BRITISH TECHNOLOGY GROUP



"British Technology Group is at the heart of technology development and technology transfer.

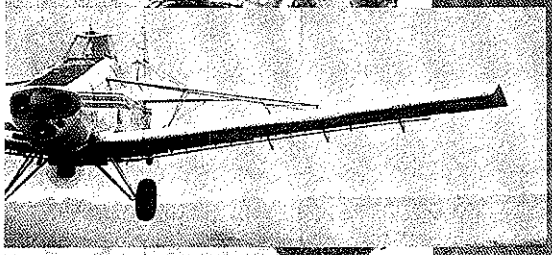
We seek out the best ideas, we finance their further development, we protect them through careful patenting, we license them to industry worldwide and we defend them against infringers —to benefit both the originators and the user.

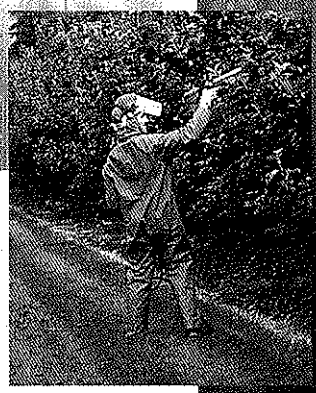
We are the world's leading technology transfer organisation, licensing and financing products worth over £600 million in annual sales."

Ian A Harvey
Chief Executive
British Technology Group

Suction net used to gather fauna from leaves of wheat during Fastac trials.
Photo: Shell

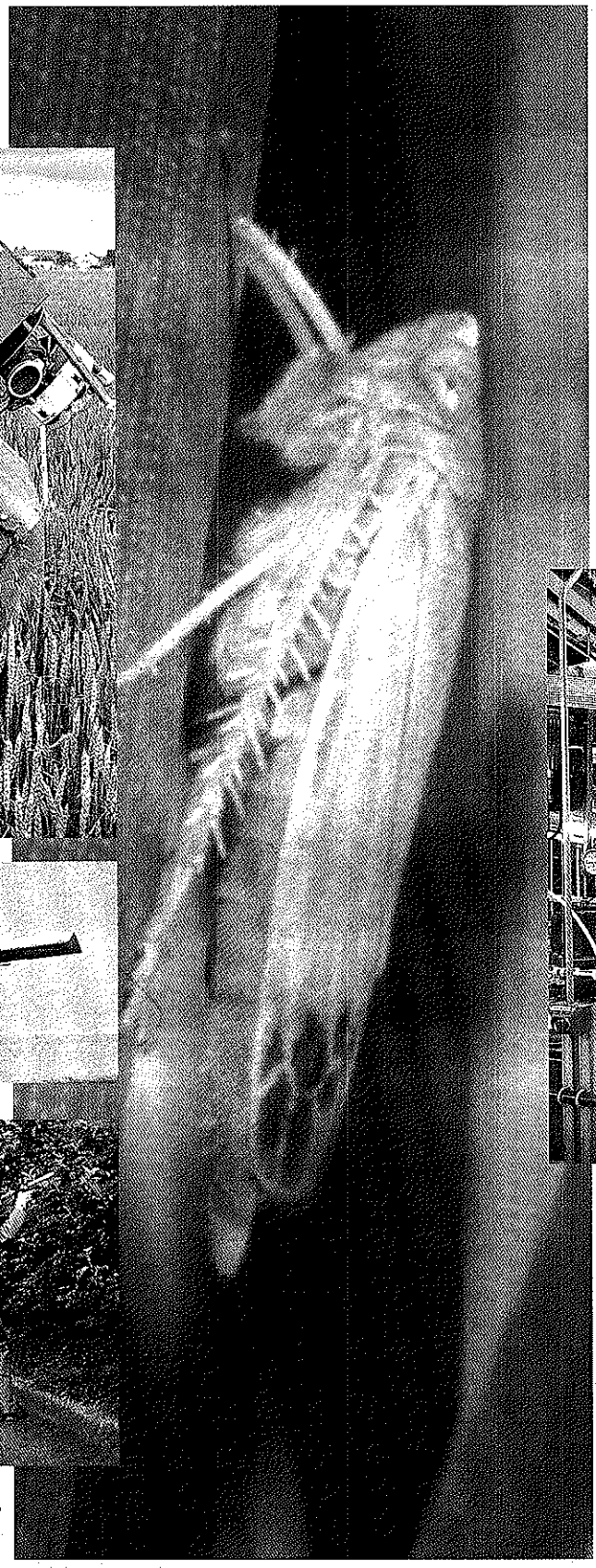




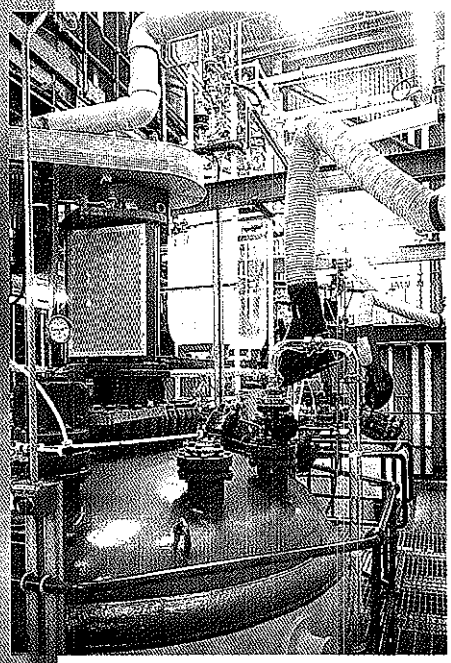


Fastac trials have also involved studies of pollen and the species from which it was gathered by honey bees.
Above: Effects of spray drift from Fastac applied under commercial conditions were monitored in adjacent ditches.
Photo: Shell

Field trials in orchards with Cypermethrin.
Photo: Mitchell Cotts



Leafhoppers are major pests in young rice because they transmit virus diseases.
Photo: Shell



Production plant for synthetic pyrethrins.
Photo: Mitchell Cotts

FINANCE FOR INDUSTRIAL INNOVATION

BTG provides finance on commercial terms for companies carrying out development work in the UK that involves a significant degree of technological innovation.

There are no formal upper or lower limits to the sums that BTG can provide, but they are confined to situations involving technological innovation and generally in the range £50,000 to £1 million. BTG funding does not preclude participation by other investors or eligibility for government grants.

Equity participation is generally the preferred method if a technology is best developed by creating a new company or expanding an existing one, or if the successful growth of a company is critically dependent on the technical innovation.

BTG welcomes opportunities to work alongside venture capitalists and other investors as part of a syndicate in which the Group's ability to assess the commercial prospects of complex technologies may be crucial to other participants.

BTG can also provide finance for academic researchers or institutions who want to set up their own companies to commercialise the results of their research activity.

Established companies may prefer a unique form of project finance devised by BTG for funding of a specific project within a company. BTG contributes a fixed proportion—up to 50%—of the company's costs as they are incurred up to an agreed limit. BTG is repaid through a levy on the company's sales of the resulting product or usage of the new process. The agreement is terminated once BTG has recovered its investment plus interest plus a 'risk premium'.

This method of funding offers several advantages to the company. BTG shares the risk of the development without taking shares in the company. Repayments do not become due until the project starts to generate sales revenue, and the cost to the company of the BTG investment is linked directly to the commercial success of the new product or process.

Further details of these industrial funding schemes are given in the BTG booklet *Finance for innovation*. Proposals involving other forms of funding will also be carefully considered.

OTHER INITIATIVES

Overseas licensing

BTG has always been alert to the global potential of its major inventions and generally negotiates licence arrangements directly with leading overseas companies.

In order to penetrate overseas markets more effectively, since 1987 BTG has appointed a network of local agents around the world to assist in the international presentation of a larger range of BTG technologies. Most are appointed on a performance-related basis and territories covered include the East and West Coast of the USA, Japan, Europe, Australia and India.

Inward licensing

Although BTG still sees British universities, polytechnics and research establishments as the prime sources of the inventions in its portfolio, other countries plainly produce plenty of good inventions.

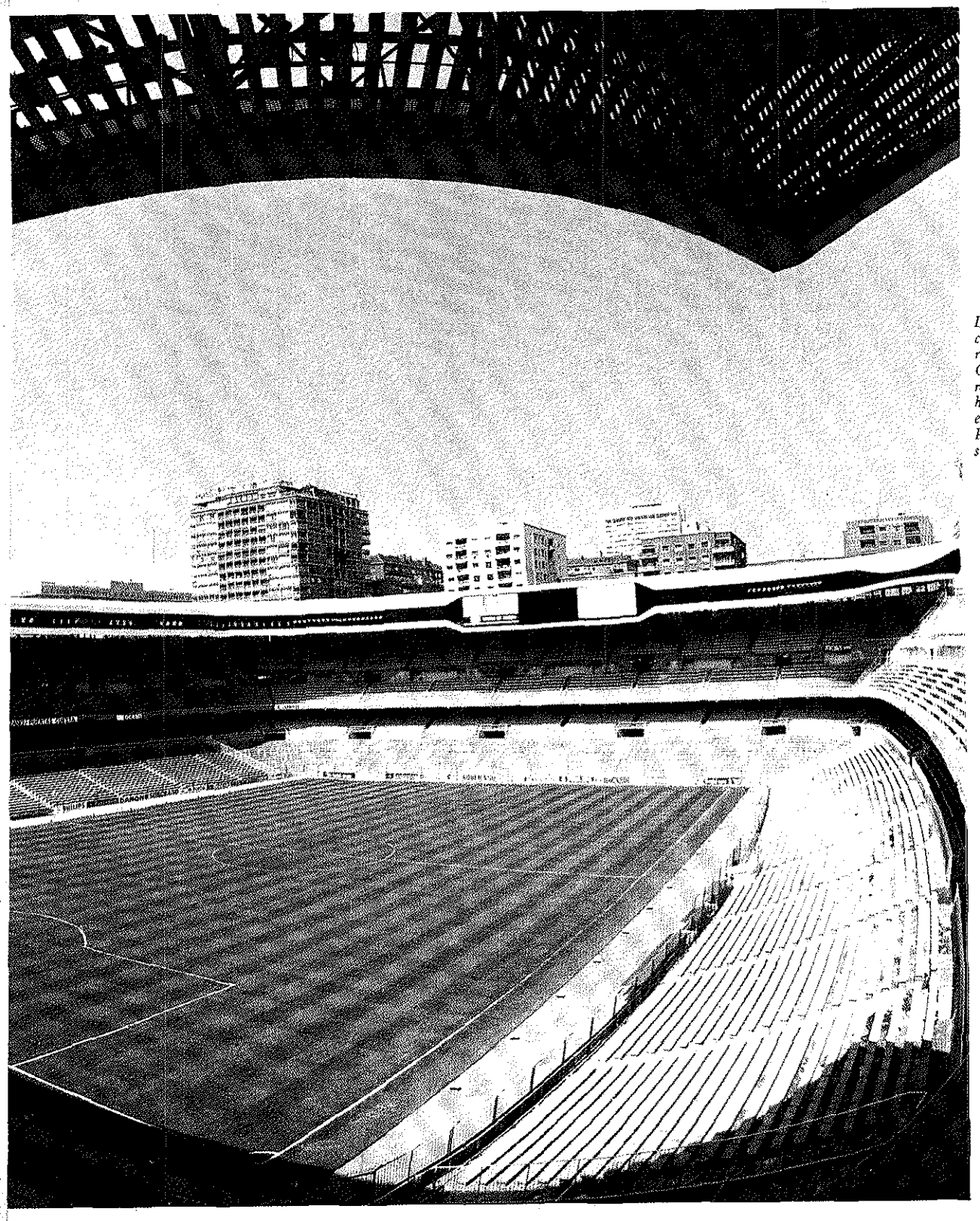
BTG has therefore begun to set up arrangements to license in the best of these from selected centres of excellence around the world. Links have already been forged with a number of universities in the USA, and with exploitation agencies in Japan.

Inter-corporate licensing

BTG's skills in transferring technology from the public to the private sector are now being applied to technology transfer between companies following the creation during 1987 of an Inter-Corporate Licensing Group within BTG.

Proven industrial technology offered to BTG for exploitation is assessed to determine the patent position and business potential. If the products look capable of generating significant royalty-bearing income, BTG takes on the task of exploitation by licensing to other companies on an international basis.

Further information on this service is given in the BTG brochure *Inter-Corporate Licensing.*



Lightweight concrete components reinforced with Cem-Fil alkali-resistant glass fibres have been used extensively at the Real Madrid football stadium.

PYRETHRIN ANALOGUE INSECTICIDES

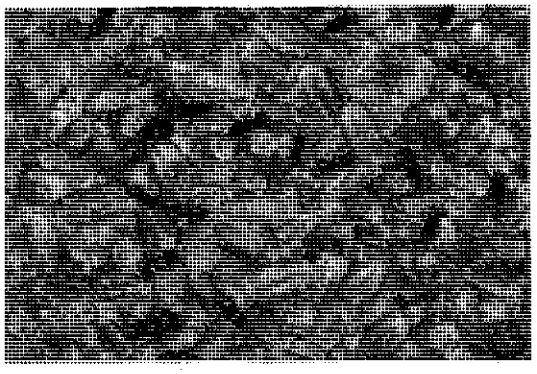
The successful development of the pyrethrin analogue insecticides has resulted in a revolution in agriculture world wide. Extremely high effectiveness against insect pests combined with a lack of adverse effects on the environment or on mammals has led to synthetic pyrethrins rapidly replacing older products in many agricultural uses. They are also highly effective as public health and veterinary insecticides.

Synthetic pyrethrins now account for one-quarter of the global insecticide market. BTG-licensed formulations constitute about 65% of the pyrethrin market, representing sales at the end-user level of nearly £1000 million.

The main BTG products were invented in 1973 by a team led by Dr Michael Elliott in a BTG-funded project at the AFRC's **Rothamsted Experimental Station**. The formulations of the pyrethrin analogues derive from natural pyrethrum present in flowers of the chrysanthemum family. BTG's funding, which built on AFRC's core programme, began in 1962 and is still continuing. Rothamsted's involvement in pyrethrin research dates back to the late 1920s.

BTG has protected the results of the research programme with a portfolio of more than 500 separate patents, patent applications or registrations, involving 34 basic inventions.

Patents are licensed by BTG to a number of companies world wide. The first commercial products appeared in the late 1970s. In the UK, licences have been granted to **The Wellcome Foundation, Mitchell Cotts, ICI and Shell**. In the USA, licensees are **FMC** and **ICI Americas Inc.** **Sumitomo** is licensed in Japan, and **Roussel Uclaf** in France.



Pyrethrins are also used to control infestation of crops in store by pests such as grain weevils.

Photo: The Wellcome Foundation



Trials using Fastac pyrethrins on rice in Indonesia to test for any adverse effects on fish held in cages in the paddy fields.

Photo: Shell

OTHER PEST CONTROL PRODUCTS

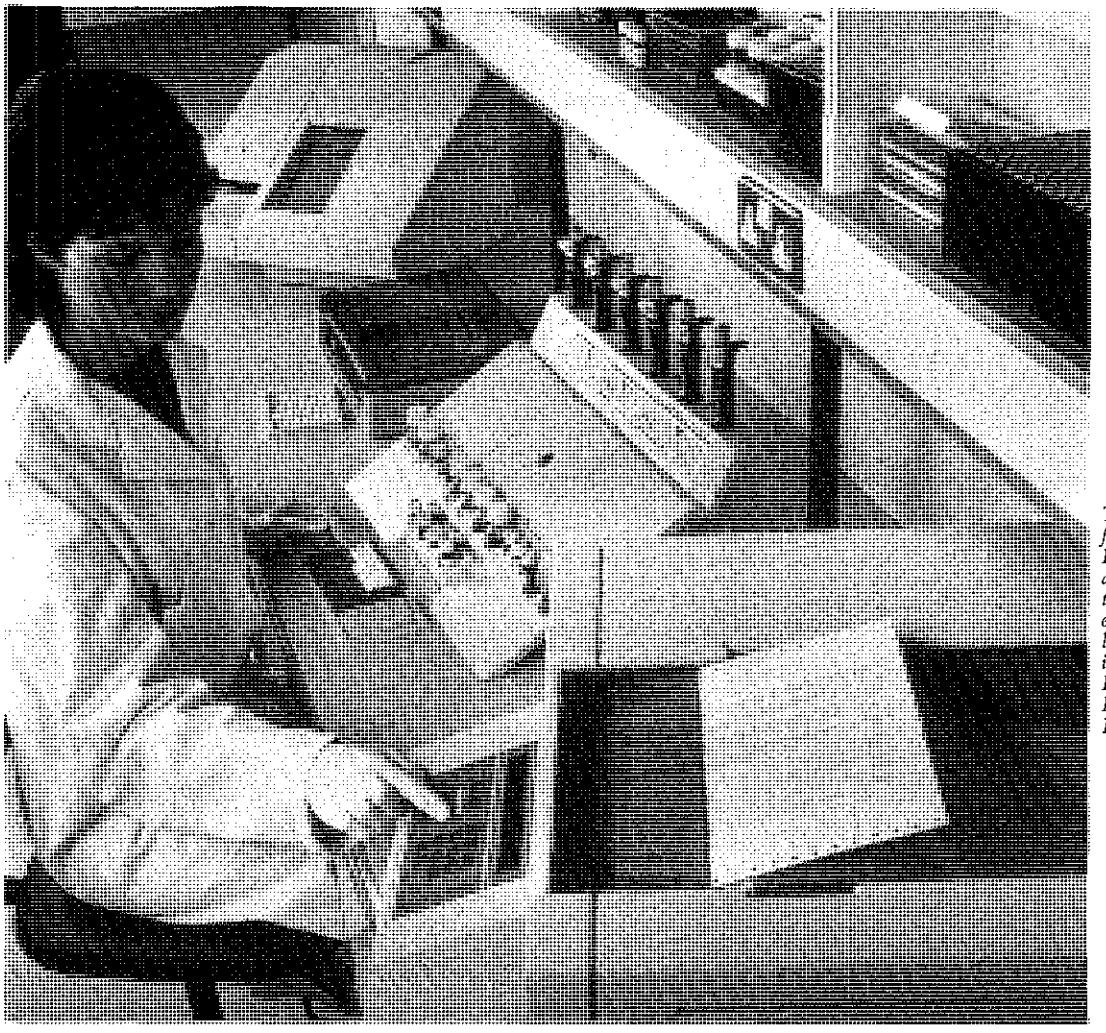
Notwithstanding their remarkable success, pyrethroid insecticides are not equally effective against all species of insect. Strains of at least 19 important agricultural pests have been reported as being resistant to pyrethroids and the problem is of increasing commercial significance.

However, work funded by BTG at **Rothamsted Experimental Station** in anticipation of this problem has resulted in a patented group of non-pyrethroid lipophilic insecticides. The intellectual property is the subject of an exclusive arrangement with **Wellcome** for collaborative development of commercial insecticides.

Insect pheromones have generated considerable interest as a means of monitoring and controlling insect populations, especially as part of integrated pest management programmes.

A collaboration between **The London School of Hygiene & Tropical Medicine** and **Rothamsted Experimental Station** has resulted in the development of a pheromone for use in controlling Culex mosquitoes. These are important vectors of diseases such as elephantiasis, and are widespread in Africa, North and South America, and Asia.

The researchers have shown that gravid (pregant) female mosquitoes are attracted to favourable breeding sites such as shallow water



The Amerlite system from Amersham International takes advantage of techniques for enhancing luminescence devised in the Wolfson Research Laboratories at Birmingham.

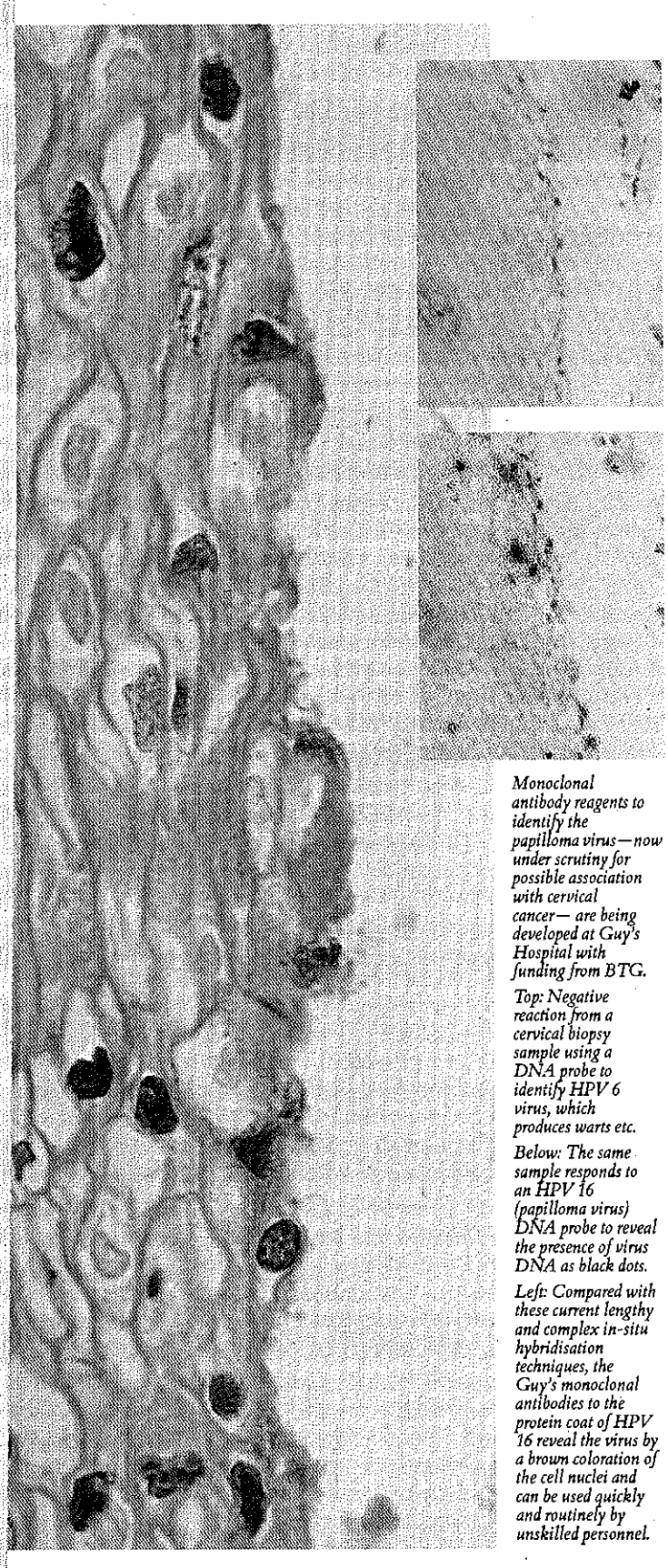
A licence has been granted to **PPR Diagnostics**, a company set up by the inventors to commercialise their research. A diagnostic kit for NAG measurement was launched in the UK in October 1987. Distribution in other territories is also planned and terms for a licence to sell in Japan are being negotiated.

A patented technique from **St Mary's Hospital**, London, uses a specific combination of enzyme substrates for rapid bacterial identification. The process eliminates the customary necessity for prolonged incubation and could have wide application. However, some radical changes in present clinical bacteriology testing methods will be required if the technique is to achieve its full potential.

The technique has been licensed exclusively by BTG to the Microscan Division of **Baxter Healthcare Corporation.**

A broadly applicable method of enhancing and sustaining the emission of light from the horseradish-peroxidase-induced breakdown of luminol in the presence of hydrogen peroxide has been devised at the Wolfson Research Laboratories in the Queen Elizabeth Medical Centre at the **University of Birmingham.** The technique has been assigned to BTG via **DHSS.** Products from BTG's licensee, **Amersham International**, are already on the market in Europe under the trade name *Amerlite*.

The technique promises to provide an order of magnitude increase in sensitivity over competitive methods. This, coupled with its potential ease of automation, could make it an attractive technique for the next generation of automated immunoassay equipment. The increase in sensitivity could be of crucial importance in the gene-probe area.



Monoclonal antibody reagents to identify the papilloma virus—now under scrutiny for possible association with cervical cancer— are being developed at Guy's Hospital with funding from BTG.

Top: Negative reaction from a cervical biopsy sample using a DNA probe to identify HPV 6 virus, which produces warts etc.

Below: The same sample responds to an HPV 16 (papilloma virus) DNA probe to reveal the presence of virus DNA as black dots.

Left: Compared with these current lengthy and complex in-situ hybridisation techniques, the Guy's monoclonal antibodies to the protein coat of HPV 16 reveal the virus by a brown coloration of the cell nuclei and can be used quickly and routinely by unskilled personnel.

therapeutic use. Terms have been agreed with the Scottish Health Service for scale-up production of the monoclonal and its use in clinical trials.

Despite a national screening programme involving an annual total of some 3 million tests based on the 'pap' smear cytology staining technique, deaths among younger women in the UK attributable to cervical cancer have doubled in recent years.

In the search for the causative agent of the disease, attention has increasingly focussed on the papilloma virus, certain strains of which are known to cause genital warts. Recent studies have confirmed this association.

Workers at Guy's Hospital, London, have now successfully prepared parts of this virus and opened up the possibility of performing screening tests employing simple, standard immunoassay techniques, eliminating subjective assessment and increasing sample throughput. Licensees are being sought by BTG for those reagents already available. A BTG-funded project at Guy's is establishing a further range of complementary reagents.

Monoclonal antibodies to herpes simplex virus developed in the Department of Pathology at the University of Cambridge have proved to be useful in diagnostic tests for herpes. The Wellcome Foundation, Boots-Celltech Diagnostics, IQ Bio and Baxter Healthcare are all licensees.

Following a blood clot, processes leading to its dissolution are triggered naturally in the human body. Thus the presence of soluble cross-linked fibrin and its degradation products (FDP) is likely to be a valuable diagnostic pointer to those patients who are at imminent risk of thrombosis.

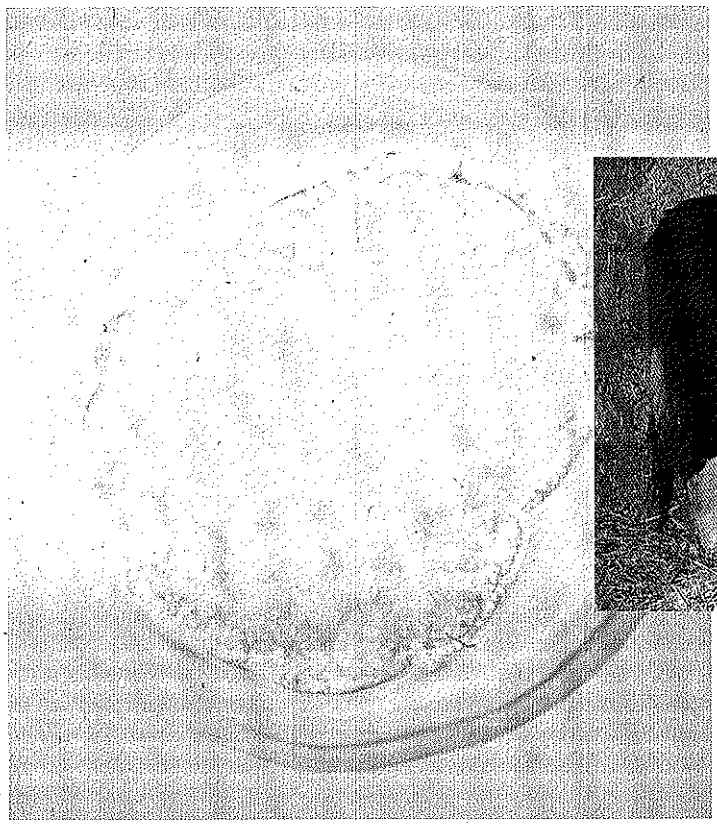
Conventional assays for FDP have employed a polyclonal reagent that also reacts with the precursor of fibrin, which circulates normally in the blood of healthy people. These reagents have therefore given only a poor indication of the risk of thrombosis.

Work at the National Institute for Biological Standards & Control has succeeded in producing monoclonal antibodies which correlate well with the presence of clinically confirmed thrombosis and complications in pregnancy. Evaluations are in progress with two companies.

Silceram is a range of patented glass ceramics with exceptionally high resistance to erosion by fluid-borne solid particles. Glass ceramics are formed by the devitrification (crystallisation) of some glasses under suitable temperature conditions. They combine many of the properties of ceramics, such as high-temperature stability, with the ease of fabrication of glasses. *Silceram* was developed at Imperial College with support from BTG as well as SERC and the EEC.

There is potentially a high-volume use for *Silceram* as a technically superior replacement for the imported Czechoslovakian cast basalt used in the linings of metal pipes and chutes for the pneumatic conveying of solids and slurries. Some low-volume, high-margin applications have also been identified.

BTG has provided financial backing to **Epi Materials Ltd**, an operation unique in Europe for independent manufacture and marketing of advanced semiconductor wafers based on gallium arsenide, indium phosphide and cadmium mercury telluride produced using metal organic vapour phase epitaxy (MOVPE) techniques.



Initial funding of £570,000 has been provided equally by BTG and Air Products (UK) Ltd by way of equity and preference share capital.

APPLIED BIOTECHNOLOGY

One key Science Division investment is in **Agricultural Genetics Company Ltd** (AGC). This company was launched by BTG and a consortium of private-sector investors in 1983 to exploit world-wide market opportunities in agriculture by the development and application of biotechnology. Further funds were raised by a private placing of shares in November 1984.

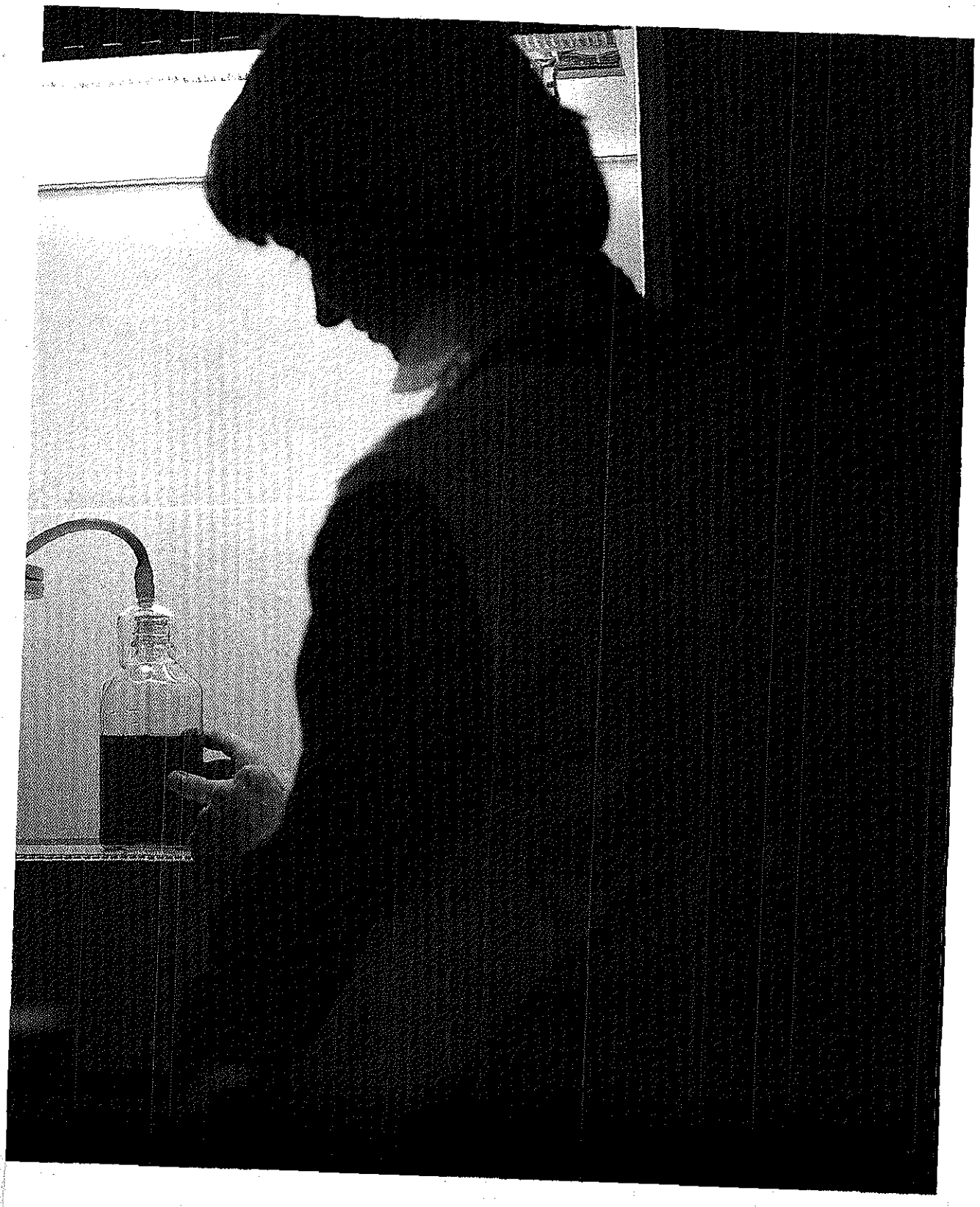
AGC draws on the considerable resources of the Agricultural & Food Research Council (AFRC) laboratories, which are recognised as world leaders in several areas. It is concerned particularly to capitalise on the commercial opportunities presented by AFRC's work on non-conventional plant breeding, microbial inoculants and biological control products. In addition, AGC has obtained access to breeding programmes for oil-seed rape and wheat.

£1 million was committed to **Premier Breeders Holdings Ltd** (PBH) in 1986. PBH is the largest private-sector supplier of semen to the dairy-cattle industry in the UK and the leading embryo-transfer company.



Moet Premier Ambassador A was imported from the USA by Premier Breeders as one of 29 embryos and was the first calf from this breeding programme to be born in the UK.

BTG invested alongside Agricultural Technology Ltd with the aim of supporting the development and application of multiple-ovulation and embryo-transfer techniques to enhance the genetic standards of British dairy cattle.



The Campath monoclonal antibodies for therapeutic use have been developed in the Department of Pathology at the University of Cambridge *(see p 22).*

synthesis and evaluation of more than 500 compounds with potential as anticancer drugs. The prospect of at least one of these compounds being developed and marketed for the benefit of cancer patients now appears to be very good.

In a less direct approach, BTG has obtained patent protection on a range of compounds from the **MRC's Radiobiology Unit** that sensitise cancer cells to radiation treatment.

A major US pharmaceutical company, **Warner Lambert**, was developing the lead compound, RU 1069, under an exclusive licence from BTG but abandoned the compound because it causes severe emesis. However a second 'back-up' compound covered by the original and subsequent BTG patents has been identified.

It is becoming clear that tissue oxygenation, on which these 'first-generation' products depend, has far-reaching value in the development of new anticancer agents. BTG has therefore invested in work at the Unit (and also provided magnetic resonance imaging equipment) to produce and evaluate compounds which act in a similar way.

A possible novel treatment for hormone-dependent cancer using pyridoglutethimide has emerged from a BTG-supported project at the **Institute for Cancer Research**. BTG has arranged for trial material to be manufactured under contract and the **Cancer Research Campaign** Clinical Trials Committee is carrying out studies of the product in patients. BTG is already negotiating licence rights with companies who specialise in new products for the treatment of cancer.

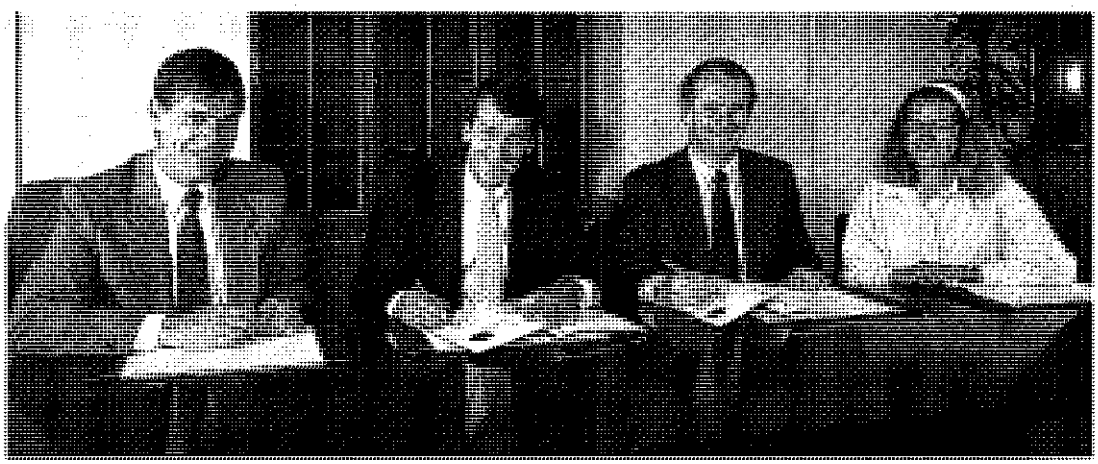
SOME EXCITING NEW DRUGS

Many drugs commonly used in the treatment of anxiety also cause drowsiness and impair the patient's ability to operate machinery or to drive a car. It is hoped that the compound coded BTG 1501 will prove to be an effective anxiolytic without a sedative effect.

BTG owns a portfolio of patents and patent applications on BTG 1501 based on research carried out by a number of scientists, including staff at the **Universities of Bradford** and **Cardiff**. These studies have revealed an exciting and unusual profile of activity and further BTG projects are being progressed to broaden patent protection. **G D Searle & Co** signed an exclusive option agreement relating to BTG 1501 in June 1988.

A BTG-funded project at the **University of Edinburgh** discovered a range of selective blockers of the actions of thromboxane, a substance released by the body when tissue is damaged or inflamed. These compounds were some of the earliest examples of a new class of drug, now called thromboxane A_2 antagonists, which are causing considerable excitement in the pharmaceutical industry. A number of major companies are actively investigating and developing potential products.

The primary clinical uses are likely to be in the treatment of cardiovascular and respiratory disease but elucidation of the true potential of this class awaits the results of clinical testing in a wide variety of diseases. Potential utility in angina, after strokes and heart attacks, in autoimmune disease, in asthma and as a prophylactic anti-inflammatory agent has been proposed.



Signing of an exclusive option agreement relating to BTG 1501 between G D Searle & Co and BTG. Left to right: Peter Geuze and Dr Ronald Goode (Searle); Dr Derek Schafer and Dorothy Saul (BTG).

Age-related illnesses such as Alzheimer's disease are of growing concern as life expectancy generally increases. Alzheimer's disease is a neurodegenerative illness resulting in the loss of the neurotransmitter acetylcholine from the brain. Cholinergic drugs with a selective action in the brain to replace the acetylcholine function may offer a therapeutic treatment.

BTG is supporting research at a number of universities in an interdisciplinary approach to the development of cholinergic drugs for use in senile dementia and other diseases. The research centres include the University of Southampton, the University of Surrey, the School of Pharmacy, and the National Institute of Medical Research.

Research has shown that many of the basic processes carried out by the brain are controlled or mediated by simple amino acids. There is a growing realisation of the enormous potential of excitatory amino acid antagonists, particularly in the development of anticonvulsant therapies and neuroprotective agents, for example in the treatment of strokes.

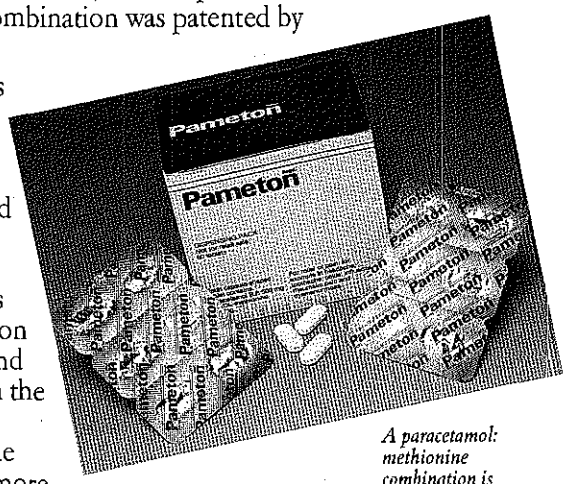
BTG has secured patent protection on an important group of compounds developed at the University of Bristol which affect this process strongly in animal models. Development of products is under way by the Swiss pharmaceutical and chemical major, Sandoz AG, which has recently exercised an option for an exclusive licence from BTG.

SAFER PARACETAMOL

Paracetamol is one of the most widely used pain-relieving drugs and has proved to be safe and free of side effects if taken within the recommended dose regime. However, its ready availability means that it has often been chosen as the vehicle for suicide, and accidental overdose is a risk with any drug, particularly with children. Taken in overdose, paracetamol does not kill immediately but through its action on the liver, so that a prolonged and painful death ensues.

There are known antidotes to paracetamol poisoning but these must be given quickly after the overdosing to be effective. Andre McLean, Professor of Toxicology at University College Hospital, London has suggested incorporating an antidote in each paracetamol tablet. His choice is methionine, a naturally occurring amino acid which is also used as a food additive, and the paracetamol: methionine combination was patented by BTG in 1973.

The product is available in the UK from Sterling Winthrop and is marketed as *Pameton*. At present it is only available on prescription and excluded from the DHSS list of reimbursable products. As more evidence of its usefulness is accumulated, it is hoped that *Pameton* will become more widely available. BTG is willing to grant further licences to other manufacturers interested in marketing the paracetamol:methionine combination, especially for 'over the counter' sales.

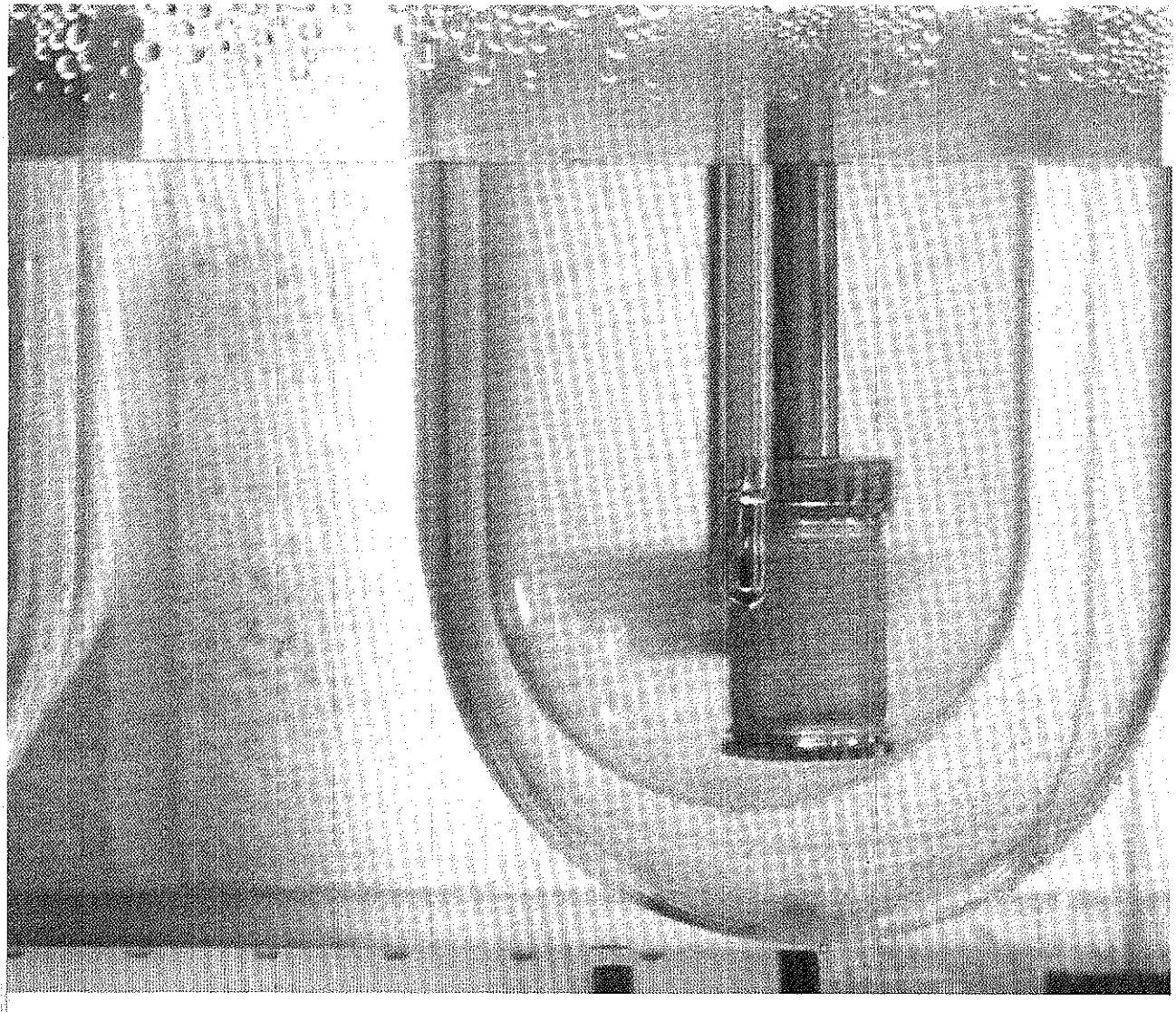


A paracetamol: methionine combination is marketed in the UK as Pameton by Sterling-Winthrop under BTG licence.

METALLIC ELEMENTS IN HUMAN PATHOLOGY

At least 14 metallic elements are required by the body for healthy tissue function. BTG is supporting projects at King's College, London, the University of York, St Thomas's Hospital, the University of Essex, the University of Cambridge, Harwell, University College London and the London Hospital researching the involvement of iron, zinc, chromium, copper and aluminium in human pathological processes. These programmes have generated an extensive patent portfolio and BTG is seeking industrial licensees in several areas to take the work forward.

In particular, at King's College, Professor Bob Hider is carrying out research into chemical compounds that interact with zinc with the objective of modifying its distribution within the body. Work with St Thomas's Hospital and University College London has shown that the level of zinc in white blood cells is a good measure of the amount of zinc in body tissues.



Special polymers developed at Strathclyde University for controlled release of drugs are being licensed to the pharmaceuticals industry by BTG with the support of Polysystems, a university spin-off company.

DRUG-DELIVERY SYSTEMS

Ways of using special polymers to release drugs in a controlled manner to give improved medical results have been developed over a number of years with BTG support at the University of Strathclyde. The physical properties of the polymers allow pharmaceuticals to be loaded without chemical processing.

More than 20 basic inventions have been assigned to BTG from the project and rights have been granted to Glaxo, Chas F Thackray and Controlled Therapeutics Inc. The latter US company, based in Philadelphia, has recently invested in major manufacturing facilities in Scotland largely to produce the licensed products. Further licences are under negotiation.

The BTG investment in the project and associated patents is approaching £1 million. Work is continuing on several fronts, including the development of animal-health products in collaboration with AFRC research institutes.

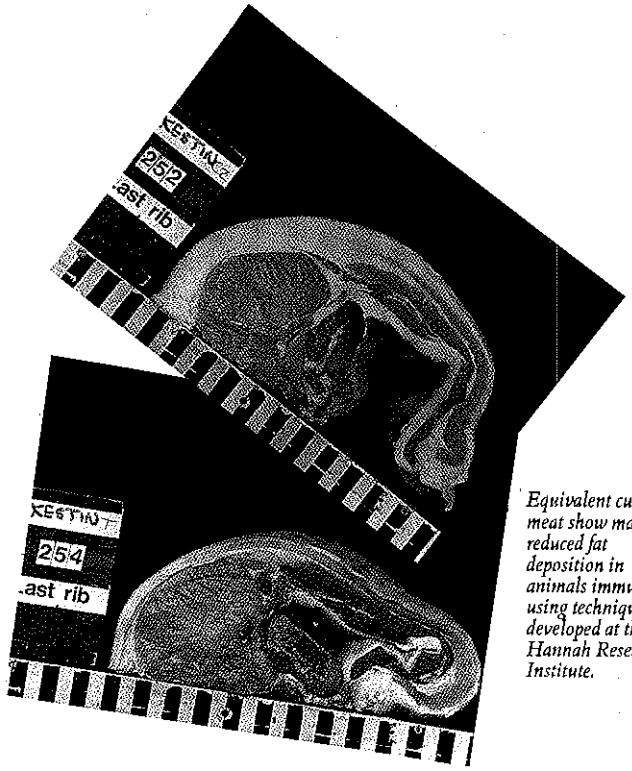
BTG has also participated in the creation of Polysystems Ltd, a company set up jointly with Strathclyde University and Professor Neil Graham to collaborate with licensees in the development of products. Polysystems itself is a licensee for certain non-medical applications.

Products from Controlled Therapeutics for release of prostaglandin E_2, of morphine, and for wound healing are likely to be the first items to reach the market.

In 1983 workers at the **AFRC Institute for Animal Health** identified a non-pathogenic strain of *T. hyodysenteriae* in pig herds not suffering from the disease. Combinations of oral dosing with this live strain, together with injection of a dead virulent strain of the organism, results in a high degree of protection against the disease. This vaccine regime has been patented worldwide by BTG and is being developed for commercial use with **Hoechst UK Ltd.**

Hoechst is already marketing a range of vaccines to prevent pasteurellosis and other diseases in sheep. The pasteurella components of these vaccines are based on work carried out at the **Moredun Institute** of the **Animal Disease Research Association** at Edinburgh.

The collaboration results from a tripartite agreement between BTG, the Institute and the company; the intellectual property is assigned to BTG and licensed to Hoechst. It is hoped that improved vaccines for sheep will emerge, as well as the first pasteurellosis vaccines for cattle.



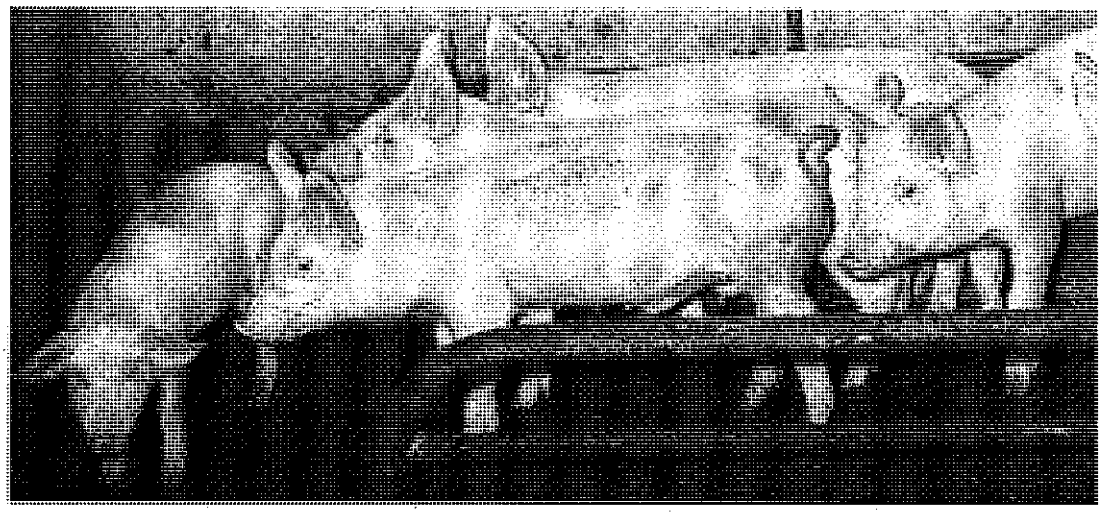
Equivalent cuts of meat show markedly reduced fat deposition in animals immunised using techniques developed at the Hannah Research Institute.

Respiratory disease in young calves may be caused by a variety of infectious agents. Work at the **Compton Laboratory** supported in part by BTG has led to a multicomponent vaccine which has been effective in field trials and is ready for launch in the UK by **Pitman-Moore.**

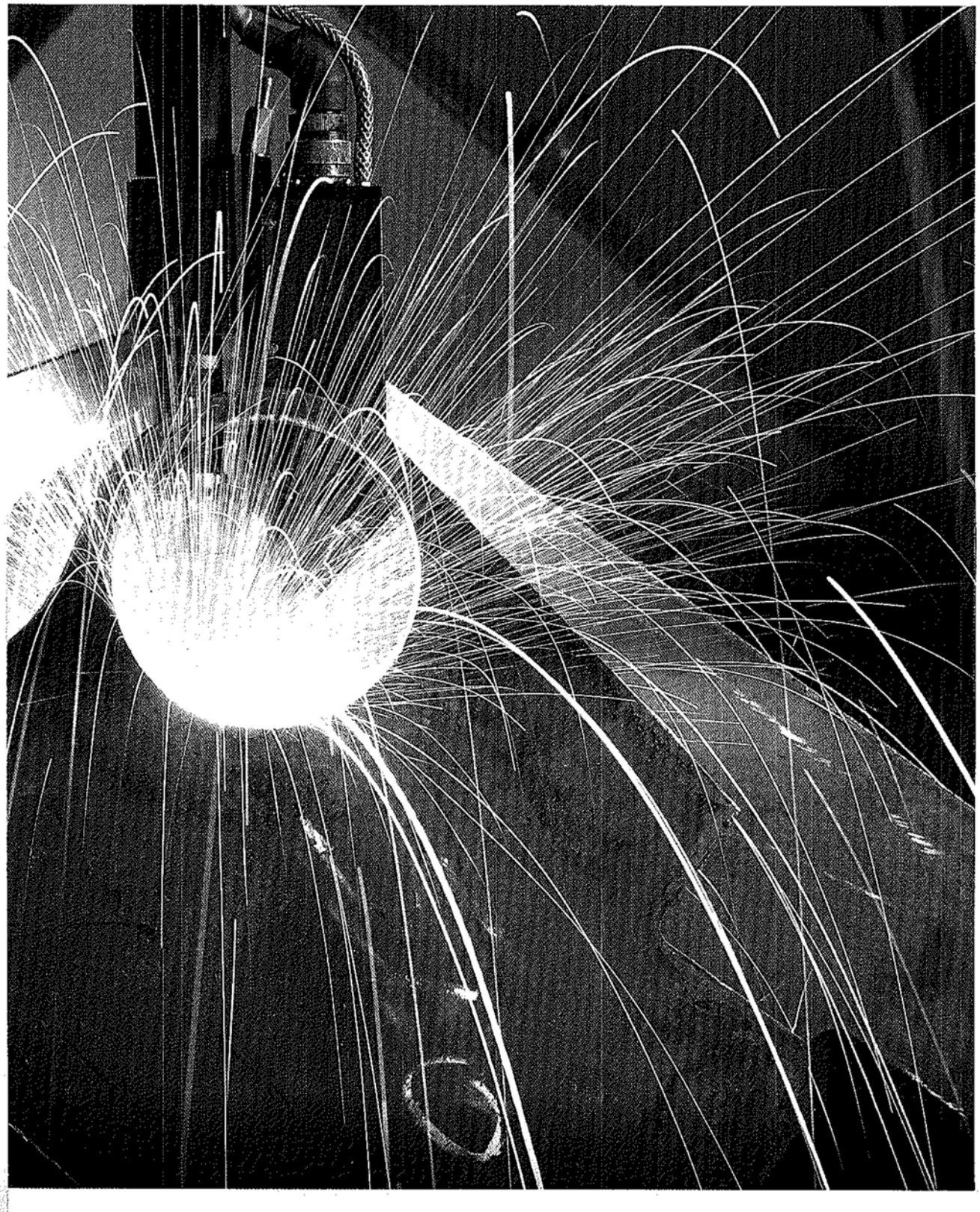
The commercial vaccine will contain two viral components and one mycoplasma component. The method of production of the key viral component—RSV (respiratory syncytial virus)—is the subject of patent applications filed by BTG.

Excessive fat deposition in food animals is inefficient and undesirable on health grounds. Workers at the **Hannah Research Institute,** Ayr, have devised techniques to immunise growing animals against their own fat cells.

BTG is supporting a collaborative programme in five research centres to develop and refine this technique for commercial use. Efficacy has now been demonstrated in several animal species and BTG is seeking to develop this work further in conjunction with licensees.



Swine dysentery has obviously retarded the growth of the pig on the left in comparison with the other healthy animals.



Meta Machines's technology for automatically tracking and welding seams has been developed by the original research team at the University of Oxford (see p 41).

BTG has an extensive portfolio of patents relating to orthopaedics, dentistry, patient monitoring and laboratory equipment. Some 80 agreements are currently in force and BTG's licensees range from major companies in the healthcare business to small firms making specialist products. In addition, BTG is supporting about 35 different development projects relating to medical equipment.

A conventional artificial hip joint comprises two parts: a cup made of polyethylene which fits into the pelvis, and a spherical head mounted on a long tapered metal shaft which fits into the femur.

A new type of prosthesis proposed by **Dr Richard Field** seeks to replace the part of the femur above the epiphyseal plate with a composite spherical head anchored by filaments driven into the bone.

BTG has supported a programme at the **University of Cambridge** to develop and evalute the mechanical properties of this hip prosthesis, taking account of the internal structure of the femur and the shape and position of the epiphyseal plate. The programme has established that the idea works on cadaveric bones under laboratory conditions, and that filamentary fixation is a practical possibility.

The next step is to manufacture components that can be tried out in patients to test dynamic performance and biocompatibility. Arrangements are in hand for a major international manufacturer of orthopaedic prostheses to fund this part of the programme.

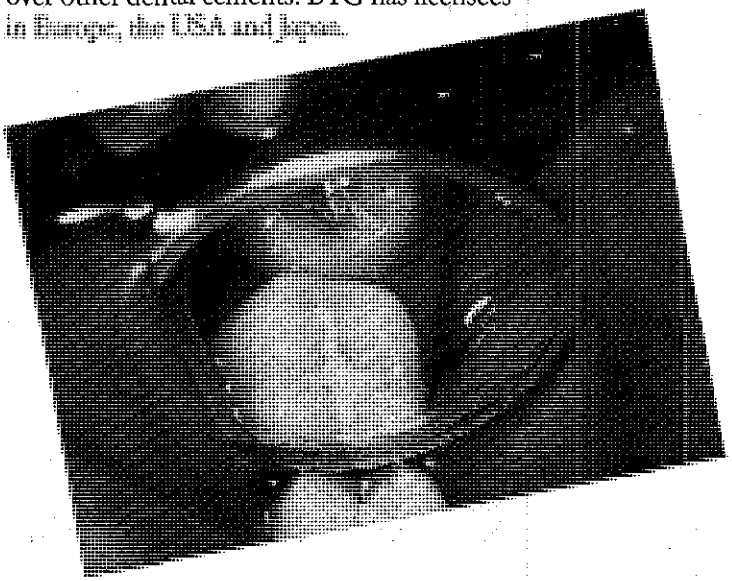
Widespread use of relatively simple and inexpensive medical instrumentation can lead to more accurate and earlier diagnosis of illness. One case in point is the Wright peak flow gauge developed at the Medical Research Council's **Clinical Research Centre (CRC)** for self monitoring of lung function by patients being treated for a variety of breathing difficulties. About 1 million of these units have been produced by BTG's licensee **Clement Clarke** and distributed through GPs.

Another invention from the CRC being sold in large numbers by **Graysby Medical Ltd** is the Neonatal Respirometer, which monitors respiratory behaviour in premature babies. New ideas involving the detection of fetal distress during labour are being developed at the **University of Nottingham** and it is expected that these ideas too will be licensed successfully.

The DACOS blood analyser, which is a discrete analyser with continuous optical scanning, was conceived at the CRC in 1973. Similar equipment was also developed independently at about the same time at the Wolfson Research Laboratories at the **University of Birmingham**. Patent rights from both groups were assigned to BTG and licensed to **Coulter Electronics Inc** in the USA and its British subsidiary Coulter Electronics Ltd. The major Japanese optical company **Olympus** was licensed by BTG during 1988. Cuvettes may be inserted in random order and the apparatus provides a series of measurements on each sample—rather than one fixed endpoint—completely automatically.

Dental materials represent another area where BTG has successfully exploited a number of inventions. One example is glass ionomer cement, which was developed at the **Laboratory of the Government Chemist (LGC)** in the early 1970s with financial support from BTG.

This is currently one of the most important dental materials world wide. It is used primarily for filling anterior teeth, as a cavity liner and for general cementation purposes. Its ability to bond with tooth material and its role in preventing caries make it a significant advance over other dental cements. BTG has licensees in Europe, the USA and Japan.



Glass ionomer cement, now one of the world's most important dental materials, was developed with BTG funding by the Laboratory of the Government Chemist.

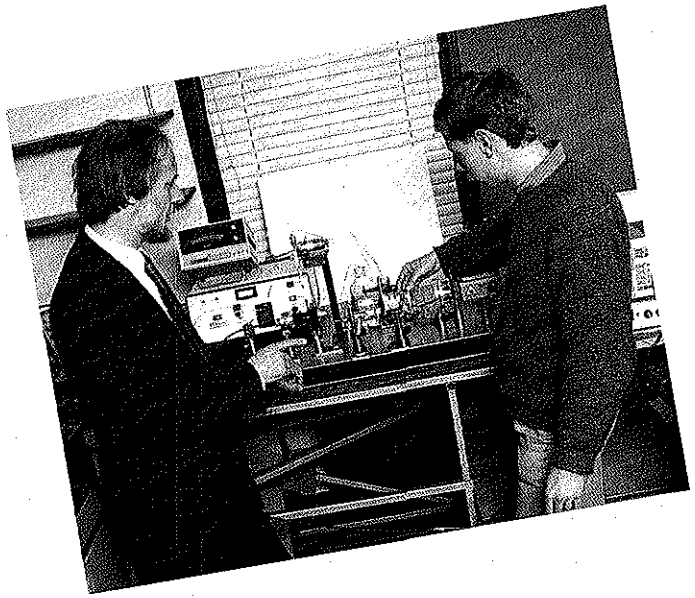
LABORATORY EQUIPMENT

Magnetic resonance imaging (MRI) in medical applications observes nucleii in mobile environments—usually protons in water molecules within living tissue. Extending MRI to the study of solids poses problems, primarily because dipolar and quadrupolar interactions between adjacent nuclei broaden the spectral lines to the extent that spatial encoding by magnetic field gradients is impossible.

Research at the **University of Surrey** has addressed various ways of overcoming this limitation, and has produced the first ever two-dimensional images from protons in crystalline solids. Applications envisaged include non-destructive examination of polymer extrusions and injection mouldings, testing of composites, and medical imaging of bone.

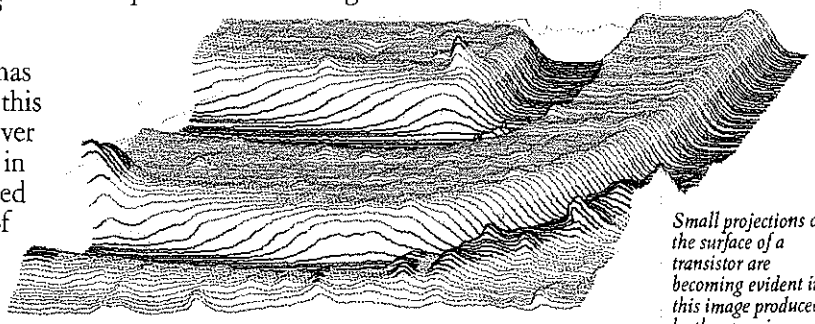
Researchers at the **University of York** have devised a miniaturised laser-diode optical-rotation detector that represents an important advance in high-pressure liquid chromatography, particularly with the advent of column materials capable of separating optical isomers. Applications include separations of biological materials, foodstuffs and pharmaceutical products.

A prototype system has been built and is being evaluated at York with BTG funding. **Applied Chromatography Systems Ltd** of Macclesfield has introduced a commercial system under BTG licence.



Dr David Goodall (left) and David Lloyd with a prototype optical-rotation detector constructed at the University of York for chromatographic applications.

A scanning microscope developed at the **University of Nottingham** uses capacitance for non-contacting measurement of surface topography. In the prototype a fine tip is held adjacent to the surface under test and capacitance measured in a precision bridge as the tip is raster scanned across the test piece. Extensive computer software has been written to control the tip-to-surface distance and present the data so gathered.



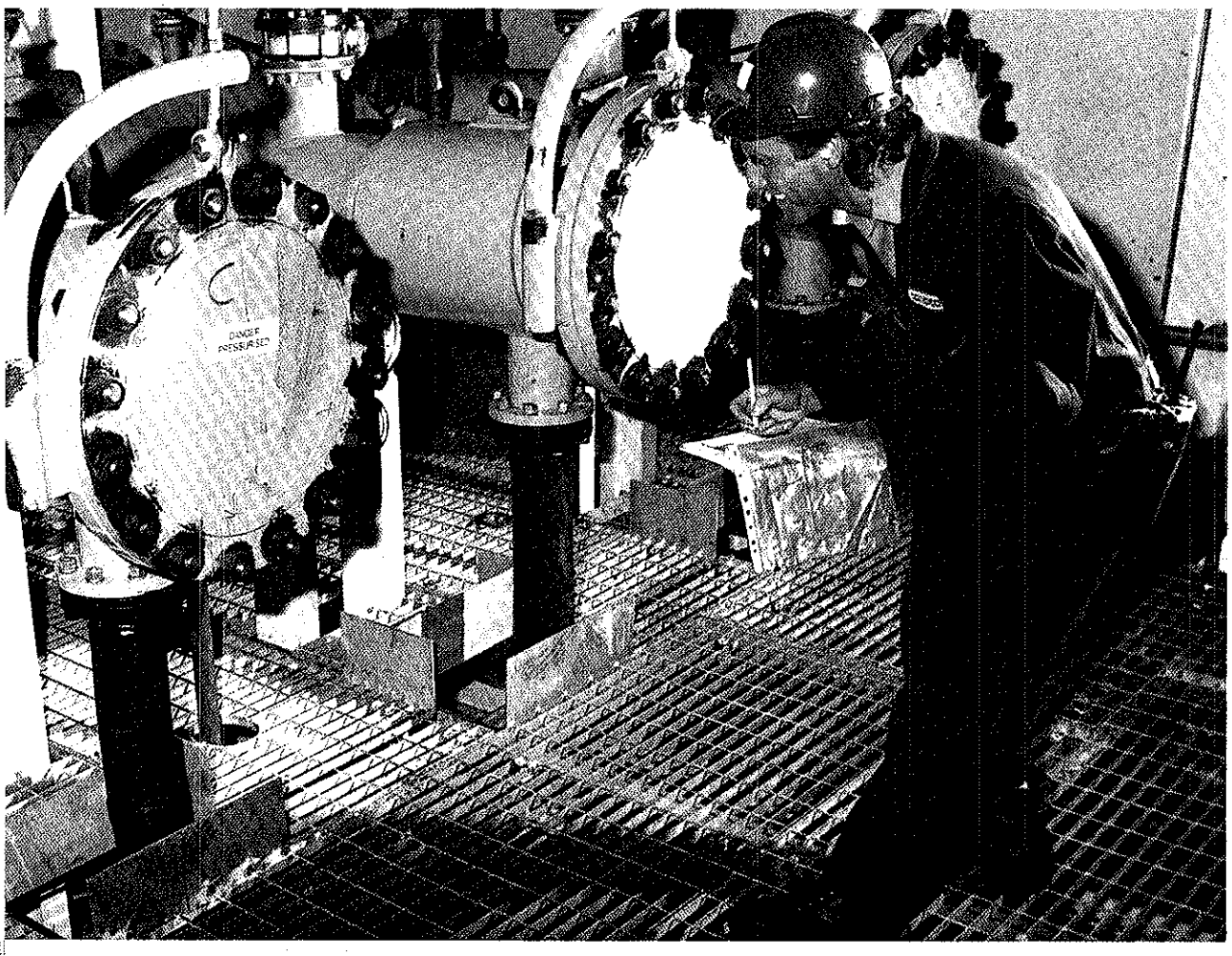
Small projections on the surface of a transistor are becoming evident in this image produced by the scanning capacitance microscope developed at the University of Nottingham. The area shown measures 130 μm x 130 μm.

Applications so far include non-contact imaging and measurement of integrated circuit features—demonstrating vertical resolution of a few nanometres and lateral resolution of 1 μm—and examination of surface finish and surface defects in a variety of materials. The system is currently being developed commercially for measurement of wet ink films produced by silk screening processes used in the manufacture of hybrid thick-film integrated devices.

A long-term research programme at the **National Physical Laboratory** into the quality of optical thin films has revealed a correlation between film structure and surface imperfections.

The hypothesis that such imperfections are characterised by local concentrations of charge was tested by writing a charge pattern into a surface using a mask and thermal electrons to simulate imperfections. Evaporation of zinc or zinc sulphide reproduced the pattern with high fidelity. Subsequent experiments have demonstrated that extremely sharp edge definition can be achieved.

Experiments with scanning electron beams show that maskless deposition of zinc sulphide or similar materials at high resolution by evaporation or sputtering is also feasible. The technique thus offers the opportunity for high-resolution, maskless writing of patterns for integrated circuits without using photoresist.



Four of the 17 60 mm Vortoil hydrocyclones installed on the Conoco Hutton tension-leg platform that are capable of treating 200,000 barrels per day of produced water to meet Government discharge requirements of less than 40 ppm of suspended oil.

The *Aztec* gold/uranium analyser takes a completely new approach to gold assay. The existing method of fire assay is expensive in terms of time, labour, chemicals and power for furnaces running 24 hours per day. It cannot be automated, one sample might typically be handled by at least 12 people, and there are inherent hazards from airborne lead.

Aztec represents four years of development by **KX Technology Ltd** with financial support from BTG and the co-operation of a leading mining house. It employs X-ray fluorescence techniques to measure the K X-rays characteristic of gold using a special high-sensitivity, low-noise detector in combination with sophisticated electronics and high-speed computing.

Compared with fire assay, *Aztec* offers reduced sample handling, lower method errors and fast turnround time. It measures only gold and uranium, so there is no need for silver correction or parting procedures.

PROCESS TECHNOLOGY

Innovations in process technology can affect a wide range of industries processing liquids, solids or gases. If an invention constitutes a breakthrough in one of the steps that have been a limiting factor in the overall industrial process, the economic benefits can be considerable and may influence the development of a whole area of industry.

For instance, the separation of oil suspended in water is of particular interest to the petroleum production and processing industry. Hydrocyclones invented at the **University of Southampton** and now manufactured and sold under the *Vortoil* name by BTG's licensees **BWN Vortoil Pty Ltd** have made possible high-speed separation of oil suspensions. Cyclone separators were in use in all sectors of the North Sea only three years after the product was launched.

Sterilisation of packaging materials by means of low concentrations of hydrogen peroxide in combination with ultraviolet light has been a key aspect of a new range of aseptic liquid packaging machines developed under BTG licence by **Liquipak NV**, which was acquired by the **Tetra Pak Group** in 1986. The technique, which was devised at the **Food Research Institute**, Norwich, leaves only low levels of hydrogen peroxide residues in preformed liquid packages and conforms to newly introduced US Food & Drug regulations. Negotiations are taking place with further potential licensees.

In the textiles industry, the process of spinning draws together short individual staple fibres to form a continuous length of yarn. The faster a yarn can be formed, the fewer spinning machines are required for any given output.

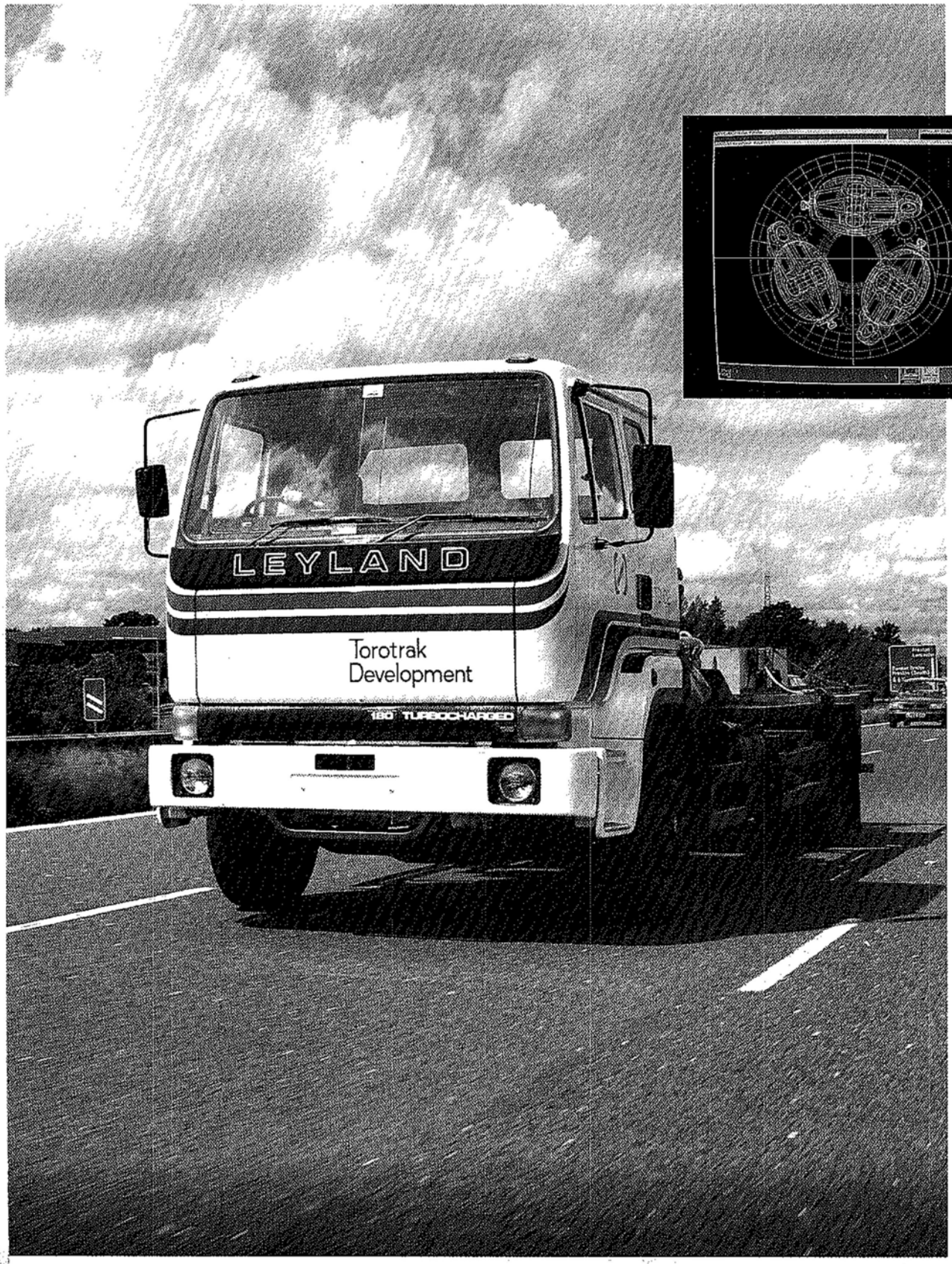
BTG is supporting a programme of work at the **University of Manchester Institute of Science & Technology** which promises significant advantages in the spinning of long staple fibres such as wool, which at present have to be spun at relatively low speeds. Early indications are that the UMIST process may be two or three times faster.

After spinning, yarns of differing colours are woven to form patterned fabrics. Production of samples in small quantities for buyers to choose from is a laborious process that requires considerable technical skill and design flair in a highly competitive and sometimes capricious business.

BTG has supported the development by the **Scottish College of Textiles** of software that simulates woven fabrics on a high-resolution graphics colour monitor in minutes, with a 'hard copy' paper printout of the final design together with a list of yarn requirements and instructions for setting up the loom for production. A palette of 16 million colours allows complete freedom of colour tint and hue, encouraging textile designers to be more adventurous without incurring the risks and costs of producing unacceptable woven samples by traditional methods.



Software developed by the Scottish College of Textiles enables woven fabrics to be simulated on a high-resolution colour monitor using a palette of 16 million colours.

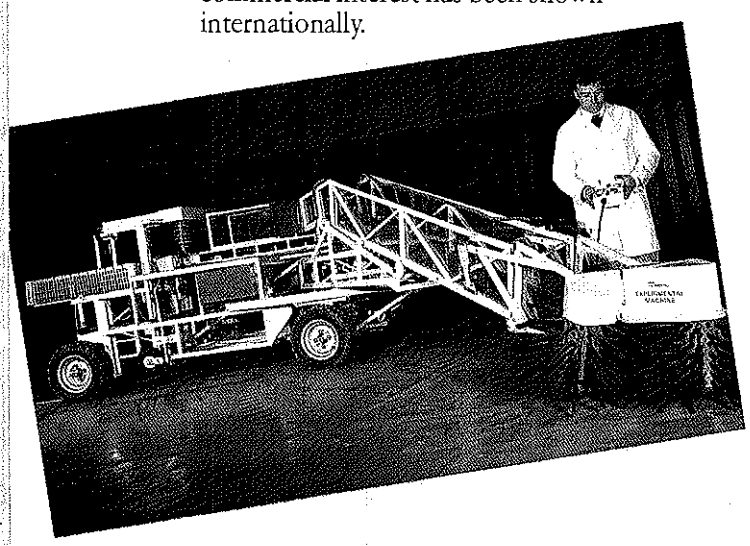


The Perbury CVT can be applied not only to cars (opposite) but right through the range to large trucks.

Another major innovation has been the development of a mechanical harvester for broiler chickens, which are collected from farms and transported live to centralised processing plants. They are normally caught in the darkened broiler houses by hand at rates of over 1000 birds per man hour. This can be enormously stressful to the birds, and may result in downgrading due to injury.

The Buildings and Livestock Division at **AFRC Engineering** has developed equipment which collects the birds much more quickly. It carefully lifts the birds off the floor of the broiler house and marshals them quietly onto a conveyor for loading into crates or specialised vehicles for transportation to processing centres.

BTG has licensed the broiler harvester to **Tamnaharry Developments Ltd** in Northern Ireland, and to **Agritec** in Wales. Considerable commercial interest has been shown internationally.



The latest prototype of the AFRC Engineering mechanical broiler harvester.

Unlike a combine harvester, the wholecrop harvester collects both the grain and the straw, breaking the latter for use as animal feed. This machine has been developed at **AFRC Engineering** under sponsorship from the Overseas Development Administration.

The major markets for the wholecrop harvester, which is designed for rear mounting on tractors of at least 45 h.p., will be in countries where wheat is a major crop and finely broken wheat straw is highly valued for animal feed, notably North Africa, the Middle and Near East, India and Pakistan.

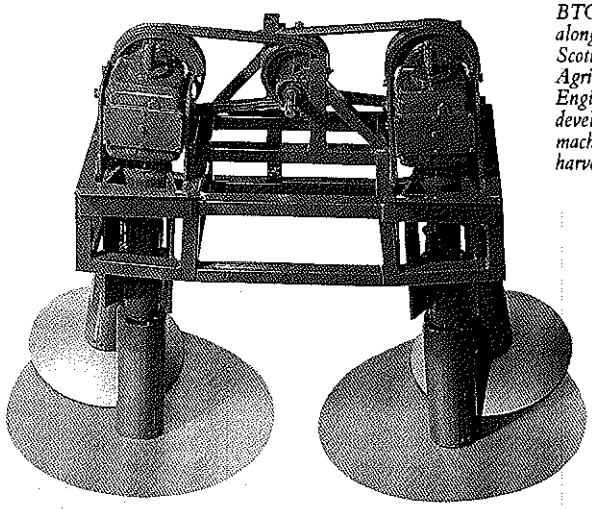
The harvester has been licensed to **Moorfield Manufacturing** in Kilmarnock.



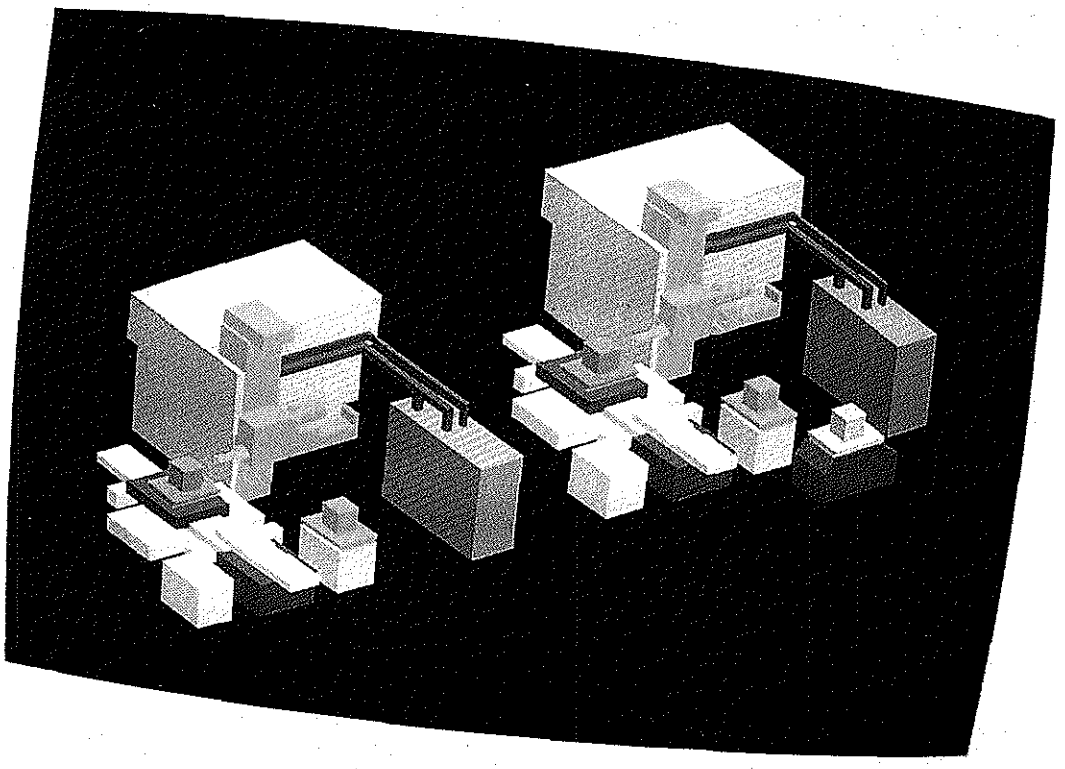
The AFRC Engineering wholecrop harvester collects both grain and straw.

BTG is taking a fresh initiative to develop, in conjunction with the **Scottish Centre for Agricultural Engineering**, a potato harvester to meet the needs and demands of farmers in the 1990s. The main objectives are to produce a machine capable of working at high speed without significant damage to the crop.

The features of the machine include disc shares driven from a tractor power take-off that lift the crop on a cushion of soil and feed it onto a separating web which is vibrated horizontally, rather than vertically as in most conventional machines.



BTG is working alongside the Scottish Centre for Agricultural Engineering to develop improved machinery for potato harvesting.



GRASP enables the feasibility of work cells involving robots, machine tools and other equipment to be evaluated prior to installation, thereby reducing the chances of costly errors.

tetrahedron and a tool located at the centre of gravity and should allow machining to nanometre precision. Applications include diamond turning or grinding of metals, single-pass preparation of optical surfaces and damage-free grinding of glass, ceramics and silicon wafers.

Work continues at NPL to characterise the system. **Ingersoll Milling Machine Co** of the USA has taken a licence to evaluate the technology for eventual incorporation into precision machine tools.

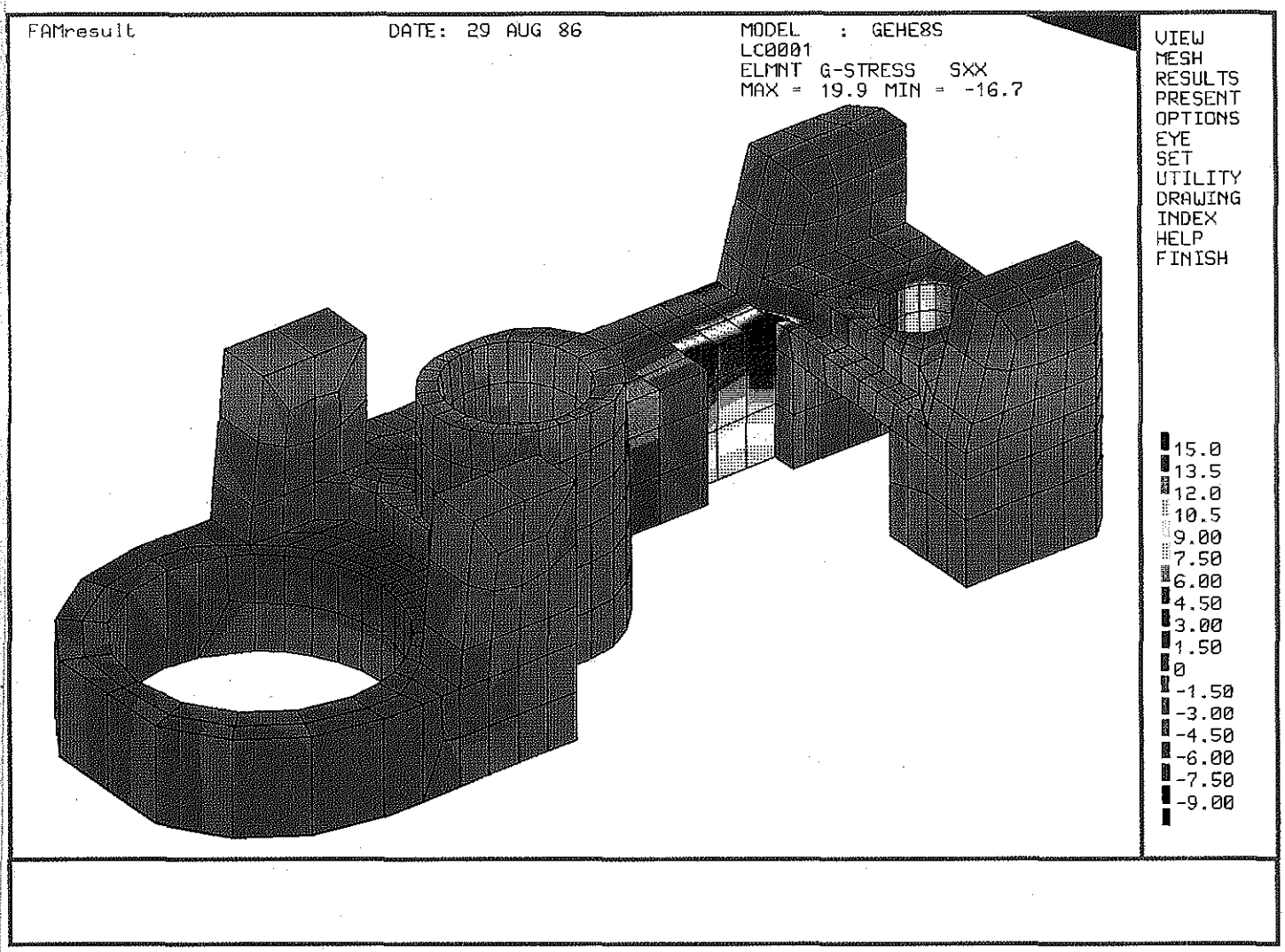
GRASP is a computer software package developed at the **University of Nottingham** that simulates the operation of industrial robots in a working environment, with one or more robots interrelating with one another, machine tools, conveyors and/or workpieces. The simulations enable work-cell feasibility, performance and safety requirements to be assessed thoroughly prior to purchasing decisions. The simulation technique also enables quantitive equipment comparisons to be carried out.

BTG has licensed **BYG Systems Ltd**, a company formed in 1984 by three leading members of the University team, to develop GRASP to a commercial standard and market the software to end users. The company has been successful on both fronts and is now extending its sales effort by appointing overseas distributors. BTG is providing BYG with support funding to enable these market opportunities to be developed quickly.

Meta Machines Ltd produces systems that automatically track and arc-weld seams and is another company formed by a team of researchers responsible for the early research and development work, in this case at the **University of Oxford.**

Originally conceived as a method of automating fabrication of light-gauge materials of the type used in motor-body manufacture, the system has since been further developed to cover a very wide range of applications from high-precision welding to heavyweight fabrications for earth-moving equipment.

BTG has overseen arrangements for industrial exploitation of the initial work at Oxford, which was funded by the Science & Engineering Research Council and received practical support from a number of major industrial companies. A licence agreement has been signed whereby **Fanuc** will manufacture and sell Meta Machines's products in Japan.



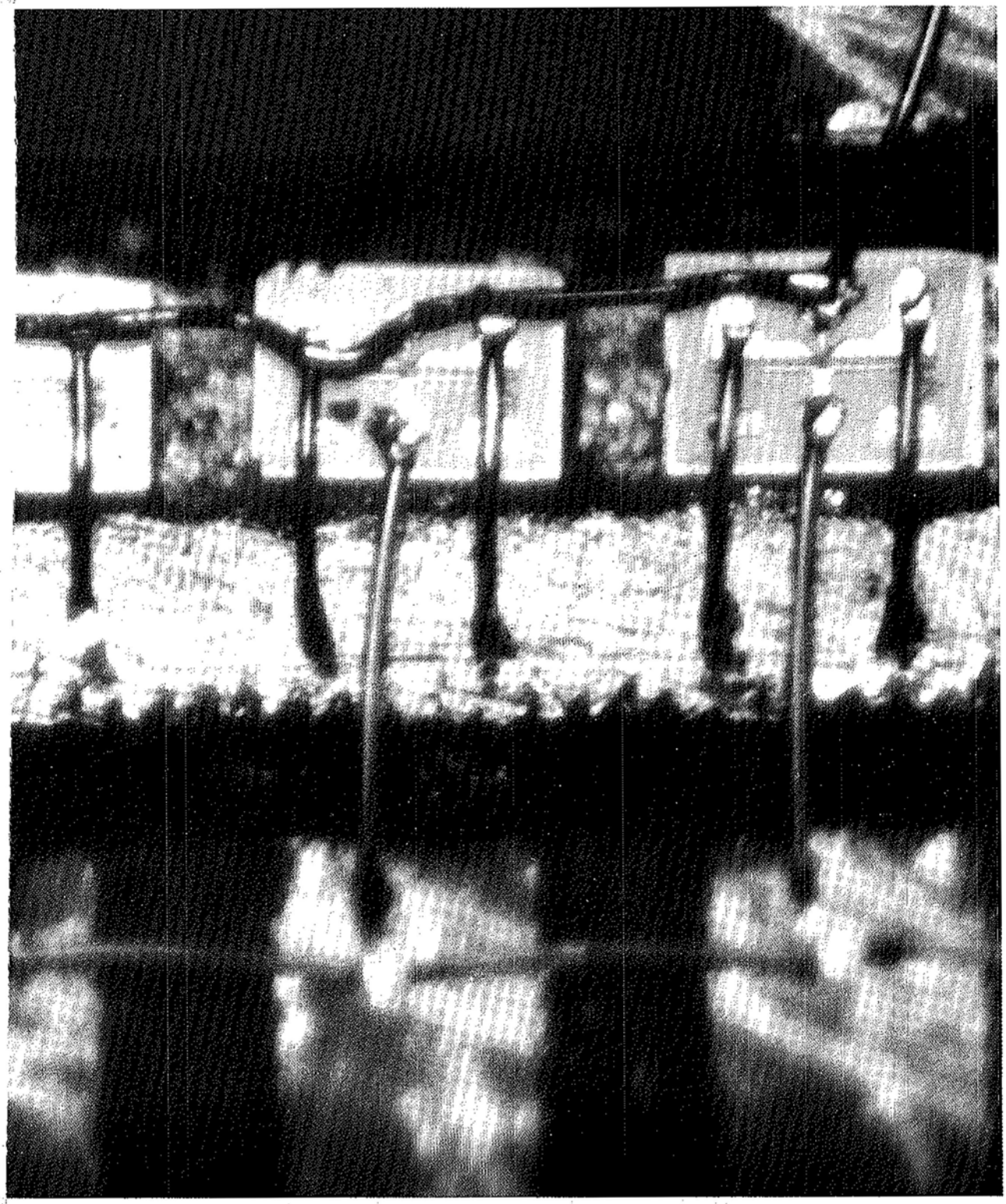
HOVERCRAFT

BTG's involvement with hovercraft dates back to 1958 when NRDC was approached by Sir Christopher Cockerell for assistance to develop his radical ideas. Subsequently it became apparent that the most significant technical challenge in hovercraft design is to maintain lift using as little power as possible.

In addressing this problem, a company set up by NRDC to develop the hovercraft concept, Hovercraft Development Ltd (HDL), made the crucial invention of a skirt system to contain the cushion of air on which a hovercraft rides. This feature has been incorporated in every practical commercial or military hovercraft ever built.

In the USA Bell Aerospace has built more than 30 craft under contract to the Department of Defense. Under US law and practice, royalties have to be sought directly by the licensor from the US Government and not the manufacturer.

Since formal claims for compensation produced no response, HDL filed a complaint in the US Court of Claims in November 1985. The US Government has formally denied liability and the case looks likely to come to trial towards the end of 1988.



BTG is working with ERA Technology on a novel development of 'distributed' broadband microwave amplifier circuits (see p 47).



Zonephone is a second-generation cordless telephone developed by Ferranti Creditphone with funding from a consortium of investors including BTG.

The first patent application on a wide-bandwidth 'distributed' amplifier was filed in the UK in 1936. BTG and ERA Technology Ltd are now working on a novel development of this circuit which is expected to give a considerable improvement in the gain and noise figure of broadband microwave amplifiers. Earlier work on a hybrid-construction distributed amplifier covering 0.5 GHz to 18 GHz has been licensed to M/A-COM Ltd of Dunstable.

Transparent tone in band (TTIB) is a technique whereby a radio signal is transmitted as two separated sub-bands and recombined exactly at the receiver with no phase or amplitude error even in the presence of severe channel distortion. This allows crucial digital or analogue signals to be carried in the gap between the sub-bands where there is least chance of corruption. Variations in the separation of the sub-bands can provide a third information channel. The original invention was made during 1983 at the University of Bath, but the work has since moved to the University of Bristol.

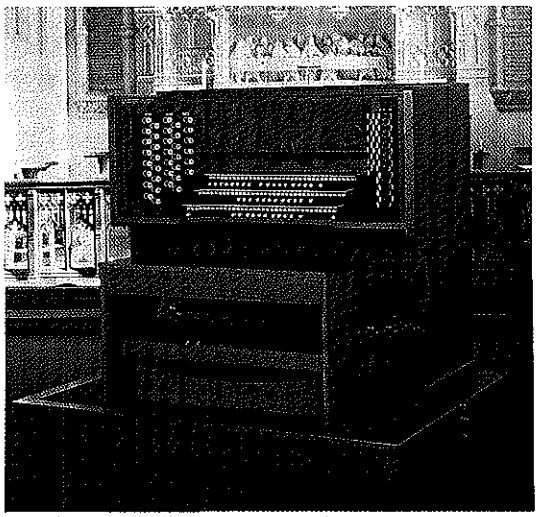
Strong interest has been shown in TTIB by the radio industry and professional user groups throughout the world.

The Department of Phonetics and Linguistics at University College London, in association with Guy's Hospital and the University of Cambridge, has developed a body-worn speech-pattern-processing hearing aid for people with profound hearing losses for whom currently available hearing aids are only marginally effective. It is estimated that in Europe and the USA alone over 250,000 people suffer from this severe disability.

In its present form, the device, called *SiVo*, uses a microprocessor to sense the speech fundamental frequency, transform its amplitude and frequency to a region appropriate to the patient, and generate a sine wave digitally—hence the term *SiVo* or sinusoidal voice. An appreciable improvement in communication ability can result when this simplified speech pattern is used as an aid to lip reading. Commercial manufacturers are being sought by BTG for this patented device.

The Bradford Musical Instrument Simulator is a software and system package from the University of Bradford available for licence through BTG. In its latest form the Bradford simulator is probably the most advanced system currently available and is firmly established at the top of the classical organ sector in the UK and West Germany.

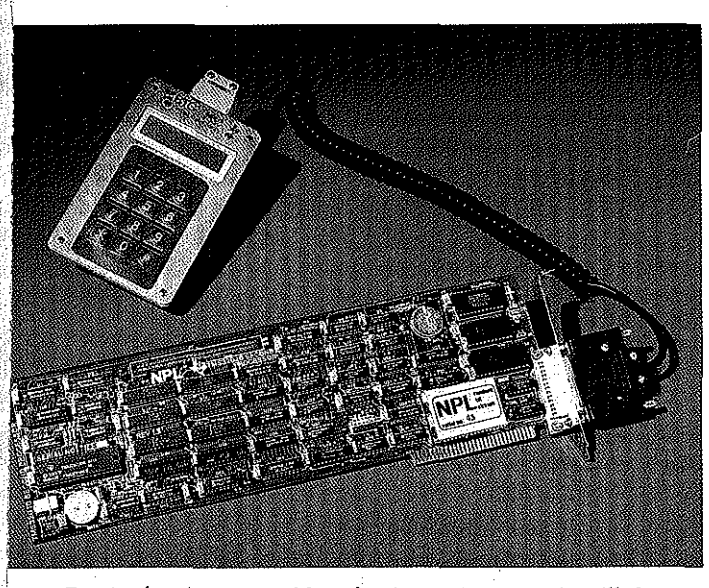
Further opportunities exist for classical organ sales, particularly in the USA. The technology could almost certainly be extended to the vast consumer market for electronic musical instruments if a licensee were prepared to invest substantially in further development and re-engineering.



This organ using Bradford simulator technology has been installed by BTG's licensee Wyvern Classical Organs in St James's Parish Church, Trowbridge, Wiltshire.

cost-effective operation of a token-based value-transfer system.

Medium-term prospects for intelligent tokens are being investigated in collaboration with Texas Instruments. Meanwhile the NPL programs and an associated processing card may find earlier application in EFTPOS (electronic funds transfer at point of sale) terminals and other security applications. To date ten licences and options have been granted by BTG.



Functional realisation by the National Physical Laboratory of an telligent token that could ultimately be produced in a credit-card format.

A personal handwritten signature is still the most common means of identification and/or authorisation, and therefore a prime target for forgery. BTG has secured patent protection for a novel device called the *Eyeball* pen invented by Mr Colin Hilton, a private inventor.

Optical interaction between a light-sensitive pen and preruled paper converts pen movement into timing data that can be fed into a computer. This timing data then can be analysed to decide whether a claimant's handwritten signature is genuine before allowing access or parting with cash, goods or services, or as a supplementary check on a personal identity number in domestic banking and cashless shopping systems.

Alternatively, the timing data can be used to identify the particular letter or number being written, enabling handwritten input to a data-processing system. Another use might be in educational toys.

Veincheck is another security invention from a private inventor (Mr Joe Rice) patented by BTG. In this case a simple photodiode array is used to take a snapshot of the position and size of the blood vessels on the back of the hand or the front of the wrist. This pattern varies from one person to another and thus constitutes a natural bar code that can be used to verify claimed identities.

BTG is also using a consortium approach to support work at the National Physical Laboratory to protect computer software. This has produced a design for a high-security software protection device (SPD) within a tamper-resistant module. If the device were penetrated, sensitive data within the SPD would be destroyed, rendering the rest of the software outside the module unusable. The SPD employs a microprocessor and store for running the protected program, together with a hardware reset system which makes the software immune to attack by Trojan horse or virus methods.

Another means of software protection costing only a few pounds and also applicable to data protection has been proposed by Mr Matthew Lynch, a private inventor. This takes the form of an optical data transducer that uses birefringence to generate colour sequences determined by random numbers generated by a program. The user must respond with numbers corresponding to the correct colour sequence in order to run the program.

A third approach proposed by Mr Stephen Ross utilises the inherent variations in the physical properties of dynamic stores arising from unavoidable (and otherwise unimportant) variations in the manufacturing process. In the absence of any refreshing signal, a dynamic store loses data but the rate at which this corruption occurs is slightly different for each element in the store. Hence every store corrupts in a different but characteristic pattern.

This enables a 'signature' to be produced which is unique to a particular system and can be tied to a program when it is first used so that thereafter the program will only run on that one computer system. The method has the advantage that it can be implemented without the legitimate user being aware of the method of protection.



BTG funding has enabled Rediffusion Simulation to hasten development of its new Digital Remote Control Unit (inset), which enables its WIDE flight simulator projection systems to be set up quickly and accurately using a single controller.

BTG has supported **Combined Power Systems Ltd** in the development of a small-scale CHP unit. The system incorporates a number of novel features such as an on-board microcomputer for engine management, system status checks and automatic restart, a remote condition-monitoring system, and an expert system to provide automatic fault diagnosis.

Development was carried out at the **University of Manchester Institute of Science & Technology**. Field trials are now running successfully at a wide variety of sites in the north-west including a hospital, a British Telecom telephone exchange, a leisure centre, a Trusthouse Forte hotel and the control tower at Manchester Airport.

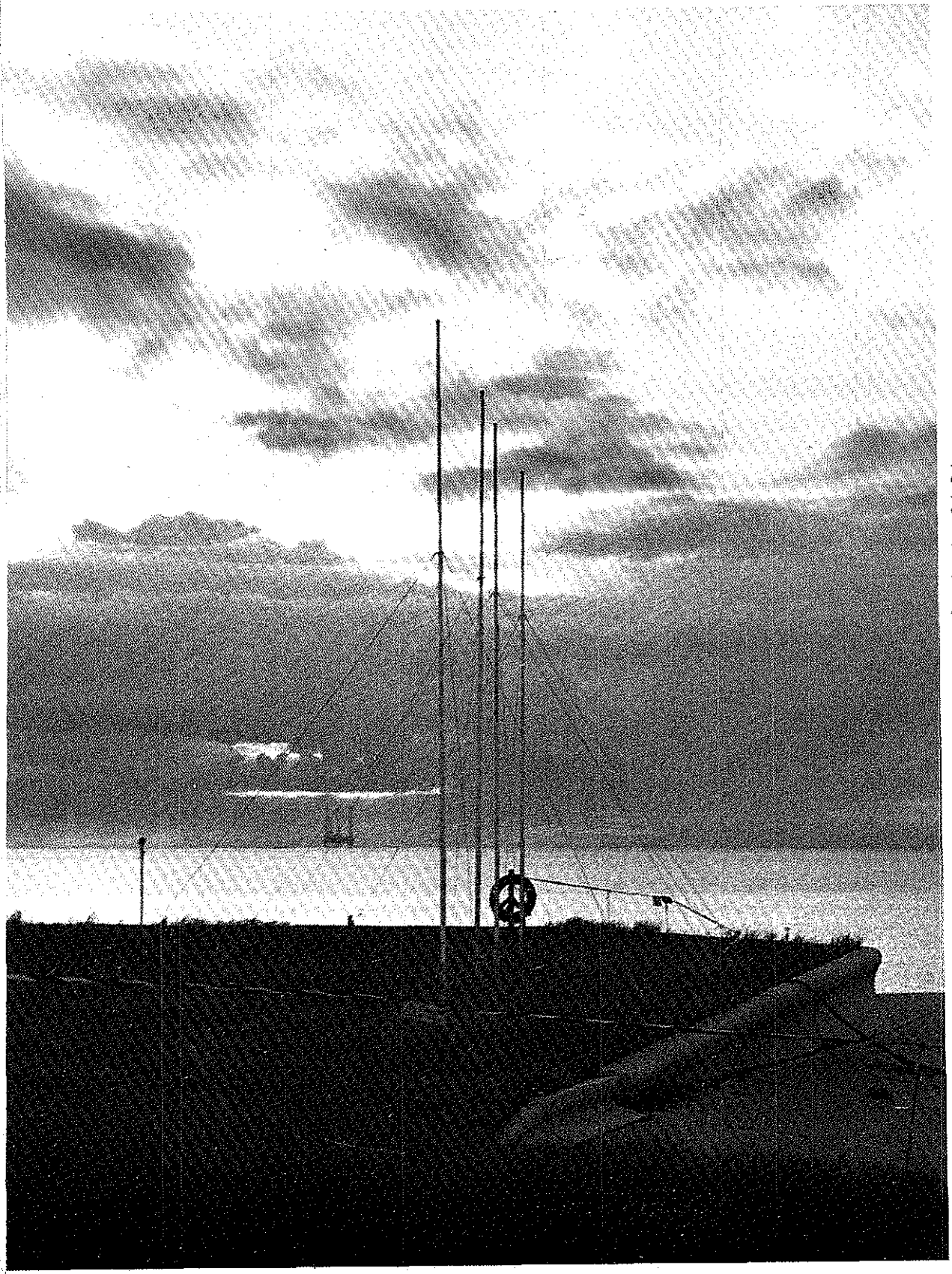
The **AFRC Institute of Arable Crops Research** at Rothamsted has devised a system for treating potatoes with fungicides prior to storage by the use of an electrostatic spray head positioned over a roller table carrying the potatoes. The spray droplets are confined to a rectangular area by a charged grid that produces very uniform deposition over the surface of the potatoes.

Trials have shown that uniform and precise fungicide deposition is the key to effective control of storage diseases, and the system is being developed under a licence option from BTG by a company in the UK.

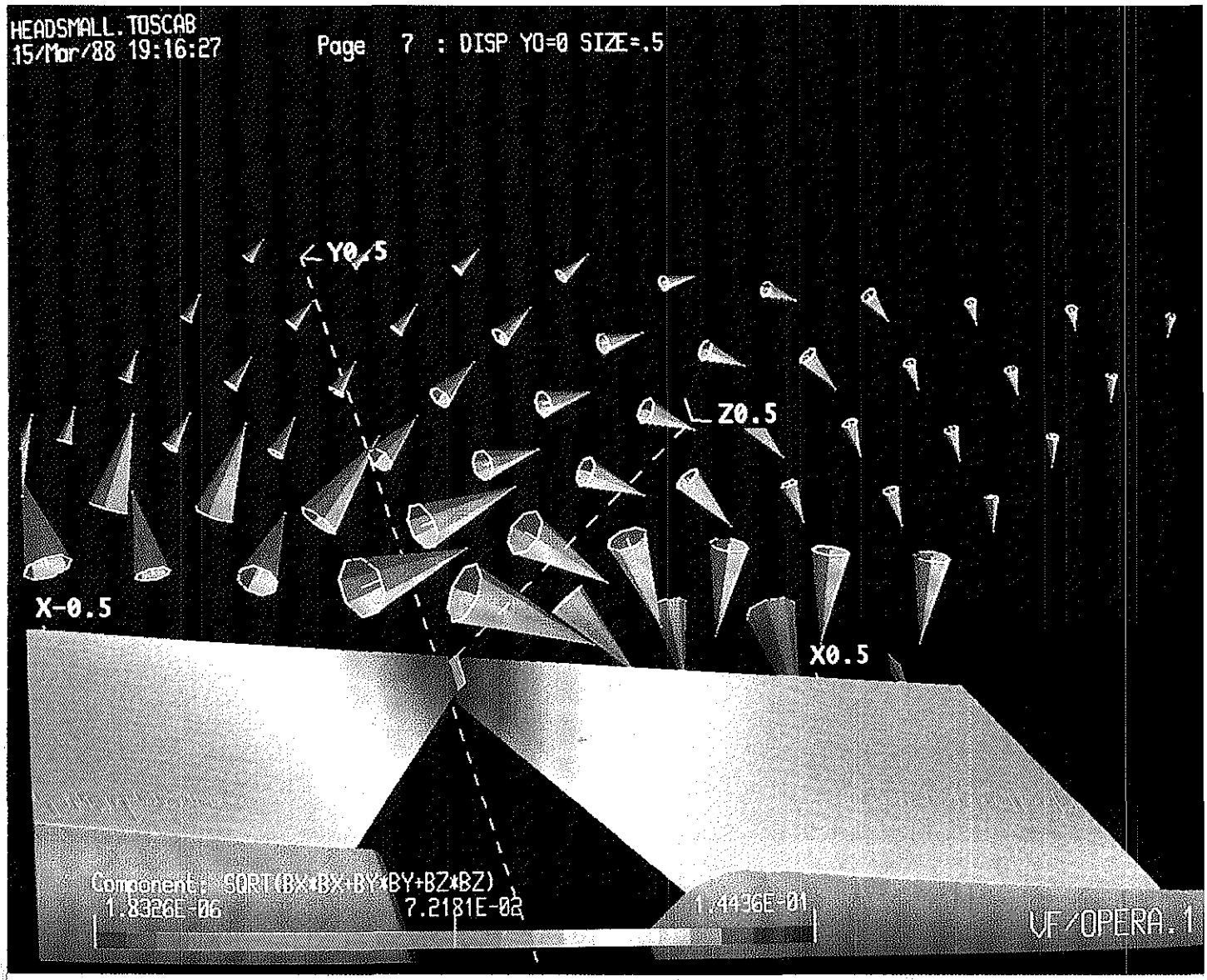
The electrostatic approach should reduce wastage of fungicide and lessen the risk of operators being contaminated with chemicals.

Apoloco Ltd of Newcastle-under-Lyme is licensed by BTG to use the CONTROL BASIC programming language developed by **Warren Spring Laboratory** and the **University of Oxford**.

As the company worked with CONTROL BASIC on its *FLEXSY* industrial microcomputer, it saw ways of upgrading the language to reduce application programming effort even further and BTG agreed to contribute £60,000 to a collaborative venture between Apoloco and Oxford. This has resulted in a number of improvements including CONTROL BASIC PLUS: a 'multitasking' version of the language distinguished by its ability to run seven 'foreground' tasks and one 'background' task



Part of an OSCR array used to map surface currents over a large area. Data derived from such surveys can help in the planning of sewage outfalls so as to minimise coastal pollution and contamination of bathing beaches.



Vectors display the direction and magnitude of the magnetic field produced by a thin-film recording head.

Photo: Vector Fields Ltd

many of the subtleties of proportioning needed to produce an attractive layout that can be easily assimilated by musicians. OMP is licensed to Oxford University Press.

Deductive Systems Ltd was formed to exploit research into fifth-generation database management techniques undertaken at the University of Strathclyde. BTG provided equity funding at an early stage alongside other investors and this initial finance, supplemented by grants from the Alvey Directorate, was used to develop the *Generis* intelligent knowledge-based management system and to progress the development of the Generic Associative Memory chip.

At the beginning of 1988 the company raised substantial additional finance from venture capital sources, the University and a number of private individuals. This will be used for the market introduction stage of the business.

In general the convergence of new technologies such as intelligent databases, expert systems and interactive video makes it possible to present facts and expertise in novel and useful forms. BTG sees 'knowledge publishing' as a new and potentially profitable area of activity, and is already considering proposals relating to computerised publications in the fields of zoology, hydraulics and agriculture.

THE FOLLOWING ORGANISATIONS ARE LICENSEES OF THE BRITISH TECHNOLOGY GROUP:

ADRIA LABORATORIES
AHLBORN ORGEL
ALLEN-BRADLEY
AMERICAN MICROSCAN
AMERICAN MONITOR CORPORATION
AMERSHAM INTERNATIONAL
ASAHI CHEMICAL INDUSTRIES
BAXTER HEALTHCARE
BDH CHEMICALS
BECKMAN INSTRUMENTS
BIOMEDICAL SENSORS
BIOMET
BOEHRINGER MANNHEIM
BRITISH INDUSTRIAL SAND
BRITISH TELECOM
BTR SILVERTOWN
BWN VORTOIL
BYG SYSTEMS
CELLTECH
CIBA-CORNING DIAGNOSTICS CORPORATION
CLEMENT CLARKE INTERNATIONAL
CONTROLLED THERAPEUTICS CORPORATION
COULTER ELECTRONICS
CROMPTON PARKINSON
DE LA RUE
DENTSPLY
DOW INSTRUMENTS & REAGENTS
DRAEGER SAFETY GROUP
DUPUY DIVISION OF BIODYNAMICS
EASTMAN KODAK
EFTPOS UK
ELECTRO-NUCLEONICS
E M INDUSTRIES
ENGELHARD INDUSTRIES
ENVIROTECH
ESPE FABRIK PHARMAZEUTISCHER PRAPARATE
FERRANTI
FIRST SECURITY GROUP
FMC CORPORATION
GEC
GEC MECHANICAL HANDLING
GENERAL ELECTRIC
GLAXO
GRASEBY MEDICAL
HEALTH IMAGES
HILTCROFT
HITACHI
HOECHST
HOFFMAN LA ROCHE
HOWMEDICA
IBM
ICI
ICI AMERICAS
INSTITUTE OF CARLO ERBA
JEOL
JOHN DEERE
KINETIC CONCEPTS
KLOCKNER HUMBOLDT DEUTZ
KUBOTA
KYOWA HAKKO KOGYO
LABORATORIES BIOTROL
LAURENCE, SCOTT & ELECTROMOTORS
LEICESTER POLYTECHNIC
LIQUIPAK INTERNATIONAL
MALTHUS INSTRUMENTS
MARI ADVANCED MICROELECTRONICS
MASKINFABRIKEN TAARUP
MEDISCUS PRODUCTS
META MACHINES
MILES LABORATORIES
MITCHELL COTTS CHEMICALS
NEGRETTI AUTOMATION
NOKIA
OCLI OPTICAL COATINGS
OLYMPUS OPTICAL
OXFORD INSTRUMENTS
PICKER INTERNATIONAL
PHILIPS RESEARCH LABORATORIES
PITMAN-MOORE
POLYSYSTEMS
PLESSEY
PRAGMA
PRIME COMPUTER CAD/CAM
PROSYS TECHNOLOGY
RACAL SAFETY
RICHARD MOZLEY
RICHARDS MEDICAL
ROLLS-ROYCE MATEVAL
ROTHEROE & MITCHELL
ROUSSEL UCLAF
ROVER GROUP
SANDOZ
SCHERING CORPORATION
G D SEARLE
SHELBOURNE REYNOLDS
SHERWOOD MEDICAL INDUSTRIES
SHOFU DENTAL MANUFACTURING
SIEMENS
SINCLAIR RESEARCH
SLUMBERLAND HOLDINGS
SMITH & NEPHEW MEDICAL
SNIA FIBRE
SPECMAT
STERLING-WINTHROP GROUP
STURTEVANT ENGINEERING
SUMITOMO CHEMICAL
TECHNICON INSTRUMENTS
TWYFORD PHARMACEUTICAL DEUTSCHLAND
VECTOR FIELDS
WARNER LAMBERT
THE WELLCOME FOUNDATION
WORMOLD INTERNATIONAL
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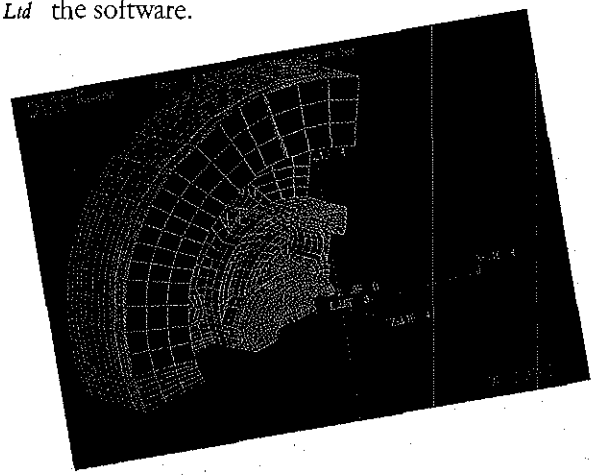
COMPUTER SOFTWARE

The creation and supply of software is now a major industry that continues to grow strongly. In the UK alone the turnover of software products and computing services reached £2,400 million in 1987, greatly exceeding that of computer hardware.

Its value and the ease with which it can be copied makes software a natural target for fraudulent activity. In addition, software is usually only protected by copyright rather than by patent, often making ownership a contentious issue. These factors make BTG's in-house legal and commercial skills especially relevant to academic authors of software, since the drafting and enforcement of licence agreements can be critical if both the sources and the distributors of software are to be fairly rewarded.

The links between inventive sources and commercial vendors need to be carefully nurtured in this rapidly advancing industry, since successful exploitation of software is often dependent on ongoing development by its originators.

In the case of the **Rutherford Appleton Laboratory** magnetics software, continuity of development effort has been achieved by the authors setting up a highly successful company, **Vector Fields Ltd**, to market and support the software.



120° section of the Texas Accelerator Laboratory cyclotron modelled using TOSCA magnetic software.
Photo: Vector Fields Ltd

In contrast, the SPEEDUP program, a world leader in dynamic chemical plant simulation, is being developed jointly by the BTG licensees, **Prosys Technology Ltd** (Cambridge) and the **Waterloo Centre for Process Development** (Ontario), in close collaboration with the originating team at **Imperial College**.

GINAS (graphical interactive network analysis and simulation) is a program written at **Leicester Polytechnic** to model water distribution networks. An initial licence was granted over five years ago and there were subsequent sales to Severn Trent, Yorkshire and Thames Water Authorities.

With the approaching privatisation of the UK Water Boards and Authorities and greater emphasis on efficiency and economy, there has been renewed interest in GINAS. Leicester Polytechnic has itself recently become a licensee and intends to market GINAS to potential customers.

Contrary to the usual view of software as an active product in which the programs themselves are important, the merits of the Protein Engineering Database compiled by researchers at the **University of Leeds** and **Birkbeck College** are largely passive: it is the data entries themselves that are valuable.

The database is one of the first results to emerge from a collaborative venture between the Science & Engineering Research Council and four industrial partners (Glaxo, ICI, Sturge and Celltech). It contains details of the structure (the atomic co-ordinates) and the sequence information (the order of the constituent amino acids) for many protein molecules.

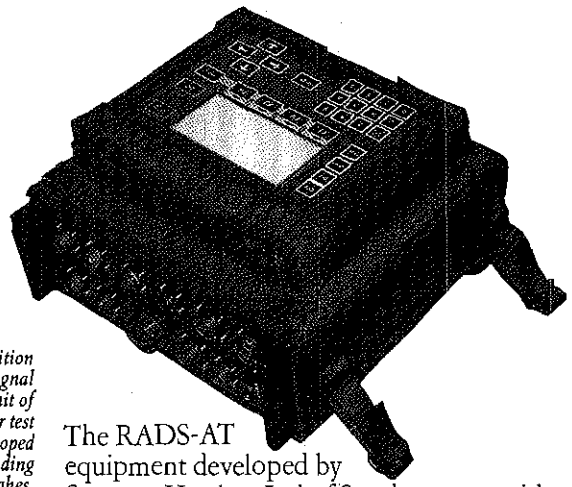
Distribution of the database among academic establishments will take place through the Daresbury Laboratory, while BTG will be the agency for commercial exploitation. The main end users of the database, which has been the subject of intensive effort over many years, are expected to be pharmaceutical companies engaged in the design of new drugs. In addition, companies selling chemical modelling software could use the database under licence to display complex models of the chemical compounds.

Oxford Music Processor (OMP) is a software package to generate musical scores that originates from the **University of Oxford** and has subsequently been developed with BTG funding to run on an IBM Personal Computer or a compatible machine.

Entries are made using a simple alphanumeric code and the package automatically deals with

concurrently plus up to 16 'event' tasks to deal with alarm interrupts.

The company has recently announced a number of other significant enhancements to the *FLEXSY* range, including a new faster central processor card and a complete data logging and control system based on an IBM Personal Computer or a compatible machine.



Data acquisition and signal processing unit of the helicopter test equipment developed with BTG funding by Stewart Hughes.

The RADS-AT equipment developed by Stewart Hughes Ltd of Southampton with BTG funding, in partnership with Scientific Atlanta Inc of the USA, enables helicopter operators to measure vibration and diagnose faults in helicopter rotors quickly and accurately.

The system uses a blade-track sensor and advanced signal-processing techniques to minimise maintenance-flight times and, consequently, the cost of carrying out these operations.

BTG has filed several patents concerning the use of optical fibres as sensors for such parameters as pressure and temperature.

Pressure sensing is accomplished by projecting light from an optical fibre onto a diaphragm whose displacement under pressure affects the light reflected back down the fibre. The patents cover work at University College London on methods of compensating for variation of parameters and drift over a period of time. This method is especially suitable for hazardous environments and enables remote location of the associated electronic circuitry.

A single optical fibre can act as a distributed temperature sensor. Minor discontinuities in the fibre at a molecular level cause small amounts of light to be reflected back from them. The amplitude of the reflection gives a measure of temperature and, by using a pulse of laser light, researchers at the University of Southampton have shown that the timing of the 'optical echo' can give the position of local hot spots along the length of the fibre. Thus a continuous fibre could be strung around several machines or other pieces of equipment so that the temperature of, say, motor bearings or industrial processes could be monitored by a single strand.

The BTG portfolio of patents from Southampton also covers means of producing the highly birefringent fibres required for these applications and designs of fibre-optic couplers and beam splitters.

OSCR—ocean surface-current radar—is a remote sensing system able to map surface currents accurately over large coastal areas. It combines measurements obtained from two intersecting high-frequency radars to produce an overall pattern of current vectors and was developed at Rutherford Appleton Laboratory as an SERC research project.

BTG licensed the results to Marex Technology Ltd, now part of the Westland Group PLC. Marex has operated the licence successfully in carrying out a number of inshore surface-current surveys. BTG is contributing to the development of OSCR Mark II.

An audiometric system based on a personal computer that integrates different types of audiological measurement has been developed with BTG support at the Institute of Sound & Vibration Research at the University of Southampton. The equipment is aimed at clinics making routine measurements to aid the diagnosis and management of a wide variety of auditory disorders of the middle and inner ear.

One important capability is measurement of the displacement of the tympanic membrane in response to an auditory stimulus. This is achieved using a microphone capable of picking up ultra-low-frequency pressure variations.

There is strong evidence that this non-invasive technique can also monitor the pressure of the fluid around the brain. It could, therefore, have application in the management of certain neurological disorders such as hydrocephalus if the early validation results are confirmed.

CONTROL AND MONITORING SYSTEMS

During 1988 **Rediffusion Simulation Ltd**, one of the world's leading designers and manufacturers of commercial flight simulators, introduced its new Digital Remote Control Unit (DRCU), which has been developed with BTG industrial project funding. The DRCU is used to set up the visual display systems used in Rediffusion's WIDE (Wide-Angle Infinity Display Equipment) projection system whereby computer-generated scenes are presented to the simulated flight deck over an uninterrupted field of view of 150° or even 200° in WIDE II.

The new device combines in a single unit the control functions which previously demanded up to five individual projector controllers, as well as those for the image generator and test-pattern projector.

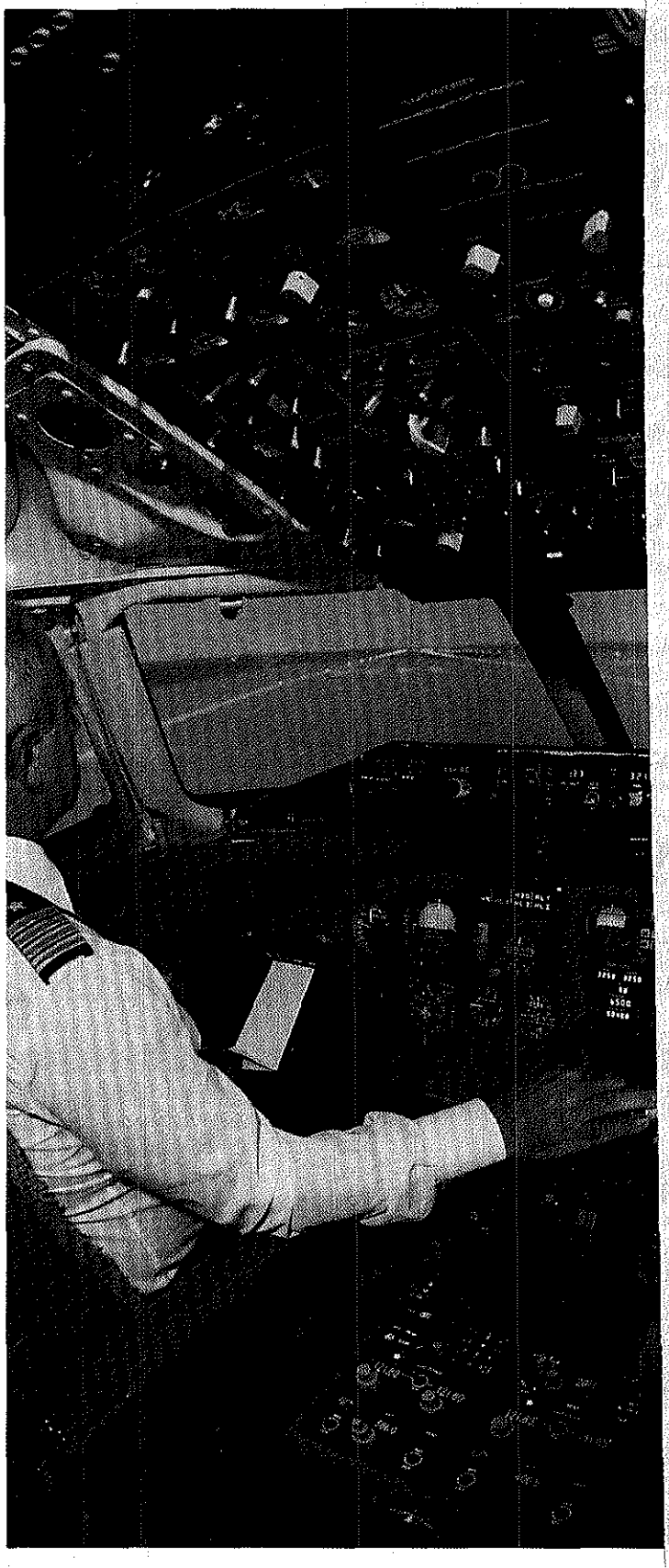
The resulting benefits include improvements in the speed, accuracy and efficiency of setting up and calibrating WIDE systems.

Rediffusion now offers the DRCU as a standard feature on all new WIDE visual systems and as a retrofit option for simulators already in the field. The company won a 1988 Queen's Award for Export Achievement and was recently acquired by Hughes Aircraft of the USA.

Mains signalling superimposes signals on power wiring for the remote control of electrical equipment. The use of existing mains wiring makes for ease of installation and flexibility, with cost benefits accruing from better energy management.

Ripul Ltd, a company in the Home Automation group, has used BTG industrial project funding to assist its development of a second-generation mains signalling system that operates in combination with photocells, active infrared switches and passive infrared occupancy detectors for even more effective management of lighting, heating, ventilation and air conditioning for all types of commercial and industrial buildings.

Combined heat and power (CHP) units make use of a single relatively low-cost fuel (usually but not exclusively gas) to generate both heat and electricity on-site more cheaply than the public utilities can supply them.

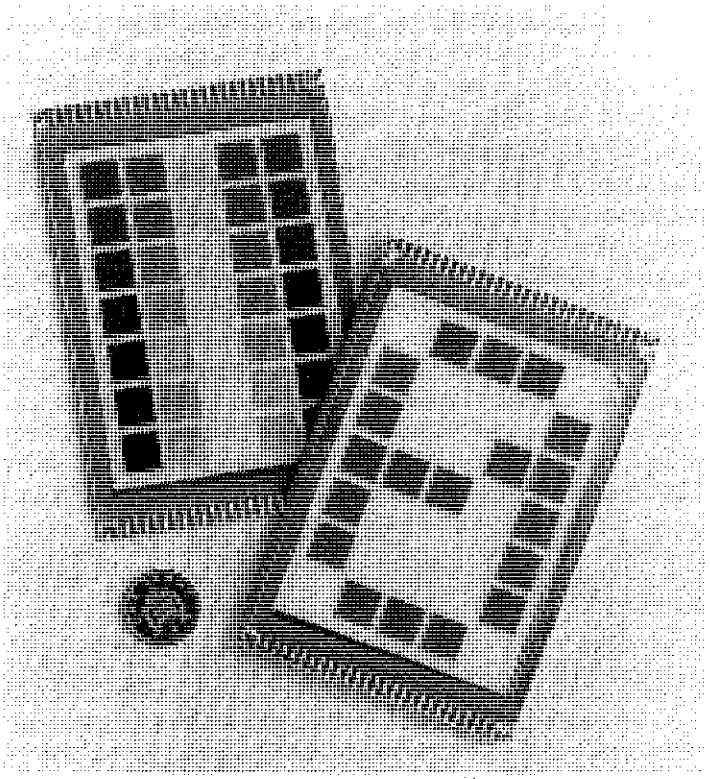


DISPLAY TECHNOLOGIES

The search for a flat-panel display as an alternative to the cathode-ray tube is a keenly competitive one that is being pursued in company laboratories and other research centres around the world.

BTG has funded development work at Imperial College on liquid-crystal display panels driven by arrays of thin-film transistors fabricated using cadmium selenide, which has much higher mobility than amorphous silicon and should be capable of producing fast, high-resolution displays with acceptable production yield. A portfolio of know-how and patents is now held by BTG and licensees are being sought for domestic and commercial applications in television, computer and projection displays.

Prototype electrochromic cells developed at Imperial College for public display systems.



BTG has also funded the development at Imperial College of robust solid-state electrochromic cells for information boards at airports, railway stations and other public areas. There are further applications in road signs, destination boards on buses and advertising hoardings. The cell has inherent memory lasting up to several months and a wide viewing angle.

Low-cost fabrication techniques have been developed utilising thick-film screen-printing technology and only one thin-film vacuum-deposition step. An important part of the development has been the formulation of a polymer electrolyte of a consistency suitable for screen printing.

Patents have also been filed by BTG on the use of electrochromic materials in windows to regulate the transmission of light and heat. Applications include energy-conscious buildings, car sun roofs and rear-view mirrors. Further research is required to generate a commercial system.

Man-machine interaction is an important aspect of display technology. Conformity with traditional procedures for circuit design has been a prime concern in the development of the MINNIE interactive graphics system for computer-aided design of electronic circuits, which BTG has funded at Imperial College and the University of Waikato in New Zealand in association with Philips Research Laboratories.

MINNIE allows designers to visualise the circuit and to link the various components in a familiar way using a 'mouse' or 'puck' without interrupting their train of thought. Entry facilities are based on a menu system that allows components and their values to be defined. These are then connected using a cursor to a matrix of nodes provided by the system. The circuit is easily modified using editing facilities and there are also features to facilitate circuit optimisation and sensitivity analysis.

SECURITY AND PERSONAL IDENTIFICATION

Working with funding and commercial guidance from an industrial consortium led by BTG, the National Physical Laboratory's Data Security Group has advanced the concept of a 'smart card' one stage further to an 'intelligent token' that incorporates an integrated-circuit computer in a credit-card format. Such tokens could one day function as an electronic current account carried about like an ordinary cheque book from which electronic 'cheques' would be issued under the control of the authorised card holder. NPL has devised special computer programs for the



Left and inset:
BTG has helped to fund development by Multitone of an improved range of pagers for both on-site and wide-area use.

COMMUNICATIONS

Ferranti Creditphone Ltd has been funded by a consortium of investors, including BTG, to produce a second-generation cordless telephone.

The design uses digitised speech which can be handled using custom very large scale integrated digital electronics. This allows the use of special protocols giving high audio quality even under adverse conditions. Adoption of a time-division duplex system makes for very efficient use of the radiofrequency spectrum.

The latest generation of pagers from **Multitone PLC** incorporates many new features to improve functionality and reliability. It includes models for both on-site and wide-area paging. The simpler pagers produce 'bleep' tones to alert the user, while the more sophisticated models allow speech transmission or can store and display visual messages. BTG has helped to fund the development of these pagers, which are sold world wide.

Widespread introduction of products and services using electronic speech recognition has been inhibited by a combination of high price and inconsistent performance.

A BTG project on automatic speech recognition implemented by **PA Technology** addresses both cost and performance barriers. The underlying principles derive from ongoing research at the **Royal Signals & Radar Establishment** involving the use of 'hidden Markov' statistical models of speech production to cope with the natural variability of human pronunciation.

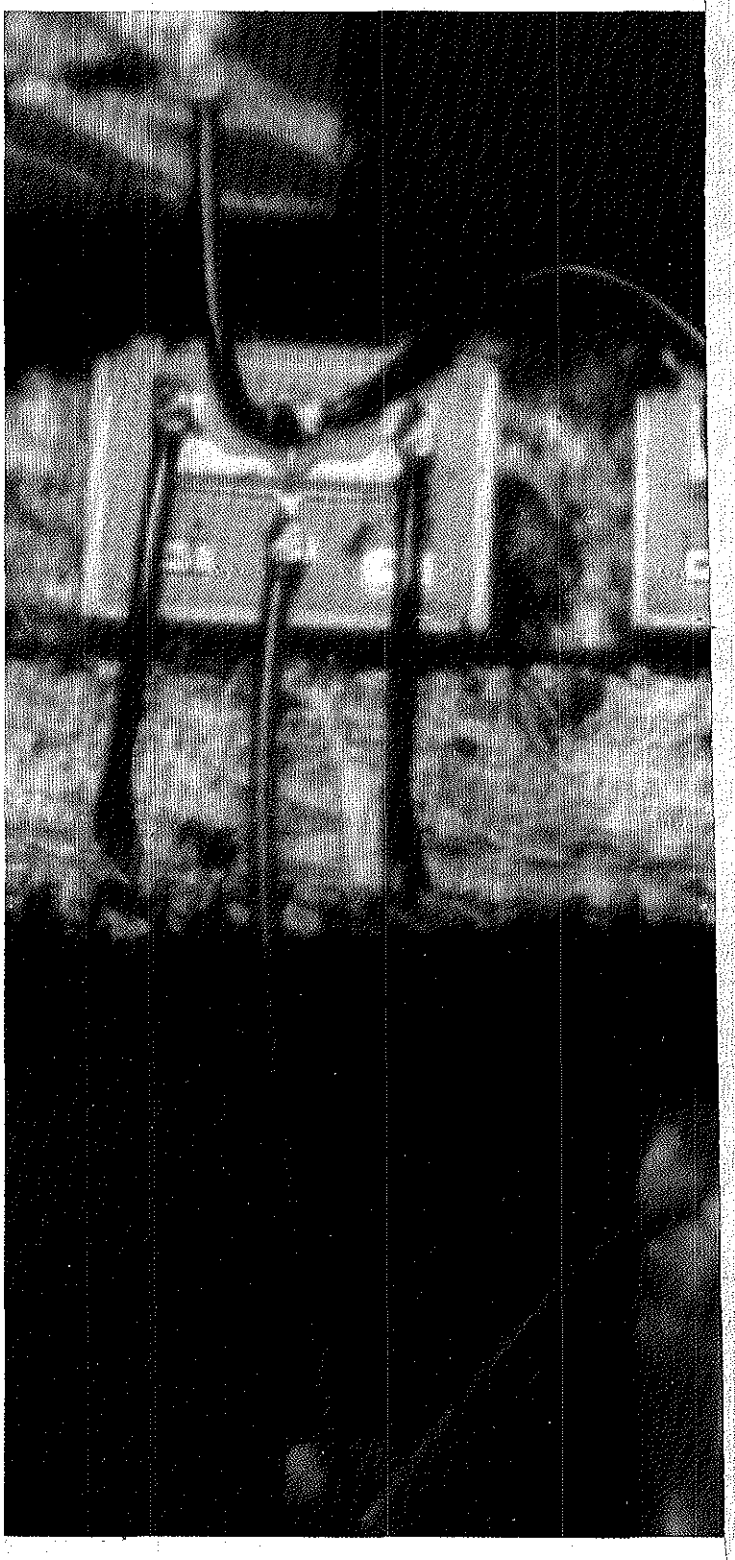
The markets for a compact, inexpensive and reliable 'hands free'/'eyes on' module are considerable, with car telephones in particular presenting an immediate opportunity.

ELECTRONICS & INFORMATION TECHNOLOGY DIVISION

BTG's Electronics & Information Technology Division is involved in principle with the transfer of technology throughout the electronics and computing sector. However, the technologies and their applications are so diverse that the Division needs to focus on areas where its particular skills can be effective, where significant market opportunities exist, and where there is matching emerging technology.

This focus is constantly changing. Thus there is little involvement now with basic silicon semiconductor devices, information storage media or general-purpose computers but a strong current interest in, among other things, communications, displays, monitoring and control, personal identification and certain aspects of software. BTG is keen to extend its involvement in all aspects of signal processing (particularly in speech and image processing and in communications), artificial intelligence and parallel computing.

The diversity and complex interaction between technologies, coupled with very short product life cycles, requires a particularly flexible approach to the process of technology transfer in this field. BTG aims to offer this flexibility not only by licensing, collaborating with established companies in new product development and by equity participation in new and start-up companies, but also by constantly considering new mechanisms whereby emerging technology can be brought to the market.

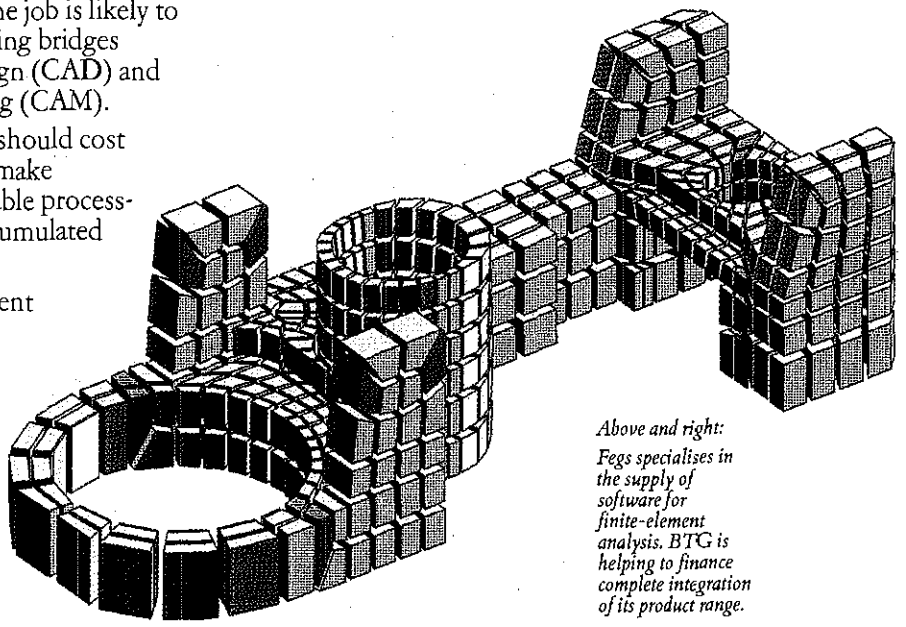


COMPUTER-AIDED DESIGN AND MANUFACTURE

BTG is investing up to £250,000 in the continuing development by **CADCentre Ltd** of the C-PLAN computer-aided process-planning (CAPP) system. Process planning determines and documents how a part or assembly is to be made, the sequence of manufacturing operations, tooling requirements and how long the job is likely to take. CAPP is one of the missing bridges between computer-aided design (CAD) and computer-aided manufacturing (CAM).

C-PLAN uses CAD data and should cost effectively reduce lead times, make standardisation easier and enable process-planning experience to be accumulated in the computer database.

As well as covering development costs, BTG's investment also extends to marketing expenditure so as to better exploit the work done so far, which has resulted in sales to Plessey, GEC and Martin Baker. BTG will recover its investment through a levy on sales of C-PLAN.

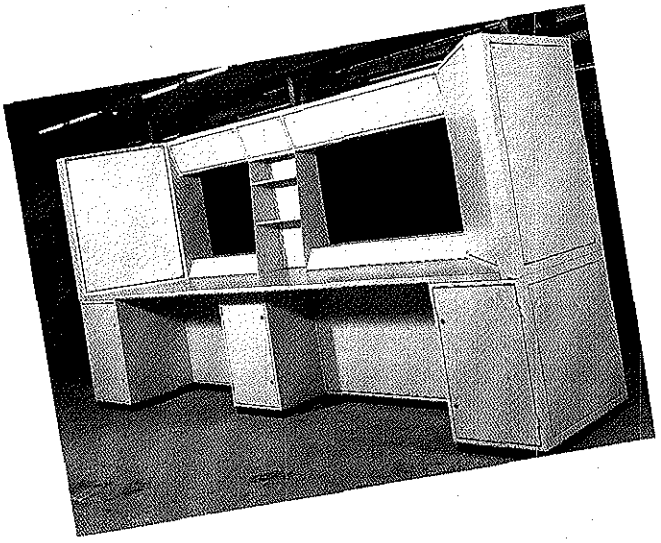


Above and right: Fegs specialises in the supply of software for finite-element analysis. BTG is helping to finance complete integration of its product range.

BTG funding is enabling Willsher & Quick to upgrade its CAD facilities for custom design of metal enclosures for control equipment and switchgear.

Willsher & Quick Ltd is an established manufacturer of custom-designed metal enclosures to house control equipment and switchgear. Its customers demand a very fast turnround from outline design to delivery of the final product. In order to achieve this reliably, the company is already using modern computer-aided techniques for product design and machine-tool control.

BTG is providing industrial project funding to enable Willsher & Quick to upgrade the integration of its management and manufacturing facility. The company does not have 'in house' capability to write new computer programmes, so this work is contracted to a specialist software house. In this instance BTG is supporting a user of innovative technology rather than the more usual scheme of supporting the manufacturer or vendor of such technology.



Fegs Ltd specialises in the supply of finite-element analysis software to solve a wide range of field-analysis problems such as stress distribution, patterns of magnetic flux, fluid flow, etc. Its present product range of preprocessor, analysis and postprocessor software originates from different sources and consequently is not fully integrated.

Fegs has, therefore, embarked on a completely new postprocessor development that will result in complete integration. The opportunity is being taken to upgrade the product and extend its range of applications.

BTG is contributing to this development by providing industrial project funding to enable the development to be accelerated and brought quickly into the market place.

ADVANCED MANUFACTURING TECHNOLOGY

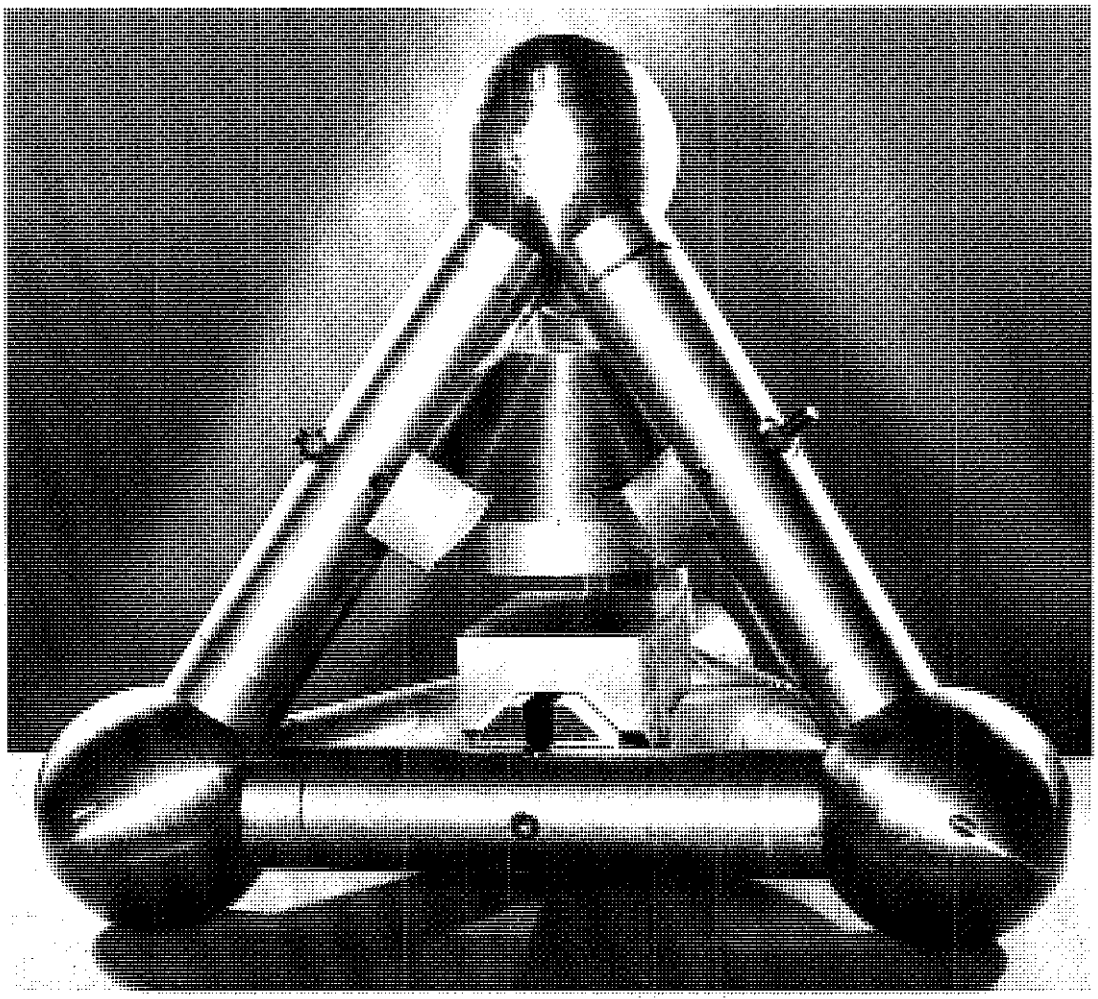
BTG broadly interprets 'advanced manufacturing technology' to be any technology that enables a product to be made or replaced at a lower cost, or to higher quality, or with greater inherent reliability. It may also enable customers' needs to be better met by new products being introduced faster, or by existing products being produced in greater variety or lower volume with no cost penalty.

Although emphasis is usually placed on the first cost of a product, advanced manufacturing technology may equally well reduce the lifetime cost to the user. The focus is on efficient production of consumer durables and industrial goods.

Tetraform is a radically new approach to the design of precision machine tools devised by staff at the **National Physical Laboratory**, Teddington. Conventional machine tools rely on massive structures with high static stiffness to achieve precision. Such structures resist deforming loads and have very low resonant frequencies, so that any structural vibration is decoupled from the high excitation frequency of workpiece/tool interaction.

The NPL design takes a different line by constructing a tetrahedral frame of large-diameter hollow tubes and incorporating internal viscous damping in each structural member. Such a structure is self compensating in respect of temperature fluctuations—the centre of gravity does not change—and possesses high static stiffness.

Although the frame is highly resonant at relatively high frequencies, the internal damping results in effective suppression of vibration in the structure. This results in effective decoupling of vibrations between a workpiece mounted on the base of the



Tetraform represents a radical new approach to machine-tool design by the National Physical Laboratory. Each side of the tetrahedron is about 1 metre long.

AGRICULTURAL ENGINEERING

The idea of taking grain from a cereal and leaving the straw standing is not new, but the design of an efficient mechanism has proved elusive.

Now scientists at **AFRC's Institute for Engineering Research** have solved the problem with a novel design of stripping rotor that is a major advance in harvesting technology.

Shelbourne Reynolds Engineering in Suffolk acted quickly to capitalise on the results of the AFRC Engineering programme, which was initiated in 1984, and swiftly converted an option arrangement with BTG to a full licence during 1986 so as to launch a commercial retrofit stripper head for combines at the 1987 Smithfield Show. This resulted in some significant sales for the 1988 harvest in the UK and overseas, including two units for the USSR.

The fundamental benefit of grain stripping is that combine throughput can be increased by up to 80% as a consequence of not needing to deal with large volumes of straw. This translates into faster harvesting or, alternatively, large-combine performance from much smaller, lighter and less powerful machines.

Moreover, the combing action of the stripping rotor means that crops beaten flat by bad weather that would usually be abandoned can be successfully havested, and in general crop losses can be reduced by up to 60%.

Trials on wheat in North America and Australia have produced excellent results. Crops other than grain, including linseed, dried peas and grass seed, have also been gathered satisfactorily, and a trial on rice in Italy is scheduled for 1988 as part of AFRC Engineering's ongoing research effort. Further licensees are being sought by BTG on an international basis.



Retrofit grain-stripping header launched by Shelbourne Reynolds under BTG licence at the 1987 Smithfield Show

AUTOMOTIVE ENGINEERING

The age of the stepless continuously variable automatic transmission (CVT) has already arrived in small cars. However, the belt system currently used is limited in torque capacity.

The Perbury CVT operates on a different principle and can be applied not only to cars but right through the range to large trucks and off-highway tracked vehicles. Prototype units are running successfully in all of these classes of vehicle. A transmission has also been combined with a flywheel energy storage system, provided by **BP**, in order to give even greater fuel economy in stop/start urban bus operation.

As a result of a deal struck with the **Rover Group** in October 1987, BTG now owns or controls intellectual property rights originating both from **Perbury Engineering Ltd** and from companies within Rover that have been active in this field.

Further development and licensing is being undertaken by two newly formed BTG subsidiary companies: **Torotrak (Development) Ltd** and **Torotrak (Holdings) Ltd**. The former employs a team of experienced CVT engineers who are carrying out a programme of system development in direct support of licensing. The latter is seeking to exploit the transmission internationally and is currently in discussion with several major companies.

Valve timing in vehicle engines operating over a wide range of loads and speeds is usually fixed at a compromise setting.

Early in 1980 BTG supported **Stephen Mitchell**, a private inventor, in his development of a simple method of varying valve timing so as to match it more closely to operating conditions. Patents have been granted for this technology and further applications were filed in April 1987.

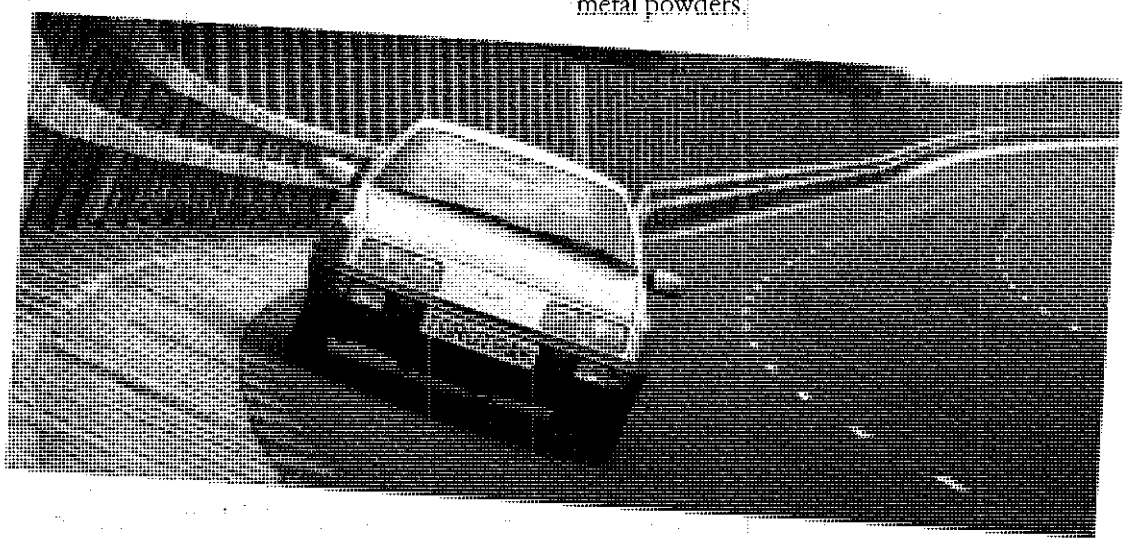
As well as improving low-speed torque and idling, savings in fuel of up to 15% appear to be achievable. A test programme carried out at **Coventry Polytechnic** has already demonstrated an 8% improvement.

The Mitchell system can be applied to single- or twin-overhead-camshaft valve trains and can be adapted to most existing engine configurations with only minor cylinder-head and valve drive-train modifications. Maximum valve lift remains unaffected.

The manufacture of mechanical components using powder metallurgy is well known in the motor industry. It reduces waste material from machining, recycling requirements and machining time, but its use is limited to components that are relatively lowly stressed.

Recent work at the **University of Nottingham** has developed a two-stage powder-compaction process operated within a single machine that can produce components suitable for highly stressed applications such as gear drives. Compactions of over 98% have been achieved.

Licences are available to companies wishing to use the technology, hopefully with the co-operation of established suppliers of equipment for fabricating components from metal powders.

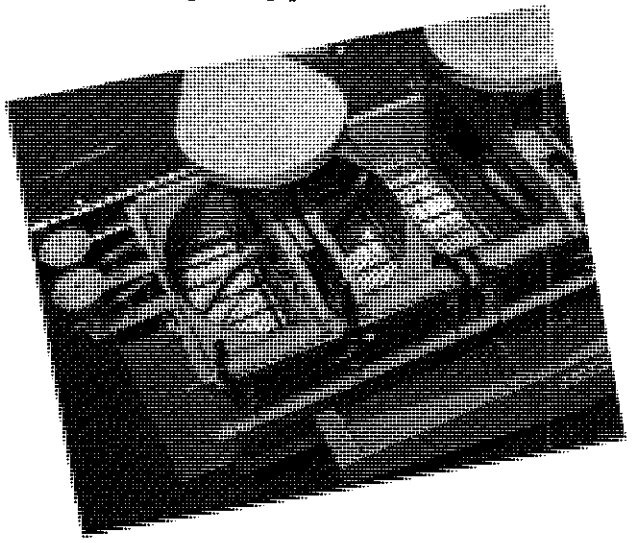


The hydrocyclones create a very high artificial gravitational field without any internal moving parts. They take up as little as one-twentieth of the space of gravity or flotation separators and are undisturbed by sea motion. Since the proportion of water to be handled increases as oil fields become depleted, these separators will extend the economic life of North Sea fields and could make hitherto uneconomic fields viable.

A multistage froth flotation system for improved cleaning of fine minerals and coal has been under extensive development in the USA by BTG's licensee Wemco since 1984. A full-scale test plant operating in Galacia, Illinois has demonstrated the advantages of the system for coal, which include reduced capital and operating costs in preparation plants. There are also benefits to coal users in the form of reduced sulphur levels and lower ash content.

The system, which was devised at the University of Leeds, uses a vertical column of froth contactors separated by patented barriers which selectively control the movement of gangue minerals and froth in each direction and allow several stages of cleaning and recovery in a compact unit without the need for separate froth cells with interconnecting pumps and pipework.

Multistage froth-flotation system devised at the University of Leeds and produced by Wemco under licence from BTG.



Ultrasonic standing waves offer an alternative to gravitational methods for the collection, separation or concentration of particles in suspension. BTG has arranged to take over a portfolio of inventions from Unilever



Stills from a cine film of blood vessels in a live 3½-day-old chick embryo showing that a 3 MHz ultrasonic standing wave can pack together red cells while plasma continues to flow. The bands disperse immediately the ultrasound is switched off.

Research in this area which complements an existing BTG invention from Imperial College and plans to develop this technology in collaboration with industrial partners.

The development is still at an early stage but could be applicable to particles below 5 μm such as blood cells, where it would offer major advantages over conventional centrifuges by avoiding the need for delicate high-speed rotary equipment and the infection risks of handling of blood in centrifuges.

SAFETY EQUIPMENT

Research into dust helmet/respirators at the laboratories of the **Health & Safety Executive** has led over the past decade to a family of successful products from manufacturers licensed by BTG. Well over half of all sales are overseas.

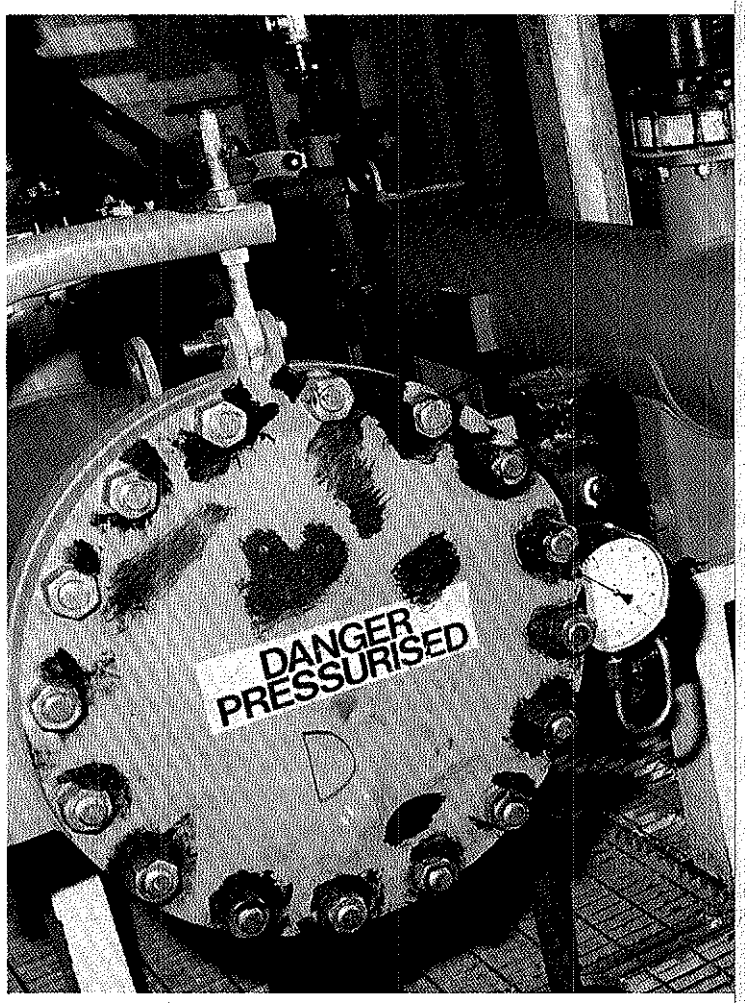
The *Airstream*, launched in 1978 by **Racal Safety Ltd**, is a combined protective helmet and dust respirator powered from a separate rechargeable battery pack. The *Pureflo* (Pureflo Safety Ltd) was introduced in 1985 as a lightweight version with an integral battery, followed in 1988 by a model with an impact-resistant helmet. Another lightweight model, though again with a separate battery pack, was launched as the *Jupiter* by Racal Safety Ltd in 1987.

The STAMP (single-tube automatic multipoint) fire-protection system successfully combines two inventions assigned to BTG: a smoke-sampling system devised at the **Ministry of Defence**, Bath, and a high-sensitivity ionisation smoke detector invented at the **Fire Research Station**. The combined technology has been licensed to **Guardian Fire Detector Systems Ltd**, with BTG also providing joint-venture finance for the company during the commercial development phase.

One of the most important applications is in computer installations, where local smoke detection within cabinets can prevent damage with the minimum of delay.



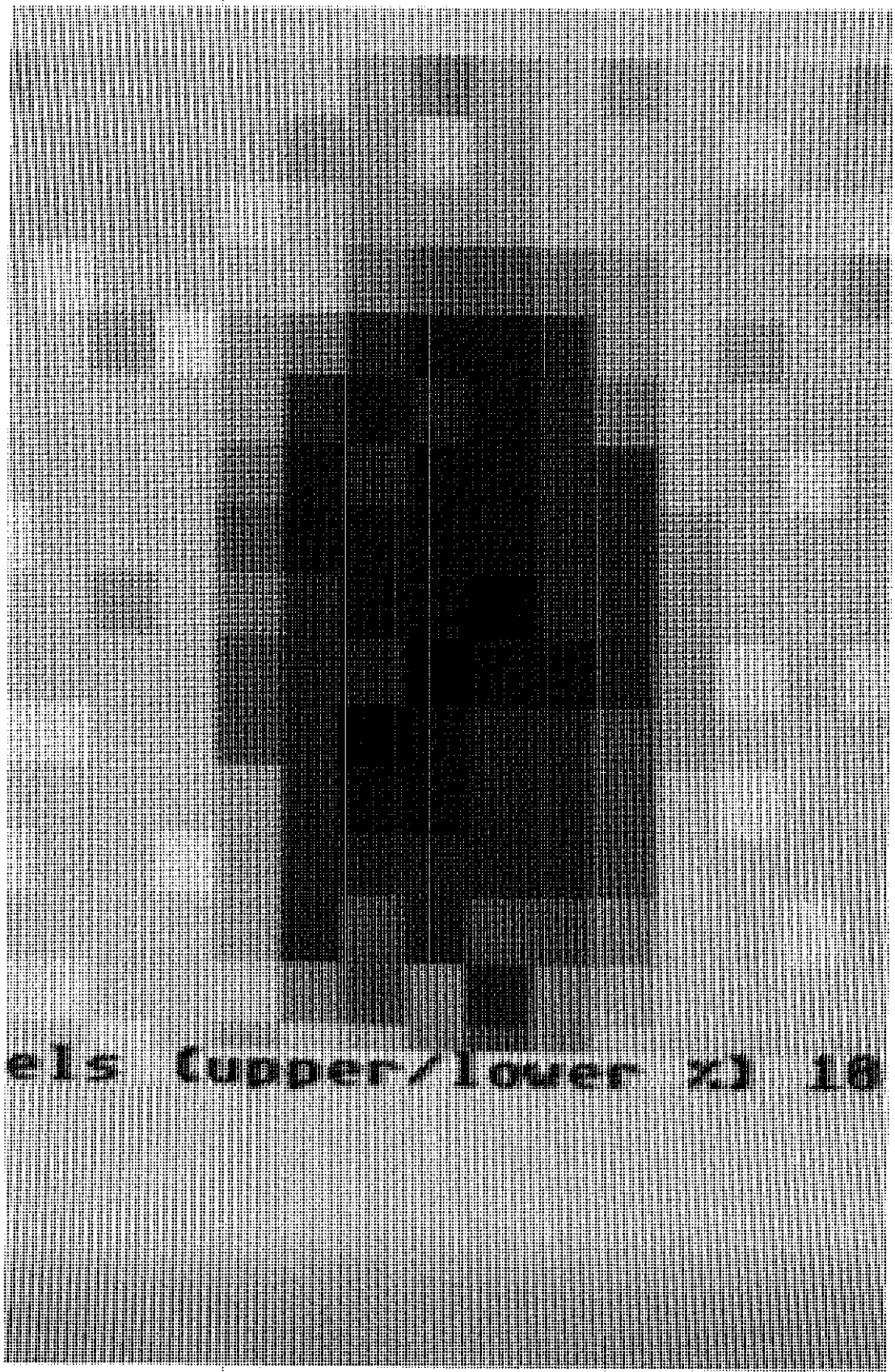
The lightweight Jupiter dust helmet/respirator was launched by Racal Safety during 1987.



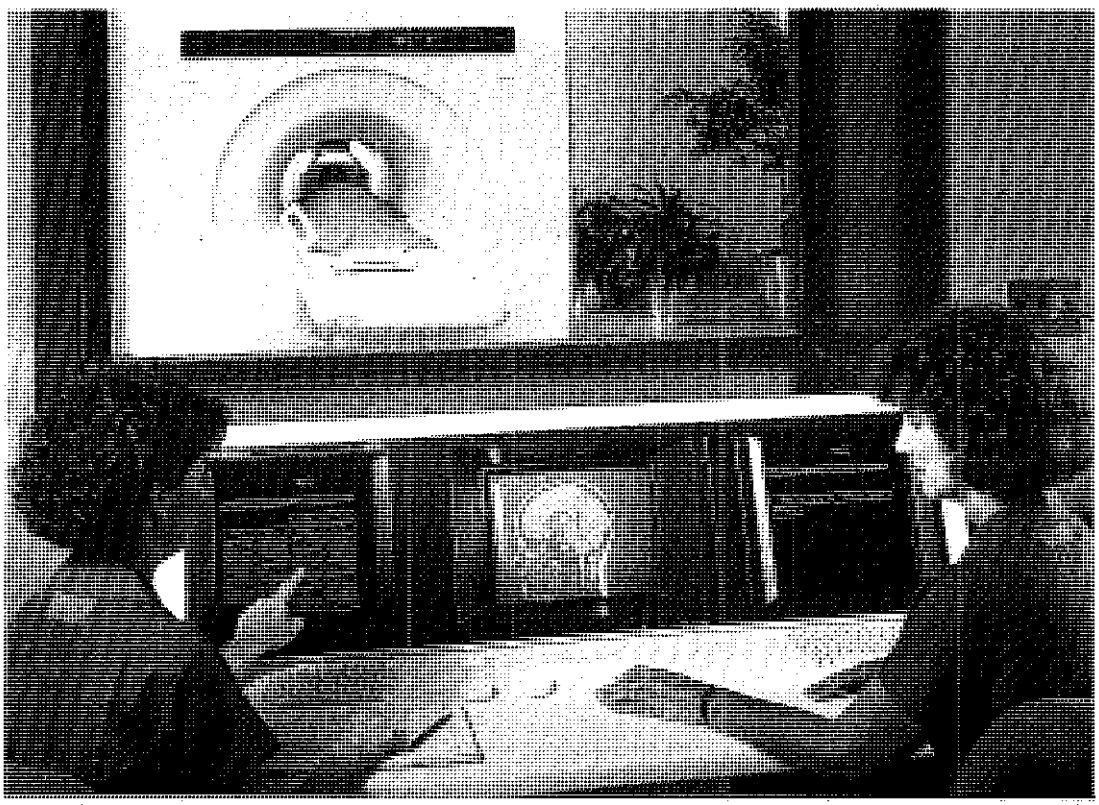
GEOLOGICAL EXPLORATION AND ASSAY

A nuclear magnetic resonance (NMR) system with a novel geometry designed for bore-hole logging of water and hydrocarbons in geological strata has been developed from early work by the **British Geological Survey** to laboratory prototype form with BTG funding. Used in oil exploration, NMR techniques can give direct measurements of the porosity and permeability of rock formations, so allowing estimates of the yield of a particular well.

The next step is to build a prototype for field trials at depths of several kilometres. Preliminary discussions have been held with wireline logging companies, oil companies and instrumentation companies to establish the requirements and decide how best to proceed, perhaps via a consortium of interested parties.



Cross-section through a rod made of the crystalline solid hexamethyl benzene produced using MRI by researchers at the University of Surrey.



Signa magnetic resonance scanner produced by General Electric; BTG announced a major licence agreement with GE in June 1987.

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) is one of the major breakthroughs in medical diagnosis this century, comparable in its importance with the discovery of X-rays. It is now used routinely to generate detailed pictures of tissue structure deep in the human body.

A number of key MRI inventions were made at the Universities of Nottingham and Aberdeen and patented by BTG, which now holds a portfolio of some 20 or so separate inventions in this field.

Three of these relate to broad basic methods of imaging. The most significant patent in the portfolio relates to slice selection, a technique employed almost universally in present-day imaging systems. Other patents in the portfolio relate to phase encoding, real-time imaging, and methods of coil screening.

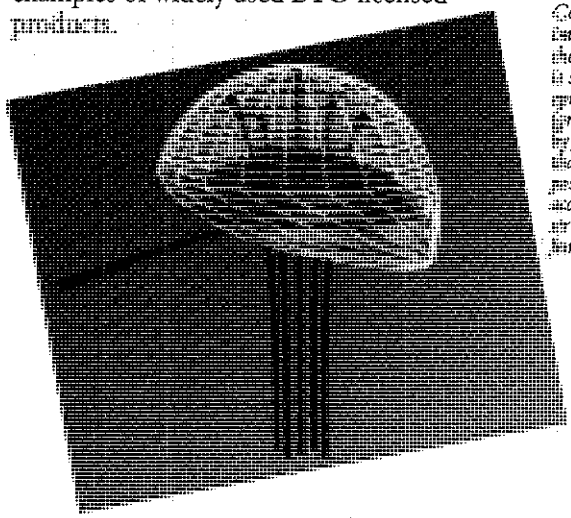
BTG licensed several companies during the early 1980s to use patents in its MRI portfolio, including Picker International, Technicare (a subsidiary of Johnson & Johnson) in the USA, and Asahi in Japan.

Subsequently important licence agreements have been signed with General Electric of the USA, the market leader in MRI, and Hitachi, Japan's largest manufacturer of electrical equipment.

Negotiations are continuing with other companies in this field, including Siemens, Philips and Toshiba.

MEDICAL ENGINEERING

The application of engineering to many aspects of medicine has been a significant factor in the improvement of health in recent years. Hip-replacement operations, for instance, are now commonplace, with the Exeter hip and the cancellous bone pin both examples of widely used BTG-licensed products.



Computer-generated image showing how the Field prosthesis is shaped to fit the epiphyseal plate (green) and is fixed by filaments (red) that are carefully positioned to take account of the structure of the femur.

ENGINEERING DIVISION

In most fields of business, success is achieved by focussing resources on the best opportunities one can find. For BTG's Engineering Division, this presents an enormous challenge because of the diverse range of interests covered by the term 'engineering'.

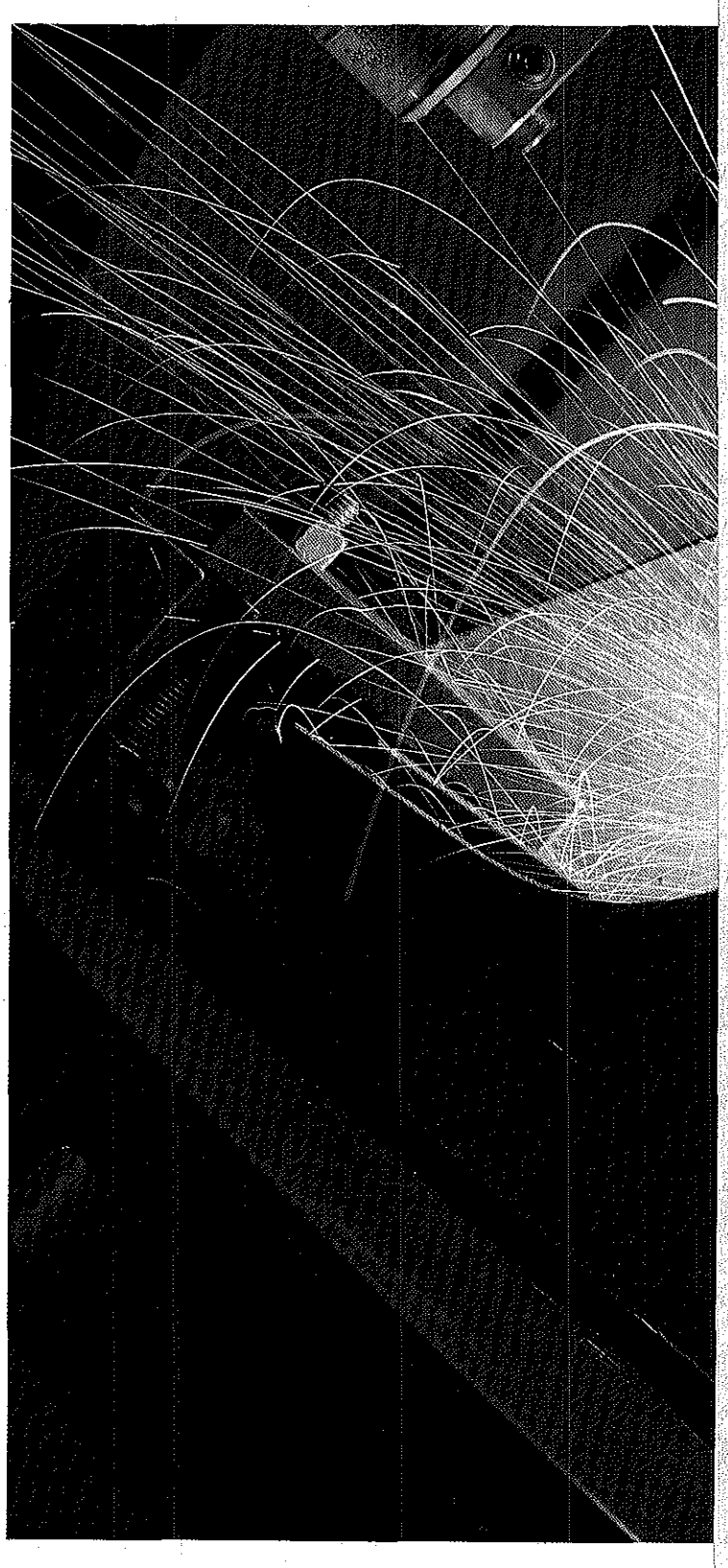
While we are prepared to consider any new invention or project in this whole field, we have chosen to concentrate on selected areas of technology. One common thread in our work is the emphasis we place on the application of advanced physics to tomorrow's new products and processes.

A major source of licence revenue arises from UK-pioneered work on magnetic resonance imaging, which has been successfully licensed by BTG on an international basis. Other medical engineering interests include clinical chemistry, orthopaedics and dental materials.

Another significant licensing and investment portfolio spans the subjects of industrial and scientific instruments, advanced manufacturing technology (including software) and safety equipment. A planned strategy for AMT is being implemented, aimed at identifying and cultivating the most likely sources of worthwhile business for BTG.

Introduction of new technology to the old 'smokestack' and process engineering industries is one of the more difficult tasks faced by Engineering Division. High-capital-value plant, large throughput, valuable work in progress, integrated processes and entrenched practices together mean that progress is at best evolutionary. However, by careful targeting it has been possible to secure successful business in this field.

Agricultural engineering inventions form a large patent portfolio, arising primarily from work at the Government-funded agricultural research establishments and also from work by industrial licensees. There is also significant licensing activity in hovercraft technology, fluid engineering and civil engineering software.





Above: About 100,000 of the parasites that cause coccidiosis could fit on the head of a pin.

Right: Chickens five days after receiving coccidial parasites. The bird on the left received normal virulent parasites; the one on the right remains healthy having received an attenuated strain.

ANIMAL HEALTH

Existing vaccines for many poultry diseases are not entirely satisfactory. Coccidiosis, for example, is a disease of major economic importance in poultry farming, caused by seven different species of *Eimeria* parasites, but for the most part is controlled by the use of drugs.

A highly effective vaccine has now been developed, with some funding from BTG, at the Houghton Laboratory of the AFRC Institute for Animal Health based on harmless strains of each of the seven species of *Eimeria*.

Glaxo Animal Health has been involved in the development since 1983 under collaboration and option/licence agreements. Good progress has been made on the production and formulation of a commercial vaccine and extensive field trials are in progress. The vaccine is clearly effective but its ultimate success will be determined largely by the economic benefits it confers. Pitman-Moore, which acquired Glaxo Animal Health during 1988, hopes to launch the vaccine on the market in 1989.

BTG is also funding a project at Houghton that uses the fowlpox virus as a vector for recombinant genes coding for important disease antigens. The fowlpox virus has capacity in its genome (non-essential regions) to allow insertion of genetic material for other antigens. This technique is analogous to that being developed for human diseases using vaccinia virus. BTG has patented gene constructs coding for antigenic determinants of infectious bronchitis virus and Newcastle disease.

Swine dysentery is one of the most serious pig diseases affecting large proportions of herds worldwide. It is caused by the bacterium *Treponema hyodysenteriae* and currently controlled by the use of antibiotics.

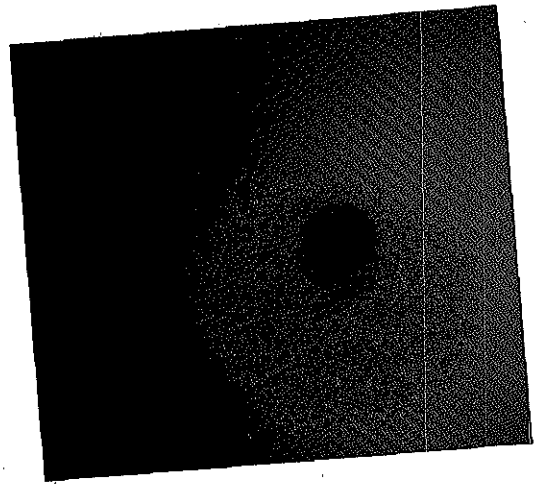
Zinc deficiency has been found in patients with cirrhosis of the liver, Crohn's disease of the bowel and cystic fibrosis. Recent findings have indicated that low levels of zinc during pregnancy may retard the growth of the fetus. Very low levels have been found in children and adults with sickle-cell disease. Preliminary studies in this latter group of patients are encouraging, suggesting that the correction of zinc deficiency results in a normalisation of the red cell and an associated improvement in oxygenation that may be translated into therapeutic treatment of these patients.

Further work on the status of zinc as a nutritional element is also indicated as a result of studying growth in children who suffer from the genetic disease beta thalassaemia, which is primarily manifested as a red-cell disorder.

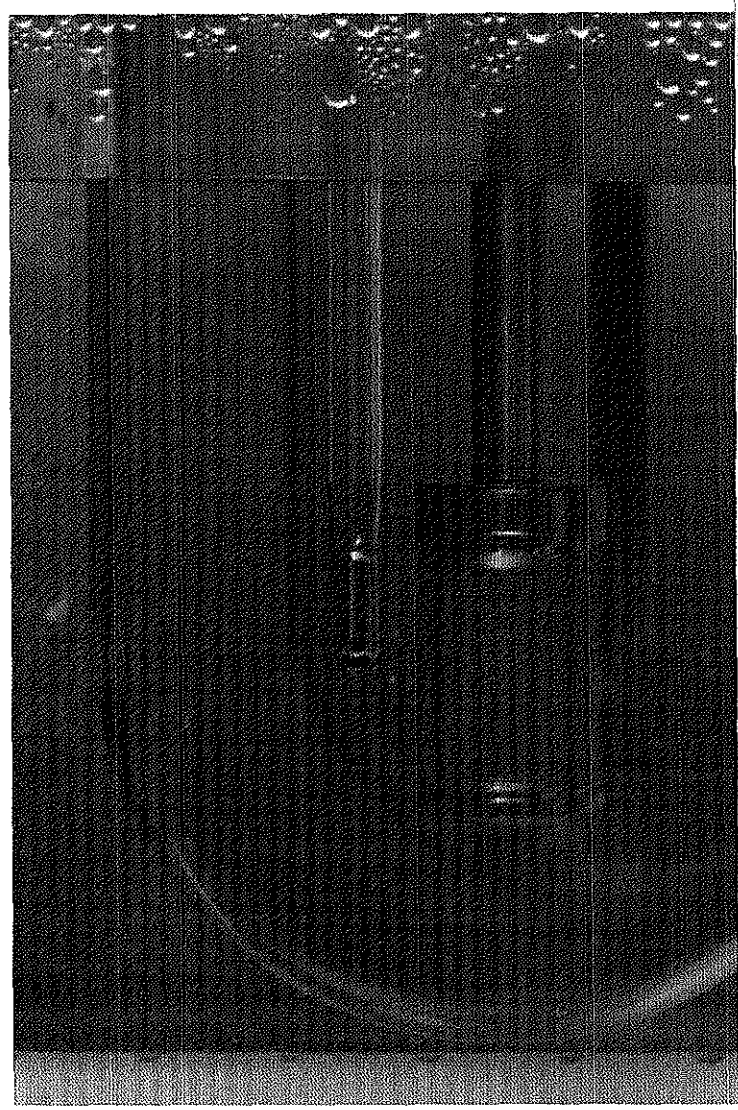
Aside from these investigations of the role of zinc in human pathology, there are some preliminary indications that certain novel zinc chelates exhibit antibacterial and antifungal properties.

THERAPEUTIC USE OF MONOCLONAL ANTIBODIES

Work in the Department of Pathology at the University of Cambridge has shown the potential for using monoclonal antibodies to target and destroy unwanted cells in the body. Campath 1 was one of the first antibodies to be used in this way—to remove unwanted cells from bone-marrow transplants in leukaemia patients—and its success (and problems) has led to the development of a family of antibodies with differing specificities.



Monoclonal antibodies produced in the Department of Pathology at the University of Cambridge.



BTG has licensed Campath 1 exclusively to Wellcome Biotechnology, which has now established its large-scale production. The agent is currently used experimentally in several of the leading bone-marrow transplant centres in the country. Recent evidence indicates that treatment of donor bone-marrow prior to transplant will become routine but that additional antibodies are needed to treat the recipient.

There may also be potential for treating other cancers and transplants, and, more speculatively, possibly in the treatment of arthritis. Recent developments include Campath 2 and 3, which are monoclonals with different and complementary specificity assigned to BTG from Cambridge.



The red and yellow areas show regions of a rat brain rich in molecules known as NMDA receptors that are involved in the processes of memory and learning but may also produce convulsions and neurological impairment if they are overstimulated. Compounds developed at Bristol University and licensed by BTG to Sandoz act on these sites and may prove to be effective in the treatment of diseases such as epilepsy and spasticity.

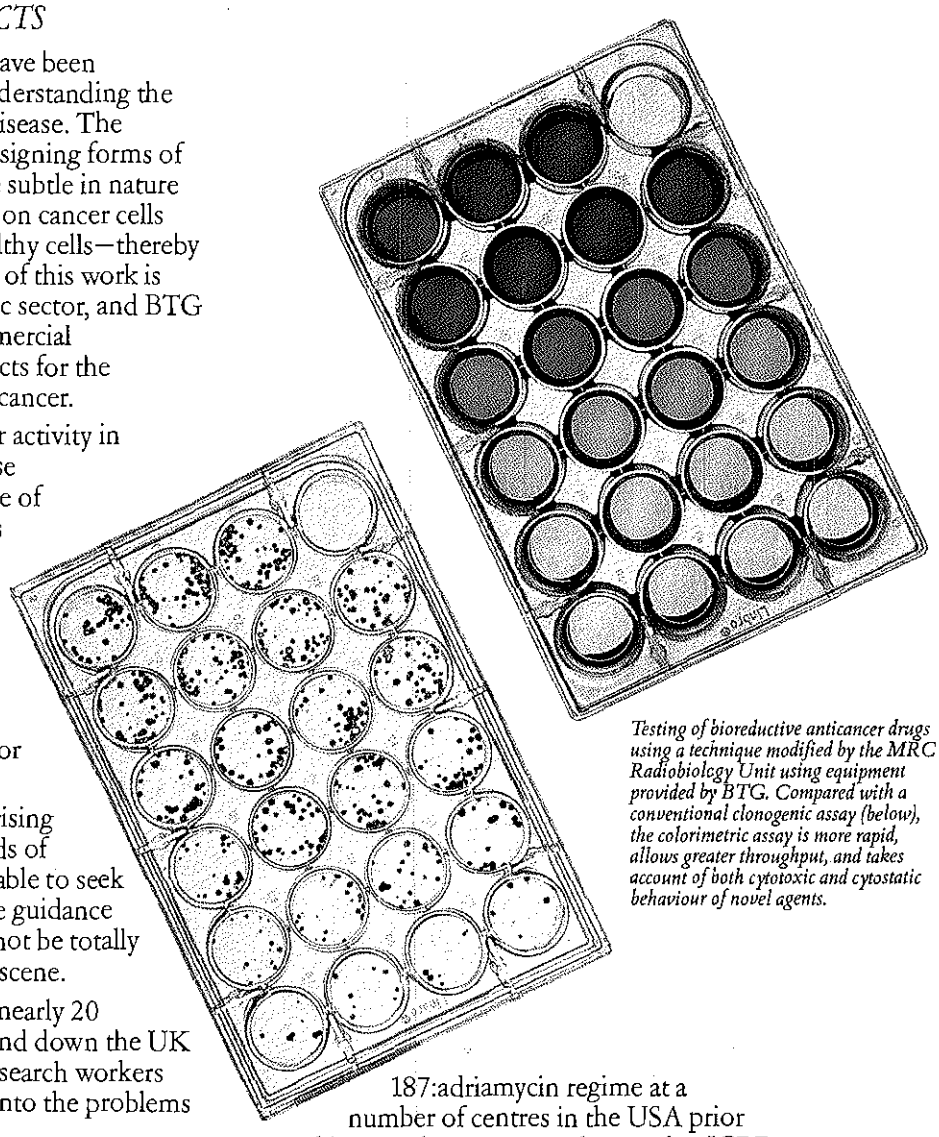
ANTICANCER PRODUCTS

In the past ten years there have been tremendous advances in understanding the mechanisms of cancerous disease. The prospect has emerged of designing forms of therapy that are much more subtle in nature and in which the agent acts on cancer cells alone without affecting healthy cells—thereby reducing side effects. Much of this work is emerging from the academic sector, and BTG is well placed to assist commercial development of new products for the diagnosis and treatment of cancer.

In order to stimulate further activity in academic circles and increase awareness of the importance of patent protection, BTG has launched a new cancer product development initiative. The key features of the scheme are:

- an earmarked fund to support the research of investigators with ideas for new products, and
- an advisory board comprising experts from various fields of cancer research who are able to seek out new ideas and to give guidance to researchers who may not be totally familiar with the current scene.

BTG is already supporting nearly 20 cancer-related projects up and down the UK and is keen to talk to any research workers with new ideas or insights into the problems of cancer.



Testing of bioreductive anticancer drugs using a technique modified by the MRC Radiobiology Unit using equipment provided by BTG. Compared with a conventional clonogenic assay (below), the colorimetric assay is more rapid, allows greater throughput, and takes account of both cytotoxic and cytostatic behaviour of novel agents.

ICRF 187 is the code number of one of the components of an anticancer drug formulated in the London laboratories of the **Imperial Cancer Research Fund** and patented by BTG.

During the early 1980s, researchers in the USA found that, given in combination with the potent anticancer drug adriamycin, ICRF 187 greatly reduced the possibility of damage to heart muscle.

BTG has licensed ICRF 187 to **Adria Laboratories** in the USA, whose major current product is adriamycin. The company, which is part of the Montedison group, is carrying out clinical trials of the ICRF 187:adriamycin regime at a number of centres in the USA prior to seeking regulatory approval to market ICRF 187. The first sales of the drug could be in 1991.

In 1980 BTG and **ICI** concluded an agreement giving the company exclusive rights to the development of a series of anticancer drugs discovered at the **Institute of Cancer Research** and patented by BTG. ICI developed and began clinical trials on CB 3717, a compound chosen from the series.

Although it was subsequently abandoned, the positive results seen in cancer patients taking CB 3717 convinced ICI scientists that a product of this type with reduced side effects would be extremely valuable. A tripartite collaboration between the Institute of Cancer Research, BTG and ICI has resulted in the

PHARMACEUTICALS DIVISION

BTG's involvement with pharmaceuticals is a long and successful one. One of the first major inventions to be taken up in the early 1950s was the cephalosporin group of antibiotics. These are closely related chemically and biosynthetically to the penicillins, which they currently outsell. Cephalosphorin royalties received by BTG and shared with the inventors have totalled more than £150 million.

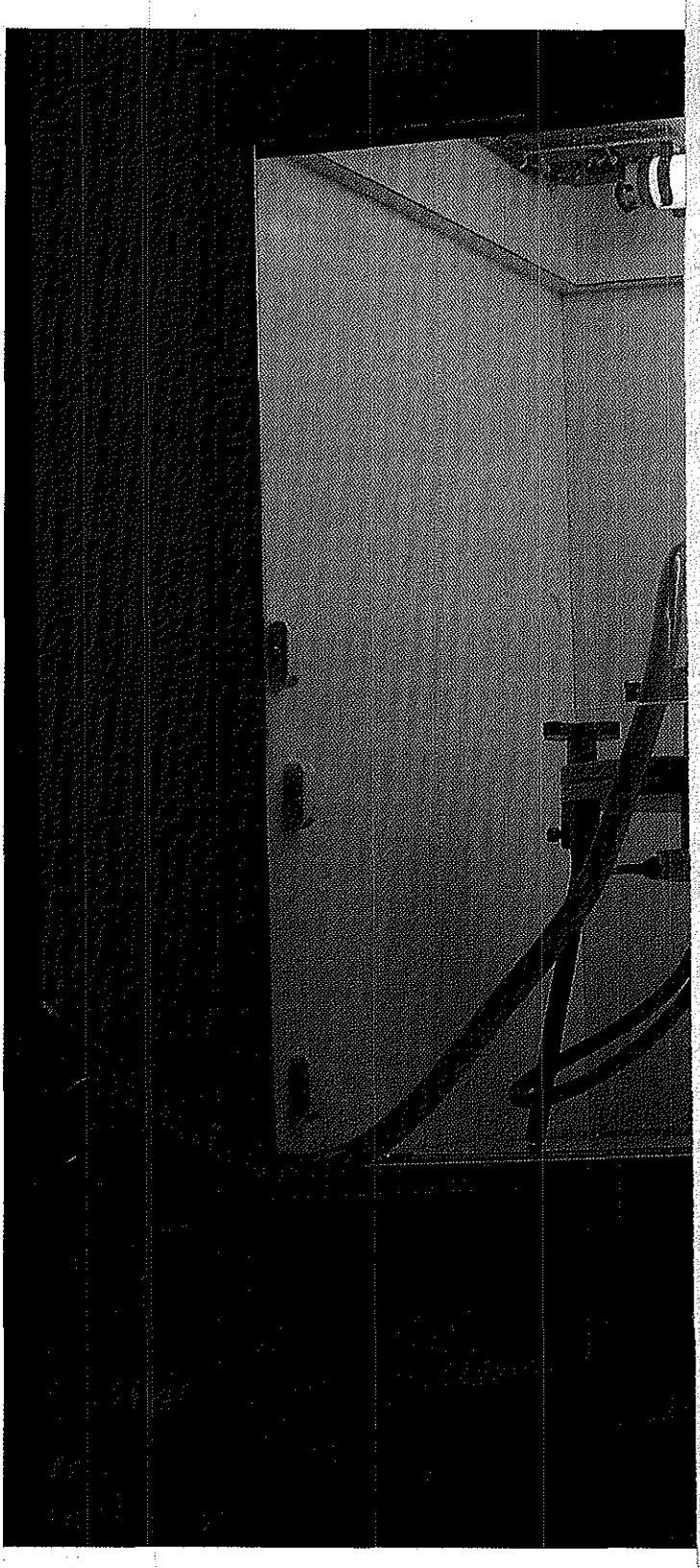
Today BTG's Pharmaceuticals Division covers pharmaceutical and biological products for both human and veterinary healthcare, with notable expertise in the fields of anti-infectives, cancer, CNS, cardiovascular products, immunology and pharmaceutical technology.

The Division's major objective is to find and develop new product opportunities for the pharmaceuticals industry. It acts as creative intermediary between the individual companies that make up the industry and the universities, research councils, medical charities and other bodies that support research likely to lead to potential new healthcare products. Total funding of such research in the UK is of the order of £500 million per annum.

BTG itself is funding some 130 projects in this field at research centres throughout Britain. These are all closely targeted with the general objective of moving research forward to the point where commercial judgements can be made by potential industrial licensees.

Often BTG is able to arrange for complementary skills from several different institutions to be brought to bear in multicentred development projects.

In seeking licensees, BTG looks to develop constructive partnerships with leading specialist companies world wide.



POLYMERS AND PLASTICS

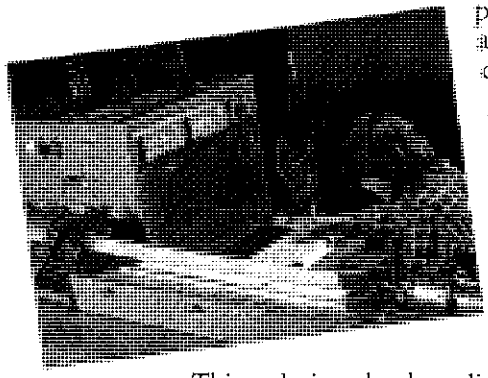
Patented processes for producing high-performance polymers have been devised over a number of years at the University of Leeds.

High-performance fibres, with properties similar to those of *Kevlar*, can be made by drawing polyethylene under carefully defined physical conditions. The original process is now quite old but recent developments have resulted in an improved end product that can resist repeated physical stresses.

The technology has been licensed by BTG to the Italian fibre company SNIA. Further licences are under negotiation on an international basis.

Applications for the fibre are foreseen in reinforcement of composites, fabrics and other areas. Trial quantities of material have been supplied to potential users from the SNIA pilot plant. Large-scale production is scheduled for 1989-90.

High-performance materials in the form of rod, tube, tape and sheet can be produced by drawing common polymers such as polyethylene or PVC through a die under carefully defined physical conditions. The process, which applies very high draw ratios to solid plastics, radically improves the modulus (stiffness) of materials as well as making them stronger and more impervious to gases.



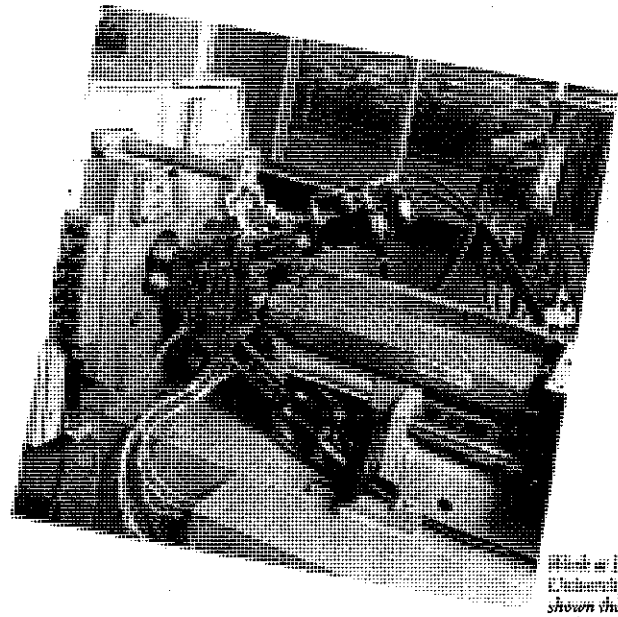
Die-drawing techniques developed at the University of Leeds enable common polymers to be converted to high modulus rod, tube, tape or sheet.

This technique has been licensed by BTG to BP Chemicals and another large UK company. Some major consumer and industrial products are under development.

The quality and strength of plastic components produced by injection moulding can be improved by applying pulsed packing pressures to the solidifying polymer by means of a relatively cheap device fitted between the mould and the nozzle of the injection machine. The process, developed at Brunel University and patented by BTG, eliminates the voids, sink marks and weld lines found in conventional mouldings.

When used with reinforced plastics, the technique gives controlled alignment of the fibres, thereby enhancing the strength of the moulding in specific locations or directions.

Several companies have expressed interest in the process and are actively evaluating its use. The technique promises to be extremely versatile and capable of application to a wide range of components in most thermoplastic polymers with any of the common reinforcement fibres. Licence negotiations are at an advanced stage with two major companies.



Brunel University has shown that application of pulsed packing pressures during injection moulding results in plastic components of improved quality.

CHEMICAL PROCESSING

Patents on a novel packed-bed electrochemical cell process that enables very efficient refining of molten alloys were first filed by BTG in 1976. Recent improvements to the original University of Cambridge design have resulted in a cell that is even more efficient, smaller, and more robust. There are possible applications in refining a number of non-ferrous metals and alloys.

A major company is evaluating the cell's performance under option arrangements offering a degree of exclusivity for certain metals. Given favourable results, this should lead to the construction of an industrial-scale pilot plant.

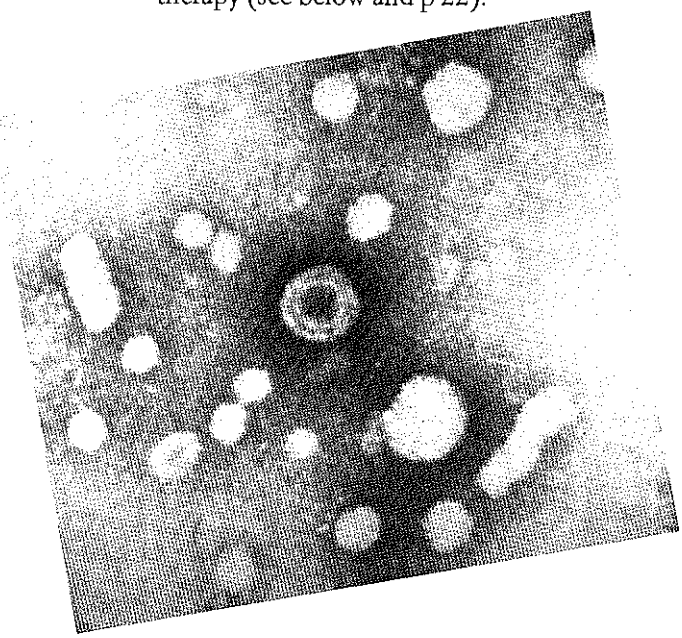
Opportunities remain open for licensees interested in applying the process to other metals, particularly aluminium and lead.

MONOCLONAL ANTIBODIES

Antibodies are proteins produced as part of the body's natural defence against infection. Although foreign bodies such as bacteria and viruses may be attacked by a range of different antibodies, each antibody-producing cell secretes only one specific antibody. Monoclonal antibodies (MABs) are pure antibodies obtained by the isolation and subsequent culture (cloning) of a single antibody-producing cell.

Commercial exploitation of individual monoclonals resulting from university or medical research is normally achieved by assignment of families of clones to BTG, which are then licensed as confidential 'know-how' to industrial companies.

Presently MABs are used principally for diagnosis, but are also finding application in therapy (see below and p 22).



Hepatitis B virus; a BTG-funded project at the Royal Free Hospital has produced monoclonal antibodies to detect the virus and perhaps confer protection against it.

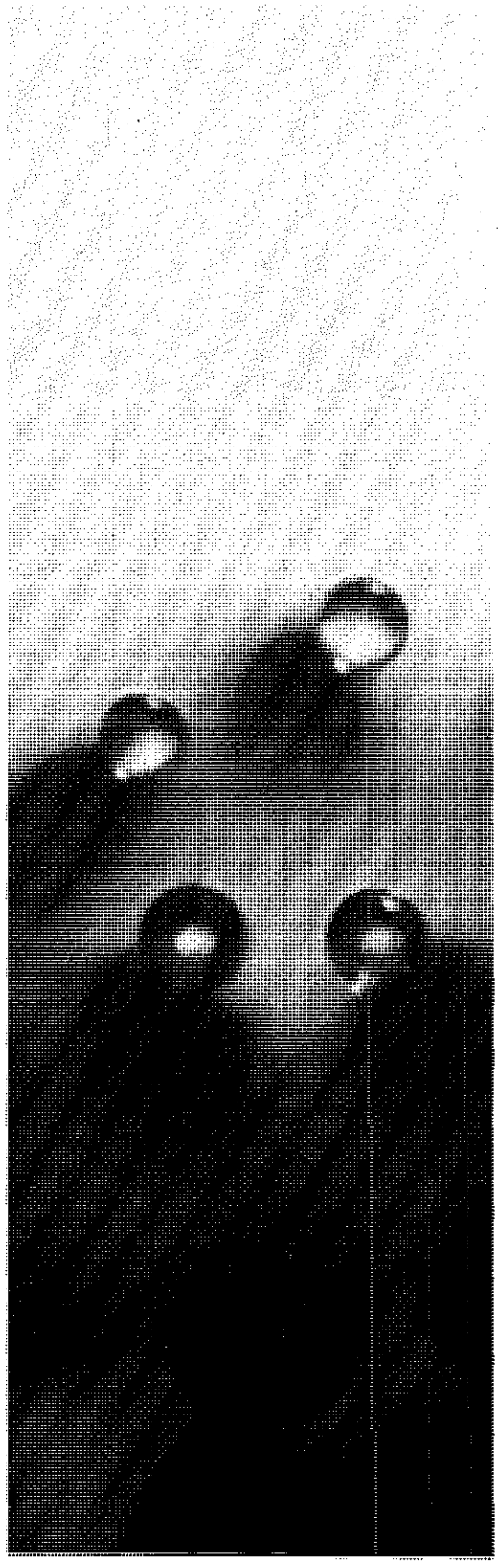
Commercial interest has increased markedly in a range of monoclonal antibodies produced in a project that BTG has funded at the Royal Free Hospital since 1980. These reagents can be used to detect various sites on hepatitis B and also other hepatitis viruses. Licence and option agreements have been concluded with five leading immunodiagnostics companies, and products should reach the market during 1989.

At least one of the monoclonals has the ability to confer protection against the hepatitis B virus, which could augur well for its



pools by a pheromone stimulus emitted from egg rafts laid by successful colonising insects. The main volatile component has been identified and the findings have been patented by BTG. Field trials in Africa have demonstrated that mosquitoes can be attracted to small areas of water to lay eggs which can be dealt with by localised use of insecticides.

BTG is also actively supporting research in other areas aimed at developing novel fungicides and molluscicides. Target areas for future involvement include products to control rodents, mites, and nematodes, and to protect crops against bird damage.

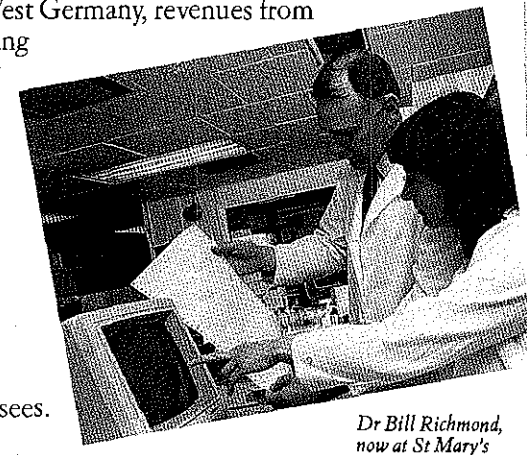


Apical droplets containing oviposition attractant pheromone on egg rafts of the Culex mosquito.

MEDICAL TESTING AND DIAGNOSTICS

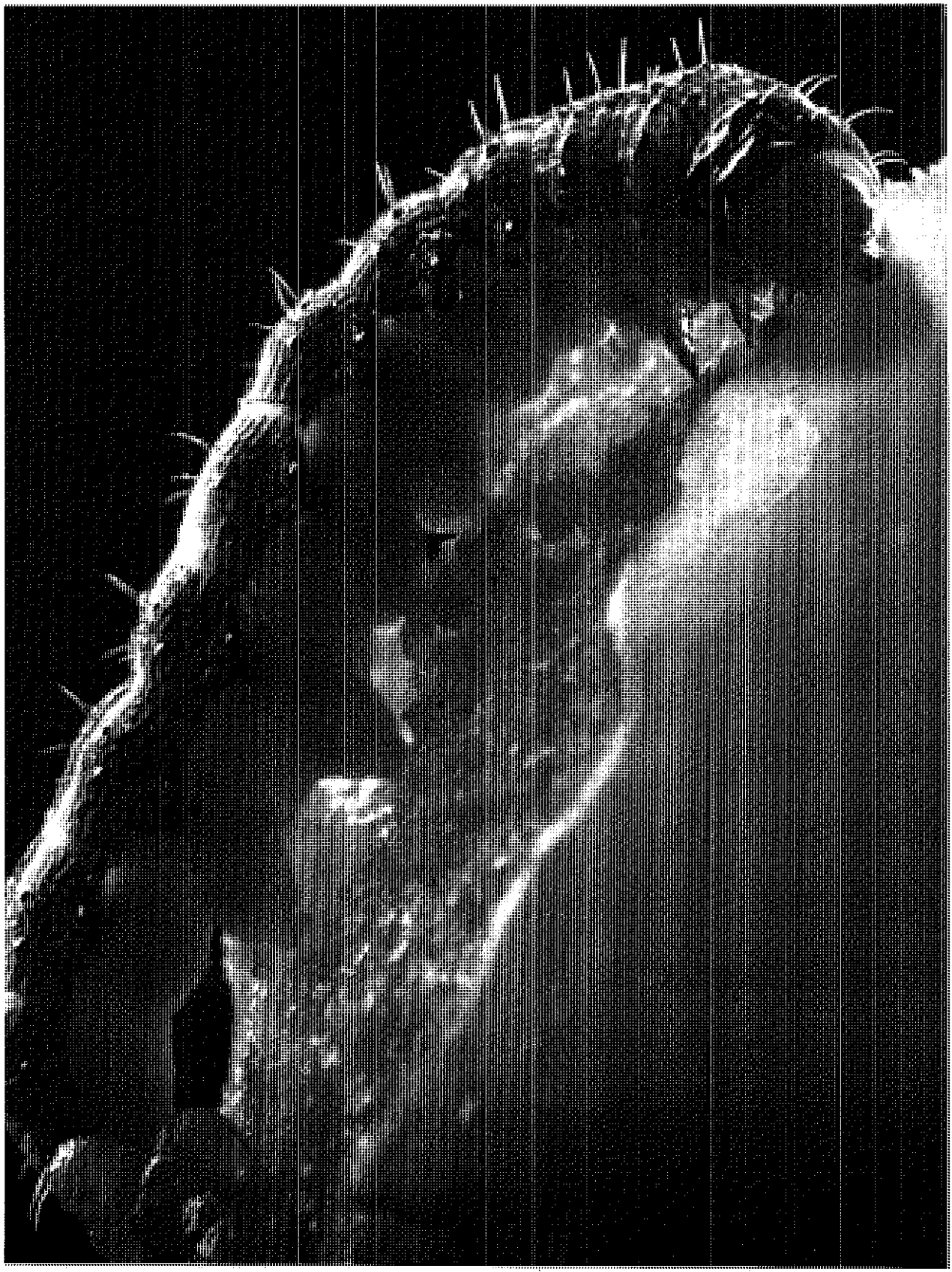
An assay technique devised in 1971 at the Clinical Research Centre and assigned to BTG for commercial exploitation is now used around the world for the measurement of cholesterol levels in blood. With an estimated 250 million determinations carried out each year, it is one of the most widely used of all diagnostic tests.

BTG has a cross-licence agreement on complementary technology with Boehringer Mannheim in West Germany, revenues from the portfolios being shared equally by BTG and Boehringer. More than 80 licences have been granted world wide, and BTG continues to receive approaches from new prospective licensees.



Dr Bill Richmond, now at St Mary's Hospital, developed the enzymatic assay for cholesterol while working at the Clinical Research Centre.

A method originally devised at Queen Elizabeth College for assessing kidney function uses a novel enzyme substrate incorporating a red chromophore. The presence in urine samples of the enzyme N-acetyl-ß, D-glucoseaminidase (NAG), which is associated with kidney damage, releases the chromophore, producing an intense coloration of the sample. A range of substrates that may be applicable to other rapid visual diagnostic tests is now available.



Synthetic pyrethrins offer high effectiveness against insect pests without adverse ecological effects. Heliothis Zea (right) attacks cotton as well as tomatoes.

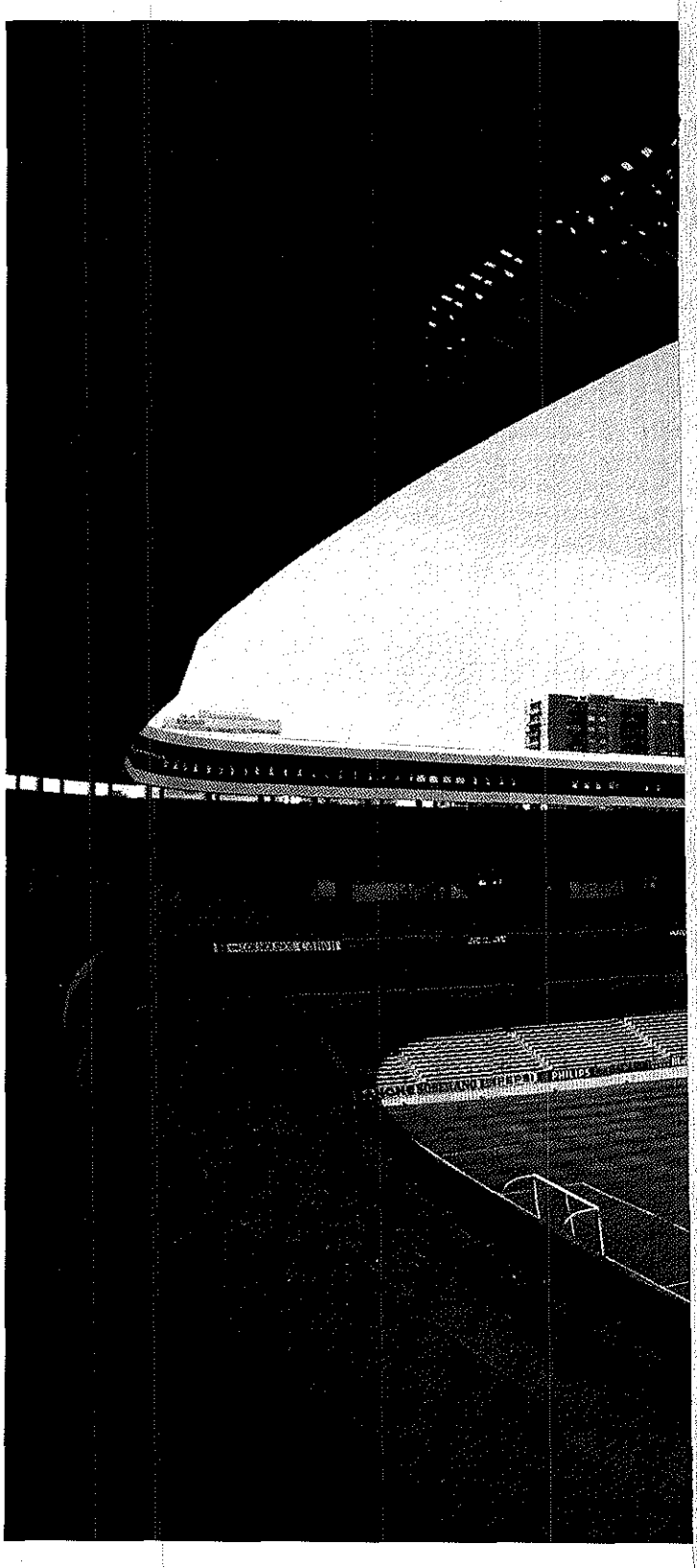
Photo: ICI Plant Protection

SCIENCE DIVISION

BTG's Science Division is concerned both with the licensing of protected inventions and with industrial investments. Technologically, the main areas of interest are crop protection, diagnostics, new materials and applications of biotechnology.

The pyrethrin analogue insecticides have been BTG's greatest success so far in crop protection. Cholesterol assay is the current leader in diagnostics. In the area of materials, BTG was actively involved in the licensing of early methods of production of carbon fibres and supported its licensee Pilkington PLC with industrial project funding for the commercial development of *Cem-FIL* alkali-resistant glass fibres.

Biotechnology embraces many industries. For BTG the earliest fruits have been in monoclonal-antibody-based diagnostics, while major investments in plant and animal breeding are expected to produce substantial rewards in the 1990s. BTG also played a leading role in setting up Celltech, now a world leader in commercial production of monoclonal antibodies.



THE CORE BUSINESS

BTG undertakes two complementary types of activity:

- the transfer of technology—prospective new products and processes—from public-sector and other sources to industrial manufacturers under licence
- the provision of funding on commercial terms for UK companies undertaking development projects involving a significant degree of technical innovation

A substantial industrial development effort may be required to transform promising research findings into a commercial product. In these circumstances BTG may combine its roles as a licensor and source of development funding to give the new technology the best possible chance of ultimate success.

INTERNAL ORGANISATION

BTG's licensing and funding activities are spearheaded by four technology-based operating divisions working in the areas of Science (p 6), Pharmaceuticals (p 16), Engineering (p 26) and Electronics & Information Technology (p 44).

These are backed by Patent, Legal, Finance and Business Development Divisions. All these teams work from BTG's London headquarters, with support from two regional offices in Edinburgh and Manchester, forming a uniquely experienced group of professionals who are collectively able to deal with every aspect of technology transfer.

BTG is large enough to retain these specialist skills as an in-house asset yet small enough to ensure short lines of communication and a minimum of bureaucracy. It has the resources not only to protect and develop inventions, but also to tackle infringements of its intellectual property.

BTG has, where necessary, taken legal action against major international companies in order to defend its rights and those of its inventive sources and legitimate licensees, and has pursued its cases in courts around the world with considerable success.

TECHNOLOGY TRANSFER

BTG provides the British research community with a comprehensive technology transfer service. BTG makes no charge for this service, relying wholly on income from successful licensing to cover its exploitation costs.

These early costs can be substantial, including the costs of making initial patent applications in the UK and overseas, and, later, renewal fees for up to 20 years to maintain the granted patents in each country. Intellectual property outside the scope of patents, such as know-how or computer software, is protected by other means.

Where necessary, BTG funds continuing development work by the inventive source to enhance the prospects of successful licensing to industry.

BTG's knowledge of companies' expertise and current interests enables it to focus in quickly on those firms likely to be receptive to new specialist technologies and to identify those companies best able to bring these to commercial reality. Major technologies are licensed around the world directly by BTG. In addition, a network of overseas agencies appointed by BTG markets licence opportunities in selected countries.

Technology is transferred to industry in return for agreed downpayments and royalties from the licensee. The latrer are usually related to sales. Details of each agreement are closely argued and negotiations on major innovations can take months or even years. Subsequently BTG monitors licensees' performance and makes periodic audits of their royalty payments.

When income begins to flow from successful licensing, BTG channels the early rewards to the inventive source. Ultimately the net licence income is shared between BTG and the source on a 50:50 basis.

Further details of this activity are given in the BTG booklet *Technology transfer*.

THE WORLD'S LEADING TECHNOLOGY TRANSFER ORGANISATION

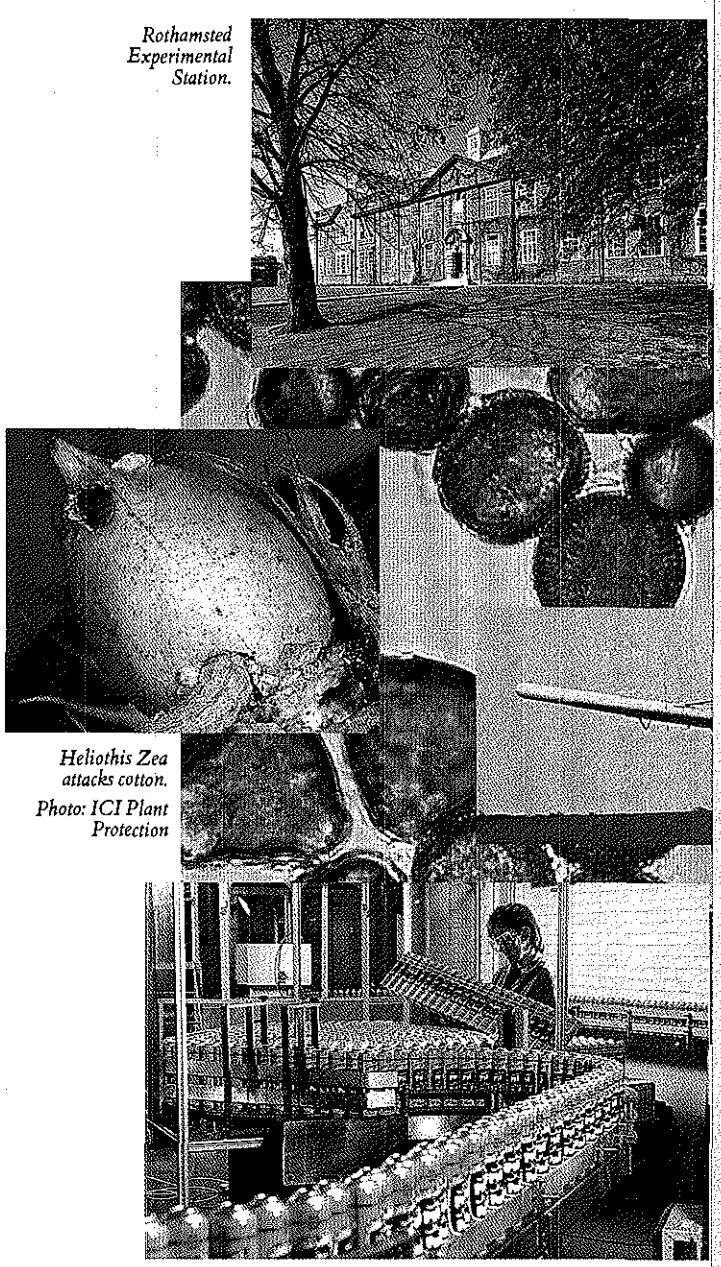
As the world's leading technology transfer organisation, British Technology Group is the principal channel to a vast pool of product opportunities constantly fed by the streams of new technical innovations arising from UK universities, polytechnics, research councils, government laboratories, charitable institutions and other sources, including companies of all sizes.

Ideas that BTG has helped to commercialise have changed the world. The cephalosporin antibiotics are the largest group of anti-infective drugs in world-wide use and outsell the penicillins. Synthetic pyrethrins account for one-quarter of the global insecticide market, protecting crops such as cotton and rice. If your blood cholesterol level is measured, the method used will be based on techniques patented by BTG and licensed to one of the many manufacturers of the test kits. The cement used for your next filling at the dentist may well be a BTG-licensed product. And when you cross the Channel by hovercraft, you will be riding on air-cushion technology that BTG backed in the 1960s on the basis of a demonstration using a couple of coffee tins.

Although universities, polytechnics and government research establishments in the UK will continue as BTG's most important inventive sources, the Group is beginning to look further afield in its search for significant innovations via its links with technology transfer organisations in other countries. An inter-corporate licensing team has also been set up within BTG, targeted on established companies around the world with underutilised technology capable of wider application.

This book summarises the services and resources that BTG can provide and outlines many of the technologies that BTG is helping forward to the marketplace.

Synthetic pyrethrins are one of the British Technology Group's greatest success stories, thanks to the ingenuity of researchers at Rothamsted Experimental Station, the efforts of BTG licensees around the world, and BTG's ability to identify, fund and license key technologies on an international basis (see p 9).



Rothamsted Experimental Station.

Heliothis Zea attacks cotton.

Photo: ICI Plant Protection

Filling aerosols with synthetic pyrethroids.

Photo: The Wellcome Foundation