II

(Preparatory Acts)

EUROPEAN ECONOMIC AND SOCIAL COMMITTEE

417th PLENARY SESSION (MEETING OF 11 AND 12 MAY 2005)

Opinion of the European Economic and Social Committee on the Proposal for a Regulation of the European Parliament and of the Council on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/83/EC and Regulation (EC) No 726/2004

(COM(2004) 599 final — 2004/0217 COD)

(2005/C 267/01)

On 12 November 2004 the Council decided to consult the European Economic and Social Committee, under Article 251 of the Treaty establishing the European Community, on the abovementioned proposal.

The Section for the Single Market, Production and Consumption, which was responsible for preparing the Committee's work on the subject, adopted its opinion on 20 April 2005. The rapporteur was Mr Braghin.

At its 417th plenary session (meeting of 11/12 May 2005), the European Economic and Social Committee adopted the following opinion unanimously.

1. **Summary of the Committee's recommendations**

1.1 The EESC considers protecting the paediatric population to be a top priority since it is a vulnerable group with specific physiological psychological, and developmental characteristics. For this reason, it believes that the decision to conduct paediatric studies should be based on clearly identified, scientifically researched needs and that compliance with the ethical conditions for the trials themselves should be ensured.

1.2 The EESC approves of the proposal to set up a Paediatric Committee within the EMEA, believing that it is an appropriate instrument for ensuring quality paediatric studies based on scientific and ethical principles. It recommends that it should include a broader spectrum of specific paediatric competences with respect to the development and use of paediatric medicines, and that the number of experts assigned to it by the Commission should be increased.

1.3 The EESC considers that the Paediatric Committee's responsibilities should be broadened at the outset. In particular, it recommends that its role be strengthened in the context of the European network of researchers and research centres for paediatric studies. It further recommends that it should be entrusted with the scientific management of the Medicines Investigation for the Children of Europe (MICE) programme that the Commission proposes to set up under an appropriate initiative.

1.4 The EESC welcomes the proposed authorisation procedure and especially supports the new PUMA procedure (the Paediatric Use Marketing Authorisation) for pharmaceuticals with existing market authorisation. It would further recommend introducing an abridged centralised procedure for cases where this is justified by the safety data, especially if gathered through the periodic safety update reports. It also suggests specifying that in cases where grounds are established for adopting orphan medicine procedures for a specific subcategory of the paediatric population, the market authorisation holder may opt for either of the two procedures.

1.5 In view of the time and resources required for paediatric studies as well as sensitive ethical and compliance issues relating to paediatric patients, the EESC agrees with the proposal to set up a system of incentives and rewards but would suggest strengthening them in certain specific situations.

1.6 The EESC supports the proposal to increase the availability of information on the use of medicines in the paediatric sector to medical and health practitioners, including greater access to information on the EudraCT Database ([1]). It further recommends adopting a broader communication strategy that facilitates a safer and more effective use of medicines in children.

1.7 The EESC considers it necessary to conduct a detailed study of the epidemiological situation for infants, therapeutic approaches and existing shortcomings in the availability of paediatric medicines, as well as a more detailed study of the paediatric use of so-called off-label prescriptions.

1.8 The EESC would therefore recommend that the Commission play an active role in setting up a network linking the relevant authorities and specialised research centres, in order to further our understanding of demand mechanisms for medicines and better therapeutic practice.

1.9 Finally, the EESC hopes that cooperation with the WHO and the dialogue with the relevant international authorities can be stepped up in order to speed up authorisation procedures for paediatric medicines and avoid any duplication or futile repetition of clinical studies.

2. **Introduction**

2.1 The paediatric population is a vulnerable group that differs from the adult population because of its specific developmental, physiological and psychological characteristics, which makes age and development related research of medicines particularly important. In contrast to the situation in adults, more than 50 % of the medicines used to treat the children of Europe have not been tested and are not authorised for use in children: the health and therefore quality of life of the children of Europe may suffer from a lack of testing and authorisation of medicines for their use.

2.2 Although there may be concerns voiced about conducting trials in the paediatric population, this has to be balanced by the ethical issues related to giving medicines to a population in which they have not been tested and therefore their effects, positive or negative, are unknown. In order to address the concerns about trials in children, the EU Directive on clinical trials ([2]) lays down specific requirements to protect children who take part in clinical trials in the EU.

2.3 The general objectives of the proposal are:

— to increase the development of medicines for use in children;

— to ensure that medicines used to treat children undergo high quality research;

— to ensure that medicines used to treat children are appropriately authorised for use in children;

— to improve the information available on the use of medicines in children, and;

— to achieve these objectives without subjecting children to unnecessary clinical trials and in full compliance with the EU Clinical Trials Directive.

2.4 The proposal includes a number of measures to achieve these objectives. The most significant are the following:

2.4.1 Setting up a Paediatric Committee within the European Medicines Agency (EMEA). The Paediatric Committee should be responsible for the assessment and agreement of paediatric investigation plans and for the relevant system of waivers and deferrals. It should also be responsible for assessing the compliance of dossiers with approved paediatric investigation plans and existing Community legislation; adopting an inventory of therapeutic needs in the paediatric population, and improving the information available on the safe use of medicines in various paediatric fields, in order, inter alia, to avoid duplicating or conducting unnecessary studies.

2.4.2 The studies in children are to be based on a paediatric investigation plan approved by the Paediatric Committee. When assessing such plans the Paediatric Committee will take into consideration two overarching principles: that studies should only be performed if there is a potential therapeutic benefit to children (and avoiding duplication of studies). The requirements for studies in children should not delay the authorisation of medicines for other populations.

2.4.3 All studies performed in accordance with a completed, agreed paediatric investigation plan are to be presented at the time of application for authorisation for new active ingredients, new indications, new pharmaceutical forms or new routes of administration for an authorised medicine, unless a waiver or a deferral has been granted by the Paediatric Committee.

2.4.4 In order to establish a vehicle for providing incentives for off-patent medicines, a new type of marketing authorisation, PUMA, is proposed. It will utilise existing marketing authorisation procedures but is specifically for medicinal products developed exclusively for use in children.

([1]) European Clinical Trials Database
([2]) OJ L 121, 1.5.2001

2.4.5 To increase the availability of medicines for children across the Community, because the requirements in the proposals are linked to Community-wide rewards and to prevent the distortion of free trade within the Community, it is proposed that an application for a marketing authorisation including at least one paediatric indication based on the results of an agreed paediatric investigation plan will have access to the centralised Community procedure.

2.4.6 For new medicines and for products covered by a patent or a Supplementary Protection Certificate (SPC), if all the measures included in the agreed paediatric investigation plan are complied with, if the product is authorised in all Member States and if relevant information on the results of studies is included in product information, the six-month SPC extension will be granted.

2.4.7 Similar incentives are proposed for orphan medicinal products, for which, provided that the requirements for data on use in children are fully met, the usual ten-year market exclusivity is extended by two years.

2.4.8 Products with existing marketing authorisation, will benefit from the data protection associated with a new marketing authorisation (PUMA).

2.5 The Clinical Trials Directive establishes a Community database of clinical trials (EudraCT). It is proposed to build onto this database an information resource of all ongoing and terminated paediatric studies conducted both in the Community and in third countries.

2.6 The Commission intends to examine the possibility of setting up a paediatric study programme: Medicines Investigation for the Children of Europe (MICE), taking into consideration existing Community Programmes.

2.7 Establishing a Community network has also been proposed. The network would link together national networks and clinical trial centres in order to build up the necessary competences at a European level and to facilitate the implementation of studies, to increase cooperation and avoid duplication of studies.

2.8 The proposal is based on Article 95 of the EC Treaty. Article 95, which prescribes the codecision procedure described in Article 251, is the legal basis for achieving the aims set out in Article 14 of the Treaty, which includes the free movement of goods (Article 14(2)), in this case human medicinal products.

3. **General comments**

3.1 *Safeguarding paediatric health and clinical trials in children*

3.1.1 The Committee considers the protection of the paediatric population to be a top priority, insofar as it is a vulnerable group with specific developmental, physiological and psychological characteristics. If this fundamental objective is to be pursued in the field of paediatric pharmaceuticals, the following conditions must be fulfilled:

— only necessary clinical trials in children are to be conducted, and futile duplication should be avoided;

— clinical tests must be adequately controlled, monitored, and conducted in accordance with the ethical imperative to provide maximum protection for the paediatric patient;

— adequate information and communication processes must guarantee a deeper understanding of recommended therapeutic approaches for this group;

— active pharmacovigilance mechanisms should facilitate the continual and scientifically grounded updating of paediatric therapeutic practice.

3.1.2 The EESC therefore considers that the decision to require and conduct clinical studies should be based on clearly defined needs supported by research. It should therefore be verified that:

— existing information on the pharmaceutical product does not adequately ensure safe and effective use in children ([3]);

— the level of (current or potential) use in children is substantial ([4]);

— the medicine is likely to have benefits;

— the additional scientific and medical information acquired through the use of a medicine with existing authorisation implies benefits for paediatric use.

([3]) In the USA, the FDA may require trials for paediatric use in cases where the inadequate labelling of a medicine on the market could expose patients to significant risk.

([4]) In the USA, the FDA defines 'substantial' as at least 50,000 patients. At this level, a company may be required to conduct clinical paediatric trials.

3.1.3 In view of the above, the EESC believes that it would be appropriate for the ethical standards and specific regulations for protecting minors laid down in the Directive on the implementation of good clinical practice in the conduct of clinical trials ([5]) to be mentioned in the Directive's articles and not only in the recitals. The Paediatric Committee's general criteria for approving the paediatric investigation plan (PIP) should take account of the recommendations of the relevant International Conference on Harmonisation ([6]), and should comply with directive 2001/20/EC on clinical trials in order to ensure compliance with the ethical conditions for the trials themselves.

3.1.4 The EESC therefore insists that the proposal's true focus should be the paediatric patient and his health needs. It is from this perspective that we should deal with issues relating to the medical approach and consequently the clinical and therapeutic information that should be available to medical personnel and, for the purposes of their specific competences, to other health care professionals to enable them to treat a specific patient requiring their care.

3.2 *Basic information gaps affecting the use of medicines*

3.2.1 The EESC considers the assessment of the present situation, causes and risks to be insufficient. The EIA dedicates only a few pages to them and the explanatory memorandum of the proposal makes no reference to them whatsoever.

3.2.1.1 It would have been appropriate to conduct a study on the epidemiological situation for infants and gaps in the existing therapeutic arsenal, thereby orientating research trends appropriately in order to identify research priorities to be supported through Community funding (within the framework of ongoing discussions on the 7th Research Framework Programme). In addition, such a study would have showcased the work of the CHMP Paediatric Expert Group, which has drawn up a list of 65 unpatented active ingredients to be treated as research and development priorities in paediatrics. It would also have facilitated and accelerated ongoing efforts to implement the abovementioned MICE paediatric study programme.

3.2.1.2 Since the return on investment is probable, the market for medicines to treat paediatric diseases with high incidence rates is substantial enough to motivate the pharmaceutical industry to develop new paediatric indications and adapt formulations for the paediatric population. However the cost of development for rarer diseases or diseases affecting specific sub age groups outweighs the return on investment. The industry (especially small/medium-sized European companies) cannot afford these costs without adequate incentives or research funding. It is precisely for these rarer diseases affecting specific sub groups that additional tools must be provided to compensate for the high cost, in terms of human, time and financial resources, of investing in paediatric research.

3.2.2 The Committee believes that it would also have been appropriate to conduct a more detailed study on the paediatric use of so-called off-label prescriptions. Such a study would have established the extent of the practice and the precise negative effects associated with the inappropriate use of medicinal products. A better insight into the situation could have facilitated a more substantiated analysis of possible remedies and incentives to be applied.

3.2.2.1 The EESC realises that the relevant information is heterogeneous, and has been gathered in the Member States by different bodies with extremely diverse, incomplete, and distortive operational procedures. As a consequence, it is doubtful whether the data will lend itself to comparison or the extrapolation of general observations that are scientifically grounded. Despite the limitations, a study of prescriptions and the use of medicines would provide a preliminary, albeit schematic, overview of obvious discrepancies in terms of the scope and use of therapeutic classes and the active ingredients used, sometimes without scientifically grounded therapeutic justification.

3.2.2.2 Another discernible shortcoming lies in the analysis of differences in medical practice in Member States, which is undoubtedly relevant on the basis of the data gathered on the classes of medicines prescribed for various diseases. The EESC not only considers that such a study can no longer be postponed, it also believes that it would be particularly effective in safeguarding public health, which is a primary asset. Bearing in mind that vocational training, health care procedures, and the administration of treatment and medicine are Member State competences, the EESC hopes that the open method of coordination will also be applied to pharmaceuticals. It also hopes that, in the interests of public health, a set of well-formulated and coordinated guidelines on best medical practice in various therapeutic fields and patient population strata, including the paediatric population, will be drafted in good time, with the active support of medical and patient associations.

([5]) OJ L 121 of 1 May 2001

([6]) With particular reference to guideline ICH E 11, which states: 'The ethical imperative to obtain knowledge of the effects of the medicinal products in paediatric patients has to be balanced against the ethical imperative to protect each paediatric patient in clinical trials'.

3.2.3 A parallel study should have been conducted on the findings of monitoring and pharmacovigilance mechanisms, an area where European legislation is undoubtedly in the vanguard. Clearly, pharmacovigilance networks should have already identified the presence or absence of cases of inappropriate use and, indirectly, therapeutic shortcomings, for which, the EU authorities, in cooperation with the relevant national authorities, could already have established an appropriate information policy.

3.2.4 Given the widespread use of off-label prescriptions, we need to question the relative efficacy of an approach based on authorisation procedures (as recommended in the proposal under consideration). The Committee believes that it would have been advisable to adopt parallel actions to encourage good practice in the use of paediatric pharmaceuticals by doctors, health operators in general, and parents, whose understandable anxieties to alleviate their children's suffering often put the doctor under pressure to prescribe short-term remedies that do not always meet the young patient's real needs.

3.2.5 Another aspect that has not been taken into proper account is the importance of the pharmacist's role in purchase decisions and in providing advice on the appropriate use of medicines. This category of health professional could provide valuable support for an active education and pharmacovigilance policy.

3.2.6 It would also be worth deepening the analysis of available data on safe use, especially pharmacovigilance, in order to assess whether the different prescriptive approaches applied in various EU Member States and the different pharmaceutical classifications have different impacts in terms of inappropriate use and adverse reactions.

3.2.7 The EESC realises that these matters go beyond the primary scope of the proposal under consideration but would nevertheless recommend that the Commission play an active role in establishing a network linking the authorities to specialist research centres in order to increase our understanding of the mechanisms that influence demand for pharmaceuticals, their rational use, best therapeutic practice, and other similar aspects, thereby facilitating the harmonisation of the internal market for pharmaceuticals too.

3.3 *The paediatric committee and clinical trials*

3.3.1 The EESC agrees with the proposal to establish a Paediatric Committee within the EMEA. The responsibilities of this committee are extremely diverse and range from the assessment of the content and modalities of all paediatric investigation plans to the preventive assessment of the potential benefits for the paediatric population; from scientific support for drafting such plans in compliance with good clinical trials practice to providing a therapeutic inventory, and support and consultancy services for setting up a European network of researchers, and centres with specific competencies in conducting studies in the paediatric population. In addition to the abovementioned responsibilities, the committee will also be responsible for avoiding the duplication of studies.

3.3.2 In view of the broad range of the Paediatric Committee's responsibilities, the EESC does not consider the competences set out in Article 4(1) to be sufficient, especially with regard to pre-clinical and clinical development methodology (in particular, experts in pharmacology, toxicology, pharmacocinetics, biometrics, and biostatistics), specialists (including neonatologists) in the paediatric fields corresponding to the most significant therapeutic groups, and experts in pharmacoepidemiology. Furthermore, the EESC would recommend that the number of experts designated by the Commission be increased to include the representatives of health care facilities for children.

3.3.3 The EESC notes that the paediatric population is defined as 'that part of the population aged between birth and 18 years' (Article 2) and realises that, to date, not even a standard ICH definition has been agreed upon. The EESC hopes that in conducting specific studies for each subpopulation, the Paediatric Committee will avoid subjecting to unnecessary studies a population whose constitution and age do not expose them to risk.

3.3.4 The EESC approves of the principle that paediatric investigation plans should be submitted during the development phase of a new pharmaceutical product and welcomes the possibility of continued dialogue between the proposer and the Paediatric Committee. The EESC is nevertheless concerned by the request to submit them 'unless otherwise justified, not later than upon completion of the human pharmaco-kinetic studies' (Article 17(1)). In fact, during this phase, safety trials in the adult patient population will not have been concluded, and consequently the safety profile will not be clearly defined. It would therefore not be possible to draw up a comprehensive, well-formulated paediatric investigation plan (especially for the various subcategories of the paediatric population). This would incur the risk of starting unnecessary studies or repeating studies with different dosages from those initially foreseen.

3.3.5 The EESC is also concerned that the request will delay the development of new medicines for the adult population, whereas at a more advanced stage of development it would be easier to identify at-risk populations, including the paediatric population, focus research efforts on important information gaps and put forward better targeted plans for active pharmacovigilance.

3.3.6 The EESC also expresses concern at the proposal that 'any studies completed before this proposed legislation is adopted will not be eligible for the rewards and incentives proposed for the EU. They will, however, be taken into account for the requirements contained in the proposals and it will be mandatory for companies to submit the studies to the competent authorities once this proposed legislation is adopted' ([7]). This proposal risks slowing down or reducing the number of ongoing or projected studies by companies, while waiting for the final version of the regulation to be implemented throughout the European Union.

3.4 *Incentive measures*

3.4.1 The EESC agrees that there is a need to create appropriate incentives to ensure that paediatric clinical trials are conducted in accordance with principles of best practice and ethical standards, and that paediatricians, paediatric clinics and wards are provided with an enhanced therapeutic arsenal, including safe, effective, high quality pharmaceuticals that have been conceived and designed for the paediatric population, following the logic of the terms of the Council Resolution of 14 December 2000 and bearing in mind experience gained in the United States in the light of specific legislation ([8]) adopted in that country.

3.4.2 The time and resources required for studies of this type, as well as sensitive ethical and compliance issues relating to paediatric patients, explain why market forces have not been sufficient to develop pharmaceutical products that may be specifically categorised as 'paediatric'. In view of this fact, the EESC considers that the incentives and rewards granted in certain situations are not always sufficient.

3.4.2.1 In particular, the six-month extension of the Supplementary Protection Certificate does not appear to adequately compensate for the higher costs, risks and delays in completing the dossier and obtaining authorisation that paediatric studies could imply for a new product. Admittedly, appropriate waivers and deferrals have been foreseen. Nevertheless, if paediatric research were made compulsory, the commitment would become particularly expensive and time-consuming.

3.4.2.2 The EESC notes with concern the current tendency to focus research and development efforts on active ingredients with broad market potential, which absorb a growing proportion of investment in research and development, whereas ingredients with smaller or niche market potential are secondary priorities. If this mechanism were applied to new paediatric medicines, it would be impossible to fulfil the objective of obtaining a genuinely innovative and sufficiently diverse arsenal of paediatric medicines within a reasonable timeframe. The EESC advocates that such risks be carefully monitored and specifically assessed in the context of the proposed general report on the experience gained from the application of the regulation.

3.4.3 The new procedure outlined in Title III Chapter II (PUMA) for medicines with marketing authorisation that are not protected by a patent or supplementary protection certificate constitutes an important and viable innovation for available paediatric use marketing authorisation procedures. The possibility of following centralised procedures even if the initial authorisation for a pharmaceutical product for adults has been obtained through national procedures constitutes a genuine opportunity.

3.4.4 Welcome progress has been achieved in terms of procedural flexibility, in particular, the possibility of referring to existing data in an authorised medicine's dossier (Article 31(4)) and the possibility of using a known brand name by simply adding the letter 'P' in superscript (Article 31(5)). In such instances, the EESC recommends that the pharmaceutical form and dosage should also be prominently displayed on the packaging if they have been adapted for paediatric use.

3.4.5 However, the EESC notes that this flexibility is countered by a certain rigidity which could act as a disincentive to paediatric research, for instance, the obligation to obtain authorisation in all Member States in order to benefit from the extension of the Supplementary Protection Certificate (SPC). The Committee considers that this provision is excessive, especially in an enlarged Union. It believes that only large multinationals producing pharmaceuticals of guaranteed success will actually benefit.

3.4.6 The assertion that all data relating to development should be disclosed is also cause for concern since it changes existing legislation on the disclosure of information and data relating to marketing authorisation dossiers. This approach would also appear to act as a disincentive to launching research into new types of drugs and the appropriate dosage for paediatric use of established medicinal products that are already marketed.

3.5 *Information on the use of medicines for children*

3.5.1 One of the proposal's objectives is to increase the availability of information on the use of medicines in the paediatric sector. The EESC agrees that the increased availability of information could facilitate the safe and effective use of medicines in children and thereby promote public health. Furthermore, the availability of information could help to avoid duplicating studies or carrying out unnecessary studies on children.

([7]) See the explanatory memorandum under *Information on the use of medicines for children*, p. 7

([8]) *Best Pharmaceuticals for Children Act*, 1 April 2002, Public Law n. 107-109.

3.5.2 For this reason, the EESC also supports the proposal to use the Community clinical trials database (EudraCT), established by the Clinical Trials Directive, as a foundation for an information resource on all ongoing and terminated paediatric studies conducted in the Community and third countries.

3.5.2.1 Nevertheless, the arrangements for using this database are not sufficiently clear: who should have access, what data should be disclosed or withheld on grounds of individual privacy protection, or the need to protect sensitive or confidential industrial information.

3.5.2.2 Similarly, no clear line has been drawn between available technical information (available to health professionals) and information to be made available to the general public in the package leaflet. In this segment of the paediatric market, comprehensible and transparent package leaflets play a particularly important role in preventing behaviour that could potentially harm the paediatric patient.

3.5.3 Title VI on Communication and Coordination outlines a series of actions and obligations (for instance, the fact that available data on all existing uses of medicinal products in the paediatric population must be collected by the Member States within two years of the entry into force of the Regulation — Article 41). However, it does not tackle the issue of understanding the proper use of pharmaceutical products in the paediatric sector and the policies to be adopted vis-à-vis health professionals and the general public.

4. **Concluding comments**

4.1 The EESC reiterates its fundamental agreement with the proposed regulation, but wonders whether its legal basis, more specifically, Article 95 of the EC Treaty for implementing objectives established under Article 14(2) (free circulation of goods), is the most appropriate basis in an area of implementation with significant public health implications. Although all legislation adopted for the pharmaceutical sector is based on the abovementioned article, it should be borne in mind that, in the case under consideration, the fundamental objective is the health and protection of the paediatric population.

4.2 The EESC hopes the Commission will soon draw up another proposal that focuses on the demand for pharmaceuticals, rather than on supply. The objective would be to create an operational tool that facilitates and encourages data collection and dissemination on the availability and use of medicines; setting up epidemiological and prescriptive use data bases; as well as establishing guidelines through the increased involvement of health professionals and patient associations, thereby simultaneously extending the application of the open method of coordination to this sector.

4.3 The communication and coordination process in Title VI seems somewhat restrictive. The EESC recommends that a broader communication strategy resulting in a more rational use of medicine in paediatrics should be prepared and implemented. Furthermore, doctors and health care professionals should be supplied with all necessary information tools for their purposes. Following the same line of thought, we should reconsider whether, and under what procedures, scientific researchers and doctors should have access to the information on clinical trials that is available on the European Clinical Trials Database (EudraCT).

4.4 The EESC welcomes the proposal to set up a paediatric study programme, Medicines Investigation for Children in Europe (MICE), to provide Community funding for research carried out by groups, companies, and paediatric hospital networks on the paediatric use of unpatented medicines, or observational or cohort studies in their post-registration phase. The EESC would, however, have preferred orientation guidelines and a more precise definition of the Paediatric Committee's role in this respect. This would avoid lengthy discussions as to who should identify priority therapeutic fields requiring further information on paediatric use, the assessment of priority needs and the specific studies to be conducted, particularly in view of the considerable differences in current medical practice in Member States.

4.5 The EESC therefore recommends that these competences be specifically attributed to the Paediatric Committee under Article 7 of the regulation, in order to facilitate speedy implementation and ensure better coordination of all the Paediatric Committee's institutional activities.

4.6 At the same time, the EESC hopes that, in establishing and implementing a European network of researchers and centres with specific roles to play in carrying out studies on the paediatric population under Article 43, the Paediatric Committee will not merely assume a supportive and advisory role for the agency. It should play an active part, with the possible support of a forum that brings experts from all Member States together, be they academics or paediatric subspecialists. Furthermore, the EESC recommends including, should it be necessary to define specific research study protocols, researchers from companies involved in the protocol through their own products, insofar as they are best placed to know the specific features of these products.

4.7 The fact that the Paediatric Committee's primary role is to approve paediatric investigation plans (PIP), which is at the very heart of the proposal leads the EESC to fear that the tendency to formalise clinical paediatric studies will prevail over the pursuit of some of the objectives, including ethical objectives, cited above, such as avoiding futile duplication or paediatric studies that are not genuinely necessary.

4.8 The EESC suggests that the need to analyse information on the EudraCT database and conduct a detailed assessment of the periodic safety update reports (established under the most recent legislative amendments) should be specifically included amongst the Committee's competences. The reports include epidemiological data, prescription surveys, and the results of published studies, thereby reducing the magnitude and duration of clinical studies, or in some cases making them redundant.

4.9 From a procedural point of view, it should be assumed that, should such documentation permit the assessment of safety data for existing medicines (obtained through pharmacovigilance, information reports and the periodic safety update reports) regarding formulations and dosage for paediatric use, it will be possible to adopt a shorter, simpler centralised procedure to amend appropriately the technical information in the package leaflet, rather than the PUMA procedure, which remains lengthy and expensive ([9]).

4.10 Also from the procedural point of view, the EESC considers that it is necessary to specify that in cases where grounds are established for adopting orphan medicine procedures for a subcategory of the paediatric population, the market authorisation holder may opt for either of the two procedures.

4.11 The EESC emphasises the importance of publishing research results and approved changes to the package leaflet, and including information for paediatric use for all unpatented medicines with the same active ingredients.

4.12 The EU is already the regulatory authority for the registration of pharmaceuticals in developing countries, and the WHO already consults it when assessing medicines that can be registered in such countries. It is to be hoped that an expeditious application of this regulation in the EU will also have a positive impact on paediatric therapies available in the least developed countries. The EESC hopes that constructive cooperation with the WHO will be further strengthened and that the Commission will pursue regular dialogue with all international authorities in order to speed up approval procedures for new substances and indications, dosages and formulations that are more appropriate for paediatric use, thereby avoiding any unnecessary duplication and repetition of clinical studies.

Brussels, 11 May 2005

The President

of the European Economic and Social Committee

Anne-Marie SIGMUND

([9]) A simplified mechanism of this type has already been adopted in the United States, where 33 products now include paediatric information in their leaflet as a result of post-registration clinical studies (since periodic safety update reports do not exist in the United States such studies were required), whereas 53 are authorised for exclusive paediatric use on the basis of a complete clinical study plan.