COMMISSION OF THE EUROPEAN COMMUNITIES

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FIRST COMMISSION REPORT TO THE COUNCIL

on the functioning of the Committee for Proprietary Medicinal Products and its impact on the development of intra-Community trade

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Period 1977/1978

First Commission Report on the functioning of the Committee for Proprietary Medicinal Products and its impact on the development of intra-Community trade

Period 1977/78

Introduction

For the purpose of the progressive establishment of the common medicaments market, the Council has hitherto adopted the following four Directives:

- Directive 65/65/EEC of 26 January 1965 (OJ of 9.2.65)
- Directive 75/318/EEC of 20 May 1975 (OJ L 147 of 9.6.75)
- Second Directive 75/319/EEC of 20 May 1975 as amended by Directive 78/420/EEC of 2 May 1978 (OJ L 123 of 11.5.78)
- Directive 78/25/EEC of 12 December 1977 (OJ L 11 of 14.1.78).

This harmonization of national laws has eliminated major obstacles to the free movement of proprietary medicinal products:

- applications for marketing authorizations (M A) may be submitted to the competent authorities of the member States on the basis of the same particulars and the same analytical, toxicological, pharmacological and clinical test results;
- the proprietary medicinal products control-tested in compliance with the requirements laid down for the M A are exempted from fresh control tests when they are imported into another member State.

However, the marketing authorizations remain the responsibility of the national authorities and therefore there is a risk that the different competent authorities may take divergent decisions. This is why the Committee for Proprietary Medicinal Products was set up, in order to limit this risk by means of close cooperation between national authorities.

The Committee must give opinions on matters related to the implementation of Articles 5, 11 and 20 of Directive 65/65/EEC, and in particular on the harmlessness, efficacy and quality of the proprietary medicinal products. The Committee delivers opinions in the following three events:

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a) when a member State considers that it cannot grant the M A for an application lodged under the Community procedure as laid down in Article 9 of Directive 75/319/EEC. This procedure may be employed if the person concerned wishes to place his product on the markets of at least five other member States;

b) when different decisions are taken in respect of the same proprietary medicinal product;

c) when a member State, in specific cases of Community interest, wishes to obtain the Committee's opinion before taking a decision on an M A application, suspension or revocation.

However, the Committee issues non-binding opinions only in such a way that, in spite of the cooperation within the Committee, the same proprietary medicinal product may be allowed on the market of one or more member States and refused on the markets of other member States.

It is obvious that this situation constitutes an obstacle to the free movement of proprietary medicinal products in the Community, which is the objective of harmonization. It is for this reason that the Council has asked the Commission (Article 15(2) of Directive 75/319) to present it with a proposal on all appropriate measures for eliminating outstanding obstacles to the free movement of proprietary medicinal products, not later than four years after the entry into force of this Directive, i.e., before the end of 1980.

Article 15 of Directive 75/319 also lays down that the Commission must report to the Council every year on the operation of the procedure applied by the Committee for Proprietary Medicinal Products and its impact on the development of intra-Community trade, and shall do so for the first time two years after the entry into force of the Directive. This is the object of the present document.

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I. The functioning of the Committee for Proprietary Medicinal Products

The period covered by the report has been essentially characterized by the setting-up of the Committee and its "running-in", thanks mainly to the interest shown in it by the competent national authorities. In fact, applications from those responsible for marketing, manufacturers or importers have up to now been very few. According to the industrial circles concerned, this must not be attributed to "a traditional reluctance to follow new paths", but to very precise reasons:

- the delay in some member States in implementing the provisions of the Directives, rendering it impossible to use the Community procedure in those countries;
- the requirement to apply for marketing authorizations for at least five other member States, rendering it difficult to follow the procedure because products are generally introduced gradually on markets.

1. The setting-up of the Committee

1.1 Rules of procedure

The Committee for Proprietary Medicinal Products drew up its rules of procedure, which were forwarded to the Council on 23 December 1976 for possible comments as laid down in a declaration included in the summary record of the 769th meeting of the Permanent Representatives Committee on 7 and 12 May 1975. On 17 March 1977 an amendment to the draft rules was forwarded to the Council, which had criticized the provisions governing the languages used in the work of the Committee; in fact, the use of languages in the Communities are laid down in Council Regulation No 1 of 12 April 1958 (OJ 17/385 of 6.10.58) as amended by Annex I to the Act concerning the Conditions of Accession and the Adjustments to the Treaties.

The rules of procedure of the Committee are set out in Annex I to this report.

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In addition to the customary provisions in such rules, the Committee is in particular empowered to set up panels of experts to study matters of common interest. This right has been used three times, as will be seen later on in the report.

Furthermore, it is laid down that the work of the Committee and of the panels of experts and all the documents which are submitted to them are confidential in nature. The breaching of professional secrecy is subject in all cases to penal sanctions. This confidentiality is obviously without prejudice to the notification of the person responsible for marketing if a reasoned objection to the marketing of his product is lodged by a member State, as soon as the Committee is apprised of this.

1.2 Election of the Chairman and Deputy Chairman

Mr Léon ROBERT, the Luxembourg representative, was elected Chairman, in accordance with the procedure laid down in Article 2 of the rules of procedure.

Mr E.L. HARRIS, the United Kingdom representative, was elected Deputy Chairman. Following Mr Harris's appointment to other duties, Professor Duilio POGGIOLINI, the Italian representative, was elected Deputy Chairman. The task of the elected Deputy Chairman is mainly to deputize for the Chairman at Committee meetings.

A second Deputy Chairman, appointed by the Commission, is provided for. His main task is to deputize for the Chairman in the period between meetings. Mr D.J. DEVINE, Director, was thus appointed Deputy Chairman; he withdrew and was replaced by Mr Nicolaas BEL, Head of Division.

Attached is Annex II, which contains a list of members of the Committee.

1.3 Notifying trade circles

So as to draw the attention of the trade circles concerned to the new procedure available to them for placing proprietary medicinal products on the market, via the Committee, a notice to manufacturers and importers was published in the Official Journal of the European Communities No C 302 of 15 December 1977 and reprinted in the national official gazettes.

This notice describes the conditions to be fulfilled in order to use the Committee procedure, the procedure to be followed and the force of Committee opinions. The text of the notice can be found in Annex III.

Meanwhile, the members of the Committee and of the Secretariat have taken part in a number of talks, conferences, seminars, etc., intended to make the Committee better known. Its Chairman has been invited several times, in his capacity as Chairman, to most of the member States.

2. "Running-in" of the Committee

2.1 Developing its working methods

From the outset, the Committee has been concerned with the efficacy of its work: first, its internal functioning, by the simplification of procedures; secondly, and essentially, for the purpose of improving cooperation between the competent authorities. To this end and so as to avoid divergent national decisions as far as possible, the Committee has revised some general standards and has drawn up more specific provisions.

a) It very quickly emerged that Article 9 of Directive 75/319/EEC was unsuitable. The forwarding of dossiers to the Committee and then on to the member States concerned was liable to cause delays detrimental to the manufacturers and, in the final analysis, to the good name of the Committee. On its proposal, the Commission, after consulting the Pharmaceutical Committee set up by Council Decision 75/320/EEC, proposed to the Council that the Directive be amended to provide for the simultaneous forwarding of dossiers to the member States concerned and to the Committee. The amendment was adopted by Council Directive No 78/420/EEC of 2 May 1978 (OJ L 123 of 11 May 1978).

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b) Likewise, the Committee examined a number of problems raised by Directive 75/318/EEC of 20 May 1975 (OJ L 147 of 9.6.75) with regard to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products. It put forward a number of proposals for revisions which will, if appropriate, be subjected to the procedure described above for the amendment of the procedure for forwarding dossiers.

c) So as to facilitate the task of the applicants for marketing authorizations and of the competent authorities, the Committee drafted a document indicating, in compliance with Directive.. 65/65/EEC, 75/318/EEC and 75/319/EEC, the order in which it wishes to have the particulars in support of applications for authorization presented to it. (See attached document in Annex IV.)

d) Moreover, the Committee was aware that the general nature of the standards and protocols could not guarantee either the uniformity of the experimental work done in the different member States or the harmonization of decisions taken by national authorities. It therefore decided to draw up more specific principles to govern procedure in relation to given experiments or groups of medicaments so that the manufacturers could draw the appropriate conclusions as regards their work. In accordance with Article 13 of its rules of procedure, the Committee set up three expert panels to assist it in this task, namely:

- the "Safety of Drugs" panel, chaired by Dr J.P. GRIFFIN, Senior Principal Medical Officer at the Department of Health and Social Security, London;

- the "Efficacy of Drugs" panel, chaired by Dr M.N.G. DUKES, Vice-President of the "College ter beoordeling van geneesmiddelen" of the Netherlands;

- the "Medicinal Products of Plant Origin" panel, chaired by Professor B. SCHNIEDERS, Director of the Medicaments Institute of the Bundesgesundheitsamt, Berlin.

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The following procedure has up to now been used so as to obtain the widest possible consultations: the panels of experts draw up scientific explanatory notes covering all available data that can be gathered. These notes are forwarded by the Committee to the competent national authorities and to the trade groups organized at Community level. The national authorities send these notes on to the national groups concerned. Comments received by the Committee for Proprietary Medicinal Products are examined by the expert panels who amend the explanatory notes accordingly or explain why they have maintained their stance to the Committee.

The legal form to be assigned to these documents depends on their contents. The Pharmaceutical Committee, set up by Council Decision 75/320/EEC, has been asked to give its opinion on this point and the discussions have not yet been completed. The following five documents have been disseminated as widely as possible and the expert panels are in the process of examining the comments received:

- fixed combination products,
- non-steroidal, anti-inflammatory compounds for the treatment of chronic disorders,
- reproduction studies,
- carcinogenicity testing,
- chronic toxicity studies.

The panels on "Safety and Efficacy of Drugs" are drafting notes in the following fields:

- immunotoxicology
- mutagenicity
- pharmacokinetics
- safety pharmacology
- bioavailability
- toxicity by inhalation
- acute toxicity
- sub-acute toxicity

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These panels are still working on the following drug groups:

- anti-epileptic drugs
- cardiac glycosides
- anti-anginal drugs
- oral contraceptives.

The panel on "Medicinal Products of Plant Origin" was set up to examine the specific problems raised by this type of product. The fact is that subjecting such products to all the requirements of the M A directives might make them disappear from the market, whereas a large number of these products are still used even if on a small scale. However, research capacity in this field seems fairly limited since scientific motivation is low and considerable financial resources would be needed. The panel is accordingly trying to utilize the available scientific documentation so as to assess the efficacy and harmlessness of these products.

2.2 The functioning of the Committee

a) The Committee received two M A applications pursuant to Article 9 of Directive 75/319/EEC.

In both cases, the initial M A was granted to the United Kingdom and the M A applications concern Belgium, Denmark, Italy, Luxembourg and the Netherlands. The procedure is in progress and will not be completed by the end of the period covered by the present report.

b) Under Article 12 of Directive 75/319/EEC, the Committee has not had to deal with divergent decisions taken by the member States with respect to M A authorization, suspension or revocation.

c) Under Article 14 of the above-mentioned Directive, the Committee has been apprised of and examined about twenty medicaments, involving problems of Community interest, and in particular the following products:
Carbamazepine - Chloroform - Practolol - Chenodesoxycholic Acid - Clozapine - Aprindine - Biguanides - Paracetamol - Tofenacine - Benorylate - Catalase - Pipemidic Acid - Aminophenazone - Lynestrenol - Salbutamol - Allergens - Bismuth salts.

In addition, it has examined the following specific cases: sterilization by ethylene oxides; asbestos fibres.

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II. Development of intra-Community trade

During this setting-up and running-in period, it is doubtful whether the functioning of the Committee for Proprietary Medicinal Products procedure will have any influence on the development of intra-Community trade. Here too, statistical instruments which will enable this development to be followed need to be put into operation.

A worth-while exercise might be to take the statistics going back to 1974, the first year for which data on the nine-member Community are available.

The statistics are given in EUR and in European units of account (EUA). Table 6 can be used for conversion to national currencies.

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1. Medicaments imports for clinical and veterinary medicine

(Value : 1000 EUR)
in 1974 - 1975
(Value : 1000 EUA) in 1976 - 1977 (Chapter 30.03 of the Common Customs Tariff)

Origin	EUR 9	BE	FR	IT	NE	B - L	UK	IR	DA
1974									
Intra-Com.	523.602	101.407	12.241	66.053	112.588	135.998	45.570	28.042	21.703
Extra-Com.	177.228	49.967	4.244	21.229	19.552	34.541	29.846	2.708	15.141
Suisse	96.969	25.834	1.804	11.821	12.125	24.385	11.598	1.113	6.289
U.S.A.	33.534	9.629	1.061	4.416	4.402	5.025	7.352	751	898
1975									
Intra-Com.	579.425	131.764	14.689	65.927	122.968	145.021	46.386	29.237	23.433
Extra-Com.	203.199	64.505	3.036	25.035	19.547	38.799	32.676	3.071	16.530
Suisse	114.056	33.211	575	15.845	14.493	27.479	14.799	1.794	5.860
U.S.A.	30.852	7.256	1.057	4.550	1.091	6.610	7.159	681	2.448
1976									
Intra-Com.	744.321	160.257	17.871	82.210	174.117	176.242	63.573	36.549	33.502
Extra-Com.	289.593	98.100	3.378	34.330	24.639	53.302	43.633	5.567	22.644
Suisse	152.872	46.318	582	20.357	17.371	40.916	16.433	3.445	7.450
U.S.A.	42.629	10.977	1.286	5.831	1.096	8.480	11.116	1.114	2.695
1977									
Intra-Com.	863.446	203.934	29.645	81.185	182.117	183.123	92.996	47.688	42.758
Extra-Com.	325.549	122.190	5.403	30.607	34.798	56.699	50.173	1.136	24.543
Suisse	170.204	55.925	856	17.197	25.082	40.788	21.538	167	8.691
U.S.A.	44.273	13.080	3.034	5.567	3.153	7.408	8.964	624	2.243

Source : E U R O S T A T

2. a) Imports of medicaments prepackaged for retail sale

(Value : 1000 EUR)
in 1974 - 1975
(Value : 1000 EUA)
in 1976 - 1977

Origin	EUR 9	DE	FR	IT	NE	B - L	UK	IR	DA
1974									
Intra-Com.	363.287	59.258	9.206	44.780	80.891	90.734	33.905	26.882	17.631
Extra-Com.	81.415	21.623	2.017	13.372	6.370	11.271	12.569	2.626	12.567
1975									
Intra-Com.	401.693	81.080	8.391	45.740	90.535	97.302	34.737	28.306	15.602
Extra-Com.	99.849	30.344	1.702	15.360	8.775	14.429	12.351	3.013	13.875
1976									
Intra-Com.	527.889	102.099	12.374	53.860	130.044	122.074	44.755	35.067	27.616
Extra-Com.	140.100	41.448	1.695	20.886	12.082	18.782	19.851	5.133	19.568
1977									
Intra-Com.	625.414	115.184	19.466	56.719	144.974	125.371	72.330	44.491	34.653
Extra-Com.	157.622	63.103	3.627	18.623	14.237	14.940	19.776	992	21.424

2. b) Percentage of intra-Community imports in total imports of medicaments prepackaged for retail sale

1974	81 %	73 %	82 %	77 %	92 %	89 %	73 %	91 %	58 %
1975	80 %	73 %	83 %	74 %	91 %	87 %	74 %	90 %	53 %
1976	79 %	71 %	88 %	72 %	92 %	87 %	69 %	87 %	58 %
1977	80 %	65 %	84 %	75 %	89 %	89 %	78 %	98 %	62 %

2. c) Percentage of medicaments prepackaged for retail sale in total Community medicaments imports

In 1977 medicaments prepackaged for retail sale represented 66 % of medicaments imported by the Community (65 % in 1976, 64 % in 1975, 63 % in 1974).

If we look at intra-Community imports alone, prepackaged medicaments account for a slightly higher proportion of the total intra-Community medicaments imports: 69.3 % in 1974 and 1975, 71 % in 1976, 72.4 % in 1977. This trend might become more marked as a result of harmonization of laws, which makes importing proprietary medicinal products easier than any other forms of medicaments (in bulk or in compounded form).

3. Medicaments exports for clinical and veterinary medicine

(Value : 1000 EUR)
in 1974 - 1975

(Value : 1000 EUA) (Chapter 30.03 of the
in 1976 - 1977 Common Customs Tariff)

Destination	EUR 9	DE	FR	IT	NE	B - L	UK	IR	DA
1974									
Intra-Com.	554.006	161.099	76.599	31.350	61.318	96.587	106.623	7.192	15.033
Extra-Com.	1.073.959	344.232	203.415	60.918	60.364	57.529	288.834	4.443	54.224
Suisse	70.382	32.924	13.836	2.626	3.308	6.195	8.351	116	3.026
U.S.A.	17.064	2.010	852	5.673	66	65	8.187	92	119
1975									
Intra-Com.	585.925	162.395	91.017	31.441	61.514	112.800	98.445	9.212	19.101
Extra-Com.	1.200.476	355.310	252.999	74.808	64.147	58.389	328.487	6.535	59.801
Suisse	73.127	31.526	14.905	3.428	3.921	7.530	9.212	220	2.387
U.S.A.	25.641	1.480	59	12.024	301	305	11.351	69	52
1976									
Intra-Com.	732.547	197.223	106.794	46.364	86.792	143.301	113.913	14.272	23.888
Extra-Com.	1.451.670	445.257	300.203	90.982	92.101	76.210	361.196	7.554	76.167
Suisse	101.637	43.816	20.093	4.195	6.553	11.588	11.964	389	3.039
U.S.A.	30.832	1.071	248	15.241	2.461	742	10.880	127	62
1977									
Intra-Com.	847.668	199.576	134.043	51.746	106.616	168.859	137.252	20.592	29.1[illegible]
Extra-Com.	1.708.091	508.969	338.390	120.426	104.358	96.929	433.432	8.039	98.6[illegible]
Suisse	117.994	48.415	26.023	5.409	6.817	12.404	14.186	421	3.319
U.S.A.	35.575	1.899	262	16.523	2.769	1.378	10.833	904	29

[illegible]

4. a) Exports of medicaments prepackaged for retail sale

(Value : 1000 EUR)
in 1974 - 1975
(Value : 1000 EUA)
in 1976 - 1977

Destination	EUR 9	DE	FR	IT	NE	B - L	UK	IR	DA
1974									
Intra-Com.	413.935	137.093	57.244	17.415	32.629	92.422	63.783	3.852	9.497
Extra-Com.	868.527	278.486	183.925	49.690	50.952	50.238	207.373	2.848	47.015
1975									
Intra-Com.	439.762	135.856	67.021	19.713	29.101	106.898	61.690	5.514	13.969
Extra-Com.	990.370	291.766	229.980	61.532	54.551	53.848	244.907	3.738	51.676
1976									
Intra-Com.	557.235	168.930	78.977	29.965	51.338	134.218	65.036	9.183	19.589
Extra-Com.	1.168.131	362.169	272.880	80.759	77.546	70.650	234.047	4.144	65.936
1977									
Intra-Com.	646.974	169.777	88.852	34.070	65.768	159.199	89.082	12.664	27.562
Extra-Com.	1.408.492	421.656	300.616	106.489	88.056	91.742	107.204	5.512	82.217

4. b) Percentage of intra-Community exports in total exports of medicaments prepackaged for retail sale

1974	32 %	33 %	24 %	26 %	39 %	65 %	24 %	57 %	17 %
1975	31 %	32 %	23 %	24 %	35 %	67 %	20 %	60 %	21 %
1976	32 %	32 %	22 %	27 %	40 %	66 %	22 %	69 %	23 %
1977	31 %	29 %	23 %	24 %	43 %	63 %	45 %	70 %	25 %

4. c) Percentage of medicaments prepackaged for retail sale in total Community medicaments exports

In 1977 medicaments prepackaged for retail sale accounted for 80.5 % of medicaments exported by the Community (79 % in 1976, 80 % in 1975, 79 % in 1974).

5. Development of trade in medicaments prepackaged for retail sale (Index 100 in 1974)

		DE	FR	IT	NE	B - L	UK	IR	DA
Index in 1977									
Imports	intra-Com.	194	211	127	179	138	213	165	196
	extra-Com.	292	180	139	223	132	157	38	170
Exports	intra-Com.	124	155	196	201	172	140	329	290
	extra-Com.	152	163	214	173	183	52	193	175

6. a) Value of the EUR

	DE 1 EUR = ... DM	FR 1 EUR = ... FF	IT 1 EUR = ... LIT	NE 1 EUR = ... HFL
1974	3,21978	6,01	813	3,35507
1975	3,20684	5,68	863	3,35507

6. b) Value of the European unit of account (EUA)

	1 EUA = ... DM	1 EUA = ... FF	1 EUA = ... LIT	1 EUA = ... HFL
1976	2,81545	5,34486	930,150	2,95515
1977	2,64832	5,60608	1006,790	2,80011

6. c) Conversion rate

1974 : 0,954980

1975 : 0,938341

	B - L 1 EUR = ... FB/FLux.	UK - IR 1 EUR = ... UKL/IRL	DA 1 EUR = ... DKR
1974	48,6572	0,511	7,57831
1975	48,6572	0,534	7,57831

	1 EUA = ... FB/FLux.	1 EUA = ... UKL/IRL	1 EUA = ... DKR
1976	43,1654	0,621578	6,76176
1977	40,8827	0,653701	6,85568

7. Comments

a) In intra-Community trade, the Benelux countries account for almost half of prepackaged medicaments imports:
47 % in 1974 and 1975, 48 % in 1976, 43 % in 1977.

Intra-Community exports are also highly concentrated: Germany and Belgium-Luxembourg account for more than half of intra-Community prepackaged medicaments exports: 33.1 + 22.3 % in 1974, 30.8 + 24.3 % in 1975, 30.3 + 24 % in 1976, 26.2 + 24.2 % in 1977.

b) The figure for French intra-Community imports of prepackaged medicaments is of a token nature - 2.5 % of total intra-Community imports in 1974, 2 % in 1975, 2.3 % in 1976 and 3.1 % in 1977. This is evidence of the obstacles to the importing of medicaments. The results of the Commission's efforts to eliminate these obstacles in conjunction with the Council's efforts to harmonize laws are not yet reflected in the statistics.

c) Since 1974 the percentage of intra-Community imports and exports in the total imports of prepackaged medicaments has been stable and this conceals the effect harmonization of laws has had on intra-Community trade. On the other hand, the accession of new member States seems to be modifying the pattern of their trade, increasing the percentage of intra-Community imports and exports, the record going to Ireland, which in 1977 imported prepackaged medicaments almost solely from the Community (98 %).

d) The procedure applied by the Committee for Proprietary Medicinal Products has had practically no impact during the period covered by the report. However, it is no doubt too much to expect great changes in trade patterns in the future, even if this procedure were widely used, when at the present time 80 % of imports of medicaments prepackaged for retail sale already derive from imports between member States.

Rules of Procedure
of the
Committee for Proprietary Medicinal Products

THE COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS,

Having regard to Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, and in particular Article 8(3)[1] thereof,

HAS DRAWN UP ITS RULES OF PROCEDURE AS FOLLOWS :

[1] OJ No L 147, 9.6.75

Article 1

1. The Committee shall consist of one representative for each Member State and one representative of the Commission. One alternate shall be appointed for each of the representatives.

2. The Committee members and the alternates shall be appointed by the Member States for three years provided they continue to be national officials responsible for examining applications for authorization to market proprietary medicinal products. Their appointments shall be renewable.

3. An alternate shall sit in this capacity on the Committee only if the full member is absent or is unable to discharge his duties.

4. Each representative may arrange to be accompanied at Committee meetings by not more than three experts.

5. Even after their duties have ceased, members, alternates and experts shall be required not to disclose information of the kind covered by the obligation of professional secrecy.

Article 2

The Committee shall elect its Chairman from among its members by absolute majority and secret ballot. If, after two ballots, nobody has obtained an absolute majority of the votes, the member who obtains the relative majority at the third ballot shall be elected. In the event of a tie the oldest candidate shall be declared elected.

Article 3

The term of office of the Chairman shall be three years. He shall be eligible for re-election once only.

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Article 4

As soon as he takes up his duties, the Chairman shall cease to be a representative and shall be replaced in that capacity.

Article 5

Two Deputy Chairmen shall be appointed to replace the Chairman when he is absent or unable to discharge his duties. One shall be elected by the Committee and the other appointed by the Commission.

The provisions of Articles 2 and 3 of these Rules of Procedure shall apply to the election and the term of office of the elected Deputy Chairmen.

Article 6

The Committee shall be convened by its Chairman, either on his own initiative or at the request of a member.

Article 7

The Chairman shall draw up the agenda, in which distinctions shall be made between:

(a) objections to applications for marketing authorizations submitted to the Committee for an opinion under Article 11 (1) of Directive 75/319/EEC;

(b) refusals, suspensions or revocations of marketing authorizations submitted to the Committee for an opinion under Article 12 (2) of Directive 75/319/EEC;

(c) fresh examinations of previous opinions under Article 13 of Directive 75/319/EEC;

(d) specific cases submitted under Article 14 of Directive 75/319/EEC.

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Article 8

Requests to convene the Committee which are made by a member must be drawn up in accordance with the classification set out in the foregoing Article and be reasoned such that they may constitute the working paper of the Committee.

Article 9

1. Pursuant to Article 9 (1) of Directive 75/319/EEC, the Member State concerned shall forward to the Committee a dossier containing :

   (a) a copy of the request for forwarding to the competent authorities of the Member States specified;

   (b) a copy of the marketing authorization;

   (c) the particulars and documents listed in the second paragraph of Article 4 of Directive 65/65/EEC.

   There shall be forwarded as many dossiers as there are Member States specified, plus one for the secretariat of the Committee.

2. Pursuant to Article 9 (2) of Directive 75/319/EEC, the Committee shall forthwith forward this dossier to the competent authorities of the Member States specified.

3. The Committee shall send to the members of the Committee the documents referred to in paragraph 1 (a) and (b) above.

Article 10

The dossier kept by the secretariat of the Committee may be consulted by any member of the Committee or by the experts referred to in Article 1(4) having the written authority of the member.

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Article 11

1. The notification of the meeting, the agenda and the working papers shall be forwarded by the Chairman to the members of the Committee in accordance with the procedure laid down in Article 18 (2) and (3).

2. These papers shall be delivered to the Permanent Representatives of the Member States and to the Commission not later than fifteen days before the date of the meeting.

3. In urgent cases, the Chairman may, at the request of a member of the Committee or on his own initiative, shorten this period of notice by up to three clear working days, stating the grounds for his decision.

Article 12

1. Meetings of the Committee shall be validly held if six Member States are represented.

2. The representative of a Member State may, if necessary, undertake the representation of one other Member State. The Chairman of the Committee shall be informed accordingly by the Permanent Representative of the Member State wishing to be so represented.

Article 13

The Committee may convene panels of experts to study matters of common interest.

Article 14

The secretarial services for the Committee shall be provided by the Commission, assisted, if necessary, by experts.

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Article 15

1. The Member States concerned shall be informed forthwith of the reasoned opinions delivered pursuant to Articles 11 and 12 of Directive 75/319/EEC in accordance with the procedure set out in the first subparagraph of Article 18(2).

2. A summary record shall be prepared under the responsibility of the Chairman for each meeting; it shall be forwarded to the members of the Committee in accordance with the procedure set out in Article 18 (2) and (3). Any comments which the members may wish to make shall be communicated to the Chairman in writing. The Chairman shall pass them on to the Committee; if there is disagreement, the proposed amendment shall be discussed at the following meeting. If disagreement persists, this amendment shall be appended to the relevant record.

Article 16

The Chairman of the Committee shall act as proxy for the Committee to perform the formal recording referred to in Article 10(1) of Directive 75/319/EEC.

He shall forthwith inform the Member States of this formal recording in accordance with the procedure set out in the first paragraph of Article 18(2).

Article 17

1. The secretariat of the Committee shall act as proxy for the Committee to forward the dossier referred to in Article 9(2) to the competent authorities of the Member States in accordance with the procedure set out in the first paragraph of Article 18(2) and, in the same way, the documents referred to in Article 9(3).

2. The information forwarded to the Committee in accordance with Article 11(3), Article 12(4) and Article 33 of Directive 75/319/EEC shall be brought to the knowledge of the members of the Committee by the secretariat in accordance with the procedure set out in the second paragraph of Article 18(2).

Article 18

1. Correspondence of concern to the Committee shall be addressed to the secretariat of the Committee, Directorate-General for Internal Market and Industrial Affairs, for the attention of the Chairman.

2. Correspondence intended for the representatives of the Member States shall be addressed to the Permanent Representations.

   Copies of such correspondence shall be addressed directly to the representatives of the Member States.

3. Correspondence intended for the representative of the Commission shall be adressed to the Commission, Directorate-General for Internal Market and Industrial Affairs.

Article 19

Notwithstanding the provisions of Article 214 of the Treaty, the work of the Committee and of the panels of experts and all the documents submitted to them shall be treated as confidential. Nevertheless, the representatives of the Member States may, in accordance with the national laws in force, inform the person responsible for marketing a medicinal product or products of the reasoned objection of a Member State, as referred to in Article 10(2) of Directive 75/319/EEC.

ANNEX II

COMITE DES SPECIALITES PHARMACEUTIQUES

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS

Président / Chairman :

M. Léon ROBERT	Président de la Commission d'Enregistrement des Médicaments Ministère de la Santé publique Luxembourg

Vice-Présidents / Deputy Chairmen :

1. Prof. Duilio POGGIOLINI	Direttore Generale del Servizio Farmaceutico Ministero della Sanità Roma
2. M. Nicolaas BEL	Chef de Division à la Direction générale du marché intérieur et des affaires industrielles - CCE

a) Représentants / Representatives :

b) Suppléants / Deputies :

BELGIQUE

a) M. Ben HUYGHE	Inspecteur général, Inspection générale de la Pharmacie Ministère de la Santé publique
b) Mme Denise TORFS-BRUDER	Pharmacien-Inspecteur, Inspection générale de la Pharmacie Ministère de la Santé publique

DANMARK

a) Mr. Steen ANTONSEN	Laboratoriechef Sundhedsstyrelsen, Farmaceutiske Laboratorium
b) Mr. Hans Otto ANDERSEN	Sekretariatschef Sundhedsstyrelsen, Farmaceutiske Laboratorium

.../...

B. R. DEUTSCHLAND

a) Prof. Dr. Bernhard SCHNIEDERS	Leiter des Instituts für Arzneimittel des Bundesgesundheitsamtes
b) Prof. Dr. Günter Aßmann	Leiter der Abteilung "Pharmazeutische Fragen der Arzneimittelzulassung" des Instituts für Arzneimittel des Bundesgesundheitsamtes

FRANCE

a) M. Jean WEBER	Directeur de la Pharmacie et du Médicament, Ministère de la Santé publique et de la Sécurité sociale
b) M. GRECH	Pharmacien-Inspecteur de la Santé au Service Central de la Pharmacie et des Médicaments Ministère de la Santé publique et de la Sécurité sociale

IRELAND

a) Dr. Alene SCOTT	Medical Director National Drugs Advisory Board
b) Prof. Oliver FitzGerald	Chairman of the National Drugs Advisory Board

ITALIA

a) Prof. Duilio POGGIOLINI	Direttore Generale del Servizio Farmaceutico Ministero della Sanità
b) Dott. Romano CAPASSO	Consigliere Ministeriale Ministero della Sanità Direzione Generale del Servizio Farmaceutico

LUXEMBOURG

a) Mlle Josannette WEYDERT	Pharmacien, Inspection des Pharmacies Ministère de la Santé publique
b) Mlle Marie-Thérèse STRONMENGER	Pharmacien attaché à l'Inspection des Pharmacies Ministère de la Santé publique

.../...

NEDERLAND

a) Dr. C.A. TEIJGELER — Voorzitter van het College ter Beoordeling van Geneesmiddelen
Ministerie van Volksgezondheid

b) Dr. M.N.G. DUKES — Vice-Voorzitter van het College ter Beoordeling van Geneesmiddelen
Ministerie van Volksgezondheid

UNITED KINGDOM

a) Dr. J.P. GRIFFIN — Senior Principal Medical Officer
Medicines Division
Department of Health and Social Security

b) Dr. P.A. FLETCHER — Principal Medical Officer
Medicines Division
Department of Health and Social Security

C.C.E. / C.E.C.

a) M. N. BEL — Chef de Division à la Direction générale du marché intérieur et des affaires industrielles

b) M. Pierre DUPRAT — Administrateur principal
Direction générale du marché intérieur et des affaires industrielles

ANNEX III

Notice to manufacturers and importers of Proprietary Medicinal Products

I. A new procedure for placing proprietary medicinal products on the market

Following the European Community Directives adopted in 1975 (Official Journal of the European Communities No L 147 of 9/6/1975) all manufacturers of and persons responsible for marketing proprietary medicinal products may now use a new procedure for placing their products on the markets of the Member States: they may go through the Committee for Proprietary Medicinal Products attached to the Commission of the European Communities in Brussels.

II. Conditions to be fulfilled in order to use this procedure

(1) The Proprietary medicinal product in question must first have obtained a marketing authorization (subsequently referred to as M.A.) in one of the Member States, as laid down in Directives 65/65/EEC, 75/318/EEC and 75/319/EEC.

Vaccines, toxins and serums, proprietary medicinal products based on human blood or blood constituents, radioactive isotopes and homeopathic proprietary medicinal products may not benefit from this procedure (Article 34 of Directive 75/319/EEC).

(2) Applications for M.A. via the Committee must relate to at least five other Member States.

III. Procedure to be followed

(a) Documents to be supplied to the competent authority of the Member State which has granted the initial M.A.:

1. Request that the documents be forwarded to at least five named Member States through the Committee for Proprietary Medicinal Products,

2. Information and documents listed in the second paragraph of Article 4 of Directive 65/65/EEC,

3. Copy of the M.A.

(b) The number of copies of these documents to be supplied is one for each Member State concerned plus one for the Committee secretariat.

(c) The languages in which the documents must be presented:

1. The documents referred to in items 1 - 7 and 9 - 11 of the second paragraph of Article 4 must be provided in one of the official languages of each of the Member States concerned.

2. The documents referred to in item 8 of the second paragraph of Article 4 may, alternatively, be presented for

   - Germany, in English
   - Belgium, in English
   - Denmark, in German, English or French
   - Italy, in English or French
   - Luxembourg, in German, English, Italian or Dutch
   - The Netherlands, in German, English or French.

3. The copy intended for the Committee secretariat must be in English or French

(d) No special fee is payable to the Committee for Proprietary Medicinal Products, but national registration fees remain applicable.

IV. Consideration of divergent decisions

Directive 75/319/EEC also makes provision for consideration by the Committee of divergent decisions taken by the Member States as regards the authorization, suspension or revocation of an M.A.

Any one of the Member States concerned may request the opinion of the Committee concerning the grounds for refusal, suspension or revocation of the M.A. as given by the authorities of another Member State.

Within 30 days, the Member States shall notify the Committee of the action they intend to take following the opinion.

V. Force of the opinions of the Committee

The opinions of the Committee shall not be binding on Member States and shall not replace national decisions.

The opinions of the Committee, which will be based on information contained in the application for an M.A., shall not be regarded as M.A. in any Member State.

VI. Additional information

For additional information, please apply to the Secretariat, Committee for Proprietary Medicinal Products, 3 Rond-Point Schuman, 1049 Brussels; or to the appropriate national licensing authority.

COMMISSION
OF THE
EUROPEAN COMMUNITIES

Directorate-General
for internal market and industrial affairs

Orig.: F

ANNEX IV

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS

Application for marketing authorization for
a proprietary medicinal product

The Committee for Proprietary Medicinal specialities wishes in respect of Council Directives 65/65/EEC, 75/318/EEC and 75/319/EEC that the particulars in support of applications for authorizations to place proprietary medicinal products on the market are presented in the following way in order to facilitate the task of the applicants and the competent authorities.

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Flyleaf

1. Name or business name of applicant for marketing authorization

2. Full Address

3 (a) Name and address of manufacturer

3 (b) Name and address of importer

4. Name of the proprietary medicinal product

5. Pharmaceutical form

6. Method and route of administration

7. Number of annexes supplied in support of the application

Annex I : General information

- Name of the proprietary medicinal product
- Pharmaceutical form
- Qualitative and quantitative composition in terms of active principles
- Therapeutic indications
- Dosage
- Contra-indications
- Warnings and precautions (including during pregnancy)
- Side-effects
- Directions for use (where applicable)
- Shelf life and storage precautions

Annex II: Information and documents concerning physico-chemical, biological or microbiological tests

Annex II A: Complete qualitative und quantitative composition

- Name of product
- Composition

Names of constituents	Quantity	Reference to standards
Active principles		
Other constituents		

- Container (brief description)

Annex II B: Method of preparation

1. Manufacturing formula

2. Manufacturing process including in-process control and the pharmaceutical assembly process

Annex II.C: Control of starting materials

1. Active principles

(a) Active principles described in a pharmacopoeia

(b) Active principles not described in a pharmacopoeia

Annex II C: Control of starting materials

2. Other constituents

(a) Constituents described in a pharmacopoeia

(b) Constituents not described in a pharmacopoeia

Annex II 01 Control tests on intermediate products

(if necessary)

Annex II E: Control tests on the finished product

1. General characteristics, other quality control tests required by the nature of the product

   (appearance, dimension, shape, colour, odour, distinguishing features, etc.)

Annex II E: Control tests on the finished product

2. Identification and quantitative determination of the active principle or principles, other quality control tests, with a description of the methods employed (including, if necessary, and depending on the nature of the product, biological and microbiological methods)

Annex II E: Control tests on the finished product

3. Identification and quantitative determination of the other constituents (if necessary)

Annex II F1 Stability tests

1. Proposed shelf life (depending on the type of container)

2. Information concerning stability, including physical stability:

   - number of batches tested
   - storage conditions
   - methods employed
   - description of containers

Annex II f: Stability tests

3. Results and interpretations

Annex II G: Conclusions

Certificate by the expert analyst on the application of the methods and justification of the control methods to be used by the manufacturer

Annex III: Toxicological and pharmacological tests *
(Summary of the tasks performed by the expert pharmacologist)

The following information must be provided in respect of each test:

1. Animals used (species, strain, sex, etc.)
2. Experimental conditions including diet
3. Results

Annexe III A: Acute toxicity

* If use is made of a list of published references pursuant to point 8 of the second paragraph of Article 4 of Council Directive 65/65/EEC (OJ No 22 of 9 February 1966), the expert must show that this is justified.

Annex III: Toxicological and pharmacological tests

Annex III B: Toxicity with repeated administration

1. Subacute toxicity trials

Annex III: Toxicological and pharmacological tests

Annex III B: Toxicity with repeated administration

2. Chronic toxicity trials

Annex III: Toxicological and pharmacological tests

Annex III C: Foetal toxicity

(a) tests for teratogenicity (dosing during period of organogenesis)

(b) pre- and postnatal dosing of the mother to demonstrate effects on late pregnancy, parturition and lactation

Annex III: Toxicological and pharmacological tests

Annex III D: Fertility studies

Annex III: Toxicological and pharmacological tests

Annex III E: Carcinogenicity and mutagenicity

Annex III: Toxicological and pharmacological tests

Annex III F: Pharmacodynamics

1. Actions relevant to the proposed therapeutic uses

2. Other actions investigated

3. Interactions

Annex III: Toxicological and pharmacological tests

Annex III G: Pharmacokinetics

1. Absorption (serum levels of the medicinal product)

2. Distribution of the medicinal product

3. Biotransformation

4. Excretion of the medicinal product or metabolites

Annex IV: Clinical trials *

(Summary of the tasks performed by the expert clinician)

Annex IV A: Human pharmacology

* If use is made of a list of published references pursuant to point 8 of the second paragraph of Article 4 of Council Directive 65/65/EEC (OJ No 22 of 9 February 1965), the expert must show that this is justified.

Annex IV: Clinical trials

Annex IV B: Clinical data

1. Individual data - clinical reports

Annex IV: Clinical trials

Annex IV B: Clinical data

2. Summary

Annex IV: Clinical trials

Annex IV B: Clinical data

3. Conclusions

Annex IV: Clinical trials

Annex IV C: Side-effects and interactions

Information on side-effects and interactions observed when used in other countries (the extent of usage in terms of number of prescriptions and duration of use is useful in assessing the frequency of the adverse reaction).

Annex V: Special particulars

Annex V A: Dosage form

1. Packaging

2. Label

3. Package insert

Annex V: Special particulars

Annex V B: Samples

Annex V: Special particulars

Annex V Cf: Manufacturer's authorization

Annex V: Special particulars

Annex V D: Marketing authorization