

# Standard Operating Procedure

## MDA (Micropipette-guided Drug Administration) Method

|                                                    |                           |
|----------------------------------------------------|---------------------------|
| Species: Mice                                      |                           |
| Version 4                                          | Date: 03.06.2020          |
| Authors: Juliet Richetto, Urs Meyer, Paulin Jirkof | Last Modified: 15.07.2026 |

### Objective

Pharmacological administration method for per os treatments in mice. This method can potentially be used for different drugs, the preparation of the drug solution depends on the drug's properties. Below an example preparation procedure is described.

### Equipment, materials

1. Sweet condensed milk (e.g. MIGROS Kondensmilch™, Migros, Zurich, Switzerland)
2. Regular Tap Water
3. 15 or 50ml Falcon Tubes
4. Ultrasonic water bath\*
5. Magnetic Stirrer\*
6. Channel p200 Micropipette
7. p200 Pipette Tips

\*Depending on characteristics of drug to be administered

*Administration of Tamoxifen or other substances that do not emulsify in the sweet condensed milk solution:* Add some drops of Tween20 (Polyethylene glycol sorbitan monolaurate, e.g. Sigma- Aldrich).

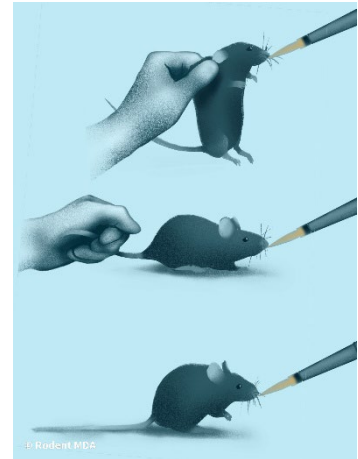
### Procedure Preparation Drug Solution\*\*:

1. Dilute condensed milk with regular tap water in an e.g. 4:10 (condensed milk to water) ratio. This solution is used as vehicle.
2. Dilute the drug to be administered per os in water and sonicate for 20 min.
3. Mix suspended drug with vehicle solution to reach the desired concentration.
4. Keep drug and vehicle solution in constant agitation using a magnetic stirrer.
5. Drug and vehicle solution are administered at a volume of e.g. 2 ml/kg.

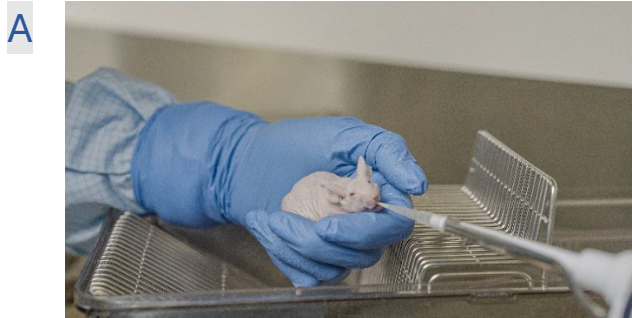
\*\* This section depends on the characteristics of the drug to be administered and might need adaptation.

## MDA Training & Procedure

1. Prepare the desired amount (2 ml/kg) of drug or vehicle solution in the tip of the p200 micropipette. For training you should use vehicle solution only.
2. Training Day 1: Restrain the mouse gently or cup it in your hand and expose it to the milk solution for the first time, by offering the pipette tip to the mouth until the mouse begins to drink (see figure 1 top and figure 2A).
3. Training Day 2: Restrain mouse solely by the base of the tail on the metal grid of the food hopper or cup it in your hand and position the pipette continually next to the mouse's mouth until it drinks (see figure 1 center and 2B). The animal should ingest the complete volume.
4. (Optional) Training Day 3-7: If necessary, repeat the procedure from training day 2 to familiarize the mouse with the milk solution even further. The animal should ingest the complete volume.
5. MDA: Place the mouse on the metal grid of the food hopper with no or minimal restraint and offer pipette tip until the mouse voluntarily begins to drink the solution (see figure 1 bottom and 2C).



**Figure 1:** Training Day 1-3 and MDA (from top to bottom)



**Figure 2:**

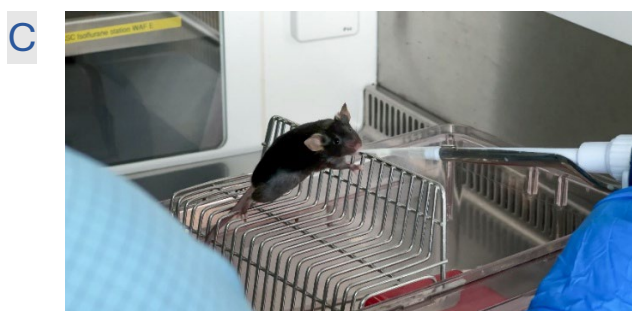
*Phases of the micropipette-guided drug administration (MDA) method in different strains.*

**(A)** Training Day 1: Mice can be cupped in the hand instead of full restraint (c.f. figure 1) and exposed to the sweetened condensed milk solution for the first time via a conventional micropipette (see also [Video](#)).

**(B)** Training Day 2 (& 3-7): Mice are restrained solely by the tail and exposed to the sweetened condensed milk solution via a micropipette (see also [Video](#)).

**(C)** MDA treatment: Mice are no longer restrained and drink the sweetened condensed milk solution voluntarily from the micropipette (see also [Video](#)).

Images: RodentMDA by MELS, UZH.



## References

- Krzyzaniak O, Steiner S, Nilsson FAM, Dietrich M, Kämpfen L, Johansen P, Jirkof P, Meyer U (2026). Carprofen and buprenorphine delivery using micropipette-guided drug administration (MDA) in mice. *Neuropsychopharmacology* (online ahead of print). doi: 10.1038/s41386-026-02445-8.
- Krzyzaniak O, Steiner S, Nilsson FAM, Dietrich M, Kämpfen L, Johansen P, Jirkof P, Meyer U (2025). Applicability of the micropipette-guided drug administration (MDA) method for assessing reward-related behaviors in mice. *Physiol Behav* 299:114967. doi: 10.1016/j.physbeh.2025.114967.
- Nilsson FAM, Krzyzaniak O, Dietrich M, Steiner S, Kämpfen L, Jirkof P, Meyer U, Johansen P (2026). Moving beyond oral gavage: micropipette-guided drug administration (MDA) as a 3R refinement for voluntary oral drug delivery in rodents. *Lab Anim* 55(6):193-195. doi: 10.1038/s41684-026-01746-1.
- Steiner S, Krzyzaniak O, Nilsson FAM, Dietrich M, Kämpfen L, Johansen P, Jirkof P, Meyer U (2025). Sex and strain differences in the micropipette-guided drug administration (MDA) method in mice. *Lab Anim* 59(5):578-587. doi: 10.1177/00236772251320843.
- Scarborough J, Mueller F, Arban R, Dorner-Ciossek C, Weber-Stadlbauer U, Rosenbrock H, Meyer U, Richetto J (2020). Preclinical validation of the micropipette-guided drug administration (MDA) method in the maternal immune activation model of neurodevelopmental disorders. *Brain Behav Immun* 88:461-470. doi: 10.1016/j.bbi.2020.04.015.
- Schalbetter SM, Mueller FS, Scarborough J, Richetto J, Weber-Stadlbauer U, Meyer U, Notter T (2021). Oral application of clozapine-N-oxide using the micropipette-guided drug administration (MDA) method in mouse DREADD systems. *Lab Anim (NY)* 50(3):69-75. doi: 10.1038/s41684-021-00723-0.
- Scarborough J, Mattei D, Dorner-Ciossek C, Sand M, Arban R, Rosenbrock H, Richetto J, Meyer U (2021). Symptomatic and preventive effects of the novel phosphodiesterase-9 inhibitor BI 409306 in an immune-mediated model of neurodevelopmental disorders. *Neuropsychopharmacology* 46(8):1526-1534. doi: 10.1038/s41386-021-01016-3.

### For further information please contact

Dr. Paulin Jirkof  
Office for Animal Welfare and 3R  
University of Zurich  
Winterthurerstrasse 190  
8057 Zurich, Switzerland  
E-mail: rodentmda@uzh.ch

### Further data/recordings available:

Video figure 2, A-C  
<https://doi.org/10.6084/m9.figshare.32923325>  
Full SOP Video  
<https://youtu.be/b8adBybZgzs?si=63H7SVFrBeGFglLU>

Rodent MDA Website  
<https://www.rodentmda.ch/>