

Mutant Mouse Regional Resource Centers Distribution Policies

1 Overview

This document describes the MMRRC Distribution policies and the procedures by which an investigator requests and receives strains distributed from an MMRRC. Definitions of terms and abbreviations used in this document are listed at the end.

2 Terms and Conditions of Distribution

The MMRRC Program is committed to advancing biomedical research by the preservation and distribution of valuable mutant mouse strains. Donating Investigators (DIs) agree to transfer strains to the MMRRC Program under the least restrictive terms to allow the MMRRC to distribute strains to Requesting Investigators or Institutions (RIs) with the fewest administrative burdens, which could delay distribution.

The MMRRC distributes mice and cryopreserved material under its Material Transfer Agreement (MTA), which must be signed by the recipient investigator and their institution's technology transfer representative. (See [sample User MTA](#).) Currently, the BayGenomics ES cell lines distributed by UC-Davis do not require an MTA.

The terms of use in the MMRRC User MTA are:

1. The strain, descendants, derivative biological products and any cryopreserved material are the property of the Donating Investigator and are provided through the MMRRC to the RI as a service to the research community.
2. The strain, descendants and any derivative biological products are **not for use in human subjects**, including diagnostic testing.
3. Strains or biological material obtained from an MMRRC and descendants and derived biological products will be used only for non-commercial, biomedical research. An RI must obtain appropriate authorization from the DI or their institution, and any patent holders (as appropriate) prior to any commercial use.
4. The strain, derivative biological products and any strain descendants will not be bred for sale or distributed to any third party outside the RI's institution. An RI should refer other potential RIs to the MMRRC Program website or the ICSC Customer Service Center.
5. An RI agrees to cite (in bibliography) the donor (e.g., first published reference on strain) and cite (in "materials and methods" and/or "acknowledgements" section) the MMRRC Program in any publication or

- presentation of research involving any strains received from an MMRRRC. The MMRRRC will provide citation information on the Strain Detail page for each strain in which we acknowledge the DI and cite their primary reference.
6. The recipient understands that the strain and any biological products are experimental in nature and may have hazardous properties; the recipient assumes all responsibility for the use, storage and disposal of mice or biological materials.
 7. The mice and any derivative biological products must be used in compliance with applicable statutes and regulations including all applicable Federal statutes and Public Health Service policies relating to the use and care of laboratory animals.
 8. The strain or biological products are made available to the recipient for a transmittal fee (distribution fee), solely to reimburse the MMRRRC for its preparation and distribution costs.

2.1 Applicable Patent Restrictions

Certain strains may involve patents. An RI should work directly with the patent holder institutions to obtain appropriate user licenses as necessary.

2.2 Statement of warranties and limitations of liability

1. Mice and cryopreserved DNA material:
An RI understands that any strain or cryopreserved material obtained from an MMRRRC is experimental in nature and may have hazardous properties. The DI, the supplying MMRRRC, and the MMRRRC Program make no representations and extend no warranties of any kind, either expressed or implied. There are no express or implied warranties of merchantability or fitness for a particular purpose, or that the use of the material will not infringe any patent, copyright, trademark, or other proprietary rights.
2. Cryopreserved embryos and germplasm:
An RI understands that any strain distributed as cryopreserved embryos and/or germplasm from an MMRRRC is supplied as is, without warranty as to quality, exact quantity, recoverability or particular genotype(s). The MMRRRC has no control over the cryo-recovery methods and procedures used by an RI; therefore, an RI cannot assign to the MMRRRC, MMRRRC Program and/or the DI or their institution any responsibility for failure to recover live mice after cryopreserved embryos and/or germplasm are thawed.
3. ES cell line clones:
Recipients may obtain ES cell line clones with or without sequence verification in order to confirm that the cells are the identified cell line. When requested without sequence verification, the recipient assumes any risk that the material may not correspond to the desired DNA sequence.

2.3 International Requests

Acceptance of international requests is at the discretion of the supplying MMRRC. The RI must check the country's requirements for importing animals into the RI's institution before placing an order for a strain. The RI must send certified copies of relevant documents in English to the supplying MMRRC before an order can be fulfilled. If the institution in the importing country requires import permits, or any special labels (e.g. rabies), an RI must provide these materials to the supplying MMRRC before shipment is scheduled.

3 Distribution and Processing Fees

3.1 Summary:

The philosophy of the MMRRC distribution fee policy is to ensure the broadest possible availability of MMRRC mice to the research community by charging fees that are reasonable and consistent among the supplying MMRRCs. The framework of the MMRRC distribution policy is based on:

1. the real cost to the supplying MMRRC for importing, maintaining, archiving, genotyping, phenotyping, and distributing MMRRC mice
2. the amount of support provided by the base grant to each of the supplying MMRRCs.

Distribution fees are subject to review and revision annually by the MMRRC Coordinating Committee.

3.2 About MMRRC Mice Distribution Fees

MMRRC distribution fees are intended to help cover the costs associated with specialized mouse breeding, genetic quality and animal health monitoring, cryopreservation, customer service, technical information and support, and maintaining updated scientific information on all genetically-altered mice within the MMRRC Program.

Distribution fees for MMRRC mice are in U. S. dollars and are exclusive of shipping and container charges. Distribution fees include a per-mouse fee and (if applicable) a cryo-recovery fee, or a cryo-distribution fee. The per-mouse fee defrays the cost of importing, rederiving, maintaining, genotyping, phenotyping, and health monitoring of MMRRC mice.

The cryo-distribution fee defrays the cost of cryopreservation and cryo-replacement of a mouse strain to be distributed as cryopreserved material, and that is maintained only as a cryopreserved archive. The cryo-distribution fee entitles an RI to receive either cryopreserved embryos, germplasm, or ovaries.

The cryo-recovery fee partially offsets the cost of cryo-resuscitation, in addition to cryopreservation and cryo-replacement, of a mouse strain to be distributed as live mice, and that is maintained only as a cryopreserved archive.

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The cryo-recovery fee entitles an RI to receive a recovered litter that would include at a minimum a sufficient number mice to start a breeding line. In some cases, depending on the nature of the strain and size of the litter recovered, this could be a single heterozygous or homozygous mutant carrier of either gender that could be mated to a commonly available inbred mouse. A litter, of course, could and usually does include more than such a minimum, and normally the entire litter would be sent to the investigator.

To obtain mice from the recovery of specific genotype(s) or specific quantities greater than the litter size, the request must include per-mouse fees for each requested item.

3.3 Deposits and Prepayments to Cover Processing

At the discretion of the supplying MMRRC, an RI may be required to post a deposit or prepayment prior to fulfillment of a request by an MMRRC. At the time an order is confirmed, an RI will be informed as to any advance fees that are required by the supplying MMRRC.

3.4 Distribution Fees

Current distribution fees are noted on the MMRRC web at:
<http://www.mmrrc.org/distribution/fees.html>

3.5 Shipping and container charges

Shipping and container costs are not included in the published distribution fees. Shipping charges will reflect the actual carrier freight charges for air and/or ground transport. Shipping and container charges will be determined by the supplying MMRRC and will be itemized separately on invoices.

- **Live mice:**
Container charges will reflect the actual cost to the supplying MMRRC of protective, filtered containers used for distribution of live mice.
- **Cryopreserved materials obtained from a cryopreserved archive:**
An RI will be charged a \$500 deposit for the cryo-material shipping container prior to shipping an order. An RI must return the cryo-material shipping container by prepaid freight promptly after delivery and in a serviceable condition to the originating MMRRC; failure to return the cryo-material shipping container in serviceable condition within 7 business days will result in forfeiture by the RI of the deposit for the cryo-material shipping container.

3.6 Special Requests

1. The supplying MMRRC may assess additional fees for any special requests (e.g., specific age or weight of mice, etc.).
2. Agreement to fulfill special requests is at the discretion of the supplying MMRRC. The ICSC CSC representative will note on the request any

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special requests or requirements; these will be communicated to the supplying MMRRC with the request.

3.7 Document Preparation Fee for International Shipments

An RI will be charged an additional fee (currently \$75) per order by the MMRRC for the preparation of export documents.

4 Processing and Delivery of Distribution Requests

4.1 Items available

By looking in the MMRRC Program Catalog, an RI may determine the available strains, the forms of the material, their maintenance level, and distribution fees associated with each strain. The ICSC CSC will only accept requests for items listed as available in the MMRRC Strain Catalog on the MMRRC web site.

4.2 Distribution Request

To initiate a distribution request, an RI contacts the ICSC CSC. The CSC will manage acceptance and processing of all order requests. Before forwarding the request to the supplying MMRRC, the Recipient Institution must submit the required MMRRC User MTAs. (Request processing will not proceed until the required MTAs are received at the MMRRC's Customer Service Center; see section 4.3 below.)

4.3 User MTA

Except for the BayGenomic ES cell lines, the MMRRC requires receipt of two original copies of the MMRRC's User MTA, properly completed and signed by the recipient investigator and an authorized representative of the requesting institution (usually a Technology Transfer official). Request processing cannot proceed until the required MTAs are received at the MMRRC's Customer Service Center. A representative from the supplying MMRRC will complete execution of the MTAs and return one signed original to the requesting institution.

4.4 Quantities

The MMRRC Program is not a commercial breeder; being a non-profit repository, the MMRRC Program supplies limited quantities of breeders. Requests for quantities in excess of the listed availability level for any strain will be considered by the supplying MMRRC based on its ability to supply the requested quantities while maintaining the strain's availability to the general research community.

1. The CSC staff will record requests for distributions in quantities greater than the published availability level so that the supplying MMRRC can determine whether they are able to fulfill the request for excess quantity.
2. The CSC representative will inform an RI requesting greater quantities that the supplying MMRRC will determine acceptance of quantities above the availability level. The quantity requested by an RI does not constitute

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an actual order until the supplying MMRRC agrees to provide the quantities requested in excess of the listed available quantities, normally at the time the order request is booked by the supplying MMRRC.

In order to obtain greater quantities, an RI may request custom, contract breeding by directly contacting the supplying MMRRC.

4.5 Requests from Cryopreserved Archive

Before fulfilling a request for a strain or material from a cryopreserved archive, an MMRRC may require that the RI establish a written agreement (*e.g.*, email or FAX) with the supplying MMRRC that states the following terms:

1. By filing an order request, an RI agrees to be responsible for paying a cryo fee for cryo-distribution or resuscitation of live mice from a cryopreserved archive. Should an RI subsequently decide to cancel, or not accept delivery of mice recovered or material from the cryopreserved archive, the MMRRC will still invoice for the cryo-recovery or cryo-distribution service which the RI agrees to pay.
2. An RI agrees to be invoiced a deposit for each cryo-material shipping container prior to booking; this deposit fee will be forfeited to replace a cryo-material shipping container that is not returned to the originating MMRRC in serviceable condition by prepaid freight within 7 business days of receipt (See Shipping and container charges in section 3.5 above).

4.6 Order Confirmation

At the time of finalizing the distribution request, the supplying MMRRC will provide full details of fees for the requested material and estimates of the shipping costs.

- All mice will be shipped in protective, filtered containers.
- All cryopreserved material will be shipped in cryo-material shipping containers.

When finalizing the order request, the supplying MMRRC will also inform the RI of the date they estimate they will ship the strain or material. Prior to shipment, the center will contact the RI to finalize the schedule for delivery.

For additional information concerning transportation to a recipient's institution, RIs should contact the MMRRC providing the strain they wish to request; the ICSC CSC can assist an RI in contacting the appropriate person or department at the supplying MMRRC.

4.7 Customer and Technical Services at an MMRRC

RIs should contact MMRRC's ICSC Customer Service Center (ICSC CSC) for requesting mice strains or material.

Additionally, RIs may contact the ICSC CSC for assistance with requests, fulfillment and technical services questions; the ICSC CSC will put the caller in

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contact with the appropriate person at the supplying MMRRC Center. (The ICSC CSC does not itself handle issues related to order fulfillment, shipping, invoicing, collection or technical questions related to breeding and husbandry.)

Each MMRRC provides access to a CS contact at their facility. Once a request is confirmed with the supplying MMRRC, the RI may contact the center directly for further assistance with that request. The MMRRC website's Members page lists the Customer/Technical Services contact for each center. This person or group will assist recipients with questions about booked order requests, shipping and collection. They will also route requests for technical assistance with breeding or husbandry of an MMRRC strain distributed from their facility.

4.8 Changes and Cancellations

1. Once a request is made and processing begun, an RI is liable for all costs incurred in processing the request.
2. To request cancellation, suspension, rescheduling of a shipment or change to an order, the RI must submit the request to the supplying Center's CS contact in writing by email or fax before 12:00 PM noon (by that MMRRC's local time) three (3) business days prior to shipment. An RI should contact the appropriate MMRRC by telephone to confirm receipt of the written cancellation, suspension, rescheduling of shipment or change to the order.
3. An RI may not cancel, suspend, reschedule shipment, or change order requests for cryo-recovery or cryo-distribution once order processing commences. An RI agrees to be responsible for payment of the cryo fee upon submitting an order request.
4. An RI will be invoiced for the full distribution fee and any unavoidable shipping costs (e.g., cost of shipping containers) for any cancellations, suspensions, and rescheduling of shipment that occur on the day of shipment.
5. Special requests may involve conducting procedures several weeks in advance of shipment. An RI may request cancellation, suspension, rescheduling of shipment or change to an order for these services, however acceptance of such modifications is at the sole discretion of the supplying MMRRC. The supplying MMRRC will invoice for any service once the service is initiated.

4.9 Returns

An RI should not return to an MMRRC any mice, embryos, germplasm or other mouse products, or any shipping containers used to ship live mice. However, cryo-containers used to ship cryopreserved materials must be returned promptly or the RI forfeits the container deposit.

4.10 Breeding protocols involving a non-MMRRC mouse strain

When a breeding-maintenance protocol requires the use of a strain (e.g., wild type background strain) not offered through the MMRRC Program, an MMRRC may or may not be able to supply the necessary strain. The MMRRC will inform an RI of the preferred control strain.

5 Terms of Credit, Invoicing and Collection:

Credit, invoicing and collection are handled independently by each MMRRC. Credit arrangements with each RI are solely at the discretion of each MMRRC.

5.1 Purchase Orders

Usually arrangements can be made to request materials from the MMRRC using a Purchase Order (PO). When requesting materials from the MMRRC using a PO, the PO must be drawn with the supplying MMRRC as the vendor.

5.2 Payments

An RI should direct payments to the supplying MMRRC according to instructions in the invoice from the MMRRC; payment by money order, major credit card and check drawn on the recipient's institutional bank account are accepted by each MMRRC.

The MMRRC centers accept MasterCard, Visa, and American Express. We will also accept payment by a USA or an international Postal Money Order, made payable to the name of the supplying MMRRC from where mice were shipped.

Please include invoice number(s) on all remittances. For payment sent by mail, please send to the address of the supplying MMRRC (found on invoice)

Some MMRRCs may accept payment via wire transfer. If accepted by the MMRRC, wire transfers should include:

- a. the name of the institution making the payment
- b. the invoice number(s) for which the payment applies

Please fax copies of wire transfer information to the supplying MMRRC from where mice were shipped. Please follow the instructions from the supplying MMRRC to send wire transfers.

For questions concerning outstanding invoices, a requesting investigator should call the Customer Service representative at the supplying MMRRC from where mice were shipped.

5.3 Payment Terms

Terms are net 30 days payable in U.S. currency. Shipping and container charges are prepaid by the supplying MMRRC and are thus added to the invoice as separate items.

5.4 Delinquent Accounts

In the event of collection difficulties, an MMRRC may request the ICSC place a credit-hold on any requests from the Recipient Institution; a credit-hold will prevent the CSC from completing a distribution request for an RI until the originating MMRRC releases the credit-hold.

5.5 Replacement and Refunds

All distributions of strains, either as mice or as cryopreserved material, to an RI from an MMRRC are final.

5.5.1 For Live Mice:

An RI may be issued credit or replacement mice when:

- a. An MMRRC ships the incorrect strain, gender or genotype of mice; an RI should notify the supplying MMRRC as soon as the mistake is detected;
- b. Mice arrive dead or moribund, or become sick within 3 days of arrival, provided that the problem is reported to the supplying MMRRC within 5 business days after receipt;
- c. Mice arrive in damaged containers; an RI should note damage on the delivery manifest at the time of receipt of the shipment and notify the supplying MMRRC immediately.

An RI must report requests for credit and carrier-related complaints by telephone to the supplying MMRRC CS within 5 business days after receipt of shipment, and follow up this report by written (e.g., email, fax) confirmation.

5.5.2 For Cryopreserved Embryos and/or Germplasm:

An RI will be issued credit or replacement of cryopreserved embryos and/or germplasm by an MMRRC for the following reasons:

- a. The supplying MMRRC ships an incorrect strain or type of cryopreserved material;
- b. Cryo-material arrives in damaged containers compromising the integrity of the cryopreserved material; an RI should note damage on the delivery manifest at the time of receipt of the shipment and notify the originating MMRRC within 5 business days after receipt.

5.5.3 Limitations:

In case of dissatisfaction with any strain or biological material shipped for a valid reason as determined by the MMRRC, liability will be limited, at the option of the supplying MMRRC, to replacement of the strain or biological material provided. Replacement of strain or material shall be the exclusive remedy of the recipient.

6 Cryopreservation-related Issues:

Recovery of mice of a strain maintained only as cryopreserved embryos and/or germplasm in a cryopreserved archive is a complex task; while techniques and performance continually improve, the process is by no means guaranteed. Once mice are resuscitated, they must be bred sufficient to supply the requested order(s) and to restock the repository. Time to breed can vary greatly from strain to strain.

1. Recovery of live mice of a strain maintained only in a cryopreserved archive (as cryopreserved embryos and/or germplasm) requires a minimum of 15 weeks to complete request fulfillment.
2. An RI will not be billed for a cryo-recovery procedure by an MMRRC in the event that it is unable to successfully resuscitate mice for distribution.
3. An RI will receive the requested number of mice following resuscitation of the strain; requests for larger quantities of mice can be made by special arrangements with the supplying MMRRC.

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7 Abbreviations and Definitions:

CC: Coordinating Committee of the MMRRRC Program

CS: Customer Service at an individual MMRRRC

CSC: ICSC Customer Service Center serving the MMRRRC Program

Cryopreserved Material: Cryopreserved embryos or germplasm

DI: Donating Investigator(s) or Institution

IACUC: Institutional Animal Care and Use Committee

ICSC: Informatics, Coordination and Service Center of the MMRRRC Program

MMRRRC: individual Center(s) participating in the MMRRRC Program

MMRRRC Program: Mutant Mouse Regional Resource Centers Program

MTA: Material Transfer Agreement

RI: Requesting Investigator(s) and/or Institution

Strain: any mutant mouse maintained and distributed by an MMRRRC