ANNEX XIV

CLINICAL EVALUATION AND POST-MARKET CLINICAL FOLLOW-UP

PART A

CLINICAL EVALUATION

1. To plan, continuously conduct and document a clinical evaluation, manufacturers shall:

(a) establish and update a clinical evaluation plan, which shall include at least:

- an identification of the general safety and performance requirements that require support from relevant clinical data;
- a specification of the intended purpose of the device;
- a clear specification of intended target groups with clear indications and contra-indications;
- a detailed description of intended clinical benefits to patients with relevant and specified clinical outcome parameters;
- a specification of methods to be used for examination of qualitative and quantitative aspects of clinical safety with clear reference to the determination of residual risks and side-effects;
- an indicative list and specification of parameters to be used to determine, based on the state of the art in medicine, the acceptability of the benefit-risk ratio for the various indications and for the intended purpose or purposes of the device;
- an indication how benefit-risk issues relating to specific components such as use of pharmaceutical, non-viable animal or human tissues, are to be addressed; and
- a clinical development plan indicating progression from exploratory investigations, such as first-in-man studies, feasibility and pilot studies, to confirmatory investigations, such as pivotal clinical investigations, and a PMCF as referred to in Part B of this Annex with an indication of milestones and a description of potential acceptance criteria;

(b) identify available clinical data relevant to the device and its intended purpose and any gaps in clinical evidence through a systematic scientific literature review;

(c) appraise all relevant clinical data by evaluating their suitability for establishing the safety and performance of the device;

(d) generate, through properly designed clinical investigations in accordance with the clinical development plan, any new or additional clinical data necessary to address outstanding issues; and

(e) analyse all relevant clinical data in order to reach conclusions about the safety and clinical performance of the device including its clinical benefits.

2. The clinical evaluation shall be thorough and objective, and take into account both favourable and unfavourable data. Its depth and extent shall be proportionate and appropriate to the nature, classification, intended purpose and risks of the device in question, as well as to the manufacturer's claims in respect of the device.

3. A clinical evaluation may be based on clinical data relating to a device for which equivalence to the device in question can be demonstrated. The following technical, biological and clinical characteristics shall be taken into consideration for the demonstration of equivalence:

— Technical: the device is of similar design; is used under similar conditions of use; has similar specifications and properties including physicochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and software algorithms; uses similar deployment methods, where relevant; has similar principles of operation and critical performance requirements;

— Biological: the device uses the same materials or substances in contact with the same human tissues or body fluids for a similar kind and duration of contact and similar release characteristics of substances, including degradation products and leachables;

— Clinical: the device is used for the same clinical condition or purpose, including similar severity and stage of disease, at the same site in the body, in a similar population, including as regards age, anatomy and physiology; has the same kind of user; has similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.

The characteristics listed in the first paragraph shall be similar to the extent that there would be no clinically significant difference in the safety and clinical performance of the device. Considerations of equivalence shall be based on proper scientific justification. It shall be clearly demonstrated that manufacturers have sufficient levels of access to the data relating to devices with which they are claiming equivalence in order to justify their claims of equivalence.

4. The results of the clinical evaluation and the clinical evidence on which it is based shall be documented in a clinical evaluation report which shall support the assessment of the conformity of the device.

The clinical evidence together with non-clinical data generated from non-clinical testing methods and other relevant documentation shall allow the manufacturer to demonstrate conformity with the general safety and performance requirements and shall be part of the technical documentation for the device in question.

Both favourable and unfavourable data considered in the clinical evaluation shall be included in the technical documentation.

PART B

POST-MARKET CLINICAL FOLLOW-UP

5. PMCF shall be understood to be a continuous process that updates the clinical evaluation referred to in Article 61 and Part A of this Annex and shall be addressed in the manufacturer's post-market surveillance plan. When conducting PMCF, the manufacturer shall proactively collect and evaluate clinical data from the use in or on humans of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence.

6. PMCF shall be performed pursuant to a documented method laid down in a PMCF plan.

6.1. The PMCF plan shall specify the methods and procedures for proactively collecting and evaluating clinical data with the aim of:

(a) confirming the safety and performance of the device throughout its expected lifetime,

(b) identifying previously unknown side-effects and monitoring the identified side-effects and contraindications,

(c) identifying and analysing emergent risks on the basis of factual evidence,

(d) ensuring the continued acceptability of the benefit-risk ratio referred to in Sections 1 and 9 of Annex I, and

(e) identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

6.2. The PMCF plan shall include at least:

(a) the general methods and procedures of the PMCF to be applied, such as gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of clinical data;

(b) the specific methods and procedures of PMCF to be applied, such as evaluation of suitable registers or PMCF studies;

(c) a rationale for the appropriateness of the methods and procedures referred to in points (a) and (b);

(d) a reference to the relevant parts of the clinical evaluation report referred to in Section 4 and to the risk management referred to in Section 3 of Annex I;

(e) the specific objectives to be addressed by the PMCF;

(f) an evaluation of the clinical data relating to equivalent or similar devices;

(g) reference to any relevant CS, harmonised standards when used by the manufacturer, and relevant guidance on PMCF; and

(h) a detailed and adequately justified time schedule for PMCF activities (e.g. analysis of PMCF data and reporting) to be undertaken by the manufacturer.

7. The manufacturer shall analyse the findings of the PMCF and document the results in a PMCF evaluation report that shall be part of the clinical evaluation report and the technical documentation.

8. The conclusions of the PMCF evaluation report shall be taken into account for the clinical evaluation referred to in Article 61 and Part A of this Annex and in the risk management referred to in Section 3 of Annex I. If, through the PMCF, the need for preventive and/or corrective measures has been identified, the manufacturer shall implement them.

Status:
Point in time view as at 05/04/2017.

Changes to legislation:
There are currently no known outstanding effects for the Regulation (EU) 2017/745 of the European Parliament and of the Council, ANNEX XIV.