

## Description of business

The Description of business discusses the activities, the resources and the operating environment of the business and identifies developments and achievements in 2000, under the following headings:

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Discussion of the Group's management structures and corporate governance procedures is set out in Corporate governance (pages 29 to 36).

Discussion of the Group's operating and financial performance and financial resources is given in the Operating and financial review and prospects (pages 47 to 68).

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In this report: 'GlaxoSmithKline' or the 'Group' means GlaxoSmithKline plc and its subsidiary and associated undertakings and the 'company' means GlaxoSmithKline plc; 'GlaxoSmithKline share' means an Ordinary Share of GlaxoSmithKline plc of 25p.

Throughout this report, figures quoted for market size, market share and market growth rates relate to the year ended 30th September 2000 (or later where available). These are GlaxoSmithKline estimates based on the most recent data from independent external sources, valued in sterling at relevant exchange rates. Figures quoted for product market share reflect sales by GlaxoSmithKline and licensees.

Brand names appearing in italics throughout this report are trade marks of GlaxoSmithKline plc, its subsidiaries or associated companies, with the exception of *Nicoderm*, a trade mark of Hoechst Marion Roussel Inc; *Bexxar*, a trade mark of Corixa Corporation, Inc; *Coreg*, a trade mark under licence from Roche Laboratories, Inc; *Factive*, a trade mark of LG Chemical, Ltd; *Navelbine*, a trade mark of Pierre Fabré Médicament and *Panorex*, a trade mark of Centocor, Inc, all of which are used under licence by the Group.

## The business

### History and development of the company

GlaxoSmithKline plc, and its subsidiary and associated undertakings, constitute a major global healthcare group engaged in the creation and discovery, development, manufacture and marketing of pharmaceutical products, vaccines, over-the-counter (OTC) medicines and health-related consumer products.

GlaxoSmithKline has its corporate head office in the London area at:

Glaxo Wellcome House  
Berkeley Avenue  
Greenford  
Middlesex UB6 0NN  
England  
Tel: 020 8966 8000

GlaxoSmithKline has an operational headquarters in Philadelphia, USA, and operating companies in some 70 countries, with products sold in over 140 countries. The principal research and development (R&D) facilities are in the UK, USA, Japan, Italy and Belgium and products are currently manufactured in some 41 countries.

The major markets for the Group's products are the USA, Japan, the UK, France, Germany and Italy.

GlaxoSmithKline plc is a public limited company incorporated on 6th December 1999 under English law. On 27th December 2000 the company acquired Glaxo Wellcome plc and SmithKline Beecham plc, both English public limited companies, by way of a scheme of arrangement for the merger of the two companies. Both Glaxo Wellcome and SmithKline Beecham were major global healthcare businesses.

### Business segments

GlaxoSmithKline operates principally in two industry segments:

- Pharmaceuticals (prescription pharmaceuticals and vaccines)
- Consumer Healthcare (over-the-counter medicines, oral care and nutritional healthcare).

The businesses in the Healthcare Services segment (primarily Clinical Laboratories and Diversified Pharmaceutical Services) were disposed of in 1999.

## Products – pharmaceuticals

Therapeutic area	Trade mark	Compound	Mechanism	Indication (may vary by country)
<b>CNS disorders</b>	<i>Seroxat/Paxil</i>	paroxetine	selective serotonin reuptake inhibitor	depression, panic, anxiety
	<i>Wellbutrin</i>	bupropion	noradrenaline reuptake inhibitor	depression
	<i>Imigran/Imitrex</i>	sumatriptan	5-HT <sub>1</sub> agonist	migraine, cluster headache
	<i>Naramig/Amerge</i>	naratriptan	5-HT <sub>1</sub> agonist	migraine
	<i>Lamictal</i>	lamotrigine	sodium channel modulator	epilepsy
	<i>Requip</i> <i>Zyban</i>	ropinirole bupropion SR	dopamine D2 agonist noradrenaline reuptake inhibitor	Parkinson's disease smoking addiction
<b>Respiratory</b>	<i>Flixotide/Flovent</i>	fluticasone propionate	inhaled anti-inflammatory	asthma, bronchial conditions
	<i>Serevent</i>	salmeterol xinafoate	bronchodilator	bronchial asthma, bronchitis
	<i>Seretide/Advair</i>	salmeterol and fluticasone propionate	bronchodilator/anti-inflammatory	asthma
	<i>Flixonase/Flonase</i>	fluticasone propionate	intranasal anti-inflammatory	hayfever, perennial rhinitis
	<i>Ventolin</i> <i>Becotide/Beclivent</i> <i>Beconase</i>	salbutamol/albuterol beclomethasone dipropionate beclomethasone dipropionate	bronchodilator inhaled anti-inflammatory intranasal anti-inflammatory	bronchial asthma, bronchitis hayfever, perennial rhinitis
<b>Anti-bacterials</b>	<i>Augmentin</i>	amoxicillin/ clavulanate potassium	broad spectrum antibiotic	common infections
	<i>Zinnat/Ceftin</i>	cefuroxime axetil	oral antibiotic	common infections
	<i>Fortum/Fortaz</i>	ceftazidime	injectable antibiotic	severe, life threatening infections
	<i>Amoxil</i>	amoxicillin	broad spectrum antibiotic	common infections
	<i>Zinacef</i>	cefuroxime	injectable antibiotic	surgical infections
<b>Anti-virals</b>	<i>Trizivir</i>	lamivudine, zidovudine and abacavir	reverse transcriptase inhibitor	HIV/AIDS
	<i>Combivir/Biovir</i>	lamivudine and zidovudine	reverse transcriptase inhibitor	HIV/AIDS
	<i>Epivir/3TC</i>	lamivudine	reverse transcriptase inhibitor	HIV/AIDS
	<i>Retrovir/AZT</i>	zidovudine	reverse transcriptase inhibitor	HIV/AIDS
	<i>Ziagen</i>	abacavir	reverse transcriptase inhibitor	HIV/AIDS
	<i>Agenerase</i>	amprenavir	protease inhibitor	HIV/AIDS
	<i>Valtrex/Zelitrex</i>	valaciclovir	DNA polymerase inhibitor	shingles, genital herpes
	<i>Zovirax</i>	aciclovir	DNA polymerase inhibitor	herpes infections, shingles, chicken pox, cold sores
	<i>Zeffix/Heptavir/ Heptodin/Epivir HBV</i>	lamivudine	reverse transcriptase inhibitor	chronic hepatitis B infection
	<i>Relenza</i> <i>Malarone</i>	zanamavir atovaquone	neuraminidase inhibitor electron transport system inhibitor	influenza treatment malaria treatment/prophylaxis
<b>Metabolic and gastro-intestinal</b>	<i>Avandia</i>	rosiglitazone	PPAR-gamma agonist	type 2 diabetes
	<i>Zantac</i>	ranitidine hydrochloride	anti-secretory	duodenal ulcers, stomach ulcers, reflux and dyspepsia
	<i>Pylorid/Tritec</i>	ranitidine bismuth citrate	anti-secretory plus antibiotic	eradication of H pylori
<b>Vaccines</b>	<i>Havrix</i> <i>Engerix-B</i> <i>Twinrix</i> <i>Infanrix</i>			hepatitis A hepatitis B hepatitis A and B diphtheria, tetanus, acellular pertussis
<b>Oncology and emesis</b>	<i>Zofran</i>	ondansetron	5-HT <sub>3</sub> receptor antagonist	nausea and vomiting from cancer therapy
	<i>Hycamtin</i> <i>Navelbine</i>	topotecan vinorelbine	topoisomerase 1 inhibitor cytotoxic	ovarian cancer, small cell lung cancer non-small cell lung cancer, breast cancer
	<i>Panorex</i>	Mab17-1A	monoclonal antibody	colorectal cancer as adjuvant therapy
<b>Cardiovascular</b>	<i>Coreg</i> <i>Lanoxin</i>	carvedilol digoxin	alpha/betablocker cardiac anti-arrhythmic	congestive heart failure congestive heart failure, cardiac arrhythmia
	<i>Flofan</i> <i>Lacipil</i> <i>Pritor</i>	epoprostenol lacidipine telmisartan	inhibitor of blood clotting calcium channel blocker angiotensin II antagonist	primary pulmonary hypertension hypertension hypertension

## Products – Pharmaceuticals

GlaxoSmithKline's principal pharmaceutical products are presently directed to 10 major therapeutic areas. An analysis of sales by these therapeutic areas, and a description of the principal products, are set out below:

Sales by therapeutic area	2000 £m	1999 £m	1998 £m
Central nervous system disorders	3,279	2,720	2,400
Respiratory	2,789	2,382	2,096
Anti-bacterials	2,472	2,383	2,278
Anti-virals	1,899	1,610	1,347
Metabolic and gastro-intestinal	1,232	886	908
Vaccines	842	776	726
Oncology and emesis	710	613	549
Cardiovascular	463	449	390
Dermatologicals	249	254	243
Arthritis	210	275	301
Others	837	842	949
Divested products	447	428	376
	<b>15,429</b>	<b>13,618</b>	<b>12,563</b>

### Central nervous system (CNS) disorders

*Seroxat/Paxil* is a selective serotonin reuptake inhibitor (SSRI) approved for depression, panic, obsessive compulsive disorder and social anxiety disorder, with approvals being obtained for generalised anxiety disorder and post traumatic stress disorder.

*Wellbutrin* is also an anti-depressant, available in the USA in normal or sustained release tablet formulations.

*Imigran/Imitrex* is a 5HT<sub>1</sub> receptor agonist used for the treatment of severe or frequent migraine and cluster headache, and has become the reference product in this sector. *Naramig/Amerge* is the Group's newer migraine product.

*Lamictal* is a treatment for epilepsy. Used alone or in combination with other products, it has achieved penetration of this mature market through successful treatment of severe cases.

*Requip* is a specific dopamine D2-like receptor for the treatment of Parkinson's disease.

*Zyban* is a novel, nicotine-free prescription medicine, available as a sustained-release tablet, for treating the problem of smoking addiction.

### Respiratory

*Serevent* is a long-acting bronchodilator, and *Ventolin* a selective short-acting bronchodilator, for the treatment of asthma.

*Flixotide/Flovent* and *Becotide/Beclovent* are inhaled steroids for the treatment of inflammation associated with bronchial asthma and chronic bronchitis.

*Seretide/Advair*, a combination of *Serevent* and *Flixotide*, offers a long-acting bronchodilator and an anti-inflammatory in a single inhaler.

*Flixonase/Flonase* and *Beconase* are intra-nasal preparations for the treatment of perennial and seasonal rhinitis.

The Group's respiratory products are now available in a wide choice of delivery systems, including the *Diskus/Accuhaler*, a dry powder multi-dose inhaler.

### Anti-bacterials

The Group markets a range of antibiotics.

*Augmentin* is a broad-spectrum antibiotic suitable for the treatment of a wide range of common bacterial infections, and is particularly effective against respiratory tract infections.

*Zinnat* is an oral antibiotic used primarily for community-acquired infections of the lower respiratory tract. *Fortum* and *Zinacef* are used in the hospital-based injectable antibiotics market.

### Anti-virals

*Combivir*, a combination of *Retrovir* and *Epivir*, has consolidated the position of these two reverse transcriptase inhibitors as the cornerstone of many multiple anti-HIV product regimens. Physician acceptance has clearly demonstrated the value placed on minimising the 'pill burden' faced by patients.

*Ziagen* is the Group's new reverse transcriptase inhibitor. The product's potency, ease of use and resistance profile will allow it to play a significant role in a variety of highly active, well tolerated, and simplified HIV treatment regimens.

*Trizivir* is a combination of *Combivir* and *Ziagen*, combining three anti-HIV therapies in one tablet, for twice daily administration.

*Agenerase* is a new protease inhibitor for the treatment of HIV, the first medicine of this class to be brought to the market by GlaxoSmithKline. *Agenerase* has a twice daily dosing regime and no significant food or drink restrictions.

*Zeffix* has been approved for marketing in the USA, Europe, China and other markets for the treatment of chronic hepatitis B.

*Zovirax* is used for the treatment of herpes infections such as chicken pox, genital herpes, shingles and cold sores. The newer anti-herpes compound, *Valtrex*, reinforces the Group's presence in this market as a treatment for zoster and the episodic and long-term suppression of genital herpes.

*Relenza*, the Group's novel treatment for influenza, is the first of a new class of drug known as a neuraminidase inhibitor, and targets the primary site of viral replication through direct delivery to the airways via an inhaler.

### Metabolic and gastro-intestinal

*Avandia* is the most potent of a novel class of oral anti-diabetic agents called thiazolidinediones or PPAR-gamma agonists, for the treatment of type 2 diabetes.

*Zantac*, for the treatment of peptic ulcer disease and a range of gastric acid related disorders, continues to play a major role in treatment in a number of markets, even where patent protection has been lost. *Pylorid/Tritec* is used, in combination with antibiotics, for the eradication of *helicobacter pylori*, a causative agent in ulcers.

*Lotronex*, a novel treatment for the multiple symptoms of irritable bowel syndrome, was approved for use in the USA following priority review and launched in 2000, but was subsequently withdrawn following discussions with the US Food and Drug Administration over the interpretation of data relating to gastro-intestinal side effects.

## Vaccines

GlaxoSmithKline markets a range of hepatitis vaccines. *Havrix* protects against hepatitis A and *Engerix-B* against hepatitis B. *Twinrix* is a combined hepatitis A and B vaccine, protecting against both diseases with one vaccine and available in both adult and paediatric strengths.

*Infanrix* is a range of paediatric vaccine combinations. *Infanrix* provides protection against diphtheria, tetanus and pertussis (whooping cough). *Infanrix PeNta* provides additional protection against hepatitis B and polio, and *Infanrix HeXa* further adds protection against haemophilus influenzae type b, which causes meningitis.

Additionally GlaxoSmithKline markets *Priorix*, a measles, mumps and rubella vaccine, *Typherix*, a vaccine for protection against typhoid fever, *LYMERix*, a vaccine for protection against LYME disease.

## Oncology and emesis

*Zofran* is used to prevent nausea and vomiting associated with chemotherapy and radiotherapy for cancer, and is available in both oral and injectable forms. It is also approved for use in the prevention and treatment of post-operative nausea and vomiting.

*Hycamtin* is a second line treatment both for ovarian cancer and for small cell lung cancer.

*Panorex* is the first monoclonal antibody to be licensed for cancer therapy.

## Cardiovascular

*Coreg* is a blocking agent which has been proven to be effective in treating mild and moderate congestive heart failure.

## Dermatologicals

The Group's principal dermatological products, *Betnovate*, the higher potency *Dermovate* and the newer *Cutivate* are anti-inflammatory steroid products used to treat skin diseases such as eczema and psoriasis.

## Divested products

In accordance with agreements for regulatory approvals of the merger between Glaxo Wellcome and SmithKline Beecham, the products *Kytril*, for the treatment of chemotherapy – and radiotherapy – induced nausea and vomiting, and *Famvir*, an anti-viral for the treatment of shingles and herpes, were divested in December 2000.

## Products – Consumer Healthcare

GlaxoSmithKline's principal consumer products are presently directed to three major areas. An analysis of sales by these areas is set out below:

	2000 £m	1999 £m	1998 £m
Over-the-counter medicines	1,454	1,434	1,328
Oral care	642	614	584
Nutritional healthcare	535	488	459
Divested products	19	10	4
	<b>2,650</b>	2,546	2,375

Category	Product
<b>Over-the-counter medicines</b>	
Analgesics	<i>Panadol</i>
Dermatologicals	<i>Oxy</i>
Gastro-intestinal	<i>Tums</i>
	<i>Tagamet HB</i>
	<i>Zantac Relief</i>
Respiratory tract	<i>Contac</i>
	<i>Beechams</i>
	<i>Beconase Hayfever</i>
Smoking control	<i>Nicorette</i>
	<i>NicoDerm CQ</i>
	<i>NiQuitin CQ</i>
	<i>Nicabate</i>
Vitamins and naturals	<i>Abtei</i>
<b>Oral care</b>	
	<i>Aquafresh</i>
	<i>Macleans</i>
	<i>Odol</i>
	<i>Dr Best</i>
<b>Nutritional healthcare</b>	
	<i>Lucozade</i>
	<i>Ribena</i>
	<i>Horlicks</i>

## Over-the-counter medicines

The most significant products are *Panadol*, a widely available non-aspirin analgesic; the smoking cessation products *Nicorette*, *NicoDerm CQ*, *NiQuitin CQ* and *Nicabate*; *Tums*, the calcium-based antacid and *Tagamet HB* for the prevention and relief of heartburn; *Contac* and the *Beechams* range for the treatment of colds and influenza; and a variety of vitamin and tonic products led by *Abtei* in Germany. Consumer Healthcare will market additionally OTC versions of *Zantac* and *Beconase*.

## Oral care

The leading oral care products are *Aquafresh*, *Macleans* and *Odol* toothpastes and toothbrushes sold under the *Aquafresh* and *Dr Best* trademarks.

## Nutritional healthcare

In this category the principal products are *Lucozade*, the glucose energy drink; *Ribena*, a line of juice drinks rich in vitamin C; and *Horlicks*, a range of milk-based malted food and chocolate drinks.

## Block Drug

In January 2001 GlaxoSmithKline completed the acquisition of Block Drug. This will add to the product range *Sensodyne* toothpaste, *Poli-Grip* denture adhesive and *Polident* denture cleaner.

## Operating environment

### Competition – Pharmaceuticals

The pharmaceutical industry is highly competitive. GlaxoSmithKline's principal competitors are large international pharmaceutical companies with substantial resources. Some of these companies and their major products are mentioned below.

Medicines may be subject to competition from different therapies during the period of patent protection and, once off patent, from generic versions. The manufacturers of generic products typically do not bear research and development costs and consequently are able to offer their products at considerably lower prices than the branded competitors. A research and development-based pharmaceutical company will normally seek to achieve a sufficiently high profit margin and sales volume during the period of patent protection to repay the original investment and to fund research for the future.

Competition from generic products generally occurs as GlaxoSmithKline's patents in major markets expire. In response, GlaxoSmithKline undertakes a range of activities, including:

- introducing innovative products into as many markets as possible
- accelerating the process by which new products are brought to market
- increasing brand share among customers.

Ultimately, GlaxoSmithKline believes that its competitive position is dependent upon the discovery and development of new products, together with effective marketing of existing products. Within the pharmaceutical industry, the introduction of new products and processes by competitors may affect pricing levels or result in product replacement, and there can be no assurance that GlaxoSmithKline's products may not become outmoded, notwithstanding patent or trademark protection. In addition, increasing government and other pressure for physicians and patients to use generic pharmaceuticals rather than brand-name medicines may increase competition for products that have gone off patent.

### CNS disorders

Major competitors to *Paxil* in the US selective serotonin reuptake inhibitor (SSRI) market are Prozac from Eli Lilly, Zoloft from Pfizer and Forest Laboratories' Celexa. The success of *Seroxat/Paxil* has made it a target for generic manufacturers, against whom GlaxoSmithKline continues to respond appropriately (see note 31 to the Financial statements, 'Legal proceedings').

*Imigran* has grown to be one of GlaxoSmithKline's leading products through addressing the previously unmet needs of migraine sufferers. Although other companies have launched competing products, newer formulations of *Imigran*, such as the nasal spray, and the introduction of *Naramig* have helped GlaxoSmithKline to retain its lead over its competitors in the migraine market.

### Respiratory

Growth of GlaxoSmithKline's newer respiratory products, *Flixotide*, *Serevent* and the recently launched *Seretide*, have continued to drive growth in this market. The established products such as *Ventolin* and *Becotide* have faced generic competition for some years but have maintained significant sales. A major competitor to GlaxoSmithKline's respiratory products is Singulair from Merck.

### Anti-bacterials

Major products competing with GlaxoSmithKline's semi-synthetic penicillins are other anti-infectives including, but not limited to, generic brands, cephalosporins and, to an increasing degree, particularly in Japan, quinolones. *Augmentin* has been experiencing increased competition in the USA, particularly from Pfizer's Zithromax, Bayer's Cipro and Abbott's Biaxin, and has lost patent protection in various countries in Europe. *Amoxil* has been without patent protection for a number of years and is subject to competition from generic brands.

### Anti-virals

GlaxoSmithKline's drive to create sustainable leadership in selected therapy areas is underlined by its pioneering role in the HIV market, with *Retrovir* and *Epivir* acting as the cornerstone of combination therapy, and available as *Combivir* in a single tablet. The launch of *Ziagen* and *Agenerase* and more recently *Trizivir* further broaden the Group's portfolio of HIV products. *Zovirax* faces competition from generic acyclovir, although *Valtrex* has helped strengthen the company's position in the anti-herpes area.

### Metabolic and gastro-intestinal

Major competitors for *Avandia* are Takeda Chemical's Actos, which is co-promoted with Eli Lilly in the USA. In the gastro-intestinal market, *Zantac* faces significant competition from omeprazole, a proton pump inhibitor, and from generic ranitidine hydrochloride.

### Vaccines

GlaxoSmithKline's major competitors in the vaccine market include Aventis Pasteur, Merck and American Home Products. *Engerix-B* and *Havrix* compete with vaccines produced by Merck – Comvax and Recombivax HB for hepatitis B and Vaqta for hepatitis A. *Infanrix*'s major competitors are Aventis Pasteur's Tripedia and TriHIBit, and Wyeth Ayerst's Acel-Imune and Tetramune.

### Competition – Consumer Healthcare

The major competitors in the consumer healthcare markets are Procter & Gamble, Colgate-Palmolive, American Home Products, Unilever and Johnson & Johnson. All of these companies are major international companies and continue to be extremely active in what is a highly competitive market. In addition, there are many other large and small companies that compete with GlaxoSmithKline in selected markets.

In the USA, the major competitor products in OTC medicines are: Tylenol Cold (cold remedy), Clearasil (acne treatment), Pepcid (indigestion) and private label in smoking cessation. In the UK the major competitor products are: Lemsip (cold remedy), Nurofen and Anadin (analgesics) and Nicotinell (smoking cessation remedy).

In nutritional healthcare the major competitors to *Horlicks* are Ovaltine and Milo malted food and chocolate drinks. The competitors to *Ribena* are primarily local fruit juice companies while *Lucozade* competes with other energy drinks.

The Consumer Healthcare business relies on the development of high-quality branded products with good consumer acceptance, supported by advertising and brand promotion, line extensions, new formulations and packaging innovations. GlaxoSmithKline's ability to compete effectively is dependent on its skills in developing new scientifically supported products and line extensions with performance superior to those of its competitors, backed up by compelling advertising.

## Regulation – Pharmaceuticals

The international pharmaceutical industry is highly regulated. National regulatory authorities administer a panoply of laws and regulations governing the testing, approval, manufacturing, labelling and marketing of drugs and also review the safety and effectiveness of pharmaceutical products. These regulatory requirements are a major factor in determining whether a substance can be developed into a marketable product and the amount of time and expense associated with such development.

Of particular importance is the requirement in many countries that products be authorised or registered prior to marketing and that such authorisation or registration be maintained subsequently.

The national regulatory authorities in many jurisdictions, including the USA, the European Union, Japan and Australia, have high standards of technical appraisal and consequently the introduction of new pharmaceutical products generally entails a lengthy approval process.

In the European Union, there are two procedures for obtaining marketing authorisations for medicinal products:

- The Centralised Procedure, with applications made direct to the European Medicines Evaluation Agency and leading to an authorisation valid in all member states, is compulsory for products derived from biotechnology and optional for new active substances and other innovative medicinal products
- The Mutual Recognition Procedure, which is applicable to the majority of conventional medicinal products, operates by mutual recognition of national marketing authorisations; where this is not possible, the matter is resolved by a binding arbitration. National authorisations are still available for medicinal products to be marketed in only one member state.

Grant of a marketing authorisation affords the company a data protection period during which a competitor cannot rely on confidential data in the regulatory file as a basis for its own marketing authorisation. The data protection period begins on the date an authorisation is first granted in the European Union and expires after ten years for authorisations granted via the Centralised Procedure, or ten or six years for authorisations granted via the Mutual Recognition procedure, depending on the country concerned.

GlaxoSmithKline anticipates that the introduction of new products will continue to require substantial effort, time and expense to comply with regulatory requirements.

### Price controls

In addition to the forms of regulation already referred to, in many countries the prices of pharmaceutical products are controlled by law.

Governments may also influence the prices of pharmaceutical products through their control of national healthcare organisations which may bear a large part of the cost of supplying such products to consumers.

In some countries, such as France and Japan, the prices of individual products are regulated. In the UK, prices are controlled by reference to limits upon the overall profitability, measured by the rate of return on capital employed, of sales of products supplied under the National Health Service.

In the USA, debate over the reform of the healthcare system has resulted in an increased focus on pricing. Although there are currently no government price controls over private sector purchases in the USA, federal legislation requires pharmaceutical manufacturers to pay prescribed rebates on certain drugs to enable them to be eligible for reimbursement under Medicaid healthcare programmes.

During 2000 the pharmaceutical market worldwide continued to experience increasing pressure on pricing and reimbursement from governments and healthcare providers, though it is non-price factors (new products and higher volumes) which are principally driving the growth of pharmaceutical expenditure.

In Europe, historically affected by government regulation in pricing and reimbursement, the pharmaceutical industry continued to experience pressure on its prices through a range of measures, including across-the-board price cuts, linking of prices to low-cost countries (price referencing) and delays in agreeing reimbursement. There is an increasing pressure for generic substitution and demonstration of the added value of new medicines. In some countries cross-border imports from low-priced markets exert a commercial pressure on in-country pricing.

In Japan the government has measures to curb the growth of healthcare expenditure including biennial price cuts.

### Value for money

It is becoming increasingly necessary to demonstrate the value for money of new products, in particular the overall effect on healthcare costs. In some markets, the need to satisfy healthcare purchasers as to value for money is becoming a hurdle in terms of product acceptance additional to the regulatory tests of safety, efficacy and quality.

In most markets it is difficult to obtain a premium price for new chemical entities, even if they represent a significant improvement over existing therapy. In the USA, however, some new products have been able to command prices reflecting a clear recognition of their value.

### Future developments

It is not possible to predict whether, and to what extent, the Group's business may be affected by future legislative and regulatory developments relating to specific pharmaceutical products or the pricing of such products.

## Regulation – Consumer Healthcare

The consumer healthcare industry is subject to national regulation regarding the testing, approval, manufacturing, labelling and marketing of products. In many countries high standards of technical appraisal entail a lengthy approval process before a new product is launched.

National regulatory authorisation is also required to approve the switch of products from prescription to OTC. The requirements include long-term experience of the quality, safety and efficacy of the product in a wide patient population and data to confirm that the relevant condition is both self-limiting and can easily be diagnosed by the consumer.

## Operating activities

### Marketing and distribution

GlaxoSmithKline sells its products worldwide through an extensive network of subsidiaries, licensees and distributors.

The gross profit margins earned on sales of pharmaceutical products are generally higher than those earned on sales of consumer products, reflecting the many risks and uncertainties inherent in developing and marketing pharmaceuticals. These risks include the high level of research and development expenditure required to discover, test and obtain patent protection for new products and the competition from new and generic products.

GlaxoSmithKline's worldwide business is subject to a number of risks inherent in conducting business in certain countries, including possible nationalisation, expropriation and other restrictive government actions such as capital regulation. In addition, currency fluctuations and other changes in economic conditions occur from time to time, which can have either a favourable or unfavourable effect on trading income. GlaxoSmithKline does not regard these factors as deterrents to further expansion of its international operations. However, the company closely reviews its methods of operation, particularly in developing countries, and develops strategies to respond to changing economic and political conditions.

### Marketing and distribution – Pharmaceuticals

An analysis of pharmaceutical sales by geographic region is set out below:

Sales by geographic region	2000 £m	1999 £m	1998 £m
USA	<b>7,705</b>	6,276	5,635
Europe	<b>4,268</b>	4,288	4,059
Rest of World:			
Asia Pacific	<b>1,049</b>	929	876
Japan	<b>832</b>	704	592
Latin America	<b>682</b>	636	662
Middle East, Africa	<b>511</b>	461	468
Canada	<b>382</b>	324	271
	<b>15,429</b>	13,618	12,563

GlaxoSmithKline sells its prescription medicines primarily to wholesale drug distributors, independent and chain retail pharmacies, physicians, hospitals, clinics, government entities and other institutions. These products are ordinarily dispensed to the public by pharmacies through prescriptions written by physicians.

In the USA, the world's largest pharmaceutical market, the pressure to contain healthcare costs has encouraged the growth of managed care organisations and pharmacy benefit managers. These intermediaries use a range of methods to lower costs, including the substitution of generic products or other cheaper therapies for branded products prescribed by doctors. GlaxoSmithKline contracts with the managed care sector due to its increasing importance as a supplier of healthcare to the community.

In each market, GlaxoSmithKline deploys sales forces of representatives and supporting medical staff to promote its prescription products to medical prescribers and healthcare purchasers through personal visits.

Promotion of GlaxoSmithKline's products is supplemented by scientific seminars, advertising in medical and other journals, television advertising, the provision of samples, the direct mailing of printed material and information contained on the company's site on the World Wide Web.

Direct-to-consumer (DTC) advertising is a major component of product marketing in the USA. DTC advertisements are now the primary source of information for patients requesting specific brand name products from their physicians in the USA.

Outside the USA, DTC is either prohibited or has a more limited role in informing patients. In the European Union and in Canada, DTC is currently prohibited. In Australia, the government allow DTC advertising of pharmacy-only products subject to certain safeguards. In New Zealand, DTC is allowed and self regulated by the industry in collaboration with the Advertising Standards Agency. Other markets allow DTC, but to date the impact has been more limited.

In addition to the direct marketing of products by its subsidiaries and associates, GlaxoSmithKline has entered into agreements with other pharmaceutical companies for the co-marketing and co-promotion of its products in many markets.

### Marketing and distribution – Consumer Healthcare

The principal markets for Consumer Healthcare's OTC medicines are the US, the UK, Germany, Australia, Argentina, Italy, Mexico, Japan, South Africa and France. The nutritional drinks business is particularly strong in the UK, Ireland and India, though the range of products is available in other markets. The principal markets for the Oral Care products are the US, Germany and the UK.

OTC products are distributed to retail outlets directly or through wholesalers.

Distribution of oral care and nutritional healthcare products are made through a wide selection of outlets either directly or through wholesalers. The organisation of the selling teams is dependent on the outlet pattern of individual countries.

## Manufacture and supply

GlaxoSmithKline has a portfolio of over 1,000 different products, ranging from tablets and toothpaste to inhalers and complex capsules, in over 32,000 different pack sizes and presentations.

Manufacture of medicines begins with the development of a therapeutic active ingredient in a selected formulation. Global Manufacture & Supply (GMS) develops manufacturing processes for full scale volume production of active compounds at 'primary' manufacturing sites. Converting active compounds into a finished dosage formulation is the responsibility of the 'secondary' manufacturing sites.

Following the merger between Glaxo Wellcome and SmithKline Beecham in December 2000, GMS operates as a single global network of 108 sites in 41 countries employing over 39,000 people. Each year GMS produces around 5,900 tonnes of bulk actives and over 3.8 billion packs, which are packaged and delivered for sale in 138 countries. It also manages approximately 1,800 new product launches a year.

GMS is focused on delivering:

- a secure source of supply of high quality products
- compliance with regulatory requirements and customer expectations
- best in class cost
- leading edge practices and performance – at sites, in procurement and in other global functions.

## Organisation

GMS operations are structured into Supply Chains and Regions.

**Actives supply.** The active ingredients of non-antibiotic products are produced at ten sites across the network, located in Australia, India, Ireland, Singapore, the UK and the USA. Approximately 3,750 staff are employed in manufacturing and supplying these active ingredients to the secondary pharmaceutical sites.

**Antibiotics supply.** This is a global organisation with 18 sites, spread across 11 countries. In total, around 6,200 staff are employed across all of these sites, where a broad range of antibiotic products are manufactured and packaged.

**European region.** There are 15 sites in the European region spread across nine countries employing around 9,250 people in total. Between them the European sites manufacture nearly all of the major pharmaceutical products marketed by GlaxoSmithKline in a wide variety of finished dosage forms.

**North America region.** There are three pharmaceutical sites in the North America region located in Puerto Rico, Canada and the USA. These sites employ around 1,750 staff.

**International region.** The International region comprises 38 manufacturing sites in 20 countries spread across five distinct areas and employs around 10,600 people. There are five sites in Middle East/Africa, 19 sites spread across the Asia Pacific area, five sites in China and two in Japan. In Latin America there are seven sites.

**Consumer Healthcare supply.** There are 24 Consumer Healthcare manufacturing sites spread across 16 countries, employing around 7,000 staff. The Consumer Healthcare supply chain is diverse and includes the manufacturing and supply of OTC medicines, oral care, nutritional healthcare and smoking cessation products.

## Strategic Master Plan

The Strategic Master Plan (SMP) is a long-term programme of integrated changes to enhance competitiveness and productivity in Glaxo Wellcome manufacturing sites announced in October 1999. It is based around three interdependent initiatives – Manufacturing Excellence, Network Rationalisation and Procurement Excellence, applied across the whole network of manufacturing and supply locations.

The programme includes using LeanSigma tools and techniques to challenge current ways of working. As well as the forecast financial benefits this leads to improvements in areas such as reduced cycle time, increased productivity and improved delivery performance. SMP implementation is proceeding as planned for completion in 2003.

## Global Supply initiative

Global Supply Initiative (GSI) is a four year programme, announced in February 1999, to restructure the SmithKline Beecham supply network to align manufacturing strategy with business needs through network rationalisation and purchasing initiatives. Implementation is at an advanced stage, with 65 per cent of benefits delivered. Sites at Plelan, France; Camacari, Brazil; Toledo, Spain and Baranzate, Italy were sold during 2000.

## GlaxoSmithKline integration

The merger of Glaxo Wellcome and SmithKline Beecham manufacturing and supply organisations presents synergy opportunities in addition to the significant savings already forecast from the Glaxo Wellcome SMP and SmithKline Beecham GSI programmes. SMP and GSI implementation programmes will be aligned with integration related changes to deliver these synergies while maintaining security of supply.

## Vaccines

Vaccine production is located principally at Rixensart, Belgium and at Dresden, Germany.

## External suppliers

Procurement is a global function supporting all functions and areas of the GlaxoSmithKline business. Manufacturing is one of the largest areas with over £2 billion spend with external suppliers every year, including the purchase of active ingredients, chemical intermediates, part finished and finished products. GMS has taken appropriate steps to protect its supply chains from any disruption resulting from interrupted external supply through appropriate stock holding, contracting and alternative registered suppliers.

## Block Drug

The acquisition of Block Drug Company Inc in January 2001 has added seven further sites and over 1,450 employees to GMS, within the Consumer Healthcare Supply chain.

## Research and development – Pharmaceuticals

The global biological and pharmaceutical Research and Development (R&D) function in GlaxoSmithKline is responsible for the generation of information and the acquisition of knowledge required to discover, develop, register, commercialise and effectively market innovative prescription medicines, vaccines and delivery systems for the treatment and prevention of human disease.

Fundamental to this goal is a thorough understanding of the diseases under investigation, increasingly through original work in genetics and predictive medicine research. In addition to the work to create new medicines and vaccines, extensive efforts are made to gain a clear understanding of the unmet needs of patients and healthcare providers as a contribution to the overall direction of R&D.

In 2000 Glaxo Wellcome and SmithKline Beecham together invested over £2.4 billion in pharmaceuticals R&D.

Approximately 16,000 staff are involved in biological and pharmaceutical R&D activities, at more than 20 sites worldwide. These sites include:

- UK: Beckenham, Cambridge, Dartford, Greenford, Harlow, Stevenage, Tonbridge, Ware, Welwyn Garden City
- USA: Research Triangle Park, North Carolina; Philadelphia, Upper Merion and Upper Providence, Pennsylvania; Santa Clara and Palo Alto, California
- Belgium: Rixensart
- Canada: Mississauga
- France: Les Ulis, Rennes
- Italy: Verona, Milan
- Japan: Tsukuba Science City and Takasaki
- Spain: Madrid
- Switzerland: Geneva.

During 2000 a significant amount of work in R&D went into preparing plans and procedures for the optimal integration of key Glaxo Wellcome and SmithKline Beecham R&D processes, so that GlaxoSmithKline would be able to operate effectively and efficiently from day one of the merger. Despite the resources devoted to these activities, several significant new medicines were delivered on schedule to the markets.

### Product approvals and submissions

In 2000 approvals were received for a number of new medicines and vaccines as well as several significant new indications and formulations for existing products, as summarised in the table opposite.

A number of other approvals were also received during 2000. Notable among these were US approvals for *Malarone*, a combination of atovaquone and proguanil to treat and prevent malarial infections and for the paediatric use of *Relenza* to treat influenza. European and US approvals were also received for a 2mg chewable-dispersible tablet formulation of *Lamictal* for the treatment of paediatric epilepsy.

A number of significant regulatory submissions were made during 2000. In the USA these included:

- the first submission for GI198745, a 5-alpha reductase inhibitor for the treatment of benign prostatic hyperplasia, submitted to the FDA in late December 2000
- a submission for a non-CFC metered dose inhaler formulation of *Advair* for asthma
- a submission for the use of *Avandia* in combination with insulin, for the treatment of type 2 diabetes
- a revised submission for an extra strength formulation of the antibiotic *Augmentin* for use in children
- a submission for a sustained release formulation of the antibiotic *Augmentin* for use in adults (both Europe and USA)
- a submission for the adolescent use of intranasal *Imitrex* for the treatment of migraine
- submissions for *Seroxat/Paxil* for the treatment of Generalised Anxiety Disorder and Post-Traumatic Stress Disorder
- submissions for *Infanrix PeNta 5*, a combined diphtheria, tetanus, pertussis, polio and hepatitis B paediatric prophylactic vaccine
- a submission for *Twinrix*, a combined hepatitis A and B prophylactic vaccine
- in addition, the BLA for *Bexxar*, a novel treatment for non-Hodgkins lymphoma, was re-submitted to the FDA in September and is now under priority review.

In Europe significant regulatory submissions in 2000 included:

- a once-daily dosing regimen for *Epivir* for HIV infections
- the fluoroquinolone antibiotic *Factive*
- a malaria prophylaxis indication for *Malarone*.

The product development pipeline, set out on pages 16–19, shows considerable breadth and depth.

During 2000 several discovery projects were progressed through non-clinical safety testing and into early (Phase I) clinical development. These are listed in the table opposite.

These compounds are now undergoing rigorous non-clinical, clinical and commercial assessments leading to 'proof of concept' decisions over the next 12–18 months.

In addition to those compounds identified in the table opposite, the following compounds were also in-licensed during 2000:

- GW650250, a mixed monoamine re-uptake inhibitor in Phase II development, in-licensed from NeuroSearch in January 2000
- SB596168, a selective RNA polymerase inhibitor in Phase II development, for the treatment of solid tumours, in-licensed from Taiho in July 2000
- repifermin, keratinocyte growth factor-2 in Phase II development, for wound care, mucositis and the treatment of inflammatory bowel disease, in-licensed from Human Genome Sciences in October 2000
- SB683698, a dual alpha4 integrin antagonist entering Phase II development, for the treatment of a range of inflammatory diseases including asthma, rheumatoid arthritis, inflammatory bowel disease and multiple sclerosis, in-licensed from Tanabe in December 2000.

In February 2001 GlaxoSmithKline completed two further in-licensing agreements. The first was with E Merck for SB 659746, a SSRI + 5HT1a receptor partial agonist in Phase II development for the treatment of depression and other mood disorders. The second was with Sepsicure for GR270773, a phospholipid anti-endotoxin emulsion entering Phase II development for the treatment of sepsis.

### Products delivered to market

Product	Approval date (Country/Region)	Description
<i>Advair</i>	August 2000 (USA)	A dry powder combination formulation of the long-acting bronchodilator salmeterol and the glucocorticoid anti-inflammatory agent fluticasone in the <i>Diskus</i> delivery system for the treatment of asthma
<i>Agenerase</i>	October 2000 (Europe)	A potent protease inhibitor for the treatment of HIV infections
<i>Avandia</i>	July 2000 (Europe)	A selective (PPAR agonist) oral combination treatment for type 2 diabetes in specific sub-groups of patients in combination with metformin or sulphonylurea
<i>Flovent Diskus</i>	September 2000 (USA)	A dry powder formulation of fluticasone in the multi-dose <i>Diskus</i> delivery system for the treatment of asthma
<i>Infanrix HeXa</i>	October 2000 (Europe)	A conjugated, recombinant paediatric vaccine for diphtheria, tetanus, pertussis, hepatitis B, inactivated polio prophylaxis and <i>H. influenzae</i> type B prophylaxis
<i>Infanrix PeNta</i>	October 2000 (Europe)	A recombinant paediatric vaccine for diphtheria, tetanus, pertussis, hepatitis B, and inactivated polio prophylaxis
<i>Seretide</i>	June 2000 (UK, as <i>Viani</i> ) December 2000 (Europe)	A non-CFC metered dose inhaler formulation of the long-acting bronchodilator salmeterol and the glucocorticoid anti-inflammatory agent fluticasone for the treatment of asthma
<i>Seroxat</i>	September 2000 (Europe)	A selective serotonin reuptake inhibitor for the treatment of Post-Traumatic Stress Disorder
<i>Seroxat</i>	November 2000 (Europe)	A selective serotonin reuptake inhibitor for the treatment of Generalised Anxiety Disorder
<i>Trizivir</i>	November 2000 (USA) January 2001 (Europe)	A combination of three reverse transcriptase inhibitors in a single tablet that will significantly reduce the 'pill burden' and improve compliance for patients with HIV infections

### Compounds progressed into Phase I clinical development

Compound	Mechanism	Indication
GW473178	thrombin inhibitor	atrial fibrillation and venous thrombosis
GW501516	peroxisome proliferator-activator receptor agonist	dyslipidaemia
GW660511	ACE/NEP inhibitor	hypertension (in-licensed from Zambon in October 2000)
SB 435495	Lp-PLA2 inhibitor	atherosclerosis
SB 207266	5HT receptor antagonist	atrial fibrillation
SB 273005	osteoclast vitronectin receptor antagonist	osteoporosis & rheumatoid arthritis
SB 418790	beta3 adrenergic receptor agonist	type 2 diabetes and obesity (in-licensed from Asahi in February 2000)
GW406381	second generation COX-2 inhibitor	inflammatory pain
GW468816	glycine receptor antagonist	migraine prophylaxis & smoking cessation
SB 641257	reversible proton pump inhibitor	gastro-esophageal reflux disease (in-licensed from Yuhan in October 2000)
GW572016	Erb-B2 & EGRF dual kinase inhibitor	solid tumours
GW150013	CCK-B receptor antagonist	anxiety disorders
GW597599	NK1 receptor antagonist	depression
Vaccines	conjugated vaccine	prophylaxis against <i>S. pneumoniae</i> infections in the elderly population
	recombinant vaccine	prophylaxis against hepatitis E
	subunit vaccine	prophylaxis against influenza with new delivery method

### Discontinuations

Following a request from the FDA, *Lotronex*, a treatment for irritable bowel syndrome, was voluntarily withdrawn from the US market in November 2000. This step was taken after in-depth discussions with the FDA about the interpretation of data relating to gastro-intestinal side effects which have occurred among patients treated with the product. These have included rare reports of fatalities, although no causal relationship with *Lotronex* has been established. Regulatory submissions in the rest of the world have now also been withdrawn.

The final analysis of data from the second of two Phase III clinical trials with GV150526, a glycine antagonist for the acute treatment of stroke, demonstrated no difference in clinical outcome from that seen with placebo and further work with this product has now been stopped. In addition, development of lotrafiban, an oral platelet aggregation inhibitor was stopped because of concerns over the safety of the compound.

## Product development pipeline – as published in February 2001

## Key

<b>MAA</b>	Marketing authorisation application (EU)
<b>NDA</b>	New drug application (USA)
<b>*</b>	New indications and line extensions for marketed product
<b>(v)</b>	Vaccine
<b>(p)</b>	Pharmaccine
<b>S</b>	Date of first submission to regulatory agency
<b>A</b>	Date of first regulatory approval (for MAA, this is the first EU approval date)
<b>AL</b>	Approvable letter
<b>†</b>	Label update

<b>Phase I</b>	Evaluation of clinical pharmacology, usually conducted in volunteers
<b>Phase II</b>	Determination of dose and initial evaluation of efficacy, conducted in a small number of patients
<b>Phase III</b>	Large comparative study (compound versus placebo and/or established treatment) in patients to establish clinical benefit and safety

Compound	Type	Indication	Phase	Estimated filing dates	
				MAA	NDA
<b>Anti-microbials &amp; Host Defence</b>					
SB 275833	bacterial protein synthesis inhibitor (BPSI)	prevention of recurrent sinusitis	I		
SB 249417	anti-Factor IX monoclonal antibody	severe sepsis & septic shock (also stroke)	I		
<i>Factive</i>	broad spectrum fluoroquinolone antibiotic	respiratory tract infections – i.v. formulation	III	2003	2003
<i>Factive</i>	broad spectrum fluoroquinolone antibiotic	respiratory & urinary tract infections – oral formulation	Submitted	S:Feb00	S:Dec99
<i>Bactroban</i>	nasopharyngeal BPSI	prevention of recurrent sinusitis	II		
<i>tafenoquine</i> (SB 252263)	8-aminoquinoline	malaria prophylaxis (adults)	III	2002	2002
<i>Augmentin SR</i>	beta lactam antibiotic	respiratory tract infections (incl. penicillin-resistant <i>S. pneumoniae</i> ) – modified release formulation	Submitted	S:Dec00	S:Dec00
<i>Augmentin ES</i>	beta lactam antibiotic	acute otitis media (incl. penicillin-resistant <i>S. pneumoniae</i> ) – paediatric high-dose suspension	Submitted	N/A	S:Oct97
<i>Malarone</i>	electron transport system inhibitor	malaria treatment & prophylaxis	Approved	S:Sep00	A:Jul00
<b>Anti-virals</b>					
GR270773	phospholipid anti-endotoxin emulsion	sepsis	II		
<i>Ziagen</i>	reverse transcriptase inhibitor	HIV infection – in combination with Epivir	II	2003	2003
GW433908	protease inhibitor; Agenerase pro-drug	HIV infection	III	2002	2002
<i>Epivir</i>	reverse transcriptase inhibitor	HIV infection – once daily dosing	Submitted	S:Sep00	2001
<i>Trizivir</i>	Epivir/Retrovir/Ziagen combination tablet	HIV infection	Approved	A:Jan01	A:Nov00
<i>Zeffix</i>	reverse transcriptase inhibitor	paediatric hepatitis B	III	2001	2001
<i>Valtrex/Zelitrex</i>	nucleoside analogue	cold sores	III	N/A	2001
<i>Valtrex/Zelitrex</i>	nucleoside analogue	HSV suppression in immunocompromised patients	III	N/A	2002
<i>Valtrex/Zelitrex</i>	nucleoside analogue	prevention of HSV transmission	III	2002	2002
<i>Relenza</i>	neuraminidase inhibitor	influenza prophylaxis	III	2001	2001
<i>Relenza</i>	neuraminidase inhibitor	influenza treatment in patients with asthma/COPD†	III	2001	2001
<b>Cardiovascular &amp; Urogenital</b>					
GW409544	PPAR alpha/gamma dual agonist	dyslipidaemia	I		
GW473178	thrombin inhibitor	atrial fibrillation & venous thrombosis	I		
GW501516	PPAR agonist	dyslipidaemia	I		
GW660511	ACE/NEP inhibitor	hypertension	I		
SB 223412	tachykinin (NK3) receptor antagonist	urinary incontinence (also COPD)	I		
SB 249417	anti-Factor IX monoclonal antibody	stroke (also severe sepsis & septic shock)	I		
SB 424323	indirect thrombin inhibitor	atrial fibrillation & stroke prevention	I		
SB 435495	Lp-PLA2 inhibitor	atherosclerosis	I		
SB 207266	5HT <sub>4</sub> receptor antagonist	atrial fibrillation	II		
SB 237376	potassium-calcium channel blocker	cardiac arrhythmia	II		
enrasentan (SB 217242)	endothelial cell receptor antagonist	congestive heart failure	II	2004	2004
telmisartan	angiotensin II antagonist	hypertension – in combination with hydrochlorothiazide	III	2001	N/A
GI198745	5-alpha reductase inhibitor	benign prostatic hyperplasia (also alopecia)	Submitted	2001	S:Dec00
GI198745	5-alpha reductase inhibitor	alopecia (also BPH)	II		
<i>Tranilast</i>	endothelial cell proliferation/migration inhibitor	restenosis	III	2001	2001
<i>Coreg</i>	beta blocker	severe heart failure	III	N/A	2001

Compound	Type	Indication	Phase	Estimated filing dates	
				MAA	NDA
<b>Metabolic &amp; Musculoskeletal</b>					
repifermin	Keratinocyte Growth Factor-2	wound care & IBD	II		
GI181771	CCK-A receptor agonist	obesity & gallstone prophylaxis	I		
GW427353	beta3 adrenergic receptor agonist	type 2 diabetes & obesity	I		
SB 418790	beta3 adrenergic receptor agonist	type 2 diabetes & obesity	I		
GI262570	PPAR gamma agonist	type 2 diabetes	III	2003	2003
<i>Avandia</i>	insulin action enhancer	type 2 diabetes – in combination with insulin	Submitted		S:Feb00
SB 273005	osteoclast vitronectin receptor antagonist	osteoporosis (also rheumatoid arthritis)	I		
<b>Neurology &amp; Gastro-intestinal</b>					
GW273293	sodium channel inhibitor	epilepsy (also bipolar disorder)	II		
GW406381	Cox-2 inhibitor (second generation)	pain including inflammatory pain	I		
GW468816	glycine receptor antagonist	migraine prophylaxis (also smoking cessation)	I		
SB 204269	anticonvulsant	epilepsy	II		
SB 271046	5HT <sub>6</sub> receptor antagonist	cognitive impairment	I		
SB 641257 (YH 1885)	reversible proton pump antagonist	gastro-esophageal reflux disease	I		
<i>ReQuip</i>	non-ergot dopamine agonist	Parkinson's disease – controlled release formulation	II	2003	2003
nabumetone Q	non-steroidal anti-inflammatory	osteoarthritis & pain	III	2002	2002
<i>Imigran/Imitrex</i>	5HT <sub>1</sub> agonist	migraine – needle-free injection formulation	II	2003	2003
<i>Imigran/Imitrex</i>	5HT <sub>1</sub> agonist	adolescent migraine – nasal formulation	Submitted	S:Feb00	S:Dec99
<i>Naramig/Amerge</i>	5HT <sub>1</sub> agonist	menstrual migraine prophylaxis	III	2001	2001
<b>Oncology</b>					
GW572016	Erb-B2 and EGFR dual kinase inhibitor	solid tumours	I		
SB 251353	CXC chemokine	prevention of chemotherapy-induced cytopenias & stem cell mobilisation	I		
SB 408075	tumour activated pro-drug (maytansine-antibody conjugate)	colorectal cancer – second line therapy	I		2004
SB 596168	selective RNA polymerase inhibitor	solid tumours	II		
<i>Hycamtin</i>	topo-isomerase I inhibitor	colorectal cancer – second line therapy	II	2004	2004
<i>Hycamtin</i>	topo-isomerase I inhibitor	small cell & non-small cell lung cancer – first line therapy	II	2004	2004
<i>Hycamtin</i>	topo-isomerase I inhibitor	myelodysplastic syndrome	III	2001	2001
<i>Hycamtin</i>	topo-isomerase I inhibitor	small cell lung cancer – oral second line therapy	III	2002	2002
<i>Hycamtin</i>	topo-isomerase I inhibitor	ovarian cancer – first line therapy	III		2004
<i>Bexxar</i>	<sup>131</sup> I radiolabelled anti-B1 monoclonal antibody	non-Hodgkin's lymphoma	Submitted	N/A	S:Sep00
<b>Psychiatry</b>					
GW468816	glycine receptor antagonist	smoking cessation (also migraine)	I		
GW150013	CCK-B receptor antagonist	anxiety disorders	II		
GW597599	NK1 receptor antagonist	depression	I		
SB 243213	5HT <sub>2c</sub> receptor antagonist	depression	I		
SB659746A (EMD68843)	SSRI + 5HT <sub>1a</sub> receptor partial agonist	depression	II		2004
GW320659 (1555U88)	noradrenaline re-uptake inhibitor	attention deficit hyperactivity disorder	II		2004
GW650250	mixed monoamine reuptake inhibitor	depression	II		
<i>Seroxat/Paxil</i>	selective serotonin reuptake inhibitor	depression – dispersible tablets	III	2002	TBD
<i>Seroxat/Paxil CR</i>	selective serotonin reuptake inhibitor	premenstrual dysphoric disorder – controlled release formulation	III	TBD	2002
<i>Seroxat/Paxil</i>	selective serotonin reuptake inhibitor	generalised anxiety disorders	Approved	A:Nov00	S:Apr00
<i>Seroxat/Paxil</i>	selective serotonin reuptake inhibitor	post-traumatic stress disorder	Approved	A:Sep00	S:Jul00

Compound	Type	Indication	Phase	Estimated filing dates	
				MAA	NDA
<b>Respiratory &amp; Inflammation</b>					
GW328267	adenosine A2 agonist	asthma & COPD	I		
fluticasone/salmeterol	beta2 agonist/inhaled corticosteroid	rhinitis – intranasal combination product	I	2003	2003
SB 223412	tachykinin (NK3) receptor antagonist	COPD (also urinary incontinence)	I		
SB 683698 (TR14035)	dual alpha4 integrin antagonist (VLA4)	asthma & rheumatoid arthritis	II		
SB 273005	osteoclast vitronectin receptor antagonist	rheumatoid arthritis (also osteoporosis)	I		
Ariflo	PDE IV inhibitor	asthma	II		
Ariflo	PDE IV inhibitor	COPD	III	TBD	2002
mepolizumab (SB240563)	anti-IL 5 monoclonal antibody	asthma – steroid sparing	II		
Flovent	inhaled corticosteroid	asthma – once daily dosing	III	N/A	2001
Flixotide/Flovent	inhaled corticosteroid	COPD	Approved	A:Sep99	2001
<b>Non-CFC Metered Dose Inhaler propellants (GR106642)</b>					
Serevent	beta2 agonist	asthma & COPD	III	2003	2003
Flixotide/Flovent	inhaled corticosteroid	asthma & COPD	Approved	A:Apr97	2001
Ventolin	beta2 agonist	asthma & COPD	Approved	A:Jun97	AL:Jan01
Seretide/Advair	beta2 agonist/inhaled corticosteroid	asthma	Approved	A:Jun00	S:Dec00
<b>Diskus/Accuhaler (dry powder inhaler)</b>					
Seretide/Advair	beta2 agonist/inhaled corticosteroid	COPD	III	2001	2001
Seretide/Advair	beta2 agonist/inhaled corticosteroid	paediatric asthma	Approved	A:Sep98	2002
Seretide/Advair	beta2 agonist/inhaled corticosteroid	asthma – first line therapy	III	2001	2001
Serevent	beta2 agonist	COPD	III	2001	2001
Ventolin	beta2 agonist	asthma & COPD	Approved	A:Dec95	AL:Jul00
<b>Hepatitis Vaccines (child/adol.)</b>					
Twinrix 2 doses	recombinant	combined hepatitis A and B prophylaxis (child/adol.)	III	2001	2002
Twinrix 3 doses (US)	recombinant	combined hepatitis A and B prophylaxis (adults)	Submitted	N/A	Submitted
Extra strength hepatitis B	recombinant	extra strength hepatitis B prophylaxis (poor/non-responders)	III	2001	TBD
Hepatitis E	recombinant	hepatitis E prophylaxis	I		
<b>Paediatric Vaccines</b>					
Infanrix PeNta-HepB-IPV	recombinant	diphtheria, tetanus, pertussis, hepatitis B and inactivated polio prophylaxis	Approved	Approved	Submitted
Infanrix HeXa-Hep B-IPV/Hib	conjugated/recombinant	diphtheria, tetanus, pertussis, hepatitis B, inactivated polio prophylaxis and Haemophilus influenzae type B prophylaxis	Approved	Approved	TBD
S. pneumoniae paediatric	conjugated	S. pneumoniae disease prophylaxis for children	III	2003	
MMR – varicella	live attenuated	measles, mumps, rubella and varicella prophylaxis	III	2002	TBD
Rotarix	live attenuated – oral	rotavirus prophylaxis	II	2004	2004
N. meningitidis A/C	conjugated	meningitis prophylaxis	II	2004	
Meningitis B (Cuba)	subunit	meningitis B prophylaxis	II		TBD
<b>Other Vaccines</b>					
Boostrix	subunit	adolescent/adult booster for diphtheria, tetanus and pertussis	Approved	Approved	2002
Epstein-Barr Virus	recombinant	EBV prophylaxis	II		
Malaria	recombinant	malaria prophylaxis	II		
Human papillomavirus	recombinant	prophylaxis of HPV infections	II		
Simplrix	recombinant	genital herpes prophylaxis	II		
New influenza	subunit	influenza prophylaxis (new delivery)	I	2004	
HIV	recombinant	HIV prophylaxis	I		
S. pneumoniae elderly	conjugated	S. pneumoniae disease prophylaxis	I		
<b>Pharmaccines for Treatment of Chronic Infectious Diseases or Cancer</b>					
SB M00026	recombinant	treatment of chronic hepatitis B	II		
SB 249553	recombinant	treatment of lung cancer/melanoma	II		
GW419458	DISC	treatment of genital herpes	II		
GW/PowderJect	recombinant	hepatitis B treatment	I		

## Summary of pipeline

Phase I	Phase II	Phase III	Filed
SB 275833	<i>Bactroban*</i>	<i>Factive*</i>	<i>Factive</i>
SB 249417	<i>Ziagen*</i>	tafenoquine (SB 252263)	<i>Augmentin*</i>
GW409544	SB 207266	GW433908	<i>Malarone*</i>
GW473178	SB 237376	<i>Zeffix*</i>	<i>Epivir*</i>
GW501516	enrasentan (SB 217242)	<i>Valtrex/Zelitrex*</i>	<i>Trizivir</i>
GW660511	GI198745	<i>Relenza*</i>	GI198745
SB 223412	<i>ReQuip*</i>	telmisartan*	<i>Imigran/Imitrex*</i>
SB 424323	<i>Imigran/Imitrex*</i>	<i>Tranilast</i>	<i>Bexxar</i>
SB 435495	<i>Hycamtin*</i>	GI262570	<i>Seroxat/Paxil*</i>
GI181771	GW320659 (1555U88)	nabumetone Q*	<i>Flixotide/Flovent*</i>
GW427353	GW650250	<i>Naramig/Amerge*</i>	<i>Ventolin*</i>
SB 418790	mepolizumab (SB 240563)	<i>Hycamtin*</i>	<i>Seretide/Advair*</i>
SB 273005	GR270773	<i>Seroxat/Paxil*</i>	<i>Avandia*</i>
GW406381	GW273293	<i>Ariflo</i>	<i>Twinrix 3 doses (v)</i>
GW468816	SB 596168	<i>Flovent*</i>	<i>Infanrix PeNta – Hep B-IPV (v)</i>
SB 271046	SB 683698 (TR14035)	<i>Serevent*</i>	<i>Infanrix HeXa – Hep B-IPV/Hib (v)</i>
SB 641257 (YH1885)	<i>Ariflo</i>	<i>Seretide/Advair*</i>	<i>Boostrix (v)</i>
GW572016	repifermin	<i>Coreg*</i>	
SB 251353	SB 204269	<i>Twinrix 2 doses (v)</i>	
SB 408075	GW150013	Extra strength Hepatitis B (v)	
GW597599	SB 659746A (EMD 68843)	<i>S pneumoniae (v)</i>	
SB 243213	N. Meningitidis A/C (v)	MMR-varicella (v)	
GW328267	<i>Rotarix (v)</i>		
fluticasone/salmeterol*	Epstein-Barr virus (v)		
SB 223412	Malaria (v)		
Hepatitis E (v)	Human papilloma virus (v)		
New Influenza (v)	<i>Simplirix (v)</i>		
HIV (v)	Meningitis B (Cuba) (v)		
<i>S. pneumoniae (v)</i>	SB-M00026 (p)		
GW/PowderJect technology (p)	SB 249553 (p)		
	GW419458 (p)		

The content of the drug development portfolio will change over time as new compounds progress from discovery to development and from development to the market. Owing to the nature of the drug development process, it is not unusual for some compounds, especially those in early stages of investigation, to be terminated as they progress through development.

For competitive reasons, new projects in pre-clinical development have not been disclosed and some project types may not have been identified.

### R&D processes

Much of the process re-design work conducted by Glaxo Wellcome and SmithKline Beecham in earlier years has now been fully implemented within R&D. In both organisations the focus during 2000 was on the consolidation of these new processes within a unified GlaxoSmithKline organisation. Considerable effort has gone into aligning quantitative performance measures with the new processes, so that the productivity of R&D can be effectively monitored in terms of the value added to the overall business. There are already benefits from these initiatives and many high quality new molecules are now in early clinical assessment. There is also good evidence from independent benchmarking that both Glaxo Wellcome and SmithKline Beecham have some of the fastest product development times within the industry.

The learnings from previous re-design work have been brought into full effect within GlaxoSmithKline so that the traditional functional barriers between Research, Development, Commercial and Manufacturing no longer exist within the organisation. Several key multi-disciplinary matrix organisations have been created to ensure continuity across the whole discovery to launch process. These include:

- Centres of Excellence for Drug Discovery to effectively integrate late-stage research and early-stage development
- New Product Development to integrate clinical, regulatory and commercial activities
- New Product Supply to align the scale-up and subsequent manufacture of the physical product.

These are described in more detail below.

There is now a clear focus on a unified approach to the generation and demonstration of commercial product value to customers. These customers include patients, healthcare professionals, budget holders and regulators, and each population has its own needs in terms of assessing the value of a new product. R&D is now positioned to ensure that, as well as developing the right products, it also generates the right information about these products. Increasingly this means not only safety, efficacy and quality information but also evidence of product value through measures such as overall reductions in healthcare utilisation, increasing length or quality of life and increased workplace productivity.

### Early drug discovery and new technologies

Over the past five years both Glaxo Wellcome and SmithKline Beecham invested heavily in establishing and integrating new technologies that will harness the full therapeutic potential offered by the elucidation of the human genome. High-throughput (HT) technologies such as HT gene sequencing, HT chemistry and HT screening are now fully established and mean that GlaxoSmithKline has substantial resources to identify significant numbers of novel molecular targets, make structurally diverse compounds and efficiently screen these compounds against such targets. In addition, HT biology technologies will help us determine the most relevant therapeutic applications of new drugs modulating pathological mechanisms that may underpin several different diseases. These technologies are the cornerstone of activities within Genetics and Discovery Research and are designed to provide a steady stream of validated drug targets and suitable series of lead compounds to the newly-created Centres of Excellence for Drug Discovery.

Complementary to these new technologies has been the work carried out in Glaxo Wellcome over the past three years to develop ways of associating disease with a patient's genetic make up. GlaxoSmithKline now aims to identify the genes most relevant to common diseases with large unmet medical needs, such as asthma, non-insulin dependent diabetes, migraine, osteoarthritis, metabolic syndrome, depression, chronic obstructive pulmonary disease, early onset heart disease and Alzheimer's disease. To further these initiatives, large international collaborative studies have now been initiated for six of these diseases. These networks bring together clinicians and other experts in the diagnosis of these diseases with centres skilled in analysing genetic and clinical data.

Many of the applications of genetic science to healthcare will be driven by single nucleotide polymorphism (SNP) high-density mapping. This new technology can be likened to a road map, with SNPs acting as signposts that tell scientists where they are on the genome. Both Glaxo Wellcome and SmithKline Beecham were members of The SNP Consortium launched in April 1999. The consortium, which comprises 12 pharmaceutical and technology companies, five academic centres and The Wellcome Trust, is producing an ordered high-density SNP map of the human genome. This work has progressed ahead of schedule, and the data are being placed in the public domain.

### Centres of Excellence for Drug Discovery

Both Glaxo Wellcome and SmithKline Beecham have experimented with a number of ways to manage drug discovery in order to optimise the progression of new medicines. During 2000, it was agreed that, for GlaxoSmithKline, a novel approach to the integration of late-stage discovery and early-stage development – the critical drug discovery phase – would be adopted. This approach is based on a sound understanding of the creative and entrepreneurial environment needed to enhance the scientific knowledge and expertise required to discover new drugs of proven value.

Six Centres of Excellence for Drug Discovery (CEDDs) have been created in GlaxoSmithKline, each focusing on specific disease areas, as summarised below:

- **Anti-bacterials & Host Defence**, centred in Upper Providence (USA)
- **Cardiovascular, Cancer and Urogenital**, centred in Upper Merion (USA)
- **Metabolic, Musculoskeletal & Viral Diseases**, centred in Research Triangle Park (USA)
- **Neurology**, centred in Harlow (UK)
- **Psychiatry**, centred in Verona (Italy)
- **Respiratory, Inflammation and Respiratory Pathogens**, centred in Stevenage (UK).

CEDDs have the autonomy to select new compounds from either internal or external sources. Each CEDD is responsible for selecting the optimal candidate from a series of similar chemical compounds and for ensuring this candidate is safe in animal models and can be developed from a technical perspective. Once this is achieved, the CEDDs are responsible for conducting the pre-clinical and early clinical work required to prove that the compound is safe and efficacious in patients – the proof-of-concept or provision-of-confidence decision point. Following a thorough senior review of the information generated, a decision is then made to progress the compound into late stage drug development where the necessary large-scale clinical trials are conducted to successfully register and commercialise the product.

### New product development

To provide focus for the development and commercialisation process, which must proceed in unison, all the major functional components, Medical, Regulatory and Product Strategy, have been integrated into one management organisation. Late-stage product development in both Glaxo Wellcome and SmithKline Beecham was organised by therapeutic areas and eight such areas have been identified for GlaxoSmithKline:

- Anti-microbials & Host Defence
- Anti-virals
- Cardiovascular & Urogenital
- Metabolic & Musculoskeletal
- Neurology & Gastro-intestinal
- Oncology
- Psychiatry
- Respiratory & Inflammation.

Worldwide vaccines R&D is conducted by the Biologicals Division, located principally at Rixensart, Belgium. It is managed independently from pharmaceuticals development. However, essentially similar approaches to development are adopted for both vaccines and prescription medicines.

The eight pharmaceutical therapy areas and vaccines development are managed by cross-functional matrix teams responsible for maximising the worldwide development opportunities for each product. The teams work to ensure that there is alignment between regional marketing needs and the clinical and commercial information generated for a new product as it is developed. The teams also collaborate at an early stage with integrated technical development and manufacturing functions to ensure rapid, effective launch and delivery of the product.

By increasingly incorporating genetic research into clinical trials of new and innovative medicines, GlaxoSmithKline will enable healthcare providers to prescribe medicines more accurately based on a patient's predicted response profile (in terms of both drug safety and efficacy). In addition, genetic research will enable a better understanding of the causes of common diseases. Many such diseases arise through complex interactions between a number of gene variants and environmental factors. Identifying the genes that predispose patients to a particular disease and understanding their role in disease progression will lead to the identification of new ways to intervene in these diseases. This understanding will also provide greater confidence that existing drug targets are relevant to the disease.

### New product supply

The efficient delivery and rapid worldwide uptake of our new products are closely linked to their ease of manufacture. Such issues as scale-up and manufacturing technology are considered at an early stage of product development, so that the process of moving from small-scale production of experimental materials for early clinical studies through to large-scale industrial manufacturing for product supply can be fast and efficient. This is the responsibility of 'New Product Supply', a partnership between R&D preclinical staff and Global Manufacturing & Supply. The partnership ensures that the Development organisation delivers a product that has already been optimised in terms of large-scale commercial manufacturing.

### Animals and research

For ethical, scientific and legal reasons, animal experimentation remains essential in the discovery and subsequent safety evaluation of new medicines. GlaxoSmithKline policy is to replace animal experiments where at all possible and use alternatives such as *in vitro* cell culture or computer modelling techniques. If animal experiments are unavoidable, our approach is to seek to reduce the number of animals used, through improved techniques and methodology. Examples of this approach include:

- the use of transgenic animals bred with genetic changes that better model human disease
- work to use non-invasive imaging to understand pathological processes and the effects of experimental drugs in far fewer animals than are required by traditional *in vivo* pharmacological methods
- the development of more sensitive assay methodologies to reduce the number of animals required to assess the effects of novel drug candidates.

Additionally, every effort is made to minimise discomfort in those animals used for such studies.

### Research and development – Consumer Healthcare

The principal centres for Consumer Healthcare research and development are in the UK and in the USA. Consumer Healthcare liaises closely with Pharmaceuticals to ensure that commercial opportunities in the OTC field are identified as quickly as possible. GlaxoSmithKline also pursues, whenever possible, opportunities to switch prescription products to OTC products.

## Operating resources

### Intellectual property – Pharmaceuticals

The table below sets out patent expiry dates for the active ingredients in significant GlaxoSmithKline products.

Therapeutic area	Product	Active ingredient(s)	Patent expiry dates for active ingredient(s) in major countries
<b>CNS disorders</b>	<i>Seroxat/Paxil</i>	paroxetine	During or after 2006
	<i>Wellbutrin</i>	bupropion	Basic compound patents have expired. Formulation patents will expire during or after 2013
	<i>Imigran/Imitrex</i>	sumatriptan	During or after 2003 (USA 2006/8)
	<i>Naramig/Amerge</i>	naratriptan	During or after 2010
	<i>Lamictal</i>	lamotrigine	During or after 2005
	<i>Requip</i> <i>Zyban</i>	ropinirole bupropion	During or after 2007 Basic compound patents have expired. Formulation patents will expire during or after 2013
<b>Respiratory</b>	<i>Flixotide/Flovent</i>	fluticasone propionate	During or after 2003
	<i>Serevent</i>	salmeterol xinafoate	During or after 2003 (USA 2008)
	<i>Seretide/Advair</i>	fluticasone propionate & salmeterol xinafoate	Patents covering the combination will expire during or after 2010
	<i>Flixonase/Flonase</i>	fluticasone propionate	During or after 2003
<b>Anti-bacterials</b>	<i>Augmentin</i>	co-amoxiclav	Basic compound patents have expired, with the exception of the USA (2017), France (2002) and Italy (2007)
	<i>Zinnat/Ceftin</i>	cefuroxime axetil	Patents to cefuroxime axetil per se have generally expired, although SPCs exist in Europe until 2002. Patents on the amorphous form of cefuroxime axetil will expire during or after 2003
	<i>Fortum/Fortaz</i> <i>Amoxil</i>	ceftazidime amoxicillin	Basic compound patents have expired Basic compound patents have expired
<b>Anti-virals</b>	<i>Combivir</i>	lamivudine + zidovudine	Patents on the combination of the two active ingredients will expire during or after 2012
	<i>Epivir</i>	lamivudine	During or after 2009
	<i>Retrovir</i>	zidovudine	Basic compound patents have expired. Patents on use in HIV infection will expire during or after 2005
	<i>Ziagen</i>	abacavir	During or after 2009
	<i>Agenerase</i>	amprenavir	During or after 2013
	<i>Valtrex</i>	valaciclovir	During or after 2009
	<i>Zovirax</i>	aciclovir	Basic compound patents have expired
	<i>Zeffix/Epivir-HBV</i> <i>Relenza</i>	lamivudine zanamivir	During or after 2009 During or after 2013
<b>Metabolic and gastro-intestinal</b>	<i>Avandia</i>	rosiglitazone	During or after 2013
	<i>Zantac</i>	ranitidine	Basic compound patents have expired.
<b>Oncology and emesis</b>	<i>Zofran</i>	ondansetron	During or after 2005. During or after 2006 for patents to its use in emesis

The patent position on Hepatitis vaccines (*Engerix* and *Havrix*) and on *Infanrix* and *LYMERix* is highly complex. GlaxoSmithKline is licensed under several US patents pertaining to *Engerix*, the latest of which expires in 2014. A recently granted US patent pertaining to *Havrix* expires in 2017. For *Infanrix* US patents expire during or after 2014. GlaxoSmithKline is licensed under a US patent covering *LYMERix* that will provide protection until 2014.

GlaxoSmithKline highly values its intellectual property and believes that its worldwide portfolio of patents and trade marks is of particular value.

Intellectual property includes patents, trade marks, registered designs and copyrights.

#### Patents

GlaxoSmithKline has obtained patents in many countries for the significant products discovered or developed throughout its R&D activities. Patent protection is available in the United States, Europe, Japan and most other significant markets for new active ingredients, as well as for pharmaceutical formulations, manufacturing processes and medical uses.

GlaxoSmithKline continues to have patent protection for one or more forms of most of its key pharmaceutical products in major markets and, in addition, either has obtained patents or anticipates that patent protection will be granted for the new drugs, which are in development. However, the absence of effective patent protection for pharmaceuticals in some developing countries continues to have an adverse effect on pharmaceutical companies, including GlaxoSmithKline.

GlaxoSmithKline is routinely engaged in disputes over its patented products and processes to protect its intellectual property rights (see Note 31 to the Financial statements 'Legal proceedings').

#### Trade marks

All GlaxoSmithKline's pharmaceuticals products are protected by registered trade marks in major markets, and GlaxoSmithKline pursues a policy of enforcing its trade mark rights vigorously against infringements and other unauthorised uses. These trade marks are used in many countries, although there may be local variations for each. For example, in the United States, the trade mark *Paxil* is used instead of *Seroxat* and *Advair* is used instead of *Seretide*.

Trade mark protection continues in some countries as long as a trade mark is used and renewed at appropriate times. GlaxoSmithKline's trade mark with respect to a pharmaceutical product generally assumes increasing importance when the patent for that product expires in a particular country.

#### Intellectual property – Consumer Healthcare

GlaxoSmithKline's Consumer Healthcare businesses are brand-oriented and the company considers its trademarks for these products to be of particular value. Consumer brands are protected by trademarks in the majority of the markets where these brands are sold, and GlaxoSmithKline vigorously protects these trademarks from infringement.

#### Information technology

Information technology plays three strategic roles in GlaxoSmithKline:

- it facilitates communication and access to information on a global basis
- it supports key business processes at the local, regional, functional and global levels
- it enables the transformation and extension of key business activities.

#### Support for the merger process

Information technology played a key part in providing the planning information for the merger, much of which was derived from the existing systems in Glaxo Wellcome and SmithKline Beecham. Of major importance was ensuring that the new company had the IT systems in place to function effectively as soon as the merger was complete. From the first day of GlaxoSmithKline, the 80,000 employees in 58 countries with e-mail accounts were able to contact their colleagues electronically. Employees could also use short codes for dialling between sites, search on-line phone directories, and access both companies' intranet sites. Cross-site links to key business applications were provided.

#### Global communications

The past year has seen major growth in the number of internal websites. These allow information to be shared across the company on a global basis and are supported by internal search engines analogous to those used externally on the Internet. The ability to provide shared access to information has enabled the growing use of 'virtual teams', that work collaboratively, spanning multiple geographies and time zones, often subject to stringent time constraints.

Information is also exchanged electronically with a broad array of suppliers, customers and partners. Hence, protection against unauthorised access to key systems, and the growing risks posed by computer viruses, is a major issue. Intruder detection software has been added to company firewalls and virus scanning has been implemented at the gateway, server and desktop levels. The separate approaches adopted by Glaxo Wellcome and SmithKline Beecham are being integrated in a common standard approach for GlaxoSmithKline.

#### Enhancing business performance

Virtually all GlaxoSmithKline's major business processes rely heavily on the use of information technology. Within R&D in both SmithKline Beecham and Glaxo Wellcome there have been major programmes to capture key information, at source, in electronic form and make it available wherever required. As a result of these efforts, it was possible to make a number of regulatory drug submissions during the past year solely in electronic form. New drug submissions can be 50,000 to 250,000 pages in size and the ability to avoid generating paper submissions gives rise to significant savings in time and cost.

As part of the project to implement standard systems for Manufacturing Resource Planning in Glaxo Wellcome, eight sites, seven in the UK and one in Jurong, Singapore, have been supported for the past year from a single system. Further along the supply chain, SmithKline Beecham introduced standard enterprise financial and commercial software into 108 locations. The ability to consolidate mission critical operations in this way reflects the growing availability and reliability of global data networks and ensures that common processes and standards are implemented across sites, in addition to providing lower operating costs.

Both Glaxo Wellcome and SmithKline Beecham have installed major systems in the USA to analyse commercially available prescribing data. By better understanding locally of how GlaxoSmithKline's products are used in the marketplace, it is possible to target promotional and detailing activities and measure the market response. Information from these systems is transmitted electronically to the field sales forces and their responses are then uploaded to the system. With the growing availability of the required technology and infrastructure, sales force automation systems are being deployed in most major commercial markets.

### Transforming and extending business activities

Insights gained from genomics and proteomics are transforming the way that disease targets are identified and validated. Information generated from a variety of external sources needs to be integrated with internally generated information in a rapid and flexible manner that relies heavily on information technology support. The analysis of these databases also requires significant amounts of processing power, taking full advantage of advances in computer technology.

### e-business

Both Glaxo Wellcome and SmithKline Beecham recognised the growing importance of e-business and had already put small dedicated teams in place. Web based interfaces to major customers have been implemented in the USA. Current projects span a broad range of key audiences including opinion leaders, healthcare professionals, patients and the public.

### GlaxoSmithKline people

The skills and intellect of GlaxoSmithKline employees are fundamental to the current and future success of the business. It is GlaxoSmithKline's human capital that maximises the potential of the Group's scientific, commercial and financial assets. The objective of human resources policy is to maintain the reputation of GlaxoSmithKline as an employer of choice: the role of Human Resources is to provide alignment between business strategy and people strategy.

### Performance and reward

The importance of people as an operating resource has to translate into employment practices that recognise the value of each individual. Compensation and benefit packages are designed to be enlightened, competitive and attuned to the local market.

Compensation includes both skill- and performance-based pay, contributing to retention of key skills and consistent recognition and reward of superior performance and accomplishment of business targets.

Alternative work schedules, such as flex-time, teleworking, adjusted work weeks, recognise that employees work best in an environment that integrates both their family and personal life.

### Communication and involvement

An extensive range of communications programmes stimulates involvement in GlaxoSmithKline goals and progress, including presentations of business results, Group-wide magazines, site newspapers, videos, recorded voice mail messages from senior executive officers and access to the GlaxoSmithKline intranet.

Share ownership schemes encourage participation as owners of the business, increasing awareness of short- and long-term business objectives.

### Diversity

Diversity is central to the effective deployment of the skills needed to compete in the modern global economy. The Group values diversity of opinion, perspective and background.

GlaxoSmithKline remains committed to employment policies which do not discriminate between potential or existing staff on the grounds of colour, race, ethnic and national origin, gender, marital status, religious beliefs or disability. In the UK, if an employee becomes disabled whilst in employment and, as a result, is unable to perform normal duties, every effort is made to offer suitable alternative employment and assistance with retraining.

### Training and development

Comprehensive training and development opportunities are available to all employees at all levels, including access to self-help computer-based training modules. Development planning is a key element in overall performance planning each year.

Executive and leadership development programmes have been designed to identify and prepare the key talent necessary for growing the business worldwide. In particular, these programmes develop skills identified as critical to future business success, such as entrepreneurship, partnering, cross-functional collaboration and global problem solving.

### Property, plant and equipment

GlaxoSmithKline has operating establishments in some 70 countries. The geographical spread of the Group's activities, and the headquarters' location in each country, are indicated in the list of Group companies (page 136). GlaxoSmithKline conducts research and development at more than 20 sites and manufactures product at more than 100 sites in 41 countries. Refer to 'Research and development – Pharmaceuticals' (page 14) and 'Manufacture and supply' (page 13).

GlaxoSmithKline has invested nearly £4 billion in its property, with a carrying value in the financial statements of £3 billion, with a further £3.5 billion at carrying value invested in plant and equipment. In 2000 GlaxoSmithKline invested £1 billion in new and renewal property, plant and equipment. Property is mainly held freehold. New investment is financed from existing Group liquid resources. The Group had at 31st December 2000 contractual commitments for future expenditure of some £300 million and operating lease commitments in 2001 of approximately £130 million.

GlaxoSmithKline's business is science-based, technology-intensive and highly regulated by governmental authorities. GlaxoSmithKline allocates significant financial resources to the renewal and maintenance of its property and plant to minimise risks of interruption of production and to achieve compliance with regulatory standards. The research and development and manufacture of active pharmaceutical ingredient require the use of chemicals and hazardous materials. GlaxoSmithKline observes stringent procedures and uses specialist skills to manage environmental risks from these activities. Environmental issues, sometimes dating from operations now modified or discontinued, are referenced under Environment, health and safety (page 25) and in Note 31 to the Financial statements.

GlaxoSmithKline believes that its facilities are adequate for its current needs. The integration of Glaxo Wellcome and SmithKline Beecham operations in 2001 and subsequently is likely to involve the rationalisation, and disposal, of a number of sites and properties.

## The business and the community

### Environment, health and safety

In keeping with GlaxoSmithKline's global quest to improve the quality of human life, environment, health and safety (EHS) issues are very important to the new company. The GlaxoSmithKline Vision for Environment, Health and Safety has been adopted and work is proceeding on agreeing the EHS policy. A corporate EHS function has been formed and is responsible for recommending policy and strategy, providing direction and support for significant issues. It will also develop standards appropriate to business needs.

The main task in 2001 will be to integrate programmes from both companies into new GlaxoSmithKline EHS programmes that take the best from both companies. In view of the similarities and the commitment of all managers and staff to high standards of EHS practice, it is expected that the merger will result in continued improvement in EHS performance. GlaxoSmithKline will monitor progress and report against a set of goals and targets that will be developed during 2001.

Further information on EHS in GlaxoSmithKline can be found in the EHS Review available from the Secretariat at the company's head office.

### EHS management system

Successful management of environment, health and safety has been a high priority for both Glaxo Wellcome and SmithKline Beecham. Both companies had global standards and guidelines on Environment, Health and Safety issues. These set key requirements for implementation of policy and programmes based on the management systems model of the International Standards Organisation (ISO). The GlaxoSmithKline EHS department will be evaluating the possibility of Group-wide ISO certification of the new EHS management system that will be put in place.

Glaxo Wellcome and SmithKline Beecham both performed audits to assess and report on implementation of corporate policy and performance against the established global standards. In 2000 the two companies performed over 57 audits in 26 countries including 19 contract manufacturing and key supplier audits.

### EHS awards

Both Glaxo Wellcome and SmithKline Beecham had internal award schemes designed to reward innovation and outstanding achievements in EHS management. Further information can be found in the EHS Review.

### Goals and targets

The broad goal for EHS in the new company is to integrate the best of each company into a combined EHS programme that will be recognised as a leader in the industry. In the first year the Group expects to develop EHS standards and a management system and start the process for company-wide ISO 14001 certification. The data that each company has collected will be analysed and evaluated to develop a baseline for the combined company with annual improvement targets through to 2005.

It is also intended to explore the impact of implementation of sustainable development principles in GlaxoSmithKline.

### Chlorofluorocarbons (CFCs)

As the world's leading provider of metered-dose-inhalers (MDIs) for the treatment of respiratory tract diseases, GlaxoSmithKline is currently changing the propellant in MDIs from CFCs to non-ozone depleting HFC 134a. *Ventolin* MDIs using the new propellant have been launched in 41 countries and *Flixotide* MDIs using HFC134a launched in 22 countries. The aim is to make the transition as smooth as possible so that doctors, nurses, pharmacists and most importantly, patients feel comfortable with, and continue to use, the reformulated products. In addition, sales of *Diskus*, the dry powder inhaler continue to grow and demonstrate the commitment to providing choice for healthcare providers and patients.

### Contract manufacturing

Because of the increasing use of external contract manufacturers and suppliers for supplying active ingredients, fine chemical intermediates and finished products, GlaxoSmithKline will continue to integrate EHS into contracts, audit contract manufacturers and key suppliers against GlaxoSmithKline EHS standards and measure their EHS performance to manage potential threats to supply chain security.

### Contaminated land

In the UK, statutory provisions for dealing with historically contaminated land have been introduced by virtue of Part IIA of the Environmental Protection Act 1990 (by insertion of Section 56 of the Environment Act 1995). A review has been carried out of all available data at 12 operational facilities in the UK to determine if any could be designated as contaminated land under the new regime. The review indicated that eight facilities are unlikely to be designated as contaminated land and that additional data was needed for the other four facilities. Further studies at these sites are being arranged to collect more data. In the USA in 2000, the Group remained actively involved in the resolution of 11 remedial sites, all of which are in mid to late stages of remediation.

More recent contaminated land issues include a site in the UK for which agreement has been reached with the local planners regarding demolition and remediation. Negotiations are currently underway to agree cleanup standards with the North Carolina State regulatory agency to remediate soil and groundwater contamination at two sites.

Provision has been made in the financial statements for estimated costs of remediation.

### Regulatory compliance

Although every effort is made to ensure full and effective legal compliance, an occasional event may result in permit or regulatory breaches. If they occur, they are taken very seriously and steps are taken to prevent any future occurrences.

### Major environmental improvement projects

The Ulverston antibiotics site in the UK is currently engaged in a £7 million project to upgrade the treatment of its site wastewater. At the Irvine, Scotland antibiotics facility, £8 million has been approved for the construction of a high temperature composting unit for waste sludge generated by the onsite wastewater treatment plant.

### Global community partnerships

GlaxoSmithKline recognises that corporate social responsibility in today's business environment requires innovative programmes to help build healthy and successful communities around the world.

By creating a blend of traditional philanthropy with major commitments to new partnerships in public health for the developing world, GlaxoSmithKline is working harder and more creatively than ever to enable people to do more, feel better and live longer.

The remit of GlaxoSmithKline's Global Community Partnerships encompasses some of the greatest challenges facing society and includes some of the most ambitious corporate citizenship projects ever embarked upon:

- efforts to tackle parasitic diseases such as malaria and lymphatic filariasis in the developing world and to combat the scourge of human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) in countries without the safety net of a state-funded healthcare system
- the challenge of empowering communities to affect their own social environments, both through traditional 'philanthropic' means and through innovative programmes designed to further strengthen those who are already expert in their particular field
- the management of an active programme of science education for children of all ages who live in the communities around major GlaxoSmithKline locations.

### HIV and AIDS

GlaxoSmithKline has provided further support for the existing UN-led programme to reduce Mother-to-Child Transmission of HIV in 25 developing countries.

Positive Action – the long-term international programme of HIV education and community care – launched a new initiative to increase the involvement of people living with HIV in support of the UN International Partnership Against AIDS in Africa.

In July 2000 GlaxoSmithKline was a principal sponsor of the 13th World AIDS Conference in Durban, South Africa, reinforcing the company's commitment to the fight against HIV/AIDS.

### Lymphatic Filariasis

In the third year of its global humanitarian programme to help eliminate lymphatic filariasis (LF, a disabling tropical disease also known as elephantiasis) GlaxoSmithKline donated over 34 million treatments of its antiparasitic drug albendazole to more than 20 developing world countries in 2000.

It is estimated that GlaxoSmithKline will provide about five billion treatments of albendazole over the next 20 years in the fight to break transmission of LF, a parasitic disease that is spread by mosquitoes. To prevent the disease, the World Health Organisation advises that albendazole is co-administered with either diethylcarbamazine (DEC) or ivermectin as a single annual treatment for four to six years to entire endemic communities.

GlaxoSmithKline also actively participates in the LF Global Alliance – a coalition of GlaxoSmithKline, the World Health Organisation and some 30 public, private and academic institutions and the Ministries of Health in the 80 endemic countries.

### Malaria

GlaxoSmithKline is working in partnership with Roll Back Malaria and other international and national stakeholders to develop and implement innovative and sustainable plans to reduce suffering and deaths from malaria.

The company has been undertaking pilot programmes in Kenya and Uganda to assess the feasibility of using donations of its product *Malarone*. In order to preserve the efficacy of *Malarone* and, as far as possible, prevent the emergence of resistance to it, it is important that the product is reserved for use when first and second-line anti-malarials are ineffective. Pilot sites have been successfully following a protocol for determining which patients require treatment with *Malarone* and which patients can be treated with standard therapies.

### Tuberculosis

Action TB was launched in July 1993 when GlaxoSmithKline committed £10 million over five years to fund research in universities in the UK, South Africa and Canada. On World TB day in 1998, GlaxoSmithKline announced a further £10 million to fund Action TB for another five years.

The goals of the programme are to deliver: a drug in early stages of development together with a backup or alternative candidate; a vaccine in early stages of development including identification of candidate antigens; and identification of surrogate markers for use in drug and vaccine trials.

### Community programmes – United Kingdom

The company's partnership with the Department of Health and the charity Barnardo's to establish the Right Fit programme is in its third year. Right Fit is a major initiative which helps young people, teachers and youth workers tackle smoking, diet and fitness. GlaxoSmithKline's donation of £3 million, spread over the three-year life of the project, is the largest single contribution made by the company in the UK. The objective of the programme is to make a positive impact on the health of young people in the UK and the results so far have been very encouraging with 175 projects being supported, benefiting over 150,000 young people.

GlaxoSmithKline provided £500,000 for medical research. This is an annual scheme, with £3.7 million awarded to over 40 medical research projects in the last eight years. Eight charities are invited to apply each year and five projects are selected for funding of approximately £100,000 each. The charities funded through this programme in 2000 were: Diabetes UK, Cystic Fibrosis Trust, Digestive Disorders Foundation, Meningitis Research Foundation and the Motor Neurone Disease Association.

GlaxoSmithKline's annual IMPACT Awards programme recognises the excellent work of small charities working in the healthcare sector. Ten winners each received an award of an unrestricted £25,000. Winning charities ranged from those supporting the health needs of male and female sex workers to community care services and carer support in isolated areas of the Scottish Highlands.

A joint venture between VSO and the Royal College of Paediatrics and Child Health received a £150,000 donation to fund ten trainee consultant paediatricians (five in 2000 and five in 2001), to spend a year of their higher specialist training in a developing country as a VSO volunteer. The focus is on providing and sharing paediatric skills in areas where they are most needed for the benefit of poor and disadvantaged children.

A £45,000 donation enabled the charity Beating Bowel Cancer to provide equipment for centres which will assist in the early diagnosis of the disease. Bowel cancer is the second biggest cancer killer in the UK and causes almost 50 per cent more deaths than breast cancer.

### **Community programmes – Europe**

Programmes in Europe focused on children's health:

Support was provided for Reaching Young Europe, run by Befrienders International (the umbrella organisation for the Samaritan movement worldwide), which helps children develop skills to cope with stress (£200,000).

Funding was provided for two programmes run by the aid organisation, Project HOPE: in Russia, to combat substance abuse (£100,000); in Bosnia, a paediatric rehabilitation programme (£130,000).

The Barretstown Gang Camp in Ireland, which supports seriously ill children from all over Europe, received £420,000.

### **Community programmes – North America**

Community Partnership focused on better access to better healthcare. Grants of \$4.0 million were awarded through the North America Community Partnership Team.

There is a \$4.5 million (three-year) initiative by GlaxoSmithKline and the University of Pennsylvania's Institute on Ageing.

A three-year Children's Health Fund grant of \$2.1 million was made to support the Referred Initiative Programme, ensuring children without medical insurance receive healthcare services.

In the US IMPACT Awards programme, ten grants of \$40,000 were made to healthcare organisations in recognition of their exceptional work in the delivery of community healthcare.

### **Community programmes – Rest of World**

Outside Europe and the USA the focus was on health education.

GlaxoSmithKline's PHASE (Personal Hygiene and Sanitation Education) is a health education programme that targets primary school children aged 6 to 13 years, with the goal of reducing diarrhoea-related disease associated with poor hygiene. This schools initiative was extended from its pilot countries of Kenya and Côte d'Ivoire to include Uganda, Peru and Nicaragua (£575,000).

GlaxoSmithKline's two indigenous community healthcare initiatives in Northern Queensland, Australia, are designed to implement community-led programmes that will improve the health of indigenous communities. These are now developing into replicable community-led models (£110,000).

### **Charitable support**

Charitable donations by GlaxoSmithKline companies around the world totalled approximately £30 million in 2000.

In the UK GlaxoSmithKline made charitable donations of some £6 million for projects both in the UK and in the developing world, with particular emphasis in the areas of UK and international healthcare, medical and scientific education, the environment and the arts. Additionally GlaxoSmithKline UK operating companies contributed a further £1 million by way of community investment in the communities local to their factories and sites.

### Access to medicines

GlaxoSmithKline is determined to play its full part in improving access to medicines for the world's poorest people. Millions of people in developing countries do not have ready access to basic healthcare services, including safe and effective medicines.

The company is involved in many initiatives to improve health in the developing world, including tackling major killers such as HIV/AIDS, malaria and TB. Both Glaxo Wellcome and SmithKline Beecham had a history of addressing developing world diseases, in terms both of the R&D they undertook and the efforts made to improve access to existing medicines.

### R&D for diseases of the developing world

GlaxoSmithKline makes very significant investments in researching new products to prevent and treat developing world diseases. The company has extensive research programmes into both the prevention and treatment of the three diseases that are the focus of international efforts – HIV/AIDS, malaria and TB. GlaxoSmithKline is the only company working to develop vaccines for all three diseases. It also has a dedicated specialist team within the company working on treatments for tropical diseases, with programmes to develop anti-malarials, de-worming agents and anti-diarrhoeals.

Development of these drugs and vaccines involves external research collaborations. For example, the company has an agreement with the Malaria Vaccine Initiative, a non-profit organisation, to test the only malaria vaccine candidate yet to show effectiveness in preventing malaria. This will speed the development of the vaccine, with the potential to save the lives of millions of children.

Other collaborative projects include two commissioned under the Medicines for Malaria Venture and the Action TB programme which harnesses academic expertise in order to develop new TB treatments.

However, efforts to develop incentives and joint funding are essential to stimulate such research. In addition to its own research efforts, GlaxoSmithKline will continue to work with donor agencies to identify additional research and development funding so that developing country diseases can be effectively tackled.

### Commitment to lower prices

Both Glaxo Wellcome and SmithKline Beecham have offered lower prices for a range of medicines for use in developing countries. Most significantly this has covered vaccines and anti-retroviral therapies for HIV/AIDS. The company is a leading provider of vaccines to the developing world, and has been offering very substantial discounts to governments, charities and agencies for public health programmes for nearly 20 years.

GlaxoSmithKline is one of five companies offering low price anti-retrovirals as part of the Accelerating Access Initiative (AAI). This aims to accelerate sustained access to appropriate interventions for the prevention, care and treatment of people living with HIV/AIDS. AAI is a partnership between the pharmaceutical industry and five UN agencies, which works with governments to ensure appropriate treatment of patients, both in terms of their overall health care and their use of drugs.

The prices available through the AAI – which represent discounts of some 90 per cent on world prices – are also being offered by GlaxoSmithKline to not-for-profit organisations that are able to deliver anti-retrovirals to patients in developing countries, including selling directly to aid organisations and UN agencies for use in their own programmes.

Additionally, the company is working with employers in Africa who offer HIV/AIDS care and treatment directly to their staff through their own workplace clinics.

### Working in partnership

GlaxoSmithKline is committed to maximising affordable access to medicines in the developing world and is exploring a framework in which the company can offer lower prices for all medicines for those who most need them in developing countries.

In addition to the acknowledgement that improving access to medicines is a shared responsibility, this framework needs to embrace three core principles – partnership, protection of products from diversion and parallel trade, and agreement that developing country prices should not be used as a benchmark for prices in developed countries. Although this framework does not currently exist, the company is working hard with all stakeholders to make products available at discounted prices while the framework develops.

To make real progress in tackling the HIV/AIDS pandemic, particularly in Sub-Saharan Africa, increased donor funding from the developed world is needed to enhance healthcare capacity and to facilitate the purchase of the anti-retroviral medicines. Even at such significantly reduced prices, the cost of the anti-retroviral therapy and the associated health care infrastructure that is necessary to deliver this to patients is way beyond the means of many developing country governments.

While the pharmaceutical industry has a role to play in improving access, significant barriers exist, most notably poverty, inadequate public spending and weak healthcare infrastructures. These problems must be addressed as a shared responsibility by all sectors of society, including governments in both the developed and developing world, international agencies, non-governmental agencies and pharmaceutical companies.