

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

DISTRICT OFFICE ADDRESS AND PHONE NUMBER

FDA/CBER/OCBQ/DMPQ
10903 New Hampshire Avenue, Silver Spring, MD 20993
Attention: Jay Eltermann, Building 71, Room 6038
Telephone: (240) 402-9168
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

April 18 - 22, 2016

FEI NUMBER

3000209996

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Robert Munday, General Manager

FIRM NAME

CMC ICOS Biologics, Inc.

STREET ADDRESS

22021 20th Avenue SE

CITY, STATE AND ZIP CODE

Bothell, Washington 98021

TYPE OF ESTABLISHMENT INSPECTED

Biologics Manufacturer

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

1. Process validation is incomplete. Specifically,

a. (b) (4) was initially assigned as "low risk" and was not included in the process validation studies.

Investigations of deviations in yield (low) under DEV-1484 and DEV-1573 at the (b) (4) step identified (b) (4) as the probable root cause. Changes were implemented to reduce the

(b) (4) of the (b) (4) used in this (b) (4) operation. Small-scale studies to evaluate the effect of (b) (4)

(b) (4) on (b) (4) are incomplete.

b. Investigations of out-of-specification (OOS) results for the (b) (4) under

DEV-1632 concluded that the initial acceptance criterion did not fully represent assay and process variability.

Again, (b) (4) was identified as a probable root cause. Small-scale studies to evaluate the effect of (b) (4) on (b) (4) are incomplete.

c. On October 17, 2015, the (b) (4) could not be (b) (4) due to (b) (4) (b) (4) contrary to the (b) (4)

d. Investigation on deviations in trend under DEV 2259 was opened on April 18, 2016 for three OOS results for the in-process parameter (b) (4)

e. Current small-scale validation study on hold times, VAL-30234-01, identified an increase in (b) (4) which might be resulted from (b) (4). The investigation is incomplete.

2. Deviations during production have not been thoroughly investigated. Specifically,

a. (b) (4) documented in deviation DEV-1498 did not trigger impact assessment on previous batches manufactured (b) (4). The impact on product quality of (b) (4) that might have been damaged

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Jay Eltermann
Michael Ovanov
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JAY ELTERMANN, CSD
MICHAEL OVANOV, RESEARCH BIOLOGIST
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Vanessa Y. Gelsey, Investigator

DATE ISSUED

4/22/16

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because of (b) (4) was not investigated. Corrective actions are not implemented to ensure that (b) (4)

b. "Reinstallation of (b) (4) was identified as the root cause for (b) (4) failure and loss of (b) (4). However, the cause for (b) (4) reinstallation, i.e., incorrect installation of (b) (4) due to failure to follow written batch record procedures, was not investigated or documented in DEV-1824.

3. Preventative maintenance of critical equipment is not performed per written procedures. Specifically,

a. Preventative maintenance for (b) (4) was not performed as scheduled. Daily tasks are not documented. Between June 7, 2015 and April 21, 2016, of 47 required weekly PM activities, eight that were late, 15 were missed, and two were not scheduled. Over the ten month period, only one of three quarterly maintenance activities was performed, due on August 31, 2015, completed on April 19, 2016. Semi-annual preventative maintenance performance was two months overdue.

b. Preventative maintenance for (b) (4) was not performed as scheduled. Daily tasks are not documented. Between September 20, 2015 through April 21, 2016, of 14 weekly PM activities, five were missed, and, of five quarterly maintenance activities, two were late.

4. Failure to follow standard operating procedure for deviation management. Specifically,

a. Critical deviations DEV-1484, DEV-1632, and DEV-2081 were initiated, respectively, 1, 5, and 2, days past the (b) (4) window as required by the deviation management procedure, GMP-0263, Rev 16. In all cases, the client was notified and initial investigations started within (b) (4) but the official documentation of the deviations were not initiated within the (b) (4) window.

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