

**PORTOLA PHARMACEUTICALS, INC.  
 PROTOCOL FOR THE HUMANE CARE AND  
 USE OF LIVE VERTEBRATE ANIMALS**

*Federal animal welfare regulations require that the Institutional Animal Care and Use Committee (IACUC) must review and approve all activities involving the use of vertebrate animals prior to their initiation. This includes animals used for experimental method development or for instructional purposes. In addition, approved protocols for ongoing activities must be reviewed by the IACUC at least annually.*

*To avoid the proliferation of submissions, please provide generic descriptions which include multiple routes of compounds administration, minor procedural variances, etc. Note, however, that a separate protocol is to be submitted for each species, even though the procedure may be similar. Your Institute IACUC member is a resource to help you. Protocols are to be submitted to the IACUC Chairperson.*

New Protocol:

First Annual Review:

Second Annual Review:

3 Year Full Committee Review: **X Conducted on October 26, 2018**

**[22 mice, 0 rats, 0 guinea pigs, and 0 rabbits were used under this protocol in 2017-2018]**

**[19 mice, 0 rats, 0 guinea pigs, and 6 rabbits were used under this protocol in 2016-2017]**

**[55 mice, 4 rats, 0 guinea pigs, and 2 rabbits were used under this protocol in 2015-2016]**

**1a. Protocol Title (should be descriptive of the animal use activity):**

Blood Harvests from Mice, Rats, Rabbits, and Guinea Pigs

**b. Protocol Purpose:**

[REDACTED]

Mice were used to provide plasma for assay development for two of Portola's research programs last year. Although few animals were used under this protocol in the past year, it remains important to be able to supply blood and plasma upon request for the various research programs at Portola.

Study designs will be written describing the specific method of blood collection, volume of blood required, and animal species to be used.

**2. Principal Investigator / Additional Personnel:**

Francis DeGuzman/ Dodie Canivel, Eduardo Escobar, Jiajia Feng, and John Malinowski



3. **Institute and Department:**

Portola Pharmaceuticals, Inc. /Biology and Pharmacology

4. **Others involved in procedural activities using live animals (other than LAF personnel.):**

Only Pharmacology personnel trained in the described procedures will participate in the execution of this protocol and its study designs. All Pharmacology personnel listed above have several years of experience in the collection of blood from conscious and anesthetized mice, rats, guinea pigs, and rabbits. Qualifications of personnel for handling, anesthetizing, and blood collection are on file with the Animal Facility Manager. Dr. Feng is a new addition to this protocol.

5. **Species:** Rat (Rt), Rabbit (R), Mouse (M), and Guinea Pig (GP)

**Strain:** SD, Lewis (Rt), NZW (R), Balb/c, Swiss Webster, IRCF1, and C57/Bl (M), and other strains of mice and rats, and Hartley (GP)

**Sex:** M/F

**Vendor:** Charles River (M, Rt, GP, R), Jackson Labs and Taconic (M), and other vendors as required.

**Weight/Age Range:** Adult

**Number of animals to be used annually:** 150 (Rt), 500 (M), 75 (GP), and 36 (R)

These numbers reflect the anticipated use based on compounds from all Portola programs to be evaluated using a variety of in vitro assays.

19 mice, 0 rats, 0 guinea pigs, and 6 rabbits were used under this protocol in 2016-2017

55 mice, 4 rats, 0 guinea pigs, and 2 rabbits were used under this protocol in 2015-2016

6. **Provide a complete description of the proposed use of animals.**

(Note: Please refer to questions 6a. through 6g. to avoid duplication of information.)

The purpose of these procedures is to provide blood and blood products to investigators for use in various types of studies and procedures, including, but not limited to assay development, platelet aggregation experiments, antidote studies, gene mapping/cloning, etc. For the majority of studies the blood harvest will involve a complete exsanguination and termination of an anesthetized animal. However, because of their larger size and total blood volume per animal, rabbits may not necessarily be exsanguinated on a terminal basis. For these studies, the rabbit will be conscious but may be lightly sedated if necessary to facilitate easy handling.

Tissues from the exsanguinated animals may also be collected to support the research programs.

a. **Experimental administrations.**

(Under Agent, identify biological materials, reference or control standards, general category of test compounds, etc. List each administration separately.)

<u>AGENT</u>	<u>VEHICLE</u>	<u>ROUTE</u>	<u>VOLUME</u>	<u>FREQUENCY</u>	<u>DURATION</u>
none	none	n/a	n/a	n/a	n/a



**7. Provide a rationale for involving animals, and for the appropriateness of the species and numbers of animals to be used:**

In *in vivo* drug development, there is a critical need to be able to screen new potential drug candidates for affinity to a particular receptor as well as potency for the biological function of interest in a high through put method prior to study in whole animals. These assays are typically cell based or rely on a blood or tissue medium on which a physiologically relevant reaction or parameter can be measured. While numerous tissues are used, blood and blood products are most heavily relied upon. This supply of blood and plasma from the various laboratory animal species are used in experiments and assays to compare various biological properties to human blood and plasma. This is perhaps the most widely used method for preclinical drug development. The need for the various species is a result of several things: the wide variety of questions posed by investigators, the techniques and technologies available and regulatory (FDA) compliance associated with filing an IND.

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The numbers of animals cited in this protocol reflect the expected use in 1 year's time based on previous years records.

**8. This section is required for any protocol/procedure that may cause more than momentary or slight pain or distress to the animals regardless of whether or not pain/distress will be ameliorated by the use of drugs or other techniques/methods. [Please refer to Animal Welfare Act, Sub-part C,2.31(d)(IV)(A,B,C)].**

**a. Provide a written narrative of alternative procedures/protocols considered and rejected. Include a description of the methods and sources used to determine that alternatives were not available:**

Blood and plasma are used in a wide variety of biological assays to characterize and differentiate the different chemical compounds under investigation at Portola. One alternative may be to purchase blood products, serum, and plasma from a commercial source. However, the volume of blood required, and the specific animal species and strain (mouse) may not be available in a timely manner. Therefore, an in-house program to supply blood and blood products to investigators in a timely manner to allow them to conduct their studies is appropriate.

A literature search was performed on the National Library of Medicine's PubMed.

Keywords: rat, mouse, rabbit, guinea pig, techniques/methods for blood collection

A literature search was conducted on October 19, 2018, using the PubMed database with the keywords listed above. For mice, 631 (1964-2018) citations were found on the database and 841 (1964-2018) citations were listed for rats.

Rabbit blood collection yielded 215 (1964-2018) articles and guinea pig had 62(1964-2017) citations from the database.

The Altweb database listed 103 citations using the keywords blood collection techniques in mouse, rat, guinea pig, and rabbit.