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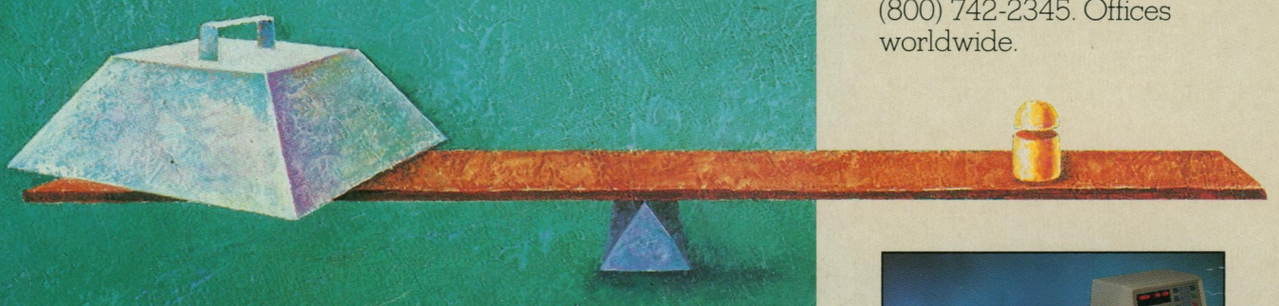

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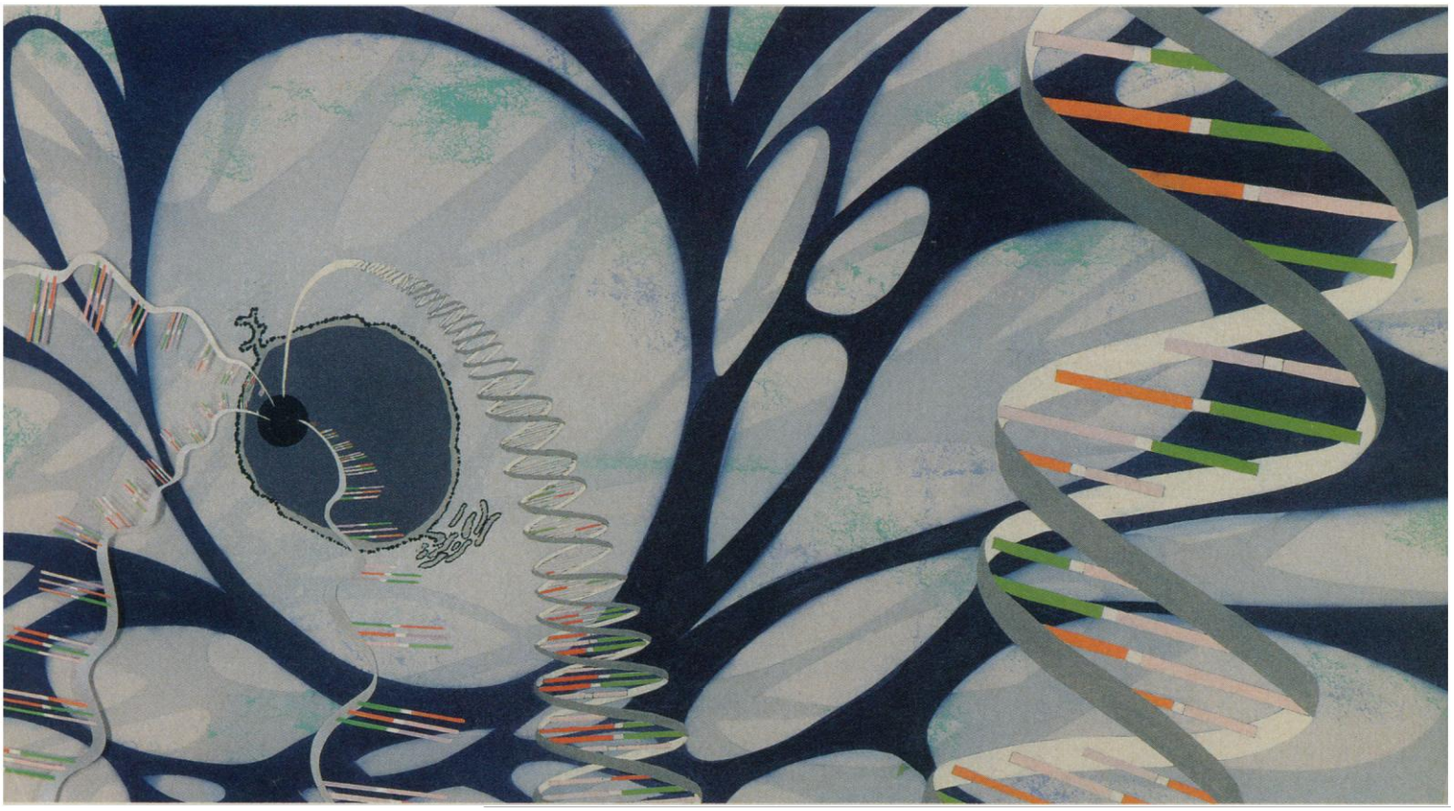

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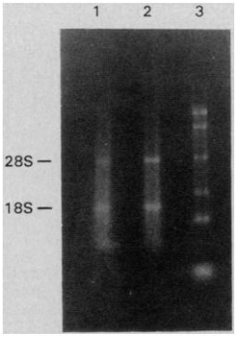

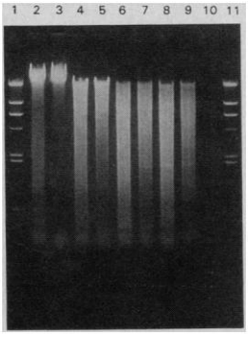

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COVER A partial cross section of a biocompatible polymer system that delivers medications, including proteins, in a controlled manner. This high-powered light micrograph was taken after the polymer matrix had been releasing protein for more than 5 months. See page 1527. [Photomicrography by Rajan Bawa]

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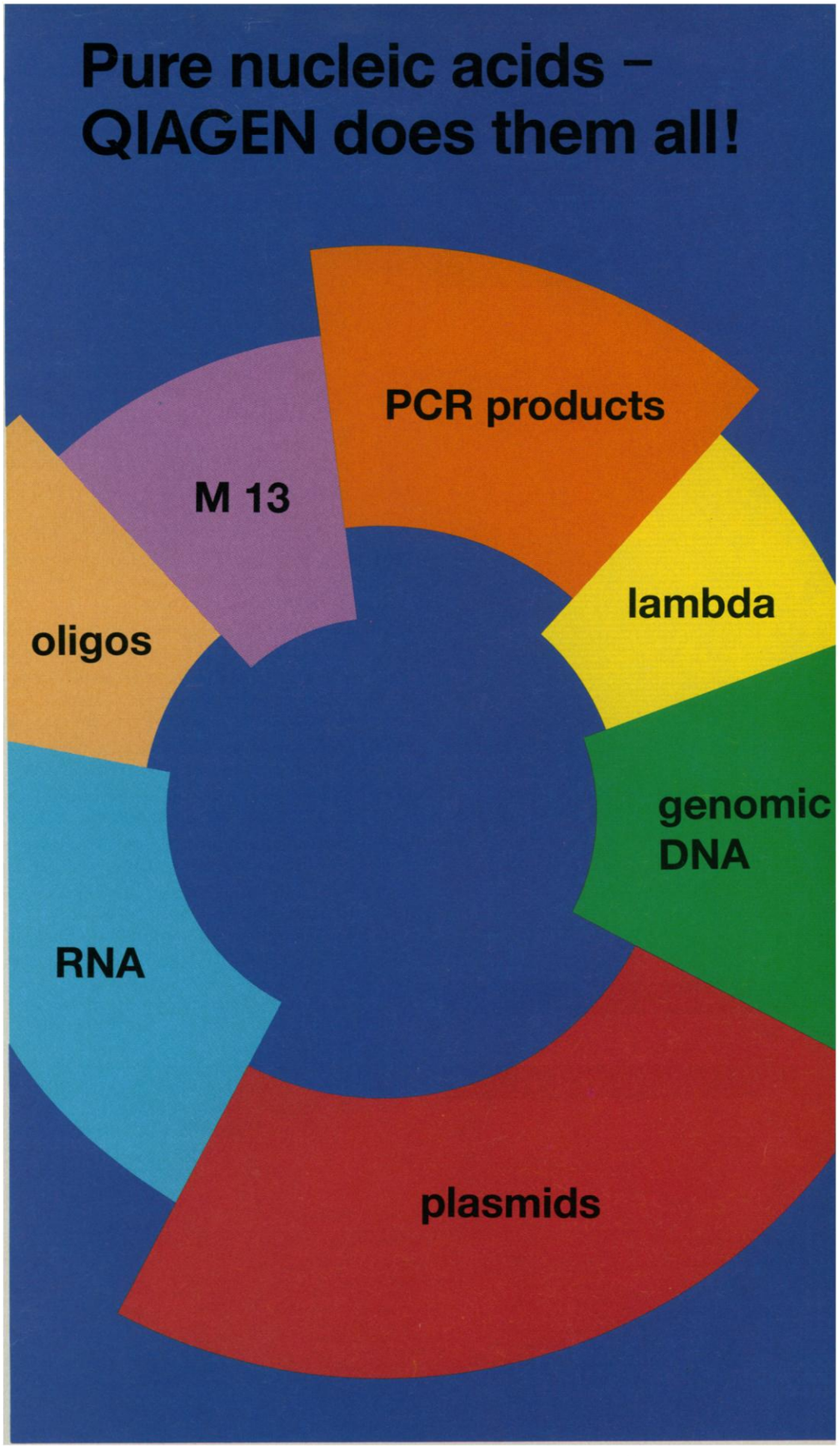

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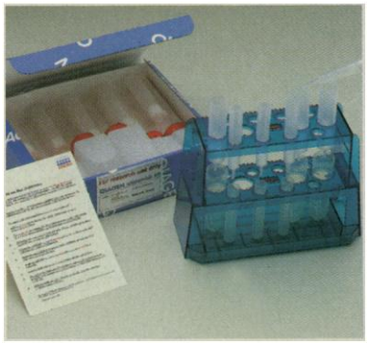

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Drug delivery systems

No longer are clinicians limited to prescribing pills, drops, and injections for their patients. Recent advances in biotechnology, chemical engineering, and materials science and a growing understanding of human physiology and immunology have resulted in the development of many new approaches for preparing and delivering therapeutic drugs (cover). Drugs can now be absorbed from skin patches, delivered by external or implanted polymer systems and pumps, or administered embedded in vesicles (including such exotica as magnetic microparticles that can be guided through the body with external magnetic fields). The drugs themselves can be chemically altered in ways that make them more stable and soluble and able to enter previously inaccessible areas of the body. Drug release can be regulated, optimum concentrations can be maintained in the blood stream, and defined areas of the body can be targeted to receive high concentrations of the drug. An overview of these and other new possibilities for diversifying therapies is presented by Langer on page 1527.

Superconducting films

Success in making multilayer electronic devices from high-temperature superconductors has been elusive because fabrication is difficult to control. Smooth films have been grown with their *c*-axis perpendicular to the surface; for device applications, *a*-axis films would be desirable. Of special interest are superconducting films with a sandwich-type configuration—a Josephson junction consisting of two superconducting materials separated by a thin insulating barrier through which electron pairs might tunnel. Progress in this direction is reported by Eom *et al.* who have grown high-quality thin films of $YBa_2Cu_3O_7$ epitaxially—the atoms of the overlying film crystal and those of the substrate are in perfect alignment—on two different substrates (page 1549). Characterization of film microstructures and surface morphologies indicated that they grew with the *a*-axis perpendicular to the surface and were atomically smooth, the latter a prerequisite for production of films with sandwich configuration tunnel junctions. Physical features that enhance or impede current flow and other structure-function relations can now be assessed for these new materials.

Alopecia model

Hair loss (alopecia) is one of the more demoralizing side effects of chemotherapy. It can occur in conjunction with the use of a number of chemotherapeutic drugs, including cytosine arabinoside (ARA-C), doxorubicin (DX), and cyclophosphamide (CTX). An animal model of alopecia has now been developed and an antidote to alopecia may even be in the offing (page 1564): in young rats the bacterial product (and potential chemotherapeutic agent) ImuVert appears to prevent chemotherapy-induced hair losses. Hussein *et al.* report that in a protocol designed to test whether combinations of ImuVert and ARA-C would prevent development of leukemia in rats, alopecia was coincidentally prevented. ImuVert also prevented DX-induced alopecia but not CTX-induced alopecia. The distinction between ARA-C and DX on the one hand and CTX on the other suggests that different mechanisms may be involved in the induction of alopecia by these agents. Tests of whether ImuVert can prevent alopecia in humans may not be too far off: the level of toxicity of ImuVert in humans has already been determined and its efficacy as a chemotherapeutic agent against brain tumors is currently being evaluated.

Cellular lifespans

In culture, human endothelial cells typically undergo about 60 population doublings and then stop growing and dividing. What accounts for this shift from active proliferation to senescence? One substance that appears to play a part is the protein interleukin-1α (IL-1α). Senescent endothelial cells contain excess amounts of transcript (messenger RNA) for IL-1α. In contrast, transformed cells, which are immortal, and young cells do not contain detectable amounts of this transcript. Daily exposure of cultured cells to oligodeoxynucleotides that have an antisense sequence—one that is complementary to that of the IL-1α transcript—blocks the onset of senescence (page 1570). The cells keep on dividing and have the appearance of young endothelial cells. Later, when exposure to antisense molecules is stopped, the cells senesce, which indicates that the effects of antisense molecules are distinct from immortalization. Maier *et al.* propose that the antisense molecules may be repressing the translation of the IL-1α transcript. The still-unanswered fundamental questions are why IL-1α transcripts accumulate inside cells at the end of the cell's proliferative phase and exactly what happens when they do.

Flip and flop

Structural variations in receptors may help an important neurotransmitter, L-glutamate, produce its diverse effects. L-Glutamate is the major excitatory substance in the mammalian nervous system; for fast neurotransmission, L-glutamate can bind to four types of related receptors. Each of the four receptors has been found to exist in two alternate active forms (page 1580): the so-called "flip" and "flop" forms differ by only a few amino acids. Whether the flip or flop form of the receptor is generated at any given time in any specific cell depends on how messenger RNA molecules are spliced. Sommer *et al.* have characterized the functional differences between the flip and flop forms of the receptors and have identified where in the brain and in which cells flip and/or flop is expressed. They speculate that at different times and places in development and in association with learning one form may be favored for carrying out requisite neurophysiologic functions and that inappropriate production of flip or flop may be at the root of certain neuropathologies.

■ Ruth Levy Guyer

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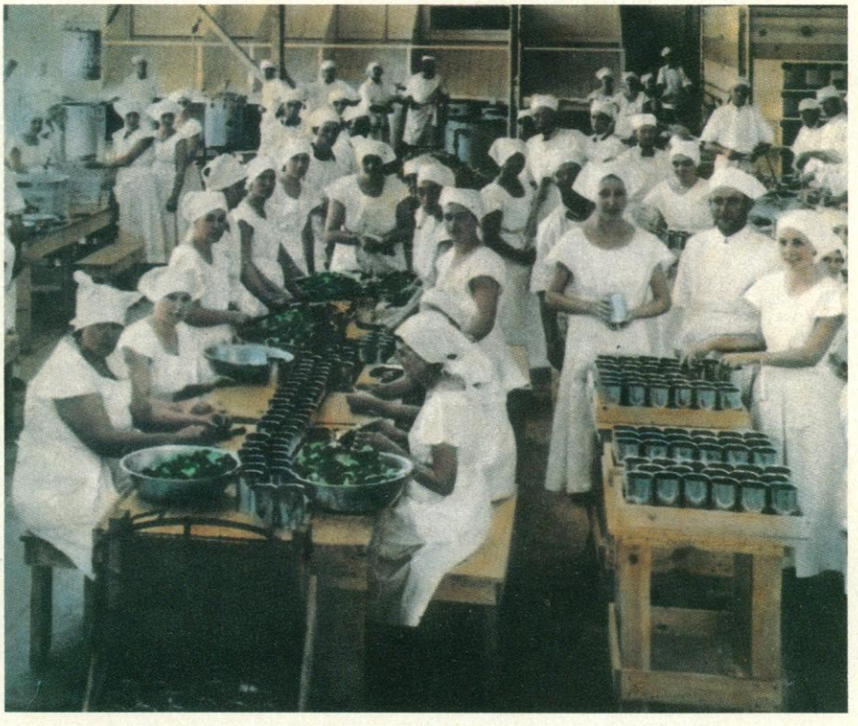

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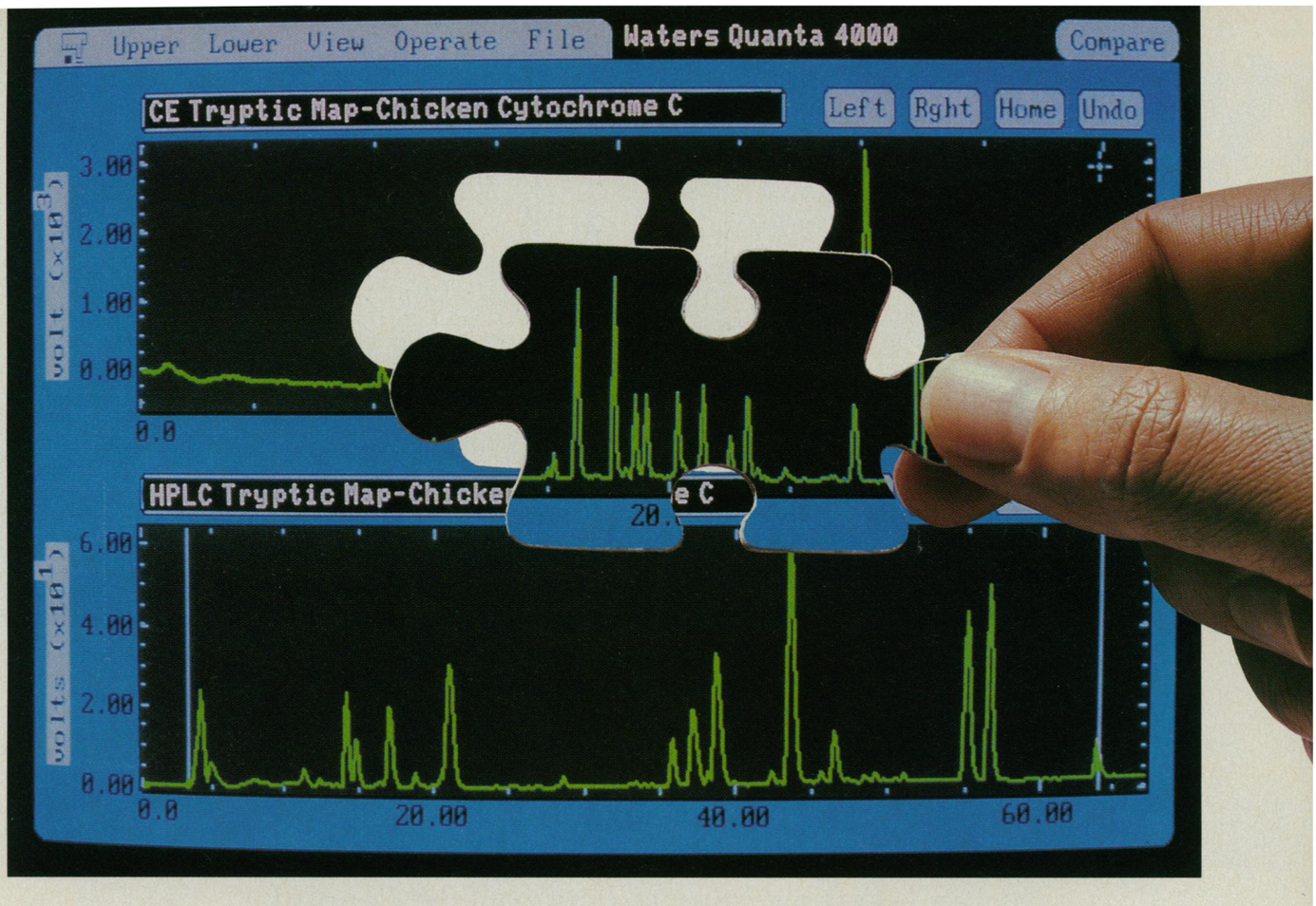

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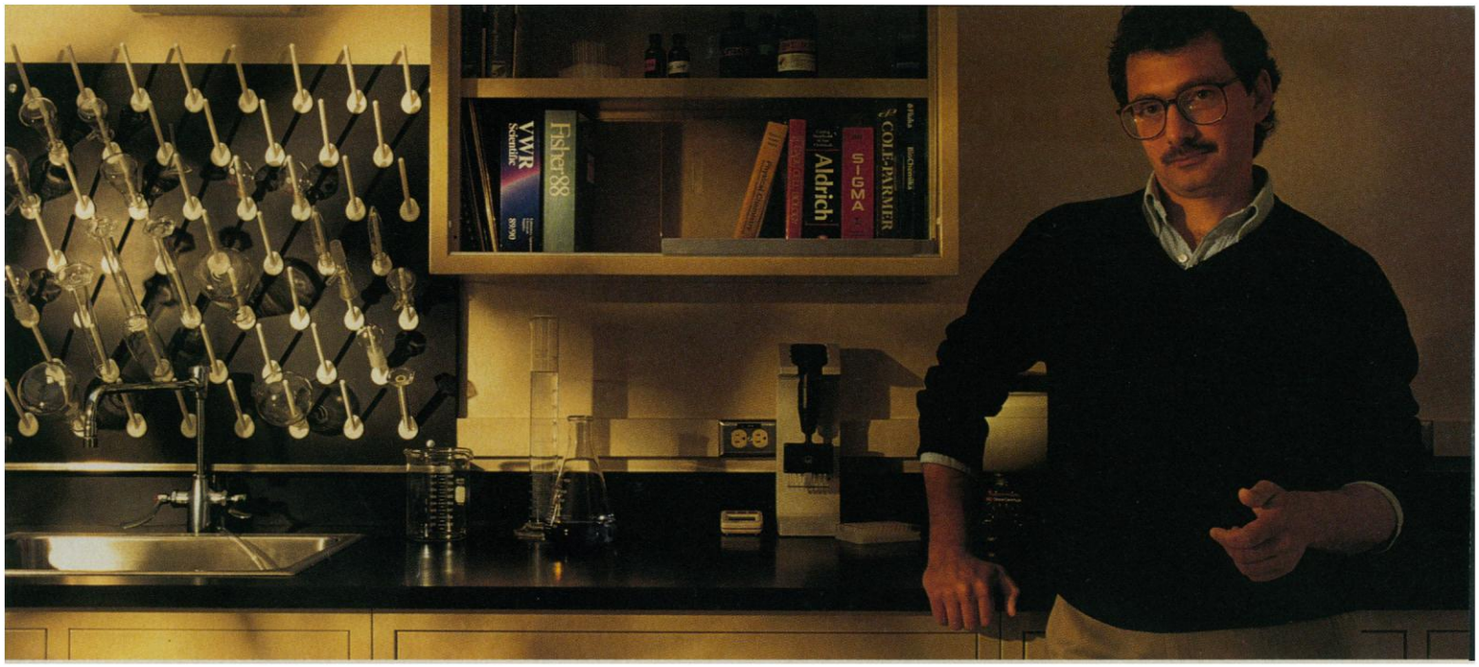

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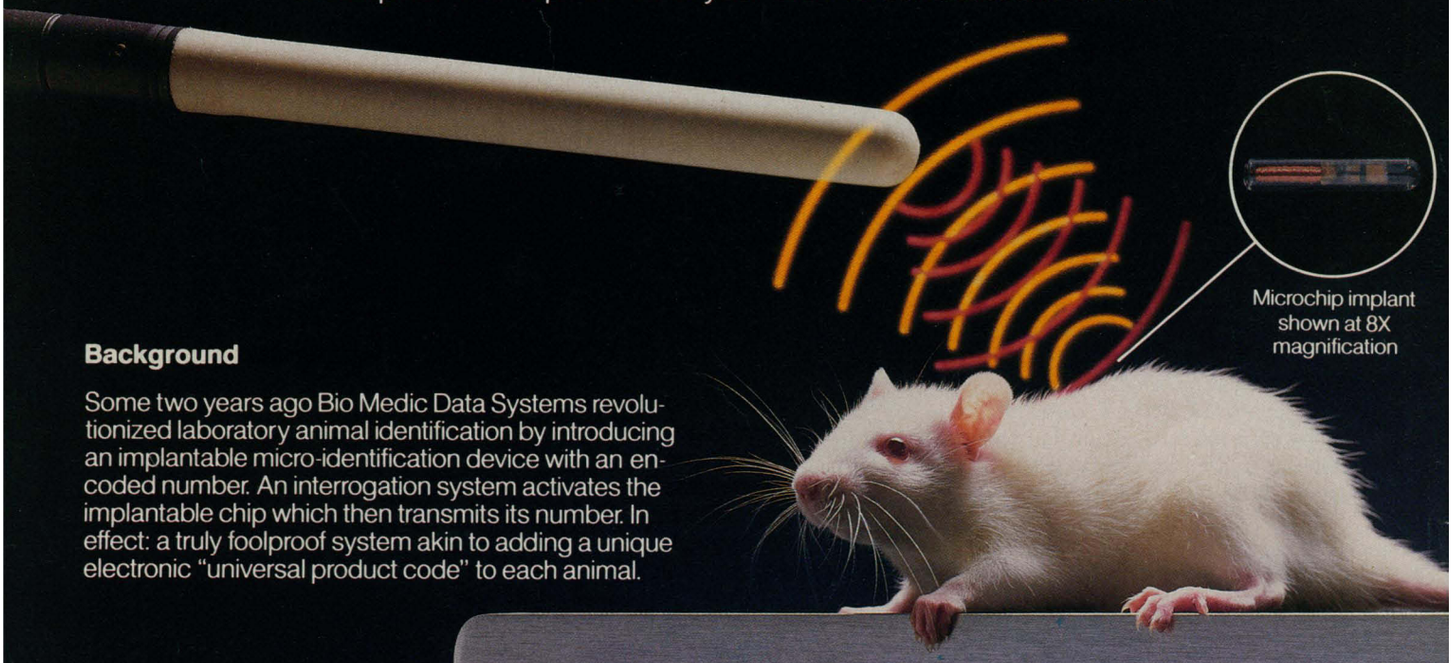

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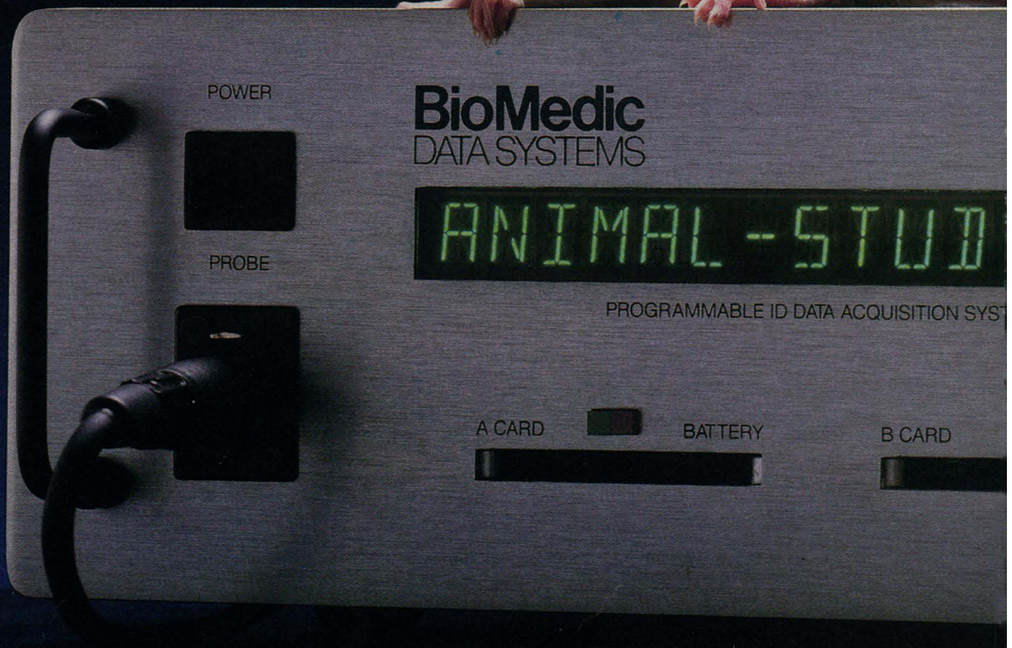

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This simple system obsoletes the traditional ear punching or tagging, toe clipping, and tail tattooing. As such, the age-old labor intensive techniques—in terms of the initial identification, the subsequent reading, and the inevitable re-dos—are replaced by a simple, easy, humane and remarkably efficient system. (A dramatic example: 200 animals can be identified in about 45 minutes.)

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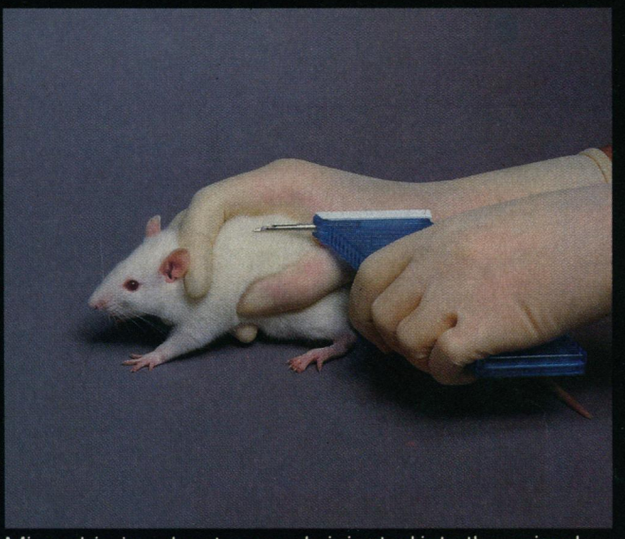

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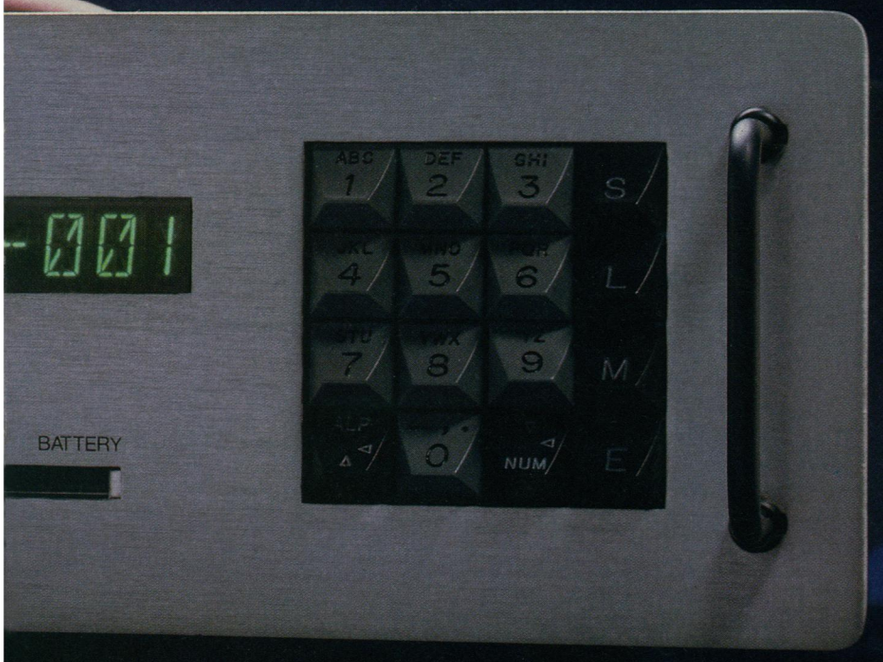

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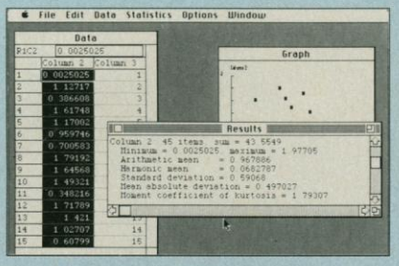

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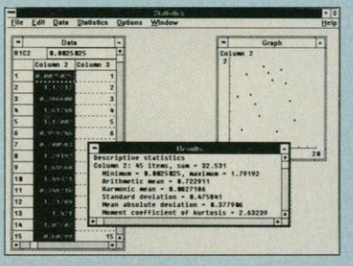

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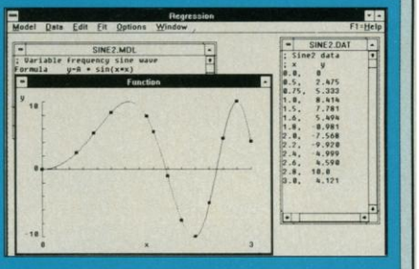

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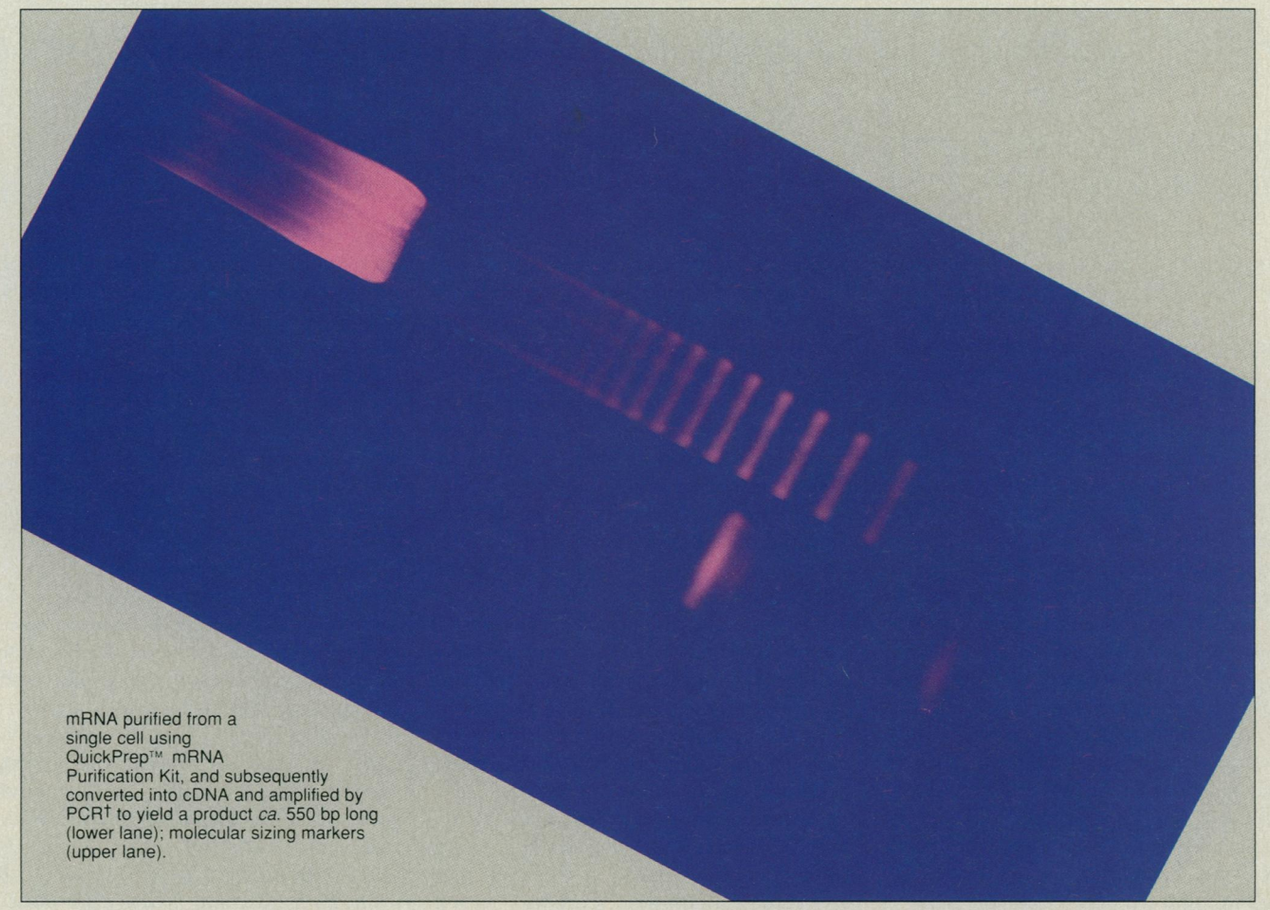

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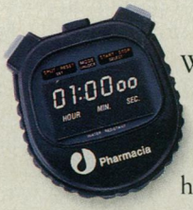

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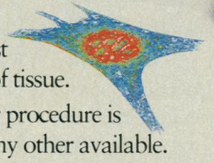

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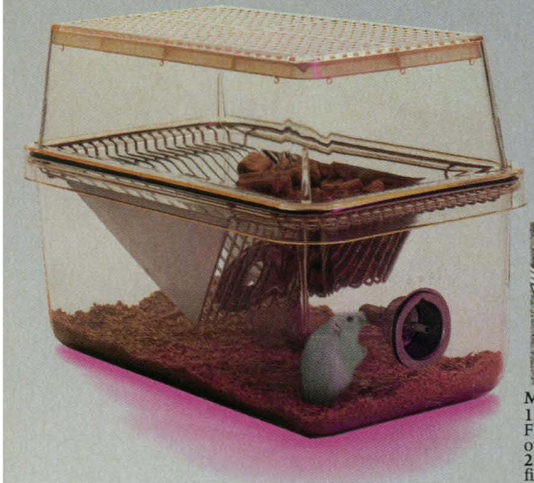
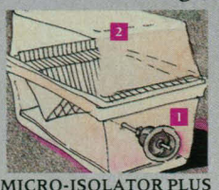
The new Micro-Isolator Plus™ System with Improved Environmental Control.





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* Testing shows ammonia levels are maintained well below 10 ppm with only one cage change for up to a two-week period.

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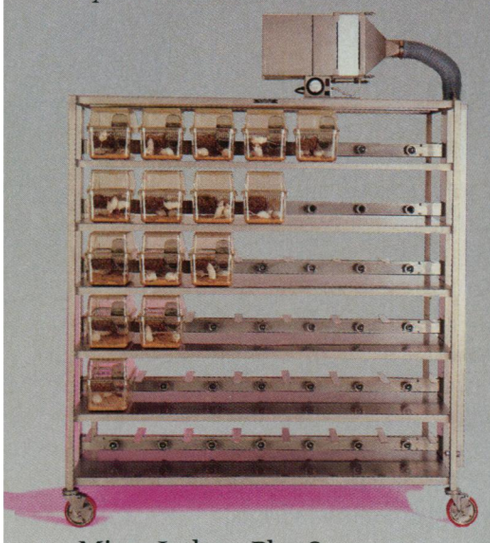
In one simple motion the individual Micro-Isolator Plus™ cage is slipped onto a shelf of one of a variety of Lab Products rack systems that support the HEPA air supply and integrated water manifold docking systems. Each shelf's air manifold is designed to supply balanced, low-velocity air to each cage regardless of the number of cages being docked. And it does so at very low levels of noise and vibration.

The Open-Shelf Rack System is used with the



Micro-Isolator Plus System when isolation at the rack level is not required, thus the cage is positive to the room.

The Ventilated Rack Systems provide additional isolation by exhausting air from each shelf to the building exhaust ventilation or through a HEPA filter module that exhausts into the room. This puts each shelf space under negative pressure relative to the room and to each cage.

Our mobile, Laminar Flow Stay-Clean™ Workbench II just got even better.

Because handling equipment must maintain the aseptic integrity of housing and be practical and efficient, Lab Products Inc. continuously performs R&D in this area. Example: our newly improved workbench with easier access, cleaning and maintenance, greater user comfort, and improved mobility and safety features.

Through extensive testing we found that Class 100 horizontal air flow patterns from back to front more effectively protect animals and control particulate from spreading across cages and work area than vertical air flow systems. We combined this with a full-length front edge air intake which then pulls the air down, creating a vertical air flow curtain at the face opening of the workbench to minimize the escape of allergens and other cage effluent into the room. One new Stay-Clean Workbench II can easily be moved around to accommodate several projects daily.**

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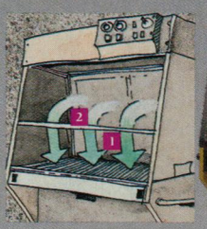

STAY-CLEAN WORKBENCH II
1. Airflow allows maximum product protection.
2. New design features adjustable sash for improved access.

Unit, these components complete a comprehensive system that ensures the integrity of complex animal research at cage barrier levels. Now you can house and process hundreds of small animals of varying species involving a variety of research in one small facility with greater effectiveness and greater efficiency. And it can all be done in a pleasant, virtually-odorless environment.

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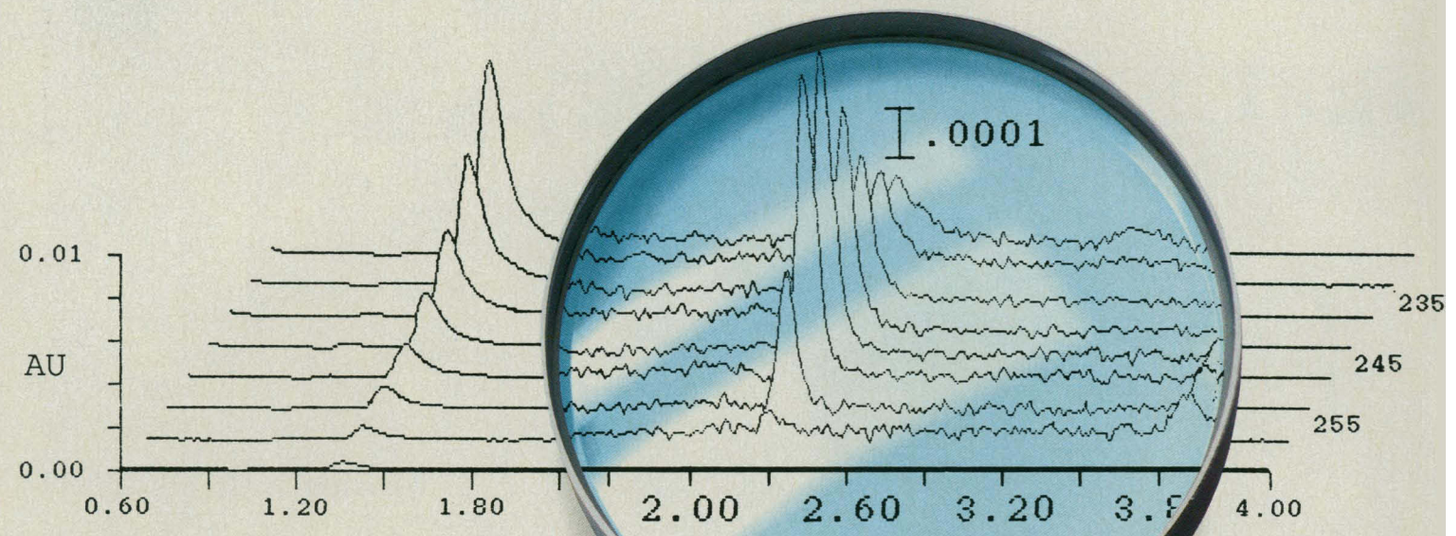

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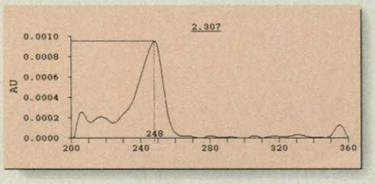

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Grants awarded are expected to be paid out before the end of June 1991.

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