



## Information on production practices, health testing and health designation for huNOG products

HSCCB-NOG-F, HSCCB-NOG-M, HSCFTL-NOG-F, HSCFTL-NOG-M,  
HSCFTL-13395-F, HSCCB-13395-F

huNOG products are generated via sublethal irradiation and engraftment of NOG mice with human hematopoietic stem cells. They are housed for 12+ weeks post-engraftment prior to shipment.

### **Source of mice, housing and procedure locations**

The NOG mice used for this engraftment are sourced from one of Taconic's Excluded Flora™ Isolated Barrier Unit production colonies and moved to a semi-rigid isolator at the humanization facility. Mice are removed from the isolator and into a procedure room for irradiation, engraftment and any blood sampling activities. The isolator is sentinelized with SW mice as well as NOG mice, sourced from a Taconic Defined Flora colony. The sentinel program involves weekly exposure of the sentinel mice to soiled bedding and used feed and water from cages within the isolator. Additionally, the sentinel mice accompany the NOG mice during transit to the procedure room and remain in close proximity to the NOG mice during all manipulations within the procedure room; sentinel mice and manipulated NOG mice are transported back to the housing isolator together. The housing isolators are monitored for contamination via modified IHMS™ testing and monthly Restricted Flora™ monitoring. IHMS™ testing is rotated between IHMS-6, IHMS- 13, IHMS-26 and IHMS-52 test panels with IHMS-52 testing occurring once per quarter to allow transit on Taconic trucks. Monthly Restricted Flora™ testing involves pooled fecal samples from both line animal and sentinel cages in addition to oral swab testing. Animals are expected to maintain Restricted Flora™ health status.

### **Human cell source and testing**

The human hematopoietic stem cells are provided to Taconic as dissected tissue or isolated cells. They have been tested by the vendor and certified negative of hepatitis B, hepatitis C, HIV and LCMV prior to receipt at Taconic.



## **Basic engraftment procedure description**

NOG mice are sublethally irradiated between 4-24 hours prior to IV injection with human hematopoietic stem cells. The mouse is restrained and cells are administered via IV tail vein injection.

## **Quality control**

Post-procedure observations include daily examination of mice for health, appearance and injection site healing. huNOG mice are tested by flow cytometry to quantify the level of human leukocytes in peripheral blood.



## Recommended Care and Housing for Human Immune System NOG Mice

HSCCB-NOG-F, HSCCB-NOG-M, HSCFTL-NOG-F, HSCFTL-NOG-M,  
HUPBMC-NOG-F, HUPBMC-NOG-M, R-HUPBMC-NOG-F,  
R-HUPBMC-NOG-M, BLT-NOG-F, BLT-NOG-M

### **Production at Taconic**

The CIEA NOG mouse<sup>®</sup> is severely immunodeficient. Human Immune System NOG mice reconstitute some portions of the human immune system, but must still be carefully handled. Taconic and CIEA recommend the highest level of care possible for these mouse models. More information regarding [production practices for the CIEA NOG mouse<sup>®</sup>](#) and for [Human Immune System NOG models](#) is available online.

At Taconic, all items that enter the isolator housing Human Immune System NOG mice are sterilized, including the feed and water. Mice are housed in polycarbonate cages with wire bar lids. Groundwater is passed through a 10 micron filter, and the water is acidified to a pH target of 2.5. After acidification, the water is passed through a 1.2 micron filter, a 0.2 micron filter and finally a 0.1 micron filter prior to being placed into sealed pouches. The water pouches fitted with drinking valves are provided to the mice inside the isolators. Water for transit is packaged as hydrogel packs which are gamma irradiated.

## **Recommendations for maintenance by users**

1. All materials for housing or experimentation should be sterilized by autoclave, chemical disinfection or irradiation, including food and water. Water treatment such as hyper chlorination, acidification, or other treatment to minimize bacterial exposure is recommended.
2. Microbiological monitoring should be performed monthly or bimonthly using sentinels. Testing should include opportunistic agents such as *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Pneumocystis murina*. Taconic offers animal health testing [services](#), and the Taconic International Health-Monitoring System™ (IHMS™) can supply the confidence needed to work with immunodeficient models.
3. Human Immune System NOG mice should be housed in the cleanest portion of the animal facility. If possible, maintain the Human Immune System NOG model in its own room or in an immunodeficient mouse room.
4. Personnel movement policies are important to reduce the chance of contamination. The most desirable arrangement is to have dedicated personnel for the Human Immune System NOG model room. If separate technicians are not available to care for the Human Immune System NOG model only, then personnel should enter the room housing the Human Immune System NOG model prior to going into areas which have a lower health status. They should not return to the Human Immune System NOG room during the day unless proper personnel decontamination procedures have taken place.
5. Illness or other adverse effects may be linked to infection by opportunistic agents or excessive stress on the mice. Care should be taken to maintain a high health standard and minimize stress on the mice.
6. As with other immunodeficient models, the Human Immune System NOG model may benefit from housing in microisolator cages. Using proper decontamination procedures between the changing of cages is recommended. One such approach is to use forceps that are disinfected before use with each new cage to pick up the tail of the mouse.
7. Move animals to a class II laminar flow hood for cage changes and research protocols. Cages can also be changed in HEPA filtered animal cage change stations.
8. Human Immune System NOG mice are generally non-aggressive and may be group housed, including males.



## **Specific notes and recommendations for individual models**

**huPBMC-NOG:** NOG mice engrafted with human PBMCs will develop Graft vs. Host Disease (GvHD) within 5-7 weeks. GvHD manifests as weight loss, poor clinical condition, infiltration of immune cells into organs and liver damage. PBMC-engrafted NOG mice should be monitored closely for condition and be humanely euthanized when found moribund.

**BLT-NOG:** Under certain circumstances, NOG mice modified with the BLT procedure may exhibit a wasting-type syndrome as they age. This appears to be related to activation of the immune system, presumably due to microbiological status of the facility. BLT-NOG mice may otherwise maintain stable engraftment and good health in long term studies.

**HUNOG-EXL:** We have seen that this model engrafts extremely well with chimeric ratios averaging 60% and sometimes over 80%. One of the potential adverse effects we have seen in some animals as a result, is the development of a clinical anemia. Our process improvements have decreased the incidence to 5-10% of mice. Nevertheless, it is recommended that all animals receive a bolus of sub-cutaneous fluids when blood samples are collected.

Requirements for care will vary by facility. Please consult your veterinarian or facility manager for more information on working with immunocompromised animals.