

***Case No COMP/M.1846 -
GLAXO WELLCOME /
SMITHKLINE
BEECHAM***

Only the English text is available and authentic.

**REGULATION (EEC) No 4064/89
MERGER PROCEDURE**

Article 6(1)(b) NON-OPPOSITION
Date: 08/05/2000

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COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 08.05.2000

In the published version of this decision, some information has been omitted pursuant to Article 17(2) of Council Regulation (EEC) No 4064/89 concerning non-disclosure of business secrets and other confidential information. The omissions are shown thus [...]. Where possible the information omitted has been replaced by ranges of figures or a general description.

PUBLIC VERSION

MERGER PROCEDURE
ARTICLE 6(2) DECISION

To the notifying parties

Dear Sirs,

Subject: Case No COMP/M.1846-GLAXO WELLCOME/SMITHKLINE BEECHAM
Notification of 20.3.2000 pursuant to Article 4 of Council Regulation No 4064/89¹

1. On 20 March 2000, the Commission received a notification of a proposed concentration pursuant to Article 4 of Council Regulation (EEC) No 4064/89 ("the Merger Regulation") by which the undertaking Glaxo Wellcome plc ("GW") and SmithKline Beecham plc ("SB") notified their intention to enter into a full merger within the meaning of Article 3(1)a of the Merger Regulation. The merger was announced on 17 January 2000.
2. In the course of the proceedings, the parties submitted undertakings designed to eliminate competition concerns identified by the Commission, in accordance with Article 6(2) of the Merger Regulation. In the light of these modifications, the Commission has concluded that the notified operation falls within the scope of the Merger Regulation as amended and does not raise serious doubts as to its compatibility with the common market and with the functioning of the EEA Agreement.

I. THE PARTIES

¹ OJ L 395, 30.12.89 p.1; corrigendum OJ L 257 of 21.09.90, p.13; Regulation as last amended by Regulation (EC) No 1310/97 (OJ L 180, 09.07.97, p.1, corrigendum OJ L 40, 13.02.98, p.17).

3. SB and GW both are active in human pharmaceuticals. SB is also active in vaccines, OTC products and health-care related products. GW was formed in 1995 following Glaxo's acquisition of Wellcome (Case IV/M.555 - Glaxo/Wellcome).

II. THE OPERATION

4. The proposed concentration is a merger of equals in the meaning of article 3(1)(a) of the Merger Regulation.
5. The merger is to be effected by way of a scheme of arrangement of GW and SB under Section 425 of the United Kingdom Companies Act ("the Scheme") and is subject to conditions, including the approval of the High Court of England and Wales. The new company will be called Glaxo SmithKline plc ("Glaxo SmithKline")
6. Post-merger, the new entity will rank first in the world in terms of total sales and will have 7.3% of world-wide pharmaceutical sales. Glaxo SmithKline will be followed by Pfizer/Warner-Lambert², AstraZeneca and Aventis.

III. CONCENTRATION

7. Following the merger, GW shareholders will hold approximately 58.75% and SB shareholders approximately 41.25% of the issued ordinary share capital of Glaxo SmithKline. The initial Board of Glaxo SmithKline will consist of 14 directors drawn equally from the Boards of GW and SB. The operation will result in a full merger between GW and SB and, therefore, is a concentration within the meaning of Article 3(1)(a) of the Merger Regulation.

IV. COMMUNITY DIMENSION

8. The undertakings concerned have a combined aggregate world-wide turnover of more than EUR 5 billion³ (GW: EUR 12,888 million, SB: EUR 11,763 million). Each of them have a Community-wide turnover in excess of EUR 250 million (GW: EUR [...] million, SB: EUR [...] million), but they do not achieve more than two-thirds of their aggregate Community-wide turnover within one and the same Member State. The notified operation therefore has a Community dimension.

V. COMPETITIVE ASSESSMENT

A. Relevant product markets

9. SB is mainly active in pharmaceuticals, vaccines, OTC products and health-care related products. GW has its main business activities in human pharmaceuticals, which is therefore the only area where the activities of the two parties materially overlap. While SB is relatively strong in the supply of human vaccines, GW is scarcely active in this market.

² Pending case COMP/M.1878- Pfizer/Warner-Lambert

³ Turnover calculated in accordance with Article 5(1) of the Merger Regulation and the Commission Notice on the calculation of turnover (OJ C 66, 2.3.1998, p. 25). To the extent that figures include turnover for the period before 1.1.1999, they are calculated on the basis of average ECU exchange rates and translated into EUR on a one-for-one basis.

10. The Commission has on many occasions dealt with the definition of the relevant market in the case of pharmaceutical products and has established a number of principles in its previous decisions⁴. On the basis of these decisions, product markets in the pharmaceutical industry can be grouped into pharmaceutical specialities, active substances and future products.

1. Pharmaceutical specialities

11. Pharmaceutical products are used for the treatment of human illnesses and diseases. Prescription/ethical medicines are pharmaceutical products exclusively accessible by way of medicinal prescription and subject, for the main part, to reimbursement through social security schemes. OTC drugs are “over-the-counter” pharmaceutical products certain of which can be prescribed by a doctor and may be reimbursable through a social security scheme.
12. In its previous decisions, the Commission noted that medicines may be subdivided into therapeutic classes by reference to the “Anatomical Therapeutic Chemical” classification (ATC), devised by European Pharmaceutical Marketing Research Association (EphMRA) and maintained by EphMRA and Intercontinental Medical Statistics (IMS). It is to be noted that whilst similar in concept to the EphMRA ATC system, the classification system prepared by the World Health Organisation (WHO) differs to some extent from it. The parties have used the EphMRA ATC system as a starting point in their pharmaceutical products market definition. The ATC is hierarchical and has 16 categories (A, B, C, D, etc.) each with up to four levels. The first level (ATC 1) is the most general and the fourth level (ATC 4) the most detailed. The third level (ATC 3) allows medicines to be grouped in terms of their therapeutic indications, i.e. their intended use, and can therefore be used as an operational market definition. These groups of products generally have the same therapeutic indication and cannot be substituted by products belonging to other ATC 3 classes.
13. However, the Commission has in earlier decisions considered that the third level of the ATC is not in all cases an appropriate basis for the definition of products markets and that it may be appropriate in certain cases to carry out analyses at other levels of the ATC classification. For example, it may be necessary to combine certain groups of pharmaceutical specialities. This would be the case where certain products from different ATC classes are substitutes for the treatment of a specific illness or disease.
14. On the other hand, it may also be appropriate to apply a narrower market definition where the pharmaceutical specialities forming part of a certain ATC 3 class have clearly differing indications. In certain cases, pharmaceuticals may be further subdivided into various segments on the basis of a variety of criteria, and in particular demand-related criteria. A possible distinction is that between medicines, which can be issued only on prescription and those, which can be sold over the counter (OTC). Most medicines issued only on prescription are reimbursed, whereas most of those, which may be sold over the

⁴ Case IV/M.072 – Sanofi/Sterling Drug; IV/M.323 – Procordia/Herbamond; IV/M.426 – Rhône-Poulenc/Cooper; IV/M.457 – la Roche/Syntex; IV/M.500 – AHP/Cynamid; IV/M.555 – Glaxo/Wellcome; IV/M.495 – Behringwerke AG/Armour Pharmaceutical Co.; IV/M.587 – Hoechst/Marion Merell Dow; IV/M.631 – Upjohn/Pharmacia; IV/M.737 – Ciba-Geigy/Sandoz; IV/M.950 – Hoffman La Roche/Boehringer Mannheim; IV/M.1229 – American Home Products/Monsanto; IV/M. 1403 – Astra/Zeneca; IV/M.1397 – Sanofi / Synthélabo; IV/M.1378 – Hoechst/Rhône-Poulenc.

counter, are not reimbursed. There are also other key considerations such as indications variances between prescription and OTC products, disease severity, demographic differences in consumers who refer to prescription as opposed to OTC products, driven by attitudinal differences and pricing factors. Prescription medicines and OTC products can belong to different markets, even if they are indicated in the same diseases because the customers, the legal background, the inherent risk, the marketing and distribution may be different. The allocation of a medicine to the prescription or the OTC segment is based on decisions by the authorities, which may lead to changes between segments according to the country concerned. There are different overlaps between the prescription and OTC market depending to a large degree on the reimbursement systems of different Member States.

15. In this case, the parties have used ATC 3 classification as a starting point in their analysis and accept this as the market definition for most product markets. However, for some product markets which are further discussed below, the parties have suggested alternative market definitions.
16. In human pharmaceuticals, the parties have overlapping activities in 7 treatment areas where the combined market shares will remain below 15%. These treatment areas do not, therefore, give rise to competition concerns. These treatment areas are stomatological preparations (A1A), topical anithaemorroid (C5A), calcium antagonist – plain (C8A), anti-fungals, dermatological (D1A), thyroid preparations (H3A), nootropics (N6D) and nasal decongestants (R1B).
17. The parties' combined market shares exceed 15% in 12 product areas based on the ATC 3 classification: anti-virals, excluding anti-HIV (J5B), topical anti-virals (D6D), anti-emetics (A4A), broad spectrum penicillins (J1C), cephalosporins (J1D), anti-malarials (P1D), topical nasal decongestants (R1A), anti-peptic ulcerants (A2B), anti-epileptics (N3A), topical antibiotics (D6A), anti-Parkinson preparations (N4A) and expectorants (R5C). These treatment areas will be discussed in more detail below.

a) Anti-virals (J5B)

18. According to the parties, the ATC classification distinguishes at ATC 3 level between J5B (anti-virals excluding anti-HIV) and J5C (anti-virals for AIDS/HIV). The parties submit that the category for J5B covers anti-virals other than for HIV and includes drugs both for oral and parenteral administrations.
19. The parties submit that the greater part of this category is accounted for by anti-herpes treatments (most importantly treatments against *herpes simplex*, *varicella zoster* and *cytomegalovirus* (“CMV”) but it also includes treatments for other viruses ranging from influenza to *hepatitis B*. According to the parties, the J5B systemic anti-herpes products are predominantly used in relation to *herpes simplex* (*HSV-1* and *HSV-2*) and *varicella zoster*, which together account for over three quarters of usage of level J5B anti-virals. The parties' products in this area include most importantly “Zovirax”, “Famvir” and “Valtrex”.
20. The parties further submit that other J5B anti-virals include *ribavirin* for *hepatitis B* (from ICN, sold under various names including “Virazid”) and *ganciclovir* for a particular herpes virus *CMV* (principally Roche's “Cymevene”). The parties submit that *CMV* is predominantly treated using *ganciclovir* although GW's “Valtrex” is also

indicated in a limited number of EU markets for prophylaxis of *CMV*. GW also markets in certain Member States “Zeffix” for *hepatitis B* and “Relenza” for influenza.

21. The parties submit that the gold standard in the treatment of herpes has, since the early 1980's, been *aciclovir*, which was the first anti-viral agent to demonstrate selective and specific inhibition of viral replications. *Aciclovir* was initially introduced by GW under the “Zovirax” brand and has since been used to treat virtually all clinical manifestations of the *herpes simplex* and *herpes zoster* infections. The parties argue that the patent protection for *aciclovir* has been lost in most European markets and, in consequence, the first generation drug “Zovirax” faces competition from generic *aciclovir*.
22. Both parties have developed second generation drugs for the treatment of herpes. GW markets “Valtrex” or *valaciclovir*, a prodrug of *aciclovir* which, once orally administered, is metabolised to *aciclovir* in the body. SB's anti-herpes product is “Famvir” or *famciclovir*, which is the prodrug of *penciclovir* and metabolises to *penciclovir* in the body.
23. The parties submit that the principal advantage of the second generation drugs “Valtrex” and “Famvir” over *aciclovir* lies in their greater oral bio-availability, thereby permitting a more favourable dosing regime involving reduced frequency of oral daily doses. The parties submit nevertheless that these compounds are available only as tablets and are indicated for a less extensive range of treatments than *aciclovir*, and do not have the benefit of the long-established efficacy and safety profile of *aciclovir*.
24. The parties argue that where a drug has a well established efficacy and safety profile, a physician is likely to choose it and will consistently prescribe it for the majority of patients unless there are strong reasons not to. The parties argue that this approach favours *aciclovir* in the cases of first and recurrent *herpes simplex* or *herpes zoster* infections, where the treatment regime is episodic and of short duration (5-10 days). The parties submit that improved bio-availability and dosing regimes may have greater significance in cases where the physician decides on a suppressive therapy involving continuous medication (90-365 days per year). The parties nevertheless submit that a suppressive dosing is required only in 10% of cases of genital herpes and seldom with *herpes zoster*.
25. The Commission's investigation shows that most third parties consider the ATC 3 level as a proper starting point for the assessment of the markets. Some customers have, however, submitted that it is not correct to include for instance drugs treating influenza in the relevant product market as there is no substitutability with these drugs and anti-herpes drugs. Therefore, it has been submitted that anti-herpes drugs should constitute a separate relevant product market in themselves. This approach is supported by the fact that for instance *ganciclovir* and *ribavirin* are prescribed for the treatment of viruses other than *herpes simplex* and *variella zoster*, and “Relenza” is specifically targeted for influenza.
26. As to the question whether the first generation drug (“Zovirax”) and the second generation drugs (“Famvir” and “Valtrex”) should be considered to constitute separate product markets, the majority of third parties who replied to the Commissions enquiries have indicated that the first and the second generation drugs are substitutable. Although, the investigation shows that there are differences in frequency of administration and bioavailability of the drugs, the first and the second generation compounds have the same indications. In this respect, the investigation shows that

“Zovirax” shows some limits due to its pharmacological characteristics in that it is quickly eliminated by the human body. As a result, patients have to take “Zovirax” in certain cases five times a day to ensure an efficient action of the drug. Therefore, if the treatment of the drug is not respected, the effect of the molecule is rendered inefficient. “Valtrex” allows dosage to be limited to twice a day in contrast with the need to administer “Zovirax” five times a day. A number of competitors have indicated that the less frequent dosage of the second generation drugs gives them an advantage over the first generation drugs and generics.

27. However, the Commission considers that given the same indications for first and second generation drugs, the less frequent dosing alone is not sufficient to warrant a market definition placing first and second generation drugs in separate markets. Therefore, for the purposes of this decision, first and second generation anti-viral compounds are considered to constitute one market. As to the question whether anti-herpes drugs should constitute a separate relevant product market from for instance drugs treating influenza, this question can be left open as serious doubts exist as to the compatibility of the common market on all alternative market definitions considered.

b) Topical anti-virals (D6D)

28. The parties submit that the principal use of prescription topical anti-virals is in the treatment of *herpes labialis* (“cold sores”). The parties submit that patients with *herpes labialis* can be treated with topical creams and ointments. Formulations are applied to the skin to treat labial herpes or, less commonly, outbreaks of genital herpes.
29. The parties submit the relevant product market as the ATC 3 level of topical anti-virals, that is, D6D. The parties’ products include GW’s “Zovirax” (*aciclovir*) and SB’s “Vectavir” (*penciclovir*). “Vectavir” is a second generation drug and was previously only available on prescription. It has only recently been launched OTC in Sweden, Denmark, Finland and the Netherlands.
30. According to the parties, the normal treatment for cold sores is self-medication with OTC products and only a very small proportion (some [$<10\%$]) of outbreaks of cold sores are treated on prescription. The parties argue that, exceptionally, in this market prescription and OTC medicines are functionally substitutable in the treatment of the same condition. The parties further submit that there is no necessary supply-side distinction between the two, as in some Member States “Zovirax” is available both on prescription and OTC, the only distinction being the size of the unit sold, with the formulation being the same. The parties therefore argue that the grounds for market separation rely principally on dispensing occasion, different distribution channels and absence of direct price correlation between OTC and prescription prices (except in those Member States⁵ in which the pharmaceutical pricing rules require OTC products to be priced by reference to the prescription products).
31. Third parties agree in general terms that the ATC 3 level is suitable for the assessment of this treatment area. In particular, they have submitted that while a distinction could be made between OTC and prescription only products, this would not materially affect the market position of the parties as GW is the market leader with similar market

⁵ Belgium, Austria, Denmark and Germany

shares in both segments. Therefore, for the purposes of this decision, the question whether or not OTC and prescription only compounds constitute separate markets will be left open.

c) Anti-emetics/anti-nauseants (A4A)

32. Anti-emetics are most generally drugs that prevent or relieve nausea and vomiting. Nausea and vomiting can have various causes. They may be associated with no obvious disease process but with psychological determinants, due to symptoms of disease process or they may be a response to stimuli such as drugs (e.g. chemotherapy), radiation or motion. The parties submit that the main indications fall within post-operative nausea/vomiting, radiotherapy induced nausea/vomiting and chemotherapy induced nausea/vomiting. Chemotherapy induced nausea/vomiting is the major indication area.
33. The parties argue that, within the chemotherapy induced nausea/vomiting, the choice of anti-emetics is often based on the likely severity of emetic reaction. Chemotherapy generally falls into three segments: highly, moderately and low emetic risk. Emetic risk depends on the chemotherapeutic agent used. In this respect, the parties have submitted that for instance Cisplatin carries the highest risk, with 98% or more patients experiencing emesis, while less than 10% of patients treated with vinca alkaloids experience emesis. The parties therefore submit that there is a broad spectrum of chemotherapy induced nausea/vomiting for which a wide range of drugs is available.
34. The parties submit that because the anti-emetics field comprises a large number of drugs for a variety of different uses and with different modes of action, the relevant product market is wider than ATC third level A4A and comprises also ATC third level A3F (gastroprokinetics). The parties contend that while not every one of these products may be substitutable in every given case, they form a range of anti-emetics products from which the most appropriate drug must be selected given the individual circumstances. The parties further argue that, given the high cost of one group of products within the A4A category, 5HT₃-antagonists, physicians will often prescribe dopamine antagonists and gastroprokinetics in preference to 5HT₃-antagonists, particularly where the risk of emesis is low or moderate. The parties argue more particularly that cancer research centres recommend a number of different drugs for the prevention of emetic reactions caused by chemo- and radiotherapy treatment. These according to the parties include 5HT₃-antagonists (such as *ondansetron* and *granisetron*), dopamine antagonists (such as *phenothiazines* and *butyrophenones*) and gastroprokinetics (such as substituted *benzamides*). 5HT₃-antagonists and dopamine antagonists are classed with ATC 3 category A4A (anti-emetics), while the gastroprokinetics fall within the third level ATC category A3F.
35. The parties submit that 5HT₃-antagonists (*serotonin*) act to block the nausea and vomiting reflexes by blocking binding of 5HT₃ to its receptor in both the small intestine and the brain. According to the parties, 5HT₃-antagonists are generally thought to be more effective than the earlier developed dopamine antagonists, especially in treating highly emetic cases of chemotherapy and radiotherapy induced nausea and/or vomiting related to cancer treatment. GW's "Zofran" (*ondansetron*) and SB's "Kytril" (*granisetron*) are both 5HT₃-antagonists. There are also two further 5HT₃-antagonists on the market in Europe: "Navoban" (*tropisetron*), which is marketed by Novartis, and "Anzemet" (*dolasetron*), marketed by Aventis.

36. With regard to dopamine antagonists, the parties submit that even though these are older drugs, they are still widely used. They comprise *phenothiazines* and *butyrophenones* which are used for treatment of drug-induced nausea and vomiting or associated with gastro-enteritis, pregnancy or uremia. SB has a *phenothiazine* product called “Compazine”.
37. As for gastroprokinetics (A3F), the parties argue that they have a number of indications, but those used in hospitals are predominantly for anti-emetic use. The parties contend that oral or parenteral *metoclopramide* relieves the symptoms associated with acute and recurrent diabetic gastroparesis or gastroparesis related to delayed gastric emptying (e.g. nausea, vomiting). The parties submit that *metoclopramide* is also used for nausea and vomiting associated with for instance surgery, radiotherapy, chemotherapy, pregnancy and gastric ulcers. *Trimethobenzamide* is, according to the parties, used in preventing post-anaesthetic nausea. Moreover, the parties submit that corticosteroids (such as *dexamethasone*) are often used in conjunction with the 5HT3-antagonists, dopamine antagonists and gastroprokinetics.
38. Third parties in their replies to the Commission’s enquiries have, however, dismissed largely the parties’ argument according to which the relevant product market should be extended to include gastroprokinetics (A3F). The investigation shows that most products within the gastroprokinetic class are not indicated for emesis and nausea caused by cancer treatment and, therefore, do not play an important role in anti-emesis during cancer therapy. With the exception of *metoclopramide*, all other gastroprokinetic products are used for gastric motility (esophageal reflux and nocturnal heartburn). While it has been widely recognised that for instance *metoclopramide* is indicated as anti-emetics for use during cancer therapy, this is not indicated for severe and moderate emesis and, therefore, the use of that compound is limited. Moreover, the investigation shows that *metoclopramide* is used only relatively little in comparison with the use of 5HT3-antagonists in the treatment of cytotoxic nausea and vomiting. In this respect, the investigation shows that *metoclopramide* represents only 1% by value of the sales in gastroprokinetics class. Finally, the investigation shows that the majority of gastroprokinetics are considered to be less suitable for the treatment of cytotoxic nausea and vomiting due to labyrinthine disorders and the side-effect profile.
39. According to third parties, 5HT3-antagonists are the gold standard in chemotherapy induced emesis and 90% of cancer patients receiving chemotherapy are treated prophylactically with 5HT3-antagonists. Given that chemotherapy is the most commonly used form of cancer treatment, 5HT3-antagonists therefore represent a key class of anti-emetics used in patients undergoing treatment for cancer. “Zofran” and “Kytril” are both considered by many to be intrinsically linked to chemotherapy treatment.
40. As to the question whether corticosteroids should be considered as belonging to the relevant product market in this treatment area, third parties have indicated that although a number of compounds, such as corticosteroids, have a role in anti-emesis for patients undergoing treatment for cancer, each of these compounds has a distinct and non-overlapping role to play.
41. On the basis of the foregoing, there are clear indications that the relevant product market should not be extended to include also gastroprokinetics (A3F). The exact market definition can, however, be left open because the operation would lead to the

creation of a dominant position in most Member States regardless of the market definition used.

d) Antibiotics (J1)

42. Antibiotics are antibacterial agents that inhibit the growth of certain micro-organisms. Systemic antibiotics (J1) are classes of semi-synthetically or fully synthetically prepared antibiotics, which followed the development of penicillin into second and third generation products. The parties submit that specific antibiotics are applied with regard to the suspected causative organism, its antibiotic sensitivity and the suitability for the specific patient. In cases where the organism causing the disease is not precisely known, the prescribing physician will choose an antibiotic with a broad spectrum of activity both in terms of organisms targeted and indication. A narrow spectrum antibiotic is likely to be chosen in those rarer cases where the organism responsible for the disease has been identified.
43. The parties submit that the market for antibiotics is dynamic due to the prescribing behaviour of the physician. They argue that factors related to the patient must be considered as well as the known or likely causative organism and its antibiotic sensitivity. The final choice of the physician depends on the microbiological, pharmacological, toxicological properties and local epidemiology. According to the parties, due to the development of pathogen resistance to antibacterial agents - which is one of the main problems in antibiotics - prescribing physicians select the following strategy, comprising first line agents, second line agents and reserve agents: The first line agents are used as the first prescription for most infections and suitable for most patients; the second line agents are used less frequently and usually where the first line agent is not appropriate for the patient or considered as unlikely to work against the suspected causative organism of infection due to resistance; reserve agents are used infrequently and held in reserve for special circumstances. The parties argue that the selection of what is used as first, second or reserve level antibiotic varies from one Member State to another.
44. The parties conclude that all systematic antibiotics classified on ATC third level are not directly substitutable for the same patient but form a range of drugs available for the treatment of bacterial infection. A range of different antibiotics is always required in order to meet individual needs. The parties contend that all major indications like throat, bronchitis, urinary tract infection, ear infection, sinusitis and pneumonia are treated by specific antibiotics, falling into the ATC third level penicillins (J1C), cephalosporins (J1D) and macrolides (J1F). Quinolones (J1G) are used against all major indications but *otitis media* (ear infection).
45. Third parties have supported the parties' view insofar as broad-spectrum penicillins (J1C), cephalosporins (J1D), macrolides (J1F) and fluoroquinolones (J1G) are all used as first line treatment for common infections, namely the largest indication of community acquired pneumonia. Thus, compounds of each of the distinct classes may be regarded as alternative treatment for the same condition from a medical diagnosing and prescribing perspective. Penicillin/cephalosporin resistant bacterial strains can be sensitive to macrolides and reciprocally. According to susceptibility of the microbe causing the disease, the risk for antibiotics resistance development, patient hypersensitivity, potential risk for complications from the disease etc., the prescribing physician will choose from a basket of compounds mentioned above.

46. However, third parties consider a market definition according to the ATC second level (J1) to be too wide. While there are occasions where cephalosporins, macrolides, fluoroquinolones and broad-spectrum penicillins are interchangeable, each class has also varying spectra of activity and differing modes of action (bacteriostatic versus bacteriocidal). Interchangeability is therefore limited by patient hypersensitivity and because agents may only have specific fields of activities, with respect to atypical pathogens. Quinolones, for example, are original in their different side effects profiles and [...]. Thus quinolones are still contraindicated for children up to 16 years of age. Since the usage of antibiotics broadly depends on indication, pharmacokinetics and particular spectrum, substitutability is limited.
47. Some replies to the Commission's market investigation suggest that a market definition according to diseases/indications would be appropriate because the effect on the microbe causing the disease is the main criterion for an antibiotic product to be chosen. However, the Commission notes that 70% of the Community market is related to respiratory tract infections, followed by urinary tract infections (8%) and skin/soft tissue infections (8%). For the reasons outlined below, market definition according to disease groups would not create significant differences in market shares compared to ATC levels. In addition, it is to be noted that the parties' products have strong competitors in each of the different indications.
48. Other third parties who replied to the Commission's market investigation support the view that a distinction should be made between place and mode of usage, particularly between hospital use (mainly injectable antibiotics) and community use (mainly oral antibiotics). Parenteral preparations are mainly limited to a hospital setting, as are certain classes of antibiotics, in order to prevent the build up of resistance. Additionally, treatment within hospitals is more likely to be initiated following identification of the infecting organism, whilst in an out patient setting treatment is frequently commenced before test results are available. On the other hand, third parties submit that a further delineation of the market according to hospital or community use would be misleading. Often, treatment is begun with a parenteral drug in the hospital and is then continued with the oral form of the same drug when the patient is leaving the hospital. Furthermore, in hospital settings, due to cost-containment efforts, a significant trend can be identified towards an early switch from injectable antibiotics to oral therapies.
49. On the basis of the foregoing, the Commission considers that for the purposes of the present case the ATC third level appears to be the most appropriate market definition. As the parties, customers and competitors have pointed out, different antibiotics within ATC second level may be interchangeable to a certain extent but they are not completely substitutable. Within the ATC third level, three separate markets, namely broad-spectrum penicillins (J1C), cephalosporins (J1D) and fluoroquinolones (J1G) can be identified, in which both parties are active. The assessment of this case will therefore be carried out for each of these categories separately, so as to examine the narrowest possible market.

e) Anti-malarials (PID)

50. Both GW and SB currently market anti-malarial products in Europe. GW's "Daraprim" (*pyrimethamine*) is indicated for prophylaxis and the treatment of malaria and has been off patent since 1967. GW's "Malarone" is currently marketed for the treatment of

malaria [...]. SB's "Halfan" (*halofantrine*) is intended for the treatment of malaria and has lost its patent protection.

51. The parties submit anti-malarials (P1D) as the relevant product market. Given that the market investigation does not suggest otherwise, the assessment will be carried out on the basis of this ATC 3 category.

f) Topical nasal decongestants (R1A)

52. The parties consider ATC third level of topical nasal preparations too wide for an appropriate definition of the market. The parties submit that the third level category of topical nasal preparations comprises a number of drugs for the topical application to the nose which cover different indications and offer different modes of action. Such products, according to the parties, are not substitutable beyond the indication they are designed to treat.
53. The parties' products include SB's "Bactroban Nasal" and "Rinazina", and GW's "Flixonase" and "Beconase". The parties submit that SB's "Bactroban Nasal" falls within category R1A3 (nasal anti-infectives without corticosteroids) and is indicated for the prevention of nasal colonisation and subsequent infections. SB's other product "Rinazina" falls within category R1A7 (nasal decongestants) and is indicated for the symptomatic relief of nasal congestions. GW's "Flixonase" and "Beconase" by contrast fall within the category R1A1 (nasal corticosteroids without anti-infectives) which treat rhinitis, which is an inflammation of the nasal mucus membrane, principally caused by allergies.
54. The parties further submit that nasal anti-infectives (R1A3) are used to treat bacterial infections of the nose and eliminate nasal colonisation by bacteria, thereby preventing patients from spreading infection to others who may be vulnerable. "Bactroban Nasal", an anti-infective product, is used as part of a hospital infection control programme to eliminate nasal carriage of the bacterium methicillin-resistant staphylococcus aureas (MRSA). GW has no nasal anti-infective product and "Flixonase" and "Beconase" cannot be used for this purpose.
55. By contrast, the parties submit that nasal corticosteroids (R1A1) have no effect on bacteria of the nasal mucosa. According to the parties, these products affect the mucus membrane itself to reduce an inflammation of the nasal membrane (rhinitis) which is mainly caused by an allergy but can also be caused non-allergically (smoking, pollution, central heating). GW's "Flixonase" and "Beconase" are corticosteroids used for the treatment of allergic as well as non-allergic rhinitis. SB has no rhinitis product and "Bactroban Nasal" cannot be used for this purpose.
56. On the basis of the foregoing, the parties submit that their activities should not be regarded as overlapping in this area. Most third parties in their replies to the Commission's enquiries support the parties' view and have confirmed that the different products discussed above are not designed to treat the same indications. Third parties have confirmed that different products will be used for decongestant purposes only and for allergies, such as hay fever.
57. On the basis of the foregoing, the Commission considers that the parties' existing products do not overlap and, therefore, this treatment area will not be discussed any further.

g) Anti-peptic ulcerants (A2B)

58. The parties submit that anti-peptic ulcerants encompass a variety of drugs used to treat a range of common disorders considered to be related to acid secretion by the stomach. These disorders include peptic ulcer diseases and gastroesophageal reflux disease. The parties' products include GW's "Zantac" and SB's "Tagamet".
59. The parties have provided data on the basis of the ATC 3 class A2B. The market investigation does not suggest that any other market definition should be used.

h) Anti-epileptics (N3A)

60. Epilepsy results from an altered neurochemical state, leading to excess electrical activity in the brain. Anti-epilepsy treatments are aimed at controlling this activity through various mechanisms.
61. The parties submit that the relevant product market for anti-epileptics is the ATC level category N3A and they have provided data on this basis. This market definition has not been contested by third parties either.

i) Topical antibiotics (D6A)

62. Topical antibiotics are antibiotics used to treat bacterial infection of the skin and are applied topically, usually as a cream or ointment but also sometimes as a spray or powder.
63. The parties submit that their topical antibiotics are for different indications and therefore do not overlap. In this respect the parties submit that SB markets "Bactroban" (*mupirocin*) which is only indicated for the topical application for the treatment of primary skin infections, principally impetigo, where a pre-existing abrasion is not required for the infection. GW's "CicatrIn" (*neomycin sulphate/bacitracin zinc*) and "Polyfax" (*polymyxin B sulphate/bacitracin zinc*) are indicated for topical application for the treatment of secondary superficial skin infections where abrasions of the skin have become infected and for other skin infections such as infection of the hair follicle.
64. While some third parties in their replies to the Commission's enquiries have confirmed that primary skin infections, principally impetigo, and skin infections following abrasion represent two different diagnostic situations, some third parties contend, however, that the minor difference in indications between the products does not materially affect the interchangeability of the products concerned and that the parties' products do overlap to a significant extent.
65. It is not necessary, however, to reach a definite conclusion on the scope of the relevant product market, because regardless of the market definition used, competition concerns would not arise in this treatment area.

j) Anti-Parkinson preparations (N4A)

66. Parkinson's disease is caused by a shortage of dopamine, a chemical messenger in the brain. Dopamine, in combination with another messenger, acetylcholine, is responsible for feedback mechanisms in the brain which enable movement to be undertaken.

67. The parties submit that the third level ATC category N4A, anti-Parkinsons's preparations, generally aim to restore the balance between dopamine and acetylcholine in the brain and have provided information on this bases. Third parties have not contested this market definition.

k) Expectorants (R5C)

68. Expectorants are medicines which promote the secretion of sputum by the air passages, used especially to treat coughs. GW and SB both sell expectorants which fall within the ATC 3 category R5C.
69. Given that the market investigation has not suggested that some other market definition should be used, the assessment will be carried out at the ATC 3 level of R5C.

2. Future markets

70. In the pharmaceuticals industry, a full assessment of the competitive situation requires examination of the products which are not yet on the market but which are at an advanced stage of development, (normally after large sums of money have been invested). These products are called pipeline products. As noted in the Ciba-Geigy/Sandoz decision⁶, research and development projects undergo three different phases of clinical testing: Phase I marks the start of clinical testing on humans, currently some eight to ten years before a product is marketed. Statistically, projects in phase I generally have no more than a 10% chance of being successful. Phase II, some four to five years before the product is marketed, involves working out the proper dose for the patient and defining the areas of application. The success of phase II is generally acknowledged to be approximately 30%. Phase III, starting three years before the product is marketed, involves establishing the product's effectiveness on larger groups of patients. The risk of failure in phase III is reported to be over 50%.
71. The potential for these products to enter into competition with other products which are either at the development stage or already on the market can be assessed by reference to their characteristics and intended therapeutic use. The Commission has to look at R&D potential in terms of its importance for existing markets, but also for future market situations.
72. In so far as research and development must be assessed in terms of its importance for future markets, the relevant product market can, in the nature of things, be defined in a less clear cut manner than in the case of existing markets. Market definition can be based either on the existing ATC classes or it can be guided primarily by the characteristics of future products as well as by the indications to which they are to be applied.

B. Relevant geographic markets

1. Pharmaceutic specialities

73. The Commission has previously defined the geographic markets for pharmaceutical products as being national in scope, despite the trend towards standardisation at a European level. The sale of medicines is influenced by the administrative procedures or

⁶ IV/M.737 – Ciba-Geigy/Sandoz, Commission decision of 4.2.1998

purchasing policies which the national health authorities have introduced in Member States. Some countries exercise a direct or indirect influence on prices, and there are different levels of reimbursement by the social security system for different categories of medicines. For this reason, the prices for medicinal products may differ from one Member State to another. In addition, there are far reaching differences in terms of brand and pack-size strategies and in distribution systems. These differences lead to national market characteristics.

74. The results of the investigation do not suggest that the Commission should deviate from its previous practice in assessing pharmaceutical markets at the national level. Therefore, the markets for pharmaceutical specialities affected by the concentration will be regarded as national.

2. Future products

75. To the extent that products not yet on the market must be taken into account on the basis of research and development in particular areas, national restrictions do not have the same degree of effectiveness than for existing pharmaceuticals. Normally, a characteristic of such products is that they have not yet been registered. Because research and development is normally global, the consideration of future markets should therefore at least focus on the territory of the Community and, possibly, on world-wide markets.

C. Assessment

1. Pharmaceutical specialities

76. The operation involves a number of treatment areas where the combined market share of the parties exceeds 15%. These treatment areas are anti-virals, excluding anti-HIV (J5B), topical anti-virals (D6D), anti-emetics (A4A), broad spectrum penicillins (J1C), cephalosporins (J1D), anti-malarials (P1D), topical nasal decongestants (R1A), anti-peptic ulcerants (A2B), anti-epileptics (N3A), topical antibiotics (D6A), anti-Parkinson preparations (N4A) and expectorants (R5C).
77. For the reasons set out below, competition concerns are not likely to arise in anti-peptic ulcerants (A2B), anti-epileptics (N3A), anti-Parkinson preparations (N4A) and expectorants (R5C). Competition concerns do not arise in the markets for broad spectrum penicillins (J1C) and quinolones (J1G) either. These markets will however be discussed in connection with antibiotics.
78. More particularly, in the market for anti-peptic ulcerants (A2B), the parties' combined market shares do not exceed [20-30%] in any Member State where both parties are present and the parties will face strong competition from a number of other companies. In particular, the Commission notes that AstraZeneca is the market leader in a number of Member States with its drug "Losec".
79. In anti-epileptics (N3A), the only overlap between the parties' activities occurs in Italy, where the combined market share is only [15-25%]. Other competitors on that market include most particularly Novartis ([20-30%] of the market), Warner-Lambert ([20-30%]) and Sanofi-Synthélabo ([10-20%]). Competition concerns are therefore unlikely to arise.

80. In the market for anti-Parkinson preparations (N4A), the only Member State where the parties' activities overlap is Italy, where the combined market share is [10-20%], with an increment of [<5%]. The leading competitors on this market are Roche ([20-30%]), DuPont Pharma ([10-20%]) and Eli Lilly ([10-20%]). The operation is therefore not expected to lead to adverse competition effects on this market.
81. Finally, in the market for expectorants (R5C), the parties' combined market share is [20-30%] in Belgium, with an increment of [<5%]. The market leader in Belgium is Zambon Group, with [30-40%] of the market. Competition concerns are therefore unlikely to arise.
82. In 18 national markets, the combined market share of the parties is over 15% but less than 40%. In 7 markets, the combined market share is above 40% but with an accretion of less than 1%. Finally, in 40 markets, the combined market share is above 40%, with an accretion of more than 1%. These markets will be discussed below.

a) Anti-virals (J5B)

83. Following the operation, the parties would attain very high market shares in a number of Member States. Based on the market share data submitted by the parties and covering the 12 month period ending 30 September 1999, the parties' combined market shares would be as follows at the ATC third category J5B: in Ireland [90-100%] (GW: [60-70%], SB: [30-40%]), Greece [90-100%] (GW: [70-80%], SB: [10-20%]), Luxembourg [80-90%] (GW: [80-90%], SB: [<10%]), Belgium [80-90%] (GW: [80-90%], SB: [<5%]), Austria [70-80%] (GW: [50-60%], SB: [10-20%]), the Netherlands [60-70%] (GW: [50-60%], SB: [10-20%]), the UK [60-70%] (GW: [30-40%], SB: [25-35%]), Sweden [60-70%] (GW: [60-70%], SB: [<5%]), Spain [60-70%] (GW: [30-40%], SB: [20-30%]), France [60-70%] (GW: [60-70%], SB: [<5%]) and Denmark [50-60%] (GW: [45-55%], SB: [<5%]). The parties' products do not overlap in Italy and Portugal, because SB's "Famvir" has not been introduced in these markets. The parties would equally achieve similarly high market shares if the compounds prescribed for the treatment of other than *herpes simplex* and *varicella zoster* were excluded from the market share calculations.
84. Although the increment of market share is less than [<10%] in France, Belgium, Luxembourg, Denmark and Sweden, the increment has to be considered sufficient to lead to the creation of a dominant position given the already very high market shares in these Member States. The only Member States where the parties' market shares are not indicative of a dominant position are Finland and Germany, where the parties account for less than [30-40%] of the markets and competitors are strong.
85. In Denmark, France, Sweden and the UK, the largest competitor accounts for some [15-25%] of the market. More particularly, in Denmark and Sweden, the Hexal Group has [15-25%] and [15-25%] of the markets respectively with its product "Geavir". In France, Schering Plough accounts for [15-25%] of the anti-virals market with its products "Rebetol" and "Virazole". Similarly, in the UK, the largest competitor has [15-25%] of the market with "Aciclovir" and "Tribavirin". However, given the fact that the new entity's market shares in these Member States would be [<5] times that of the largest competitor and that the remaining players have less than [5-15%] in market share, the Commission concludes that the competitors are not sufficiently strong to be able to offset the market power of the new entity. The new entity's position would be

even more pronounced in other Member States, where the competitors' market shares are at most around [5-15%] or less.

86. The parties argue that, over the last five years, dynamic changes in the market for anti-virals have led to the erosion of the combined market share of GW and SB in the markets for anti-virals. More precisely, the parties argue that GW has lost patent protection for the *aciclovir* molecule in all European markets save in France, where the expiration date of that patent is in [...]. The parties argue that following patent expiry, "Zovirax" faces considerable competition from generic *aciclovir*.
87. According to the parties, generic *aciclovir* competes with "Zovirax", "Valtrex" and "Famvir" across most of the EU. This, according to the parties, has led to a significant decline in the combined market share of the parties in anti-virals. In this respect, the parties argue that the market share of "Zovirax" practically [...] between 1995 and 1999 over the EU as a whole from [65-75%] to [30-40%] in terms of value. The parties argue that there is a close correspondence between the decline of "Zovirax" and the growth in generic sales of *aciclovir*. The parties claim further that this process is particularly marked in countries where patent expiry occurred relatively early.
88. The Commission notes, however, that during the same period when "Zovirax" lost market share, "Valtrex" increased its market share from [<5%] to [10-20%] and "Famvir" from [<5%] to [<10%] in value terms at the EEA level. Therefore, while it is true that "Zovirax" lost a total of [30-40%] market share between 1995 and 1999, "Famvir" and "Valtrex" increased some [15-25%] their market share. At the same time, generic products increased their market share only by some [<5%]. In volume terms, generic *aciclovir* increased its EEA-wide market share only by [<5%], although the market share of "Zovirax" decreased from [60-70%] to [35-45%].
89. With regard to the market share development in individual Member States, the parties have provided data between 1995 and 1999. According to this data, the value share of generic *aciclovir* for instance in Denmark doubled from [10-20%] in 1995 to [25-35%] in 1999. In Sweden and the UK, the value share of generic *aciclovir* grew to over [20-30%]. Moreover, based on the information submitted by the parties, between 1997 and 1999, GW's "Valtrex" practically doubled its market share in Denmark (from [5-15%] to [20-30%]) and in Sweden (from [20-30%] to [45-55%]) and SB's "Famvir" increased its market share in the UK (from [20-30%] to [25-35%]). In fact, apart from Germany, either "Valtrex" or "Famvir" or both products together gained market share in all Member States between 1997 and 1999.
90. Third parties in their replies to the Commission's enquiries have indicated that the competition from generic products is likely to have some impact on the market share of the first generation drug "Zovirax" but not on the second generation products "Famvir" and "Valtrex", because these are still protected by patents. Moreover, competitors and customers have indicated that although the competition from generic *aciclovir* has led to some price reductions of "Zovirax", generic products have not been able to counterbalance the dominating market position which "Zovirax" enjoys in a number of Member States. In this respect, the Commission notes that the share of sales of "Zovirax" in Belgium are still [70-80%] and in Luxembourg [40-50%] although the product lost its patent protection already in 1995. In Greece, where "Zovirax" is off-patent since 1990, it still accounts for [40-50%] of the market.
91. The parties argue that, in the majority of EU markets, "Valtrex" [...]

92. [...]
93. The Commission's investigation confirms the parties' argument that [...]. Third parties have submitted that pricing has been relatively low in order to induce doctors and patients to use the second generation drug instead of "Zovirax" and push them to abandon the first generation drugs altogether. In this context, some third parties have indicated that even though the first and the second generation drugs may be substitutable at the moment, the first generation drugs will be replaced by the second generation drugs and become obsolete within the next 3-5 years.
94. On the basis of the foregoing, the Commission draws the conclusion that while it is true that part of the market share lost by "Zovirax" has been taken over by generic *aciclovir*, a large part of that market share has migrated to "Valtrex" and "Famvir". The parties' submission that where "Valtrex" and/or "Famvir" are established to any significant degree, they have achieved their position at the expense of "Zovirax" rather than at the expense of generic *aciclovir* is not relevant for the analysis at hand, since this merely indicates that generic *aciclovir* has not been able to take market share from the parties' products to the extent that generic competition should be considered to counterbalance the new entity's market position in the market for anti-virals.
95. Customers and competitors have expressed serious concerns over the notified operation. They have indicated that the existing competition in the second generation drugs between "Valtrex" and "Famvir" would be completely eliminated by the merger and further consolidate the parties' position. While several new entrants into the generic *aciclovir* segment have been reported, there has been no new entry into the segment of second generation drugs for the past 3-5 years.
96. Competitors have also indicated that the operation as notified would discourage any tentative research and development attempts by third parties to develop anti-viral drugs. They have also indicated that a new but substantially smaller player would have difficulties in penetrating the market. In this respect, the investigation shows that the operation as notified would lead to a significant increase of market entry barriers for those competitors who have pipeline products in anti-virals under development. In this respect, the parties have submitted that Flamel Technologies has developed a mechanism for controlled release delivery of *aciclovir*. Although this product could be considered to compete in particular with the parties' second generation drugs, the Commission's investigation shows that the launch of this new compound has been difficult and this product cannot therefore be considered to constitute an immediate competitive constraint to the parties' products.
97. On the basis of the foregoing, serious doubts as to the compatibility of the operation with the common market exist in anti-virals.

b) Topical anti-virals (D6D)

98. According to the parties, the category for D6D is intended to comprise only prescription drugs but they submit that the data provided may also include some OTC sales of "Zovirax" in those countries where it is available OTC (the UK, France, Germany and Finland). The parties argue that the information provided exaggerates the "Zovirax" prescription market share because other topical anti-virals are not generally available both on prescription and OTC and, thus, the same double counting does not occur for these products. SB's "Vectavir" (*penciclovir*) was previously only available

on prescription but has recently been launched OTC in Sweden, Denmark, Finland and the Netherlands. These OTC sales do not, however, appear in the 1999 IMS sales data.

99. In order to assess whether the inclusion of the OTC sales of “Zovirax” would significantly distort the parties’ market position, the Commission requested the parties to estimate if the deletion of ”Zovirax” sold OTC from the market share information would materially affect the parties’ market position. On the basis of the further information provided by the parties, the Commission draws the conclusion that the changes are only few percentage points and, therefore, the parties’ market shares are not materially affected.
100. Based on the IMS data provided by the parties, their combined market shares in the ATC third level category D6D would be very high in most Member States. The parties would attain [90-100%] of the market in France (GW: [90-100%], SB: [<5%]), [80-90%] in Denmark (GW: [70-80%], SB: [10-20%]), [80-90%] in Belgium (GW: [75-85%], SB: [<5%]), [80-90%] in the UK (GW: [75-85%], SB: [<5%]), [75-85%] in Finland (GW: [60-70%], SB: [10-20%]), [70-80%] in Greece (GW: [70-80%], SB: [<5%]), [70-80%] in Luxembourg (GW: [70-80%], SB: [<5%]), [70-80%] in Austria (GW: [70-80%], SB: [<5%]), [60-70%] in Italy (GW: [50-60%], SB: [<10%]), [55-65%] in the Netherlands (GW: [50-60%], SB: [<5%]), [50-60%] in Spain (GW: [50-60%], SB: [<10%]) and [40-50%] in Germany (GW: [40-50%], SB: [<5%]). SB’s “Vectavir” has not been launched in Portugal and Ireland yet and, therefore, no overlap occurs. In Sweden, there is no overlap between the parties’ products because “Zovirax” is not approved for sale in this category there. If considering the OTC segment separately, the investigation shows that the parties’ position in those countries where overlap occurs would not be materially affected as GW would have similar market shares also in this segment.
101. The parties submit that, in Italy, they would face strong competition from Sigma Tau who currently accounts for [20-30%] of the market with this product. However, this company’s market share is only about third of that of the new entity. In Finland, Luxembourg, Germany and Spain, the largest competitor accounts for 11-13% of each of those markets. However, given that the market shares of the parties range between [40-50%] and [75-85%] in those countries, it must be considered unlikely that competitors could constrain the market behaviour of the new entity. In all other Member States, the largest competitors are small, accounting for between 2.1% and 10% of the market. In conclusion, actual competition is relatively weak in most Member States.
102. The parties argue that topical “Zovirax” is under competition from suppliers of generic topical treatments. In this respect, the parties have submitted that the patent protection for the *aciclovir* molecule in “Zovirax” has expired. The parties have provided information showing that, over the three year period 1997 to 1999, “Zovirax” has lost [<10%] market share by value and [5-15%] by volume on an EU level. At the same time, the parties argue that generic *aciclovir* gained [<5%] of the market by value and [<10%] by volume.
103. The information submitted by the parties indeed shows that, in value terms, generic *aciclovir* has gained market share in a number of Member States while the market share of “Zovirax” has declined. However, the Commission notes that in Greece, Italy and Spain “Zovirax” has more or less maintained its position while the market share of generic *aciclovir* has declined. Therefore, the Commission concludes that the evolution

of the market share of “Zovirax” is not necessary linear with the introduction of generic *aciclovir*.

104. Indeed, the market share data submitted by the parties shows that “Zovirax” has been able to maintain very high market shares despite the introduction of generic competition. On the basis of the information provided by the parties, during the period between 1997 and 1999, the market share of “Zovirax” deteriorated only relatively slightly and, in any case, did not drop below [65-75%] in Greece (from [70-80%] to [70-80%]), Austria (from [75-85%] to [70-80%]), Belgium (from [85-95%] to [75-85%]), Denmark (from [85-95%] to [70-80%]), the UK (from [90-100%] to [75-85%]) and Luxembourg (from [80-90%] to [70-80%]). The most pronounced decline in the market share of “Zovirax” can be seen in the Netherlands, where the market share fell from [90-100%] in 1997 to [50-60%] in 1999. In any event, the Commission notes that the market share of “Zovirax” has not declined below [40-50%] (in Germany), despite the fact that “Zovirax” lost the patent protection in all Member States mentioned above between 1995 and 1997, in Germany in 1993 and in Greece already in 1990.
105. In France, “Zovirax” gained market share of [<5] percentage points from [85-95%] to [90-100%] between 1997 and 1999, although the Commission notes that *aciclovir* came off patent only in 1999. However, there was a slight increase in the market share also in Spain from [45-55%] to [50-60%], although *aciclovir* came off patent in that country already in 1997.
106. In volume terms, the decline of “Zovirax” market share has been more marked than when assessed in value terms. However, the fact that “Zovirax” has been able to maintain its market position in value terms at a relatively high level despite generic competition is more relevant for the assessment of this case than the fact that the sales volumes have declined. Indeed, this demonstrates that, despite generic *aciclovir* taking sales volumes, “Zovirax” has been able to generate revenue for GW at far higher levels than competing generic products.
107. Third parties in their replies to the Commission’s enquiries have indicated that generic competition to “Zovirax” has not been very successful. In this respect, the investigation shows that “Zovirax” is a very strong, established brand on the market and is considered to constitute a significant barrier to entry for generic products. Customers have indicated for instance that, due to heavy advertising and brand awareness, the topical branded “Zovirax” holds a far higher market share than generic products. Competition against such a strong brand is reported to be difficult.
108. The Commission notes further that not all the market share lost by “Zovirax” has migrated to generic *aciclovir*. Indeed, almost half of the market share lost by “Zovirax” in value terms and some third in volume terms on an EU level migrated to SB’s “Vectavir” between 1997 and 1999. In this respect, the parties argue that, on an EU level, the market share accretion is less than [$<10\%$]. The Commission notes that “Vectavir” has been launched only very recently in a number of Member States, like in France, Italy, the Netherlands and Spain only in 1999. Therefore, in some Member States, the accretion of market share is indeed very small (for instance only [$<5\%$] in France). However, as will be explained below, “Vectavir” has gained market share rapidly in most Member States where it has been launched. It is also considered to be a very important prescription brand. Therefore, the Commission considers that even a *de minimis* accretion of market share needs to be taken into account in the assessment of

the case, especially in view of the fact that GW's "Zovirax" has a very strong market position in most Member States.

109. More particularly, on the basis of the information submitted by the parties, it can be seen that "Vectavir" has gained rapidly market share in value terms in most Member States where it has been launched. Only in the UK, the market share has remained stable. The growth of "Vectavir" has been particularly strong in Sweden, where it has taken [50-60%] of the market since its introduction in 1997. Since 1997, "Vectavir" has increased its market share to [10-20%] in Finland and, since 1996, to [10-20%] in Denmark. In Italy, "Vectavir" gained [<5%] market share in two years time, in Belgium [<5%] and in Luxembourg [<5%]. The market share data by volume shows that "Vectavir" has gained market share even more rapidly in particular in Sweden, where it has [55-65%] of the market. In Italy the market share of "Vectavir" by volume is [10-20%], in Belgium [10-20%] and in Spain [5-15%].
110. Third parties have indicated that "Vectavir" is a significantly rising prescription brand. Third parties have indicated that it is difficult to compete against an established brand in the prescription market in Europe, because no direct consumer advertising is permitted. In this respect, third parties have submitted that advertising for OTC products may lead to an increase in the market share for the prescription form also. However, given that topical anti-virals other than GW's "Zovirax" are not generally available both on prescription and OTC, this effect may be useful only to GW.
111. It has further been indicated to the Commission that a product which is well established in the prescription market will be easier to launch OTC. In this respect, "Vectavir" has only recently been launched OTC in Sweden, Denmark, Finland and the Netherlands. The Commission notes that "Vectavir" has gained rapidly market share in the prescription market in Sweden, Finland and Denmark, where it holds its highest market shares. The parties have submitted that it is their intention to launch "Vectavir" in other Member States as well.
112. Third parties have expressed concern over the operation and argue that the merger would lead to the creation of a dominant position in the market for topical anti-virals. As noted above, although competitors have entered the market with generic *aciclovir* in recent years, this has not lead to any significant changes on the market and "Zovirax" has been able to largely maintain its position. Third parties have indicated that, as in anti-virals, the operation as notified would discourage any research and development attempts by third parties to develop drugs for herpes for the topical anti-virals market and new entry would be more difficult.
113. On the basis of the foregoing and in particular in view of the new entity's very high market shares in most Member States, serious doubts exist as to the compatibility of the operation with the common market in topical anti-virals.

c) Anti-emetics/anti-nauseants (A4A)

114. Following the operation, the parties would attain very high market shares in most Member States. Apart from Germany and Portugal, where the operation does not create an overlap, only in Spain the parties' market share is not indicative of a dominant position, as they account for less than [20-30%] of that market.

115. On the ATC third level A4A, the parties' combined market shares would be as follows: in Luxembourg [85-95%] (GW: [85-95%], SB: [<5%]), Denmark [80-90%] (GW: [75-85%], SB: [<5%]), Ireland [75-85%] (GW: [60-70%], SB: [10-20%]), the Netherlands [75-85%] (GW: [60-70%], SB: [10-20%]), Belgium [65-75%] (GW: [60-70%], SB: [<10%]), France [70-80%] (GW: [40-50%], SB: [20-30%]), the UK [65-75%] (GW: [45-55%], SB: [15-25%]), Greece [60-70%] (GW: [40-50%], SB: [10-20%]), Italy [60-70%] (GW: [30-40%], SB: [25-35%]), Finland [60-70%] (GW: [35-45%], SB: [20-30%]) and Sweden [50-60%] (GW: [45-55%], SB: [<10%]). The increment of market share is less than [10%] in Denmark and Luxembourg. However, given the very high market shares attributable to GW's "Zofran" and relatively weak actual competition, the increment has to be considered sufficient to raise serious doubts also in these Member States.
116. The market shares would not change essentially if, as the parties have suggested, some gastroprokinetics would be included into the market definition: the market shares would be still far higher than those of the closest competitors and in the region of [45-55%] and more in most Member States (from [40-50%] in Greece to [80-90%] in Denmark).
117. The parties argue that effective competition exists from "Navoban" (Novartis) and, in certain countries, also from "Anzemet" (Aventis). The parties submit that "Navoban" has achieved a share of [10-20%] of all 5HT3-antagonists sold in the EU by 1999. The parties further submit that "Anzemet", which is a new market entrant, would be in a good position to compete with the parties' products. Namely, the parties argue that the ability of "Anzemet" to capture market share from "Zofran" and "Kytril" has been demonstrated by the US experience, where "Anzemet" has grown successfully after market entry. Finally, the parties submit that the existence of "Navoban" and, in some cases, "Anzemet" would be sufficient to constrain any attempt to raise prices.
118. The Commission notes, however, that the 5HT3-antagonists dominate the market for anti-emetics and that the parties' position in 5HT3-antagonists is extremely strong. GW's "Zofran" was launched in 1990 and was the first product to reach the market. It was followed by SB's "Kytril" in 1991. Currently, "Zofran" and "Kytril" are the number one and number two leading products in France, the Netherlands, the UK, Italy and Ireland. In Belgium, Austria, Denmark, Finland and Greece "Zofran" and "Kytril" are number one and three leading products. Apart from Austria and Sweden, where Novartis has a relatively strong presence, the parties' market share would be between three and eight times higher than that of the closest competitor in all other Member States.
119. The Commission also notes that, since its launch across Europe between 1992 and 1996, "Navoban" accounts only for [10-20%] of the EU market, while the parties' combined market share is currently [75-85%]. Furthermore, the Commission notes that although "Navoban" holds [30-40%] of the market in Austria (depending on the market definition used) and [30-40%] of the market in Sweden, the parties would still be twice as large as Novartis in Austria and their market share would be around [45-55%] or exceed that figure also in Sweden. Therefore, although "Navoban" has been available across EU by 1996, it has not been able to challenge the market position of the parties. Therefore, "Navoban" cannot be considered to have been particularly successful in competition against the two leading suppliers.

120. With regard to “Anzemet”, this compound was first launched in the US in 1997 and subsequently in a number of European countries between 1997 and 1999. It is currently available only in Germany, France, Austria and Italy. The Commission notes, however, that the current market share of “Anzemet” is merely [$<5\%$] at the EU level and it is also relatively weak in all those Member States where it is currently available. Third parties in their replies to the Commission’s enquiries have confirmed that “Anzemet” has had little impact on the sales of “Zofran” and “Kytril” and they do not anticipate “Anzemet” to be able to constrain the parties’ market power and their ability to raise prices. Although the parties submit that “Anzemet” has been registered to be launched in Finland, the Netherlands, Sweden and the UK and pre-registered in Spain, in view of the market development of “Anzemet” and the favourable image of the gold standard held by the parties’ compounds, the Commission does not consider it likely that “Anzemet” would be able to counterbalance the dominant market position of the new entity across the EU.
121. According to the parties, competition is intensified by the buying power and tendering practises of the major customers. 5HT₃-antagonists are predominantly used in cancer treatment and, therefore, typically purchased by hospitals (particularly those anti-emetics which are given intra-venous). The parties argue that these large buyers are in a position to exercise buyer power mainly through tenders. As a consequence, the parties argue that aggressive competition has taken place and that the majority of markets have been characterised by aggressive price competition among companies and heavy discounting.
122. Third parties have indicated to the Commission that hospitals most generally try to obtain lower prices either by tenders, buying in consortiums or agreeing to buy only one single drug from a particular category if a quantity discount is granted. In this respect, it has been indicated that the competition between GW, SB, Novartis and, recently also to some extent from Aventis, has helped in keeping the prices for 5HT₃-antagonists down. However, given that “Anzemet” is only available in a few Member States, in practice, the merger would basically reduce the number of competitors from three to two, bringing together the two leading companies in this market. Third parties in their replies to the Commission’s questionnaires have indicated that neither “Anzemet” nor “Navoban” are considered to bring substantial medical benefits over “Zofran” and “Kytril” and are not expected to replace these drugs.
123. Post-merger, the parties would capture some [$75-85\%$] of the market, leaving only some [$15-25\%$] to Novartis and Aventis. Third parties have indicated that the operation as notified would lead to the creation of a dominant position and a near monopoly in 5HT₃-antagonists indicated for the treatment of cytotoxic induced nausea and vomiting, which forms the main part of this market. In view of the parties’ post-merger strong position, the Commission considers it likely that the operation reduces the possibilities for major customers to negotiate discounts. Third parties have expressed concern that the operation as notified would lead to price increases of the two leading drugs. Moreover, the combination of the parties’ products would give them the possibility to set up barriers for market entry by granting quantity discounts for hospitals. It would be extremely difficult for the two remaining, substantially smaller competitors to respond to this.
124. In view of the foregoing, the Commission considers that serious doubts as to the compatibility of the notified operation with the common market exist in the treatment area of anti-emetics in most Member States.

d)Antibiotics (J1)

d.1) Broad Spectrum Penicillins (J1C)

125. With regard to the ATC 3 category J1C, SB holds a market share of [50-60%] in the EU. GW is not present in these market, except in Spain, where GW markets a generic product, currently purchased in bulk from SB. In Spain the market share of SB is [50-60%] and GW holds [<5%] of the market. The operation would lead to a joint market share of [50-60%].
126. The parties submit that, in Spain, their products are not protected by patents. Thus, the parties argue that they will not only be exposed to competition from other penicillins but will also face increasing competition from generic products. SB produces and markets a range of broad spectrum penicillins, the principal of which are “Augmentin” and “Amoxil”. “Amoxil” consists of *amoxillin*, a member of the penicillin antibiotic class, whereas “Augmentin” contains *amoxillin* in combination with *clavulanic acid*, a beta-lactamase inhibitor. According to the parties *Amoxillin* has been off patent for some time. SB’s “Augmentin” has recently gone off patent in the majority of EU Member States, including Spain.
127. With special regard to the Spanish market, the parties claim that a number of major manufacturers supply broad spectrum penicillins, including Columbia ([5-15%] of the market), Pharmacia & Upjohn ([<10%]) and J. Uriach ([<5%]). Additionally, a large number of pharmaceutical companies market generic *amoxicillin* in Spain, including Ratiopharm, Sabater, Norman, Geminis and Belmac.
128. As GW is not manufacturing broad spectrum penicillins but markets a product purchased from SB, the operation will have only limited effects on the level of distribution. The Commission notes that the market share increment is small and the parties are facing competition by a number of manufactures and also by generic products. Customers who replied to the Commission’s market investigation do not expect that the operation will lead to adverse competition effects. In view of the foregoing, the Commission considers that the operation does not raise serious doubts as to its compatibility with the common market in the market for broad spectrum penicillins (J1C) in Spain.

d.2) Cephalosporins (J1D)

129. As to cephalosporins (J1D), GW has a EU-wide market share of [15-25%], whereas SB’s sales amount to only [<5%]. However, the only national markets affected are those of Belgium, Italy and Spain, where SB markets its products “Monocid” and “Cefizox”.

Belgium, Italy

130. In Italy, the market share of GW and SB amounts to [10-20%] with an increment of [<5%]. Given this comparatively small combined market share and the fact that the parties face severe competition from the market leader Roche ([20-30%] of the market) and other potent pharmaceutical companies such as Aventis ([<10%]) and Bristol-Myers Squibb ([<10%]), competition concerns are unlikely to arise.

131. In Belgium, the combined market share of the parties in is [40-50%] with an increment of [<5%]. Considering in particular the *de minimis* overlap in Belgium and the fact that there is strong competition on the market, the largest competitor being Bristol-Myers Squibb accounting for [15-25%] of the market, the Commission draws the conclusion that the operation does not raise serious doubts as to its compatibility with the common market in Belgium.

Spain

132. In Spain, the merger would lead to a combined market share of [40-50%] with a significant overlap of [10-20%] arising first and foremost from SB's "Monocid". The parties argue that the market share increment results from the prescribing praxis in Spain, where for historic reasons SB's product "Monocid" is frequently used by doctors in rural areas of Spain, to provide antibiotic cover for elderly patients undergoing minor surgery, which carries a risk of infection.

133. The parties submit that except for this local prescribing habit, GW's and SB's products can not be considered to be direct competitors. GW markets four broad spectrum cephalosporins in the EU: "Zinnat", administered in oral form and covering a wide range of community indications; "Fortum", mostly used in cases of severe hospital infections; "Zinacef", which is injected; and "Ceoprex", which is orally administered for community indications. On the other hand, SB's agent "Monocid" (also distributed as "Cefonicid"), an injectable cephalosporin, is principally used only in hospitals and is limited in its use against a relatively narrow spectrum of organisms within each indication. Because of this limited applicability, the parties argue that it cannot be considered to be substitutable to GW's products "Zinacef", "Zinnat" and "Fortum". In addition, SB also distributes "Cefizox" in Spain. This injectable cephalosporin, however, accounts for only negligible sales⁷.

134. Furthermore, the parties submit that "Zinacef" and "Ceporex" are already off patent and "Zinnat" will come off patent in [...] in Spain. The parties indicate that under these circumstances, potential competition by generics is likely to increase within the next years. Also the parties argue that there are many other cephalosporins available on the market. With regard to the Spanish market, the main competitors include Eli Lilly ([10-10%] of the market), Merck ([5-15%]) and Menarini ([<10%]).

135. The arguments of the parties can not remove serious concerns on the J1D segment. GW and SB are the number one and number two suppliers on the Spanish market, and the largest competitor, Eli Lilly, would have less than one third of the aggregated market share of the parties. Both parties market a range of well established brands. Certain historic prescribing habits do exist, which are not likely to change in the short run, and do form considerable barriers to entry for new competitors. In addition, GW's product "Fortum" is still under patent protection and is, according to the parties, frequently used as an empiric initial treatment. On the basis of the foregoing, the Commission concludes that no evolution in favour of generic products or new pharmaceuticals is likely to occur.

⁷ The sales of "Cefizox" are so small that they are not even reported in IMS data.

136. On the basis of the foregoing, serious doubts as to the compatibility of the operation with the common market exist in the J1D segment in Spain.

d.3) Quinolones (J1G)

137. As to the market for quinolones (J1G), no significant market overlap occurs between the parties, due to the fact that SB's European presence is limited to the market in Italy with a negligible market share of only [$<5\%$]. The combined market share of the parties in Italy is [10-20%].

138. In addition, GW has indicated that it has withdrawn its product "Raxar" which accounted for almost all its sales in the European market (EU market share of GW of [$<5\%$]), except for the Italian market. It is to note, however, that SB currently has a quinolone, "Factive", in phase III clinical trials. This product is a [...].

139. The parties state, however, that there are several quinolones on the market and in development in Europe and in the United States. With special regard to the Italian market, competitors include leading companies such as Bayer ([40-50%] market share), Aventis ([10-20%] market share) and Ibi ([$<10\%$] market share). In addition, a number of quinolones marketed in Europe are in-licensed from Japanese pharmaceutical companies. These companies are described as "power house" for discovery and development of new quinolones with promising drugs in their R & D pipeline. The parties claim that many of those pharmaceuticals are likely to be available for in-licensing in Europe, since those Japanese companies did not have European operations.

140. On the basis of the foregoing, in view of the negligible overlap and the withdrawal of GW's "Raxar" from the market, the Commission considers that the operation does not raise serious doubts as to its compatibility with the common market in the market for quinolones (J1G) in Italy.

e) Anti-malarials (PID)

141. The parties' activities in anti-malarials overlap in Belgium, Germany, Luxembourg, the Netherlands, Spain and the United Kingdom. However, apart from Spain, the parties' combined market shares remain below [5-15%].

142. In Spain, the IMS data suggest that the parties would account for [90-100%] of the market. The parties argue, however, that a number of anti-malarial products can be acquired through "Medicamentos Extranjeros", a department of the Spanish Ministry of Health. The "Medicamentos Extranjeros" system enables physicians to prescribe a limited number of products for very specific diseases in Spain, although they are not expressly licensed in Spain. According to the parties, this is the case for malarial products, which include *mefloquine* and *chloroquine/proguanil*. The parties submit that the products which are supplied through the "Medicamentos Extranjeros" system are not sold through pharmacies but supplied directly to the physician who asked for the product. Consequently, the parties argue that such products are not registered in IMS sales audit and, therefore, the parties' market share is significantly overstated by the IMS figures. The parties estimate that, including the sale of *mefloquine* and *chloroquine/proguanil* in the Spanish market, their combined market share is below [5-15%].

143. The Commission has obtained confirmation from “Medicamentos Extranjeros” that the size of the total anti-malarials market when including *mefloquine* and *chloroquine/proguanil* is indeed considerably larger than the IMS data suggest (some EUR 1.3 million instead of EUR 50 000). On the basis of this information and together with confidential figures obtained from third parties, the Commission has estimated that the parties’ market share in the Spanish market does not exceed [5-15%]. Therefore, no competition concerns are likely to arise in this market.
144. The parties submit that SB is in the process of developing “Tafenoquine”. The product is [...].
145. Although some third parties have indicated that the parties’ pipeline products could enhance the parties’ combined market position, the Commission considers that no competition concerns are likely to arise given the parties’ current low market shares.

f) Topical antibiotics (D6A)

146. In topical antibiotics, the parties’ activities overlap in Germany, Ireland and the UK. The parties would account for [30-40%] of the market in Ireland (GW: [15-25%], SB: [5-15%]), [25-35%] in the UK (GW: [<5%], SB: [20-30%]) and [<10%] in Germany (GW: [<5%], SB: [<10%]).
147. On hypothesis that the parties’ products have different indications, no overlap occurs and there is no aggregation of market share. Assuming that the products belong to the same product market, the operation will not lead to the creation of a single dominant position because in Ireland and the UK, where the parties attain their highest market shares, they would face strong competition. The market leader Leo has [50-60%] of the market in Ireland and [40-50%] in the UK. A number of other competitors are also on the market.
148. The operation is unlikely to lead to the creation of a collectively dominant position either, even if the three largest companies active in the UK market (Leo, SB and Smith & Nephew) and in the Irish market (Leo, GW and Smith & Nephew) will have an aggregated market share of more than [75-85%]. The respective market shares of these companies are not static but fluctuate and are asymmetric. For example, in the UK, Leo increased its market share from [30-40%] in 1997 to [35-45%], while the parties’ aggregated market share fell from [30-40%] in 1997 to [25-35%] in 1999. Also, Smith & Nephew lost some market share during this period from [20-30%] to [15-25%]. It may also be noted that demand has grown from EUR 11,757 million in 1997 to EUR 12,466 million in 1999. Similarly, in Ireland, Leo increased its market share from [45-55%] to [50-60%] and Smith & Nephew its market share from [5-15%] to [5-15%] in 1997-1999. The market has grown from EUR 658,000 million in 1997 to EUR 682,000 million in 1999. Thus, each company may increase its sales without necessarily implying a reduction in the other companies’ market shares.
149. On the basis of the foregoing, the Commission does not consider that the operation as notified would lead to any adverse competition effects

2. Future markets

150. The areas of overlap where either one or both parties have existing products on the market and pipeline products are asthma/COPD, anti-migraine (N2C), therapeutic

vaccines (“pharmaccines”) and other urologicals, including antispasmodics (G4B). Areas where neither party is currently active on the market but where both parties have pipeline products are diabetes (A10B), oncology (L1) and irritable bowel syndrome. These treatment areas will be discussed in more detail below.

a) Asthma/COPD

a.1) Asthma/COPD conditions

151. The parties submit that although asthma and COPD (“Chronic Obstructive Pulmonary Disease”) are both diseases of the respiratory tract, the two diseases are characterised by different clinical presentations, different risk factors, different inflammatory processes and different therapies.
152. Asthma is an inflammatory disease which is characterised by acute episodes of airflow limitation. These episodes are transient and fully reversible. Airflow obstruction in asthma is due to bronchoconstriction and inflammation of the airway wall. The former is caused by spasms of the muscle layer within the airway wall resulting in a narrowing of the air pipes (bronchi), whereas inflammation causes a thickening of the airway wall, due to the accumulation of cells and fluid. Bronchodilators are used to reverse the bronchoconstriction, while anti-inflammatory drugs are used to treat the inflammation.
153. The Commission considered products indicated for the treatment of asthma in case *M.1403 – Astra/Zeneca*. In line with this decision, the parties submit that asthma-related respiratory drugs may broadly be categorised into short-acting treatments (or “relievers”) and treatments for prophylactic or long-term management of the illness (or “preventers”). Short-acting symptomatic treatments are aimed at reversing the bronchoconstriction which results in the wheezing and breathlessness during an asthma attack, without necessarily having any therapeutic effect on the underlying disease. Drugs used in prophylaxis or long-term management may result in the patient being symptom free for extended periods of time or having only minor symptoms which do not affect his or her daily life.
154. In *M.1403 – Astra/Zeneca*, the Commission concluded that there is a clear differentiation between the objectives of therapy for these two types of treatment and that therefore competition occurs more within than across types. This distinction is meaningful from a medical point of view as it allows the treating physician to balance the need for primary intervention with short-acting relieving agents, with or without disease modification depending on the severity, and the appropriate addition of long-term symptom controllers. Moreover, short-acting symptomatic drugs are used only on a needed basis whereas prophylactic and long-term drugs are taken regularly daily.
155. The parties submit that, broadly speaking, the prophylactic and long term management treatments of asthma tend to be regarded as those under non-steroidal respiratory anti-inflammatories (R3C), corticoids (R3D) and leukotriene receptor antagonists (“LTRAs”) (R3J). Moreover, long-acting B2-agonists (R3A), theophylline (R3B) and cromones are used. The short-term symptomatic treatments are regarded as those under B2-stimulants (R3A, short-acting B2-agonists), xanthines (R3B), anticholinergics (R3G) and R3X (all other bronchodilators). The prophylactic and symptomatic combinations are those at R3E (combinations of B2-stimulants with R3C) and R3F (combinations of B2-stimulants with corticoids R3D). The parties nevertheless submit that the distinction is not clear cut as for instance the R3A category includes drugs

which are both short and long acting. Indeed, in *M.1403 – Astra/Zeneca*, the Commission noted that for instance the long acting B2-stimulants *salmeterol* and *formoterol* in R3A are used for long-term management of asthma. There are also classes of combination drugs which combined symptomatic drugs and drugs for prophylaxis/long term management.

156. The parties argue that unlike asthma, COPD is not a single disease, but a spectrum of poorly reversible conditions including, in particular, chronic bronchitis (chronic cough and sputum production), inflammation and emphysema (permanent destruction of lung units). The key defining characteristic is airflow obstruction. Patients with COPD suffer chronic symptoms, including shortness of breath, cough, phlegm and a limitation on their ability to take an active part in daily life. According to the parties, the fact that the symptoms are chronic, i.e. continuing rather than episodic, is in sharp contrast to patients with asthma who do not suffer symptoms all the time. Patients with COPD also have an increased susceptibility to bacterial infections. Furthermore, COPD is a progressive disease, with acute severe worsening leading to hospitalisation and, even death.
157. The parties submit that whereas asthma is well understood and well treated, the products that are used to treat COPD are largely ineffective and, therefore, patients are generally treated with multiple therapy. In this respect, the parties submit that patients with mild COPD on average use between [<5] and [<5] products, while patients with severe COPD use as many as [<5] products on average.
158. As opposed to asthma, there is currently limited agreement between the various sets of COPD guidelines worldwide, in terms of diagnosis and management of the disease. The parties submit that the only point of agreement among the existing guidelines is the recommendation for first line therapy which is either inhaled anticholinergics (R3G) or short acting B2-agonists (R3A). As disease severity increases, a variety of agents are added to improve symptomatic control such as combination bronchodilators (belonging to R3G), inhaled long-acting B2-agonists (belonging to R3A), inhaled corticosteroids (R3D), xanthines, principally theophylline (R3B), B2-stimulants and corticoid inhalants (R3F) and leukotriene antagonists (R3J). Oxygen is the therapy of last resort.

a.2) Actual competition

159. While SB has not current respiratory products on the market, GW has a long-established position in the respiratory field and has products in several major categories, most importantly in R3A, R3D and R3F. GW's products include a short acting beta-agonist "Ventolin" (*salbutamol*), a long acting beta-agonist "Serevent" and inhaled corticosteroids "Becotide" (*beclomethasone*) and "Flixotide" (*fluticasone*). GW also has "Seretide", a combination product of B2 agonist/inhaled corticosteroid, in the R3F category. "Seretide" has been approved for asthma and has been launched in most EU Member States.
160. In 1999, the total sales of anti-asthmatic/COPD products (ATC level 2 - R3) in the EEA reached a value of EUR 3,099 million. At this aggregated level, GW achieved sales of EUR [...] million, corresponding to [40-50%] of the total market. GW has increased its market share from 1997, when it accounted for EUR [...] million of the total market of EUR 2,560 million, corresponding to [35-45%] of the total EEA-wide market. On this level, the largest competitors are AstraZeneca ([15-25%]), Boehringer Ingelheim ([$<10\%$]), Novartis ([$<5\%$]) and Aventis ([$<5\%$]).

161. At the national level, in R3F (combinations of B2 stimulants/corticoids), GW has currently [90-100%] of the market in ten Member States in which it is present with its combination products “Seretide” and faces no competition from other pharmaceutical companies.
162. In R3A (B2 stimulants), GW’s market position is relatively strong in most Member States. Apart from Germany and Italy, GW’s market share ranges between some [45-55%] and [75-85%] in most Member States. More particularly, GW accounts for [75-85%] of the market in Luxembourg (AstraZeneca: [10-20%]), [70-80%] in Belgium (AstraZeneca: [5-15%]), [70-80%] in the UK (AstraZeneca: [10-20%]), [60-70%] in Ireland (AstraZeneca: [10-20%]), [60-70%] in Finland (AstraZeneca: [20-30%]), [55-65%] in Greece (Novartis: [20-30%]), [55-65%] in France (Novartis: [20-30%]), [60-70%] in the Netherlands (Novartis: [10-20%]), [50-60%] in Denmark (AstraZeneca: [20-30%]), [50-60%] in Sweden (AstraZeneca: [30-40%]), [40-50%] in Spain (AstraZeneca: [10-20%]), [40-50%] in Portugal (Bial: [15-25%]) and [40-50%] in Austria (AstraZeneca: [25-35%]). In Germany and Italy, GW accounts for [30-40%] and [30-40%] of the market in each Member State respectively. It can be seen from these figures that while GW faces relatively strong competition from AstraZeneca in Austria and Sweden, in all other Member States GW’s closest competitors are much smaller.
163. In R3D (corticosteroids), where GW accounts for some [35-65%] of the market in ten Member States, the market situation is more balanced in most Member States, with a number of competitors, most importantly AstraZeneca, on the market with market shares between [25-35%] and [35-45%]. However, GW has a particularly strong position in Austria (GW: [50-60%], AstraZeneca: [35-45%]), Finland (GW: [45-55%], AstraZeneca: [30-40%]), France (GW: [50-60%], AstraZeneca: [30-40%]), Luxembourg (GW: [55-65%], AstraZeneca: [35-45%]), the Netherlands (GW: [55-65%], AstraZeneca: [25-35%]) and the UK (GW: [55-65%], AstraZeneca: [20-30%]).
164. With regard to asthma, the Commission has estimated in line with case M.1403 – Astra/Zeneca on the basis of IMS data that GW accounts, on the segment for short-term management of asthma, for some [25-35%] of the sales on an EEA level. The largest player in this segment is Boehringer Ingelheim with [30-40%] of sales. AstraZeneca accounts for some [5-15%] and Novartis [<10%] of the sales in this segment on an EEA level. On the segment for the long-term management of asthma, the Commission has estimated that GW has currently a share of sales of some [40-50%] on an EEA level. AstraZeneca holds a share of sales of [20-30%], while all the remaining competitors such as Aventis and Novartis have less than [<10%] of that segment.
165. With regard to COPD, the investigation shows that the sales attributable to COPD can be divided as follows: some 30% of the sales derive from B2-agonists (R3A), 29% from corticosteroids (R3D), 25% from anticholinergics (R3G) and 10% from xanthines (R3B). The remaining 6% is divided amongst other categories, most importantly to leukotriene receptor antagonists (R3X). Given that GW is mainly active in R3A and R3D, its products cover therefore about the half of the COPD segment.
166. The parties do not consider mild, moderate and severe COPD to constitute separate markets, the reason being that the same products are used in all three categories. The parties have not been able to supply market data split by severity of the disease as IMS does not provide these data. The parties submit that as the severity of the disease increases, the use of all products increases roughly in proportion with total increase of

products used. On this basis, GW has estimated that its market share in mild, moderate and severe COPD is [...].

167. The parties submit in the notification that although there is no observable split as between respiratory products used in treatments of asthma and COPD, as a broad indication, asthma accounts for [75-85%] and COPD [15-25%] of the total EEA-wide market encompassing all categories in R3. The parties have estimated the market position of GW in the overall COPD segment and, separately, on first and second line treatment segments [for the purposes of this decision, “second line treatment” shall refer to treatments used in combination with other therapies]. The parties have explained that it is possible to split the IMS data on the basis of prescriptions and, to this end, they have used four different types of COPD diagnoses⁸ as a basis for the market share calculations. Following this method, the parties submit that GW’s market share in the overall segment for the treatment of COPD is [30-40%] in value. AstraZeneca accounts for [10-20%] of this segment and Boehringer Ingelheim some [10-20%]. In first line therapy of COPD, GW accounts according to the parties only for [20-30%]. The parties argue that this relatively low market share can be explained by the fact that while GW is a key player in inhaled short-acting B2 agonists (R3A) with its product “Ventolin”, it is not present in anticholinergics (R3G), which is dominated by Boehringer Ingelheim with its products “Atrovent” and “Combivent”. The parties submit that Boehringer Ingelheim is the clear leader in this segment with [50-60%] of the sales. Finally, the parties submit that GW’s current market share in second line of treatment of COPD is [35-45%]. AstraZeneca has some [15-25%] of the segment and Boehringer Ingelheim only around [<5%].
168. The parties have further split the four diagnoses areas according to first and second line therapies. These market shares reflect largely the parties position in the overall first and second line segments. On the basis of this data, the position of the main players in first line therapy by value is as follows: in J41, Boehringer Ingelheim has [35-45%] of this segment, GW [30-40%] and AstraZeneca [<10%]. In J42, Boehringer Ingelheim accounts for [45-55%], GW [15-25%] and AstraZeneca [10-20%]. In J43, Boehringer Ingelheim has [55-65%] of that segment, GW [15-25%] and AstraZeneca [<10%]. Lastly, in J44, Boehringer Ingelheim has a market share of [50-60%], GW [20-30%] and AstraZeneca [<10%]. In sum, Boehringer Ingelheim is the clear market leader in all diagnoses areas in first line treatment.
169. In second line treatment, GW is the strongest player. In J41, GW has [45-55%] of that diagnosis area and AstraZeneca [25-35%]. In J42, GW’s share of sales is [25-35%] and AstraZeneca’s [10-20%]. In J43, GW accounts for [40-50%] of the segment and AstraZeneca [15-25%]. Finally, in J44, GW has [35-45%] of that segment while AstraZeneca has [20-30%]. Boehringer Ingelheim has a *de minimis* presence ([<5%]) in second line treatment diagnoses areas.
170. While the Commission’s calculations largely correspond to the market position of the main players as presented by the parties, the Commission notes that there are some important differences in the market shares calculated on the basis of the methodology suggested by the parties and on the basis of available IMS data. In view of the parties’

⁸ J41 Simple Mucopurulent Chronic Bronchitis, J42 Unspecified Chronic Bronchitis, J43 Emphysema, J44 Other Chronic Obstructive Pulmonary Disease

submission that a combination of different products are used for the treatment of COPD and that, in general terms, compounds in all different R3 categories can be used for the treatment of COPD, the Commission considers that GW's market share in the overall segment for COPD should be [40-50%], in other words, the same as in the overall R3 segment. The Commission has further estimated that, in the segment for first line treatment of COPD which includes short-acting B2-agonists and R3G, GW accounts for some [30-40%] while Boehringer Ingelheim accounts for some [35-45%] of this market. Finally, The Commission has estimated that GW's share in second line treatment (the overall market - first line treatment) is somewhat higher, around [40-50%], while AstraZeneca accounts for some [15-25%] of that segment and Boehringer Ingelheim less than [<5%].

171. In conclusion, whichever method is used to calculate market shares, GW enjoys a far stronger position in the overall treatment area for asthma/COPD in the EEA than any of its competitors. GW is also very strong in the three largest product categories it is present in at the national level. In COPD, while GW lags behind Boehringer Ingelheim in first line treatment, in second line treatment it is the clear leader with a position twice as strong as the next competitor.
172. The parties argue that GW's sales in B2-agonists and corticosteroids have remained relatively constant over time and are not expected to grow significantly in the future. In fact, the parties argue that "Ventolin" (R3A) has lost its patent protection and faces generic competition. The Commission notes, however, that while "Ventolin" has indeed lost market share ([20-30%] in 1997 and [15-25%] in 1999), GW's other compound used in asthma/COPD, "Serevent", has increased its market share from [25-35%] to [30-40%] over the same period. Moreover, IMS data shows that GW has also managed to increase its sales of corticoids from [40-50%] to [40-50%] during this period. Finally, the Commission notes that GW has been able to increase its overall market share in the respiratory market during the past three years from [35-45%] to [40-50%]. The parties have explained that GW has been able to retain its share of value as a result of the introduction of improved and thus more expensive products into each category.
173. The parties argue that GW faces competition in all the therapeutic classes in which it has a presence from companies such as AstraZeneca, Boehringer Ingelheim and Aventis. However, as seen above, GW's position is far stronger than any of the other competitors in those product categories where it is present. The parties also argue that other ATC 3 classes, in which GW is not active, are also in competition in the respiratory field. In this respect, the Commission notes that the most important categories in which GW is active (R3A, R3D, R3F) represent [75-85%] of the total EEA wide market in terms of value. In addition, GW accounts for [30-40%] of the EEA wide market in asthma devices and has increased its sales in R3G very rapidly. Therefore, the Commission considers that competition from other existing product categories in asthma/COPD is unlikely to materially affect GW's current position.
174. The parties argue that no competition concerns arise in asthma/COPD because SB does not currently produce or market any anti-respiratory products. While it is indeed true that the operation does not lead to any addition of market share, the correct assessment of the case needs to take into account SB's pipeline products in the respiratory tract. More particularly, it needs to be assessed what the impact of the transaction on existing markets and on R&D markets is.

a.3) Pipeline products

Asthma

175. With regard to asthma, SB [...]. SB 240563 is a monoclonal antibody targeted at interleukin 5 with potential for treating severe asthma and is in Phase II of development. According to the parties, this product represents a novel mechanism in this disease area, in which GW has no product in development. The second pipeline product for the treatment of asthma is SB 207499, a phosphodiesterase 4 (“PDE4”) inhibitor, which is at Phase I of development. GW has no PDE4 inhibitor in development.
176. The parties argue that no competition concerns will arise from SB’s asthma products because several other companies are developing compounds for the same treatment areas. Aventis, Merck, Byk Gulden and Schering Plough have PDE4 inhibitors in their development pipeline for asthma in Phase I and II. As regards SB’s Phase II monoclonal antibody compound, the Commission notes that Novartis has a similar compound in Phase III. AstraZeneca’s “Symbicort” is in Phase III and is expected to be launched for asthma [...]. Moreover, a number of competitors, including AstraZeneca, Pfizer and Boehringer Ingelheim have pipeline products in Phase I and II.
177. In view of the fact that GW [...], there is no risk of eliminating actual R&D competition between SB and GW. The Commission considers nevertheless that the operation would lead to a reduction of potential competition on existing markets. However, given the parties’ submission that SB’s pipeline product will be commercialised [...], that at least one similar, competing new asthma product is likely to be launched before SB’s compound reaches the market, and that there are a large number of competitors with Phase II pipeline products for asthma, the Commission does not consider that the elimination of potential competition would be likely to strengthen GW’s existing strong position in the treatment for asthma.
178. Therefore, in view of the foregoing, the Commission concludes that competition concerns are unlikely to arise in the treatment area for asthma.

COPD

179. With regard to the treatment of COPD, the parties have submitted that there is no horizontal overlap between GW’s existing products and SB’s pipeline products and, therefore, no competition concerns arise. A large number of competitors have, however, expressed concern and argued that SB’s pipeline products would further strengthen GW’s existing strong position in the field of respiratory tract. Therefore, while the market investigation has confirmed the parties’ submission that SB’s new compound is likely to be classified in a new ATC 3 category and no direct horizontal overlap occurs, it needs to be assessed whether SB’s compound is likely to affect the overall market position of the new entity in the respiratory field and whether the overall R&D potential is likely to be reduced.
180. Both GW and SB have pipeline products in the treatment of COPD. There is however no direct overlap between the parties’ pipeline products as GW and SB are developing different molecules. These molecules are indicated for both first and second line treatment of COPD.

181. GW's existing asthma product, "Seretide", is a combination of a long acting B2-agonist and a corticosteroid. This compound is currently in Phase III of development for COPD. SB has two products in pipeline for the treatment of COPD: an oral NK-3 receptor antagonist known as SB 223412 in Phase I development and a PDE4 inhibitor SB 207499 ("Ariflo") in Phase III. For the assessment of this case, only the parties' Phase III compounds are relevant.
182. The parties submit in general terms that PDE4 inhibitors represent a novel approach to the treatment of COPD which, according to the parties, may result in incrementally greater benefit compared to other therapies [...]. PDE4 inhibitors are expected to be classified within a new ATC 3 category (R3X).
183. More particularly, the parties submit that the end events in mechanism of action of COPD products are bronchodilation (to reverse contraction of the airways) and anti-inflammatory effect (to reverse inflammation). A number of pathways to achieve these end events are possible. The parties submit that "Ariflo" has a completely distinct mechanism of action from that of "Seretide". It has bronchodilation, neuromodulation⁹ and anti-inflammatory activities which are required for the treatment of COPD. According to the parties, these effects are different to those induced by corticosteroids, which are generally ineffective in modulating neutrophil driven inflammatory events, prevalent in COPD. In particular, the parties submit that the mechanism of action of "Ariflo" and of the two drugs making "Seretide" are different: [...]. The parties argue that this is the reason that "Ariflo" and "Seretide" belong to different classes of products and that there is no overlap between the parties' pipeline compounds nor between "Ariflo" and GW's existing products.
184. The parties contend that there is a large number of different classes of molecules in clinical development at this time, including those of Aventis, AstraZeneca, Bayer, Boehringer Ingelheim, Merck, Novartis, Pfizer and Schering-Plough. At present in the industry pipeline, the parties have estimated that there are as many as 30 different compounds falling into thirteen different therapeutic categories in development for COPD by over 20 different companies.
185. The Commission's investigation shows that competitors with PDE4 inhibitors in the pipeline include Byk Gulden (Altana), who has a similar compound to that of SB ("Roflumilast") in Phase III of development. Aventis and Celltech Chiroscience have a PDE4 inhibitor in Phase II each. Other competitors reported to have PDE4 pipeline products in Phase I are Basf, Bayer, Novartis, Merck, Pfizer, Napp Labs/Mundipharma, Warner-Lambert and Yamanouchi.
186. Competitors with compounds other than PDE4 inhibitors currently in development for COPD are most importantly AstraZeneca, Boehringer Ingelheim and Pfizer. [As submitted by the parties,] AstraZeneca has three compounds in Phase III development for COPD: "Symbicort", a combination of B2-agonist *formoterol* and inhaled steroid *budesonide*, a long-acting B2-agonist *formoterol turbuhaler* and a bronchodilator "Viozan". Boehringer Ingelheim has a long-acting anticholinergic compound "Spiriva"

⁹ The airways are innervated by nerves that release chemicals (neuromediators) responsible for a lot of actions such as mucus secretion by glands (sputum), inflammation or cough. Drugs blocking these chemicals have a neuromodulatory effect and can decrease inflammation, mucus secretion, or cough.

(*tiotropium bromide*) in Phase III, which according to the parties represents the most important new therapy with potential to become the next gold standard in COPD treatment. Boehringer Ingelheim has also another compound, BIL-284, under Phase II development. This compound is a long-acting leukotriene antagonist. Pfizer has one product (*revatropate*) currently in Phase II. Moreover, Medea Research has a Phase III compound in development for COPD. This compound is a protease inhibitor (*midesteine*). There are also a number of pipeline compounds in clinical trials or Phase I from competitors such as AstraZeneca, Byk Gulden and Boehringer Ingelheim.

187. The investigation shows that COPD is an attractive market for future research and development. COPD was the sixth most common cause of death world-wide in 1990 and mortality rates for COPD are increasing. COPD is expected to become the third most common cause of death by 2020. Due to the relative inefficiency of the existing products and the fact that none of the current or pipeline products act as an effective single treatment for COPD, there is a lot of unmet clinical need in this segment and a large number of pharmaceutical companies are conducting research in this area.
188. Given the attractiveness of the market and the fact that GW and SB pursue different lines of research and development in COPD, the Commission considers that the operation is unlikely to lead to an elimination of the existing R&D currently being conducted by the merging parties. While it is feasible to believe that the parties will streamline their R&D efforts in the future, given the large number of current pipeline products and resourceful competitors on the market, the Commission does not consider that this would lead to the diminution of the overall R&D potential either.
189. As to the question whether the operation is likely to lead to the strengthening of GW's position on existing products as a result of the elimination of SB as a potential entrant in the respiratory tract, the Commission takes note of the parties' submission that "Ariflo" will only be used in conjunction with other therapies [...] existing therapies in the market. Therefore, the Commission considers it appropriate to assess the potential effects of SB's pipeline products with respect to second line treatment where SB's PDE4 inhibitor is likely to be used and where GW is particularly strong. The Commission has taken into account the argument submitted by the parties according to which Boehringer Ingelheim's "Spiriva" could, if successful, reduce the need for second line therapy. The Commission considers however that while this could lead to the reduction of the total size of the second line treatment segment, it would not affect GW's position in it. Therefore, only the second line treatment area is relevant for the assessment of this case.
190. Moreover, in view of the fact that compounds in Phase III are likely to be launched on the market within three years time as opposed to Phase II, which may take 4-5 years, the assessment will focus on Phase III compounds because these are likely to provide a more immediate competitive constraint to the merged entity than Phase II products. In addition, while the risk of failure in Phase III is 50%, in Phase II it is reported to be 70%. Therefore, the assessment of Phase III pipeline products gives a more accurate estimation of new compounds entering the market in the near future.
191. In this respect, the Commission notes on the basis of its investigation that Phase III pipeline compounds potentially indicated for second line treatment are the parties' compounds "Seretide" and "Ariflo", Byk Gulden's PDE4 inhibitor and AstraZeneca's "Symbicort" and *formoterol turbuhaler*. Moreover, the protease inhibitor in development by Medea Research is also indicated for second line therapy. With regard

to Boehringer Ingelheim's *tiotropium* and AstraZeneca's "Viozan", the parties expect these to be first line therapies.

192. The parties have submitted that, as all COPD compounds, the parties' products "Seretide" and "Ariflo" will be used in all COPD diagnoses categories (J41-44). The parties submit further that the use in one category is expected to be in proportion to the size of the category within COPD. In other words, the parties contend that as J44 accounts for 83% of the value of the second line treatment, the parties expect about 80% of the prescriptions for "Ariflo" and "Seretide" to be for J44. As noted above, GW accounts for 40% in this diagnosis area and AstraZeneca 22%.
193. In total, therefore, four competing compounds for second line therapy are in Phase III development. Most particularly, the Commission notes that AstraZeneca, which is currently number two in second line therapy, has two compounds in Phase III. The Commission further notes that AstraZeneca's "Symbicort" is a combination of bronchodilator and inhaled steroids and is expected to compete with GW's similar product "Seretide". Similarly, Byk Gulden's PDE4 inhibitor can be expected to compete with SB's PDE4 inhibitor. Moreover, the Commission notes that as a resourceful company with an important position in respiratory tract with a number of existing products, AstraZeneca is in a good position to launch its new compounds on the market. In addition, the Commission also takes note of the fact that Byk Gulden is a subsidiary of a larger pharmaceutical group, Altana Industrial, which is already present in asthma/COPD market. Therefore, it is reasonable to assume that also Byk Gulden has the necessary financial resources and marketing skills to launch its product on the market.
194. The Commission notes, on the other hand, that GW's position is very strong in second line therapy for COPD. Moreover, the Commission notes that GW accounts for [35-45%] of the J44 diagnoses area where the parties' pipeline products will mostly be indicated while AstraZeneca, the largest competitor in this segment, has only [20-30%] of the sales. Therefore, the Commission considers that, in eliminating a potential entrant, the operation could further strengthen the position of GW in this segment or, overall, in second line therapy in particular if the other Phase III products for second line treatment were to fail. Therefore, serious doubts as to the compatibility of the operation with the common market exist.
195. In assessing a proper remedy to remove the serious doubts in the area of COPD, the Commission has taken into account the fact that a certain degree of uncertainty prevails in pipeline products. As noted above, the probability of success for compounds in Phase III of development is 50% which means that compounds at this stage often fail for one reason or another. Therefore, the Commission under the very special circumstances of this case has accepted an undertaking offered by the parties according to which SB's "Ariflo" will be outlicensed but only in the event that competing Phase III pipeline compounds for second line treatment fail. The undertaking has been supported by the market investigation.

b) Anti-migraine(N2C)

196. GW has two leading *triptan* products: "Imigran" (*sumatriptan*), which currently represents the gold standard in symptomatic treatment of acute migraine, and "Naramig" (*naratriptan*). SB has no existing migraine treatment but it has a compound (SB220453) on the pipeline which has completed Phase II trials. According to the

parties, SB's pipeline compound will most likely have a novel mechanism of action and does not act the same way as the *triptans*. GW has a glycine antagonist in Phase II, which is being developed for prophylaxis of migraine, but no new compounds in clinical development for the treatment of acute migraine.

197. The parties have submitted in the notification that SB220453 will be outlicensed. The parties have also given a formal commitment of this. The commitment is annexed to the decision. The Commission therefore concludes that no overlap will occur between GW's existing products and SB's pipeline product. This treatment area will therefore not be investigated any further.

c) Therapeutic vaccines

198. Therapeutic vaccines ("pharmaccines") are developed and produced according to methods similar to those of vaccines. The main difference with prophylactic vaccines is that pharmaccines will have a therapeutic purpose and will be administered for treatment after the disease has been established. The parties therefore submit that pharmaccines cannot be regarded as potential competitors with existing vaccine products.

199. At present, SB and GW have no pipeline products on the market. The only potential overlaps between the SB pipeline pharmaccines and existing or pipeline GW products would be in the treatment area anti-virals (J5B), more particularly, in the treatment of *hepatitis B* and *herpes simplex* virus.

200. GW has currently a *hepatitis B* product "Zeffix" (*lamivudine*) on the market and a *hepatitis B* pharmaccine in the Phase I of the development. SB also has a *hepatitis B* pharmaccine in the pipeline at Phase II. The parties submit, however, that [...]. With regard to *herpes simplex* virus, both SB and GW have existing drugs on the market indicated for the treatment of this virus. GW also has a pharmaccine in the pipeline. The parties submit that this pharmaccine [...].

201. The parties submit that pharmaccines are based on a new pharmaceutical concept for which testing on humans has not even substantially started. According to the parties, it is therefore difficult to ascertain whether or not pharmaccines will be a success and whether they will be able to compete with drugs currently on the market.

202. Third parties have largely confirmed that the success of pharmaccines is yet to be seen and have not raised concerns in this area. As to the question whether the new vaccine which is currently under development for *herpes simplex* virus would affect the parties' market position in the market for anti-virals (J5B), third parties have indicated that as the vaccine is still at the clinical stage, the success of the vaccine remains to be seen. Some competitors have also indicated that should the vaccine prove successful, it would constitute a third generation drug and rather be in direct competition with the parties' own second generation drugs. However, in any event, third parties believe that the vaccine would not reach the market within [...] years.

203. The foregoing applies also for pharmaccines under development for *hepatitis B*. In this respect the Commission also notes that GW's "Zeffix" has a modest presence on the market and, even if the new pharmaccine was used in combination with this drug, it is unlikely to lead to adverse competition effects.

204. Lastly, the Commission takes note of the fact that there are a large number of active players in R&D on the pharmancines market. These include for instance Aventis, Bristol-Myers Squibb, Schering-Plough and Roche.

205. Therefore, on the basis of the foregoing and in particular in view of the fact that none of the products in the pipeline are expected to be commercialised within the next 5 years and that there are competitors active in developing pharmancines, the Commission does not consider that the pipeline products in the market for anti-virals would further strengthen the position of the combined entity. Furthermore, in view of the fact that the parties have offered undertakings in the area of anti-virals where the parties' pipeline pharmancines overlap, the Commission considers that a divestment of one of the parties' current compounds is sufficient to restore competition in the market for anti-virals.

d) Other urologicals, including antispasmodics (G4B)

206. SB currently markets "Doralese" (*indoramin*) in the UK and Ireland for improved urinary flow for men with benign prostatic hyperplasia (BHP) and hypertension. GW has an agreement to co-promote Yamanouchi Pharma Ltd's product "Flomax", also known as "Harnal", (*tamsulosin/hydrochloride*) in the UK. GW's product GI198745 is in Phase III development for BPH. The parties submit that the product under development is substantially different from alpha blockers, such as SB's "Doralese", and that the new compound and SB's existing product will not compete or will only compete to a limited extent.

207. SB's current market position in the UK and Ireland is relatively weak. SB accounts for less than [5-15%] of the markets in the UK and Ireland each and the market share of GW's "Flomax" in the UK is [10-20%]. In view of this, even if GW's pipeline product was considered to fall into the same category with SB's "Doralese", the Commission considers that competition concerns are unlikely to arise.

e) Diabetes (A10B)

208. The parties submit that there are various different types of diabetes. Type 1 diabetes results from the destruction of insulin producing cells in the pancreas and insulins are used in the treatment of Type 1 diabetes. Type 2 diabetes, which tends to occur among older age groups, consists of insulin resistance and progressive failure of insulin production by the pancreas. Neither GW nor SB markets or has in development insulin for the treatment of Type 1 diabetes. Therefore, only Type 2 diabetes is relevant for the assessment of this case.

209. According to the parties, doctors have previously had three classes of oral Type 2 diabetes products to prescribe to the patient: sulphonylureas, metformin and alpha glucosidase inhibitors (*acarbose*). The parties submit that thiazolidinediones are the first generation of insulin-sensitising drugs, such as *trogliatzone*, *rosigliatzone*, *pioglitazone* and *trogliatzone*. The parties submit that *repaglinide*, which has recently been launched in Europe, represents a new type of treatment of Type 2 diabetes. In addition, a number of other drugs are under development.

210. Neither GW nor SB currently market any diabetes drugs in Europe. SB has a product "Avandia" (*rosigliatzone*) which is available in the US and is expected to be launched in Europe this year. GW has a non-thiazolidinedione pipeline product GI262570 which

recently entered Phase III. GW also has a compound GW409544 in Phase I. [...]. The parties expect GW's new compound to fall into the same ATC class as SB's "Avandia".

211. The Commission considers that competition concerns are unlikely to arise from the parties' pipeline products in this treatment area. First, the parties have no existing products in the market for diabetes in Europe. Second, there are a number of competitors including Eli Lilly, Bristol-Myers Squibb and Roche on the market with both existing products and pipeline products.

f) Oncology (L1)

212. SB and GW have compounds in different clinical trial stages of development to treat two types of cancer: colorectal cancer and non-Hodgins lymphoma. However, with regard to non-Hodgins lymphoma, the parties submit in the notification that while SB has a compound at Phase III development, GW [...]. Therefore, there is no overlap in the parties' product pipeline relating to this treatment area.

213. GW and SB have two pipeline products each for the treatment of colorectal cancer. SB's existing cancer treatment product "Hycamtin" (*topotecan*) is in Phase IIb clinical trial state development for second line treatment of colorectal cancer. SB's SB408075 is currently in Phase I development and is a tumour activated prodrug for second line treatment of colorectal cancer. GW's "Edrecolomab" is a monoclonal antibody in Phase III development. The parties submit that this compound is expected to be classified in ATC 3 class L1X. Also, GW's "Eniuracil" is in Phase III clinical trial stage. According to the parties, "Eniuracil" is expected to be classified in ATC 3 class L1C and/or L1X.

214. The Commission does not consider that the parties' overlapping activities in oncology are likely to lead to adverse competition effects. An important number of competitors, such as Merck, Pfizer, Pharmacia & Upjohn, AstraZeneca, Bristol-Myers Squibb and Roche, are active in this field. Given this and in view of the fact that the parties' current position in cancer treatment does not give rise to competition concerns, the Commission concludes that no adverse competition effects will arise.

g) Irritable bowel syndrome

215. Neither SB nor GW currently market any products in this field. The parties expect that GW will launch a product "Lotronex" (*alosetron*) in the EU shortly. According to the information submitted in the notification, SB had a pipeline product in this treatment area but this compound is currently inactive in clinical trials and the decision has been taken to terminate development for this compound.

216. In view of the foregoing, the Commission considers that no overlap occurs between the parties' existing or pipeline products and, therefore, the operation will not lead to anticompetitive effects on the market.

VI. MODIFICATIONS TO THE PROPOSED OPERATION

217. In order to remove the serious doubts resulting from the proposed transaction, the parties offered the Commission undertakings. The detailed text of these undertakings is

annexed to this decision. The full text of the annexed undertakings forms an integral part of this decision.

218. In the market for anti-virals, excluding HIV (J5B), the parties have committed to outlicense “Famvir” (*famciclovir*), for use in treatment of *herpes simplex* and *herpes zoster*, in the European Economic Area (“EEA”). The proposed undertaking will remove the entire overlap between GW and SB in this market and the undertaking has been supported by third parties.
219. In the market for topical anti-virals (D6D), the parties proposed to outlicense either “Vectavir” (*penciclovir*) or “Zovirax” (*aciclovir*) for use in topical treatment of herpes simplex, in the EEA. The market test has confirmed that a divestment of either of the products would remove the overlap between the parties activities and would, therefore, remove the serious doubts on this market.
220. In the market for anti-emetics (A4A), the parties have undertaken to outlicense “Kytril” and “Kevatril” (*granisetron*), for anti-emetic use, in the EEA. The licence will be without prejudice to any rights granted to Bristol Myers Squibb under its agreement with SB for the distribution of *granisetron* in Germany under the “Kevatril” trademark. The proposed undertaking will remove the entire overlap between GW and SB in this market.
221. In order to remove the competition concerns in the ATC 3 class J1D market in Spain, the parties have committed themselves to grant a licence of the Spanish trademark rights to SB’s “Monocid” to an unassociated third party. “Monocid” is not subject of patent protection, but the licence grant would be accompanied by product registration support, effort to transfer a contract manufacturing agreement of the bulk active ingredient and, possibly, a supply agreement. This undertaking would significantly reduce the overlap created by the concentration by 15%. The only overlap remaining would be SB’s product “Cefizox”, which is owned by Fujisawa and only distributed by SB in Spain. However, given that “Cefizox” accounts for only negligible sales, the Commission concludes that the undertaking is sufficient to address the competition concerns raised by this concentration.
222. In the area of COPD, the parties propose to license out “Ariflo” (SB207495) in Europe for COPD at the successful conclusion of Phase III clinical trials for COPD, or in the event that the new entity ceases global development of “Ariflo” for COPD, whichever is the earlier, in the event that competing Phase III pipeline compounds for second line treatment fail.
223. The Commission considers that the undertakings are sufficient to eliminate serious doubts as to the compatibility of the transaction with the common market. These commitments will solve competition concerns both by eliminating the overlap between the parties in this market and facilitating new entry to the market. The undertakings have also been supported by third parties in their replies to the Commission’s market test.

VII. CONCLUSION

224. The Commission concludes that the undertakings submitted by the parties are sufficient to address the competition concerns raised by this concentration. Accordingly, subject to the full compliance with the commitment submitted by the notifying parties, the

Commission has decided not to oppose the notified operation and to declare it compatible with the common market and with the EEA Agreement. This decision is adopted in application of Article 6(2) of Council Regulation (EEC) No 4064/89.

For the Commission,

ANNEX

Undertaking - Anti-virals, topical anti-virals and anti-emetics

Whereas on 20 March 2000, SmithKline Beecham plc and Glaxo Wellcome plc notified their agreement to merge to the Commission of the European Communities pursuant to Council Regulation (EEC) No 4064/89, as amended (the “Merger Regulation”).

In accordance with Article 6 (2) of the Merger Regulation, and subject to clearance of the Transaction under Article 6(1)(b) of the Merger Regulation, the parties agree that they will outlicense:

- Granisetron, for anti-emetic use;
- Famciclovir, for use in treatment of herpes simplex and herpes zoster; and
- Penciclovir or Aciclovir (to be determined by the Parties at their discretion), for use in topical treatment of herpes simplex;

in the European Economic Area (“EEA”) on the terms and conditions set out below.

I Definitions

- 1 “**Aciclovir**” means the pharmaceutical product manufactured by or for GW in topical form and sold in the Territory for use in topical treatment of herpes simplex under the brand name Zovirax.
- 2 “**Closing date**” means the date on which the High Court of England and Wales registers the Order sanctioning the Scheme of Arrangement bringing about the Transaction.
- 3 “**Commission**” means the Commission of the European Communities.
- 4 “**Famciclovir**” means the pharmaceutical product manufactured by or for SB in oral form and sold in the Territory for use in treatment of herpes simplex and herpes zoster principally under the brand name Famvir.
- 5 “**Glaxo SmithKline**” means the company to be known as Glaxo SmithKline plc as a result of the Transaction and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by Glaxo SmithKline plc.
- 6 “**Granisetron**” means the pharmaceutical product manufactured by or for SB in oral and injectible form and sold in the Territory for anti-emetic use under the brand names Kytril and Kevatril.
- 7 “**GW**” means Glaxo Wellcome plc and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by GW.
- 8 “**Know-how**” means relevant confidential business information and know-how owned by SB in relation to the Product, including
 - relevant information concerning the research, development, marketing, distribution, costs, pricing, sale and commercialisation of the Product for their Licensed Use in the Territory;

- relevant data materials and information relating to obtaining marketing authorisations for the Product for their Licensed Use in the Territory; as well as
 - relevant technological, technical, scientific, chemical, biological, pharmacological, toxicological, regulatory, marketing and other information relating to the Product for their Licensed Use in the Territory, including without limitation all formulae, techniques, patents, patent applications, discoveries, compounds, compositions of matter, assays, reagents, and biological materials, research data, technical data and information, testing data, preclinical and clinical data, toxicological and pharmacological data, statistical analysis, analytical data, clinical protocols, specifications, processes, testing and quality assurance/quality control data, manufacturing data and regulatory submissions.
- 9** “**Licence**” means irrevocable exclusive licences granting the proposed licensee (or licensees) the exclusive right to use the Know-how used in the development, manufacture, marketing, sale and distribution of the Product for the Licensed Use within the Territory. Hereby it is expressly stipulated that the Parties continue to have exclusive rights to the Product outside the Territory and with respect to any use other than the Licensed Use within the Territory.
- 10** “**Licensed Use**” means:
- (i) in respect of Granisetron, anti-emetic use;
 - (ii) in respect of Famciclovir, use in treatment of herpes simplex and herpes zoster;
 - (iii) in respect of Penciclovir, use in topical treatment of herpes simplex; and
 - (iv) in respect of Aciclovir, use in topical treatment of herpes simplex.
- 11** “**Territory**” means the European Economic Area.
- 12** “**Ondansetron**” means the pharmaceutical product manufactured by or for GW in oral and injectible form and sold in the Territory for anti-emetic use under the brand name Zofran.
- 13** “**Penciclovir**” means the pharmaceutical product manufactured by or for SB in topical form and sold in the Territory for use in topical treatment of herpes simplex under the brand name Vectavir.
- 14** “**Transaction**” means the proposed merger between SB and GW as notified to the Commission on 20 March 2000 pursuant to the Merger Regulation.
- 15** “**SB**” means SmithKline Beecham plc and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by SB.
- 16** “**Product**” means (i) Granisetron, (ii) Famciclovir and (iii) Penciclovir or Aciclovir (to be determined by the Parties at their discretion).

II Object of the Undertaking

- 17** SB, GW and, after the Closing Date, Glaxo SmithKline (hereinafter collectively referred to as the “Parties”) undertake to:
- (a) grant, for adequate remuneration, the Licence for an unlimited period of time to a third party (“the Licensee”) who will have the right to grant sublicences to third parties or grant distribution rights to third parties.
 - (b) transfer, for adequate remuneration, to the Licensee:

- (i) only in so far as the Licensed Use is concerned, the existing national marketing authorisations for the Product granted by the competent regulatory authorities in the Territory and the grant of technical support necessary for the transfer of the authorisations;
 - (ii) those trademarks owned by the Parties under which the Product are marketed for the Licensed Use in the Territory. It is hereby expressly stipulated that the Parties continue to have exclusive rights to the Zovirax trade mark with respect to use in systemic treatment of herpes simplex and herpes zoster.
 - (c) Upon request of the Licensee, in case the Licensee does not have production facilities of its own, to enter into an agreement for the supply, for adequate remuneration, of any of the Product for a reasonable transitional period of up to five years.
- 18** The Licensee will be a viable third party independent of the Parties and possessing the financial resources and expertise to enable it to develop and market the Product for the Licensed Use within the Territory in active competition with the Parties. The Licensee has to be approved for the purpose by the Commission.
- 19** The Licence will be without prejudice to any rights granted to Bristol Myers Squibb under its agreement with SB for the distribution of Granisetron in Germany under the Kevatril trademark.
- 20** Nothing provided in this Undertaking shall limit any right of the Parties to (i) develop, manufacture, distribute or sell the Product outside the Territory or in respect of any use other than the Licensed Use or (ii) participate in the development, manufacture, distribution or sale of the Product outside the Territory or in respect of any use other than the Licensed Use or (iii) to award licence rights for the development, manufacture, distribution or sale of the Product outside the Territory or in respect of any use other than the Licensed Use or (iv) to manufacture the Product within the Territory for any of the above purposes (i), (ii) or (iii) or to supply the Licensee for a reasonable transitional period pursuant to paragraph 16 (c) above. In this context, the Parties will maintain all the rights to the Know-how and patents in relation to the Product outside the Territory or in respect of any use other than the Licensed Use and to manufacture the Product in the Territory for sale outside the Territory or in respect of any use other than the Licensed Use. In particular and for the avoidance of doubt, the Parties will maintain all the rights to the Know-how and Zovirax trade mark in relation to Aciclovir with respect to use in systemic treatment of herpes simplex and herpes zoster. The Licence will be without prejudice to Glaxo SmithKline's right to use such of the Know-How to the extent that such Know-how is necessary to enable Glaxo SmithKline to manufacture, distribute or sell Ondansetron.

III Appointment of a Trustee

- 21** Within seven (7) working days after the Closing Date, the Parties will propose to the Commission two trustees, who are independent of the Parties ("Proposed Trustees"). The appointment of the Proposed Trustees is subject to approval of the Commission. If the Commission does not reject the Proposed Trustees by notice in writing to the Parties within ten (10) Commission working days of the proposal, the Proposed Trustees shall be deemed to have been approved. If only one of the Proposed Trustees

has been approved, then that trustee shall be appointed. If both Proposed Trustees have been approved, then the Parties shall, at their own discretion, appoint one of them.

- 22** If the Proposed Trustees are rejected, the Parties will propose the name of a new trustee (“New Trustee”) within seven (7) working days of being informed of the rejection. If the Commission does not reject the New Trustee by notice in writing to the Parties within ten (10) Commission working days of the new proposal, the New Trustee shall be deemed to have been approved.
- 23** If the New Trustee is rejected by the Commission, the Commission shall nominate a suitable Trustee (“the Commission Trustee”) which the Parties will appoint or cause to be appointed. The Commission Trustee shall be an expert in the negotiation of licensing agreements and shall have substantial experience in the pharmaceutical industry.

IV Trustee’s mandate

- 24** Within seven (7) days of the date on which the Commission has approved or is deemed to have approved either the Proposed Trustees, the New Trustee or the Commission Trustee in accordance with Section III above, the Parties shall enter into a mandate agreement (the “Mandate”) with the approved trustee (“the Trustee”), the terms of which shall have previously been agreed with the Commission which confers on the Trustee all the rights and powers necessary to permit the Trustee to monitor the Parties’ compliance with the terms of this undertaking and in a manner consistent with the purpose of this undertaking.
- 25** Throughout the duration of the Trustee’s appointment the Trustee shall:
- 25.1** have full and complete access to the Parties’ personnel, books, records, documents, facilities and technical information relating to the research, regulatory approvals, development, manufacture, distribution and sale of the Product for the Licensed Use in the Territory, or to any other relevant information, as the Trustee may reasonably request provided, however, such request is limited to the Licensed Use in the Territory and to what is reasonably necessary for the Trustee to fulfil its Mandate. The Parties shall co-operate with any reasonable request of the Trustee.
 - 25.2** provide written reports (the “Trustee Reports”) to the Commission on the progress of the discharge of its duties under the Mandate, identifying any respects in which the Trustee has been unable to discharge such duties. The Trustee Reports shall be provided at regular monthly intervals, commencing one month after the date of the appointment of the Trustee, or at such other times or time periods as the Commission may specify and are notified in writing to the Parties;
 - 25.3** monitor and advise the Commission as to the development of the procedure for selecting a Licensee and as to the conduct of the negotiations;
 - 25.4** monitor and advise the Commission as to whether prospective Licensee(s) with whom the Parties are or intend to negotiate are likely to satisfy the Licensee requirements.
 - 25.5** monitor the maintenance of the viability of the Product for their Licensed Use in the Territory and that they are managed for their Licensed Use in the Territory in the ordinary course of business, pursuant to good business practice.

- 26** The Trustee's duties and functions as set out above shall not be extended or varied in any way by the Parties, save with the express written consent of the Commission. Any instruction or request to the Trustee from the Parties which conflicts with the terms of the Mandate and duties and functions as set out above will be considered null and void.
- 27** After [...] (or any extension agreed by the Commission) have lapsed from the Closing Date without the Parties having entered into a binding agreement for the obligations set forth in Section II of this undertaking, the Trustee shall be given an irrevocable mandate to negotiate and conclude a similar arrangement within [...] with a viable and independent third party at a fair market price.
- 28** If, however, the Trustee is unable to conclude such an arrangement at the end of the [...] period (or any extended period agreed by the Commission) within which the Trustee is required to conclude an arrangement, the Trustee is entitled to enter into this arrangement at no minimum price for a further maximum and non-extendable period of [...].

V Interim position

Pending completion of the Undertaking, the Parties undertake to use reasonable efforts to ensure that, so far as relevant, the Product shall be managed in respect of their Licensed Use in the Territory in the ordinary course of business, pursuant to good business practices, including that all contracts necessary to preserve their viability are continued in accordance with their terms.

VI Miscellaneous

- 29** The Trustee will provide the Parties with all reasonable assistance and will procure that all relevant third parties provide such assistance required to ensure compliance with this Undertaking. The Parties will provide or cause to be provided to the Trustee all such assistance and information, including copies of all relevant documents accessible by the Parties as the Trustee may require in carrying out its Mandate, and to pay reasonable remuneration for its services.
- 30** Notwithstanding the Trustee's overall responsibility to discharge its functions and in particular notwithstanding the Trustee's position as an independent unrelated third party, the Trustee (who shall undertake in the Mandate to do so) shall have to the extent possible given the nature of its tasks due regard to the commercial interests of the Parties.
- 31** The Mandate and this Undertaking shall be deemed to be discharged and the Trustee's appointment shall be deemed to be terminated if the Parties should jointly announce that the Transaction has been irrevocably abandoned.
- 32** The Trustee's and all other relevant third parties' powers of attorney and appointment shall be irrevocable.
- 33** The Commission for its part declares that it will use its best endeavours to inform the Parties, as soon as reasonably practicable, as regards the suitability of any proposed Licensee. If there has been no rejection of the proposed Licensee by the Commission within ten (10) Commission working days after submission of a proposal by the Parties or the Trustee, the proposed Licensee will be deemed to have been approved by the Commission. In determining whether any proposed Licensee is suitable, it will take into account inter alia whether the proposed Licensee (i) appears to possess the

status and resources necessary to manufacture and develop the Product for the Licensed Use within the Territory over the long term as a viable, active and significant competitor to the Parties, (ii) is independent of the Parties and (iii) can be shown not to have significant and relevant commercial connections with the Parties.

- 34 For the avoidance of doubt, there may be a separate Licensee and thus a separate Licence entered into in respect of each of the Product and, subject always to the Commission's approval in accordance with paragraph 33 above, more than one Licensee in respect of each of the Product within the Territory.
- 35 The obligations entered into in this Undertaking are conditional upon clearance pursuant to Article 6(1)(b) of the Merger Regulation by the Commission of the Transaction no later than 8 May 2000.

VII Governing Law and Provisions

This Undertaking is governed by, and shall be construed in accordance with, the laws of England and Wales.

Undertaking - Monocid

Whereas on 20 March 2000, SmithKline Beecham plc and Glaxo Wellcome plc notified their agreement to merge to the Commission of the European Communities pursuant to Council Regulation (EEC) No 4064/89, as amended (the "Merger Regulation").

In accordance with Article 6(2) of the Merger Regulation, and subject to clearance of the Transaction under Article 6(1)(b) of the Merger Regulation, the parties agree that they will outlicense:

- the rights to market the product cefonocid under the trademark "Monocid" in Spain on the terms and conditions set out below.

I Definitions

- 1 "Closing date" means the date on which the High Court of England and Wales registers the Order sanctioning the Scheme of Arrangement bringing about the Transaction.
- 2 "Commission" means the Commission of the European Communities.
- 3 "Glaxo SmithKline" means the company to be known as Glaxo SmithKline plc as a result of the Transaction and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by Glaxo SmithKline plc.
- 4 "GW" means Glaxo Wellcome plc and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by GW.
- 5 "Licence" means the irrevocable exclusive licence without limit of time granting the proposed licensee the exclusive right to use the Trademark in respect of the Product within the Territory. Hereby it is expressly stipulated that the Parties continue to have exclusive rights to the Trademark outside the Territory.

- 6 **“Manufacturing Contract”** means the contract manufacturing agreement between SB and a third party manufacturer for the manufacture of bulk active ingredient for the Product.
- 7 **“Product”** means the cephalosporin antibiotic cefonicid formulated in injectable form by SB, for which the active ingredient is manufactured for SB by a third party, and sold by SB in the Territory under the brand name Monocid.
- 8 **“SB”** means SmithKline Beecham plc and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by SB.
- 9 **“Territory”** means Spain.
- 10 **“Third Party Manufacturer”** means the third party manufacturer party to the Manufacturing Contract.
- 11 **“Trademark”** means the trademark “Monocid” under which the Product is sold by SB in the Territory.
- 12 **“Transaction”** means the proposed merger between SB and GW as notified to the Commission on 20 March 2000 pursuant to the Merger Regulation.

II Object of the Undertaking

- 13 SB and, after the Closing Date, Glaxo SmithKline (hereinafter collectively referred to as the “Parties”) undertake:
- (d) to grant, for adequate remuneration, the Licence to a third party (“the Licensee”) who will have the right to grant sublicences to third parties or grant distribution rights to third parties.
 - (e) to transfer, for adequate remuneration, to the Licensee the existing national marketing authorisation(s) for the Product granted by the competent regulatory authorities in the Territory and the grant of technical support necessary for the transfer of the authorisations;
 - (f) to use reasonable efforts to obtain the consent of the Third Party Manufacturer to transfer the Manufacturing Contract to the Licensee. If such consent is not forthcoming, the Parties will supply the bulk active ingredient for the Product to the Licensee on arm’s length terms until expiry of the Manufacturing Contract.
- 14 The Licensee will be a viable third party independent of the Parties and possessing the financial resources and expertise to enable it to market the Product within the Territory in active competition with the Parties. The Licensee has to be approved for the purpose by the Commission.
- 15 Nothing provided in this Undertaking shall limit any right of the Parties to (i) develop, manufacture, distribute or sell the Product outside the Territory or (ii) participate in the development, manufacture, distribution or sale of the Product outside the Territory or (iii) to award licence rights for the development, manufacture, distribution or sale of the Product outside the Territory or (iv) to manufacture the Product within the Territory for any of the above purposes (i), (ii) or (iii) or to supply the Licensee with bulk active ingredient pursuant to paragraph 13(c) above. In this context, the Parties will maintain all the rights to the Trademark outside the Territory.

III Appointment of a Trustee

- 16** Within seven (7) working days after the Closing Date, the Parties will propose to the Commission two trustees, who are independent of the Parties (“Proposed Trustees”). The appointment of the Proposed Trustees is subject to approval of the Commission. If the Commission does not reject the Proposed Trustees by notice in writing to the Parties within ten (10) Commission working days of the proposal, the Proposed Trustees shall be deemed to have been approved. If only one of the Proposed Trustees has been approved, then that trustee shall be appointed. If both Proposed Trustees have been approved, then the Parties shall, at their own discretion, appoint one of them.
- 17** If the Proposed Trustees are rejected, the Parties will propose the name of a new trustee (“New Trustee”) within seven (7) working days of being informed of the rejection. If the Commission does not reject the New Trustee by notice in writing to the Parties within ten (10) Commission working days of the new proposal, the New Trustee shall be deemed to have been approved.
- 18** If the New Trustee is rejected by the Commission, the Commission shall nominate a suitable Trustee (“the Commission Trustee”) which the Parties will appoint or cause to be appointed. The Commission Trustee shall be an expert in the negotiation of licensing agreements and shall have substantial experience in the pharmaceutical industry.

IV Trustee’s mandate

- 19** Within seven (7) days of the date on which the Commission has approved or is deemed to have approved either the Proposed Trustees, the New Trustee or the Commission Trustee in accordance with Section III above, the Parties shall enter into a mandate agreement (the “Mandate”) with the approved trustee (“the Trustee”), the terms of which shall have previously been agreed with the Commission which confers on the Trustee all the rights and powers necessary to permit the Trustee to monitor the Parties’ compliance with the terms of this undertaking and in a manner consistent with the purpose of this undertaking.
- 20** Throughout the duration of the Trustee’s appointment the Trustee shall:
- 20.1** have full and complete access to the Parties’ personnel, books, records, documents, facilities and technical information relating to the research, regulatory approvals, development, manufacture, distribution and sale of the Product in the Territory, or to any other relevant information, as the Trustee may reasonably request provided, however, such request is limited to the Territory and to what is reasonably necessary for the Trustee to fulfil its Mandate. The Parties shall co-operate with any reasonable request of the Trustee.
 - 20.2** provide written reports (the “Trustee Reports”) to the Commission on the progress of the discharge of its duties under the Mandate, identifying any respects in which the Trustee has been unable to discharge such duties. The Trustee Reports shall be provided at regular monthly intervals, commencing one month after the date of the appointment of the Trustee, or at such other times or time periods as the Commission may specify and are notified in writing to the Parties;
 - 20.3** monitor and advise the Commission as to the development of the procedure for selecting a Licensee and as to the conduct of the negotiations;

- 20.4** monitor and advise the Commission as to whether prospective Licensee with whom the Parties are or intend to negotiate are likely to satisfy the Licensee requirements.
- 20.5** monitor the maintenance of the viability of the Product in the Territory and that it is managed in the Territory in the ordinary course of business, pursuant to good business practice.
- 21** The Trustee's duties and functions as set out above shall not be extended or varied in any way by the Parties, save with the express written consent of the Commission. Any instruction or request to the Trustee from the Parties which conflicts with the terms of the Mandate and duties and functions as set out above will be considered null and void.
- 22** After [...] (or any extension agreed by the Commission) have lapsed from the Closing Date without the Parties having entered into a binding agreement for the obligations set forth in Section II of this undertaking, the Trustee shall be given an irrevocable mandate to negotiate and conclude a similar arrangement within [...] with a viable and independent third party at a fair market price.
- 23** If, however, the Trustee is unable to conclude such an arrangement at the end of the [...] period (or any extended period agreed by the Commission) within which the Trustee is required to conclude an arrangement, the Trustee is entitled to enter into this arrangement at no minimum price for a further maximum and non-extendable period of [...].

V Interim position

Pending completion of the Undertaking, the Parties undertake to use reasonable efforts to ensure that, so far as relevant, the Product shall be managed in respect of the Territory in the ordinary course of business, pursuant to good business practices, including that all contracts necessary to preserve its viability are continued in accordance with their terms.

VI Miscellaneous

- 24** The Trustee will provide the Parties with all reasonable assistance and will procure that all relevant third parties provide such assistance required to ensure compliance with this Undertaking. The Parties will provide or cause to be provided to the Trustee all such assistance and information, including copies of all relevant documents accessible by the Parties as the Trustee may require in carrying out its Mandate, and to pay reasonable remuneration for its services.
- 25** Notwithstanding the Trustee's overall responsibility to discharge its functions and in particular notwithstanding the Trustee's position as an independent unrelated third party, the Trustee (who shall undertake in the Mandate to do so) shall have to the extent possible given the nature of its tasks due regard to the commercial interests of the Parties.
- 26** The Mandate and this Undertaking shall be deemed to be discharged and the Trustee's appointment shall be deemed to be terminated if the Parties should jointly announce that the Transaction has been irrevocably abandoned.
- 27** The Trustee's and all other relevant third parties' powers of attorney and appointment shall be irrevocable.

- 28** The Commission for its part declares that it will use its best endeavours to inform the Parties, as soon as reasonably practicable, as regards the suitability of any proposed Licensee. If there has been no rejection of the proposed Licensee by the Commission within ten (10) Commission working days after submission of a proposal by the Parties or the Trustee, the proposed Licensee will be deemed to have been approved by the Commission. In determining whether any proposed Licensee is suitable, it will take into account inter alia whether the proposed Licensee (i) appears to possess the status and resources necessary to market the Product within the Territory over the long term as a viable, active and significant competitor to the Parties, (ii) is independent of the Parties and (iii) can be shown not to have significant and relevant commercial connections with the Parties.
- 29** The obligations entered into in this Undertaking are conditional upon clearance pursuant to Article 6(1)(b) of the Merger Regulation by the Commission of the Transaction no later than 8 May 2000.

VII Governing Law and Provisions

This Undertaking is governed by, and shall be construed in accordance with, the laws of England and Wales.

Undertaking - COPD

Whereas on 20 March 2000, SmithKline Beecham plc and Glaxo Wellcome plc notified their agreement to merge to the Commission of the European Communities pursuant to Council Regulation (EEC) No 4064/89, as amended (the “Merger Regulation”).

In accordance with Article 6 (2) of the Merger Regulation, and subject to clearance of the Transaction under Article 6(1)(b) of the Merger Regulation, the parties agree that they will outlicense:

- compound SB207499 for use in treatment of Chronic Obstructive Pulmonary Disease in the European Economic Area (“EEA”) on the terms and conditions set out below.

I Definitions

- 30** “**Closing date**” means the date on which the High Court of England and Wales registers the Order sanctioning the Scheme of Arrangement bringing about the Transaction.
- 31** “**Commission**” means the Commission of the European Communities.
- 32** “**Competing Pipeline Products**” [...].
- 33** “**COPD**” means Chronic Obstructive Pulmonary Disease.
- 34** “**Divestment Conditions**” means those conditions set out in paragraph 17 below.
- 35** “**Divestment Period**” means a period of [...] from the date on which all the Divestment Conditions are satisfied.
- 36** “**Glaxo SmithKline**” means the company to be known as Glaxo SmithKline plc as a result of the Transaction and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by Glaxo SmithKline plc.

- 37** “**GW**” means Glaxo Wellcome plc and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by GW.
- 38** “**Know-how**” means relevant confidential business information and know-how owned by SB in relation to the Product, including
- relevant information concerning the research and development of the Product for its Licensed Use in the Territory;
 - relevant data materials and information reasonably necessary for the Licensee to apply for and obtain marketing authorisations for the Product for its Licensed Use in the Territory; as well as
 - relevant technological, technical, scientific, chemical, biological, pharmacological, toxicological, regulatory, and other information relating to the Product for its Licensed Use in the Territory, including without limitation all formulae, techniques, patents, patent applications, discoveries, compounds, compositions of matter, assays, reagents, and biological materials, research data, technical data and information, testing data, preclinical and clinical data, toxicological and pharmacological data, statistical analysis, analytical data, clinical protocols, specifications, processes, testing and quality assurance/quality control data, manufacturing data and regulatory submissions.
- 39** “**Licence**” means an irrevocable exclusive licence granting the proposed licensee the exclusive right to use the Know-how in the development, manufacture, marketing, sale and distribution of the Product for the Licensed Use within the Territory. Hereby it is expressly stipulated that the Parties continue to have exclusive rights to the Product outside the Territory and with respect to any use other than the Licensed Use within the Territory.
- 40** “**Licensed Use**” means use in treatment of COPD.
- 41** “**Other Competing Products**” means a compound excluding the parties’ own products and the Competing Pipeline Products which is being or has been developed for COPD and is likely to be used or is being used in second-line therapy for COPD and is not currently marketed at the date of this Undertaking.
- 42** “**Territory**” means the European Economic Area.
- 43** “**Transaction**” means the proposed merger between SB and GW as notified to the Commission on 20 March 2000 pursuant to the Merger Regulation.
- 44** “**SB**” means SmithKline Beecham plc and, where the context admits and requires, the subsidiaries, divisions, groups and affiliates which are directly or indirectly controlled by SB.
- 45** “**Product**” means compound SB207499.

II Object of the Undertaking

- 46** SB and, after the Closing Date, Glaxo SmithKline (hereinafter collectively referred to as the “Parties”) undertake:
- (g) To grant within the Divestment Period, for adequate remuneration, the Licence for an unlimited period of time to a third party (“the Licensee”) who will have the right to grant sublicences to third parties or grant distribution rights to third parties.

To grant, for adequate remuneration, to the Licensee the technical support reasonably necessary for the Licensee to apply for and obtain national marketing authorisations for the Product from the competent regulatory authorities in the Territory.

provided that all the following conditions (“Divestment Conditions”) are satisfied:

- (h) Phase III clinical trials for the Product for the Licensed Use have been completed.
 - (i) All the Competing Pipeline Products have failed Phase III clinical trials and their clinical development for COPD has been discontinued.
 - (j) There is no Other Competing Product which has completed or is about to complete and subsequently completes Phase III clinical trials for COPD.
- 47** The Licensee will be a viable third party independent of the Parties and possessing the financial resources and expertise to enable it to develop and market the Product for the Licensed Use within the Territory in active competition with the Parties. The Licensee has to be approved for the purpose by the Commission.
- 48** Nothing provided in this Undertaking shall limit any right of the Parties to (i) develop, manufacture, distribute or sell the Product outside the Territory or in respect of any use other than the Licensed Use or (ii) participate in the development, manufacture, distribution or sale of the Product outside the Territory or in respect of any use other than the Licensed Use or (iii) to award licence rights for the development, manufacture, distribution or sale of the Product outside the Territory or in respect of any use other than the Licensed Use or (iv) to manufacture the Product within the Territory for any of the above purposes (i), (ii) or (iii). In this context, the Parties will maintain all the rights to the Know-how and patents in relation to the Product outside the Territory or in respect of any use other than the Licensed Use and to manufacture the Product in the Territory for sale outside the Territory or in respect of any use other than the Licensed Use.

III Appointment of a Trustee

- 49** Within seven (7) working days after the Closing Date, the Parties will propose to the Commission two trustees, who are independent of the Parties (“Proposed Trustees”). The appointment of the Proposed Trustees is subject to approval of the Commission. If the Commission does not reject the Proposed Trustees by notice in writing to the Parties within ten (10) Commission working days of the proposal, the Proposed Trustees shall be deemed to have been approved. If only one of the Proposed Trustees has been approved, then that trustee shall be appointed. If both Proposed Trustees have been approved, then the Parties shall, at their own discretion, appoint one of them.
- 50** If the Proposed Trustees are rejected, the Parties will propose the name of a new trustee (“New Trustee”) within seven (7) working days of being informed of the rejection. If the Commission does not reject the New Trustee by notice in writing to the Parties within ten (10) Commission working days of the new proposal, the New Trustee shall be deemed to have been approved.
- 51** If the New Trustee is rejected by the Commission, the Commission shall nominate a suitable Trustee (“the Commission Trustee”) which the Parties will appoint or cause to be appointed. The Commission Trustee shall be an expert in the negotiation of licensing agreements and shall have substantial experience in the pharmaceutical industry.

IV Trustee's mandate

- 52** Within seven (7) days of the date on which the Commission has approved or is deemed to have approved either the Proposed Trustees, the New Trustee or the Commission Trustee in accordance with Section III above, the Parties shall enter into a mandate agreement (the "Mandate") with the approved trustee ("the Trustee"), the terms of which shall have previously been agreed with the Commission which confers on the Trustee all the rights and powers necessary to permit the Trustee to monitor the Parties' compliance with the terms of this undertaking and in a manner consistent with the purpose of this undertaking.
- 53** Throughout the duration of the Trustee's appointment the Trustee shall:
- 53.1** have full and complete access to the Parties' personnel, books, records, documents, facilities and technical information relating to the research, regulatory approvals and development of the Product for the Licensed Use in the Territory, or to any other relevant information, as the Trustee may reasonably request provided, however, such request is limited to the Licensed Use in the Territory and to what is reasonably necessary for the Trustee to fulfil its Mandate. The Parties shall co-operate with any reasonable request of the Trustee.
 - 53.2** provide written reports (the "Trustee Reports") to the Commission on the progress of the discharge of its duties under the Mandate, identifying any respects in which the Trustee has been unable to discharge such duties. The Trustee Reports shall be provided at regular three monthly intervals, commencing one month after the date of the appointment of the Trustee, until the Divestment Period begins and at regular monthly intervals thereafter, or at such other times or time periods as the Commission may specify and are notified in writing to the Parties;
 - 53.3** advise the Commission as to whether and, if so, the date on which, Phase III clinical trials for the Product for the Licensed Use are completed or SB (or, after the Closing Date, Glaxo SmithKline) ceases global development of the Product for the Licensed Use.
 - 53.4** monitor and advise the Commission as to the development of the procedure for selecting a Licensee and as to the conduct of the negotiations;
 - 53.5** monitor and advise the Commission as to whether prospective Licensee(s) with whom the Parties are or intend to negotiate are likely to satisfy the Licensee requirements.
- 54** The Trustee's duties and functions as set out above shall not be extended or varied in any way by the Parties, save with the express written consent of the Commission. Any instruction or request to the Trustee from the Parties which conflicts with the terms of the Mandate and duties and functions as set out above will be considered null and void.
- 55** After the Divestment Period (or any extension agreed by the Commission) has expired without the Parties having entered into a binding agreement for the obligations set forth in Section II of this undertaking, the Trustee shall be given an irrevocable mandate to negotiate and conclude a similar arrangement within [...] with a viable and independent third party at a fair market price.

- 56** If, however, the Trustee is unable to conclude such an arrangement at the end of the [...] (or any extended period agreed by the Commission) within which the Trustee is required to conclude an arrangement, the Trustee is entitled to enter into this arrangement at no minimum price for a further maximum and non-extendable period of [...].

V Interim position

Pending completion of the Undertaking, the Parties undertake to use reasonable efforts to ensure that, so far as relevant, development of the Product for the Licensed Use shall be managed in the ordinary course of business, pursuant to good business practices.

VI Miscellaneous

- 57** The Trustee will provide the Parties with all reasonable assistance and will procure that all relevant third parties provide such assistance required to ensure compliance with this Undertaking. The Parties will provide or cause to be provided to the Trustee all such assistance and information, including copies of all relevant documents accessible by the Parties as the Trustee may require in carrying out its Mandate, and to pay reasonable remuneration for its services.
- 58** Notwithstanding the Trustee's overall responsibility to discharge its functions and in particular notwithstanding the Trustee's position as an independent unrelated third party, the Trustee (who shall undertake in the Mandate to do so) shall have to the extent possible given the nature of its tasks due regard to the commercial interests of the Parties.
- 59** The Mandate and this Undertaking shall be deemed to be discharged and the Trustee's appointment shall be deemed to be terminated if (i) the Parties should jointly announce that the Transaction has been irrevocably abandoned or (ii) SB or, after the Closing Date, Glaxo SmithKline ceases development of the Product for the Licensed Use or (iii) any of the Competing Pipeline Products completes Phase III clinical trials for COPD or (iv) otherwise agreed by the Commission.
- 60** The Trustee's and all other relevant third parties' powers of attorney and appointment shall be irrevocable.
- 61** The Commission for its part declares that it will use its best endeavours to inform the Parties, as soon as reasonably practicable, as regards the suitability of any proposed Licensee. If there has been no rejection of the proposed Licensee by the Commission within ten (10) Commission working days after submission of a proposal by the Parties or the Trustee, the proposed Licensee will be deemed to have been approved by the Commission. In determining whether any proposed Licensee is suitable, it will take into account inter alia whether the proposed Licensee (i) appears to possess the status and resources necessary to manufacture and develop the Product for the Licensed Use within the Territory over the long term as a viable, active and significant competitor to the Parties, (ii) is independent of the Parties and (iii) can be shown not to have significant and relevant commercial connections with the Parties.
- 62** The obligations entered into in this Undertaking are conditional upon clearance pursuant to Article 6(1)(b) of the Merger Regulation by the Commission of the Transaction no later than 8 May 2000.

VII Governing Law and Provisions

This Undertaking is governed by, and shall be construed in accordance with, the laws of England and Wales.

Undertaking - Anti-migraine

For the purposes of this undertaking, “Licence” means an irrevocable exclusive licence granting the proposed licensee the exclusive right to develop, manufacture, market, sell and distribute compound SB220453 for migraine within the European Economic Area (“EEA”) and the right to grant sub-licences or distribution rights to third parties. Hereby it is expressly stipulated that the Parties continue to have exclusive rights to compound SB220453 outside the EEA and with respect to any use other than migraine within the EEA.

- 63** SmithKline Beecham plc, Glaxo Wellcome plc and, after the Closing Date, Glaxo SmithKline plc undertake to grant on arm’s length commercial terms and conditions, the Licence to any third party who is willing to in-license compound SB220453 for migraine.
- 64** Any dispute arising under or in connection with this undertaking shall be determined by arbitration in London pursuant to the rules of the London Court of International Arbitration by a single arbitrator chosen by agreement between the parties, failing which the arbitrator shall be chosen by President of the Law Society of England and Wales. The arbitration shall be conducted and the award shall be made in the English language.
- 65** This undertaking is governed by, and shall be construed in accordance with, the laws of England and Wales.