large expenditures are made to develop them into marketable products.

A measurable benefit of the Ames and similar tests is the amount of money manufacturers save by avoiding the development of potentially hazardous products. Because drug and chemical firms are the most active users of short-term bioassays, a very rough estimate of benefits can be developed based on calculating the amount of development money saved as a result of prescreening:

$$A = \left(\frac{D \times Fm}{1 - Fm} - T\right)$$

Where

A = net annual benefits,
D = annual R&D outlays by drug and chemical firms,
Fm = fraction of compounds shelved as potential mutagens, and
T = annual cost of bioassays.

An estimate of the annual R&D outlays by drug and chemical firms is contained in the National Science Foundation publication *Research and Development in Industry, 1979*. The figure is $1.99 billion in 1979, or about $3.3 billion in 1982 dollars. Based on an informal survey of a number of firms, 5 percent appears to be a fair estimate for the fraction of compounds found to be potential mutagens. Dr. Ames estimated that over 3000 laboratories worldwide use his test routinely, resulting in an estimate of $35 million to the annual cost of bioassays. This results in an estimated annual cost savings of some $140 million/year in 1982 dollars.

Use of these low-cost tests to screen existing products that have never been examined for mutagenic potential represents a potential future benefit. Thousands of man-made compounds are currently in use. To date EPA has inventoried under the Toxic Substances Control Act over 60,000 such compounds that have never been tested for carcinogenic potential. Because the present capacity for animal testing in the United States is limited to a few hundred compounds per year, short-term cell bioassays are the only feasible means of screening these substances.

Analyzing Complex Mixtures for Toxic Agents By the early 1960s, existing instruments were reaching limits that would adversely affect important areas of health and environmental research and progress in increasing industrial safety. Two such limits were the inability to determine the elemental composition of nonradioactive mixtures suspected of containing trace amounts of toxic materials and the inability to ascertain the isotopic composition of complex mixtures of radioactive elements such as those being encountered in nuclear reactors and laboratory analysis. Solutions to both of these problems emerged from the OHER research program. The first solution, a semiconductor X-ray spectrometer, has been widely applied to detect pollutants in the environment, identify unknown materials in the scrap metal and metal manufacturing industries, and to locate sites for examination by electron microscopes. The second solution, a high-resolution gamma-ray spectrometer, is commonly used for identifying the elements in the cooling water of nuclear power plants that cause radioactivity, logging oil wells, studying distant planets, and analyzing laboratory samples.

Semiconductor X-ray Spectrometer (SXRS) This instrument is widely used in industry, medicine, and scientific research to determine the elemental composition of nonradioactive materials. The SXRS is a member of the family of X-ray fluorescence spectrometers and is also known as the energy-dispersive X-ray spectrometer.

The SXRS has three primary components: a radiation source, a semiconductor detector, and a processor. The radiation source can be any material or device that emits X-rays; an isotope of iron that naturally emits X-rays is frequently used. X-rays from the source are directed at the sample to be analyzed, causing the sample to emit other X-rays. The semiconductor detector is made of silicon with lithium added (lithium drifted into it) to obtain the desired detection capability. When X-rays enter the detector, the resulting interaction or ionization produces current pulses that are directly proportional to the energy of the X-rays from the sample. The processor, an electronic logic circuit, counts the number of pulses and records the pattern of X-rays, the distribution of measured energies. Because each element emits a unique pattern of X-rays, the elemental composition of the sample is identified. The typical output produced by the processor is a table showing the percentage composition of the sample.

History X-ray fluorescence spectrometers have been in use since the 1930's, when the wavelength-dispersive X-ray fluorescence (WDXRF) spectrometer was developed. However, the WDXRF spectrometer has limited resolution and can only analyze one element at a time. It is, thus, a very costly method, particularly when a large number of elements must be analyzed. Older methods of chemical analysis, particularly wet chemistry, which is very slow and destructive, were still predominant in 1960.

Research on alternative methods was undertaken on a large scale in the 1950's in the United States and other countries. The electronic properties of silicon and germanium were discovered during this period, and the first silicon detector was developed in 1960. The lithium-drifting process, which permitted construction of detectors thick enough to totally absorb the X-rays, was developed in 1960 and 1961.

These first semiconductor detectors provided improved resolution to distinguish elements, but the associated electronic processors were too poor to maintain the resolution. From 1963 to 1969, research to improve the associated electronics was undertaken. By 1965 a high-resolution SXRS was developed. During this period, improvements in the detectors and further development of the entire X-ray detector system also took