Bug Banking: A Growing Business

Frozen cells and mail-order microbes are increasingly in demand

By RICK WEISS

Every afternoon, at 2:00 sharp, 10 scientists at the American Type Culture Collection (ATCC) leave their workstations for an hour to take phone calls from troubled scientists around the world.

"My culture doesn't look healthy," a worried microbiologist says. "Can I substitute minimal essential media for our RPMI 1640 and still get good growth?"

More than 60,000 times per year, these doctoral Dear Abbys share their collective expertise with inquiring microbiologists, virologists and plant pathologists — all of whom know that if the specialists in Rockville, Md., can't answer their questions, probably nobody can. That's because the Culture Collection scientists are caretakers of the world's largest microbial menagerie, featuring nearly 50,000 strains of refrigerated, frozen or freeze-dried microorganisms.

As part of their job, ATCC technicians periodically thaw a sample of each strain, test it for viability, then put it back to "sleep," ensuring the preservation of a standardized collection of living specimens for scientific investigators. Indeed, ATCC's highly respected hotline is but a spinoff of the collection's primary mission: to preserve and distribute authenticated samples of biological materials, and to serve the research community as both a "Bureau of Standards" and a not-for-profit "Sears & Roebuck." Last year, the 63-year-old institution distributed more than 90,000 specimens to researchers in 50 countries.

ATCC's coolers and freezers contain not only bacteria and viruses — including a number of disease-causing organisms — but also DNA plasmids and oncogenes, fungi and yeast, algae and protozoans, a variety of seeds and even greenhouse-grown bits of cultured plant tissue.

That menu is considerably broader than its founders ever anticipated, but stranger things may yet find a home in the collection. According to ATCC's Bobbie Brandon, its freezers someday could become a repository for genetically engineered embryos as well. With the recent U.S. Patent and Trademark Office (PTO) decision allowing patents on animals (SN: 4/25/87, p.263), deposits of frozen, patented embryos soon may be required as part of the patent application process, Brandon and PTO officials say. If so, Brandon adds, ATCC will probably start accepting and preserving early embryos of gene-altered animals — ensuring its continued preeminence as the world's biggest, and perhaps strangest, collection of little living things.

If ATCC were just another cold-storage company specializing in microbes, it might not consider moving into the frozen-animal-embryo business. But in addition to serving as a nonprofit "cell bank," ATCC is one of two internationally recognized patent depositories in the United States. (The other is the U.S. Department of Agriculture's Agricultural Research Culture Collection in Peoria, Ill.) As such, ATCC maintains — in a separate, closely guarded facility — microorganisms and other genetic material critical to pending patent applications.

William Siegel

A technician retrieves from a liquid nitrogen freezer a glass ampule containing a preserved microbial specimen. Multiple locks and alarms, back-up power systems and the maintenance of duplicate specimens in different locations help ensure the collection's integrity.

Housing roughly 8,000 specimens, the ATCC patent depository is a small part of the Culture Collection's total operation. But recent advances in biotechnology, and a resulting evolution of patent law, have brought the collection's restricted-access iceboxes increasingly into the limelight.

Since U.S. patent law was first enacted in 1790, inventors have enjoyed exclusive rights to their inventions for limited periods, now 17 years. In return, they are required to make public a detailed description of their creation so that others might learn from and improve upon their work. That description, traditionally in writing, accompanies the patent application but is protected from public scrutiny until the patent actually is issued — sometimes years, or even decades, after the application is first filed.

In the 1940s, as scientists developed patentable processes and products that used specific microorganisms, patent examiners found the written word was sometimes inadequate for describing the microbes involved. So the Patent Office first recommended in 1949, and now often requires, that such patent applications be supplemented with the actual organism.

Scientists are asked to deposit their organism in a "bug" bank such as the ATCC, where it is kept in a high-security state of suspended animation while awaiting patent approval. Only then is the organism moved into the general collection, where — in keeping with the mandate of international law — it is made available to other scientists for at least the next 30 years.

"Most of the people who call us about patent deposits think they have an extremely important patent, and many of them do," Brandon says. "We have people who arrive here from Japan, hand-carrying these packages in dry ice."

It's understandable, she adds, that inventors take such personal interest in their bugs' frozen fates. For example, although U.S. patent deposit rules are slightly different from those of most other countries, patent-pending organisms generally must be deposited on or before

the day a patent application is filed. With biotechnology companies racing to develop very similar products, a single day's delay may mean the loss of millions of dollars of eventual sales.

Recently, Brandon says, couriers were dispatched to a Washington, D.C., airport to pick up a late-arriving microbial specimen from New Zealand that had missed its connection in Los Angeles. Since the bug's patent application had already been filed in Washington that day, the couriers rushed the specimen to Rockville, where it was logged in and deposited at 11 p.m. "We made it with an hour to spare," Brandon says with a smile.

Despite the high-stakes atmosphere surrounding the patent depository, most of the ATCC facility resembles an ordinary microbiological laboratory. There is the constant howl of fans pulling air through filtered ducts; the warm smell of freshly cooked growth media; the sloshing of shaker racks keeping finicky bacteria suspended in their favorite liquid broths.

As in many laboratories, glossies of photogenic bacteria decorate walls, and one door features a popular Gary Larsen cartoon depicting pornographic amoebas with little black bars masking their vacuole-pocked "faces."

Many of the lab's 100 or so scientists are essentially "nutritionists," experimenting with new growth media that may stimulate better microbial growth. The facility makes more than 2,000 types of media — in a rainbow of colors — many of them custom-designed to meet the dietary needs of uniquely engineered organisms. At times it has taken months or even years to come up with the ideal medium to support a new organism, Brandon says.

In addition to their search for the perfect microbial meal, scientists constantly face the challenge of discovering how best to preserve a specimen over long periods of time. Survival is not the only criterion; scientists want to minimize the possibility of mutation as well. Depending on the nature of the specimen, it may preserve best when freeze-dried and refrigerated at 5°C, frozen at −60°C to −80°C, or dunked in liquid nitrogen at −196°C.

So far, ATCC scientists are not preserving engineered embryos, Brandon says. Only one patent has been granted to a gene-altered animal in the United States (SN: 4/16/88, p.244). And although its creators — two Harvard University scientists — cite two ATCC-registered microorganisms as important to the gene-altered animal's creation, the Patent Office did not require any new deposits before issuing that patent.

If the Patent Office starts asking for deposits, Brandon says, frozen, early embryos probably will be the deposit of choice — in part because the technology for freezing embryos already is well established. But nobody knows if the Patent Office will require deposits for any of the genetically engineered animals expected to be patented — or, if so, what *kind* of deposit it may deem most appropriate.

Under current rules, says PTO Supervisory Patent Examiner Thomas Wiseman, applicants generally must deposit their patent-pending organism if it is new and unavailable, or if its taxonomic description is incomplete — conditions that foreseeably will be true for some of the engineered animals under development. In addition, he says, patent officers generally require a deposit if they think a scientist skilled in the art would have to perform "undue experimentation" to duplicate the original invention. Wiseman defines this as "the type of experimentation that is akin to invention."

According to PTO Commissioner Charles Van Horn, new rules currently being formulated should help clarify deposit requirements. But those rules will be only "procedural guidelines," and for the most part will not address *what* inventors must deposit. "We're not going to try to restrict or define what it is that one has to deposit," he says. "That will have to be decided on a case-by-case basis."

Most important, Van Horn notes, a deposit is supposed to enable other scientists to duplicate the original work, or to show the "best mode" of producing the new creation. So any decision to require animal cell deposits would depend in part on how useful such deposits proved to be.

"The deposit has to be more than a storehouse of a finite number of samples," he says, adding that if the stored specimen is not self-replicating it won't be particularly useful to anybody. He predicts the rules will continue to evolve as cell preservation and cloning technologies improve.

If the Patent Office does begin to require some animal cell deposits, those samples are bound to represent but a small part of the Culture Collection's workload, Brandon says. "The patent depository is the smallest part of our operation, even if it seems the most critical."

And although animal patents remain controversial in scientific, bioethical and congressional circles, the heated debate is not likely to penetrate the Rockville coolers. For even the oddest engineered embryo loses much of its notoriety once dipped in liquid nitrogen and stored on a shelf. Another little piece of the biotic puzzle, it will be given a number, catalogued and shown to its room. There it will take its place with the thousands of other bits of accumulated life that have gradually filled the collection's shelves since 1925. □