The European Agency for the Evaluation of Medicinal Products
Pre-authorisation Evaluation of Medicines for Human Use

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Status Report on the Implementation of the European Parliament and Council Regulation on Orphan Medicinal Products

- Legislation[1] on orphan medicinal products, eagerly awaited by patients suffering from rare diseases for many years, came into force in the European Union in April 2000.
- 'Orphan' medicinal products are for treating conditions that occur so rarely that sponsors are unwilling to develop them under normal market conditions. These medicinal products are intended to treat patients with life-threatening or very serious diseases for which today there is either no treatment or only unsatisfactory treatment options. A large number of these diseases affect children and newborn babies.
- The EMEA plays an important new role in stimulating the development of orphan medicinal products. A committee and a procedure have been established to designate 'orphans'. Sponsors will receive incentives to bring orphan medicinal products to the market and to the patient in the shortest possible timeframe. Such incentives include the possibility to request protocol assistance (scientific advice) from the EMEA and fee reductions for all types of centralised activities including, fees for protocol assistance, the application for marketing authorisation, variations and annual fees.
- The Committee for Orphan Medicinal Products (COMP), created in the EMEA in April 2000, is the first institutional Committee of the European Union where representatives of patient organisations are full members, one of which is the vice-chairman.
- Sponsors have been able to submit applications for orphan medicinal product designation to the EMEA since May 2000 and the response to date is considerable:

Intent to file notified	*Applications submitted*	*Applications withdrawn*	*Positive COMP Opinions*	*Negative COMP Opinions*	*Designations granted by Commission*
47	169	43	101	1[2]	98

Details of designated orphan medicinal products have been entered in the Community Register of Orphan Medicinal Products which is published on the web-site of the European Commission (http://pharmacos.eudra.org/F2/register/index.htm).

- Among the applications already received or expected by EMEA for rare diseases there are products for:
  - genetic diseases where the enzyme deficiency leads to metabolic disorders and ultimately to an early death,
  - diseases where transplant is today the only option,
  - patients which have intractable bowel disorders and severely deficient pulmonary function (cystic fibrosis),

1 Regulation (EC) No 141/2000 adopted of 16 December 1999 and Commission Regulation (EC) No 847/2000 of 27 April 2000

2 Of the five negative opinions adopted to date, one appeal is ongoing. Two applications have been subsequently withdrawn, one has resulted in a final negative decision and one has resulted in a final positive opinion following appeal.

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- rare cancers, such as brain cancers particularly in children and young adults. Cancer where there is no therapeutic option when all current available therapies have failed such as in certain types of cancer of the blood (leukaemias),
- neurological disorders leading to paralysis and progressively to death,
- products that will aid successful bone marrow transplantation,

A number of these medicinal products are developed by biotechnology or gene therapy, most by small and medium-sized European companies.

- In 2001 the first orphan medicinal products reached the market following the grant of marketing authorisations by the European Commission. To date 4 marketing authorisations have been granted for orphan medicinal products:

Name of product	Date of Marketing Authorisation	Orphan Condition	Estimated number[3] of EU citizens affected by condition
Fabrazyme	August 2001	Fabry disease	500-1000
Replagal	August 2001	Fabry disease	500-1000
Glivec	November 2001	Chronic myeloid leukaemia	33 000
Trisenox	March 2002	Acute promyelocytic leukaemia	30 000

- A further 15 applications for marketing authorisation and 1 additional variation for an authorised orphan medicinal product have been submitted to the EMEA and are currently in the review process.
- A total of € 1 297 500 of Community funds was used in 2001 to fund fee exemptions for orphan medicinal products.
- In 2002 the funds made available by the Community for fee exemptions for orphan medicinal products amounts to € 3 300 000. In addition, € 1 900 000 of the Agency's basic subsidy has been set aside to cover meeting and staff costs. The large number of designations granted in 2001 will result in a higher than anticipated number of orphan marketing applications in 2002. To date, 50% of this year's funding for fee exemptions has already been allocated to incoming applications for protocol assistance and marketing authorisation and maintenance of the existing orphan marketing authorisations.
- For 2003, the EMEA has requested a special contribution of € 6 200 000 to fund orphan fee reductions for an estimated 20 applications for marketing authorisation and 30 requests for protocol assistance. An additional € 2 300 000 on the Agency's basic subsidy has been requested to cover staff and meeting costs for the orphan designation process and protocol assistance support.

[3] The number of patients affected by the condition is estimated and assessed for the purpose of the designation. This estimate is based on available information and calculations presented by the sponsor at the time of the application and may thus differ from the true number of patients affected by the condition.

OVERVIEW OF EMEA BUDGETARY NEEDS 2002-2003

Year	**2002**	**2003**
Number of orphan designations	85	90
Number of orphan marketing applications + protocol assistance	38	50
Number of variations + annual fee for maintenance of marketing authorisation	12	44
Special contribution for partial fee exemptions	€ 3 300 000	€ 6 200 000 (estimate)
Contribution from EU basic subsidy for EMEA meeting and staff costs	€ 1 900 000	€ 2 300 000 (estimate)

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