COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 03.07.1998
COM(1998) 407 final

COMMUNICATION FROM THE COMMISSION
TO THE COUNCIL AND THE EUROPEAN PARLIAMENT

FOR INCREASED SOLIDARITY TO CONFRONT AIDS IN DEVELOPING COUNTRIES

DOCUMENT MOTIVATION

This document aims to:

- Give a first basis for a debate on the response to the request of the European Council in Luxembourg asking the Commission "*d'étudier les modalités de l'établissement d'un fonds de solidarité thérapeutique sous l'égide de l'ONUSIDA destiné à la lutte contre le SIDA dans les pays en voie de développement*""

- respond to the request of the Parliament, approved by the Council of Ministers, within the framework of the regulation of the AIDS (Acquired Immune Deficiency Syndrome) budgetline n° B7. 6211 "Studying ways and means of improving access to treatment for people infected with HIV in the poorest countries ... in close collaboration with the United Nations agencies, concerned NGO's, pharmaceutical laboratories and the Members States of the European Union."

- recognise and welcome all of the calls for increased and enhanced international solidarity to confront AIDS, including those made at the Denver and Birmingham G8 meeting, the UNAIDS (United Nations Joint Programme on AIDS) meeting on perinatal transmission, the International AIDS Vaccine Initiative (IAVI) and the World Bank's call for the creation of a vaccine purchase fund.

- recapitulate the Commission's existing priorities with respect to HIV (Human Immuno-deficiency Virus) and AIDS in developing countries.

- outline the Commission's position on several recent calls for increased international solidarity to confront AIDS in developing countries and the possible EC specific contribution to a new international initiative.

- propose a framework for an additional strategy and some elements to consider in relation to financial resources through which the EU could participate in an enhanced international solidarity effort to confront AIDS in the domains of prevention (vaccine) and improved care in developing countries.

COMMISSION COMMUNICATION

FOR INCREASED SOLIDARITY TO CONFRONT AIDS IN DEVELOPING COUNTRIES

EXECUTIVE SUMMARY

This Communication:

1) Provides a context to the calls for **international solidarity**, describing the present situation with respect to HIV/AIDS (Human Immuno-deficiency Virus and Acquired Immune Deficiency Syndrome) in developing countries.

2) Outlines the European Commission's (EC's) position on **national and international priorities** for the use of public funds in confronting AIDS in developing countries. It highlights the mutual reinforcement of prevention and care through the provision of public goods.

3) Summarises the EC's **existing efforts** in confronting HIV/AIDS in developing countries, before discussing how these may be strengthened. Firstly, it highlights the success **of *cost-effective targeted preventative interventions***, and the importance of their expansion. Secondly, it stresses the importance of support to ***strengthen health care systems***, outlining possible improvements.

4) Explores the possibility of creating **new solidarity mechanisms**, and examines and several alternatives. Firstly the prospect of financing ***care including anti-retrovirals*** in developing countries is explored, and concerns of technical uncertainties, relative priorities, affordability, and public policy are raised. Secondly the possibility of developing ***vaccines and microbicides***, and creating a purchase fund for these products once developed is discussed and given general support.

5) Outlines the potential for additional **specific contribution of the EC**, including the allocation of additional financial resources to:

- support countries in ***purchasing existing commodities***, namely, in order of priority

  a) AZT (Azidothymidine) in monotherapy for pregnant seropositive women

  b) medicines for sexually transmitted diseases (STD's), tuberculosis (TB) and other opportunistic diseases

  c) anti-retroviral (ARV) therapy for pilot testing in a few countries already selected by UNAIDS

- leverage further investment by the private sector in developing ***vaccines and microbicides*** and providing purchase funds for these commodities once they exist

6) Stresses the global responsibility of UNAIDS in the **management** of new solidarity instruments, whilst nevertheless leaving major decisions in developing countries, and underlines the importance of ***monitoring***.

TABLE OF CONTENTS

d) Public policy towards anti-retroviral treatment. Experience to date in some developing countries

B. Private and public partnership to develop a vaccine and microbicides

C. Modalities of new international solidarity instruments

V: The EC's specific contribution

A. What is to be financed by additional EC resources?

B. The main commodities which could be purchased

1. Commodities that already exist

2. Commodities still to be developed

C. A framework for what would be financed by additional resources

D. How are the funds to be to provided to the countries?

E. Some examples of conditions to be in place for the use of the EC's budget support at country level.

1. Medicines already available

2. Products not yet available

VI: Management of new solidarity instruments

A. International level.

B. National management of a fund to provide commodities for developing countries

C. Monitoring

D. Regarding management of a new international financing instrument for the testing and purchase of vaccines for developing countries

VII: Conclusion about International co-operation and the European Community's specific contribution

Annex 1 - Quotes concerning international solidarity with respect to HIV/AIDS

I: INTRODUCTION

A. The challenge for the coming decade

From the beginning of the AIDS epidemic it was recognised that AIDS could not be dealt with by households and countries alone. The international community had to be mobilised and their efforts could only be sustained through sufficient political momentum and financial resources over a long time period.

It is in this context that the European Community in 1984 first began research on HIV/AIDS, and in 1987 first became involved in actions dealing with HIV/AIDS in developing countries. At that stage the EC and the African, Caribbean and Pacific (ACP) countries agreed that "AIDS would be a major challenge for development and should be dealt with as such". Only six months after the programme started in the ACP countries, other developing countries became eligible for support through a specially created budgetline.

In the 1980's the challenge faced by the countries was to rapidly develop effective interventions to prevent the spread of AIDS, to strengthen the different systems to deal with the virus whilst at the same time increasing the scientific learning and knowledge basis. The EC together with the international community supported national and regional efforts.

The policies and strategies for EC support were widely debated as formulated in the Communication of 7th January 1994 from the Commission to the Council and the European Parliament entitled *"AIDS policy of the Community and the Member States in the developing world"*, and also in the legal basis for the special AIDS budgetline n° B7. 6211 (Ref. 95/0164(SYN) dated 26.6.95).

Now, at the end of the 1990's, the challenge is to implement the most effective interventions at a large enough scale whilst simultaneously supporting health care systems to deal with those already infected and further developing knowledge to improve interventions and develop new methods. This has been explored in detail in *"Confronting AIDS: Public priorities in a global epidemic"*, a joint exercise carried out by The World Bank, the European Commission, and UNAIDS, published in 1997.

These challenges for the future were presented by the Commission at a public hearing at the Parliament where the continuation and strengthening of support for AIDS actions in third countries in the future was announced[1]. The European Commission (EC) also proposed priorities for its financial support in the future. These priorities are summarised and explained in Chapter II.

B. Confronting HIV/AIDS

1. Care for people with HIV/AIDS: A World Apart

It is estimated that today in 1998 more than 30 million people are infected with the HIV virus world-wide, of whom 90% live in the developing world and 20 million are living in sub-Saharan Africa. Of those living in sub-Saharan Africa, half are women.

[1] Hearing at the European Parliament, 25th November 1997

Until recently, it was considered that the disease had a lethal outcome in close to 100% of all infected individuals, though there were significant differences between rich and poor countries in the prevention of mother to child transmission, the care of patients, and the course of the illness.

In rich countries, the great majority of the population received specialist care in public or private health services. Even though no cure was available, it was possible to extend life by preventing and treating opportunistic infections, making use of AZT monotherapy, providing psychological support, and ensuring good nutrition, with the result that the average duration between infection and death was around 12 years.

In poor countries, only a small proportion of patients received any specialist care, and against a background of poverty, poor nutrition, weak health sectors and insufficient treatment of opportunistic infections, duration of life after seroconversion was generally considerably less than ten years, and transmission from mother to child remains common.

However two years ago the perception that AIDS always had a fatal outcome changed with the development and introduction of therapeutic strategies involving the use of combinations of anti-retroviral drugs and protease inhibitors which not only improve the quality of life of nearly 80% of the persons under medication, but hold out the possibility that future developments in drug research may allow a permanent arrest of the disease process. Furthermore, in the richer countries, the advent in 1996 of monotherapy for pregnant women, and the availability of alternatives to breastfeeding and options for testing and counselling, has rapidly minimised the transmission of HIV during pregnancy.

For the first time, it appeared that HIV infection did not necessarily have a fatal conclusion. Following these discoveries, protease inhibitors and anti-retroviral drugs have been widely used in the richer countries.

The discovery of effective monotherapy for pregnant women and combination therapy for people with HIV has still further widened the difference in the prospects of HIV infected individuals in rich and poor countries. Whereas in the industrialised world, the number of new infections is falling (as a result of successful prevention campaigns) and the prospect of effective therapy has appeared, in the poorer countries new infections continue to occur at a high rate and the outcome is still universally fatal. Several countries in the developing world have seen a serious decrease of life expectancy due to AIDS, and adult mortality due to AIDS is still increasing in the most affected areas. It is likely that 40 million people will die as a result of HIV infection over the next decade. Children will also become infected in large numbers.

This reality of two different worlds facing AIDS and its consequences is a reminder of the major differences in quality and access to health care between industrialised and developing countries in general and the difficult choices this entails. For example 1 in 50 women in developing countries dies as a consequence of the complications of pregnancy and childbirth compared with only 1 in 2700 in the established market economies.

It is in this context, of huge disparities in health status and the capacities of health care systems dealing with all health problems including HIV/AIDS, that the call for greater international solidarity to increase the accessibility to prevention, care, and combination therapy has to be seen.

2. Preventing the spread of HIV/AIDS

It is now widely recognised that increased efforts should be made to contain the epidemic where possible through improving the efficiency of the existing interventions such as information, targeted education, counselling, testing, condom use, and treatment of sexually transmitted diseases (STD's), but also through the development of new methodologies to prevent the transmission of the virus, especially amongst populations in developing countries.

One of the additional preventive methods that became available recently is the provision of Zidovudine or AZT for pregnant women to reduce the transmission of the virus to the child. At the same time as the results became available of the clinical trials, AZT was also put on the essential drug list by WHO and the price was significantly decreased ⋘ in order to make the intervention accessible to parts of the populations.

At the present time, the undertaking to increase access to care and treatment for people with HIV goes in parallel to the efforts to make existing and new preventive interventions more available, because it is recognised that for countries to be able to deal with the increasing burden caused by AIDS, the only serious option is to stop the spread as soon and as efficiently as possible. The countries that are able to contain the epidemic will also be the optimal placed to provide the optimal and appropriate care to their populations with and without HIV.

It is therefore in this complex context that new appeals to make AZT widely available for pregnant women to enlarge access to other anti-retroviral medicines, and to develop or leverage investment in the production of products such as vaccines and microbicides are to be seen. These developments would make a real difference if supported in the near future and if new financial instruments were made available for developing countries to purchase these products once developed.

C. Political momentum for additional international efforts and renewed international solidarity

With the purpose to organise additional efforts and mechanisms to further increase international solidarity with respect to AIDS, the European Council in Luxembourg requested the Commission "*d'étudier les modalités de l'établissement d'un fonds de solidarité thérapeutique sous l'égide de l'ONUSIDA destiné à la lutte contre le SIDA dans les pays en voie de développement*" A similar request had already been introduced by the European Parliament and approved by the Council of Ministers within the framework of the regulation of the AIDS budgetline n° B7. 6211 "Studying ways and means of improving access to treatment for people infected with HIV in the poorest countries ... in close collaboration with the United Nations agencies, concerned NGO's, pharmaceutical laboratories and the Members States of the European Union."[2]

This document is a first phase of the response to these requests and is designed to spell out the specific role the Community's programme in developing countries proposes to play in contributing to **increased international solidarity** for prevention and improved care for people with HIV, recognising that this objective must be a shared responsibility. Only an increased and well co-ordinated effort will be able to confront AIDS in the larger

[2] Article 2, paragraph 2b of EC regulation no. 550/p7

context of competing priorities. The document mainly focusses at the different priorities and dicusses strategy. Once consensus is reached on the basis of this document it will be possible to go into further details and proposals for modalities and financing.

D. Document Outline

This introduction has provided a context to the calls for international solidarity, describing the present situation with respect the HIV/AIDS.

In the second chapter, the document proceeds to outline the EC's position on national and international priorities for the use of public funds in confronting AIDS in developing countries, highlighting the mutual reinforcement of prevention and care through the provision of public goods.

Chapter three then briefly summarises the EC's existing efforts in confronting HIV/AIDS, before discussing how these may be strengthened. In particular low cost prevention initiatives, and support to national health systems are explored.

In the fourth chapter the possibility of creating new solidarity instruments is discussed, and several alternatives are examined. Firstly the prospect of financing anti-retrovirals in developing countries is explored with respect to concerns of technical issues, relative priorities, affordability, and public policy. Secondly the possibility of developing vaccines and microbicides, and creating a purchase fund for these products once developed is discussed. The modalities of finding funds for new solidarity instruments are only briefly examined.

In Chapter five, the specific contribution of the EC is outlined. This includes allocating additional resources both to support countries in purchasing existing commodities, and to leverage further investment by the private sector in developing vaccines and microbicides.

An introduction to the discussion on the management of new solidarity instruments follows in Chapter six, clarifying the position of the EC in relation to other international bodies and highlighting the importance of monitoring.

Finally the conclusion summarises the major issues discussed, and suggests future action at strategic level including a refocussing of current undertakings complemented by new efforts to i) purchase medicinal commodities at the country level once they exist, and ii) leverage larger and more appropriate finances for the testing and purchase of vaccines at the international level. The annex provides a summary of various statements on international solidarity with respect to HIV/AIDS.

II: The EC's position on National and International priorities for the use of presently available public funds in confronting AIDS in developing countries.

Individuals, countries and the international community have worked hand in hand over the past ten years to deal with the new and enormous challenges created by AIDS. However in view of decreasing public funds, an increasing number of people infected world-wide and several other competing priorities facing people in developing countries, governments and donors have had to make difficult choices. The EC together with developing countries and with the major other donors have discussed the need to prioritise the use of available public funds and increase their commitments and partnerships with the private sector. The EC has also come to some conclusions about it's own comparative advantage and the way forward for the future. These choices were presented by the Commission in November 1997 and as summarised as follows:

The overall objectives of the EC's actions on HIV/AIDS at national level are to limit the spread of the virus whilst helping the health sectors in developing countries to cope with the consequences and improve quality of care without discrimination. The overall objective of the EC at the international level is to collaborate to improve knowledge and to invest in international public goods as related to HIV/AIDS.

The lessons learned over the last years show convincingly that developing countries cannot ignore the HIV/AIDS epidemic. In developing countries, where 90 percent of all HIV infections occur, AIDS is reversing hard won gains in improving quality of life. Between 1950 and 1990 average life expectancy in developing countries has increased from 40 to 63 years. But in many countries AIDS has now reduced life expectancy by more than 10 years. HIV/AIDS is also exacerbating poverty and inequality as the poor have the fewest resources to cope. It is therefore at the core of development and poverty alleviation concerns.

However poor people and poor countries face many pressing problems beside HIV/AIDS, and public resources are scarce and choices are difficult. For example, in a typical developing country it costs as much to treat one AIDS patient for a year as it does to educate 10 primary school students for a year. Balancing these objectives is difficult but essential.

The EC has therefore recognised that the essential use of national and international public funds regarding AIDS should be focused firstly at the public good nature of information, education and knowledge, and secondly at the extra benefits associated with the prevention of communicable diseases (such as HIV, tuberculosis, and sexually transmitted diseases (STD's)) which is a public as opposed to a private health issue.

Prevention is therefore essential and remains so even at later stages when the epidemic has spread throughout the general population. At the end of 1997 it was estimated that more than 250 million people lived in countries where HIV infection had spread widely. These countries have no other choice but to confront the epidemic both through further preventative efforts and through facing the rising burden of AIDS related sickness and death and the impact this has on the care given to all people within the country.

When a country reaches this stage, and when public funds are used to help the health sector to cope, AIDS can push up government spending on health care by over 40%, while people without HIV sometimes still may have less access to health care then

before. Within this concern special care should therefore be given to not discriminate between allocations for care to people with and without AIDS, and special efforts should be made to focus available public funds on basic care to the poorest .

A few hard hit countries that focused their resources in this way in the past and sustain their efforts today are now seeing results. For example Uganda, Thailand and Senegal have succeeded for the moment to relatively stabilise the epidemic through vigorous and targeted preventative efforts. However, these successes are recent and need to be sustained through continued efforts in the same direction.

The international donor community, including the EC, have given the priority to generously support developing countries efforts in response to the AIDS pandemic, and simultaneously providing ongoing funds for investment in international public goods. Examples of international public goods are operational and fundamental research into policies, systems, clinical effectiveness of mother to child prevention, and the development of microbicides and vaccines. The EC has also greatly increased its support to strengthening health sectors in developing countries.

The EC has committed itself to continue its efforts to strengthen the response organised in the developing countries and focus on the mutual reinforcement of prevention and care. At the same time, the EC is further committed to invest with its international partners in the development of new knowledge and products to increase the choice of people in protecting themselves from HIV/AIDS.

The EC recognises the importance of the political momentum created to mobilise additional support to confront AIDS in developing countries and examines the best opportunities for the EC to contribute to those efforts. With this consideration in mind this document identifies the issues and the opportunities related to an additional international support with a special focus on the specific role and comparative advantage of the EC. Only in a second stage when the strategies are discussed will it be possible to prepare more detailed discussion documents on modalities, instruments and financial requirements.

III: THE EC'S EXISTING EFFORTS IN CONFRONTING HIV/AIDS AND RECOMMENDATIONS ON STRENGTHENING THESE AREAS IN THE FUTURE

The EC's existing efforts to confront HIV/AIDS in developing countries are organised with finances from a special budgetlines, national and regional programmes under EDF in ACP countries, and country programmes in Asia, Latin America, and Meditteranean.

A. Prevention - Low cost interventions

The EC has targetted 50% of its aids programme financial resources to cost effective, preventative interventions. Initiatives have included information campaigns targetted at high-risk groups, youth education especially in schools, peer-group education for example amongst truck-drivers and sex-workers, guaranteeing safe blood transfusions, and treating STD's. These projects have met with considerable success, and prevention activities remain a priority.

The special issue of preventing mother to child transmission

In view of recent developments, if national health services are adequately strengthened and if the country considers making anti-retrovirals available within this context, priority should be given to medicines preventing the transmission from mother to child. Every year 2 million HIV positive women get pregnant and 550,000 infants are born infected with HIV. They live in the world's poorest countries. As a comparison, in Tanzania, one of Africa's poorest nations, mosquito control to prevent malaria costs $5-$250 for every year of healthy life gained. The cost of AZT for all HIV infected pregnant women in Tanzania works out at about $50 per healthy life gained. It was calculated that Tanzania already spends $3.10 per capita on AIDS prevention, and that providing AZT for seropositive pregnant women would add about 80 cents per capita to that.

Since 1987, the EC has set up and collaborated world-wide in the research and development of a strategy for preventing mother to child transmission of HIV. At the present time, further operational and clinical research is still needed while operationalisation has begun in several countries.

The EC could contribute further in this area in a preliminary stage by financing a feasibility assessment of an essential package for pregnant women in developing countries, which would include different options for HIV testing and counselling, breastfeeding or bottle feeding, and other priority interventions. Existing instruments and funds are adequate for this work for the present time. Therefore funds could be mobilised within EC's regular instruments to develop and evaluate such interventions on a large scale.

In summary the existing instruments from the EC to provide support for prevention and care for people with HIV, and the possibility to prevent perinatal transmission of HIV within the context of general health care support are appropriate but additional efforts to increase and improve the existing support could be made if more flexible instruments and more human resources were made available within the overall context of health sector support to developing countries.

B. Support to National Health Care Systems

The EC has increased its support to health sectors in developing countries over the last years both in terms of quantity and quality, including support in the fields of access to care and prevention of AIDS.

This is reflected by the fact that from the 6th to the 7 th EDF the EC's support for health projects has increased from 184 MECU to 415 MECU. In addition, 633 MECU has been used for support to national health budgets in ACP countries through the counterpart funds of structural adjustment operations. Efforts in the ALAMED countries have also significantly increased. A substantial part of these funds are used on essential drugs programmes, including restructuring central medical stores.

In order not to discriminate against or for persons with HIV, the main way the EC supports access to care and treatment for all people (including for HIV infected persons) is through general health sector support, within which access to essential drugs is a major focal area for the EC.

In addition to the main financial instruments which are used to support the health systems and fund essential drugs, the special budgets for AIDS are used to facilitate studies, innovative interventions and technical support to promote the inclusion of HIV/AIDS issues within the general health system.

EC support, as a part of national and international efforts, has ensured a greater development of the medicines system in several countries and has improved access to medicines for people in general. However, because of the scale of the problem, and the lack of financial and human resources both in the developing countries and within the EC, this is not done in all developing countries where it is needed and it is a long term process. The existing instruments are in general appropriate for the purpose for which they have been created.

However, the main constraints are insufficient funds allocated by the countries within the context of competing priorities, limited technical capacity in developing countries and in the EC, and a lack of rapid and flexible instruments to access human resources and expertise in this field. Additional efforts and instruments and a technical assistance group would be beneficial and would provide the opportunity to do more, to do it faster and with a higher degree of quality. This could be considered within the context of the EC's general health sector work strengthening activities at national level, and could specifically focus upon the following areas:

- Improve co-ordination of all efforts in the health sector at country level with a special emphasis on the provision of medicines under the leadership of the country involved and in close co-operation with the WHO and other donors.

- Consider HIV/AIDS, its consequences, and the public requirements within general public expenditure and health sector reviews, on the basis of a rapid assessment tool which should be developed and validated.

- Encourage a more rapid development of adequate sustainable medicine systems in developing countries which also includes essential drugs for STD's/HIV, opportunistic communicable diseases such as TB, and AZT to prevent transmission from mother to child, and give special attention to developing a system for nationals to decide which medicines are to be subsidised and for which illnesses the costs need to and can be recovered.

- Provide training for the adequate and appropriate use of medicines and set up monitoring systems to follow up performances and trends.

- Strengthen systems to include testing and counselling for populations which could not benefit from them otherwise.

- Strengthen collaboration of the public sector with profit and no-profit-making private sector to support general care for diseases such as AIDS, for example by providing more facilities for home care.

IV: NEW INTERNATIONAL SOLIDARITY INITIATIVES

The increased international efforts to improve world-wide solidarity in confronting AIDS are welcomed. Clearly however, the new effort should have an additional character, and must not cause a decrease in supporting existing HIV/AIDS activities.

From the discussion developed earlier in the text, the EC identifies a few priority focal areas as concerns where international renewed and additional efforts could occur. It also identifies the possibility of international co-operation in creating new initiatives.

Specifically the new international solidarity initiatives focus upon i) strengthening the health system in developing countries to enable the purchase of most needed medicines and to generally improve the quality of care for affected people, and ii) creating a new financial instrument to increase private sector investment developing new preventative methods such as vaccines and microbicides. These options are explored in detail below.

A. Financing health care and anti-retrovirals for people with HIV/AIDS in developing countries

1. The situation of the health care systems in developing countries and how to face the extra burden caused by AIDS

Even without the challenge of HIV/AIDS, the publicly funded health care systems in the poorer developing countries are under enormous pressure. Whereas the World Bank calculated that it would cost around $12 per capita or 3.4% of GNP to deliver a basic package of care, the actual levels of expenditure achieved are often much lower. For example, the average public expenditure on health for sub-Saharan African countries was 2.5% of GNP in 1990, and it fell as low as 0.5% in the case of Sudan. Total expenditure from all sources was $5 per capita or less in Mozambique, Tanzania, Ethiopia, Sierra Leone and Sudan. In comparing this figure with the required $12, it needs to be remembered that much of the actual expenditure is incurred on services outside the package. Such low levels of expenditure are manifest in minimally functional health services, with demoralised and frequently absentee labour forces, frequent drug stock-outs, and low rates of effective coverage of the population.

Faced with such momentous problems, few of the poorer countries were able to mount an effective response to HIV/AIDS using only domestic resources. The general pattern has been that a considerable proportion of public resources has been expended on curative care of AIDS patients. This has not been the intended consequence of public policy, but has arisen spontaneously as ever higher proportions of beds in public hospitals are occupied by AIDS patients. A particularly unfortunate consequence has been that patients with other diagnoses have found it increasingly difficult to gain admission to hospital, even when their prognosis is much better. Furthermore, private expenditures are almost exclusively for curative care. The great majority of funds for preventive actions, such as public education, condom promotion and treatment of STDs, have been provided by external donors. This leads to divergent patterns of expenditure, depending on the share of the public and private sectors, and the extent of external funding. In Tanzania, where the private sector is small and there has been much external support, 85% of total expenditure on HIV/AIDS has been on prevention. By contrast, in Cote d'Ivoire, the bulk of public spending has been on treatment and less external aid, with the consequence that treatment accounted in 1995 for 92% of total AIDS expenditures.

2. The specific issue of combination therapy with anti-retrovirals

The problem of lack of accessibility to anti-retrovirals in developing countries was raised acutely when scientists announced at the International AIDS Conference in Vancouver that new triple therapy for HIV was improving and extending people's lives in the West. There have since been further reports confirming these results. The question then posed is: "is it feasible and desirable to provide combination therapy to HIV infected individuals in developing countries ?"

Calls from different groups were made to make these drugs "available for all", implying availability for the majority of people infected in developing countries. However the difficulties in complying with this demand are manifold, and raise four main concerns:

a) Technical issues regarding the generalised use of combination therapy for the treatment of HIV infection.

From the clinical perspective, it is now clearly established that anti-retroviral combination therapies have beneficial effects for the quality of life of HIV/AIDS patients: they diminish morbidity and mortality, significantly improve quality of life and possibly decrease infectivity . However multiple challenges still need to be overcome.

Issues to consider include the long term effectiveness of the medicines, the absence of more patient-friendly medicine combinations or regimes (present regimes involve a multiple of pills to take at precise times), the need to have specialised laboratories, tests and clinical surveillance to ensure treatments, and the nutritional status and compliance of the patients. Only a maximum of 80% of patients respond to treatment in the industrialised world. Treatment requires indefinite disciplined compliance and extensive monitoring of liver and renal functions. It also requires expensive and yet not very efficient viral load testing as well as trained doctors to supervise the treatment. If these conditions are not in place, there is a risk of producing world-wide resistance to the new drugs. In addition to this, specific clinical problems remain unanswered due to the absence of data from the countries concerned. These issues include the use of less expensive bitherapies and drugs, the lack of experience in treating HIV-2 infections (which account for 50% of the cases in Senegal, but which are not commonly encountered in the Western countries where most treatment trials have been conducted and where HIV 1 is the most common strain) with the newest anti-retrovirals, and the reactivation of tuberculosis during anti-retroviral treatment.

b) Relative priorities

When resources are scarce, as they are in developing countries, so that it is not possible to finance all the potentially life-saving interventions, it has to be asked whether the public resources which might be allocated to combination therapy for HIV patients would be more productive if applied elsewhere, targeted towards more cost-effective interventions. This question can be asked in various contexts. In terms of existing interventions which are specific to AIDS, there is strong evidence to show that resources applied to prevention are more effective than those applied to treatment even in terms of reducing human suffering. However proven low cost preventive measures, such as treatment of other sexually transmitted diseases (STD's), are insufficiently funded, even though the cost of treating an STD case is $10.15 including only $2.11 for medications. A field trial in Tanzania has established that the cost of averting an HIV case by improved STD treatment is only $218, far less than the cost of annual treatment with

combination therapy which is at least $10,000. Given that our ultimate aim is to minimise the toll of human misery caused by HIV/AIDS, it is important to channel the available resources into those actions that are most effective in preventing the spread of the disease and in caring for those already infected.

If the context is confined to those who are already infected with HIV, there are treatment alternatives to consider. In sub-Saharan Africa, the annual cost for comprehensive care without anti-retroviral drugs is around $500 per person (only $300 if the most expensive opportunistic infections are omitted). The provision of this care can add several years to the life of an HIV infected individual. Furthermore, it is also worth remembering that treating people with HIV for their opportunistic infections is a pre-requisite for any more sophisticated treatment and in itself is also a means of improving quality of life.

However, in practice, treatment in general has encountered chronic problems in most developing countries. The treatment of the most frequent and dramatic opportunistic infection linked to AIDS, tuberculosis, costs around $20, but the effectiveness of most control programmes have decreased in the last decade and the availability of this treatment is far from universal in most countries.

In the context of anti-retroviral therapy itself, there are strong arguments to give priority to finance a short course of AZT for seropositive pregnant women in order to prevent transmission of HIV to the new-born. This monotherapy has been proven effective and decreases transmission by 50% among non-breastfeeding populations. The price has been cut by the company by 75% and comes now to $50-$150 for a short course.
If the context is widened again to consider interventions for other conditions in addition to HIV infection, there are strong inferences that a given expenditure would have greater impact if applied to other life-saving actions, such as infant immunisation, or the treatment of diarrhoea with oral rehydration salts, which all cost less than $15 per life year saved. These simple and low cost technologies remain widely neglected, and adequate financing of these should be a pre-condition for public sector spending on the extremely high cost intervention of combination therapy for HIV patients.

The potential for competition with many other public priorities in developing countries is great. Pilot programmes for combination drug therapy should also be considered in that light because even if they are largely funded by grant or loan money from outside the recipient country, they are likely to attract substantial national resources (financial or human) which could otherwise have provided effective care to many more patients or helped prevent the spread of the epidemic to thousands more.

To be fair to both people with HIV infection and those without, the heath system must first avoid discrimination against people with AIDS. It is also unfair, however, for the care of AIDS patients to be subsidised more than that of patients with similar diseases such as liver cancer or kidney diseases which are extremely frequent in Africa. Indeed, the main issue of concern is the combination of direct and indirect pressures caused by HIV, which are compromising the functioning of health structures. It appears that the emergence of the HIV mortality burden is to be considered as the most important challenge to the health sector and a strong reason to speed up and reinforce the health sector reform process including the proper organisation and financing of medicines and care. However, focusing only on specific HIV treatments could jeopardise the highly needed more general reforms in medicine financing and health care.

c) Affordability.

The annual cost for treatment with anti-retrovirals (triple therapy) is around $10-20,000 per person, the lower figure being derived from Thailand, a country which uses bitherapies excluding the expensive antiproteases, and the higher from USA and UK. These figures are a huge multiple of the average per capita expenditure on health in developing countries, and many times what is currently being spent per HIV patient. While it is to be expected that the cost of drugs may fall substantially over time, treatment of HIV patients using combination therapy will remain expensive due to the cost of testing and monitoring which must be taken into account. It has been estimated that to treat all HIV infected people in sub-Saharan Africa would cost annually $20-$40 billion. There is no indication that anyone, patients, governments or external donors, is willing and able to meet more than a tiny fraction of this cost. This clearly means that access to anti-retroviral treatment cannot be financed for all people who are seropositive. Therefore choices will have to be made, probably focusing on the poorest.

d) Public policy towards anti-retroviral treatment. Experience to date in some developing countries

The situation regarding public policy in favour of generalised use of combination therapy for treatment of HIV infection is very varied and changing constantly. The wealthiest people in many developing countries are already finding ways to get anti-retrovirals (ARV), but the poorest people are unlikely to do so. Therefore the public financing of ARV in the poorest countries could disproportionately subsidise health care for the rich unless clear criteria for targeting towards the poor are organised. Some countries provide universal health care which does not include anti-retrovirals (Kenya), and others have provided for specific legislation to provide ARV to persons living with HIV/AIDS under different health care systems: under the social security system (Argentina), or private insurance (South Africa), or from public funds (Brazil).

Most often however these decisions are taken without sufficient clarity concerning whether additional funds will be added to the health care budget or if existing funds will be reallocated (for example from prevention to care). For example, Brazil's government has guaranteed AIDS patients complete funding of ARV. The drugs alone will cost Brazil $700 million in 1998 or 4% of the Ministry Of Health's budget. This represents more than twice what the international community spends each year on AIDS prevention in the developing world.

Countries such as South Africa, Botswana, Zimbabwe or Thailand have a policy to make the short cause of AZT available for seropositive pregnant women and are prepared to strengthen the health services where needed in order to make this possible.

However in countries where STD's and tuberculosis (TB) are not adequately treated the idea of starting a national HIV/AIDS screening and treatment programme, or national HIV treatment in general seriously needs to be reconsidered at national policy level. Some of these interventions could be financed and carried out by the private sector or by NGO's in countries where governments have more pressing priorities, and where such policies could not yet be implemented at the national level.

For example, the first policy implication of the Thai trial on mother to child transmission could be that an individual woman who knows that she is HIV positive, has fully been counselled, has the resources to purchase AZT, and is willing and able to forgo

breastfeeding should be offered treatment. It could also be suggested that this could be done in the first instance through the private sector or NGO's.

B. Private and public partnership to develop a vaccine and microbicides

New investment and financial instruments are needed to facilitate the development and general availability of new preventive methodologies against HIV/AIDS for developing countries.

Over recent years several calls were made to develop additional preventive methods designed to reduce the specific vulnerability of women, such as a female condom and a vaginal microbicide. Responding to this demand, a female condom was developed and is now being used by an increasing number of women in some countries. Work is continuing to develop an effective and affordable microbicide.

However, there is a wide consensus that "in the long term, the development of safe, accessible and effective vaccines against HIV/AIDS holds the best chance of limiting, and eventually eliminating, the threat of this disease" (communiqué of G7, Denver, 1997 - see Annex 1). The development of a microbicide and a vaccine encounter several barriers, that can be categorised as scientific, technical, economic and financial.

The European Commission has in past and present R&D framework programmes put in substantial efforts in developing vaccine-orientated AIDS research in Europe. Major efforts have been invested in large scale facilities providing reagents and animals for HIV vaccine trials. These efforts will be continued through the newly established Key Action II of the FPV's Life Sciences Programme and the specific activities of the INCO programme.

The scientific and technical areas for the debate will not be further developed here but it is strongly believed that improved scientific leadership and co-ordination could make a qualitative difference and allow faster and more efficient progress.

The economic and financial issues are of more specific concern for this Communication on increased international solidarity and will therefore be developed here. In the development of new products, the traditional division of funding responsibility is between the public sector supporting pure research, and the private sector supporting the development of commercial applications. However, the fundamental issue is that there is insufficient investment by the private sector in developing microbicidal products or vaccines protecting against HIV/AIDS, as a result of the perception of inadequate purchasing power in developing countries.

Private sector spending on research and development of an AIDS vaccine for developing countries is inadequate. Evidence suggests that existing marked-based incentives are biased in favour of the development of AIDS treatments, which are products with weak external benefits demanded by high income AIDS patients, as opposed to the development of a microbicide or vaccine which are products with large external benefits, especially for residents of developing countries.

Total global research and development for preventive HIV vaccines in both the public and private sectors in 1993 was estimated by the National Institute of Health (NIH) at $160 million, which is less than 7 percent of annual global research and development

expenditure on HIV/AIDS. Within the total of $160 million spent on vaccine research, only $5 million per year is spent on vaccines for potential use in developing countries.

By contrast, there is far less uncertainty about the market and profitability of research on medicines to treat HIV/AIDS. Three million of the people infected world-wide live in industrialised countries where individual or insurance purchasing power is high. The global market for medicines for HIV/AIDS and related infections in 1995 was estimated at $1.3 billion.

The recent history of the development of other products, such as hepatitis vaccines, has demonstrated that those products are not widely purchased by individuals or governments in developing countries. One or two decades ago, the international community argued for investments in those products because of the serious consequences of those diseases in developing countries and the potentially high cost-benefit ratio of such products. The reluctance of the international bio-medical industry to invest heavily in products destined for markets in developing countries is entirely understandable in the light of this history.

The creation of a particular special research fund is probably not a solution and would add to the dispersion of ongoing efforts. Additional funding of pure research would have only a small effect on the incentives facing the private sector in incurring the high costs and high risks of developing an AIDS vaccine. What is needed is a financial mechanism ensuring that when vaccines appropriate for developing countries are developed by the private sector, there will be adequate purchasing power in the market to enable the private firms to recover the costs of their development and production.

Given the weakness of purchasing power in developing countries themselves, international public investment is needed to provide that guarantee of a sufficient market. Since the product itself does not yet exist, innovative mechanisms to assure a market for a hypothetical product are required. In this context the International AIDS Vaccine Initiative (IAVI), the World Bank (as announced in the policy research report on AIDS) and the preparatory group for the G-8 (Group of eight most industrialised countries) meeting in Birmingham are making interesting proposals to create new international solidarity instruments. One particularly attractive idea under consideration is the notion of a contingent purchase fund, whereby donors issue promissory notes for a number of years ahead, to be drawn down for vaccine purchase in the event that the conditions are met, of a safe and effective vaccine suitable for use in developing countries.

C. Modalities of new international solidarity instruments

It is recognised that the creation of new solidarity instruments at international level could only help if the purpose was well focused and collectively prepared. Problems which are related to the weakness of the economy and the social sectors in many developing countries cannot be solved through the creation of specific funds at international level. Furthermore, it is important to realise the difficulties of increasing solidarity at international level in a period of budgetary constraints at national and regional level world-wide. It would also not be an answer to the lack of rapid progress in donor co-ordination and collaboration within the EU and the international community.

Extra public funds will have to be mobilised within the context of international budgetary constraints and the relative decrease of funds available for development in general. In the EC context, a reallocation of funds in order to increase spending on HIV/AIDS related activities will have to be discussed with the budgetary authorities but

also with our developing countries partners (for example in the context of the (re)negotiations of future conventions post Lomé). Funds which were not used from previous EDF's could for example be proposed to be used by a new funding instrument.

Funds could be mobilised through two main mechanisms at EC level: firstly through the EIB (European Investment Bank), and secondly through European NGO's and foundations. EIB funds, which are traditionally applied to market oriented operations, might be used in drug manufacture and distribution. NGO's and foundations could raise funds from the citizens of European countries to provide care for HIV/AIDS patients in the developing countries.

Other options for raising funds include:

- Contributions by pharmaceutical companies. Discussions are being held by UNAIDS
- A special tax raised as a percentage of the price paid for drugs in Europe to be transferred to the fund by the European country's national security system or to the pharmaceutical industry. At this stage, such options seem difficult in view of the problems encountered by the social security systems in Europe and the already high taxes paid by European citizens.
- Voluntary contributions from health insurance systems in Europe. The potential for this option appears limited as in many countries statutory rules would exclude this kind of transfer.
- Contribution from philanthropists. These would have to be linked to tax relief but could be available. Some potential names were put forward in the communications from Abidjan, but need to be confirmed.

V: THE SPECIFIC CONTRIBUTION OF THE EC

The EC's programme on AIDS in developing countries is committed to further support countries to finance the priorities as detailed in Chapter II.

This is to be seen in the context of the EC's efforts to strengthen the social sectors and to alleviate poverty alteration through greater efficiency of public finances and equity concerns.

It is argued that the EC's instruments to finance priorities for the relevant areas in the health sector at country, regional and international level are largely adequate and in equilibrium with the human resources available. Any new effort would have to be additional to these instruments and activities, as outlined in Chapter III.

A. What is to be financed by additional EC resources?

New additional finance resources could best be used for the purchase of additional commodities to prevent HIV/AIDS and to care for people with HIV/AIDS. This should have two components, i) to support countries to purchase existing commodities, and ii)

internationally to leverage further investment by the private sector in developing vaccines and microbicides.

B. The main commodities which could be purchased

1. Commodities that already exist

- AZT in monotherapy for pregnant seropositive women
- medicines for STD's, tuberculosis and other opportunistic infections
- anti-retroviral therapy for pilot testing in a few countries selected by UNAIDS

2. Commodities still to be developed

- vaccines and microbicides

In this context, more detailed work is needed in a 2nd stage and jointly with other development partners to look into the possibilities of creating a fund which could leverage investment by i) the private sector to develop such products, and/or ii) the countries to test these products once available. The World Bank is presently examining the different options for this.

C. A framework for what would be financed by new additional resources

It is proposed that the commodities mentioned under B.1. are procured and financed by and through the national medicine systems in the respective developing countries.

However the EC's additional resources could provide funds for pilot testing and purchasing of these commodities. The country involved could then start with a revolving fund to procure those commodities in a sustainable way.

A different choice can be made for the different products. For example, vaccines, once available, could be subsidised for a certain time in a degressive manner whereas microbicides will probably be cheap enough for the majority of persons to pay for them themselves. In that case it could still be beneficial however to provide a facility for the poorest and the higher risk persons to access the commodity through a targeted system such as vouchers.

Regarding monotherapy with AZT for pregnant women and treatment for STD's, tuberculosis and other opportunistic infections it is proposed to help countries to procure these medicines through the essential drugs system and to finance the start up of the system as well as subsidise the medicines for a certain period, if it can be ensured that the poorest would be targeted through adequate systems.

Concerning combination anti-retroviral therapy, it is proposed that some additional resources be used for testing of such products in a few countries selected by UNAIDS. The provision of the medicines could be carried out by private companies involved and the EC could provide for funds of notably technical assistance to monitor and evaluate the pilot phase and to disseminate the lessons learned. This evaluation could draw easily

on experience accumulated by European research groups during projects involving the set-up of these treatments in Europe and elsewhere.

The additional financial resources could furthermore be used to set such a system in place, test it and help develop national policies concerning all those commodities, their financing and the quality control required.

D. How are the funds be provided to the countries?

Additional finances could be provided to the national budgets of developing countries which would be allocated on the basis of action plans, and which include the guarantees for conditions to be in place as required and specified further. Detailed modalities and criteria will have to be examined at a later stage.

E. Some examples of conditions to be in place for the use of the EC's budget support at country level.

1. Medicines already available on the market

The provision of those products should be integrated in the overall system of procuring, financing and distributing all essential drugs in the country. The national plan should include provision for subsidies or cost recovery in harmony with the policies of the country.

2. Products not yet available

a) Vaccines

- an integrated HIV vaccine policy should be in place.
- a sustainable plan should be proposed to ensure longer term viability including financing mechanisms

b) Microbicides

Similar to above but probably less stringent as it might be an over the counter product rather than a medicinal product

F. Modalities for mobilising additional resources at the EC level

Once an agreement has been reached on the purposes of the new debate around the present communication, several options could be available to implement the initiatives described above:

Funding could be provided from different sources (budgetlines and EDF) which allow the use of resources for aids related activities in developing countries.

A. International level.

UNAIDS has a global responsibility in the monitoring of all these initiatives in the normative and ethical domains, and the EC supports this position. If new instruments at the international level are set up, it is understood that they would be managed by existing organisations with adequate technical capabilities and capacities.

B. National management of finances to provide commodities for developing countries

The international community has the responsibility to assure that they are achieving their stated purposes and not having any perverse effects on the existing health care systems or on preventive efforts.

However, in general, it is crucial that the main decisions about systems and priorities for subsidised or other care should remain in the developing countries because the effectiveness, affordabilility, equity and sustainability concerns are primarily a national responsibility. External interventions may nevertheless strengthen national efforts in these areas.

C. Monitoring

It is crucial to set up and finance a monitoring system that can capture any impact of these initiatives on the rest of the health sector whether they are positive or negative. This could be done as follows.

In conjuncture with any pilot programme to introduce medicines including ARV therapy in a very poor setting, a responsible international institution funding country-level implementation would first do baseline surveys on the health system in the vicinity of the pilot programme to determine the quality and accessibility of curative care and the distribution of financial and human resources to the introduction of the programme. The same surveys could then be conducted after 6 months during the implementation. For ARV, the results of these surveys could then be monitored to assure that funds allocated to provide ARV therapy to AIDS patients are spent in such a way so as to:

a) Maximise patient compliance, thereby minimising the risk that ARV therapy would create new, drug resistant strains to HIV which could subsequently spread throughout the entire world.

b) Minimise the diversion of human and financial resources from:

- The prevention of AIDS
- The prevention of easy to prevent fatal illnesses like measles
- The treatment of curable illnesses, including the easily treated opportunistic infections related to HIV.

D. Regarding management of new international financing instruments for the testing and purchase of vaccines for developing countries

It is proposed that the international community of donors collaborates with existing and new mechanisms. The EC would be ready to participate in this process. Detailed modalities will have to be further analysed and discussed at later stages.

VII: CONCLUSION ABOUT INTERNATIONAL CO-OPERATION AND THE EUROPEAN COMMUNITY'S SPECIFIC CONTRIBUTION

It goes without saying that no single nation alone, nor any group of nations, can provide effective solutions to the problems created by HIV/AIDS. Rather it is crucial to secure a high degree of international co-operation if the world community is to have a chance of finding just and sustainable solutions and of achieving both intergenerational and intragenerational equity on economical and political terms.

At the international level, UNAIDS must take global responsibility for any new solidarity initiatives. Though new mechanisms are welcomed it is highly important that their financing is additional to existing efforts to confront HIV/AIDS.

Over the past 10 years, the Community has been playing an important part in international action in the field of AIDS and plans to continue to do so.

- Regarding HIV/AIDS control, a European Community commitment was made by the Commission to reinforce actions to stabilise and minimise the spread of the epidemic in most of the developing countries in the next decade.

- Regarding health services, including those dealing with people infected with HIV, the Community's commitment to support developing countries' efforts to strengthen their health systems and focus on sustainable effective systems mainly for the poorest will be a major task for next decades. The Community is also proposing to make greater efforts to implement new strategies faster and more effectively jointly with all its partners. Furthermore, it will additionally give renewed attention to developing appropriate medicines systems in the countries requesting support for HIV and include appropriate care for AIDS.

- We are at the turning point in the action related to HIV/AIDS in developing countries. The lack of effective vaccines, the lack of accessibility to medicines for STD's and opportunistic infections (including TB), and the recently discovered anti-retroviral therapy is at the heart of the concerns world-wide and especially in the poorest developing countries affected.

The EC is committed to renew its existing efforts in order to ensure a decline in infected persons in most of the developing countries where able to give support.

Furthermore, new additional efforts and additional financial resources of the EC could be concentrated in two areas:

- at the country level to purchase commodities once they are on the market

- at the international level to leverage further investment of the private sector to develop and purchase vaccines and/or microbicides

ANNEX 1

1) **Regulation for AIDS budgetline: "Art. 2b":**

"Studying ways and means of improving access to treatment for people infected with HIV in the poorest countries. This study should be conducted in close collaboration with the United Nations agencies, concerned NGO's, pharmaceutical laboratories and the Members States of the European Union."

2) **Luxemburg Council:**

"Le Conseil européen demande à la Commission d'étudier les modalités de l'établissement d'un fonds de solidarité thérapeutiques sous l'égide de l'ONUSIDA destiné à la lutte contre le SIDA dans les pays en voie de développement"

3) **Parliament ACP document amendment:**

"rappelle à la Commission que le Conseil européen de Luxembourg lui a demandé: *d'étudier les modalités de l'établissement d'un fonds de solidarité thérapeutique sous l'égide de l'ONUSIDA destiné à la lutte contre le SIDA dans les pays en voie de développement"* et demande à la Commission de prévoir la mise en oeuvre de ce fonds dans le cadre de la prochaine convention."

4) **G8 in Denver:**

"Preventing the transmission of HIV infection and the development o AIDS is an urgent global public health imperative. While other prevention and treatment methods must be pursued, in the long term the development of safe, accessible and effective vaccines against AIDS holds the best chance of limiting and eventually eliminating, the threat of this disease. We will work to provide the resources necessary to accelerate AIDS vaccines research and together will enhance international scientific cooperation and collaboration"

5) **UNAIDS statement on mother to child transmission (23-24 March 98):**

"A global effort is needed to promote the updating and scaling up of interventions to prevent mother to child transmission of HIV. Furthermore, there is on ethical imperative to support the introduction of the shorter AZT (zidovudine) regime in countries in which trials have been completed and to encourage such interventions in countries which have capacity and willingness to support them"

6) **WORLD BANK:** Vaccine Purchase Fund:

This initiative seeks to assure industry of a commercially viable market in developing countries by establishing an international Vaccine Purchase Fund. Such a fund can create a guaranteed paying market in the developing world of known minimum size. By encouraging industrial investment in vaccine development, the Vaccine Purchase Fund could be financed by current country or donor funds, or by a guaranteed line of credit through the World Bank. Ten to 15 participating countries, providing $50-$100 million each, would create a $0.5-$1.0 billion dollar developing country vaccine market. Funds would only be made available to purchase a vaccine once it was

successfully developed. A World Bank line of credit conditional loan is a particularly attractive approach as current funds allocated to HIV could continue to be used for prevention and treatment until a vaccine was developed. Ultimately, having funds available for purchase will be essential for assuring vaccine availability, but by itself will most likely not be sufficient to fully overcome the reluctance of major vaccine companies to invest in developing HIV vaccines for low income countries.

7) **UNAIDS:** HIV drugs access initiative pilot project on providing wider access.

ONUSIDA: lance l'initiative visant à améliorer l'accès aux médicaments pour la prise en charge de l'infection au VIH et du SIDA dans les pays en voie de développement.

"En raison de l'ampleur et du potentiel de destruction massive et durable dus au SIDA, il est encore plus urgent et prioritaire de renforcer et d'actualiser les systèmes de prestations de soins de santé. L'initiative de l'ONUSIDA lance un phase pilote qui englobe la mise en oeuvre et le suivi de nouvelles stratégies destinées à éliminer les obstacles entravant l'amélioration de la prise en charge de VIH/SIDA et se déroulera au Chili, en Côte d'Ivoire, en Uganda et au Vietnam, pays qui permettent une évaluation adéquate de l'initiative dans des contextes géographiques, sociaux, culturels, économiques et structurels très divers"

ISSN 0254-1475

COM(98) 407 final

DOCUMENTS

EN 05 11 15 16

Catalogue number : CB-CO-98-421-EN-C

ISBN 92-78-37558-6

Office for Official Publications of the European Communities

L-2985 Luxembourg