transgenic technology is primarily limited by whether or not the modification to the animal's genome is an inherently lethal change.

Although genetically produced animal models, natural or artificially manipulated, are very useful, it is not always necessary, or even possible, to use an animal model that is "hard wired" to produce a specific disease state or condition. In many cases, a model of a disease state or condition can be induced temporarily. Drug-induced animal models, for example, utilize pharmacological intervention in order to establish the models. In general, an otherwise healthy animal is treated with a compound known to induce a disease condition or symptoms that closely mimic the disease. The MPTP model of Parkinson's disease, for example, creates a Parkinsonian type condition in primates[7] and mice.[8] Administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) leads to rapid destruction of dopamine-synthesizing neurons in the substantia nigra region of the brain. This triggers the rapid development of Parkinson's disease symptoms in a manner consistent with the human condition. Interestingly, administration of MPTP to rats has no effect, which highlights the importance of species selection in animal models.

Animal models can also be produced by physical means (e.g., mechanical, surgical, etc.). Ischemic events can be surgically created by limiting or blocking blood flow in order to study the impact of test compounds on stroke survival[9] or cardiac reperfusion after a heart attack.[10] *In vivo* models designed to study the ability of a compound to suppress pain sensation can also be generated using physical means. The ability of an animal to tolerate contact with a heated surface, such as a hotplate underneath a paw, could be used to identify compounds that suppress pain.[11]

It is also possible to use an animal's environment to create a situation suitable for assessing the pharmacological impact of test compounds. This is especially useful in the CNS arena, as changes in behavioral response to environmental condition in the presence or absence of a test compound may be the only meaningful data available. Consider, for example, animal models designed to identify compounds that may be useful for the treatment of depression. Although it is not possible to determine if a mouse is experiencing depression, it is possible to study potential antidepressants in mice by observing their responses to various situations. In the Porsolt forced swimming test, for example, a mouse is placed in a glass cylinder containing water too deep to stand in and with walls too high to allow escape. Eventually, mice in this situation will stop attempting to reach the top of the cylinder to escape and simply float on the surface. Mice that are treated with antidepressants spend a significantly greater time attempting to find an escape than untreated mice.[12] This model has been effectively employed to identify clinically useful antidepressants, even though there is no clear relationship between a mouse's inability to escape a situation and human depression.