EN

Case No COMP/M.2517 - BRISTOL MYERS SQUIBB / DU PONT

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REGULATION (EEC) No 4064/89
MERGER PROCEDURE

Article 6(1)(b) NON-OPPOSITION
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COMMISSION OF THE EUROPEAN COMMUNITIES

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PUBLIC DECISION

MERGER PROCEDURE
ARTICLE 6(1)(b) DECISION

To the notifying party

Dear Sir/Madam,

Subject: Case No COMP/M.2517 – BRISTOL-MYERS SQUIBB/DU PONT Notification of 9 July 2001 pursuant to Article 4 of Council Regulation No 4064/89[1]

1. On 9 July 2001, the Commission received a notification whereby Bristol-Myers Squibb Company ("BMS") notified its intention to acquire sole control over Du Pont Pharmaceuticals Company ("DP") within the meaning of Article 3(1)b of Council Regulation (EEC) No 4064/89 ("Merger Regulation").

2. After examination of the notification, the Commission has concluded that the notified operation falls within the scope of the Merger Regulation and does not raise serious doubts as to its compatibility with the common market and with the EEA Agreement.

I. THE PARTIES

3. BMS is a pharmaceutical and related health care products company. In the pharmaceutical sector it is involved in a number of areas including oncology, cardiovascular and anti-infective treatments, cholesterol-fighting medications and treatments for diabetes. The company also manufactures infant formula and nutritional

[1] OJ L 395, 30.12.1989 p. 1; corrigendum OJ L 257 of 21.9.1990, p. 13; Regulation as last amended by Regulation (EC) No 1310/97 (OJ L 180, 9. 7. 1997, p. 1, corrigendum OJ L 40, 13.2.1998, p. 17).

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supplements. BMS is a public company whose shares are listed on the New York Stock Exchange and the Pacific Exchange.

4. DP is a wholly-owned subsidiary of E.I. du Pont de Nemours and Company. It is a worldwide business focusing on research, development and delivery of pharmaceutical and imaging (or radiopharmaceutical) products to treat various illnesses and diseases including HIV/AIDS, cardiovascular disease, inflammatory and neurological diseases.

5. The only overlap between the parties' activities is in the research, development, manufacture and marketing of pharmaceuticals. DP is a minor player in the pharmaceuticals sector: it accounts for only [<1%] of global pharmaceutical sales and is ranked no. 42 world-wide. Most of its pharmaceutical sales are generated in the United States. BMS is currently the 5th largest pharmaceuticals company in the world with [<5%] of worldwide pharmaceutical sales. The acquisition will result in only a minor increment in share and will not change BMS's overall ranking.

II. THE OPERATION

6. The acquisition will be effected by the transfer to BMS of all the outstanding general partnership interests in DP, together with the shares in three related entities. The consideration for the transfer is $7.8 billion in cash.

III. CONCENTRATION

7. By the proposed operation, BMS will acquire sole control over DP. Therefore, the operation is a concentration.

IV. COMMUNITY DIMENSION

8. The undertakings concerned have a combined aggregate world-wide turnover of more than EUR 5 billion[2] (BMS: 23,080.1 million EUR, DP 1,693,330 million EUR). Each of them have a Community-wide turnover in excess of EUR 250 million (BMS: […], DP […]), 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. The operation does not qualify for co-operation with the EFTA surveillance authority pursuant to the EEA Agreement.

V. COMPETITIVE ASSESSMENT

A. Relevant product markets

9. The economic sector concerned in this case is the pharmaceutical business. In previous pharmaceutical cases[3], the Commission has found that product markets in the pharmaceutical industry can be grouped into existing pharmaceutic specialities, active

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2 Turnover calculated in accordance with Article 5(1) of the Merger Regulation and the Commission Notice on the calculation of turnover (OJ C66, 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.

3 COMP/M.1378 - Hoechst/Rhône-Poulenc, COMP/M.1397 - Sanofi/Synthélabo, COMP/M.1403 - Astra/Zeneca, COMP/M.1835 - Monsanto/Pharmacia & Upjohn, COMP/M.1846 - Glaxo Wellcome/SmithKline Beecham, COMP/M.1878 - Pfizer/Warner-Lambert

substances and future products. In the present case, the parties' activities overlap only in pharmaceutic specialities and future products.

1. Pharmaceutic specialities

10. Pharmaceutical products are used for the treatment of human illnesses and diseases. 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). 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.

11. The Commission has in earlier decisions considered 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 pharmaceutic specialities or it may also be appropriate to apply a narrower market definition. In this case, BMS has used the ATC 3 classification as a starting point in the analysis.

12. The parties' product ranges are largely complementary. The only areas where their combined market shares exceed 15% at the national level based on the ATC3 classification are in plain ACE inhibitors (C9A) in Ireland and Spain; combination ACE inhibitors (C9B) in Ireland, Italy and UK; and in HIV/AIDS antivirals (J5C) in France, Germany, Ireland, Italy, Spain and UK.

(a) Plain ACE inhibitors (C9A) and combination ACE inhibitors (C9B)

13. ACE inhibitors are used to treat cardiac arrythmias and hypertension. They may either be prescribed individually or in combination tablets with diuretics, in which case they are categorised under C9B. BMS has suggested that plain ACE inhibitors (C9A) and combination ACE inhibitors (C9B) constitute relevant product markets each.

14. Some competitors have suggested that ACE inhibitors are part of the broad hypertension market, which includes such products as diuretics, beta-blockers, calcium channel blockers, ACE inhibitors and angiotensin II antagonists. However, the Commission concluded in case *IV/M.1403 - Astra/Zeneca* that ACE inhibitors should be assessed separately from other hypertension medicines. The question whether or not plain and combined ACE inhibitors (C9A/B) constitute separate product markets was left open in that case. It is not necessary to reach a definite conclusion on the relevant product market in this case either, because in all alternative market definitions considered, the operation as notified would not lead to the creation or strengthening of a dominant position.

(b) HIV/AIDS antivirals (J5C)

15. The Human Immunodeficiency Virus (HIV) is a retrovirus which progressively destroys the body's ability to fight infections and certain cancers. The term Acquired Immune Deficiency Syndrome (AIDS) applies to the most advanced stages of HIV

infection. The virus is transmitted through sexual and blood-to-blood contact. Women can transmit HIV to their baby during pregnancy, delivery or breast-feeding.

16. According to BMS, the treatment of HIV/AIDS is a complex process which varies from patient to patient and according to the stage of development of the disease. Because it is currently impossible to kill the virus, all of today's HIV/AIDS antiviral products aim to inhibit viral replication. Various treatment strategies and drug combinations have been developed to achieve this.

17. BMS submits that, at present, there are three categories of antiviral products used for the treatment of HIV/AIDS: so called *nucleoside reverse transcriptase inhibitors* (NRTIs), *protease inhibitors* (PIs) and *non-nucleoside reverse transcriptase inhibitors* (NNRTIs):

    a) NRTIs work by inhibiting the reverse transcriptase enzyme which HIV needs to infect the immune system cells. There are two principal categories of NRTIs: *non-thymidine nucleoside analogues* (such as didanosine, zalcitabine and lamivudine), which serve as substitutes for natural non-thymidine nucleosides, and *thymidine nucleoside analogues* (such as stavudine and zidovudine), which serve as substitutes for natural thymidine during viral replication.

    b) PIs (such as saquinavir, indinavir, ritonavir, nelfinavir, lopinavir and amprenavir) work at the final stage of the virus reproduction cycle. By blocking the HIV protease enzyme they inhibit the replication of HIV by host CD4+ cells and prevent the virus infecting new cells.

    c) NNRTIs (such as nevirapine and efavirenz) stop HIV production by directly attaching to the reverse transcriptase enzyme and preventing it from functioning. Unlike the NRTIs, however, the NNRTIs are not incorporated into the viral DNA molecule, and therefore these compounds require no phosphorylation by cellular enzymes in order to be active.

18. BMS's products Zerit (stavudine) and Videx (didanosine) are both NRTIs whereas DP's only product Sustiva (efavirenz) is a NNRTI.

19. BMS considers that PIs and NNRTIs should not be treated as falling within the same relevant market as NRTIs. According to BMS, NRTIs and NNRTIs are used as complements in HIV/AIDS combination therapy to enhance the efficacy of the antiviral treatment by attacking HIV in different ways. Therefore, BMS submits that there is no direct competition between the parties' products. BMS argues further that there are also differences in the therapeutic indications for PIs and NNRTIs which suggest that they may be in different markets.

20. According to BMS, the standard of care is at present a combination of three drugs for most patients, with four or more drugs sometimes prescribed for patients with advanced stages of the disease. These drug combinations, according to BMS, consist of two elements:

    a) A "backbone" consisting of two NRTIs (one thymidine NRTI and one non-thymidine NRTI).

    b) A third agent, typically a NNRTI or a PI, or, at the late stages of the disease, both a NNRTI and a PI, two NNRTIs or two PIs.

21. BMS submits that, in practice, because of their high toxicity and greater ability to suppress viral load, PIs are more commonly used later in the disease progression, with NNRTIs the preferred option for early treatments. Occasionally a third NRTI may be used but only in specific combinations, most commonly in GlaxoSmithKline's combination product Trizivir**.** According to BMS, regimens have to be changed over time because of the rapidly mutating nature of the virus and patient intolerance to the products. Combinations of drugs typically last only around 11-14 months (depending on the individual patient's reaction to the regimen) after which a new combination must be found.

22. The investigation in this case confirms BMS's argument that a combination therapy of 3-4 antiretrovirals is the current standard of care. The investigations suggests that the most typical combination currently is 2 NRTIs + 1 PI or 2 NRTIs + 1 NNRTI. According to third parties, a therapy consisting of two NNRTIs in combination is currently rare. Although there would appear to be a degree of substitutability between the different groups of compounds - such as between PIs and NNRTIs in 2-NRTI combinations - the question whether or not NRTIs, PIs and NNRTIs should be considered to belong to the same relevant product market can be left open for the purposes of this decision, because in all alternative market definitions considered, the operation as notified would not lead to the creation or strengthening of a dominant position.

2. Future products

23. As established in previous Commission decisions, a full assessment of the competitive situation in the pharmaceuticals industry requires examination of the products which are not yet on the market but which are at an advanced stage of development. As noted in the Ciba-Geigy/Sandoz decision[4], research & 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%.

24. Regarding future products, the Commission has to look at R&D potential in terms of its importance for existing markets, but also for future market situations. The relevant markets for future products often cannot be defined in the same manner as for existing products, except if the future products intend to replace existing products. 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. Market definition can thus 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

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

1. Pharmaceutic specialities

25. The Commission has previously defined the geographic markets for pharmaceutical products as being national in scope. The sale of medicines is influenced by the administrative procedures or 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.

26. The investigation in this case does not suggest that the Commission should deviate from its previous practice in assessing pharmaceutical markets at the national level. Therefore, the markets for pharmaceutic specialities affected by the concentration will be regarded as national.

2. Future products

27. As has been recognised in previous decisions, 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, the said 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. Pharmaceutic specialities

1) Plain ACE inhibitors (C9A),

28. As regards plain ACE inhibitors (C9A), the parties' combined market share in Ireland would be [15-25]% (BMS [15-25]%, DP [<5]%) and in Spain [15-25]% (BMS [10-20]%, DP [<5]%). In both countries, the new entity would face strong competition. In Ireland, AstraZeneca accounts for [20-30]% of the market, Aventis [10-20]% and Servier [10-20]%. In Spain, Merck's market share is some [10-20]%, and that of Merckle [5-15]%. Should all ACE inhibitors (C9A and C9B) be considered together, the parties' market shares would not be materially affected.

29. Therefore, given the market shares above, competition concerns are unlikely to arise as a result of the operation.

2) Combination ACE inhibitors (C9B)

30. In combination ACE inhibitors (C9B), the parties' combined market share in Italy would be [10-20]% (BMS [10-20]%, DP [<5]%), in the UK [30-40]% (BMS [25-35]%, DP [<5]%) and in Ireland some [50-60]% (BMS [50-60]%, DP [<5]%).

31. While the new entity would achieve a relatively high market share in Ireland, the increment of market share from DP is minimal. Moreover, the Commission notes that BMS's principal product, Capozide, is off patent in both Ireland and the UK, and is therefore exposed to generic competition. The market share for Capozide in Ireland has fallen from [75-85]% in 1997 and its share in the last quarter (January to March) was down further to [40-50]%. Most of this share has been lost to AstraZeneca's Zestoretic which has increased its share in Ireland from [5-15]% in 1995 to just over [30-40]% in 2000. UK sales of Capozide have halved since the product came off patent. In UK, the market leader is AstraZeneca with [40-50]% of the market.

32. Should all ACE inhibitors (C9A and C9B) be considered together, the parties' market share in Italy would not be materially affected. In the UK and Ireland, the combined market shares would be much lower (some [10-20]% in the UK and [20-30]% in Ireland).

33. In view of the foregoing and given in particular the rapid deterioration of BMS's market position in Ireland, the Commission concludes that the operation as notified would not lead to the creation or strengthening of a dominant position.

3) HIV/AIDS antivirals (J5C)

34. In case NRTIs and NNRTIs were to be considered to constitute separate relevant product markets, the operation would not lead to any increment of market share, because BMS's compounds are NRTIs and DP's compound is a NNRTI.

35. If the parties' products were to be considered as belonging to the same product market, the combined market share of the parties would be some [15-25]% in Italy (with an increment of [<5]% from DP) and some [25-35]% in France, Germany, Spain and the UK respectively (with an increment of some [5-15]% from DP). Based on the

information submitted by BMS, the new entity would attain [35-45]% of the market in Ireland (BMS [20-30]%, DP [10-20]%).

36. GlaxoSmithKline is the largest competitor in this treatment category. Based on IMS data, it is the market leader in France, Germany, Italy and the UK with market shares ranging between [20-30]% and [35-45]%. In Spain, the new entity would attain only a slightly higher market share than GlaxoSmithKline. As regards Ireland, BMS has not been able to produce reliable figures of its competitors in this country because IMS does not record hospital sales there. However, on the basis of the confidential figures obtained during the investigation, the Commission is able to conclude that GlaxoSmithKline is the largest competitor in Ireland with a market share capable of matching that of the new entity. Other competitors include Roche, who has market shares of some [5-15]-[10-20]% in the above mentioned Member States, Boehringer Ingelheim, Merck & Co, Abbott Laboratories and Agouron Pharmaceuticals.

37. As to the question whether or not BMS combining into a single product BMS's two existing NRTI products (Videx and Zerit) with DP's sole existing NNRTI product (Sustiva) would lead to the creation or strengthening of a dominant position, the Commission considers that this is not likely. Most importantly, given that one regimen period does not typically exceed 14 months, any combination tablet can be used only during this period after which the combination of drugs must be changed and the combination tablet cannot be used any more. Because of the need to combine different products, the individual components of any combination product will have to be continued to be sold also separately on the market, as is the case with GlaxoSmithKline's two combination tablets, Combivir and Trizivir. The Commission also recognises the technical impediments related to the development of combination products. BMS has marketed Zerit and Videx for the last five years […]. The parties' compounds have different dosing and food regimes, which according to BMS makes it difficult to combine them into a single tablet.

38. As to the question whether adding DP's Sustiva into the product portfolio of BMS, currently comprising two compounds, would lead to the creation or strengthening of a dominant position, the Commission considers in light of the investigation that this is unlikely. The investigation shows that GlaxoSmithKline has an extensive product portfolio and is currently the market leader in this treatment area in most Member States as well as in the EEA as a whole. GlaxoSmithKline has 5 NRTIs (two of which combination tablets) and one PI. The Commission also notes that GlaxoSmithKline has a NNRTI pipeline compound in Phase II development, which will complete its portfolio (see further below). In addition, GlaxoSmithKline has one NRTI pipeline compound and one PI in Phase III development each. Given this, the Commission considers that BMS will face intensive competition from GlaxoSmithKline in the future. There are also a number of other companies (Roche, Merck, Boehringer Ingelheim etc.) most of them both with existing and pipeline compounds.

39. On the basis of the foregoing, the Commission concludes that the operation as notified would not lead to the creation or strengthening of a dominant position in the market for HIV/AIDS antivirals (J5C)

2. Future products

40. In the current transaction, the parties overlap in the development of future products to a relatively limited extent. The treatment areas where both parties have pipeline products are specific antirheumatic agents (M1C) and HIV/AIDS antivirals (J5C). In those treatment areas where either of the parties has a pipeline compound the Commission does not consider, in view of the market shares for existing products, that competition concerns would be likely to arise.

41. As regards specific antirheumatic agents (M1C), both BMS and DP have a product in Phase II development. Neither party has existing products in this segment. There is a large number of other pharmaceutical companies with pipeline products in this segment, including British Biotech, Bayer, Aeterna, Pharmacia, Novartis, Pfizer, Roche, Kureha/Sankyo and Shiongi. Given this, the Commission does not consider that the parties' pipeline products would raise serious doubts in this field.

42. As regards HIV/AIDS antivirals (J5C), DP has the following products in clinical trials: two PIs, both on hold (DPC681 - Phase I, DPC684 - Phase I), two NNRTIs (DPC083 - Phase III, DPC961 - Phase I/II on hold) and an NRTI (DPC817 - Phase I). BMS has one PI in clinical development (BMS 232632 - Phase III).

43. If NRTIs, PIs and NNRTIs were to be considered to constitute separate relevant product markets, no overlap would arise in pipeline compounds as a result of the operation. Should these compounds be considered to belong to the same product market, the overlap at the pipeline level is minimal, because BMS has currently only one future product.

44. In terms of product portfolio, the operation would strengthen BMS's product range by adding into it one NNRTI, which is in Phase III of development. However, as discussed above, GlaxoSmithKline is the largest competitor with an extensive existing product portfolio. It also has one NNRTI in Phase II development. In addition, a large number of other companies have pipeline compounds in this sector, in particular Abbott Laboratories/Triangle Pharmaceuticals, Pharmacia and Shiuonogi/Pfizer, each with NNRTIs in Phase III development. Furthermore, GlaxoSmithKline, Abbott Laboratories/Triangle Pharmaceuticals and Gilead Sciences have NRTIs in Phase III development and a number of other companies have similar compounds in Phase II. Finally, GlaxoSmithKline has one PI is Phase III development and Boehringer Ingelheim, Merck and Japan Energy Corporation similar compounds in Phase II.

45. HIV/AIDS antivirals sector is a fast moving area where drugs and treatment regimens have evolved significantly over the last twenty years and are continuing to change rapidly. Even in the past three years there have been dramatic changes in what is considered the standard of care. By way of example, according to the information provided by BMS and confirmed by the investigation, for the past three years, the use of PIs has diminished and that of the latest arrival, NNRTIs, increased. Accordingly, a therapy comprising 2 NRTIs and one NNRTI has increased while therapy containing 2 NRTIs and one PI has diminished.

46. Therefore, in view of the rapid development of the sector and the large number of companies currently developing new compounds, the Commission concludes that the combination of the parties' pipeline products is unlikely to lead to the creation or strengthening of a dominant position in HIV/AIDS antivirals (J5C).

VI. CONCLUSION

47. For the above reasons, 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(1)(b) of Council Regulation (EEC) No 4064/89.

For the Commission

Mario Monti
Member of the Commission