Tamoxifen diets for inducible Cre-LoxP systems

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.

Envigo 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.

If you have any questions, don’t hesitate to contact a nutritionist at askanutritionist@envigo.com.

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)

References

Teklad now stocks tamoxifen and tamoxifen citrate

Tamoxifen is added to the diet as a tamoxifen-sucrose mixture. Users are encouraged to use the stocked supply. However, Envigo will continue to work with customer prepared mixes. If you choose this option, please consult a nutritionist for additional information about preparing and sending the mixture.

<table>
<thead>
<tr>
<th>Tamoxifen mg per kg diet</th>
<th>Daily tamoxifen mg per kg body weight</th>
<th>Diet code</th>
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<tbody>
<tr>
<td>250</td>
<td>40</td>
<td>TD.130855</td>
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<tr>
<td>500</td>
<td>80</td>
<td>TD.130857</td>
</tr>
<tr>
<td>400 citrate¹</td>
<td>40</td>
<td>TD.130859 ³</td>
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<td>TD.130860 ³</td>
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¹ Assumes 20-25 g body weight and 3-4 g intake
² Tamoxifen citrate is 66% tamoxifen
³ Referred to as TAM400/CreER in Europe (TD.55125)

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

Teklad Global 2016 (base diet in these examples) is only one of several minimal phytoestrogen diets Teklad produces. Consult a nutritionist about use of other base diets.

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 two weeks (four weeks if irradiated)
- Irradiation (20 - 50 kGy) is optional, and must be requested at time of order

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.