3. Availability of test techniques not readily available with other equipment;
4. Data reduction in "real time" using an on-line computer;
5. Flexibility to serve institutions having small-to-medium testing loads; and
6. Cost savings to users.

Sales of the centrifugal fast analyzer are estimated by industry sources to be at least 500 units/ year, amounting to approximately $25 million/ year. Industry sources indicate that the current number of centrifugal fast analyzers in operation is about 4000 in the United States and as many as 10,000 worldwide at purchased prices ranging from $20,000 to $70,000. While there are no statistics on the number of tests performed with the analyzer, two estimates are available: (1) approximately 175,000 tests per year per analyzer and (2) 10 to 25 percent of the 2 to 4 billion clinical chemistry tests performed in a year, probably closer to 10 percent of the total tests.

Owners indicated that they save 10 to 30 cents/test performed on centrifugal fast analyzers, mostly in reagent costs. Applying these factors to 300 million tests/year yields the estimated savings of $30 to $90 million/year.

Fast Test for Cancer-Causing Chemicals Short-term cell bioassays are used as inexpensive, fast screens prior to more costly animal tests in screening chemicals for cancer-producing or cell-altering characteristics. A number of tests are included within the scope of short-term cell bioassays.

One of the most widely used is a test using special strains of the bacterium *Salmonella* developed by Dr. Bruce Ames of the University of California at Berkeley. The uniqueness of this test involves the use of a mutant strain of this bacterium that is unable to produce the amino acid histidine, which is necessary for its reproduction. If the chemical being screened causes the organism to undergo a genetic change that allows it to produce histidine and, therefore, reproduce itself, then the chemical is considered a mutagen and potential cancer-causing agent. The mutational potency of the chemical under test is expressed in terms of the number of growing bacterial colonies that are observed after a period of incubation. The equipment required is minimal and a single technician can perform a number of tests in a day.

Because a negative Ames test does not absolutely ensure that a compound is inactive in humans, a "tiered" strategy in which the next levels of testing may include mammalian cells in tissue culture and acute animal studies is often employed. Although not quite as simple or inexpensive as the Ames test, such assays are still orders of magnitude quicker and cheaper than long-term, whole-animal testing.

Chromosomal aberration and sister chromatid exchange measurements are common bioassays performed with cultured mammalian cells. These assays are run either on cells grown in tissue cultures or on bone marrow cells, spermatogonia (a cell structure that precedes development of a sperm), or lymphocytes (a white blood cell formed in lymph nodes and several other organs) from experimental animals and human donors.

History Although short-term cell bioassays are most commonly used for measuring the response to chemical agents, the majority were developed from radiation studies sponsored by OHER. Their roots lie in two areas of investigation in radiation biology—chromosomal effects and genetic toxicology.

Scientists in the OHER-supported laboratories were the first to realize that the induction of chromosome aberrations—other than normal changes in genes manifested as mutations caused by the abnormal breaking and rejoining of chromosomes—could be used as a biological dosimeter. This was first demonstrated by exposing cells from a plant that is extremely sensitive to radiation damage to radioactive clouds during the atomic bomb test, Operation Greenhouse, in 1951. Later it was found that chromosomal aberrations in lymphocytes could also be used to measure dose. Additional studies, combined with advances in the science of somatic cell genetics, were instrumental in developing the mammalian cell assays noted above.

Genetic toxicology—the study of the nature, effects, and detection of radiation and chemicals on genes and, thus, on the characteristics passed from one generation to another—is a new field of science that developed from the discovery of DNA repair. Studies by Rasmusson and Painter at the Radiobiological Laboratory, University of California at San Francisco, in the 1970's demonstrated that exposure to radiation (and other toxins) caused some DNA to undergo unscheduled DNA (repair) synthesis (UDS), and that this UDS is quite separate from the normal synthesis process in DNA. This observation forms the basis of the commonly used UDS assay. The ability to construct and characterize bacteria with deficient DNA-repair mechanisms was a crucial step on the path to the Ames test.

Benefits The testing of new products using short-term cell bioassays has resulted in reduced costs and increased productivity. Many different new substances have been created and introduced to the environment in recent years, some of which have the potential to cause genetic damage. Before the early 1970's, animal testing was the only accepted means of evaluating a substance for carcinogenic activity. With the advent of the Ames test and other short-term cell bioassays, however, it has become possible to test substances for mutagenic or carcinogenic potential far more rapidly and cheaply. The Ames test, for example, presently costs $1000 to $1500 and takes only 48 hours. These bioassays are used routinely by many drug and chemical firms to screen substances for potential mutagenic activity before