



The rasH2 Mouse^{*}

A MODEL TO ACCELERATE
CARCINOGENICITY TESTING STUDIES

The rasH2 Mouse*



When you perform traditional carcinogenicity testing over a two-year horizon, time and costs are not the only things you are adding to your protocol. You are also exposing your research to the risk of spontaneous tumor development in your models – a risk that can skew your findings.

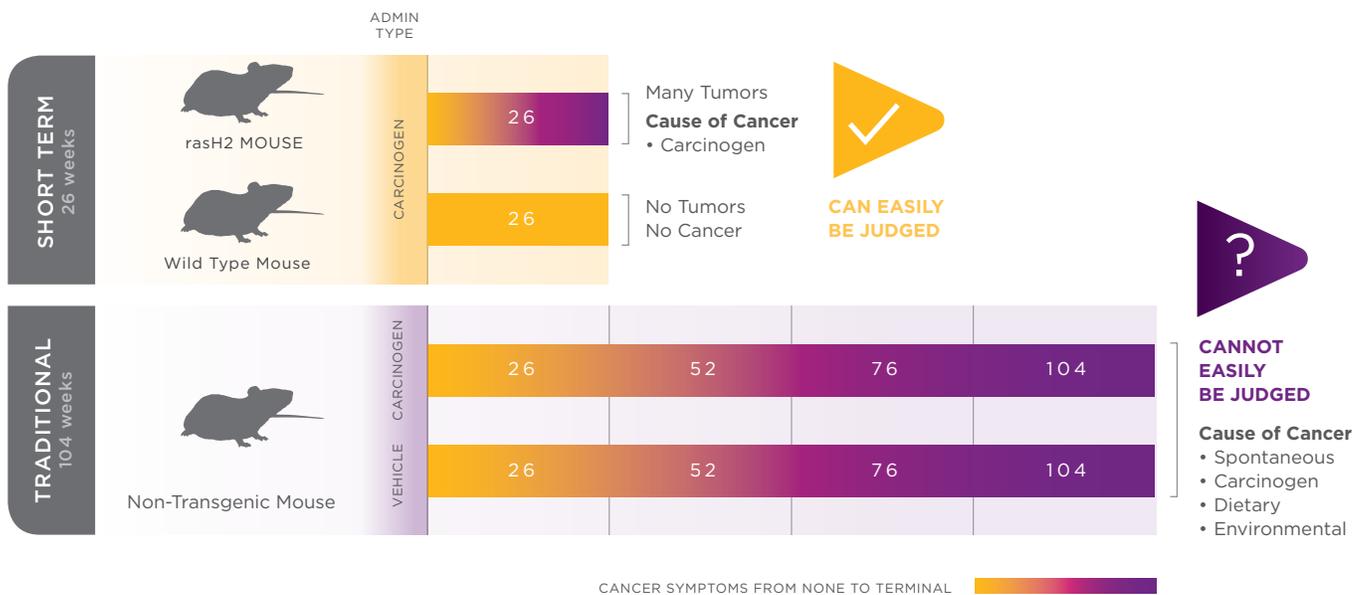
THE TACONIC rasH2 MOUSE* OFFERS A BETTER ALTERNATIVE

Taconic rasH2 mice enable you to perform short-term carcinogenicity testing of compounds on a much faster time line – reducing the in-life portion of your study to 1/4 of a traditional two year study.

The use of rasH2 is approved by the FDA and the International Conference on Harmonisation (ICH) S1B Guideline 1. Faster testing means lower costs, quicker answers on your compounds, and a significantly lower risk of spontaneous tumors.

Like all of the models in our unique Taconic Transgenic Models portfolio, rasH2 mice are sold with full research use rights and are readily available in typical study quantities – enabling you to immediately begin using them in your research.

CARCINOGENICITY TESTING (IN WEEKS)



* Developed by CIEA

TO ORDER

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ADVANTAGES OF THE rasH2 MOUSE*

- **Shorter studies.** Using Taconic's rasH2 mice, you can greatly reduce the in-life portion of your testing – cutting your study time by as much as 75 percent.
- **Lower study costs.** Taconic rasH2 mice reduce your total research costs through lower cage costs, less compound administration, and reduced labor costs.
- **Faster results.** Since Taconic's rasH2 mice allow you to complete carcinogenicity studies in a fraction of the time, you obtain critical data and answers sooner.
- **More accurate results.** With no spontaneous tumor indication up to the age of 6 months, Taconic rasH2 mice reduce the incidence of false positives.
- **Availability of Historical Data.** A substantial amount of phenotypic background data is available for

rasH2^{2,3,4,5}. These data demonstrate the low incidences of spontaneous tumors and the robustness of the model in identifying carcinogens, providing a valuable reference for current and future carcinogenicity studies.

KEY APPLICATIONS

Taconic rasH2 mice provide a fast, cost-effective option for testing for mutagenic and non-mutagenic chemically- induced tumor formation.

HOW TACONIC'S rasH2 MOUSE* WORKS

Taconic rasH2 mice carry the human c-Ha-ras oncogene in addition to the endogenous murine Ha-ras oncogene. The presence of the human c-Ha-ras gene makes hemizygous rasH2 mice highly susceptible to tumor development when exposed to compounds that cause cancer in humans.

Taconic rasH2 mice are FDA approved for use in short-term carcinogenicity testing that has an in-life portion of only six months – reducing your testing timeline by up to 75 percent. rasH2 mice also demonstrate an extremely low incidence of spontaneous tumors, with no indication of pre-neoplastic cell stages or tumors until the age of 6 months. They are also proven to provide much more rapid onset and a higher incidence of more malignant tumors after being treated with mutagenic or nonmutagenic carcinogens. By empowering you to complete carcinogenicity testing on a significantly faster timeline, Taconic rasH2 models greatly reduce your costs and help to minimize the risk of false positives as a result of spontaneous tumors.

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PROPOSED CHANGES IN THE ICH S1 GUIDELINES ON RODENT CARCINOGENICITY TESTING: THE UTILITY OF THE RASH2 MODEL

A change to the current ICH S1 guidelines on rodent carcinogenicity testing is being considered⁶. The proposal suggests that the traditional two year rat carcinogenicity assay may not be necessary for certain compounds based on the compound,- properties. For such compounds sponsors will have the choice to either conduct a traditional 2-year mouse study or to use a short term transgenic mouse testing assay, with an apparent time advantage for the latter approach. Furthermore, the ICH S1 guidelines propose a short-term transgenic carcinogenicity assay as one way of quickly determining the need for a further two year rat study.

The ICH S1 has developed a set of Weight of Evidence (WOE). Sponsors are encouraged to

develop a Carcinogenicity Assessment Document (CAD) that include this Weight of Evidence to determine the value and need for a 2-year rat carcinogenicity study. Studies using the rasH2 model can be used as part of the WOE in preparing the Carcinogenicity Assessment Document⁷.

Talk to one of our PhD scientists to learn more about these proposed guideline changes and the future utility of the rasH2 model in light of these proposals.

REFERENCES

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DISCUSS YOUR NEEDS

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GEMS DESIGN

Taconic Biosciences GEMs Design empowers our clients to develop research models specifically suited to the unique needs of their discovery and development studies or therapeutic programs.

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- Transgene Expression
- miRNA Expression
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Research organizations demand precision tools that better reflect human physiology. Taconic Biosciences leads the field delivering innovative solutions to meet these continually evolving needs. Our core competencies include the delivery of complex strategies that both integrate human genetic sequences and engraft human cells and tissues into custom mouse and rat models.

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US: 1-888-822-6642
EU: +45 70 23 04 05
INFO@TACONIC.COM

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