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’.

(**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.';