



## Inspection Report

Emd Millipore Corporation  
28820 Single Oak Drive  
Temecula, CA 92590

Customer ID: **321736**

Certificate: **14-R-0195**

Site: 001

E M D MILLIPORE CORPORATION

Type: ROUTINE INSPECTION

Date: 03-MAY-2017

### 2.31(d)(1)(ii)

#### INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

The search for alternatives for antibody production in animals is not current. The search was performed in October 2007 and included dates from 1992-2004. The search did not specifically investigate the potential pain and distress of repeated anesthetized cardiac bleeds in a guinea pig.

It is the responsibility of the IACUC to ensure that pain and distress are minimized to the greatest extent possible. Failure to question the use of repeated, invasive, potentially painful procedures (cardiac bleeds), and investigate the use of viable alternative procedures, can result in unnecessary pain and distress for the animals under study. The IACUC should ensure that procedures involving animals will avoid or minimize discomfort, distress, and pain to the animals.

Correct by 15 June, 2017.

### 2.31(d)

#### INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

The Institutional Animal Care and Use Committee (IACUC) did not adequately review animal activities being performed under the guinea pig protocol.

The IACUC approved protocol specified that serum would be collected by venipuncture, collecting 1-3 mls at a time under anesthesia. The facilities' Guinea Pig Care & Use SOP referenced in the protocol does not describe venipuncture as a route of blood collection in guinea pigs. The SOP describes cardiac bleeding under anesthesia.

The approved protocol referenced the guinea pig SOP for specifics of blood collection, which specified that two technicians are required to perform anesthetized cardiac blood draws on guinea pigs. During inspection, a single technician was observed performing cardiac blood draws under anesthesia on guinea pigs.

Adequate IACUC review of animal use is necessary to ensure that activities involving animals are being conducted appropriately. The IACUC should make certain that all activities relating to the care and use of animals receive

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adequate oversight and are conducted in accordance with the approved protocol and the Animal Welfare Act.

Correct from this day forward.

### 2.31(e)(3)

#### **INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).**

The IACUC approved protocol for Guinea Pigs did not contain a complete description of the proposed use of animals. The protocol specifies venipuncture for blood collection, with a terminal cardiac bleed yielding more blood as an approved study end-point and references an SOP that describes cardiac bleeds, not venipuncture. There is no detail regarding the frequency and duration of blood collection in the protocol or the SOP to determine the impact on the animals.

Review of the IACUC approved project starts with animal numbers did not include the bleed schedules, blood collection procedures and duration of the project. The IACUC is not able to review a complete description of the use of the animals without this information. The project schedules were reviewed for several projects, documenting that animals are bled via cardiac bleed every two weeks after injections of antigen.

It is the responsibility of the IACUC to ensure that the investigator provides a complete description of proposed activities that involve the use of animals in order that these activities may be adequately reviewed and determined to be in accordance with the Animal Welfare Act. A system should be in place to ensure that a complete description of each procedure is provided to the IACUC.

Correct by 30 May, 2017

### 2.33(b)(4)

#### **ATTENDING VETERINARIAN AND ADEQUATE VETERINARY CARE.**

Over the last two years, a total of four animals have been found dead in their enclosures in conjunction with recent cardiac bleeds and a gross necropsy has been performed. The two earlier animals were found dead the day after a cardiac bleed was performed and the cause of death was recorded as a cardiac tear in July of 2015 (12 previous cardiac bleeds) and July of 2016 (26 previous cardiac bleeds). In the last four months, two animals have been found dead in their enclosures. On 23 January 2017, animal 764 (38 previous cardiac bleeds) was found dead, 12 days after the last cardiac bleed on 11 January 2017 and the necropsy noted "Thorax noted w/ hemorrhage. Cardiac tamponade. Spontaneous myocardial rupture". On 22 April 2017, animal 781 (4 previous cardiac bleeds) was found dead, 3 days after a cardiac bleed on 19 April 2017 and the necropsy noted "pericardial sac full of hemorrhage - secondary to needle sticks most likely".

This recent increase in unexpected mortality related to cardiac abnormalities on necropsy in animals undergoing

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repeated cardiac bleeds is a change in the previous pattern. Adequate veterinary care includes guidance regarding the care and use of animals during the conduct of research. Repeated anesthetized cardiac bleeds is not a widely used method for survival blood collection in guinea pigs and in conjunction with the recent animal deaths after 4-38 cardiac bleeds in individual animals, additional guidance needs to be provided by the veterinarian regarding the care and use of animals.

Correct by 30 May 2017.

This inspection was conducted with facility representatives over several days. The exit interview was conducted over the phone.

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## Species Inspected

Cust No	Cert No	Site	Site Name	Inspection
321736	14-R-0195	001	E M D MILLIPORE CORPORATION	03-MAY-17

Count	Scientific Name	Common Name
000420	<i>Capra hircus</i>	DOMESTIC GOAT
000029	<i>Cavia porcellus</i>	DOMESTIC GUINEA PIG
000015	<i>Ovis aries aries</i>	SHEEP INCLUDING ALL DOMESTIC BREEDS
<b>000464</b>	<b>Total</b>	