COMMISSION OF THE EUROPEAN COMMUNITIES

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Proposal for a

COUNCIL REGULATION (EC)

ON FEES PAYABLE TO THE EUROPEAN MEDICINES EVALUATION AGENCY

(presented by the Commission)

Explanatory memorandum

Pursuant to Council Regulation (EEC) No 2309/93 of 22 July 1993[1] laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products ("the Agency"), the Council establishes the structure and the amount of fees paid by undertakings for obtaining and maintaining a Community marketing authorisation and for other services provided by the Agency.

After a start-up period of several years, the Agency should be capable, as far as possible, of financing itself. Fees will then constitute the Agency's main source of revenue. Therefore, the amount of fees should be fixed in such a manner that the Agency's operational capacity is not weakened due to financial shortcomings. Fees will be payable to the Agency for the examination and the review of any application for authorisations for medicinal products.

Furthermore, the Agency's budget will have to be in balance. The expenditure will have to be met by the Agency's real income.

In a general way, the fees to be levied by the Agency should neither lay an undue burden on the applicants nor endanger the achievement of the Agency's primary task of providing scientific advice of the highest possible quality in relation to the authorisation and supervision of medicinal products.

With regard to the amounts of the various fees to be laid down, account must be taken of the international character of the Agency and its obligation to work under the linguistic regime of the Community and hence in nine different languages. The corresponding additional expenditure is considerable and has not to be dealt with at national level.

More generally, any direct comparison of the structure and the amount of fees between the Agency and national authorities should bear in mind, among others, those two aspects cited above, i.e. the Agency is set up as a supranational body under the law of the EC and it will have to be self-funding.

The Agency's fee structure should be based on the principles of cost-effectiveness, payment for services effectively rendered and financial independence and should enable the Agency to live up to the high scientific and organisational standards as set out in the basic Regulation.

Therefore, the standard fee for obtaining a Community marketing authorisation in the centralised procedure should be comparable to the benefit derived from a single procedure and authorisation throughout the Community. It should be more or less equivalent to but in no case substantially higher than the total of fees charged by the 12 Member States.

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[1] OJ L 214, 24.08.1993, p. 1

On the basis of the information made available, the fees levied by Member States' authorities for a marketing authorisation for a new medicinal product, as it would be subject to the centralised procedure of the Regulation, currently total nearly 220,000 ECU for human medicines and 110,000 ECU for veterinary medicines. In view of the likely increase of national fees until the end of 1994, a Community standard fee for obtaining a marketing authorisation in the centralised procedure set at 200,000 ECU for human and 100,000 ECU for veterinary medicines meets the above requirement.

That would be even more so as the standard fee is defined as the initial comprehensive full fee covering all specific applications for the different strengths, schedules of dosage, routes and forms of administration which are made simultaneously for a given medicinal product at the time of the initial application. As regards veterinary medicinal products, applications for different species and for the establishment of Maximum Residue Limits (hereinafter referred to as MRLs) would equally be covered.

By contrast, most Member States charge, on a separate basis, for different specific applications regarding the same medicinal product, even if made simultaneously with the initial application, so that the actual sum of fees for a standard application is quite often substantially higher than the one laid down for the issuing of a marketing authorisation.

The extra work generated by the applicant's right to appeal against an opinion adversely affecting his rights would equally be comprised in the standard fee as it cannot reasonably be detached from the initial application for a Community marketing authorisation.

The comprehensive character of the fee should facilitate the collection of all necessary data at one time and, by that means, streamline the authorisation procedure and make it most cost-effectiveness.

Correspondingly and to the same end, an extension fee is laid down for the additional work and expenditure of subsequent specific applications regarding the same medicinal product whenever an applicant willingly chooses to do so.

On the other hand, applications not sustained by a full dossier pursuant to Article 4 of Directive 65/65/EEC and Article 5 of Directive 81/851/EEC respectively require less work. An initial reduced fee duly takes into account this circumstance.

For the same reasons, an application for a veterinary medicinal product for use in non-food producing animals where no MRL has to be established attracts the reduced fee.

Applying the same principle of payment for service effectively rendered, variations to the terms of existing authorisations either administrative or otherwise, which do not require full assessment of the product's quality, safety and efficacy are charged according to their complexity and the real workload linked to them and therefore far less than a standard application.

Two types of variations have then to be distinguished. The fee for an administrative variation type I can reasonably be set at 5,000 ECU whereas the one charged for all other variations type II is respectively 40,000 ECUfor human and 20,000 ECU for veterinary medicines.

The work involved in the mandatory five yearly renewal of a Community marketing authorisation justifies a corresponding fee at the level of a fee for a variation.

For the reasons stated above, fees for arbitrations under the decentralised procedure should also be fixed on the principle of service effectively rendered by the Agency. The work involved can be assessed at more or less the same level as the one of a complex variation type II.

The arbitration procedure arises from differences between Member states about the mutual recognition of marketing authorisations and is hence independent of the applicant's attitude. Therefore, the levying of an arbitration fee by the Agency must be compensated by a reduction by one half of national fees of all Member States other than the first where an application has been successfully lodged.

As regards inspections made successively to a marketing authorisation at the request or in the interest of its holder, a fee set at 10,000 ECU on a flat-rate basis is justified. It corresponds to the above principles of service effectively rendered and cost-effectiveness.

The nature of the assessment of a veterinary medicinal product as well as the size of the market involved are substantially different from those of a medicinal product for human use and do therefore justify a general reduction of the fee; furthermore, it should be possible to take account of the particular situation linked to the marketing of certain veterinary medicinal products on an individual basis and this aim could be best achieved under the special provision of a clause for reductions and waivers.

As regards the evaluation of applications for MRLs, it is up to the applicant to decide whether to apply separately for the establishment of MRLs or to do so together with an application for a Community marketing authorisation in which case the fee incurred for the evaluation of the application for authorisation covers the one for the establishment of MRLs.

If however the applicant deliberately chooses to apply separately for the establishment of MRLs, the additional work and expenditure should be recouped by means of an Isolated-MRL-fee.

As regards all other fees for the assessment of veterinary medicinal products, the reasons for levying them or to abstain from it remain identical to those stated above.

Under exceptional circumstances as for example in the case of medicinal products designed to treat only a limited number of patients of a particular disease (so-called orphan drugs), small sized businesses or for essential public health reasons, there should be provisions for waivers or reductions of the fees stated above. However, such cases should be decided only on the merits of each individual case by the management board on a proposal from the Director after hearing the competent Committee.

The same procedure should apply to the settling of disagreements which may arise about the classification of an application under one of the above fee items.

PROPOSAL FOR A COUNCIL REGULATION ON FEES PAYABLE TO THE EUROPEAN MEDICINES EVALUATION AGENCY

THE COUNCIL OF THE EUROPEAN UNION

Having regard to the Treaty establishing the European Community,

Having regard to Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products ("the Agency"), and in particular Article 58 thereof,

Having regard to the proposal from the Commission[2],

Whereas Article 58 of the Regulation requires the Council to establish the structure and the amount of fees referred to in Article 57(1);

Whereas Article 57(1)of the Regulation establishes that the revenues of the Agency shall consist of a contribution of the Community, and the fees paid by undertakings for obtaining and maintaining a Community marketing authorisation and for other services provided by the Agency;

Whereas Article 6(3) and 28(3) of the Regulation respectively require an application for authorisation for a medicinal product be accompanied by the fee payable to the Agency for the examination of the application;

Whereas the standard fee should be defined as the comprehensive full fee covering all applications for the different strengths, schedules of dosage, routes and forms of administration which are made simultaneously for a given medicinal product in the initial request in order to facilitate the collection of all necessary data at one time and, by that means, streamline the authorisation procedure and make it most cost-effective;

Whereas to the same end, an extension fee should be laid down for subsequent applications regarding a medicinal product which has already been authorised in order to take account of the additional work and expenditure where an applicant chooses to submit the applications gradually and subsequently;

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[2]OJ C

Whereas it should be provided for a reduced fee for applications not required to be sustained by a full dossier pursuant to Article 4 of Directive 65/65/EEC and Article 5 of Directive 81/851/EEC respectively and for applications concerning a medicinal product for use in non-food producing animals;

Whereas variations, either administrative or other, to the terms of existing authorisations not requiring full assessment of the product's quality, safety and efficacy should be charged according to their complexity and the real workload linked to them and therefore far less than a standard application;

Whereas the work involved in the mandatory five yearly renewal of a Community marketing authorisation justifies a corresponding fee at the level of a fee for a complex variation;

Whereas fees for arbitrations under the decentralised procedure should be fixed on the principle of service effectively rendered by the Agency; whereas that work can be assessed at more or less the same level as that involved in a variation requiring a complex evaluation; whereas furthermore the arbitration procedure arises from differences between Member States about the mutual recognition of marketing authorisations and is hence independent of the applicant's attitude; whereas, therefore, the levying of an arbitration fee by the Agency should be compensated by a reduction by one half of national fees of all Member States other than the first one where an application has been successfully lodged;

Whereas on the same grounds of service effectively rendered a fee should be levied on a flat-rate basis for any inspection made successively to a marketing authorisation at the request or in the interest of its holder;

Whereas the nature of the assessment of a veterinary medicinal product as well as the size of the market involved are substantially different from those of a medicinal product for human use and do therefore justify a general reduction of the fee; whereas it should furthermore be possible to take account of the particular situation linked to the marketing of certain veterinary medicinal products on an individual basis; whereas this aim can be best achieved under the special provisions of a clause for reductions and waivers;

Whereas as regards the evaluation of applications for MRLs it is up to the applicant to decide whether to apply separately for the establishment of MRLs or to do so together with his application for a Community marketing authorisation in which case the fee incurred for the evaluation of the application for authorisation should cover the one for the establishment of MRLs; whereas, however, the applicant deliberately chooses to apply separately for the establishment of MRLs, the additional work and expenditure should be recouped by means of an Isolated-MRL-fee;

Whereas, as regards all other fees for the assessment of veterinary medicinal products, the reasons for levying them or to abstain from it remain identical to those stated above;

Whereas it should be provided for waivers or reductions of the fees stated above under exceptional circumstances as for example in the case of medicinal products designed to treat only a limited number of patients of a particular disease (so-called orphan drugs), small sized businesses or for essential public health reasons; whereas it should be decided upon those cases only on the merits of each individual case by the management board; whereas to that effect, a proposal from the Director has to be made after hearing the competent Committee;

HAS ADOPTED THIS REGULATION:

Article 1

Scope

(1) Fees for obtaining and maintaining a Community marketing authorisation shall be levied in accordance with this regulation.

(2) They shall be laid down in ECU.

Article 2

Applications for medicinal products for human use under the centralised procedure

(1) Full fee 200.000

It is the comprehensive standard fee for an application for a Community marketing authorisation of a given medicinal product sustained by a full dossier. It covers all applications for the different strengths, schedules of dosage, routes and forms of administration which are made simultaneously for that medicinal product at the time of the initial application.

(2) Reduced fee 100.000

It is the reduced fee for an application for a Community marketing authorisation of a given medicinal product not required to be sustained by a full dossier as provided for under the exception rules of point 8 (a) of the second paragraph of Article 4 of Directive 65/65/EEC. It covers all applications for the different strengths, schedules of dosage, routes and forms of administration which are made simultaneously for that medicinal product at the time of the initial application.

(3) Extension fee 40.000

It is the fee for each supplement or extension of an existing Community marketing authorisation of a given medicinal product to different strengths, schedules of dosage, routes and forms of administration. It applies where an applicant chooses to submit the applications gradually and subsequently to take account of the additional work and expenditure hereby caused.

(4) Variation fee type I 5.000

It is the fee for an administrative or minor change to an existing marketing authorisation which would be proposed by the marketing authorisation holder and would neither change the specifications for the active ingredient(s), the release specifications or end of shelf-life-specifications as already authorised nor alter the summary of product characteristics or the labelling of the medicinal product.

(5) Variation fee type II 40.000

It is the fee for all other changes proposed by the marketing authorisation holder to the particulars referred to in article 4 of Directive 65/65/EEC of an existing authorisation not requiring a new application.

(6) Five yearly renewal fee 40.000

It is the fee due for the obligatory five yearly renewal of a Community marketing authorisation after a review of the available new information about the product.

(7) Inspection fee 10.000

It is the flat-rate fee for any inspection within the European Communities made at the request or in the interest of the holder of a marketing authorisation. For inspections outside the European Communities travel expenses will be charged extra on the basis of the effective cost.

Article 3

Applications for medicinal products for human use under the decentralised procedure

Arbitration fee 40.000

It is the flat rate fee for the work of the Agency involved in the arbitration of disagreements between Member States on the mutual recognition of a national marketing authorisation in the decentralised procedure.

Member States fees for delivering a national marketing authorisation are reduced by one half except for the first Member State that issued a marketing authorisation for that medicinal product.

Article 4

Applications for medicinal products for veterinary use under the centralised procedure

(1) Full fee 100.000

It is the comprehensive standard fee for an application for a Community marketing authorisation of a given medicinal product for use in food producing animals sustained by a full dossier. It covers all applications for the different species, strengths, schedules of dosage, routes and forms of administration and for the establishment of an MRL which are made simultaneously for that medicinal product at the time of the initial application.

(2) Reduced fee 50.000

It is the reduced fee for an application for a Community marketing authorisation of a given medicinal product not required to be sustained by a full dossier as provided for under the exception rules of point 10 (a) of the second paragraph of Article 5 of Directive 81/851/EEC or for an application concerning a medicinal product for use in non-food producing animals. It covers all applications for the different species, strengths, schedules of dosage, routes and forms of administration which are made simultaneously for that medicinal product at the time of the initial application.

(3) Isolated MRL fee 50.000

It is the fee for an isolated establishment of an MRL for a new medicinal product.

(4) Extension fee 20.000

It is the fee for each supplement or extension of an existing Community marketing authorisation of a given medicinal product to different species, strengths, schedules of dosage, routes and forms of administration. It applies where an applicant chooses to submit the applications gradually and subsequently to take account of the additional work and expenditure hereby caused.

(5) Variation fee type I 5.000

It is the fee for an administrative or minor change to an existing marketing authorisation which would be proposed by the marketing authorisation holder and would neither change the specifications for the active ingredient(s), the release specifications or end of shelf-life-specifications as already authorised nor alter the summary of product characteristics or the labelling of the medicinal product.

(6) Variation fee type II 20.000

It is the fee for all other changes proposed by the marketing authorisation holder to the particulars referred to in Article 5 of Directive 81/851/EEC of an existing authorisation not requiring a new application.

(7) Five yearly renewal fee 20.000

It is the fee due for the obligatory five yearly renewal of a Community marketing authorisation after a review of the available new information about the product.

(8) Inspection fee 10.000

It is the flat-rate fee for any inspection within the European Communities made at the request or in the interest of the holder of a marketing authorisation. For inspections outside the European Communities travel expenses will be charged extra on the basis of the effective cost.

Article 5

Applications for medicinal products for veterinary use under the decentralised procedure

Arbitration fee	20.000

It is the flat rate fee for the work of the Agency involved in the arbitration of disagreements between Member States on the mutual recognition of a national marketing authorisation in the decentralised procedure.

Member States fees for delivering a national marketing authorisation are reduced by one half except for the first Member State that issued a marketing authorisation for that medicinal product.

Article 6

Waivers, fee reductions and dispute settlement

(1) Under exceptional circumstances as for example in the case of medicinal products designed to treat only a limited number of patients of a particular disease (so-called orphan drugs), small sized businesses or for essential public health reasons, the management board may decide upon waivers and fee reductions on the merits of each individual case on a proposal from the Director who will have consulted the competent Committee.

(2) The same procedure shall apply to any disagreement which may arise about the classification of an application under one of the above fee items.

Article 7

Due date and belated payment

(1) Fees in respect of which the due date is not specified in this Regulation or Regulation (EEC) No 2309/93 of 22 July 1993 shall be due on the date of receipt of the application for the service for which the fee is incurred.

(2) Where any fee payable under this Regulation remains unpaid at its due date the Director may decide not to make or to suspend services dependent upon the advance payment of the corresponding fee.

Article 8

Implementing rules

(1) Without prejudice to other provisions of this Regulation or Regulation (EEC) No 2309/93 of 22 July 1993, implementing rules to be adopted by the Agency's management board shall lay down the due date for fees to be paid under Article 1, the methods of their payment, the consequences of belated or omitted payment and contain all other provisions needed to put the present regulation into effect.

(2) The same rules shall determine the conversion rates in national currencies of the fees and costs to be levied under this Regulation and laid down pursuant to Article 1(2) in ECU.

Article 9

Conversion of procedures

Former concertation procedures converted on 1 January 1995 to centralised procedures pursuant to Article 2 of Directive 93/41/EEC attract the arbitration fee as laid down in Articles 3 and 5.

Article 10

Entry into force and legal effect

(1) This Regulation shall enter into force on the day following its publication in the Official Journal of the European Communities.

(2) It shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, ...

EUROPEAN AGENCY FOR THE EVALUATION OF MEDICINAL PRODUCTS

PROPOSAL FOR A COUNCIL REGULATION
ON THE FEES PAYABLE BY UNDERTAKINGS

FINANCIAL STATEMENT

ARTICLE B5-306: Subsidy for the European Agency for the Evaluation of Medicinal Products

authorized appropirations 1994		appropriations requested 1995		variation %	
commitments	payments	commitments	payments	commitments	payments
1	2	3	4	5 = 3/1	6 = 4/2
7.500.000	6.800.000	9.500.000*	9.500.000*	37,8%	52 %

* APB 95

1. Title

Proposal for a Council implementing regulation on the fees paid by undertakings for obtaining and maintaining a Community marketing authorization and for other services provided by the Agency.

2. Budget headings

See above.

3. Legal basis

Articles 57 and 58 of Regulation (EEC) No 2309/93 of 22 July 1993.

4. Description of the action

4.1 General objective

Completion of the internal market in the pharmaceuticals sector (medicinal products for human and veterinary use); improved public health and consumer protection throughout the Community.

4.2 Specific objectives

Council Regulation (EEC) No 2309/93, adopted on 22 July 1993, lays down (centralized) Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishes a European Agency for the Evaluation of Medicinal Products. Three Council Directives (93/39/EEC, 93/40/EEC and 93/41/EEC), adopted on 14 June 1993, complete the system for the future authorization of medicinal products under the decentralized procedure.

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1 Including a reserve fund of 700 000 ecus

The abovementioned Regulation entered into force on the day following the decision taken by the Heads of State and Government on 29 October 1993 establishing, *inter alia*, the headquarters of the Agency in London.

As of now, the Agency officially exists and is due to become operational from 1 January 1995.

The future system will entail:

a) the creation of a centralized Community authorization issued by the Commission (compulsory in the case of biotechnology products and veterinary medicinal products used as performance enhancers, optional in the case of other innovatory medicinal products);

b) the creation of a new decentralized procedure, based on the principle of mutual recognition which will enable a marketing authorization from one Member State to be extended gradually to the others; in the event of disputes between Member States, the Agency will be asked to arbitrate, and its decision will be made binding by the Commission;

c) the introduction of consolidated Community procedures for the collection and assessment of information about adverse reactions to medicinal products and for the adoption by the Community of appropriate regulatory measures (pharmacovigilance);

d) the delivery by the Commission of a scientific opinion on the maximum veterinary medicinal product residue levels that can be permitted in foodstuffs of animal origin without entailing risks for the consumer.

Under Articles 57 and 58 of the basic Regulation, the system will be financed from the Agency's own revenues which shall consist of a contribution from the Community and the fees paid by undertakings for obtaining and maintaining a Community marketing authorization and for other services provided by the Agency.

The purpose of this implementing Regulation is to establish a structural framework for fixing the levels of the fees referred to above.

4.3 Duration

Selectively targeted measures

4.4 Sectors of the population targeted by the action

a) Approximately 2 000 European pharmaceuticals firms applying for authorization

b) Approximately 3 000 national officials required to work together through the Agency interface

c) Significant proportion of the European population (sick persons)

5. Classification of the expenditure

NCE, DC

6. Type of expenditure

Full direct subsidy in 1994, partial subsidy from 1995.

a) Initial contribution (100%) from the Community budget in 1994

In order to launch the Agency's activities, it will be necessary to make provision for a relatively high level of start-up investment which will have to be funded from the Community budget, since the Agency will not yet be in a position to provide services to the undertakings.

b) Partial subsidy from 1995

From 1995 the Agency will be required to examine applications for authorization submitted by pharmaceuticals companies on a fee-paying basis, thus generating revenue for the Agency's budget.

Thus, a contribution from the Community budget is required (albeit on a decreasing scale up to 1998) in respect of the following:

- as a balancing subsidy for the Agency's operating budget throughout the period during which proceeds from fees do not constitute a stable source of revenue capable of coping with major investment and start-up costs, i.e., until 1998;

- to cover the considerable amount of investment required for the telecommunications network to be installed for the exchange of information and warnings between Commission/Agency/competent authorities in the Member States.

7. Financial impact on the operating appropriations

7.1. Method of calculating the total cost of the action

On the basis of the study carried out by the DRT consultants, but subject to a reassessment of the foreseeable work load (reduced number of dossiers), investment and operating costs for the next five years are as follows:

Costs in thousands ECU	1995	1996	1997	1998	1999
Investment	964	704	-	-	-
operating expenditure	3.456	4.154	4.623	4.761	4.904
Rapporteurs+experts	5.979	12.393	15.510	22.420	24.307
Administrative costs + staff	12.481	16.541	18.446	27.257	30.610
Translation Center in Luxembourg	3.000	5.000	5.800	8.200	9.000
Total "Agency"	25.880	38.792	44.379	62.638	68.821

7.2 Itemized breakdown

VENTILATION	BUDGET 94	APB 95	VARIATION EN %
Investment	3.105	964	- 69 %
operating expenditure	1.756	3.456	+ 97 %
Administrative and staff costs	2.639	12.481	+ 373 %
payments rapp./experts	-----	5.979	
Translation Center	-----	3.000	
TOTAL	7.500	25.880	+ 245 %

As far as the variation in rates is concerned, it should be noted that the 1994 financial year relates to the launching of the Agency, whereas the 1995 financial year (the year when the Agency becomes operational) represents the Agency's first genuine operating budget.

7.3 Provisional schedule of commitment appropriations

Not applicable, since this is a subsidy.

7.4 Subsidy under Heading B5-306 "Agency for the Evaluation of Medicinal Products"

Since this is an autonomous body endowed with legal personality and possessing its own budget, the contribution from the Community budget will take the form of a subsidy to be entered under Heading B5-306. The amount of this subsidy is estimated on the basis of the costs referred to above and the fees expected to accrue from 1995 and beyond.

The "low" hypothesis recommended by the competent Commission departments would aim to achieve self-sufficiency towards 1998.

The "high" hypothesis would allow corrections to be made in the event of overestimates of the number of applications, and hence of the principal sources of revenue, and would provide flat-rate funding (25%) from the Community budget to cover general market-monitoring tasks incumbent on the authority responsible for taking decisions, i.e., the Commission.

a) "Low" budget estimate, aimed at achieving self-sufficiency based on fees

Under this hypothesis, preferable from the point of view of budgetary discipline, the Heading B5-306 subsidy would enable self-sufficiency to be achieved in 1998:

Thousands ECU	1995	1996	1997	1998	1999
Agency costs	25.880	38.792	44.379	62.638	68.821
(15 % Translation Center included)	(3.000)	(5.000)	(5.800)	(8.200)	(9.000)
Fees	12.545	22.347	28.284	-	-
% cover	49%	58%	64%	100%	100%
Subs.B 5-306	9.500*	**	**	**	**

* amount previewed by the Commission related to the availability of ressources in the financial perspectives. A consensus at the budgetary authority level should allow to make up the difference between the high fee and the low fee hypothesis

** Community subsidy to be determined every year taking into account the availability of budgetary ressources in the frame of financial perspectives

Revenue trends

This Regulation lays down the structure and exact amounts of the revenue expected from the pharmaceuticals industry.

The fees are fixed in such a way as not to exceed the total amount of corresponding national fees required in order to obtain a marketing authorization in the 12 Member States.

Nevertheless, these fees are high and could not be increased at present without placing an excessive burden on the economic resources of the undertakings oncerned. Revenue trends as a function of fees are indicated in the following table:

	1995	1996	1997	from 1998
Human	10.575.000	17.273.100	21.907.660	
Veterinary	1.970.000	5.073.900	6.376.037	
TOTAL	**12.545.000**	**22.347.000**	**28.283.697**	probably self-sufficient

b) "High" budget estimate, maintaining Community co-financing

Given that the total costs and the monitoring of the market would account for approximately a quarter of the activities, this proportion would continue to be chargeable to the Community budget if the "high" hypothesis of co-financing from the Community budget were to be adopted. Such a hypothesis would also facilitate adjustments as a function of the actual amount of the revenue obtained in the first few years after the new system became operational. On the other hand, the level of fees forming the basis of this proposal for a Regulation would not be sufficient in 1995, 1996 and 1997 to achieve the envisaged rate of cover of 75%.

Thousands ECU	1995	1996	1997	1998	1999
Agency costs	25.880	38.792	44.379	62.638	68.821
(15 % Translation Center included)	(3.000)	(5.000)	(5.800)	(8.200)	(9.000)
Subs.B 5-306	9.500	**	**	**	**
Level of fees to be reached	16.380	27.155	32.396	46.979	51.616
% cover	63%	70%	73%	75%	75%

** Community subsidy to be determined every year taking into account the availability of budgetary ressources in the frame of financial perspectives

8. Anti-fraud measures

Council Regulation (EEC) No 2309/93 of 22 July 1993 setting up the Agency for the Evaluation of Medicinal Products provides for specific adoption and budgetary control procedures. Each year the Management Board, made up of representatives of the Member States, the Commission and the European Parliament, shall be responsible for adopting the draft budget (Article 55). The budgetary control mechanisms are described in Article 57.

9. Aspects of cost-effectiveness analysis

9.1 Objectives

The provisions on the future system for the authorization of medicinal products seek to promote the free movement of medicinal products in the Community, while at the same time providing better public health protection. In particular, they will permit rapid access to the new medicinal products available on the single market and ensure greater harmonization of the conditions governing the placing on the market of commercial medicinal products. A single evaluation, meeting the highest possible scientific standards, will be carried out by the European Agency for the Evaluation of Medicinal Products, working in partnership with the Member States and the Commission.

Consequently, these provisions come under three major Community strategies:

- completion of the internal market in the pharmaceuticals sector;
- industrial policy to promote the competitiveness of European companies;
- creation of a trans-European communications and early warning network linking the competent authorities, the Agency and the Commission.

9.2 Justification for the action

The pharmaceuticals market is characterized by a set of highly complex technical regulations designed to protect public health and the interests of social security beneficiaries and, sometimes, to promote the national industry. The pharmaceuticals industry still occupies a position as one of the leading producers and exporters of pharmaceuticals worldwide. However, the European market remains fragmented by virtue of the existence of national marketing authorizations, resulting in the undermining of the competitiveness of this industry *vis-à-vis* the American and Japanese industries, notably in the field of advanced research.

It does not appear feasible - or, for that matter, desirable - to dismantle the national structures, only to build in their place a gigantic European Food and Drug Administration (FDA) along US lines. It should be noted, however, that a total of nearly 3 000 staff are engaged in drug regulatory activities in the Twelve Member States, i.e., as many as in the US-FDA. In order to avoid unnecessary duplication of work involving 12 separate evaluations, thus leading to the wasteful use of resources and the creation of possible sources of conflict, it would be far better to share the work among the authorities concerned by introducing not only the guarantees that are essential for public health but also sensible emulation procedures to be followed by all the competent authorities. To this end, considerable efforts are needed to strengthen the evaluation capabilities and authority of the European committees, so as to ensure that the opinions they deliver can form the basis for solutions that are accepted throughout the Community.

The Community authorization system, as adopted by the Council, will reduce the time taken to examine the dossiers to less than 300 days. The activities of the national authorities will be combined into a single European system leaving wide scope for decentralized evaluation, inspection and control activities, while at the same time providing for centralized coordination for a small number of new medicinal products and for arbitration in the event of possible conflicts involving national decisions.

In addition, the workload and the estimated costs resulting from the texts approved by the Council have been the subject of a major study carried out on behalf of the Commission by the firms Deloitte, Touche Ross and Besselaar (DRT) following a call for tenders. This study was carried out from January to December 1992 in close collaboration with the competent national authorities and the manufacturers concerned.

At the same time, it must be stressed that, for the pharmaceuticals industry, speed of access to the mass market and simplification of the authorization procedures (one evaluation instead of twelve) are crucial factors in ensuring competitiveness *vis-à-vis* manufacturers in the USA and Japan. Furthermore, a single European evaluation meeting high scientific standards will provide this industry with an important trump card as far as exports are concerned.

Research and development costs for a new medicinal product are generally estimated at more than 200 million ecus. Consequently, the amount in authorization fees, forming the basis for the financing of the Agency, appears perfectly modest and reasonable: 200 000 ecus for a new medicinal product, i.e., 0.001% of the total cost of the research. In addition, this Community fee cancels and replaces an equivalent amount in fees which the firms are currently required to pay to the national authorities.

The new system of authorization will also reduce the overall workload of the Member States which in future will be required, through the Agency, to share out the evaluation tasks hitherto repeated twelve times. At present, the cumulative operating budget of the 12 competent authorities already exceeds the 250 million ecu figure (with the clear likelihood of further increases) as against the cost of the Agency (27 million in 1995, 52 million in 1999).

Looking ahead to 1999, the introduction of the new system will be accompanied, according to the DRT report, by a reduction of at least 40% in the overall volume of business.

The cost-benefit ratio of the European Agency as compared with the continuation of twelve national evaluation systems operating along repetitive and independent lines has already been demonstrated. This multiplier effect will bring benefits not only to the relevant national budgets but also to the European pharmaceuticals firms themselves.

The creation of a European Agency with a budget of its own, funded to a large extent by fees from the industry for services rendered, clearly opens up the possibility of mobilizing alternative sources of funding.

In the event of the Agency not being set up, the Commission would have to assume direct responsibility for the management of numerous meetings of experts on the Community budget in order to ensure the necessary degree of scientific cooperation required by the single market in pharmaceuticals.

9.3 Monitoring and assessment of the action

Selected performance indicators:

The parameters for judging the efficiency of the future system of authorization and of the Agency itself fall under two main categories:

a) Actual number of applications submitted by the companies under the centralized or decentralized procedure, taking account of the choices left open to the undertakings and the largely optional character of the decentralized system up to 1998.

The DRT's forecasts for applications, revised downwards by the Commission, are as follows:

	1995	1996	1997	1998	1999
Centralized applications (no change)					
Human	30	32	34	36	38
Veterinary	5	10	16	14	12
Decentralized arbitration					
Human	60	100	100	500	480
Veterinary	20	54	64	144	120
Establishment of limits for veterinary residues	10	10	20	15	15

b) Compliance with the 300-day evaluation and decision-making deadline, as laid down by the Agency and the Commission. The speed of the new system, compared with certain national deadlines (4-6 years in Germany), is a crucial factor for the European industry.

Evaluation procedures and frequency:

The Regulation provides for the adoption by the Agency's Management Board of an annual report on the activities of the Agency to be forwarded to the Member States, the Commission, the Council and the European Parliament (Article 56). In particular, the Executive Director of the Agency will be responsible for reporting on compliance with the evaluation deadlines and on the number of different applications examined by the Agency (Article 55).

Within six years of the entry into force of the Regulation, the Commission shall publish a full general report on the experience acquired under the new system, indicating, where appropriate, any corrective measures that need to be introduced (Article 71).

IMPACT ASSESSMENT FORM

THE IMPACT OF THE PROPOSAL OF BUSINESS

with special reference to small and medium sized enterprises (SMEs)

Title of proposal : **Proposal for a Council Regulation on fees payable to the EMEA**

The proposal :

1. In order to promote the free circulation of medicinal products throughout the Community, while reinforcing the protection of public health, the Council adopted on 14 June 1993 three Directives 93/39/EEC, 93/40/EEC and 93/41/EEC and on 22 July 1993 Regulation (EEC) n° 2309/93, hereinafter referred to as the Basic Regulation. (OJ n° L214 of 24.08.93).

The Basic Regulation provides for a new centralised Community authorisation procedure for technologically advanced medicinal products leading to a single Community marketing authorisation valid in all Member States. Furthermore, it sets up the European Agency for the Evaluation of Medicinal Products to which applications both under the centralised and decentralised procedures will have to be submitted.

The Basic Regulation came into force on 30.10.93, the day following the decision of the Heads of States and Governments to choose London as the Headquarters of the EMEA.

The present proposal is an implementing Council Regulation pursuant to Art. 57 (1) and 58 of Council Regulation (EEC) n° 2309/93 which read as follows :

Art. 57 (1) : "The revenues of the Agency shall consist of a contribution from the Community, and the fees paid by undertakings for obtaining and maintaining a Community marketing authorisation and for other services provided by the Agency."

Art. 58 : "The structure and the amount of the fees referred to in Article 57 (1) shall be established by the Council acting under the conditions provided for by the Treaty on a proposal from the Commission, following consultation of organizations representing the interests of the pharmaceutical industry at Community level."

The impact on business

2. Who will be affected by the proposal ?

About 2000 operators of the European pharmaceutical industry applying for marketing authorizations are concerned by the existing and the oncoming registration procedures.

The business sector concerned by the centralised procedure, and by way of consequence, the full impact of the fees Regulation is marked by large multinational companies.

The costs of developing new medicinal products are very high (for a major innovatory product up to 200 million ECU). Therefore, companies seek to attain the "critical mass" necessary to finance research and development by way of concentration.

Smaller or medium sized companies in this business sector manufacture primarily conventional medicinal products whose patent has expired. They are mostly geared to decentralised procedures linked to national and even regional markets and would therefore prefer to obtain national marketing authorisations which would largely fall under national fee schemes, except for the costs of arbitration, in case of conflict.

Finally, there are a limited number of small, highly innovatory companies concentrating on basic research into new therapies.

3. What will business have to do to comply with the proposal ?

From 1995 onwards, the EMEA will play an active role in two out of three then available registration procedures by formulating opinions of the highest possible scientific level about the quality, safety and efficacy of a medicinal product for human and veterinary use.

Under the centralised procedure, which concerns innovatory medicinal products, the opinion of the Agency will lead to a final decision on the application for a Community marketing authorization. The decision will be taken by either the Commission within the framework of a regulatory committee procedure or the Council.

The decentralised procedure which will apply to the substantial majority of medicinal products is based upon the principle of mutual recognition by a variable number of Member States of each others existing marketing authorisations. In the event of disagreements between Member States, a binding arbitration procedure at the level of the Agency will apply from 1998 onwards (on an optional basis from 1.1.95).

National registration procedures limited to applications of local interest concerning a single Member State remain possible.

Pharmaceutical companies making use of the new registration procedures will have to pay fees to the Agency for the work done by it just as they pay fees to Member States' authorities in order

to obtain national marketing authorisations. It has to be noted that the choice of the suitable procedure, save the marketing of medicinal products derived from biotechnology, rests with the applicant.

4. Economic effects of the measure

Fees levied by Member States' authorities for 12 different marketing authorisation for a new medicinal product currently total nearly 210,000 ECU for human medicines. This concerns only the first application and does not cover different strengths etc.

Under the terms of this proposal, a pharmaceutical company applying for a Community marketing authorisation in the centralised procedure would have to pay a standard fee of 200,000 ECU. This fee would be defined as a comprehensive fee covering at the choice of the applicant a bundle of applications for different strengths, schedules of dosage, routes and forms of administration, and, as regards veterinary medicinal products, the establishment of Maximum Residue Limits. **This is meant to be a major incentive for streamlined procedures and better cost-efficiency. It meets the requirement put forward by industry of having "good value for money".**

As the overall cost of research and development of a new medicinal product in general exceeds 200 millions ECU, the comprehensive cost for industry to obtain a Community marketing authorization represents but one per thousand of the overall research cost.

Compared to the cost, the benefit derived from the new centralised procedure is significant.

- ☐ It is one single procedure throughout the Community instead of 12 national procedures.
- ☐ It is a far less time consuming procedure compared to the national procedures lasting quite often for four or five years.
- ☐ It leads to a single marketing authorisation immediately valid in all Member States.
- ☐ It is more value for less money.

As regards the decentralised procedure, an arbitration fee of 40,000 ECU would be levied by the Agency for its services in connection with the settlement of disputes between Member States about the mutual recognition of each others marketing authorizations.

Here too, the benefit derived from a system of mutually recognised national marketing authorisations after a binding Community arbitration procedure clearly outweighs the cost in form of the above mentioned arbitration fee.

In more general terms, the creation of the EMEA and its leading role in the future system's centralised and decentralised registration procedure will facilitate the access of all medicinal medicinal products to a Community scale market. This will lead to a substantial gain in

competitiveness for both large scale multinational companies **and small and medium sized entreprises.** The latter quite often lack the resources to establish local subsidiaries in the different Member States to deal directly with national regulatory authorities.

The access, especially for small and medium sized businesses, to the single European market will be further enhanced by the transparency of the future system's registration procedures.

Finally, the EMEA will foster the pre-and post-marketing co-operation between Member States to ensure the quality, safety and efficacy of all medicinal products circulating in the Single European Market and will help to achieve greater international harmonisation.

5. Measures to take account of the specific situation of small and medium sized firms.

A special derogatory clause is provided for under Art. 6 of the proposal to take due account of specific situations which might arrise for SMEs. The case of the above mentioned small sized but highly innovatory companies concentrating on basic research into new therapies can be seen in this context.

6. Consultations

Extensive consultation has preceeded the adoption of the Basic Regulation as well as the current proposal on fees payable to the Agency.

A working paper on the financial arragements for the Agency has been circulated early 1993 to industry and other interested parties with the invitation to submit comments by 1.5.93. The dialogue with industry continued in the following months leading to a final consultation of organizations representing the interests of the pharmaceutical industry at Community level in December 1993.

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