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Teklad Custom Diets

# Cuprizone diets: A trusted tool for neuroscience research

Bis(cyclohexanone)oxaldihydrazone, commonly referred to as cuprizone, causes demyelination of the central nervous system in rodents, most notably, the corpus callosum of mice. Cuprizone is a copper chelator; however, the exact mechanism of cuprizone-induced damage to the central nervous system remains unclear. Despite an unknown mechanism of action, dietary cuprizone administration is a well-characterized and reliable method used to study de- and remyelination processes involved in diseases of myelin dysfunction such as multiple sclerosis and certain psychiatric disorders.

## Cuprizone and control diets

Cuprizone %	Base diet: 2016	Base diet: 2018
0% or control	TD.00217	TD.00588
0.2%	TD.140800	TD.140803
0.2% with Red food dye	TD.140801	TD.140804
0.3%	TD.140802	TD.140805

If you require an alternate concentration, base diet, or color not shown in this table, please contact a nutritionist at [askanutritionist@envigo.com](mailto:askanutritionist@envigo.com) to assist you in setting up a new product code prior to your next diet order.

We encourage you to use our stocked supply, but if you prefer to send the cuprizone, we are happy to accommodate you. If you choose this option, please consult a nutritionist before sending your cuprizone.

## Key planning information

### Ordering

- Minimum order quantity is 3 kg, sufficient for feeding ~20 mice or four-six rats for one month.
- We make your diet fresh to order in pellet or powder form, and typical lead-time is two weeks (four weeks if irradiated).
- Irradiation (20 - 50 kGy) is optional, and must be requested at time of order. Effects of irradiation on cuprizone are unknown. However, several research groups are successfully producing demyelination with irradiated cuprizone diets.

### Packaging and labeling

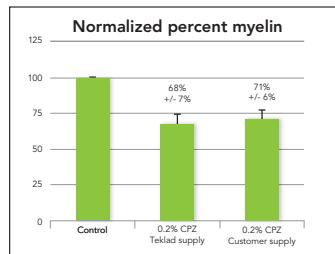
- We recommend vacuum packaging in 500 g, 1 kg, or 2 kg packs.
- Box and package labels indicate the diet code, description, batch specific lot number, and manufacture date.

### Shelf life and storage

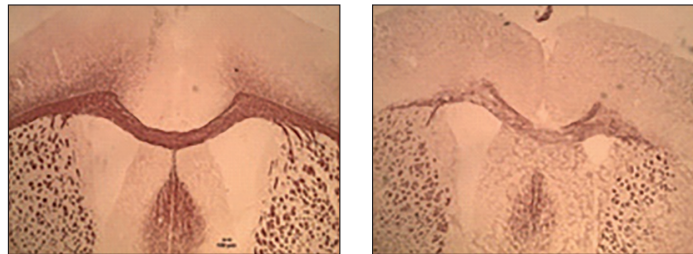
- Store diet refrigerated, away from light, and plan to use within six months.

Plan to change out feed on cage tops at least once per week. Due to cuprizone stability concerns, some researchers report changing food as frequently as every two days.

**Eight week old C57BL/6 mice fed 2016 with 0.2% cuprizone (CPZ) diet for six weeks (N=5 CPZ groups, N=2 control).**



Percent myelin in area of corpus callosum and external capsule normalized to control.



Representative image from control (left) and 0.2% CPZ- Teklad supply (right). Notice the greater amount and more organized structure of the myelin in the control vs. cuprizone treated mouse.

Data provided by NYU Researchers JL Salzer, EM Grund, and J Samanta

## Key points from literature

### Induction method

- In acute studies, cuprizone containing diets are fed for 4-6 weeks (1-13). Substantial remyelination occurs within 4-6 weeks after cuprizone withdrawal.
- In chronic studies, cuprizone is administered for 12 weeks or longer (3, 7, 10, 12). In contrast to acute treatment, remyelination is incomplete and may require 12 weeks to reach maximal levels.
- The typical dietary inclusion of cuprizone is 0.2% (1-7, 9-13). A slightly higher inclusion of 0.3% is also common (1, 4, 8, 13) and could result in more complete demyelination or shorten the treatment time. The higher level may be preferable in some mouse strains, but is not as well tolerated in others.

### Model characteristics

- C57Bl/6 is the most common mouse strain utilized (1-12) although BALB/c, CD-1, Swiss and mice with mixed background may also experience demyelination through cuprizone administration (2, 10, 13).
- Mice are usually eight weeks, but occasionally treatment is started in mice that are several months of age (9). Younger mice tend to have variable response and poor tolerance of cuprizone treatment (7).
- Male mice are predominantly used since estrogen and progesterone can influence myelination, however some researchers utilize both sexes and report that sex does not matter when using C57Bl/6 mice (5, 7, 12).

### Additional considerations

- Expect weight loss during the first week of cuprizone administration. Weight recovery typically occurs by the end of treatment or within a week of cuprizone removal (2, 5, 8, 11).
- Signs of spontaneous remyelination have been observed transiently during cuprizone administration (4, 6, 7).

## Material safety

- Cuprizone is not hazardous according to OSHA criteria. Accidental exposure can be minimized by using typical lab precautions of lab coat, gloves and mask when handling the diet.
- Your chemical safety department should be contacted for additional institution specific guidelines for handling and disposal of cuprizone-containing diets.

### References

1. Armstrong RC, Le TQ, Frost EE, Borke RC, Vana AC. 2002. Absence of fibroblast growth factor 2 promotes oligodendroglial repopulation of demyelinated white matter. *J Neurosci* 22:8574-8585.
2. Franco-Pons N, Torrente M, Colomina MT, Vilella E. 2007. Behavioral deficits in the cuprizone-induced murine model of demyelination/remyelination. *Toxicol Lett* 169:205-213.
3. Hibbits N, Yoshino J, Le TQ, Armstrong RC. 2012. Astrogliosis during acute and chronic cuprizone demyelination and implications for remyelination. *ASN Neuro* 4:393-408.
4. Lindner M, Heine S, Haastert K, Garde N, Fokuhl J, Linsmeier F, Grothe C, Baumgartner W, Stangel M. 2008. Sequential myelin protein expression during remyelination reveals fast and efficient repair after central nervous system demyelination. *Neuropathol Appl Neurobiol* 34:105-114.
5. Liu L, Darnall L, Hu T, Choi K, Lane TE, Ransohoff RM. 2010. Myelin repair is accelerated by inactivating CXCR2 on nonhematopoietic cells. *J Neurosci* 30:9074-9083.
6. Mason JL, Langaman C, Morell P, Suzuki K, Matsushima GK. 2001. Episodic demyelination and subsequent remyelination within the murine central nervous system: changes in axonal calibre. *Neuropathol Appl Neurobiol* 27:50-58.
7. Matsushima GK, Morell P. 2001. The neurotoxicant, cuprizone, as a model to study demyelination and remyelination in the central nervous system. *Brain Pathol* 11:107-116.
8. Sachs HH, Bercury KK, Popescu DC, Narayanan SP, Macklin WB. 2014. A new model of cuprizone-mediated demyelination/remyelination. *ASN Neuro* 6.
9. Shen S, Sandoval J, Swiss VA, Li J, Dupree J, Franklin RJ, Casaccia-Bonnel P. 2008. Age-dependent epigenetic control of differentiation inhibitors is critical for remyelination efficiency. *Nat Neurosci* 11:1024-1034.
10. Skripuletz T, Lindner M, Kotsiari A, Garde N, Fokuhl J, Linsmeier F, Trebst C, Stangel M. 2008. Cortical demyelination is prominent in the murine cuprizone model and is strain-dependent. *Am J Pathol* 172:1053-1061.
11. Steelman AJ, Thompson JP, Li J. 2012. Demyelination and remyelination in anatomically distinct regions of the corpus callosum following cuprizone intoxication. *Neurosci Res* 72:32-42.
12. Tobin JE, Xie M, Le TQ, Song SK, Armstrong RC. 2011. Reduced axonopathy and enhanced remyelination after chronic demyelination in fibroblast growth factor 2 (Fgf2)-null mice: differential detection with diffusion tensor imaging. *J Neuropathol Exp Neurol* 70:157-165.
13. VonDrän MW, Singh H, Honeywell JZ, Dreyfus CF. 2011. Levels of BDNF impact oligodendrocyte lineage cells following a cuprizone lesion. *J Neurosci* 31:14182-14190.

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