

Transgenic mice fall far short

are unimportant pests and that plenty of chemicals are available to control them. Therein lies the beauty of this niche product. Slugs are considerable pests. An estimated \$100 million of crops, from wheat to lettuce, are destroyed annually by slugs. Not counted in these estimates is the substantial damage to home gardens and landscapes. The most common control chemical is methiocarb pellets, which slugs ingest. Because these pellets look like cat food, they are frequently eaten by birds and small animals.

AGC's most comprehensive tests of the parasitic nematodes have involved winter wheat. The nematodes reduced crop damage from slugs by 50 percent, while methiocarb gave only a 20 percent reduction. Also, field and laboratory studies indicate that the nematodes do not harm earthworms, soil-borne insects, birds, or mammals.

Again, Professor Kotler's guidelines for ideal niches are supported. The market for natural snail and slug control agents is estimated at \$80 million at the user level in Europe, North America, and Japan. The largest unquantifiable, but obvious, segment is sales to home gardeners. The continuing call for decreases in intensive chemical usage on European cereal crops alone assures market growth. The purchasing power of farmers is unquestionable, as they are increasingly attuned to substitute natural control agents for chemicals. The apparent absence of comparable products by other agbiotech and agrichemical companies demonstrates that many have neglected natural slug-control agents. AGC is also known as an innovative supplier of other microbial crop protectants. It has been sought after as a venture sidekick in microbial agents by Idemitsu Kosan (Tokyo), Gustafson (Dallas, TX), Sandoz (Basel, Switzerland), and others. Home gardeners in England are already praising AGC's slug-control product through impromptu recommendations on gardening programs.

Other dedicated nichers sparsely populate the agbiotech industry. Perhaps other will shake their schizophrenia to join the ranks of serious niche marketers. ///

WASHINGTON, D.C.—For years researchers have dreamed of accelerating drug discovery by testing compounds in mice engineered to model such human diseases as cancer and immune-system deficiencies. Indeed, several companies are developing such transgenic mice, including DNX (Princeton, NJ), GenPharm International (Mountain View, CA), SyStemix (Palo Alto, CA), and TSI (Worcester, MA). Numerous universities are also developing these mice. Yet the market for transgenic mice has not lived up to expectations. That was the message from a recent conference sponsored by the National Academy of Sciences (Washington, DC) entitled "Workshop on Sharing of Laboratory Resources in Biological Research: A Case Study of Genetically Altered Mice."

One of the first transgenic mice—the so-called "Harvard" mouse, which contains specific human oncogenes—was developed by Philip Leder and his colleagues at Harvard Medical School (Boston, MA) and was patented in 1988. Yet the mouse, which was licensed exclusively to Du Pont (Wilmington, DE) for commercial development, has not met early commercial expectations based on its use in cancer research. One reason is that Du Pont, after reaching an agreement with Charles River Laboratory (CRL, Wilmington, MA) to maintain the mouse and distribute it commercially, established a steep fee structure and other provisions that potential users consider onerous.

In particular, many would-be Harvard-mouse users object to a "reach-through" clause that requires them to pay a share of revenues from sales of future products developed through the use of the mouse. This reach-through provision prompted a rebellion among university researchers, who have effectively boycotted the Harvard mouse. The mouse has "proved a disaster from our perspective," says CRL's Melvin Balk, and, hence, CRL has been seeking to sever its arrangement with Du Pont. More generally, Balk notes that most inventors "overestimate the value" of their transgenic mice and need to be more "realistic" about their worth.

"So far this is a non-profit venture," says CRL's Glenn Monastersky of his company's efforts with transgenic mice. David Winter of GenPharm International (Mountain View, CA) agrees that, despite high prices, the transgenic-mouse business is "not yet profitable." Winter says that it costs GenPharm as much as \$90,000 to establish a new transgenic-mouse strain and that, for some strains, steep royalties need to be paid to the academic institutions from which the mice originate. Moreover, costs for breeding pathogen-free animals and for maintaining the integrity of stocks continue to soar.

In part to respond to academic researchers who objected to the high costs of transgenic mice, GenPharm recently changed its policies for distributing the mice. Instead of insisting that university researchers purchase all mice from the company, GenPharm now allows researchers to pay an annual fee to obtain breeder-mouse pairs that allow them to produce their own colonies. Although researchers sign a "standard use agreement, much like a lease agreement that comes with computer software," to restrict their use of the mice, GenPharm makes no attempt to "reach forward to products," says Winter.

Public-sector resources also are available to maintain and distribute transgenic mice. Officials at the National Institutes of Health (NIH, Bethesda, MD) recently decided to establish a special repository that would accept and distribute transgenic animals at cost for the sake of furthering basic biomedical research. The underlying idea is that NIH will supplement the roles now played by existing commercial and non-commercial facilities.

Meanwhile, in light of the Harvard mouse and GenPharm experiences, several universities have been rethinking their transgenic-mice technology-transfer policies. The technology licensing group at the Massachusetts Institute of Technology (MIT, Cambridge, MA), for instance, now tells researchers that it is generally not worth filing patent applications for genetically engineered mice if their primary use is for basic research.—**Jeffrey L. Fox**

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