis stude reviewed and approve | ifically, our review lies have the same wed by the QC and                             |
| We were unable indicated that all sonication time of                 | Hypothesis Study  Hypothesis-1A(b) mins Hypothesis-1B, mins Hypothesis-1C, mins Hypothesis-1D, mins Hypothesis-2, (b) mins (per STP)  to determine if the hypothesis studil associated analytical worksheets of (b) minutes. The analytical worksheets   | ies were act for the purposheets were             | (b) (4)  ually conducted. Speciported hypothesis stude reviewed and approve | ifically, our review lies have the same wed by the QC and                             |
| We were unable indicated that all sonication time of QA personnel. W | Hypothesis Study  Hypothesis-1A(b) mins  Hypothesis-1B,  Hypothesis-1C,  Hypothesis-1D,  Mins  Mypothesis-2, (b)  mins (per STP)  to determine if the hypothesis studil associated analytical worksheets  of (b)  minutes. The analytical worksheets  of (c)  mins   | ies were act for the purposheets were             | (b) (4)  ually conducted. Speciported hypothesis stude reviewed and approve | ifically, our review<br>lies have the same<br>wed by the QC and<br>hypothesis studies |
| We were unable indicated that all sonication time of QA personnel. W | Hypothesis Study Hypotheis-1A(b) mins Hypothesis-1B, Hypothesis-1C, Hypothesis-1D, mins Hypothesis-2, (b) mins (per STP)  to determine if the hypothesis studil associated analytical worksheets of (b) minutes. The analytical worksheets of (a) minutes. The analytical worksheets of (b) mins (c) m | ies were act for the purposheets were             | (b) (4)  ually conducted. Speciported hypothesis stude reviewed and approve | ifically, our review lies have the same wed by the QC and hypothesis studies          |
| We were unable indicated that all sonication time of QA personnel. W | Hypothesis Study  Hypothesis-1A(4)  Hypothesis-1B,  Hypothesis-1C,  Hypothesis-1D,  mins  mins  mins  mins  mins  mins  mins  mins  mins  Hypothesis-2, (b)  mins (per STP)  to determine if the hypothesis studil associated analytical worksheets  of (b)  minutes. The analytical worksheets  of (a)  ewere unable to ascertain how the lease  employee(s) SIGNATURE  Tamil Arasu, Investigator  Jogy George, Investigator  | ies were act for the purposheets were ow Assay va | (b) (4)  ually conducted. Speciported hypothesis stude reviewed and approve | ifically, our review lies have the same wed by the QC and hypothesis studies          |
| We were unable indicated that all sonication time of QA personnel. W | Hypothesis Study  Hypotheis-1A(b) mins  Hypothesis-1B, Hypothesis-1C, Hypothesis-1D, mins  Hypothesis-1D, mins (per STP)  to determine if the hypothesis studi associated analytical worksheets of (b) minutes. The analytical work were unable to ascertain how the least temployee(s) SIGNATURE  Tamil Arasu, Investigator   | ies were act for the purposheets were ow Assay va | (b) (4)  ually conducted. Speciported hypothesis stude reviewed and approve | ifically, our review lies have the same wed by the QC and hypothesis studies          |

|   | DEPARTMENT OF HEALT<br>FOOD AND DRUG   |  |  |  |  |
|---|--|--|--|--|--|
| DISTRICT ADDRESS AND PHON   |  | 3 10 11 11 11 11 11 11 11 11 11 11 11 11   | DATE(S) OF INSPECTION  | 0.1  |  |
| ORA OPQO HQ,  | Room #2032   |  | 09/19/2019-09/27/201<br>FEI NUMBER   | 9*   |  |
|   | awn Drive, Rockville, MD 20857   |  | 3007373532   |  |  |
|   | rnational483responses@fda.hhs  |  |  |  |  |
|   |  |  |  |  |  |
| Industry Information  | : www.fda.gov/oc/industry  |  |  |  |  |
| Mr. Madan Mol   | nan Reddy, Director  |  |  |  |  |
| FIRM NAME   |  | STREET ADDRESS   |  |  |  |
| Aurobindo Pha   | arma Limited   | Unit VII   | , Formulation Plant,   | Plot S-1,  |  |
| l   |  |  | 11, 425, 434-435, 458  | , TSIIC,   |  |
| CITY, STATE, ZIP CODE, COUN   | TRY  | Green Ir   | Idustrial Park   |  |  |
| Polepally, 1  | Mahaboob Nagar,  | Finished   | ed Product Manufacturer  |  |  |
|   | 509302, India  |  |  |  |  |
| sonication of san<br>market.  (B) OOS Investig  | es were utilized to conclude that the apples. All four impacted batches congation FU7STOOS190023 for (b) (4)   | overed in th   | nis investigation are curren  USP (b)  | tly in the U.S.  (4) mg(b) (4)   |  |
| (b) (4) %, (b) (4) % w/w) found dur (b) (4) with(b) (4) experiment 1 usin requirement. Ex experiment 2 yiel solution was con the product's for for the same imp (b) (4) | mg(b) (4) was initiated on (6) for the (b) (4) Related Coming Related Substance testing at (a). The investigation concluded hur During the extended laboratory in an intentionally contaminated bear periment 1 yielded (b) (4) % for the same impurity. Sidered to confirm the presence of ced degradation study which was courity. It is unclear how the firm utility to draw an equivalent corring the hypothesis study.  | the 9-mon<br>man error convestigation<br>aker with (b)<br>the (b) (4)<br>However, 1<br>b) (4)<br>onducted usilized the (b) | gainst a specification limit that time point (25°C/ 60% aused by the use of a contain, two hypothesis studies who (4) and experiment and pH measurement of the compount in the sample. The firm a fing (b) (4) that yielded a wing | of NMT (b) % %RH, batch # minated beaker ere conducted; nt 2 as per STP d (b) whereas, original sample also referenced value of (b) (4) % ormed with (b) |  |
| (C) OOS Investi   | gation FU7STOOS190044 for (b) (  | (4)  | Т  | ablets (b) mg,   |  |
| batch #s(b) (4)   | was in   | itiated on 0   | 7/29/2019 to investigate th  |  |  |
|   | 3-month stability testing (25°C/ 60  |  | he OOS results were obtain   |  |  |
| Organic Impurity testing (by HPLC). Specifically, (b) (4) yielded OOS   |  |  |  |  |  |
|   | $\frac{1}{6}$ (w/w) and $\frac{1}{6}$ (b) (4) $\frac{1}{6}$ (w/w) agains   |  |  |  |  |
| (b) (4)   |  |  | ation concluded that the ro  |  |  |
| to analyst error  | (i.e. sample sonication at the inco  | orrect temp  | perature of 40°C vs. the S   | TP sonication  |  |
|   | EMPLOYEE(S) SIGNATURE  | -1   |  | DATE ISSUED  |  |
| SEE REVERSE   | Tamil Arasu, Investigator  | TA   | E  | 09/27/2019   |  |
| OF THIS PAGE  | Jogy George, Investigator  |  | (Ja)   |  |  |
|   | Emmanuel J. Ramos, Investiga   | ator   |  |  |  |
|   | The state of the s |  |  |  |  |
| FORM FDA 483 (09/08)  | PREVIOUS EDITION OBSOLETE INSP   | PECTIONAL O  | BSERVATIONS  | PAGE 3 OF 14 PAGES   |  |

| DEPARTMENT OF HEALTH AND HUMAN SERVICES  |  |  |                                |                 |  |  |
|--|--|--|--------------------------------|-----------------|--|--|
| DISTRICT ADDRESS AND PHON  | FOOD AND DRUG  | ADMINISTRATIO  | N DATE(S) OF INSPECTION        |                 |  |  |
| Dietitio Fiberico Fito   | The Court of the C |  | 09/19/2019-09/27/2019*         |                 |  |  |
|  | ORA OPQO HQ, Room #2032  |  | FEI NUMBER                     |                 |  |  |
|  | wn Drive, Rockville, MD 20857  |  | 3007373532                     |                 |  |  |
| ORAPHARMINTE   | rnational483responses@fda.hhs  | .gov   |                                |                 |  |  |
| Industry Information   | : www.fda.gov/oc/industry  |  |                                |                 |  |  |
| Service and the service and th |  |  |                                |                 |  |  |
| Mr. Madan Mol  | nan Reddy, Director  | STREET ADDRESS   |                                |                 |  |  |
| Aurobindo Pha  | arma Limited   | 15 Maria Conservation  | , Formulation Plant, Plot S-1, |                 |  |  |
| narobinao in   | alia de la constanta de la con |  | 11, 425, 434-435, 458, TSIIC,  |                 |  |  |
|  |  | Green In   | dustrial Park                  |                 |  |  |
| CITY, STATE, ZIP CODE, COUNT   |  | TYPE ESTABLISHME   | Product Manufacturer           |                 |  |  |
|  | Mahaboob Nagar,<br>509302, India   | rinished   | Product Manufacturer           |                 |  |  |
| Terangana,   | 509502, India  |  |                                |                 |  |  |
| temperature requ   | irement of 5±3°C). The hypothesis  | studies that   | t were conducted to substa     | ntiate the root |  |  |
|  | gested that the impurity increases b   |  |                                |                 |  |  |
|  | sample is sonicated at 40°C. The   |  |                                | prove that the  |  |  |
|  | c is the root cause of significantly hi  | The state of the s |                                |                 |  |  |
|  | The initial results were invalidated   |  |                                |                 |  |  |
| result of record. H  |  |  | both commercially distribu     |                 |  |  |
|  | xpiry date of 01/31/2021.  | arc  | both commercially distribu     | ted in the O.S. |  |  |
| market with an e.  | xpiry date of 01/31/2021.  |  |                                |                 |  |  |
| Product Complai  | nt Investigations:   |  |                                |                 |  |  |
| 1 Todact Compiai   | nt investigations.   |  |                                |                 |  |  |
| (D) Savaral of v   | our complaint investigations of bro  | ven tablets  | or cancules since 2017 con     | sclude that the |  |  |
|  | ect was obtained after the product I   |  |                                |                 |  |  |
|  | applaint investigation and the packag  |  |                                |                 |  |  |
|  |  |  |                                |                 |  |  |
| observed that all the product rejects were re-inspected and repackaged after visual inspection. Broken or defective units (tablets/capsules) are part of the rejection criteria on the packaging lines. For example:   |  |  |                                |                 |  |  |
| detective diffic (tablets/capsules) are part of the rejection effects on the packaging lines. For example,   |  |  |                                |                 |  |  |
| 1. Complaint APL-7-2018-PC-1-54327337 was received on 10/16/2018 because the customer  |  |  |                                |                 |  |  |
| found several bottles containing broken capsules of (b) (4)  Capsules USP  |  |  |                                |                 |  |  |
|  |  |  |                                |                 |  |  |
| (4) ng   | (b) ng, batch #(b) (4) Complaint investigation APL-FU7-2018-USA-PCM-00375 was opened by the firm on 17/10/2018. The packaging batch record for this lot has documented   |  |                                |                 |  |  |
|  |  |  |                                |                 |  |  |
| that a   | pproximately (b) (4) capsules wer  | e rejected o   | auring initial primary pack    | les were good   |  |  |
| Visual   | inspection of the rejected capsule<br>les and were repackaged (no broke  | s it was io  | ware noted). The details       |                 |  |  |
|  |  |  |                                | or tills visual |  |  |
| inspection were not documented such as how it was performed.   |  |  |                                |                 |  |  |
| 2 G 1 1 1 PG2010 0672 are received an 07/22/2010 because the systeman found 27 broken  |  |  |                                |                 |  |  |
| 2. Complaint PC2019-0672 was received on 07/22/2019 because the customer found 27 broken tablets throughout (b) bottles of (b) (4) Tablets USP (b) mg, batch #(b) (4)  |  |  |                                |                 |  |  |
| tablet   | s throughout (4)   | Table  | is OSF (b) ling, batch #(b)    | . 7)            |  |  |
|  |  |  |                                |                 |  |  |
|  |  |  |                                |                 |  |  |
|  | EMPLOYEE(S) SIGNATURE  | TA   |                                | DATE ISSUED     |  |  |
| SEE REVERSE  | Tamil Arasu, Investigator  | (1)  | (Fa)                           | 09/27/2019      |  |  |
| OF THIS PAGE   | Jogy George, Investigator  |  | (00)                           |                 |  |  |
|  | Emmanuel J. Ramos, Investiga   | ator   |                                |                 |  |  |

INSPECTIONAL OBSERVATIONS

FORM FDA 483 (09/08)

PREVIOUS EDITION OBSOLETE

PAGE 4 OF 14 PAGES

| DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION |               |                                  |  |                                      |
|--|---------------|----------------------------------|--|--------------------------------------|
| DISTRICT ADDRESS AND PHONE NUMBER                                    |               | DATE(S) OF INSPECTION            |  |                                      |
|  |               | 09/19/2019-09/27/2019*           |  |                                      |
| ORA OPQO HQ, Room #2032<br>12420 Parklawn Drive, Rockville, MD 20857 |               | 3007373532                       |  |                                      |
|  |               |                                  |  | ORAPHARMInternational483responses@fd |
| URAPHARMINTELNACIONAL4031eSponSeSeld                                 | la.IIIIS.gov  |                                  |  |                                      |
| X 1 2 X 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2                              |               |                                  |  |                                      |
| Industry Information: www.fda.gov/oc/industry                        |               |                                  |  |                                      |
| 7. H. C.                         |               |                                  |  |                                      |
| Mr. Madan Mohan Reddy, Director                                      |               |                                  |  |                                      |
| FIRM NAME  | STREET ADDRE  | SS                               |  |                                      |
| Aurobindo Pharma Limited   | Unit V        | II, Formulation Plant, Plot S-1, |  |                                      |
|  | Survey        | 411, 425, 434-435, 458, TSIIC,   |  |                                      |
|  |               | Industrial Park                  |  |                                      |
| CITY, STATE, ZIP CODE, COUNTRY                                       | TYPE ESTABLIS | HMENT INSPECTED                  |  |                                      |
| Polepally, Mahaboob Nagar,   | Finishe       | ed Product Manufacturer          |  |                                      |
|  |               |                                  |  |                                      |
| Telangana, 509302, India   |               |                                  |  |                                      |

Complaint investigation APL-FU7-2019-USA-PCM-00728 was opened by the firm on 07/24/2019. The packaging batch record for this lot has documented that approximately tablets were rejected during initial primary packaging. After visual inspection of the rejected tablets it was found that all (b) (4) tablets were good tablets and were repackaged (no broken tablets were noted). The details of this visual inspection were not documented such as how it was performed.

- 3. Complaint PC2018-0010 was received on 01/16/2018 because the customer found 42 broken tablets throughout (b) bottles of (b) (4) Tablets USP (b) mg, batch #(b) (4) Complaint Investigation CU02018-U07 was opened by the firm on 01/17/2018. The packaging batch record for this lot has documented that approximately (b) (4) tablets were rejected during initial primary packaging. After visual inspection of the rejected tablets it was found that all (b) (4) tablets were good tablets and were repackaged (no broken tablets were noted). The details of this visual inspection were not documented such as how it was performed.
- 4. Complaint PC2018-0326 was received on 08/13/2018 because the customer found one bottle with 32 broken tablets of (b) (4) Tablets USP (b) ng, batch # (b) (4) Complaint investigation APL-FU7-2018-USA-PCM-00257 was opened by the firm on 16/08/2018. The packaging batch record for this lot has documented that approximately (b) (4) tablets were rejected during initial primary packaging. After visual inspection of the rejected tablets it was found that all (b) (4) tablets were good tablets and were repackaged (no broken tablets were noted). The details of this visual inspection were not documented such as how it was performed.
- 5. Complaint PC2018-0338 was received on 08/16/2018 because the customer found a broken tablet of (b) (4) Tablets USP (b) (4) mg, batch (b) (4)

  Complaint investigation APL-FU7-2019-USA-PCM-00261 was opened by the firm on

| SEE REVERSE<br>OF THIS PAGE | Tamil Arasu, Investigator  Jogy George, Investigator  Emmanuel J. Ramos, Investigator | 09/27/2019 |
|-----------------------------|---|------------|
|-----------------------------|---|------------|

| DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION  |  |  |  |  |
|---|--|--|--|--|
| DISTRICT ADDRESS AND PHONE NUMBER   | DATE(S) OF INSPECTION 09/19/2019-09/27/2019*   |  |  |  |
| ORA OPQO HQ, Room #2032<br>12420 Parklawn Drive, Rockville, MD 2085<br>ORAPHARMInternational483responses@fda.hr | 7 3007373532   |  |  |  |
| Industry Information: www.fda.gov/oc/industry  NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED               |  |  |  |  |
| Mr. Madan Mohan Reddy, Director   |  |  |  |  |
| FIRM NAME   | STREET ADDRESS   |  |  |  |
| Aurobindo Pharma Limited  | Unit VII, Formulation Plant, Plot S-1,<br>Survey 411, 425, 434-435, 458, TSIIC,<br>Green Industrial Park |  |  |  |
| CITY, STATE, ZIP CODE, COUNTRY  | TYPE ESTABLISHMENT INSPECTED   |  |  |  |
| Polepally, Mahaboob Nagar,<br>Telangana, 509302, India  | Finished Product Manufacturer  |  |  |  |

(b) (4) tablets were rejected during initial primary packaging. After visual inspection of the rejected tablets it was found that all tablets were good tablets and were repackaged (no broken tablets were noted). The details of this visual inspection were not documented such as how it was performed.

- (E) Product complaint Number APL-FU7-2019-USA-00068 for (b) (4) Tablets USP (b) (4) batch (b) (4) was initiated following a complaint received on 01/23/2019. The complaint reported from this U.S. distributed batch was for an unknown discolored (i.e. greyish) material embedded in the tablet. The investigation concluded that the greyish foreign material could be due to 'processing of hard remnants settled at the bottom of the (b) (4) equipment utilized during batch manufacturing. Additionally, UV spectrum of the purported complaint sample (b) (4) mg) was generated and compared with a (b) (4) standard solution (b) (4) mg) using an Assay method. Deficiencies with the investigation include, but are not limited to:
  - Failure to investigate the root cause of greyish discoloration. The finished product is a (b) (4) (b) (4)
  - Failure to describe in the UV analysis work sheet if the sample prepared representing the complaint sample of (b) (4) mg included the greyish unknown material from the returned complaint sample. This is not specifically described in the work sheet. Additionally, the UV spectrum only indicates the presence of (b) (4) in the purported complaint sample that was analyzed. However, there is no evidence provided to conclusively substantiate that the greyish material is free of other potential degradants. No other physiochemical analysis was considered to positively identify the structure/composition of the greyish foreign material.
  - The retain samples from this batch were visually checked as part of the complaint investigation.
     The samples were not checked to verify if any embedded material is inside the retain tablets.
- (F) A product complaint report APL-FU7-2019-USA-PCM-00774 reported from the U.S market was

| SEE REVERSE          | Tamil Arasu, Investigator                           | 09/27/2019         |
|----------------------|---|--------------------|
| OF THIS PAGE         | Jogy George, Investigator                           |                    |
|                      | Emmanuel J. Ramos, Investigator                     |                    |
| FORM FDA 483 (09/08) | PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS | PAGE 6 OF 14 PAGES |

| DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION  |  |  |  |  |
|---|--|--|--|--|
| DISTRICT ADDRESS AND PHONE NUMBER   | DATE(S) OF INSPECTION  |  |  |  |
|   | 09/19/2019-09/27/2019*   |  |  |  |
| ORA OPQO HQ, Room #2032   | 3007373532   |  |  |  |
| 12420 Parklawn Drive, Rockville, MD 2   | 20857  |  |  |  |
| ORAPHARMInternational483responses@fda   | a.hhs.gov  |  |  |  |
| Industry Information: www.fda.gov/oc/industry  NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  M.S. Madara Mohara Baddy Disposit or a |  |  |  |  |
| Mr. Madan Mohan Reddy, Director   |  |  |  |  |
| FIRM NAME   | STREET ADDRESS   |  |  |  |
| Aurobindo Pharma Limited  | Unit VII, Formulation Plant, Plot S-1,<br>Survey 411, 425, 434-435, 458, TSIIC,<br>Green Industrial Park |  |  |  |
| CITY, STATE, ZIP CODE, COUNTRY  | TYPE ESTABLISHMENT INSPECTED   |  |  |  |
| Polepally, Mahaboob Nagar,<br>Telangana, 509302, India  | Finished Product Manufacturer  |  |  |  |

found in the QA documentation room on inspection day 1 (09/19/2019). This document was signed by the author on 09/14/2019 indicating all associated tasks during the complaint investigation (including control sample evaluation) was completed on or before 09/14/2019. However, review of your control sample retrieval history in LIMS and other associated documentation indicate the control samples were not evaluated until 2 days after the report was authored (i.e., on 09/16/19). The document's author did not provide any explanation for the discrepancy in control sample evaluation dates in the report and LIMS.

## **OBSERVATION 2**

There are no written procedures for production and process controls designed to assure that the drug products have identity, strength, quality, and purity they purport or are represented to possess.

Specifically,

(A) We observed the presence and use of executed batch manufacturing records that were not identified in the records presented during the inspection. When requested for the complete list of executed batches for(b) (4) Capsules (b) mg and (b) mg (b) (4) your firm provided a list of (4) full batches (each involving (b) stages) of which 3 of them were submission batches. The Vice President of Quality stated that no additional batches were made other than the batches included on the list. However, review of the firm's record management system (Data Storage and Retrieval System) audit trail showed that additional batch records have been issued and executed. For example, the following issued batch records were not included in the provided list but shown in the audit trail:

| SEE REVERSE    |
|----------------|
| OLL ILLITOR    |
| OF THIS PAGE   |
| 01 11110 17100 |

EMPLOYEE(S) SIGNATURE

Tamil Arasu, Investigator

Jogy George, Investigator

Emmanuel J. Ramos, Investigator



DATE ISSUED

09/27/2019

FORM FDA 483 (09/08)

INSPECTIONAL OBSERVATIONS

| DISTRICT ADDRESS AND PHONE NUMBER             | DATE(S) OF INSPECTION                 |
|---|---------------------------------------|
|   | 09/19/2019-09/27/2019*                |
| ORA OPQO HQ, Room #2032                       | FEI NUMBER                            |
| 12420 Parklawn Drive, Rockville, MD           | 20857 3007373532                      |
| ORAPHARMInternational483responses@f           | da.hhs.gov                            |
|   |                                       |
| Industry Information: www.fda.gov/oc/industry |                                       |
|   |                                       |
| Mr. Madan Mohan Reddy, Director               |                                       |
| FIRM NAME                                     | STREET ADDRESS                        |
| Aurobindo Pharma Limited                      | Unit VII, Formulation Plant, Plot S-  |
|   | Survey 411, 425, 434-435, 458, TSIIC, |
|   | Green Industrial Park                 |
|   | TYPE ESTABLISHMENT INSPECTED          |
| CITY, STATE, ZIP CODE, COUNTRY                |                                       |
| Polepally, Mahaboob Nagar,                    | Finished Product Manufacturer         |
|   | Finished Product Manufacturer         |
| Polepally, Mahaboob Nagar,                    | Finished Product Manufacturer         |

According to the firm's electronic records, approximately (b) additional batch records for this product have been issued but not executed. The (b) (4) application for (b) (4)

Capsules (b) mg and (b) mg (b) (4) is currently under is currently under review by the FDA.

(B) Review of the re-issuance of records maintained by the Quality Assurance department indicated more than 100 logged events of batch record (or related documents) issuance in an uncontrolled Excel Sheet. The reasons for re-issuance identified in the file was either 'server is down', 'half pages downloaded', 'due to printer error', etc. However, several records have remained unaccounted for and the firm was unable to provide any record of reconciliation during the inspection. In addition, the destruction records maintained by the QA department do not include any printed/unexecuted batch records. Examples of unaccounted documents include batch records, protocols, etc. For example;

Capsules, USP (b) mg) Batch record (b) (4) (b) (4)

Tablets, USP(b) (4)mg) Batch record (b) (4) ((b)(4)

Capsules,  $USP_{(4)}^{(b)} mg_{(4)}^{(b)} mg$ ) Batch record BRSA18053-A (b) (4)

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE

Tamil Arasu, Investigator

Jogy George, Investigator

Emmanuel J. Ramos, Investigator

TA

DATE ISSUED 09/27/2019

INSPECTIONAL OBSERVATIONS FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE

PAGE 8 OF 14 PAGES

|  | DEPARTMENT OF HEALT<br>FOOD AND DRUG                 |                                   |  |                 |  |
|--|--|-----------------------------------|--|-----------------|--|
| DISTRICT ADDRESS AND PHONE NUMBER  |  | DATE(S) OF INSPECTION             | - 100 <sub>0</sub> 2   |                 |  |
| ORA OPQO HQ, Room #2032  |  | 09/19/2019-09/27/201<br>FEINUMBER | 9*   |                 |  |
| PLATERIAL DE PRINCIPAL DE L'ADRIGUE DE L'ADR | wn Drive, Rockville, MD 20857                        |                                   | 3007373532   |                 |  |
|  | rnational483responses@fda.hhs                        |                                   |  |                 |  |
| Industry Information   | Eda govlaslindustm                                   |                                   |  |                 |  |
| NAME AND TITLE OF INDIVIDU   | n: www.fda.gov/oc/industry  AL TO WHOM REPORT ISSUED |                                   |  |                 |  |
|  | han Reddy, Director                                  |                                   |  |                 |  |
| FIRM NAME  | Ti-i4-J  | STREET ADDRESS                    | The second secon |                 |  |
| Aurobindo Ph   | arma Limited   | Survey 4                          | , Formulation Plant, 1<br>11, 425, 434-435, 458,   | Plot S-1,       |  |
|  |  | Green In                          | Industrial Park  |                 |  |
| CITY, STATE, ZIP CODE, COUN  |  | TYPE ESTABLISHME                  | NT INSPECTED   |                 |  |
| The state of the s | Mahaboob Nagar,<br>509302, India                     | Finished                          | Product Manufacturer   |                 |  |
| Totaligalia,   | JUJJUZ, IIIGIA                                       |                                   |  |                 |  |
| OBSERVATIO   | N 3  |                                   |  |                 |  |
| Control proced   | ures are not established which                       | of those n                        | nanufacturing processes  | that may be     |  |
| responsible for  | causing variability in the char-                     | acteristics                       | of in-process material a   | and the drug    |  |
| product.   |  |                                   | GARAGE CO.   |                 |  |
|  |  |                                   |  |                 |  |
| Specifically,  |  |                                   |  |                 |  |
| (A) Your approa  | nch to commercial process validation                 | on (PV) is                        | deficient Several example  | es were found   |  |
|  | e first attempted commercial valid                   |                                   |  |                 |  |
|  |  |                                   |  |                 |  |
|  | lidation campaigns have intermitted                  |                                   |  |                 |  |
|  | initial commercial PV attempt. The                   |                                   |  |                 |  |
|  | dly with a root cause, and 3 PV batc                 |                                   |  |                 |  |
|  | ess performance qualification lacks                  |                                   |  |                 |  |
|  | examples of U.S. marketed product                    |                                   |  | dation batches  |  |
| failed or during s   | subsequent post-validation commerc                   | ial campaig                       | ns that failed are:  |                 |  |
| 1. (b) (4) Tablets USP (b) mg (first 3 commercial batches failed)  |  |                                   |  |                 |  |
| Tablets USP(b) mg (4 PV batches failed)  |  |                                   |  |                 |  |
| 3.   | (4)  |                                   |  |                 |  |
| 4. <b>(b) (4)</b>  | Capsules USP (1 post valida                          |                                   |  | .aneu)          |  |
| 4. (6)(.)  | Capsules OSF (1 post valida                          | llon ( )                          | batch failed)  |                 |  |
| (B) The sample of  | uantities used to establish (b) (4) hol              | d time are r                      | ot representative of the bu  | ]k(b) (4) batch |  |
| sizes. For examp   | le, the sample quantity used to esta                 | ablish hold                       | time for several (b) (4)   | products is     |  |
| approximately (b   | grams irrespective of the batch                      | size. This                        | approach was utilized b  | v the firm in   |  |
|  | hold time for approximately (b) (4)                  |                                   | products intended for the U  |                 |  |
| VV   | note that to approximately                           |                                   | producto intended 101 mil  | J.O. Hamile     |  |
|  |  |                                   |  |                 |  |
|  |  |                                   |  |                 |  |
|  |  |                                   |  |                 |  |
|  | EMPLOYEE(S) SIGNATURE                                | -1                                |  | DATE ISSUED     |  |
| SEE REVERSE  | Tamil Arasu, Investigator                            | TA                                |  | 09/27/2019      |  |
| OF THIS PAGE   | Jogy George, Investigator                            |                                   | (FG)   |                 |  |
|  |  | tor                               |  |                 |  |
|  | Emmanuel J. Ramos, Investiga                         | 101                               |  |                 |  |

INSPECTIONAL OBSERVATIONS

PAGE 9 OF 14 PAGES

FORM FDA 483 (09/08)

#### DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION DISTRICT ADDRESS AND PHONE NUMBER 09/19/2019-09/27/2019\* ORA OPQO HQ, Room #2032 FEI NUMBER 3007373532 12420 Parklawn Drive, Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry Mr. Madan Mohan Reddy, Director FIRM NAME STREET ADDRESS Aurobindo Pharma Limited Unit VII, Formulation Plant, Plot S-1, Survey 411, 425, 434-435, 458, TSIIC, Green Industrial Park TYPE ESTABLISHMENT INSPECTED CITY STATE ZIP CODE COUNTRY Polepally, Mahaboob Nagar, Finished Product Manufacturer Telangana, 509302, India

## **OBSERVATION 4**

Laboratory records do not include complete data derived from all tests, examinations and assay necessary to assure compliance with established specifications and standards.

Specifically,

Review of the electronic audit trails from the Tiamo software application that operates Auto titrators Karl-Fischer titrators indicated repeated events of 'Determination stopped', 'Determination reprocessed', 'Determination interrupted' and 'Determination error' during the progress of test runs. For example, during the test runs, the following incidents were observed between April 2018 and September 2019:

| Instrument ID | Number of Times<br>Stopped | Number of Times<br>Error Message | Number of Times<br>Interruption | Number of Times<br>Reprocessed |
|---------------|----------------------------|----------------------------------|---------------------------------|--------------------------------|
| KFAZ0001      | 3                          | 0                                | 2                               | 3                              |
| KFAZ0003      | 4                          | 8                                | 3                               | 6                              |
| KFAZ0004      | 7                          | 6                                | 1                               | 3                              |
| KFAZ0006      | 3                          | 5                                | 6                               | 5                              |
| KFAZ0007      | 7                          | 0                                | 10                              | 15                             |
| KFAZ0008      | 7                          | 21                               | 2                               | 2                              |
| POAZ0001      | 7                          | 4                                | 3                               | 3                              |

The 'Determination error' message included event such as Communication lost with device. However, your quality unit did not periodically review these audit trails and assess what may have caused these events. You also failed to investigate what those interruptions are and why the analysts may have stopped during a run. Some of the products that were running during this purported communication loss include,

| but are not limited to, (b) (4) | USP, (b) (4)      | USP, (b) (4) | USP, (b) (4) | USP,      |
|---------------------------------|-------------------|--------------|--------------|-----------|
| (b) (4)                         | Capsules, (b) (4) | Capsules,    | (b) (4)      | Capsules, |

| <br>MPLOYEE(S) SIGNATURE  Tamil Arasu, Investigator  Jogy George, Investigator | 09/27/2019 |
|--|------------|
| Emmanuel J. Ramos, Investigator  |            |

FORM FDA 483 (09/08)

PREVIOUS EDITION OBSOLETE

|  | HEALTH AND HUMAN SERVICES ID DRUG ADMINISTRATION   |
|--|--|
| DISTRICT ADDRESS AND PHONE NUMBER  | DATE(S) OF INSPECTION 09/19/2019-09/27/2019*   |
| ORA OPQO HQ, Room #2032 12420 Parklawn Drive, Rockville, MD ORAPHARMInternational483responses@fd Industry Information: www.fda.gov/oc/industry |  |
| NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED   |  |
| Mr. Madan Mohan Reddy, Director  |  |
| FIRM NAME  | STREET ADDRESS   |
| Aurobindo Pharma Limited   | Unit VII, Formulation Plant, Plot S-1,<br>Survey 411, 425, 434-435, 458, TSIIC,<br>Green Industrial Park |
| CITY, STATE, ZIP CODE, COUNTRY   | TYPE ESTABLISHMENT INSPECTED   |
| Polepally, Mahaboob Nagar,   | Finished Product Manufacturer  |

(b) (4) Capsules, etc. The following table summarizes the approximate number of OOS investigations pertaining to Karl-Fischer auto titrators since January 2017:

|                             | Valid OOS | Invalid OOS |
|-----------------------------|-----------|-------------|
| Stability                   | 4         | 8           |
| Others (RM, In-Process, FP) | 7         | 47          |

## **OBSERVATION 5**

The responsibilities and procedures applicable to the quality control unit are not fully followed.

Specifically,

(A) Several lists of documents requested were either provided as incomplete, inaccurate, and or explained with potentially misleading statements throughout the inspection. For example, on 09/24/2019 (day 4 of the inspection), two (2) representatives from the Corporate Quality group stated independently that there are no Aberrant Results Investigations associated with In-Process testing of product lots manufactured at Unit VII. The same quality personnel stated that they are also responsible for review of Aberrant Results investigations. However, the list of Aberrant Results investigations provided on day 1 included approximately 11 investigations for in-process results directly contradicting the statements provided. The corporate quality personnel who answered our questions were later found not to have undergone training on the Aberrant Results investigation SOP.

(B) An original Aberrant Investigation Report Form (No. ABR/QC/030/19, date of initiation: 04/08/2019) for (b) (4) Tablets, USP (b) batch #(b) (4) and (b) (4) Tablets USP (b) mg/ (b) (4) mg batch #s (b) (4) was found in the QA documentation room. The 10-page document with attachments had the original signatures of the author (signed 04/21/2019) and reviewer

| SEE REVERSE  | The state of the s | tor TA                    | 09/27/2019    |
|--------------|--|---------------------------|---------------|
| OF THIS PAGE | Jogy George, Investiga   | tor (OG)                  |               |
|              | Emmanuel J. Ramos, Inv   | estigator                 |               |
|              | AND AND TO STOLE OF STATE  | INSPECTIONAL OBSERVATIONS | PAGE II OF 14 |

|  | ALTH AND HUMAN SERVICES<br>RUG ADMINISTRATION  |
|--|--|
| DISTRICT ADDRESS AND PHONE NUMBER  | DATE(S) OF INSPECTION 09/19/2019-09/27/2019*   |
| ORA OPQO HQ, Room #2032  12420 Parklawn Drive, Rockville, MD 208  ORAPHARMInternational483responses@fda.h  Industry Information: www.fda.gov/oc/industry |  |
| Mr. Madan Mohan Reddy, Director  |  |
| FIRM NAME  | STREET ADDRESS   |
| Aurobindo Pharma Limited   | Unit VII, Formulation Plant, Plot S-1,<br>Survey 411, 425, 434-435, 458, TSIIC,<br>Green Industrial Park |
| CITY, STATE, ZIP CODE, COUNTRY   | TYPE ESTABLISHMENT INSPECTED   |
| Polepally, Mahaboob Nagar,<br>Telangana, 509302, India   | Finished Product Manufacturer  |

(signed 04/22/2019) with no signature of the final QA approver. Your DGM-QA stated that the document was intended for destruction. However, no explanation was provided when the index list of 2019 Aberrant Investigation Reports had ABR/QC/030/19 listed as a "closed" investigation. This aberrant investigation report was initiated to investigate the below LOQ results obtained and reported for the (b) (4) content in the batches listed above.

- (C) An original Aberrant Investigation Report Form (No. ABR/QC/058/19) for (b) (4)

  (b) (4) Tablets USP(b) mg (batch(b) (4) ) was found in the QA documentation room. This 24-page document details the manufacturing investigation conducted to determine the root cause of total impurities result of (b) (4) % against a specification limit of NMT(b) %. The report had signatures of the author (dated 06/28/2019) and reviewer/department head (dated 06/28/2019) with missing signatures of the QA in-Charge and Head QA/Corporate Quality Head. Your DGM-QA did not provide a clear explanation for the status of the report and why it had remained unsigned while the 2019 Aberrant Investigation Reports index (provided during the investigation) had ABR/QC/058/19 assigned to another unrelated product lot.
- (D) Several product samples in (b) (4) bottles with labels that indicated "Samples for Analysis" and other unknown product samples in Ziplock bags containing no identifiable information were found in the QA documentation room. Your DGM-QA stated that the samples pertain to complaint samples however, no accompanying documentation was available to substantiate the claim. In addition, the samples with the labels "Samples for Analysis" as per the DGM-QA were allegedly pulled based on Inter Office Communication(s). No documentation was available for our review to substantiate the origin or the intended purpose of the product samples that were found in the QA documentation room.
- (E) Too numerous to count executed batch records were found stored in an In-Process QA (Packing) room in the (b) (4) block on day 1 of the inspection. The batch records were stored under a section labelled "Waiting for COA". The GM-Production explained that batch records awaiting release of FP COAs are stored in the area. However, several batch records with accompanying COAs were found in the area and

| SEE REVERSE<br>OF THIS PAGE   | Emmanuel J. Ramos, In     | gator                     | 09/27/2019    |
|-------------------------------|---------------------------|---------------------------|---------------|
| FORM FDA 483 (09/08)<br>PAGES | PREVIOUS EDITION OBSOLETE | INSPECTIONAL OBSERVATIONS | PAGE 12 OF 14 |

|  | F HEALTH AND HUMAN SERVICES<br>AND DRUG ADMINISTRATION   |
|--|--|
| ORA OPQO HQ, Room #2032 12420 Parklawn Drive, Rockville, MD ORAPHARMInternational483responses@f Industry Information: www.fda.gov/oc/industry NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Mr. Madan Mohan Reddy, Director | DATE(S) OF INSPECTION 09/19/2019-09/27/2019* FEI NUMBER 3007373532                                       |
| FIRM NAME  | STREET ADDRESS   |
| Aurobindo Pharma Limited   | Unit VII, Formulation Plant, Plot S-1,<br>Survey 411, 425, 434-435, 458, TSIIC,<br>Green Industrial Park |
| CITY, STATE, ZIP CODE, COUNTRY   | TYPE ESTABLISHMENT INSPECTED   |
| Polepally, Mahaboob Nagar,<br>Telangana, 509302, India   | Finished Product Manufacturer  |

several had missing final approval by Quality Assurance on the batch records. In addition, finished product lots with unapproved batch records (by QA) were found in a released status in the Oracle based ERP system. For example, the following U.S marketed batches had a released status in the ERP system:

| # N / A | Product | Batch Number | Release Status in<br>Batch Record as<br>of 9/19/19 | ERP Release<br>Date/Time | Batch<br>Shipment<br>Date |
|---------|---------|--------------|--|--------------------------|---------------------------|
| (b) (4) |         |              | Incomplete   | 30-AUG-2019 10:38:14     | 11-SEP-2019               |
|         |         |              | Incomplete   | 31-AUG-2019 10:32: 23    | 06-SEP-2019               |
|         |         |              | Incomplete   | 05-SEP-2019 13:07:35     | 13-SEP-2019               |

- **(F)** Your computer system administrator for multiple laboratory equipment was discovered to have a reporting structure directly within the quality assurance department. The system administrator stated during the inspection that he is involved in the review of electronic audit trails from multiple laboratory systems. This reporting structure provides no confidence in maintaining the integrity of electronic data without potential conflict of interest.
- (G) On 09/19/2019, we discovered the use of uncontrolled documents in the QC laboratory. This included a large bound log book that included entries of OOS investigations. This log book is not part of any QC-related SOPs and not officially issued by the Quality unit.

#### **OBSERVATION 6**

Equipment and utensils are not cleaned at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

PAGES

| SEE REVERSE          | ()   | 09/27/2019    |
|----------------------|--|---------------|
| OF THIS PAGE         | Jogy George, Investigator  Emmanuel J. Ramos, Investigator |               |
|                      | Emmanuel J. Ramos, Investigator                            |               |
| FORM FDA 483 (09/08) | PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS        | PAGE 13 OF 14 |

| ORA OPQO HQ, Room 2032 12420 Parklawn Drive, Rockville, MD 20857 ORAPHARMINTERNATIONAL 83 responses 8 fda.hhs.gov  Industry Information www.fda.gov/Orindustry Wark Montrol Forecout Township Report Township  |  | DEPARTMENT OF HEALT<br>FOOD AND DRUG    |                |                                 |   |  |
|--|--|---|----------------|---------------------------------|---|--|
| DRA OPOO HQ, Room #2032 12420 Parklam Drive, Rockville, MD 20857 ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/toc/industry  www.material 9 selector towardsaferation  Mr. Madan Mohan Reddy, Director  **Monitor  Mr. Madan Mohan Reddy, Director  **Monitor  Aurobindo Pharma Limited  On September 19, 2019, a cleaned (b) (d)  Area (b) was found with visible unknown residue inside the (b) (d)  Area (b) was found with visible unknown residue inside the (b) (d)  Area (b) was found with visible unknown residue inside the (b) (d)  The location was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (b) (d) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (b) (d)  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (d)  **DATES OF INSPECTION  **DATES OF INSPECTION  9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE  OF THIS PAGE  **DATES OF INSPECTION  10  | DISTRICT ADDRESS AND PHON  |   | IDMINISTRATIC  | DATE(S) OF INSPECTION           |   |  |
| TORSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handlling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (1914)  **DATES OF INSPECTION*  SINGER PROCESS  STATE OF THIS PAGE  DIALY 17 PROCESS  DIALY 17 PROCESS  STATE OF THIS PAGE  DIALY 17 PROCESS  DIALY 17 PROCESS  STATE OF THIS PAGE  DIALY 17 PROCESS  DIALY 17 PROCESS  STATE OF THIS PAGE  DIALY 17 PROCESS  DATE SEARCH 17 PRO | ORA OPOO HO  | Room #2032                              |                |                                 | 3*  |  |
| Discussive Information www.fda.gov/cofindustry  Mr. Madan Mohan Reddy, Director  FRANCE  FROM Madan Mohan Reddy, Director  FRANCE  FRA |  |   |                | 3007373532                      |   |  |
| Mr. Madan Mohan Reddy, Director    Marobindo Pharma Limited   Street Roomes    |  |   |                |                                 |   |  |
| Mr. Madan Mohan Reddy, Director    Marobindo Pharma Limited   Street Roomes    |  |   |                |                                 |   |  |
| Mr. Madan Mohan Reddy, Director    Marobindo Pharma Limited   STREETAGRESS   Unit VII, Formulation Plant, Plot S-1, Survey 411, 425, 434-435, 458, TSIIC, Green Industrial Park   Prolepally, Mahaboob Nagar, Telangana, 509302, India   Prolepally, 40001, 10cated in Manufacturer   Prolepal | Industry Information   | : www.fda.gov/oc/industry               |                |                                 |   |  |
| Aurobindo Pharma Limited    Single Aurobindo Pharma Limited   Unit VII, Formulation Plant, Flot S-1, Survey 411, 425, 434-435, 458, TSIIC, Green Industrial Park   Polepally, Mahaboob Nagar, Telangana, 509302, India   (Equip No. 1014)   (Aurobina Park Transparent Park Transparent Park Transparent Park   (Equip No. 1014)   (Equip No. 10 |  |   |                |                                 |   |  |
| Survey 411, 425, 434-435, 458, TSIIC, Creen Industrial Park Polepally, Mahaboob Nagar, Telangana, 509302, India  On September 19, 2019, a cleaned (b) (4) (Equip No. (b) (4) (A) (A) (A) (A) (A) (A) (A) (A) (A) (A  |  | ian nadaj, birabat                      | STREET ADDRESS |                                 |   |  |
| Green Industrial Park Polepally, Mahaboob Nagar, Telangana, 509302, India  On September 19, 2019, a cleaned (b)(4)  Area (b) a found with visible unknown residue inside the (b)(4)  Area (b) a found with visible unknown residue inside the (b)(4)  Area (b) a found with visible unknown residue inside the (b)(4)  The location was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (b)(4)  In a (cation that was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (b)(4)  In a (cation that was found in an analysis to identify the source of powder ferside. The body in a cation that was found in accessible when required during product than analysis to identify the source of powder ferside. The body in a cation that was found in accessing the source of powder ferside. The body in a cation that was found in accessing the source of powder ferside. The body i | Aurobindo Pha  | arma Limited                            | Unit VII       | , Formulation Plant, 1          | Plot S-1,   |  |
| Polepally, Mahaboob Nagar, Telangana, 509302, India  On September 19, 2019, a cleaned (b) (4) (Equip No. (b) (4) (M) in a location that was approximately (b) (9) behind the (b) (9) The location was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (b) (9) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (b) (4) In a (b) (7) has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (4) mg batch (4) (6) (7) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION  9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  Tamil Arasu, Investigator  Jogy George, Investigator  Jogy George, Investigator  Jogy George, Investigator  Jogy George, Investigator  |  |   |                |                                 | TSIIC,  |  |
| On September 19, 2019, a cleaned (D) (4) (Equip No. (D) (4) A0001, located in (D) (4) Area (D) was found with visible unknown residue inside the (D) (4) in a location that was approximately (D) (4) behind the (D) (4) The location was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (D) (4) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (D) (4) in a (D) (4) has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a property labelled red crate. However, during inspection of your packaging operation of U.S. bound product (D)   | CITY, STATE, ZIP CODE, COUN  | TRY                                     |                |                                 |   |  |
| On September 19, 2019, a cleaned (b) (d) (Equip No. (b) (4) A0001, located in (b) (4) Area (b) was found with visible unknown residue inside the (b) (4) in a location that was approximately (b) (d) behind the (b) (d) The location was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (b) (d) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (b) (d) (d) has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (d) Capsules (d) mg batch (d) (d) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION  9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  OF TH | Polepally, 1   | Mahaboob Nagar,                         | Finished       | Product Manufacturer            |   |  |
| Area (b) was found with visible unknown residue inside the (b) (d) . The location that was approximately (b) (d) behind the (b) (d) . The location was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (b) (d) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (b) (d) in a (b) has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (d) Capsules (d) in giaspection of your packaging operation of U.S. bound product (b) (d) Capsules (d) in giaspection of the material status.  *DATES OF INSPECTION  9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  OF THIS PAGE  DATE SURVEY SEARCH UNDER THE PAGE THE PAGE OF THE BABBOR THE BABBOR OPERATIONS  Joy George, Investigator  Emmanuel J. Ramos, Investigator  DATE SURVEY SEARCH OPERATIONS  PAGE OF THIS PAGE OF THIS PAGE THE PAGE OF THE BABBOR OPERATIONS  PAGE OF THIS PAGE |  |   |                |                                 |   |  |
| Area (b) was found with visible unknown residue inside the (b) (d) . The location that was approximately (b) (d) behind the (b) (d) . The location was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (b) (d) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (b) (d) (d) with a state potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (d) Capsules (d) mg batch (d) (d) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  OF THIS PAGE  DATE SURVEY BEAUTION  1  |  |   |                | (h) (4)                         | (b) (4)   |  |
| approximately (b)(4) behind the (b)(4). The location was found inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (b)(4) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (b)(4) (b) in a (b)(4) has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b)(4) (Capsules (b) (a) (Capsules (b) (d) (Capsules (b) (d) (d) (d) (d) (d) (d) (d) (d) (d) (d   |  |   |                |                                 |   |  |
| inaccessible when requested to take a swab sample and conduct an analysis to identify the source of powder residue. The (D)(4) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (D)(4) (D) in a (D)(4) has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (D)(4) (Capsules (D)(4) (D) (D) (D) (D) (D) (D) (D) (D) (D) (D   |  |   | side the (b)   |                                 |   |  |
| powder residue. The (b)(4) was documented on the log book as C-cleaned and verified by production personnel. The C-cleaning is procedurally required during product changeovers. An unclean (b)(4) has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7 Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b)(4) Capsules (h) mg batch #(b)(4)  the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  OATE INSURED  DATE INSURED  DAT |  |   |                |                                 |   |  |
| personnel. The C-cleaning is procedurally required during product changeovers. An unclean (b) (4)  (b) in a (b) (4) has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (h) mg batch #(b) (4) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  Tamil Arasu, Investigator Jogy George, Investigator Jogy George, Investigator Jogy George, Investigator Jogy George, Investigator  |  |   |                |                                 |   |  |
| has the potential to contaminate products that are loaded on to the machine during routine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (4) In good batch (b) (4) Capsules (4) In good batch (b) (4) In good batch (b) (5) Capsules (6) In good batch (c) (c) Capsules (d) In good batch |  |   |                |                                 |   |  |
| Toutine operation.  OBSERVATION 7  Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (4) mg batch #(b) (4) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  EMPLOYEE(9) SIGNATURE Tamil Arasu, Investigator Jogy George, Investigator Emmanuel J. Ramos, Investigator Emmanuel J. Ramos, Investigator   |  |   |                |                                 |   |  |
| OBSERVATION 7 Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4)  Capsules (4)  Table (4)  The procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4)  Capsules (b)  Table (b) (4)  The procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4)  The procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in specific of your packaging operation of your packaging operation of your packaging operation of U.S. bound product (b) (4)  The procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of your packaging operation of the must be collected in blue crates without proper identification of the material status.  *DATE ISBURD O9/27/2019  DATE ISBURD O9/27/2019   |  |   | products t     | that are loaded on to the m     | achine during   |  |
| Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (2) ng batch #(b) (4) Capsules (3) ng batch #(b) (4) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  EMPLOYEE(R) SIGNATURE Tamil Arasu, Investigator Jogy George, Investigator Emmanuel J. Ramos, Investigator   | routine operation  |   |                |                                 |   |  |
| Written production and process controls procedures are not followed in the execution of production and process control functions.  Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (2) ng batch #(b) (4) Capsules (3) ng batch #(b) (4) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  EMPLOYEE(R) SIGNATURE Tamil Arasu, Investigator Jogy George, Investigator Emmanuel J. Ramos, Investigator   |  |   |                |                                 |   |  |
| Specifically,  Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (4) mg batch #(b) (4) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  Tamil Arasu, Investigator Jogy George, Investigator Emmanuel J. Ramos, Investigator   |  |   |                |                                 |   |  |
| Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (b) (4) Report of the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE Tamil Arasu, Investigator Jogy George, Investigator Emmanuel J. Ramos, Investigator   |  |   | res are not    | followed in the execution       | of production   |  |
| Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (4) mg batch #(b) (4) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  OF THIS PAGE  Tamil Arasu, Investigator  Jogy George, Investigator  Emmanuel J. Ramos, Investigator  | and process con  | trol functions.                         |                |                                 |   |  |
| Procedure FU7-PR-PK-GEN-011, Handling of Rejects in Packing, states that all rejected material must be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (4) mg batch #(b) (4) the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  OF THIS PAGE  Tamil Arasu, Investigator  Jogy George, Investigator  Emmanuel J. Ramos, Investigator  |  |   |                |                                 |   |  |
| be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (b) (a) Ramos, Investigator  Capsules (b) (d) Red back (d) (d) Red back (d) (d) Red back (e) | Specifically,  |   |                |                                 |   |  |
| be collected and stored in a properly labelled red crate. However, during inspection of your packaging operation of U.S. bound product (b) (4) Capsules (b) (a) Ramos, Investigator  Capsules (b) (a) Ramos, Investigator  Capsules (b) (d) Reverse (during inspection of your packaging operation of U.S. bound product (b) (d) Capsules (d) Reverse (during inspection of your packaging operation of U.S. bound product (b) (d) Capsules (d) Republic (d) Re | D 1 DVIII 1  | D DV CENTALL II. III. CD.               | n 1            | ·                               |   |  |
| operation of U.S. bound product (b) (4)  the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  Tamil Arasu, Investigator  Jogy George, Investigator  Emmanuel J. Ramos, Investigator  DATE ISSUED  09/27/2019  |  |   |                |                                 |   |  |
| the inline rejected material was noted as being collected in blue crates without proper identification of the material status.  *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  Emmanuel J. Ramos, Investigator  Jogy George, Investigator  Emmanuel J. Ramos, Investigator  |  |   | ate. Howe      | ver, during inspection of y     | our packaging   |  |
| *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  OF THIS PAGE  EMPLOYEE(S) SIGNATURE Tamil Arasu, Investigator Jogy George, Investigator Emmanuel J. Ramos, Investigator  |  |   |                |                                 |   |  |
| *DATES OF INSPECTION 9/19/2019(Thu), 9/20/2019(Fri), 9/23/2019(Mon), 9/24/2019(Tue), 9/25/2019(Wed), 9/26/2019(Thu) and 9/27/2019(Fri)  SEE REVERSE OF THIS PAGE  Tamil Arasu, Investigator Jogy George, Investigator Emmanuel J. Ramos, Investigator  DATE ISSUED 09/27/2019  |  |   |                |                                 |   |  |
| SEE REVERSE OF THIS PAGE  SEE REVERSE Tamil Arasu, Investigator  Jogy George, Investigator  Emmanuel J. Ramos, Investigator  Emmanuel J. Ramos, Investigator   | material status.   |   |                |                                 |   |  |
| SEE REVERSE OF THIS PAGE  SEE REVERSE Tamil Arasu, Investigator  Jogy George, Investigator  Emmanuel J. Ramos, Investigator  Emmanuel J. Ramos, Investigator   |  |   |                |                                 |   |  |
| SEE REVERSE OF THIS PAGE  SEE REVERSE Tamil Arasu, Investigator  Jogy George, Investigator  Emmanuel J. Ramos, Investigator  Emmanuel J. Ramos, Investigator   | *DATES OF IN   | CDECTION                                |                |                                 |   |  |
| SEE REVERSE OF THIS PAGE  SEE REVERSE OF THIS PAGE  Ogy George, Investigator  Emmanuel J. Ramos, Investigator  DATE ISSUED  09/27/2019   |  |   | ue) 9/25/201   | 9(Wed) 9/26/2019(Thu) and 9/2   | 7/2019(Fri)   |  |
| OF THIS PAGE  Jogy George, Investigator  Emmanuel J. Ramos, Investigator   | 9/19/2019(111u), 9/2   | 0/2019(11), 9/23/2019(Non), 9/24/2019(1 | de), 7/25/201  | (Wed), 7/20/2019 (11td) and 7/2 | 2//2017(11)   |  |
| OF THIS PAGE  Jogy George, Investigator  Emmanuel J. Ramos, Investigator   | l  |   |                |                                 |   |  |
| OF THIS PAGE  Jogy George, Investigator  Emmanuel J. Ramos, Investigator   | l  |   |                |                                 |   |  |
| OF THIS PAGE  Jogy George, Investigator  Emmanuel J. Ramos, Investigator   | I  |   |                |                                 |   |  |
| OF THIS PAGE  Jogy George, Investigator  Emmanuel J. Ramos, Investigator   | l  |   |                |                                 |   |  |
| OF THIS PAGE  Jogy George, Investigator  Emmanuel J. Ramos, Investigator   |  | EMBLOVECO SIGNATURE                     | 0              | 1 /                             | DATE ISSUED   |  |
| OF THIS PAGE  Jogy George, Investigator  Emmanuel J. Ramos, Investigator   | SEE REVERSE  |   | 1 Grani        | Kraku                           | ASSESSMENT TO THE PARTY OF THE |  |
| Emmanuel J. Ramos, Investigator  | The second secon |   | _              | 200                             |   |  |
| DISPOSITIONAL OPERBUATIONS   |  |   | 2              | 108mg                           |   |  |
| DISDECTIONAL OPERAL TIONS  |  | Emmanuel J. Ramos, Investiga            | itor           |                                 |   |  |
| DIODECTIONAL ODCEDNATIONS  |  |   |                |                                 |   |  |
| FORM FDA 483 (09/08) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 14 OF 14 PAGES   | FORM ED 4 462 (00/06)  | PREVIOUS EDITION OBSOLETE INSP          | ECTIONAL O     | BSERVATIONS                     | PAGE 14 OF 14   |  |