DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
FDA/CDER/OPQ/OPMA/Division of Biotechnology Manufacturing Attn: Zhihao Peter Qiu, PhD, Acting Division Director White Oak Bldg 22, Room 5112, 10903 New Hampshire Ave; Silver Spring, MD 20903 Email: OPFBLAinspection483Responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	14-15, 18-22 November 2019
	FEI NUMBER 3010630287

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Domagoj Runac, Managing Director & Site Leader

FIRM NAME	STREET ADDRESS
Hospira Zagreb d.o.o.	Prudnička cesta 60
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
10291 Prigorje Brdovečko, Croatia	Drug Substance & Drug Product Manufacturing Facility

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 (I) (WE) OBSERVED:

OBSERVATION #1:

Your firm was unable to manufacture (b) (4) drug product purporting to be sterile because of a critical malfunction of the (b) (4) assembly. Specifically, during our observation of the (b) (4) (b) (4) of batch (b) (4) on 19 November 2019, tw (b) (4) bags (b) (4) containing the sterile bulk drug product fell onto the floor of the grade B environment, and the sterile bulk drug product solution leaked onto the floor. A deviation (4398034) was opened on 19 November 2019 your firm's quality unit; the aseptic processing operations were aborted, and the batch rejected.

OBSERVATION #2:

Written procedures are inadequate in the manufacture and testing of (b) (4) drug substance and drug product. Specifically,

a. "Determination of (b) (4) DS and DP potency by cell-based bioassay" (LAB-31261, v. 1.0; dated 11 May 2018) describes the method for potency testing of (b) (4) DS and DP release and stability samples. Page 10 of 13 of the procedure indicates that "a maximum of (b) (4) dose group and/o (b) (4) raw readouts/wells per Standard, Control or sample curves may be masked due to outliers." These instructions are inadequate for objective elimination of outliers in a way that ensures adequate assay performance and tracking of data masking events.

c. (b) (4) impurities—IC HPLC" (LAB-31157, v. 3.0; dated 13 November 2019), (b) (4) identity and quantitation of related compounds in drug substance and drug product by reverse phase high performance liquid chromatography" (LAB-3164, v. 4.0, date 13 November 2019), (b) (4) size variants—(b) (4) (LAB-31156, v. 3.0, dated 21 March 2019), and (b) (4) impurities an (b) (4) assay— (MPC008843/4, dated 17 December 2004) describe chromatography methods for testing of (b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (*Print or Type*)	DATE ISSUED
		Scott Nichols, Ph.D., Microbiologist Lindsey Brown, Ph.D., Microbiologist Merry Christie, Ph.D., Lead Chemist Ram Sihag, Ph.D., Lead Biologist	11/22/2019

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DS and DP in-process, release, and stability samples. The method descriptions allow for use of equivalent columns; however, there are no written procedures for how to determine columns are equivalent.

SN 22 Nov 2019

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SEE REVERSE OF THIS PAGE	HH Lindsey Brown mchristie	Scott Nichols, Ph.D., Microbiologist Lindsey Brown, Ph.D., Microbiologist Merry Christie, Ph.D., Lead Chemist Ram Sihag, Ph.D., Lead Biologist	11/22/2019