DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Donors were not screened by a review of relevant medical records for risk factors of communicable disease agents and diseases.

Specifically, you have received (b)(4) donors of umbilical cord blood units since January 2019 from your main supplier located in (b)(4) which is an area identified as an active transmission risk area. From the umbilical cord blood units you received, you produced (b)(4) of which (b)(4) vial were further distributed.

A. For example, FDA has identified Zika virus (ZIKV) as a relevant communicable disease agent or disease (RCDAD) under 21 CFR 1271.3(r)(2). Therefore, review of relevant medical records, as defined in 21 CFR 1271.3(s), must indicate that a potential donor is free from risk factors for, or clinical evidence of, ZIKV infection for the purpose of determining donor eligibility. Form DT-001 “Donor Risk Assessment Interview” utilized by your main supplier of umbilical cord blood located in (b)(4) does not include the full complement of questions required to assess a donor's relevant communicable disease risk as it relates to ZIKV. Form DT-001 only asks donors “Have you ever been diagnosed with or suspected of having dengue, chikungunya or Zika virus.” The following questions are missing:

1. Whether the donor has resided in or traveled to an area with increased risk for Zika virus transmission at any point during pregnancy or
2. Had sex at any point during pregnancy with a person who has resided in or traveled to an area with increased risk for Zika virus transmission or
3. Had sex at any point during pregnancy with a person who had a medical diagnosis of ZIKV infection.

B. The firm accepted deficient relevant medical records from their umbilical cord blood supplier that were subsequently used to evaluate donor eligibility. Form DT-001 “Donor Risk Assessment Interview” does not...
include complete and/or accurate screening questions related to the following conditions and behaviors that increase a donor's relevant communicable disease risk. For example:

1. Appropriate ZIKV questions as listed above, and
2. Persons who have been diagnosed with vCJD or any other form of CJD.

**OBSERVATION 2**

HCT/P donors were not determined to be eligible based on the results of donor screening and testing.

Specifically, (b) (4) [contracted recovery firm] is not properly determining donor eligibility based on donor screening for Zika and CJD risk.

You have received (b) (4) [donors of umbilical cord blood units since January 2019 from your main supplier located in (b) (4)] which is an area identified as an active transmission risk area. From the umbilical cord blood units you received, you produced (b) (4) [of which (b) (4) vial were further distributed].

**OBSERVATION 3**

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile did not include validation of the aseptic process.

Specifically, since January 16, 2019 to May 21, 2019 your firm processed (b) (4) [donations of human umbilical cord blood into (b) (4) vials of biological products of which (b) (4) were distributed, however your firm did not adequately validate the aseptic process used to produce the biological products.

a) You failed to adequately validate your manufacturing process for aseptic controls. For example, your media fill batch sizes are not at least equal to the maximum commercial product batch size made. Your aseptic validation denotes (b) (4) media fills that validated batch sizes of (b) (4) vials, respectively. From (b) (4), you manufactured 17 lots where the lot size ranged from (b) (4) of PURE products.
b) Your firm failed to adequately validate the aseptic process as demonstrated by environmental organisms being detected in product samples as well as environmental monitoring samples. From January 16, 2019 to present, three pre- and post-processing sterility samples that yielded microbial growth with the following identification:

<table>
<thead>
<tr>
<th>Donor Number</th>
<th>Lot Number</th>
<th>Pre Sterility</th>
<th>Post Sterility</th>
<th>Organism ID</th>
<th>Disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>(b)(6)</td>
<td>(b)(6)</td>
<td>FAIL</td>
<td>PASS</td>
<td>Staphylococcus hominis</td>
<td>Destroyed</td>
</tr>
</tbody>
</table>

Lot Number | Vials Frozen | Vials Released
---|-------------|-------------
(b) (6) | (4) | (b) (4) |
From January 16, 2019 to May 10, 2019, Environmental Monitoring of in process settling plates within the ISO 5 Biological Safety Cabinets (BSC) included growth and identification of *Paenibacillus glucanolyticus* on two separate occasions.

<table>
<thead>
<tr>
<th>Date</th>
<th>Area of failure</th>
<th>Sample type</th>
<th>Organism(s) Id</th>
<th>Number of CFU’s</th>
<th>Lot Number</th>
<th>Disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/17/2019</td>
<td>BSC (b) (4)</td>
<td>Air (In Process Settle plate)</td>
<td><em>Paenibacillus glucanolyticus</em></td>
<td>1</td>
<td>(b) (6)</td>
<td>Released</td>
</tr>
<tr>
<td>2/20/2019</td>
<td>BSC (b) (4)</td>
<td>Air (In Process Settle plate)</td>
<td><em>Paenibacillus glucanolyticus</em></td>
<td>1</td>
<td>(b) (6)</td>
<td>Released</td>
</tr>
</tbody>
</table>

From February 20, 2019 – May 10, 2019, the Environmental Monitoring sampling of ISO 7 gown and clean rooms as well as personnel sampling included the following microbial growths with speciation:
<table>
<thead>
<tr>
<th>Computer Table (Middle)</th>
<th>ISO Class</th>
<th>Count Below Action Level</th>
<th>Count</th>
<th>(Staphylococcus hominis)</th>
<th>&lt;2 (no growth)</th>
<th>** (b) (6)</th>
<th>**Destroyed</th>
<th>Released</th>
<th>Released</th>
<th>Released</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gowning Room (Center)</td>
<td>ISO Class</td>
<td>Count Below Action Level</td>
<td></td>
<td>(Staphylococcus hominis, Bacillus Spp.)</td>
<td>N/a</td>
<td>same lots as above</td>
<td>Released</td>
<td>Released</td>
<td>Released</td>
<td>Released</td>
</tr>
<tr>
<td>Door Handle Exterior</td>
<td>ISO Class</td>
<td>Count Below Action Level</td>
<td></td>
<td>(Staphylococcus hominis)</td>
<td>N/a</td>
<td>same lots as above</td>
<td>Released</td>
<td>Released</td>
<td>Released</td>
<td>Released</td>
</tr>
<tr>
<td>Gowning Room (Center)</td>
<td>ISO Class</td>
<td>Count Below Action Level</td>
<td></td>
<td>(Staphylococcus hominis)</td>
<td>1</td>
<td>** (b) (6)</td>
<td>Released</td>
<td>Released</td>
<td>Released</td>
<td>Released</td>
</tr>
<tr>
<td>Upper Torso</td>
<td>ISO Class</td>
<td>N/A</td>
<td></td>
<td>Staphylococcus haemolyticus</td>
<td>1</td>
<td>** (b) (6)</td>
<td>Released</td>
<td>Released</td>
<td>Released</td>
<td>Released</td>
</tr>
</tbody>
</table>
** Lot (b) (6) post-sterility sample and (b) (4) ISO 14644 surface samples both identified Staphylococcus hominis.

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c) You failed to conduct sampling according to LL-QA-005 Environmental Monitoring (EM) operating procedure, version 1, effective date 5/14/2019. Section 7.4.4 states that (b) (4) shall be performed on a (b) (4) basis in (b) (4) to schedule to capture all shifts. From January 18, 2019 - May 20, 2019, the firm failed to conduct (b) (4) EM sampling for a total of 3 weeks.

<table>
<thead>
<tr>
<th>Dates of missing environmental monitoring sampling</th>
<th>Lots processed</th>
<th># Vials manufactured and released</th>
</tr>
</thead>
<tbody>
<tr>
<td>(b) (4)</td>
<td>(b) (6)</td>
<td></td>
</tr>
<tr>
<td>(b) (4)</td>
<td>(b) (6)</td>
<td></td>
</tr>
<tr>
<td>Total (b) (4)</td>
<td>Total (b) (6)</td>
<td>Total (b) (4)</td>
</tr>
</tbody>
</table>

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SEE REVERSE OF THIS PAGE

Abby L. Mozeke-Baker, Investigator
Tania Y. Hall, Investigator

Abby L. Mozeke-Baker, Investigator
Tania Y. Hall, Investigator

DATE ISSUED 5/23/2019
e) The raw materials and supplies are labeled for in vitro diagnostic use, or research use and are used in the production of PURE products since production began in January 2019. From January 16, 2019 to May 20, 2019, your firm processed approximately \( (b) (4) \) donations of human umbilical cord blood have been processed and approximately \( (b) (4) \) vials of biological products were manufactured of which \( (b) (4) \) were distributed.
f) You failed to adequately validate your processing for aseptic controls. For example, Validation of Processing, LL-VAL-005, version 1, effective 01/14/2019, section 1 states that this validation shall define On 02/26/2019, batch record and were processed by the same operator. You did not validate the processing of two cord blood units by the same operator. Senior laboratory technician and Chief Compliance Officer approximate that processing is being performed of the time.

OBSERVATION 4
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, You failed to challenge your BSC cleaning described in Validation of Biological Safety Cabinet Cleaning, version 1, effective 05/15/2019, with standard organisms to demonstrate that cleaning and sanitization procedures are effective. Since January 16, 2019 to May 20, 2019, your firm processed approximately donations of human umbilical cord blood have been processed and approximately vials of biological products were manufactured of which were distributed.

OBSERVATION 5
Procedures designed to prevent objectionable microorganisms in drug products not required to be sterile are not established, written and followed.

Specifically, the following procedures were not established, written, or followed:

Operating procedure, LL-QA-005 Environmental Monitoring, version 1, effective 05/14/2019, was not established:

a. You failed to establish an appropriate sampling frequency. You are not conducting surface sampling
You are currently conducting surface sampling on a (b) (4) basis according to LL-QA-005 Environmental Monitoring operating procedure, version 1, effective 05/14/2019, despite conducting manufacturing on (b) (4) basis between 1/16/2019 to 5/23/2019.

b. You failed to establish alert and action levels related to microbe or airborne particle levels and appropriate steps to take when alert or action levels are exceeded in your LL-QA-005 Environmental Monitoring, operating procedure, version 1, effective 05/14/2019. Additionally, you have recovered as many as (1) colony in ISO 5, (6) colonies in ISO 7, and (12) colonies in ISO areas without taking corrective action.

Operating procedure, LL-QA-005 Environmental Monitoring, version 1, effective 05/14/2019, was not followed:

c. According to LL-QA-005 Environmental Monitoring operating procedure, version 1, effective 05/14/2019, Table 1 - Air Classification, microbiological settling plate action levels for ISO 5 designation is <1 CFU. From 1/15/2019 - 05/10/19, processing settling plates used to assess conformance of ISO 5 yielded 6 growths with 1 CFU’s.

d. From 02/09/2019 to 02/13/19, you used (b) (4) contact plate during processing of (b) (4) vials. You failed to validate the use of (b) (4) plates during in-processing. You did validate the use of settle under plates in the BSC cleaning validation and aseptic processing validation. You substituted contact plates instead of settle due to no inventory of settle plates. No action was taken by the firm when action levels were met. According to the certificate of analysis, the substituted contact plates do not recover the organisms.

<table>
<thead>
<tr>
<th>Deviation #</th>
<th>Affected lots</th>
<th># of vials manufactured</th>
<th>Disposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>DV 19-004</td>
<td>(b) (6)</td>
<td></td>
<td>Shipped</td>
</tr>
<tr>
<td>DV 19-005</td>
<td></td>
<td></td>
<td>Shipped</td>
</tr>
<tr>
<td>DV 19-006</td>
<td></td>
<td></td>
<td>Shipped, (b) (4) vials</td>
</tr>
</tbody>
</table>
DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

PISTRCIC AIOd ASS /
CATIDS) 01' INSPECTION

19701 Fairchild
Irvine, CA 92612-2445
(949) 608-2900 Fax: (949) 608-4417

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Erin M. Sairafe, Chief Compliance Officer

Firm Name: Liveyon Labs Inc  
22667 Old Canal Rd  
Yorba Linda, CA 92887-4601

Type Establishment Inspected: Biological Drug Manufacturer

<table>
<thead>
<tr>
<th>Operating Procedure Title</th>
<th>Document No.</th>
<th>Version</th>
<th>Effective Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterility Testing &amp; Investigation of Failures</td>
<td>LL-QA-008</td>
<td>1</td>
<td>none</td>
</tr>
<tr>
<td>Product Quarantine &amp; Release</td>
<td>LL-LAB-006</td>
<td>1</td>
<td>none</td>
</tr>
<tr>
<td>Validation of Pure Products' Stability</td>
<td>LL-LAB-0069</td>
<td>1</td>
<td>none</td>
</tr>
<tr>
<td>Nonconformance</td>
<td>LL-QA-016</td>
<td>1</td>
<td>none</td>
</tr>
</tbody>
</table>

e. You have not established an aseptic gowning qualification as of 5/21/2019.

f. You began manufacturing on (b) (4) As of 5/13/2019, The following procedures were not reviewed, approved, and implemented:

OBSERVATION 6
There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically, You failed to investigate and document 5 of 6 microbial growths of in processing settling plates (EM). While you identified the species on a summary chart, you did not identify a trend of repeating microorganisms such as Paenibacillus glucanolyticus species.

OBSERVATION 7
A standard operating procedure for the release of HCT/Ps from donors that test reactive for cytomegalovirus (CMV) was not established, maintained, defined and documented.

SEE REVERSE OF THIS PAGE
Abby L Mozeke-Baker, Investigator
Tania Y Hall, Investigator

DATE ISSUED: 5/23/2019

FORM FDA 483 (09/98) PREVIOUS SECTION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 10 of 12 PAGES
Specifically, there is no procedure that describes the current practice of additional or further testing performed for CMV IgG and CMV IgM when the CMV total antibody test is reactive and how to evaluate the further testing results for purposes of donor eligibility and release to the distributor.

**OBSERVATION 8**
Procedures describing the handling of written and oral complaints related to drug products are deficiently written or followed.

Specifically, the Product Complaints procedure (LL-Q-015) lacks detailed instructions.

1. The procedure does not provide time frames in which complaints received by the sales force must be forwarded to log the complaint into the complaint system. It does not provide a time frame in which the complaint form must be initiated, a time frame in which a decision to investigate or not be determined, a time frame in which the investigation must be initiated and completed, and a time frame in which the complaint must be closed.

2. The procedure is not reflective of current practice. It instructs customer service/sales receiving complaints to forward the complaint to the QA department for follow up. Current practice is to forward all complaints to the CCO of Liveyon Labs, Inc. to log into the complaint system and then route to QA for follow up.

**OBSERVATION 9**
Drug products do not bear an expiration date determined by appropriate stability data to assure they meet applicable standards of identity, strength, quality and purity at the time of use.
Specifically, you failed to determine an appropriate expiration date. Your stability study titled LL-VAL-019 Validation of PURE Product Stability, version 1, has not been reviewed and approved by a responsible person prior to implementation on 11/30/2018 and is ongoing.

On 5/15/2019, I observed final labeling for batch (b)(6) that denotes a 1-yr expiration date. Chief Compliance Officer of Liveyon Labs Inc. stated that the one-year expiry was assigned on or before 01/15/2019 and was assigned without accelerated studies or other provisional data. Since that time, your firm processed approximately (b)(4) donations of human umbilical cord blood have been processed and approximately (b)(4) vials of biological products were manufactured of which (b)(4) were distributed.

*DATES OF INSPECTION