ANNEX I

Annexes 1 to 7 to Directive 90/385/EEC shall be amended as follows:

1. Annex 1 shall be amended as follows:

(a) the following Section shall be inserted:

5a. Demonstration of conformity with the essential requirements must include a clinical evaluation in accordance with Annex 7.;

(b) in Section 8, the fifth indent shall be replaced by the following:

— risks connected with ionising radiation from radioactive substances included in the device, in compliance with the protection requirements laid down in Council Directive 96/29/Euratom of 13 May 1996 laying down basic safety standards for the protection of the health of workers and the general public against the dangers arising from ionising radiation[(1)] and Council Directive 97/43/Euratom of 30 June 1997 on health protection of individuals against the dangers of ionising radiation in relation to medical exposure[(2)].;

(c) in Section 9, seventh indent, the following phrase shall be added:

For devices which incorporate software or which are medical software in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification.;

(d) Section 10 shall be replaced by the following:

10. Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in Article 1 of Directive 2001/83/EC, and which is liable to act upon the body with action ancillary to that of the device, the quality, safety and usefulness of the substance must be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC.

For the substances referred to in the first paragraph, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking account of the intended purpose of the device, seek a scientific opinion from one of the competent authorities designated by the Member States or the European Medicines Agency (EMEA) acting particularly through its committee in accordance with Regulation (EC) No 726/2004[(3)] on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the substance into the device. When issuing its opinion, the competent authority or the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body.

Where a device incorporates, as an integral part, a human blood derivative, the notified body shall, having verified the usefulness of the substance as part of the device and taking account of the intended purpose of the device, seek a scientific opinion from the EMEA, acting particularly through its committee, on the quality and safety of the substance, including the clinical

benefit/risk profile of the incorporation of the human blood derivative into the device. When issuing its opinion, the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body.

Where changes are made to an ancillary substance incorporated in a device, in particular related to its manufacturing process, the notified body shall be informed of the changes and shall consult the relevant medicines competent authority (i.e. the one involved in the initial consultation), in order to confirm that the quality and safety of the ancillary substance are maintained. The competent authority shall take into account the data related to the usefulness of the incorporation of the substance into the device as determined by the notified body, in order to ensure that the changes have no negative impact on the established benefit/risk profile of the addition of the substance in the device.

When the relevant medicines competent authority (i.e. the one involved in the initial consultation) has obtained information on the ancillary substance, which could have an impact on the established benefit/risk profile of the addition of the substance to the device, it shall provide the notified body with advice, whether this information has an impact on the established benefit/risk profile of the addition of the substance to the device or not. The notified body shall take the updated scientific opinion into account in reconsidering its assessment of the conformity assessment procedure.;

(e) Section 14.2 shall be amended as follows:

(i) the first indent shall be replaced by the following:

— the name and address of the manufacturer and the name and address of the authorised representative, where the manufacturer does not have a registered place of business in the Community,;

(ii) the following indent shall be added:

— in the case of a device within the meaning of Article 1(4a), an indication that the device contains a human blood derivative.;

(f) the following indent shall be added to the second paragraph of Section 15:

— date of issue or the latest revision of the instructions for use.;

2. Annex 2 shall be amended as follows:

(a) in Section 2, the third paragraph shall be replaced by the following:

This declaration shall cover one or more clearly identified devices by means of product name, product code or other unambiguous reference and must be kept by the manufacturer.;

(b) in the second paragraph of Section 3.1, the first sentence of the fifth indent shall be replaced by the following:

— an undertaking by the manufacturer to institute and keep updated a post-marketing surveillance system including the provisions referred to in Annex 7.;

(c) Section 3.2 shall be amended as follows:

(i) the following sentence shall be added to the second subparagraph:

It shall include in particular the corresponding documentation, data and records arising from the procedures referred to in point (c).;

(ii) the following indent shall be added to point (b):

— where the design, manufacture and/or final inspection and testing of the products, or elements thereof, is carried out by a third party, the methods of monitoring the efficient operation of the quality system and in particular the type and extent of control applied to the third party.;

(iii) the following indents shall be added to point (c):

— a statement indicating whether or not the device incorporates, as an integral part, a substance or a human blood derivative referred to in Section 10 of Annex 1 and the data on the tests conducted in this connection required to assess the safety, quality and usefulness of that substance or human blood derivative, taking account of the intended purpose of the device,

— the pre-clinical evaluation,

— the clinical evaluation referred to in Annex 7.;

(d) in Section 3.3, the last sentence of the second subparagraph shall be replaced by the following:

The evaluation procedure shall include an inspection on the manufacturer's premises and, in duly substantiated cases, on the premises of the manufacturer's suppliers and/or subcontractors to inspect the manufacturing processes.;

(e) Section 4.2 shall be amended as follows:

(i) the first paragraph shall be replaced by the following:

The application shall describe the design, manufacture and performances of the product in question, and it must include the documents needed to assess whether the product conforms to the requirements of this Directive, and in particular Annex 2, Section 3.2, third paragraph, points (c) and (d).;

(ii) in the fourth indent of the second paragraph, the word ‘data’ shall be replaced by the word ‘evaluation’;

(f) in Section 4.3, the following paragraphs shall be added:

In the case of devices referred to in Annex 1, Section 10, second paragraph, the notified body shall, as regards the aspects referred to in that section, consult one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC or the EMEA before taking a decision. The opinion of the competent national authority or the EMEA shall be drawn up within 210 days after receipt of valid documentation. The scientific opinion of the competent national authority or the EMEA must be included in the documentation concerning

the device. The notified body will give due consideration to the views expressed in this consultation when making its decision. It will convey its final decision to the competent body concerned.

In the case of devices referred to in Annex 1, Section 10, third paragraph, the scientific opinion of the EMEA must be included in the documentation concerning the device. The opinion shall be drawn up within 210 days after receipt of valid documentation. The notified body will give due consideration to the opinion of the EMEA when making its decision. The notified body may not deliver the certificate if the EMEA's scientific opinion is unfavourable. It will convey its final decision to the EMEA.;

(g) in Section 5.2, the second indent shall be replaced by the following:

— the data stipulated in the part of the quality system relating to design, such as the results of analyses, calculations, tests, pre-clinical and clinical evaluation, post-market clinical follow-up plan and the results of the post-market clinical follow-up, if applicable, etc.;

(h) Section 6.1 shall be replaced by the following:

6.1. For at least 15 years from the last date of manufacture of the product, the manufacturer or his authorised representative shall keep available for the national authorities:

— the declaration of conformity,

— the documentation referred to in the second indent of Section 3.1, and in particular the documentation, data and records referred to in the second paragraph of Section 3.2,

— the amendments referred to in Section 3.4,

— the documentation referred to in Section 4.2,

— the decisions and reports of the notified body referred to in Sections 3.4, 4.3, 5.3 and 5.4.;

(i) Section 6.3 shall be deleted;

(j) the following Section shall be added:

7. Application to the devices referred to in Article 1(4a):

Upon completing the manufacture of each batch of devices referred to in Article 1(4a), the manufacturer shall inform the notified body of the release of the batch of devices and send to it the official certificate concerning the release of the batch of human blood derivative used in the device, issued by a State laboratory or a laboratory designated for that purpose by a Member State in accordance with Article 114(2) of Directive 2001/83/EC.;

3. Annex 3 shall be amended as follows:

(a) Section 3 shall be amended as follows:

(i) the first indent shall be replaced by the following:

— a general description of the type, including any variants planned, and its intended use(s),;

(ii) the fifth to eighth indents shall be replaced by the following:

— the results of design calculations, risk analysis, investigations and technical tests carried out, etc.,
— a declaration stating whether or not the device incorporates, as an integral part, a substance or a human blood derivative as referred to in Section 10 of Annex 1 and the data on the tests conducted in this connection required to assess the safety, quality and usefulness of that substance or human blood derivative, taking account of the intended purpose of the device,
— the pre-clinical evaluation,
— the clinical evaluation referred to in Annex 7,
— the draft instruction leaflet.;

(b) the following paragraphs shall be added to Section 5:

In the case of devices referred to in Annex 1, Section 10, second paragraph, the notified body shall, as regards the aspects referred to in that section, consult one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC or the EMEA before taking a decision. The opinion of the competent national authority or the EMEA shall be drawn up within 210 days after receipt of valid documentation. The scientific opinion of the competent national authority or the EMEA must be included in the documentation concerning the device. The notified body will give due consideration to the views expressed in this consultation when making its decision. It will convey its final decision to the competent body concerned.

In the case of devices referred to in Annex 1, Section 10, third paragraph, the scientific opinion of the EMEA must be included in the documentation concerning the device. The opinion shall be drawn up within 210 days after receipt of valid documentation. The notified body will give due consideration to the opinion of the EMEA when making its decision. The notified body may not deliver the certificate if the EMEA's scientific opinion is unfavourable. It will convey its final decision to the EMEA.;

(c) in Section 7.3, the words ‘five years from the manufacture of the last appliance’ shall be replaced by the words ‘15 years from the manufacture of the last product’;

(d) Section 7.4 shall be deleted;

4. Annex 4 shall be amended as follows:

(a) in Section 4, the words ‘post-marketing surveillance system’ shall be replaced by the words ‘post-marketing surveillance system including the provisions referred to in Annex 7’;

(b) Section 6.3 shall be replaced by the following:

6.3. Statistical control of products will be based on attributes and/or variables, entailing sampling schemes with operational characteristics which ensure a high level of safety and performance according to the state of the art. The sampling schemes will be established by the harmonised standards referred to in Article 5,

taking account of the specific nature of the product categories in question.;

(c) the following Section shall be added:

7. Application to the devices referred to in Article 1(4a):

Upon completing the manufacture of each batch of devices referred to in Article 1(4a), the manufacturer shall inform the notified body of the release of the batch of devices and send to it the official certificate concerning the release of the batch of human blood derivative used in the device, issued by a State laboratory or a laboratory designated for that purpose by a Member State in accordance with Article 114(2) of Directive 2001/83/EC.;

5. Annex 5 shall be amended as follows:

(a) in Section 2, second paragraph, the words 'identified specimens of the product and shall be kept by the manufacturer' shall be replaced by the words 'devices manufactured, clearly identified by means of product name, product code or other unambiguous reference and must be kept by the manufacturer';

(b) in the sixth indent of Section 3.1, the words 'post-marketing surveillance system' shall be replaced by the words 'post-marketing surveillance system including the provisions referred to in Annex 7';

(c) in Section 3.2(b), the following indent shall be added:

— where the manufacture and/or final inspection and testing of the products, or elements thereof, are carried out by a third party, the methods of monitoring the efficient operation of the quality system and in particular the type and extent of control applied to the third party.;

(d) in Section 4.2, the following indent shall be inserted after the first indent:

— the technical documentation,;

(e) the following Section shall be added:

6. Application to the devices referred to in Article 1(4a):

Upon completing the manufacture of each batch of devices referred to in Article 1(4a), the manufacturer shall inform the notified body of the release of the batch of devices and send to it the official certificate concerning the release of the batch of human blood derivative used in the device, issued by a State laboratory or a laboratory designated for that purpose by a Member State in accordance with Article 114(2) of Directive 2001/83/EC.;

6. Annex 6 shall be amended as follows:

(a) Section 2.1 shall be amended as follows:

(i) the first indent shall be replaced by the following two indents:

— the name and address of the manufacturer,

— the information necessary for the identification of the product in question,;

(ii) in the third indent, the word 'doctor' shall be replaced by the words 'duly qualified medical practitioner';

(iii) the fourth indent shall be replaced by the following:

— the specific characteristics of the product revealed by the prescription,;

(b) Section 2.2 shall be replaced by the following:

2.2. For devices intended for clinical investigations covered in Annex 7:

— data allowing the devices in question to be identified,

— the clinical investigation plan,

— the investigator's brochure,

— the confirmation of insurance of subjects,

— the documents used to obtain informed consent,

— a statement indicating whether or not the device incorporates, as an integral part, a substance or human blood derivative referred to in Section 10 of Annex 1,

— the opinion of the ethics committee concerned and details of the aspects covered by its opinion,

— the name of the duly qualified medical practitioner or other authorised person and of the institution responsible for the investigations,

— the place, date of commencement and duration scheduled for the investigations,

— a statement affirming that the device in question complies with the essential requirements apart from the aspects constituting the object of the investigations and that, with regard to these aspects, every precaution has been taken to protect the health and safety of the patient.;

(c) in Section 3.1, the first paragraph shall be replaced by the following:

For custom-made devices, documentation, indicating manufacturing site(s) and enabling the design, manufacture and performances of the product, including the expected performances, to be understood, so as to allow conformity with the requirements of this Directive to be assessed.;

(d) in Section 3.2, the first paragraph shall be amended as follows:

(i) the first indent shall be replaced by the following:

— a general description of the product and its intended use,;

(ii) in the fourth indent, the words ‘a list of the standards’ shall be replaced by the words ‘the results of the risk analysis and a list of the standards’;

(iii) the following indent shall be inserted after the fourth indent:

— if the device incorporates, as an integral part, a substance or human blood derivative referred to in Section 10 of Annex 1, the data on the tests conducted in this connection which are required to assess the safety, quality and usefulness of that substance, or human blood derivative, taking account of the intended purpose of the device,;

(e) the following two sections shall be added:

4. The information included in the declarations covered by this Annex shall be kept for a period of at least 15 years from the date of manufacture of the last product.

5. For custom-made devices, the manufacturer must undertake to review and to document experience gained in the post-production phase, including the provisions referred to in Annex 7, and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them and the relevant corrective actions:

(i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;

(ii) any technical or medical reason connected with the characteristics or performance of a device for the reasons referred to in point (i) leading to systematic recall of devices of the same type by the manufacturer.;

7. Annex 7 shall be amended as follows:

(a) Section 1 shall be replaced by the following:

1. General provisions

1.1. As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances referred to in Sections 1 and 2 of Annex 1 under the normal conditions of use of the device and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio referred to in Section 5 of Annex 1, must be based on clinical data. The evaluation of this data (hereinafter referred to as clinical evaluation), where appropriate taking account of any relevant harmonised standards, must follow a defined and methodologically sound procedure based on:

1.1.1. Either a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device where:

— there is demonstration of equivalence of the device to the device to which the data relates and,

— the data adequately demonstrate compliance with the relevant essential requirements;

1.1.2. Or a critical evaluation of the results of all the clinical investigations made,

1.1.3. Or a critical evaluation of the combined clinical data provided in 1.1.1 and 1.1.2.

1.2. Clinical investigations shall be performed unless it is duly justified to rely on existing clinical data.

1.3. The clinical evaluation and its outcome shall be documented. This documentation shall be included and/or fully referenced in the technical documentation of the device.

1.4. The clinical evaluation and its documentation must be actively updated with data obtained from the post-market surveillance. Where post-market clinical follow-up as part of the post-market surveillance plan for the device is not deemed necessary, this must be duly justified and documented.

1.5. Where demonstration of conformity with essential requirements based on clinical data is not deemed appropriate, adequate justification for any such exclusion has to be given based on risk management output and under consideration of the specifics of the device/body interaction, the clinical performances intended and the claims of the manufacturer. Adequacy of demonstration of conformity with the essential requirements by performance evaluation, bench testing and pre-clinical evaluation alone has to be duly substantiated.

1.6. All data must remain confidential unless it is deemed essential that they be divulged.

(b) Section 2.3.5 shall be replaced by the following:

2.3.5. All serious adverse events must be fully recorded and immediately notified to all competent authorities of the Member States in which the clinical investigation is being performed.

(c) In Section 2.3.6, the words ‘appropriately qualified medical specialist’ shall be replaced by the words ‘duly qualified medical practitioner or authorised person’.

ANNEX II

Annexes I to X to Directive 93/42/EEC shall be amended as follows:

1. Annex I shall be amended as follows:

(a) Section 1 shall be replaced by the following:

1. The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their intended use constitute acceptable risks when weighed

against the benefits to the patient and are compatible with a high level of protection of health and safety.

This shall include:

— reducing, as far as possible, the risk of use error due to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and

— consideration of the technical knowledge, experience, education and training and where applicable the medical and physical conditions of intended users (design for lay, professional, disabled or other users).;

(b) the following Section shall be inserted:

6a. Demonstration of conformity with the essential requirements must include a clinical evaluation in accordance with Annex X.;

(c) in Section 7.1, the following indent shall be added:

— where appropriate, the results of biophysical or modelling research whose validity has been demonstrated beforehand.;

(d) Section 7.4. shall be replaced by the following:

7.4. Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in Article 1 of Directive 2001/83/EC and which is liable to act upon the body with action ancillary to that of the device, the quality, safety and usefulness of the substance must be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC.

For the substances referred to in the first paragraph, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking account of the intended purpose of the device, seek a scientific opinion from one of the competent authorities designated by the Member States or the European Medicines Agency (EMEA) acting particularly through its committee in accordance with Regulation (EC) No 726/2004[(4)] on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the substance into the device. When issuing its opinion, the competent authority or the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body.

Where a device incorporates, as an integral part, a human blood derivative, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking into account the intended purpose of the device, seek a scientific opinion from the EMEA, acting particularly through its committee, on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the human blood derivative into the device. When issuing its opinion, the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body.

Where changes are made to an ancillary substance incorporated in a device, in particular related to its manufacturing process, the notified body shall be

informed of the changes and shall consult the relevant medicines competent authority (i.e. the one involved in the initial consultation), in order to confirm that the quality and safety of the ancillary substance are maintained. The competent authority shall take into account the data related to the usefulness of incorporation of the substance into the device as determined by the notified body, in order to ensure that the changes have no negative impact on the established benefit/risk profile of the addition of the substance in the medical device.

When the relevant medicines competent authority (i.e. the one involved in the initial consultation) has obtained information on the ancillary substance, which could have an impact on the established benefit/risk profile of the addition of the substance in the medical device, it shall provide the notified body with advice, whether this information has an impact on the established benefit/risk profile of the addition of the substance in the medical device or not. The notified body shall take the updated scientific opinion into account in reconsidering its assessment of the conformity assessment procedure.

(e) Section 7.5 shall be replaced by the following:

7.5. The devices must be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction, in accordance with Annex I to Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances[(5)].

If parts of a device (or a device itself) intended to administer and/or remove medicines, body liquids or other substances to or from the body, or devices intended for transport and storage of such body fluids or substances, contain phthalates which are classified as carcinogenic, mutagenic or toxic to reproduction, of category 1 or 2, in accordance with Annex I to Directive 67/548/EEC, these devices must be labelled on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging as a device containing phthalates.

If the intended use of such devices includes treatment of children or treatment of pregnant or nursing women, the manufacturer must provide a specific justification for the use of these substances with regard to compliance with the essential requirements, in particular of this paragraph, within the technical documentation and, within the instructions for use, information on residual risks for these patient groups and, if applicable, on appropriate precautionary measures.

(f) in Section 8.2, the word ‘transferable’ shall be replaced by the word ‘transmissible’;

(g) the following Section shall be inserted:

12.1a For devices which incorporate software or which are medical software in themselves, the software must be validated according to the state of the art taking into account the principles

of development lifecycle, risk management, validation and verification.;

(h) in Section 13.1, the first paragraph shall be replaced by the following:

13.1. Each device must be accompanied by the information needed to use it safely and properly, taking account of the training and knowledge of the potential users, and to identify the manufacturer.;

(i) Section 13.3 shall be amended as follows:

(i) point (a) shall be replaced by the following:

(a) the name or trade name and address of the manufacturer. For devices imported into the Community, in view of their distribution in the Community, the label, or the outer packaging, or instructions for use, shall contain in addition the name and address of the authorised representative where the manufacturer does not have a registered place of business in the Community;

(ii) point (b) shall be replaced by the following:

(b) the details strictly necessary to identify the device and the contents of the packaging especially for the users;

(iii) point (f) shall be replaced by the following:

(f) where appropriate, an indication that the device is for single use. A manufacturer's indication of single use must be consistent across the Community;

(j) Section 13.6 shall be amended as follows:

(i) the following subparagraph shall be added to point (h):

If the device bears an indication that the device is for single use, information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used. If in accordance with Section 13.1 no instructions for use are needed, the information must be made available to the user upon request;

(ii) point (o) shall be replaced by the following:

(o) medicinal substances, or human blood derivatives incorporated into the device as an integral part in accordance with Section 7.4;

(iii) the following point shall be added:

(q) date of issue or the latest revision of the instructions for use.;

(k) Section 14 shall be deleted.

2. Annex II shall be amended as follows:

(a) Section 2 shall be replaced by the following:

2. The EC declaration of conformity is the procedure whereby the manufacturer who fulfils the obligations imposed by Section 1 ensures and declares that the products concerned meet the provisions of this Directive which apply to them.

The manufacturer must affix the CE marking in accordance with Article 17 and draw up a written declaration of conformity. This declaration must cover one or more medical devices manufactured, clearly identified by means of product name, product code or other unambiguous reference and must be kept by the manufacturer.;

(b) in Section 3.1, second paragraph, the introductory part of the seventh indent shall be replaced by the following:

— an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase, including the provisions referred to in Annex X, and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:;

(c) Section 3.2 shall be amended as follows:

(i) the following paragraph shall be inserted after the first paragraph:

It shall include in particular the corresponding documentation, data and records arising from the procedures referred to in point (c).;

(ii) in point (b), the following indent shall be added:

— where the design, manufacture and/or final inspection and testing of the products, or elements thereof, is carried out by a third party, the methods of monitoring the efficient operation of the quality system and in particular the type and extent of control applied to the third party;

(iii) point (c) shall be replaced by the following:

(c) the procedures for monitoring and verifying the design of the products, including the corresponding documentation, and in particular:

— a general description of the product, including any variants planned, and its intended use(s),

— the design specifications, including the standards which will be applied and the results of the risk analysis, and also a description of the solutions adopted to fulfil the essential requirements which apply to the products if the standards referred to in Article 5 are not applied in full,

— the techniques used to control and verify the design and the processes and systematic measures which will be used when the products are being designed,

- if the device is to be connected to other device(s) in order to operate as intended, proof must be provided that it conforms to the essential requirements when connected to any such device(s) having the characteristics specified by the manufacturer,
- a statement indicating whether or not the device incorporates, as an integral part, a substance or a human blood derivative referred to in section 7.4 of Annex I and the data on the tests conducted in this connection required to assess the safety, quality and usefulness of that substance or human blood derivative, taking account of the intended purpose of the device,
- a statement indicating whether or not the device is manufactured utilising tissues of animal origin as referred to in Commission Directive 2003/32/EC[6],
- the solutions adopted as referred to in Annex I, Chapter I, Section 2,
- the pre-clinical evaluation,
- the clinical evaluation referred to in Annex X,
- the draft label and, where appropriate, instructions for use.

(d) the second paragraph of Section 3.3 shall be replaced by the following:

> The assessment team must include at least one member with past experience of assessments of the technology concerned. The assessment procedure must include an assessment, on a representative basis, of the documentation of the design of the product(s) concerned, an inspection on the manufacturer's premises and, in duly substantiated cases, on the premises of the manufacturer's suppliers and/or subcontractors to inspect the manufacturing processes.;

(e) in Section 4.3, the second and third paragraphs shall be replaced by the following:

> In the case of devices referred to in Annex I, Section 7.4, second paragraph, the notified body shall, as regards the aspects referred to in that section, consult one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC or the EMEA before taking a decision. The opinion of the competent national authority or the EMEA must be drawn up within 210 days after receipt of valid documentation. The scientific opinion of the competent national authority or the EMEA must be included in the documentation concerning the device. The notified body will give due consideration to the views expressed in this consultation when making its decision. It will convey its final decision to the competent body concerned.
>
> In the case of devices referred to in Annex I, Section 7.4, third paragraph, the scientific opinion of the EMEA must be included in the documentation concerning the device. The opinion of the EMEA must be drawn up within

210 days after receipt of valid documentation. The notified body will give due consideration to the opinion of the EMEA when making its decision. The notified body may not deliver the certificate if the EMEA's scientific opinion is unfavourable. It will convey its final decision to the EMEA.

In the case of devices manufactured utilising tissues of animal origin as referred to in Directive 2003/32/EC, the notified body must follow the procedures referred to in that Directive.;

(f) in Section 5.2, the second indent shall be replaced by the following:

— the data stipulated in the part of the quality system relating to design, such as the results of analyses, calculations, tests, the solutions adopted as referred to in Annex I, Chapter I, Section 2, pre-clinical and clinical evaluation, post-market clinical follow-up plan and the results of the post-market clinical follow-up, if applicable, etc.,;

(g) Section 6.1 shall be amended as follows:

(i) the introductory part shall be replaced by the following:

The manufacturer or his authorised representative must, for a period ending at least five years, and in the case of implantable devices at least 15 years, after the last product has been manufactured, keep at the disposal of the national authorities:;

(ii) the following phrase shall be added to the second indent:

and in particular the documentation, data and records referred to in the second paragraph of Section 3.2,;

(h) Section 6.3 shall be deleted;

(i) Section 7 shall be replaced by the following:

7. Application to devices in Classes IIa and IIb.

7.1. In line with Article 11(2) and (3), this Annex may apply to products in Classes IIa and IIb. Section 4, however, does not apply.

7.2. For devices in Class IIa the notified body shall assess, as part of the assessment in Section 3.3, the technical documentation as described in Section 3.2(c) for at least one representative sample for each device subcategory for compliance with the provisions of this Directive.

7.3. For devices in Class IIb the notified body shall assess, as part of the assessment in Section 3.3, the technical documentation as described in Section 3.2(c) for at least one representative sample for each generic device group for compliance with the provisions of this Directive.

7.4. In choosing representative sample(s) the notified body shall take into account the novelty of the technology, similarities in design, technology, manufacturing and sterilisation methods, the intended use and the results of any previous relevant assessments (e.g. with regard to physical, chemical or biological properties) that have

been carried out in accordance with this Directive. The notified body shall document and keep available to the competent authority its rationale for the sample(s) taken.

7.5. Further samples shall be assessed by the notified body as part of the surveillance assessment referred to in Section 5.;

(j) in Section 8, the words 'Article 4(3) of Directive 89/381/EEC' shall be replaced by the words 'Article 114(2) of Directive 2001/83/EC';

3. Annex III shall be amended as follows:

(a) Section 3 shall be replaced by the following:

3. The documentation must allow an understanding of the design, the manufacture and the performances of the product and must contain the following items in particular:

— a general description of the type, including any variants planned, and its intended use(s),

— design drawings, methods of manufacture envisaged, in particular as regards sterilisation, and diagrams of components, sub-assemblies, circuits, etc.,

— the descriptions and explanations necessary to understand the abovementioned drawings and diagrams and the operation of the product,

— a list of the standards referred to in Article 5, applied in full or in part, and descriptions of the solutions adopted to meet the essential requirements if the standards referred to in Article 5 have not been applied in full,

— the results of the design calculations, risk analysis, investigations, technical tests, etc. carried out,

— a statement indicating whether or not the device incorporates, as an integral part, a substance, or human blood derivative, referred to in Section 7.4 of Annex I, and the data on the tests conducted in this connection which are required to assess the safety, quality and usefulness of that substance, or human blood derivative, taking account of the intended purpose of the device,

— a statement indicating whether or not the device is manufactured utilising tissues of animal origin as referred to in Directive 2003/32/EC,

— the solutions adopted as referred to in Annex I, Chapter I, Section 2,

— the pre-clinical evaluation,

— the clinical evaluation referred to in Annex X,

— the draft label and, where appropriate, instructions for use.;

(b) in Section 5, the second and third paragraphs shall be replaced by the following:

In the case of devices referred to in Annex I, Section 7.4, second paragraph, the notified body shall, as regards the aspects referred to in that section, consult one of the authorities designated by the Member States in accordance with Directive 2001/83/EC or the EMEA before taking a decision. The opinion of the competent national authority or the EMEA

must be drawn up within 210 days after receipt of valid documentation. The scientific opinion of the competent national authority or the EMEA must be included in the documentation concerning the device. The notified body will give due consideration to the views expressed in this consultation when making its decision. It will convey its final decision to the competent body concerned.

In the case of devices referred to in Annex I, Section 7.4, third paragraph, the scientific opinion of the EMEA must be included in the documentation concerning the device. The opinion of the EMEA must be drawn up within 210 days after receipt of valid documentation. The notified body will give due consideration to the opinion of the EMEA when making its decision. The notified body may not deliver the certificate if the EMEA's scientific opinion is unfavourable. It will convey its final decision to the EMEA.

In the case of devices manufactured utilising tissues of animal origin as referred to in Directive 2003/32/EC, the notified body must follow the procedures referred to in that Directive.;

(c) Section 7.3 shall be replaced by the following:

7.3. The manufacturer or his authorised representative must keep with the technical documentation copies of EC type-examination certificates and their additions for a period ending at least five years after the last device has been manufactured. In the case of implantable devices, the period shall be at least 15 years after the last product has been manufactured.;

(d) Section 7.4 shall be deleted;

4. Annex IV shall be amended as follows:

(a) in Section 1, the words ‘established in the Community’ shall be deleted;

(b) in Section 3, the first paragraph shall be replaced by the following:

3. The manufacturer must undertake to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase, including the provisions referred to in Annex X, and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:;

(c) Section 6.3 shall be replaced by the following:

6.3. Statistical control of products will be based on attributes and/or variables, entailing sampling schemes with operational characteristics which ensure a high level of safety and performance according to the state of the art. The sampling schemes will be established by the harmonised standards referred to in Article 5, taking account of the specific nature of the product categories in question.;

(d) in Section 7, the introductory part shall be replaced by the following:

The manufacturer or his authorised representative must, for a period ending at least five years, and in the case of implantable devices at least 15 years, after the last product has been manufactured, make available to the national authorities:;

(e) in the introductory part of Section 8 the word ‘exemptions’ shall be deleted;

(f) in Section 9, the words ‘Article 4(3) of Directive 89/381/EEC’ shall be replaced by the words ‘Article 114(2) of Directive 2001/83/EC’;

5. Annex V shall be amended as follows:

(a) Section 2 shall be replaced by the following:

2. The EC declaration of conformity is the part of the procedure whereby the manufacturer who fulfils the obligations imposed by Section 1 ensures and declares that the products concerned conform to the type described in the EC type-examination certificate and meet the provisions of this Directive which apply to them.

The manufacturer must affix the CE marking in accordance with Article 17 and draw up a written declaration of conformity. This declaration must cover one or more medical devices manufactured, clearly identified by means of product name, product code or other unambiguous reference, and must be kept by the manufacturer.;

(b) in the eighth indent of the second paragraph of Section 3.1, the introductory part shall be replaced by the following:

— an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase, including the provisions referred to in Annex X, and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them;;

(c) in point (b) of the third paragraph of Section 3.2, the following indent shall be added:

— where the manufacture and/or final inspection and testing of the products, or elements thereof, are carried out by a third party, the methods of monitoring the efficient operation of the quality system and in particular the type and extent of control applied to the third party;

(d) in Section 4.2, the following indent shall be inserted after the first indent:

— the technical documentation,;

(e) in Section 5.1, the introductory part shall be replaced by the following:

The manufacturer or his authorised representative must, for a period ending at least five years, and in the case of implantable devices at least 15 years, after the last product has been manufactured, make available to the national authorities:;

(f) Section 6 shall be replaced by the following:

6. Application to devices in Class IIa

In line with Article 11(2), this Annex may apply to products in Class IIa, subject to the following:

6.1. By way of derogation from Sections 2, 3.1 and 3.2, by virtue of the declaration of conformity the manufacturer ensures and declares that the products in Class IIa are manufactured in conformity with the technical documentation referred to in Section 3 of Annex VII and meet the requirements of this Directive which apply to them.

6.2. For devices in Class IIa the notified body shall assess, as part of the assessment in Section 3.3, the technical documentation as described in Section 3 of Annex VII for at least one representative sample for each device subcategory for compliance with the provisions of this Directive.

6.3. In choosing representative sample(s) the notified body shall take into account the novelty of the technology, similarities in design, technology, manufacturing and sterilisation methods, the intended use and the results of any previous relevant assessments (e.g. with regard to physical, chemical or biological properties) that have been carried out in accordance with this Directive. The notified body shall document and keep available to the competent authority its rationale for the sample(s) taken.

6.4. Further samples shall be assessed by the notified body as part of the surveillance assessment referred to in Section 4.3.;

(g) in Section 7, the words ‘Article 4(3) of Directive 89/381/EEC’ shall be replaced by the words ‘Article 114(2) of Directive 2001/83/EC’;

6. Annex VI shall be amended as follows:

(a) Section 2 shall be replaced by the following:

2. The EC declaration of conformity is the part of the procedure whereby the manufacturer who fulfils the obligations imposed by Section 1 ensures and declares that the products concerned conform to the type described in the EC type-examination certificate and meet the provisions of this Directive which apply to them.

The manufacturer affixes the CE marking in accordance with Article 17 and draws up a written declaration of conformity. This declaration must cover one or more medical devices manufactured, clearly identified by means of product name, product code or other unambiguous reference, and be kept by the manufacturer. The CE marking must be accompanied by the identification number of the notified body which performs the tasks referred to in this Annex.;

(b) in the eighth indent of the second paragraph of Section 3.1, the introductory part shall be replaced by the following:

— an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase, including the provisions referred

to in Annex X, and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:;

(c) in Section 3.2, the following indent shall be added:

— where the final inspection and testing of the products, or elements thereof, are carried out by a third party, the methods of monitoring the efficient operation of the quality system and in particular the type and extent of control applied to the third party;

(d) in Section 5.1, the introductory part shall be replaced by the following:

The manufacturer or his authorised representative must, for a period ending at least five years, and in the case of implantable devices at least 15 years, after the last product has been manufactured, make available to the national authorities:;

(e) Section 6 shall be replaced by the following:

6. Application to devices in Class IIa

In line with Article 11(2), this Annex may apply to products in Class IIa, subject to the following:

6.1. By way of derogation from Sections 2, 3.1 and 3.2, by virtue of the declaration of conformity the manufacturer ensures and declares that the products in Class IIa are manufactured in conformity with the technical documentation referred to in Section 3 of Annex VII and meet the requirements of this Directive which apply to them.

6.2. For devices in Class IIa the notified body shall assess, as part of the assessment in Section 3.3, the technical documentation as described in Section 3 of Annex VII for at least one representative sample for each device subcategory for compliance with the provisions of this Directive.

6.3. In choosing representative sample(s) the notified body shall take into account the novelty of the technology, similarities in design, technology, manufacturing and sterilisation methods, the intended use and the results of any previous relevant assessments (e.g. with regard to physical, chemical or biological properties) that have been carried out in accordance with this Directive. The notified body shall document and keep available to the competent authority its rationale for the sample(s) taken.

6.4. Further samples shall be assessed by the notified body as part of the surveillance assessment referred to in Section 4.3.;

7. Annex VII shall be amended as follows:

(a) Sections 1 and 2 shall be replaced by the following:

1. The EC declaration of conformity is the procedure whereby the manufacturer or his authorised representative who fulfils the obligations imposed by Section 2 and, in the case of products placed on the market in a sterile condition and devices with a

measuring function, the obligations imposed by Section 5 ensures and declares that the products concerned meet the provisions of this Directive which apply to them.

2. The manufacturer must prepare the technical documentation described in Section 3. The manufacturer or his authorised representative must make this documentation, including the declaration of conformity, available to the national authorities for inspection purposes for a period ending at least five years after the last product has been manufactured. In the case of implantable devices the period shall be at least 15 years after the last product has been manufactured.;

(b) Section 3 shall be amended as follows:

(i) the first indent shall be replaced by the following:

— a general description of the product, including any variants planned and its intended use(s),;

(ii) the fifth indent shall be replaced by the following:

— in the case of products placed on the market in a sterile condition, description of the methods used and the validation report,;

(iii) the seventh indent shall be replaced by the following indents:

— the solutions adopted as referred to in Annex I, Chapter I, Section 2,

— the pre-clinical evaluation,;

(iv) the following indent shall be inserted after the seventh indent:

— the clinical evaluation in accordance with Annex X,;

(c) in Section 4, the introductory part shall be replaced by the following:

4. The manufacturer shall institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase, including the provisions referred to in Annex X, and to implement appropriate means to apply any necessary corrective actions, taking account of the nature and risks in relation to the product. He shall notify the competent authorities of the following incidents immediately on learning of them:;

(d) in Section 5, the words ‘Annex IV, V or VI’ shall be replaced by the words ‘Annex II, IV, V or VI’;

8. Annex VIII shall be amended as follows:

(a) in Section 1, the words ‘established in the Community’ shall be deleted;

(b) Section 2.1 shall be amended as follows:

(i) the following indent shall be inserted after the introductory phrase:

— the name and address of the manufacturer,;

(ii) the fourth indent shall be replaced by the following:

— the specific characteristics of the product as indicated by the prescription,;

(c) Section 2.2 shall be amended as follows:

(i) the second indent shall be replaced by the following:

— the clinical investigation plan,;

(ii) the following indents shall be inserted after the second indent:

— the investigator's brochure,

— the confirmation of insurance of subjects,

— the documents used to obtain informed consent,

— a statement indicating whether or not the device incorporates, as an integral part, a substance or human blood derivative referred to in Section 7.4 of Annex I,

— a statement indicating whether or not the device is manufactured utilising tissues of animal origin as referred to in Directive 2003/32/EC,;

(d) in Section 3.1, the first paragraph shall be replaced by the following:

3.1. For custom-made devices, documentation, indicating manufacturing site(s) and allowing an understanding of the design, manufacture and performances of the product, including the expected performances, so as to allow assessment of conformity with the requirements of this Directive.;

(e) Section 3.2 shall be replaced by the following:

3.2. For devices intended for clinical investigations, the documentation must contain:

— a general description of the product and its intended use,

— design drawings, methods of manufacture envisaged, in particular as regards sterilisation, and diagrams of components, sub-assemblies, circuits, etc.,

— the descriptions and explanations necessary to understand the abovementioned drawings and diagrams and the operation of the product,

— the results of the risk analysis and a list of the standards referred to in Article 5, applied in full or in part, and descriptions of the solutions adopted to meet the essential requirements of this Directive if the standards referred to in Article 5 have not been applied,

— if the device incorporates, as an integral part, a substance or human blood derivative referred to in Section 7.4 of Annex I, the data on the tests conducted in this connection which are required to assess the safety, quality and usefulness of that substance or human blood derivative, taking account of the intended purpose of the device,

— if the device is manufactured utilising tissues of animal origin as referred to in Directive 2003/32/EC, the risk management measures in this connection which have been applied to reduce the risk of infection,

— the results of the design calculations, and of the inspections and technical tests carried out, etc.

The manufacturer must take all the measures necessary to ensure that the manufacturing process produces products which are manufactured in accordance with the documentation referred to in the first paragraph of this Section.

The manufacturer must authorise the assessment, or audit where necessary, of the effectiveness of these measures.;

(f) Section 4 shall be replaced by the following:

4. The information contained in the declarations concerned by this Annex shall be kept for a period of time of at least five years. In the case of implantable devices the period shall be at least 15 years.;

(g) the following section shall be added:

5. For custom-made devices, the manufacturer must undertake to review and document experience gained in the post-production phase, including the provisions referred to in Annex X, and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them and the relevant corrective actions:

(i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;

(ii) any technical or medical reason connected with the characteristics or performance of a device for the reasons referred to in subparagraph (i) leading to systematic recall of devices of the same type by the manufacturer.;

9. Annex IX shall be amended as follows:

(a) Chapter I shall be amended as follows:

(i) in Section 1.4, the following sentence shall be added:

Stand alone software is considered to be an active medical device.;

(ii) Section 1.7 shall be replaced by the following:

1.7. Central circulatory system

For the purposes of this Directive, “central circulatory system” means the following vessels:

arteriae pulmonales, aorta ascendens, arcus aorta, aorta descendens to the bifurcatio aortae, arteriae coronariae, arteria carotis communis, arteria carotis externa, arteria carotis interna, arteriae

cerebrales, truncus brachiocephalicus, venae cordis, venae pulmonales, vena cava superior, vena cava inferior.;

(b) in Chapter II, Section 2, the following section shall be added:

2.6. In calculating the duration referred to in Section 1.1 of Chapter I, continuous use means "an uninterrupted actual use of the device for the intended purpose". However where usage of a device is discontinued in order for the device to be replaced immediately by the same or an identical device this shall be considered an extension of the continuous use of the device.;

(c) Chapter III shall be amended as follows:

(i) the introductory phrase of the first paragraph of Section 2.1 shall be replaced by the following:

All invasive devices with respect to body orifices, other than surgically invasive devices and which are not intended for connection to an active medical device or which are intended for connection to an active medical device in Class I:;

(ii) Section 2.2 shall be replaced by the following:

2.2. Rule 6

All surgically invasive devices intended for transient use are in Class IIa unless they are:

— intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with these parts of the body, in which case they are in Class III,

— reusable surgical instruments, in which case they are in Class I,

— intended specifically for use in direct contact with the central nervous system, in which case they are in Class III,

— intended to supply energy in the form of ionising radiation in which case they are in Class IIb,

— intended to have a biological effect or to be wholly or mainly absorbed in which case they are in Class IIb,

— intended to administer medicines by means of a delivery system, if this is done in a manner that is potentially hazardous taking account of the mode of application, in which case they are in Class IIb.;

(iii) in Section 2.3, the first indent shall be replaced by the following:

— either specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with these parts of the body, in which case they are in Class III,;

(iv) in Section 4.1, first paragraph, the reference '65/65/EEC' shall be replaced by the reference '2001/83/EC';

(v) in Section 4.1, the second paragraph shall be replaced by the following:

> All devices incorporating, as an integral part, a human blood derivative are in Class III.;

(vi) in Section 4.3, second paragraph, the following phrase shall be added:

> unless they are specifically to be used for disinfecting invasive devices in which case they are in Class IIb.;

(vii) in Section 4.4, the words 'Non-active devices' shall be replaced by the word 'Devices';

10. Annex X shall be amended as follows:

(a) Section 1.1 shall be replaced by the following:

1.1. As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I, under the normal conditions of use of the device, and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio referred to in Section 6 of Annex I, must be based on clinical data. The evaluation of this data, hereinafter referred to as "clinical evaluation", where appropriate taking account of any relevant harmonised standards, must follow a defined and methodologically sound procedure based on:

1.1.1. Either a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device, where:

— there is demonstration of equivalence of the device to the device to which the data relates, and

— the data adequately demonstrate compliance with the relevant essential requirements.

1.1.2. Or a critical evaluation of the results of all clinical investigations made.

1.1.3. Or a critical evaluation of the combined clinical data provided in 1.1.1 and 1.1.2.

(b) The following Sections shall be inserted:

1.1a In the case of implantable devices and devices in Class III clinical investigations shall be performed unless it is duly justified to rely on existing clinical data.

1.1b The clinical evaluation and its outcome shall be documented. This documentation shall be included and/or fully referenced in the technical documentation of the device.

1.1c The clinical evaluation and its documentation must be actively updated with data obtained from the post-market surveillance.

Where post-market clinical follow-up as part of the post-market surveillance plan for the device is not deemed necessary, this must be duly justified and documented.

1.1d Where demonstration of conformity with essential requirements based on clinical data is not deemed appropriate, adequate justification for any such exclusion has to be given based on risk management output and under consideration of the specifics of the device/body interaction, the clinical performances intended and the claims of the manufacturer. Adequacy of demonstration of conformity with the essential requirements by performance evaluation, bench testing and pre-clinical evaluation alone has to be duly substantiated.;

(c) in Section 2.2, the first sentence shall be replaced by the following:

Clinical investigations must be carried out in accordance with the Helsinki Declaration adopted by the 18th World Medical Assembly in Helsinki, Finland, in 1964, as last amended by the World Medical Assembly.;

(d) Section 2.3.5 shall be replaced by the following:

2.3.5. All serious adverse events must be fully recorded and immediately notified to all competent authorities of the Member States in which the clinical investigation is being performed..

(**1**) OJ L 159, 29.6.1996, p. 1.

(**2**) OJ L 180, 9.7.1997, p. 22.';

(**3**) Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1). Regulation as last amended by Regulation (EC) No 1901/2006.';

(**4**) Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1). Regulation as last amended by Regulation (EC) No 1901/2006.'

(**5**) OJ 196, 16.8.1967, p. 1. Directive as last amended by Directive 2006/121/EC of the European Parliament and of the Council (OJ L 396, 30.12.2006, p. 850).'

(**6**) Commission Directive 2003/32/EC of 23 April 2003 introducing detailed specifications as regards the requirements laid down in Council Directive 93/42/EEC with respect to medical devices manufactured utilising tissues of animal origin (OJ L 105, 26.4.2003, p. 18).'