FOOD AND DRUG ADMINISTRATION	ROCKVILLE, MD 20852 (301) 827-6191	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: ROBERT G. KRAMER	PERIOD OF INSPECTION 10/10-26/00	C.F. NUMBER 1873886
TITLE OF INDIVIDUAL [redacted] / CHIEF OPERATING OFFICER	TYPE OF ESTABLISHMENT INSPECTED Vaccine/Blood Products Manufacturer	
FIRM NAME BioPort Corporation	NAME OF FIRM, BRANCH OR UNIT INSPECTED same	
STREET ADDRESS 3500 N. Martin Luther King, Jr. Blvd.	STREET ADDRESS OF PREMISES INSPECTED same	
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

1. The design and construction of the filling suite (Rms [redacted], environmental monitoring, cleaning and employee practices do not assure sterility of products filled in the suite, in that,

A. concerning the design and construction:

1. seams around the hot air oven are not sealed, such that during the smoke study of 7/28/00, smoke from the unclassified Room [redacted] was seen coming through to Room [redacted] around the hot air oven.

2. floors in room [redacted] are not of a material that is easily cleanable, and walls have seams.

3. the curtain separating the class 10,000 area from the class 100 area of room [redacted] is approximately 6", above the work surface height and smoke was observed flowing from the class 10,000 area into the class 100 area during the smoke study of 7/28/00.

4. the curtain separating the class 10,000 area from the class 100 area of room [redacted] is discolored where employees enter/exit, appearing to be rust from weights in the curtain and is taped at seams in several areas.

5. the in-line HEPA filter box for the hot air oven is located in the class 10,000 area of room [redacted].

6. gowning room ([redacted]) does not contain an air return, only a vent opening into room [redacted].

7. rust was observed on hinges of the hot air oven, the floor at the base of the hot air oven, grates for HEPA filters [redacted] and [redacted] (in the class 10,000 area at the beginning of the filling line and exit of the gowning room respectively).

8. temperature and humidity specifications for Room [redacted] are not met when the hot air oven is operating.

9. smoke studies show there is turbulence in the area where employees exit the gowning room and enter room [redacted], directly beneath HEPA [redacted]

10 smoke studies indicate the floor returns in room [redacted] do not all return air uniformly.

[redacted]

SEE REVERSE OF THIS PAGE

DATE ISSUED
10/26/00

FORM FDA 483 (5/85)

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: ROBERT G. KRAMER	10/10-26/00	1873886
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
# 4 Top CHIEF OPERATING OFFICER	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

11. The gowning room for filling (Building [redacted], Room [redacted]) has airlock doors that interlock. An interlocking mechanism overide allows for the doors to be opened both at the same time. The lock has only the word "exit" printed on it. The SOP for gowning (#FP01-006-01) does not address airlocks and proper use of the airlocks.

B. concerning environmental monitoring:

1. There is no assurance that environmental samples taken in the filling suite in Building [redacted] Room [redacted] and the capping area Building [redacted] Room [redacted] are representative of actual conditions in the filling suite. For example:

   a. Tryptic soy agar (TSA) plates used for environmental surface and personnel monitoring are growth promoted using bacteria, yeast, and molds. During growth promotion, plates are incubated at 30-35 degrees C for bacteria and at 20-25 degrees C for yeast and mold. However, incubation for plates used for surface and personnel sampling are incubated only at 30-35 degrees C.

   b. The sampling procedure for environmental surface sampling in the filling and packaging suites is not representative of the entire work areas. Samples in the capping area are limited to one side of the room. Samples in the filling suite in both the class 10, 000 area and the class 100 filling area (separated by vinyl curtain) are not taken in critical areas that are most often in contact with personnel. For example, the areas not sampled include: the vinyl curtain that separate class 10,000 from class 100 is not sampled; the doors to the dry heat oven are not sampled; the autoclave door is not sampled.

   c. Environmental samples are taken prior to and after filling operations. Surfaces sampled for environmental monitoring are not always cleanable. For example, the turntable for the empty vials in the class 100 filling portion has holes in it to allow for air to pass through. This turntable is sampled both before and after filling operations. It was observed during mock sampling that media remained inside the holes after sampling and after the technician wiped the residue from the top of the surface.

[redacted]

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: ROBERT G. KRAMER	10/10-26/00	1873836
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
PRESIDENT/CHIEF OPERATING OFFICER	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

d. The firm does not always identify environmental contaminants when they exceed the action limits ~~are all exceeded.~~ [redacted] 10/26/00

e. Corrective action stated in sterility test failure investigations for at least the last 24 months state that the firm intended to use a barrier isolator to perform sterility testing to eliminate what the firm refers to as "false positives" in sterility failures. To date, the barrier isolator has not been validated.

f. Samples have been taken "for information only" since 1997 in the sterility gowning room and the sterility test suite. Occasionally these samples exceed the action level and the firm does not always identify the contaminant. Though these samples are taken in critical areas, the results are not used routinely in failure investigations.

C. concerning cleaning of room [redacted]

1. one solution is used for cleaning surfaces including the curtain, floor, walls, ceiling and oven and autoclave doors of room [redacted] consisting of a [redacted] solution of [redacted]

2. there is no data that the cleaning solution is effective in removing microorganisms from surfaces in room [redacted]

3. cleaning of room [redacted] is performed up to [redacted] days prior to filling product, despite the length of time from the last cleaning.

D. concerning employee practices:

1. employees routinely exit and enter through the curtain in Room [redacted] during product filling, moving between a class 10,000 area and a class 100 area, and do not always sanitize their hands after touching the curtain between the [redacted] areas, as seen in the media fill of 7/00.

2. operators enter the class 100 area from the class 10,000 area the barrier curtains are moved in such a way as to pass over the empty sterile vials which allows for the vials to be exposed to class 10,000 conditions.

[redacted]

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: ROBERT G. KRAMER	10/10-26/00	1873886
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
PRESIDENT/COO	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

3. There is no mirror in gowning room [redacted] to assure that employees comply with gowning procedures.

2. The following product lots failed initial sterility testing for release or for stability testing:

Test date	Product	Lot number	Test Purpose	Test Time Point	Microbial Identification
3/1/99	Albumin	HA1204	Stability	O Month	*Staphylococcus epidermidis*
11/17/99	Anthrax Vaccine sublot	AV824	Sublot Release	N/A	*Bacillus spaericus* *
12/29/99	Anthrax Vaccine	FAV014	Release	N/A	*Bacillus mecerans*
1/28/00	Anthrax Vaccine	FAV011	Release	N/A	*Propionibacterium acnes*
4/13/00	Rabies Vaccine	RV167	Release	N/A	*Staphyloccus epidermidis*

*Lot AV824 was retested and failed the retest.

Investigations into these initial sterility test failures are incomplete in that:

A. The firm examined sterility test suite environmental monitoring, media, and testing procedures and was unable to determine that the failure was related to testing error.

B. The firm did not evaluate environmental monitoring conducted at the time of the filling operation.

C. The firm did not attempt to associate the organisms isolated from the sterility failures to organisms isolated previously from the environment.

D. Several failure investigations state in the conclusion that the firm has proven anti-microbial effectiveness testing.

E. The firm does not address corrective actions relating to personnel in their investigation of sterility failures though the firm concludes in several incidences that the cause of the sterility failure is technician error.

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: ROBERT G. KRAMER	10/10-26/00	1873886
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
PRESIDENT / CEO	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

These lots were re-tested, those that passed the sterility re-test, were released.

3. Investigations are incomplete, inaccurate, or not conducted. For example:

A. Investigation report for the media fill that took place on July 13, 2000, states that based on investigation findings, the filling room (Building [redacted] room [redacted] appears to have been contaminated with organisms that had not been previously detected by BioPort's environmental monitoring program. The organisms isolated from the media fill are as follows: *Cephalosporium* species; *Staphylococcus epidermidis*; *Curvularia* (fungi) species, *Aspergillus* (fungi)species, Yeast, *Penicillium* (fungi) species; *Micrococcus* species; *Cladosporium* (fungi) species.

The firm's microbiological trend analysis for environmental isolates from the period of October 1,1999 through March 30, 2000 found some of the organisms in the environment that were isolated from the media fill. Those organisms include *Micrococcus* species (isolated from personnel and air); *Staphylococcus epidermidis* (isolated from personnel, air and surfaces. Fungi were isolated from air and equipment but those fungi were not identified by genus.

Cladosporium (fungi) species and *Alternaria* (fungi) species were isolated from equipment in the filling area (Building [redacted] room [redacted]) in 1995.

Tryptic Soy Broth (TSB) vials used for the media fill were incubated at [redacted] degrees C (though the protocol indicated that it should be 20-25 degrees C). The manufacturers recommended temperature for incubation of TSB is 20-25 degrees C.

B. Investigations were not conducted when alarms occurred for non-viable particulate (NVP) monitoring in room [redacted] Class 100 fill area. For example:

1. During lot FAV059 fill on 5/3/00, [redacted] particles ([redacted] µm) per ft^3 were noted at 10:26 am at the turntable point. A comment in records noted an operator was removing tipped vials near the probe.

2. During lot IG149 fill on 4/7/00, [redacted] particles were noted at 12:43 pm at the turntable point. A record comment attributed this to an operator in the curtain area.

[redacted]

SEE REVERSE OF THIS PAGE

DATE ISSUED 10/26/00

FORM FDA 483 (5/85)

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: ROBERT G. KRAMER	10/10-26/00	1873886
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
PRESIDENT/COO	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

C. Investigation #99-0072 into "flaking" found during visual inspection of Albumin, beginning with lot #HA1200 on 11/2/98 is incomplete in that there are no protocols, with acceptance criteria addressing the "mock lots", repooling and refiltering of lots, pasteurizing samples of lots and changing process parameters. No report has been written as a result of the investigation. Multiple lots of Albumin failed visual inspection and are included in this deviation report, which concludes that the flakes are caused by ineffective filtering that resulted from using a plastic lock nut used as a replacement part, even though subsequent lots of Albumin continue to contain "flakes".

D. SOP #CW00-004-03, Sampling and Testing of the Water for Injection and Clean Steam Systems does not address the action to be taken if action limits are exceeded in the system. A deviation report is issued, however, additional samples are taken until the results are within specification. In addition the action limits for microorganisms do not address the types of organisms found, such as gram negatives. For example:

For example on 8/18/99, Steam outlet #[redacted] had a total microbial count of [redacted] CFU, gram negative bacilli, reported on Deviation #9900865. The site was resampled on 8/26 &27/99 and no CFU's were found. On 8/18/99 the same site failed to meet its Conductivity specification. And on 8/11/99 2 CFU's were found at Steam outlet #[redacted], and identified as *Chryseobacterium meningosepticum*. This organism (1 CFU) was found at this site again on 9/28/99.

4. QA unit has not assured completeness, accuracy, of records, reports, and testing documents. For example:

A. concerning the report of the 7/00 media fill, which did not pass specifications:

1. The investigation report, approved by management 10/11/00, indicated that [redacted] positives were found in [redacted] vials; however, batch production records indicated that only [redacted] vials were incubated.

2. Batch production records indicate that [redacted] filled vials were removed during filling; however, the reasons for removal or rejection were not recorded.

3. the investigation report does not mention multiple design and construction deficiencies mentioned above.

[redacted]

SEE REVERSE OF THIS PAGE

DATE ISSUED 10/26/00

FORM FDA 483 (5/9

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: Robert G. Kaminski	10/10-26/00	1873886
TITLE OF INDIVIDUAL Vice President / Chief Operating Officer	TYPE OF ESTABLISHMENT INSPECTED Vaccine/Blood Products Manufacturer	
FIRM NAME BioPort Corporation	NAME OF FIRM, BRANCH OR UNIT INSPECTED same	
STREET ADDRESS 3500 N. Martin Luther King, Jr. Blvd.	STREET ADDRESS OF PREMISES INSPECTED same	
CITY AND STATE (Zip Code) Lansing, MI 48909	CITY AND STATE (Zip Code) same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

B. concerning the log for maintenance, cleaning, and use (LUMAC) for building [redacted] aseptic filling room and equipment:

1. entries are missing or inaccurate entries; for example:

a. Product lots HA1209, HA1210, HA1211, FAV052, and FAV053, filled between 11/5/99 and 12/8/99 were not entered. A log entry dated 12/8/99 noted the log had been misplaced; however, a backup log was not used during this period.

b. Product lot HA1204 filled on 3/3/98, and lots FAV048, FAV048B, and BP7012, filled between 12/23/98 and 1/7/99 were not entered.

c. Media fill #63, which was a special fill for a pasteurization study, was performed on 5/17/99, but was not recorded on the log.

d. Media fill #64 was performed on 7/26/99; however, the log does not record this. It only indicates the set up date of 7/22/99.

e. Several entries in August 1999, on 5/27/99, 9/30/99, and 3/29/00 were not made concurrently, but were made later after omissions were discovered (they were then appropriately post-dated and initialed).

f. Second check initials and dates were inconsistently recorded between 12/18/98 and 10/7/99.

g. The log records filling of Lot FAV049 on 8/20/99, and 10/7/99. The latter is the correct fill date, but an explanation was not made in the log.

h. The date 10/2/98 appears before 9/30/98; the date 3/31/00 appears before 3/29/00 and 4/5/00 appears before 4/4/00, with no explanation.

2. The LUMAC is not periodically reviewed for accuracy and completeness by the quality unit.

C Recorder charts for temperature and relative humidity monitoring in room [redacted] between 1/5/00 and 3/28/00 indicate there were several temperatures above [redacted]C (specification [redacted]C) and humidity readings below [redacted] (specification [redacted]). However, there were no notations to indicate these

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: Robert G. Kremer	10/10-26/00	1873886
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
Pres. / Chief Operating Officer	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

deviations were evaluated. (No increased temperatures were observed during product filling, and conditions were corrected.) Recorder charts were not reviewed and approved by Manufacturing Supervision until 6/21/00. No comments were included, concerning the out of range readings.

D. The P&ID drawing for the clean steam system in Bldg [redacted] does not include the [redacted] Autoclave in Room [redacted]

E. Annual reports for 1998 and 1999 are incomplete and have not been submitted to FDA.

F. SOP #FP01-005-002 states the drying cycle for the [redacted] Autoclave is [redacted] minutes. Since approximately 3/8/00, the cycle has been extended to [redacted] minutes because loads were not drying adequately. The QA Unit has approved batch records affected by this change

5. regarding adverse events:

A. The military reported a death of an individual who had received Anthrax vaccine lot # FAV031. The individual was inoculated on 3/14/00 and died on 6/14/00. The cause of death is reported as Aplastic Anemia and Invasive Aspergillosis. The firm received information in a Vaccine Adverse Event Reporting System (VAERS) form but there is no documentation as to when that report was received by the firm.

1. The firm has not reported the death to FDA in a 15-day report.

2. The firm has not conducted an investigation as a result of this VAERS report.

B. The firm does not trend data received relating to adverse events. Further, there is no documentation to show that the firm investigates adverse events when received.

C. The firm has not investigated adverse events for anthrax vaccine that are different from those stated in the package insert. Examples include, but are not limited to, the following: FAV030 and FAV041 have numerous complaints for nausea, diarrhea, and vomiting; FAV030 also reports double vision, dizziness, memory loss, and shortness of breath and FAV020 reports memory loss , dizziness, and "black outs".

D. There is no documentation to show when adverse events are received by the firm.

[redacted]

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: Robert C Kramer	10/10-26/00	1873886
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
President / Chief Operating Officer	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

6. There is no assurance equipment is operating as designed:

A. concerning the passthrough [redacted] Autoclave used to sterilize stoppers and processing equipment in Room [redacted] Bldg [redacted]

1. there is no documentation that the vent filter has been changed, or integrity tested.

2. the pure clean steam supplied to the autoclave is not monitored.

3. the vent filter is not included in the preventive maintenance program.

4. there is no documentation that annual preventive maintenance for the autoclave, due 7/00 has been performed.

5. there is no documentation that the autoclave has been repaired since the observation of water remaining in the chamber, loads of stoppers not being adequately dried, and drying temperatures not being met during cycles as noted 3/9 -14/00.

B. Concerning the passthrough [redacted] Oven in room [redacted] Bldg [redacted]

1. the 7/99 requalification:

a. The approved protocol for cold spot determination did not specify acceptable variance for distribution thermocouple temperatures. A temperature variation of approximately [redacted]C was observed, between the lowest to highest thermocouple. In addition, the cold spot determination was performed with equipment in the chamber, rather than an empty chamber.

b. The summary report notes that the 3 coldest thermocouples were no. 3, 4 and 13; however, data indicates no. 10 was colder throughout the run. (No. 10 was located at a [redacted] rather than inside the chamber; however, this was not explained in the report.)

c. There was a temperature variation during loaded chamber run [redacted] mL vials, of approximately [redacted]C between the lowest and highest thermocouple, at about [redacted]

[redacted]

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: Robert G. Kruse	10/10-26/00	1873886
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
President / Chief Operating Officer	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

hours into the [redacted] hour cycle (though all thermocouples were above the specified [redacted] C).

d. The summary report, prepared 9/20/99 by Validation personnel, was not finally approved by Manufacturing management until 6/5/00.

2. Loaded chamber cold spot determinations have not been performed for minimum and maximum loads, for each vial size. Studies in 1996 were performed with mixed glassware loads. Requalification sterilization and depyrogenation studies in 7/99 did not include [redacted] mL or [redacted] mL vials.

3. Empty chamber cold spot heat distribution studies in 1996 indicate that protocol specifications were not met, in that thermocouple ranges were not within [redacted] C from mean temperatures. The stated corrective action was to not use the lower shelves of the oven.

C. concerning the [redacted] air handling unit that supplies air to rooms [redacted] and [redacted], Bldg [redacted]

1. the report for the air balance of 1996 contains blanks, does not always indicate acceptance criteria, and was performed under static conditions, for example;

a. the report lists acceptance criteria, under static conditions, for the specification for pressure differentials of room [redacted], [redacted] and [redacted]. All readings are above the specifications, but there is no specification for the maximum air pressure allowed.

b. pages 50 through 53 list the supply volume for a room, and the room volume, but do not list the room exhaust volume, yet air changes/hour is calculated.

c. there is no written report of the results found during the air balance, including failure to meet acceptance criteria, and whether the system is balanced.

D. Concerning plant compressed air, used in room [redacted] (for product movement through the [redacted] micron filter) and in room [redacted] (for fill equipment operation) prior to 7/00:

1. There was no routine monitoring of the air quality at these use points.

[redacted]

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: Robert G Kramer	10/10-26/00	1873886
TITLE OF INDIVIDUAL: President / Chief Executive Officer	TYPE OF ESTABLISHMENT INSPECTED: Vaccine/Blood Products Manufacturer	
FIRM NAME: BioPort Corporation	NAME OF FIRM, BRANCH OR UNIT INSPECTED: same	
STREET ADDRESS: 3500 N. Martin Luther King, Jr. Blvd.	STREET ADDRESS OF PREMISES INSPECTED: same	
CITY AND STATE (Zip Code): Lansing, MI 48909	CITY AND STATE (Zip Code): same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

2. There was no preventive maintenance program, including filter inspection and replacement for coalescing filters that were previously in place at the use points.

7. Change control system:

A. New clean compressed air system piping, fittings, filters and use points are installed in room [redacted] and room [redacted], however, the subject Change Control Request #0824, dated 7/7/00, has not been signed by QA to proceed with the change.

B. Change Control #0783, dated 3/3/00 changes the drying cycle for the [redacted] Autoclave from [redacted] minutes to [redacted] minutes because loads aren't being adequately dried, and does not address the reason the loads are wet at the end of a cycle. It is signed by QA, 10/24/00 and does not address comments made by Regulatory asking for an assessment of the effect of the extended cycle on autoclave loads.

C. During Phase I facility changes in rooms [redacted] and [redacted], a new air duct was installed from the main air handling unit (AHU) [redacted] into room [redacted]. This change was not included in the Phase I Change Control Report No. 0551, subsequent memos describing additional changes, or other records. In addition, the change was not included on updated HVAC drawings. A formal documented evaluation was not made for the impact of this change on existing air system balance.

8. Some work orders for corrective maintenance or repairs were marked as "Critical Systems Work Order," however, were not signed/dated as reviewed by Quality Assurance, Quality Control, Critical Systems Committee, or other management as required. In addition, there was no indication that product impact was evaluated. For example:

A. W/O #0030706, dated 3/7/00 states the [redacted] Autoclave does not adequately dry stoppers.

1. the autoclave was not taken out of use during test cycles, and remains in use.

2. Work order #30706 remains open, and there is no documentation the autoclave was repaired Production was told which areas of the chamber not to use during loading to avoid wetness after a cycle

[redacted]

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: Robert G. Kramer	10/10-26/00	1873886
TITLE OF INDIVIDUAL	TYPE OF ESTABLISHMENT INSPECTED	
~~Vice~~ President, Chief Operating Officer	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)	
Lansing, MI 48909	same	

DURING THE INSPECTION OF YOUR FIRM WE OBSERVED:

B. W/O #99030804, dated 3/8/99 states the [redacted] system is not working
W/O #99110110, dated 11/1/99 states the [redacted] system is out of temperature range
W/O #99122103, dated 12/21/99 states the [redacted] system is out of temperature range
W/O #00031601, dated 3/15/00 states the [redacted] system is out of temperature range.
W/O #00032205, dated 3/22/00 states the [redacted] system, is out of temperture range.
W/O #00032801, dated 3/28/00, states the HEPA filter indicator lights are flashing.

C. Work order 00041408 was initiated by Production management on 4/13/00, to request room [redacted] room pressure reduction, to prevent backflow into filling room [redacted]. However, the concern was not evaluated completely at the time by Engineering, Quality Assurance, or Validation management. Further evaluation (based on verbal request) by pressure differential measurement was not performed until 6/2/00. Product lots IG150 and FAV059 were filled in room [redacted] between 4/18 and 5/1/00. (The room was not used for product after 5/1/00 until media fill of 7/00).

9. The Out Of Specifications (OOS) SOP, #AL00-021-02, dated 11/18/99, allows two independent re-tests to be performed on a sample with initially OOS test results, even though the laboratory investigation did not find a cause for the initial OOS result. It states the two independent tests shall be performed, one by the original analyst and one by a second analyst, as "confirmatory testing". If the confirmatory testing fails to cnfirm the initial test result, then a series of [redacted] re-tests by a second analyst may be performed.

On 12/6/99. finished product Human Albumin, lot #1209 was tested and failed to meet the protein specification (23.5% to 26.5%) with a result of [redacted] and the result was considered valid. The results of "Confirmatory testing" by two analysts were [redacted] (12/7/99) and [redacted] (12/9/99). A second calculation, to determine whether these [redacted] results were in the [redacted] confidence interval concluded the OOS result was confirmed.

On 1/4/00, bulk Human Albumin, lot #1215 was tested and failed to meet the protein specification (23.5% to 26.5%) with a result of [redacted] and the result was considered valid. The results of "confirmatory testing "by two analysts were [redacted] and [redacted] (1/5/00) and [redacted] (1/6/00) A second calculation, to determine whether these 3 results were in the 95% confidence interval concluded the OOS result was not confirmed. It was tested [redacted] additional times by the second analyst, the results were averaged with the test result of 1/6/00 and the average of [redacted] reported.

On 1/4/00, finished product Human Albumin, lot #1215 was tested and failed to meet the protein specification (23.5% to 26.5%) with a result of [redacted] and the result was considered valid. The results of

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President, Chief Operating Officer	Vaccine/Blood Products Manufacturer	
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED	
BioPort Corporation	same	
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED	
3500 N. Martin Luther King, Jr. Blvd.	same	
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Lansing, MI 48909	same	

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"confirmatory testing" by two analysts were [redacted] and [redacted] (1/5/00) and [redacted] (1/6/00). A second calculation, to determine whether these 3 results were in the 95% confidence interval concluded the OOS result was not confirmed. It was tested [redacted] additional times by the second analyst, the results were averaged with the test result of 1/6/00 and the average of [redacted] reported..

There is no report addressing the fact that both the bulk and finished product of Human Albumin, lot #1215 initially failed to meet protein specifications. There is no SOP for calculating the 95% confidence level.

10. The firm has not set specifications for bioburden testing though they began testing for pre-filtration bulk on 2/20/97. Organisms found include but are not limited to *Bacillus* species, *Corynebacterium* species, *Pseudomonas* species, *Micrococcus* species, and *Acinetobacter* species. Further, the firm does not have a procedure for dealing with bulk product that tests positive for gram negative organisms. The following are several examples: [redacted]

A. Albumin lot HA 1205 was bioburden tested prior to sterile filtration. The firm recovered [redacted] cfu/ml organisms. *Bacillus thuringiensis*, *Acinetobacter* species were found as well as *Chyseobacterium meningosepticum*, a gram negative organism .

B. Immune Globulin lot IG 143 was found to have [redacted] cfu/ml organisms of gram negative *Pseudomonas flourescens* in batch bioburden sample prior to sterile filtration.

C. Albumin lot HA 1212 was found to have [redacted] cfu/ml of gram negative *Pseudomonas* species.

D. Albumin lot HA 1217 was found to have [redacted] cfu/ml of gram negative *Pseudomonas flourescens* and a gram positive spore forming bacilli.

11. There is no documentation of review and approval of major Quality decisions by Senior Quality Management. For example:

A. the Investigation Report for the media fill failure, dated 10/10/00, is signed by the Director of Manufacturing and Director of QA.

[redacted]

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B. lots of Human Albumin that did not meet their specification for appearance were sold for Diagnostic use. There is no documentation of the review and approval to release this product nor for the labeling used for this product.

C. there is no documentation of review and approval of consultant reports, such as the "Action Level Recommendation and Statistical Summary Report", dated 6/27/00 and whether recommendations in this report are to be incorporated into the firm's procedures; similarly, there is no documentation of a decision on recommendations contained in a document from [redacted] dated 7/28/99 addressing the "flakes" in lots of Human Albumin.

D. Changes were made to the manufacturing process for Human Albumin. There is no documentation for review and approval of these changes by the quality unit.

12. "Planned Deviations" allow departures from procedures or manufacturing processes and no reports are written about the acceptability of the product manufactured under the deviation. For example:

A. Planned Deviation, #99-1438, dated 12/7/99 – Albumin Paste lots #FVR865 and FVR866 were shipped under colder temperature conditions and were used prior to older lots of paste to determine whether the colder temperature would reduce particles (flakes) in finished Albumin. No report was written after the finished lot was manufactured, or whether the problem of "flakes" in the product was corrected.

B. Planned deviations #99-1319 and 99-1320 -- allow powder from small experimental fraction V reworks using different ethanol concentrations and the formulation of lots of varying sizes. No report was written about finished lots #HA1209 and #HA1210 and the effect, if any of these changes.

C. Planned deviation #99-1403 -- allows a draft of a new batch record to repool Albumin lot #HA1200 into lot #HA1213. No report was written about the finished lot #HA1213 and the effect, if any of repooling.

13. SOP's are incomplete

A. Filling SOPs do not address glass vial resterilization, or the number of times that vials can be resterilized.

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B. Fill SOPs do not address the actions to take when filling is interrupted. Batch records for lot FAV057 indicate that filling began on 1/27/00, but was not continued. Filling was then actually performed on 2/8/00; however, there was no explanation in the batch records for this interruption.

14. Failure to follow CBER approved process for manufacture of blood derivatives; failure to submit changes to CBER; failure to validate the new process:

[redacted]

A. Since approval of a manufacturing departure in 5/97, the firm has been departing from approved IN HOUSE manufacturing procedures, including but not limited to the following:

1. different centrifuge rates other than the rate approved in the firm's product license.

2. changed addition rate ranges for addition of [redacted]

3. changed addition temperature ranges of [redacted]

4. reagent to product ratios instead of being used are changed not to be product specification but "for information only"

15. Validation and Requalification Documents are deficient, for example:

A. Concerning smoke airflow visualization testing for the room [redacted] class 100 laminar air flow [redacted] HEPA filters:

1. Original testing was done in February 1995, where average filter velocity ranged from [redacted] to [redacted] fpm. Changes in the air system were then made, as documented in 3/96 requalificaion records, so that average filter velocity ranged from [redacted] to [redacted] fpm. However, additional smoke testing was not performed at that time.

2. Smoke testing was not performed in conjunction with allowable low and high air velocity range, for the HEPA filter bank. For example, specifications are that each filter velocity should be > or = 90 fpm.

[redacted]

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3. A smoke test was performed (and videotaped) in April 1999; however, there are no records to indicate the reason, or to provide an evaluation of its acceptability and Quality Assurance approval.

B. No media fills were performed between 7/26/99 and 7/13/00. In addition, both of these media fills were performed using [redacted] mL vials, and none were performed on [redacted] mL vials (used for albumin). Media fill SOPs 12635, effective 9/12/95 and FP01-021-00, effective 11/30/99 specify that media fills will be conducted on each of the two vial sizes (2 or 5 mL and 50 mL) once per year. The previous media fill for [redacted] mL vials was performed on 1/13/99.

There is a lack of reconciliation of vials that are returned to the firm from customers:

A. Lot # FAV030, Anthrax Vaccine was returned. The documentation from the military states that [redacted] vials were returned on 5/6/98. The firm's documentation shows that 10 vials were received on 5/26/98. The vials were sent for disposal at the firm but disposal records show that on 10/26/99 only [redacted] of the [redacted] vials were received for disposal.

B. Lot # FAV017, Anthrax Vaccine was returned from the military. Documentation shows that [redacted] vials were returned and received by the firm on 6/16/98. The firm's records dated 10/26/99, show the original number of vials received was [redacted] but the records were changed to show that 6 vials were received for destruction.

17. Regarding documentation:

A. Documentation of destruction for lots AV824 and AV825 was incorrect and/or inadequate in that the records show that the lots were destroyed but the lots remain in quarantined inventory.

B. There is no documentation of destruction for [redacted] gallons DPT intermediate product listed as having been destroyed in the Product Discard Log.

C. Expired reagent ([redacted] lot 121703SA) was used as the toxin diluent for bioassay for IG 141 without prior supervisory approval.

D. Numerous incidences were observed where QA did not sign final approval as required by procedure.

[redacted]

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E. Batch records contain numerous deviations and do not document actual chain of events. For example, lot HA 1204 was placed on quarantine on 3/9/99 but there is no documentation as to v the lot was placed on quarantine. The bulk pre-filtration sample shows growth of a gram negati bacteria but the document shows that the sample was a final filled sample not bulk.

F. The document used as accountability for filled vials still shows a column where the firm docum rejected vials labeled as re-pool vials though the firm does not re-pool any rejected vials.

G. Documentation of the inspection of vials for HA1207 shows that the inspection list is incomple that it does not state the rejects.

18. Regarding Sterility testing:

[redacted]

A. There is no mirror located in the gowning area for sterility testing of. During observations of th gowning operation for sterility testing the sterility test technician had a suit that had a hole in th back of the suit. She did not know about the hole in her suit but if she would have observed her gowning in a full length mirror, she would have known.

B. Observations of sterility test gowning found that sterility test personnel sample the outside of th gown with TSA media prior to testing and do not remove the residue of the media.

[redacted]

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to the health. A copy of such report shall be sent promptly to the Secretary."