

Tamoxifen diets for inducible Cre-LoxP systems

(Available in Europe)



Diets with tamoxifen activate CreER

Tamoxifen-containing diets should be considered an option if you are using a model with Cre under the control of a mutated estrogen receptor.

Inotiv makes a variety of tamoxifen-containing diets customized to meet your research needs. We also make a variety of doxycycline-containing diets for Tet regulated systems.

For questions, contact
a nutritionist at
askanutritionist@inotivco.com
or your local European Inotiv office.

Key points from literature

- Length of treatment varies from 1-2 weeks^(1,2,5,6,7,8) to 1-2 months^(3,4,8)
- Pure tamoxifen^(1,5,8) and tamoxifen citrate^(1,2,3,4,6,7) are both effective
- Usual tamoxifen doses are ~40-80 mg per kg body weight per day
- Typical inclusion for pure tamoxifen is 250 mg⁽⁸⁾ or 500 mg^(1,5) and for tamoxifen citrate is 400 mg per kg diet^(1,2,3,4,6,7)
- Initial weight loss of 10% is reported^(1,2,4,7,8), associated with reduced food intake⁽²⁾
- Subsequent recovery of body weight after returning to regular diet may be compromised by gene inactivation^(2,7)

1. **Andersson KB, Winer LH, Mork HK, Molkentin JD, Jaisser F. 2010.** Tamoxifen administration routes and dosage for inducible Cre-mediated gene disruption in mouse hearts. *Transgenic Res* 19:715-725.
2. **Chiang PM, Ling J, Jeong YH, Price DL, Aja SM, Wong PC. 2010.** Deletion of TDP-43 down-regulates Tbc1d1, a gene linked to obesity, and alters body fat metabolism. *Proc Natl Acad Sci U S A* 107:16320-16324.
3. **Kardakaris R, Gareus R, Xanthoulea S, Pasparakis M. 2011.** Endothelial and macrophage-specific deficiency of P38alpha MAPK does not affect the pathogenesis of atherosclerosis in ApoE^{-/-} mice. *PLoS One* 6:e21055.
4. **Kiermayer C, Conrad M, Schneider M, Schmidt J, Brielmeier M. 2007.** Optimization of spatiotemporal gene inactivation in mouse heart by oral application of tamoxifen citrate. *Genesis* 45:11-16.
5. **Koitabashi N, Bedja D, Zaiman AL, Pinto YM, Zhang M, Gabrielson KL, Takimoto E, Kass DA. 2009.** Avoidance of transient cardiomyopathy in cardiomyocyte-targeted tamoxifen-induced MerCreMer gene deletion models. *Circ Res* 105:12-15.
6. **Kratsios P, Catela C, Salimova E, Huth M, Berno V, Rosenthal N, Mourkioti F. 2009.** Distinct roles for cell-autonomous Notch signaling in cardiomyocytes of the embryonic and adult heart. *PCirc Res* 106:559-572.
7. **Miro-Murillo M, Elorza A, Soro-Arnaiz I, Albacete-Albacete L, Ordonez A, Balsa E, Vara-Vega A, Vazquez S, Fuertes E, Fernandez-Criado C, Landazuri MO, Aragonés J. 2011.** Acute Vhl gene inactivation induces cardiac HIF-dependent erythropoietin gene expression. *PLoS One* 6:e22589.
8. **Welle S, Burgess K, Thornton CA, Tawil R. 2009.** Relation between extent of myostatin depletion and muscle growth in mature mice. *Am J Physiol Endocrinol Metab* Oct;297(4):E935-40.



Tamoxifen diet options

The standard version for tamoxifen citrate produced in EU is 400 mg per kg diet. Teklad Global 2016 is used as the base diet to provide a minimal phytoestrogen background. Red color is added to differentiate from regular diet.

| TAMOXIFEN MG PER KG DIET | DAILY TAMOXIFEN MG PER KG BODY WEIGHT ¹ | DIET CODE | |
|--------------------------------|--|-----------------------|------------|
| | | NON- IRRADIATED | IRRADIATED |
| 400 citrate ² | 40 | TD.55125 ³ | TD.55125.I |

¹ Assumes 20-25 g body weight and 3-4 g intake

² Tamoxifen citrate is 66% tamoxifen

³ Referred to as TAM400/CreER

This example diets has tamoxifen premixed with ~5% sucrose as a palatability enhancer; however, feed aversion may still occur.

If you require an alternate concentration, base diet, or color not shown, please contact a nutritionist at askanutritionist@inotivco.com.

Key planning information

- Minimum order quantity is 3 kg, sufficient for feeding ~20 mice for one month
- Store diet refrigerated and plan to use within six months
- Typical lead time is 3-4 weeks (4-5 weeks if irradiated)
- Irradiation at a minimum dose of 21 kGy

For more information contact us at
askanutritionist@inotivco.com

Mice need time to adjust.

Plan for:

- Initial reduction in food intake and weight loss
- Daily observation of animal tolerance - consult your IACUC for monitoring metrics
- Intervene when necessary (see below)

Other researchers have the following advice if intake seems to be a problem:

- Determine if a lower dose is effective for your model by conducting a tamoxifen dose feeding trial.
- Gradually acclimate mice by mixing tamoxifen-containing pellets with regular feed pellets.
- Wet the food, then place in a dish inside the cage (requires daily replacement).
- Feed tamoxifen diet on weekdays, regular diet on weekends.
- Alternate weeks (two weeks on tamoxifen diet, one week off) for longer treatments.

Safe handling of tamoxifen diets

- Tamoxifen is a selective estrogen receptor modulator (SERM) meaning it can repress actions of estrogen or have pro-estrogen effects.
- Usual dose for therapeutic effects in humans is 20 mg/day. Tamoxifen diets for rodents typically contain ~1-2 mg/pellet.
- Accidental tamoxifen 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 tamoxifen containing diets.