

Guidance document for the interpretation of significant changes in the framework of article 120: “Transitional provisions” of Regulation (EU) 2017/745.

**April 2019**

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## 1 – Background

Article 120 of Regulation (EU) 2017/745 provides transitional provisions, including the possibility of maintaining until 27 May 2024, if certain conditions are fulfilled, the validity of the certificates of conformity with Directives 93/42/EEC and 90/385/EEC valid on 26 May 2020.

One of the main conditions to continue to place on the market or put into service a medical device covered by a valid certificate issued pursuant to Directives 93/42/EEC and 90/385/EEC is the absence of any significant change in the design and intended purpose of the medical device covered by the scope of this certificate.

From 26 May 2020, any significant change in the design and intended purpose of a medical device covered by a certificate of conformity with the directives will result in invalidating the existing certificate. This provision applies regardless of the type of certificate to Directives 93/42/EEC and 90/385/EEC and concerns all classes of medical devices.

Manufacturers wishing to make such changes will have to submit an initial application for a conformity assessment of their medical device with Regulation (EU) 2017/745 in order to continue to place on the market or put into service their medical device.

Note: During the transition period, manufacturers are still allowed to make changes to their medical device and/or to introduce changes or enhancements to their quality management system provided that these actions do not affect the validity of certificates issued or do not constitute a significant change in the design or intended purpose of the device covered by this certificate.

## 2 – Scope and application

The purpose of this guidance document, developed by GMED, is to assist manufacturers in determining whether the change in the intended purpose or design of the device is a significant change referred to in Article 120 paragraph 3 of Regulation (EU) 2017/745, invalidating the certificates of conformity with the directives 93/42/CEE and 90/385/CEE for the modified medical device.

This guidance document constitutes a tool for identifying the regulatory consequences of modification project in terms of placing on the market or putting into service a medical device. Some changes will allow to continue to place on the market or put into service modified

medical device under the certificates of conformity to the applicable European directive. Other changes will require obtaining a certificate of conformity with Regulation (EU) 2017/745 before placing the device on the market or put into service the modified medical device. These regulatory consequences have a direct impact on the deployment of the marketing plan for the modified medical device both in terms of conformity assessment and deadline.

Are excluded from the scope of this guidance document:

- Organizational or administrative changes (manufacturing site, distributor, subcontractor, including their name, address and respective legal status), changes to the quality management system and any other change not impacting, directly or indirectly, the design or intended purpose of the medical device.
- Any changes in the design and intended purpose of the medical device related to a Field Safety Corrective Action (FSCA) assessed and accepted by the relevant Competent Authority. Therefore any change in the design and intended purpose of the medical device following a FSCA will not be considered as a significant change in accordance with Article 120 of Regulation (EU) 2017/745.

This document does not replace GMED guidance document for the interpretation of significant changes in the framework of EC type and EC design assessment (720 DM 0701-49) in accordance with Directives 93/42/EEC and 90/385/EEC.

For each change project, regardless of the class of the device concerned and regardless of the type of certificate of conformity to directives, the manufacturer shall use this guidance document to assess whether the change that he wishes to make to his medical device is a significant change in the design or intended purpose. This would impact the maintenance or not of the CE marking certificate in accordance with Directives, with regard to the provisions of article 120 of Regulation (EU) 2017/745. If the analysis concludes that there is a significant change in the design or intended purpose, an initial application for CE marking in accordance with Regulation (EU) 2017/745 must be submitted to GMED.

In case of devices subject to EC design examination or EC type examination, the manufacturer must also use GMED guidance document for the interpretation of significant changes in the framework of EC type and EC design assessment (720 DM 0701-49) to determine if the change to its device must be notified to GMED, including changes in the design and intended purpose that result to a FSCA evaluated and accepted by the relevant Competent Authority.

Therefore, the manufacturer's obligations to notify substantial changes to GMED under the applicable European Directives remain in effect throughout the transitional period. GMED continues to evaluate substantial changes in the quality management system, the product range covered and/or the approved model covered by one or more certificates of conformity with directives.

This guidance document based on NBOG's Best Practice Guide "Guidance for manufacturers and Notified Bodies on reporting design changes and changes of quality system" - NBOG BPG 2014-3. However, all changes to be reported to Notified Bodies in accordance with NBOGBPG 2014-3 shall not be considered as significant changes in design or intended purpose as mentioned in Article 120 of Regulation (EU) 2017/745.

The manufacturer is solely responsible for analyzing its change project to its medical device to determine whether or not the change will result in the invalidity of its certificate of conformity with Directives. If there are outstanding questions about a particular change, please contact your Certification Project Manager.

Warning:

This guidance document does not replace or affect regulatory documents, legislation, official guidelines and regulations. The definitions in this document are provided to clarify the meaning of terms used in this document. They do not replace or in any way affect definitions from regulatory documents, legislation, guidelines or official regulations.

GMED cannot be held responsible to different interpretation concerning the significant change in the design and intended purpose of a medical device under Article 120 of Regulation (EU) 2017/745 issued after this guide document by the European Commission.

### **3 – How to use this document**

The guidance document contains a detailed description of changes in the intended purpose and changes in the design of medical device considered significant in the context of the application of Article 120 of Regulation (EU) 2017/745.

For each change project, the manufacturer shall refer to this guidance document to assess whether the change will invalidate the existing certificate or not.

In addition to the changes described in parts 5 and 6 of this document, the manufacturer can refer to the flowcharts, which show various types of changes. These flowcharts allow the

manufacturer to decide whether the changes made to its medical device are considered significant changes or not according to Article 120 of Regulation (EU) 2017/745:

Flowchart n°1: Significant changes in the intended purpose

Flowchart n°2: Significant changes in the design

Flowchart n°3: Significant Changes in the design - Changes of a component or a material

Flowchart n°4: Significant changes in the design - Changes of sterilization method or packaging with impact to the sterilization

Flowchart n°5: Significant Changes in the design - Software Changes

When the manufacturer plans to change intended purpose of medical device, he must refer to Chapter 5 and use Flowchart n°1.

When the plan to change concerns the design of the device, the manufacturer must always refer to Chapter 6 paragraph (a) and use Flowchart n°2.

After having used Flowchart n°2 and rules defined in Chapter 6 (a) and when the proposed change project of the design of the medical device concerns more particularly a component or a material, the method of sterilization or the packaging necessary to preserve sterilization or software, the manufacturer must refer to the corresponding paragraph and Flowchart that has been developed in addition to Chapter 6 paragraph (a) and Flowchart n°2.

When considering several simultaneous changes, this guidance document must be used to assess each change separately, as well as the collective impact of changes.

## 4 – Definitions

"Significant change": A change is considered significant change when it is likely to have an impact in terms of:

- Safety, efficiency or performance;
- Compliance with the essential requirements of the applicable directive;
- Claims and intended use.

“intended purpose” : means the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation

“Field Safety Correction Action (FSCA)” is an action taken by the manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of the medical device that is already placed on the market.

For example, a FSCA might be performed by the manufacturer after becoming aware that the device:

- (1) May be hazardous to health;
- (2) May fail to conform to any claim made by the manufacturer relating to its effectiveness, benefits, performance characteristics or safety; or,
- (3) May not meet the requirements of the MDD.

Such actions, whether associated with direct or indirect harm, should be reported and should be notified to the Notified Body via a Field Safety Notice.

“Software” means the set of instructions used to control the actions or output of a medical device, to provide input to or output from a medical device, or to provide the actions of a medical device. This definition includes software that is imbedded or permanently a part of a medical device, software that is an accessory to a medical device, or software that is itself a medical device.

“Control mechanism” is a mean of verifying or checking that the specifications or outputs of the device meet a standard or predetermined result. They are mechanisms put in place to maintain on-going control or regulate the output of a device.

“Operating principles” are the means by which a device produces or leads to an intended or appropriate effect. They are the means by which a device is able to have a certain influence on a person or its surroundings.

“Supplier” designates the company supplying the raw material to a finished device manufacturer.

## **5 – Significant changes in the intended purpose – Flowchart n°1**

The following changes are considered significant changes in the intended purpose:

- Any changes related to the intended purpose excluding limitation of the intended purpose (example: when the manufacturer decides to restrict the use of its device to a particular user category due to analyzes of data collected in the post-market follow-up);

- Any changes about addition of final users or new patient target group;
- Any changes regarding a new indication or clinical practice.

## 6 – Significant changes in the design

Changes that could occur in the medical device design of are of various types. Thus GMED has defined very broadly the significant changes in design.

Further details about qualification criteria for significant changes in the design to component or material of device, sterilization method or sterile barrier system and software are also provided.

### a) Changes in the design – Flowchart n°2

Generally, any change in medical device design is considered to significant change when it has an impact in terms of safety, performance or usability and this impact requires the implementation of one of the following actions:

- Analysis of further clinical data;
- Analysis of further usability data;
- Analysis of a new risk introduced following change with need to have additional control means;
- Analysis of an already identified risk negatively impacted by the change.

Taking this into account, GMED considers the following changes as significant:

- Change of built-in control mechanism;
- Change in operating principle or mode of action;
- Change in type of energy source of medical device (e .g. transition from a thermal energy to electric).

### b) Changes related to a component or a Material - Flowchart n°3

Any change impacting a component or material is considered significant when it meets one of the following conditions:

- the component or material is human or animal origin;
- the change impacts the quality, safety or efficacy of a pharmaceutical substance\*;
- the change concerns a component or material that contains a pharmaceutical substance\* and impacts the component, material or quality, safety or efficacy of pharmaceutical substance\*;

- the component or material is in contact with body fluids or tissues for more than 30 days\*\*;
- the component or material is absorbed\*\*.

\*Pharmaceutical substance: Substance which, if used separately, can be considered to be a medicinal product, as defined in point 2 of Article 1 of Directive 2001/83/EC, and that has an action ancillary to that of the devices. GMED also considers that any active substance or active pharmaceutical ingredient in a device must be considered as a pharmaceutical substance, including when this substance is not used for its pharmacological, immunological or metabolic properties.

\*\* For this type of component or material, the change is not significant if and only if one of the following criteria is met:

- Modified or replaced component or material comes from the same supplier and meets the same specifications as the original component or material;
- Modified or replaced component or material comes from the same supplier and equivalence to the original component or material has been demonstrated;
- The component or material comes from a new supplier and meets the same specifications as the component or material provided by the original supplier;
- The component or material comes from a new supplier and equivalence with the original component or material has been demonstrated.

The demonstration of equivalence shall relate to characteristics and performances of the component or material. Differences shall not affect the characteristics or specifications of the finished product.

### **c) Changes of sterilization method or sterile barrier packaging - Flowchart n°4**

The following changes are considered significant changes in the design:

- Change of sterilization mode (e.g. the device is sterilized by irradiation and manufacturer wants to sterilize its device with ethylene oxide) ;
- Change of a material of the device having an impact on sterilization\*\*\* (e.g. addition of a new material known to retain a larger quantity of residues of ethylene oxide);

- Change in the design of the device having an impact on the sterilization\*\*\* (e.g. change of lumen dimension for an aspiration catheter or a drip chamber for an Infusion set);
- Change in packaging may adversely affect the function, safety, stability of the device or the integrity of the seal;
- Change of the lifetime and/or shelf-life validated by other methods or protocols than those of reference.

\*\*\*For Ethylene Oxide sterilization, please refer to standard EN ISO 11135 and guidance document AAMI TIR 28. For Radiation sterilization, please refer to standard EN ISO 11137-1. For Moist heat sterilization, please refer to EN ISO 17665-1. For Aseptic Process sterilization, please refer to EN ISO 13408-1.

#### **d) Software changes - Flowchart n°5**

Changes to software are considered significant when the functionality related to the diagnosis or therapy delivered to the patient are modified (e.g. change of usage or interpretation parameters) and relate to at least one of the following elements:

- major change of operating system requires a change in functionality of the software or system;
- new operating system (e.g. the software is only compatible with Android and manufacturer wants to extend the compatibility to iOS);
- new or modified architecture or database structure;
- change which impacts the control of the device;
- change of algorithm or data presentation with impact on software or system functionality;
- introduction of a new feature;
- introduction or removal of an alarm;
- data user input is no longer necessary because now the software makes a closed-loop decision ;
- New channel of inter-operability.

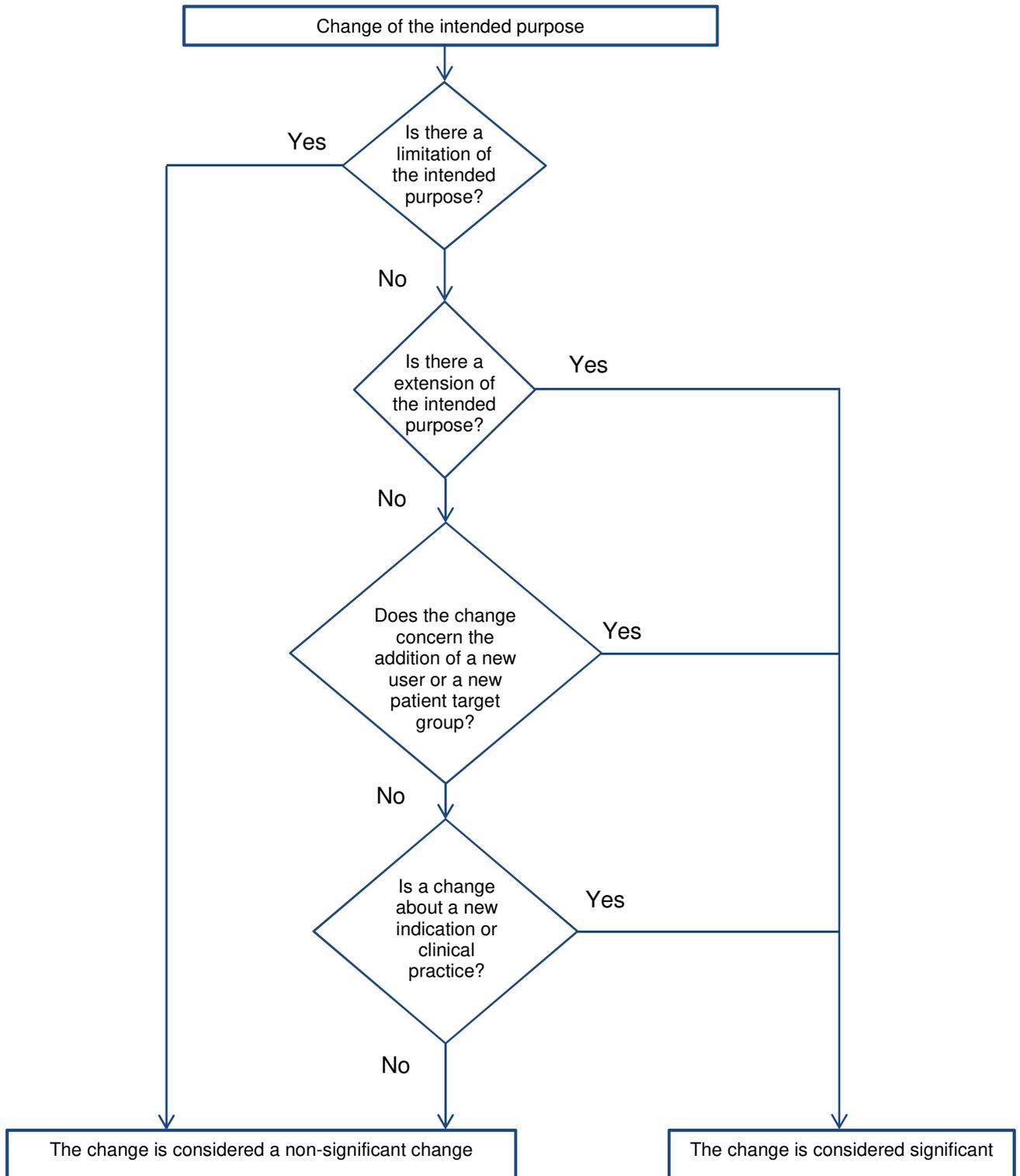
Software changes that have no impact on the diagnosis or therapy delivered to the patient can be considered as changes related to:

- an error correction that does not present risk for device safety and does not modify software or the system functionality ;

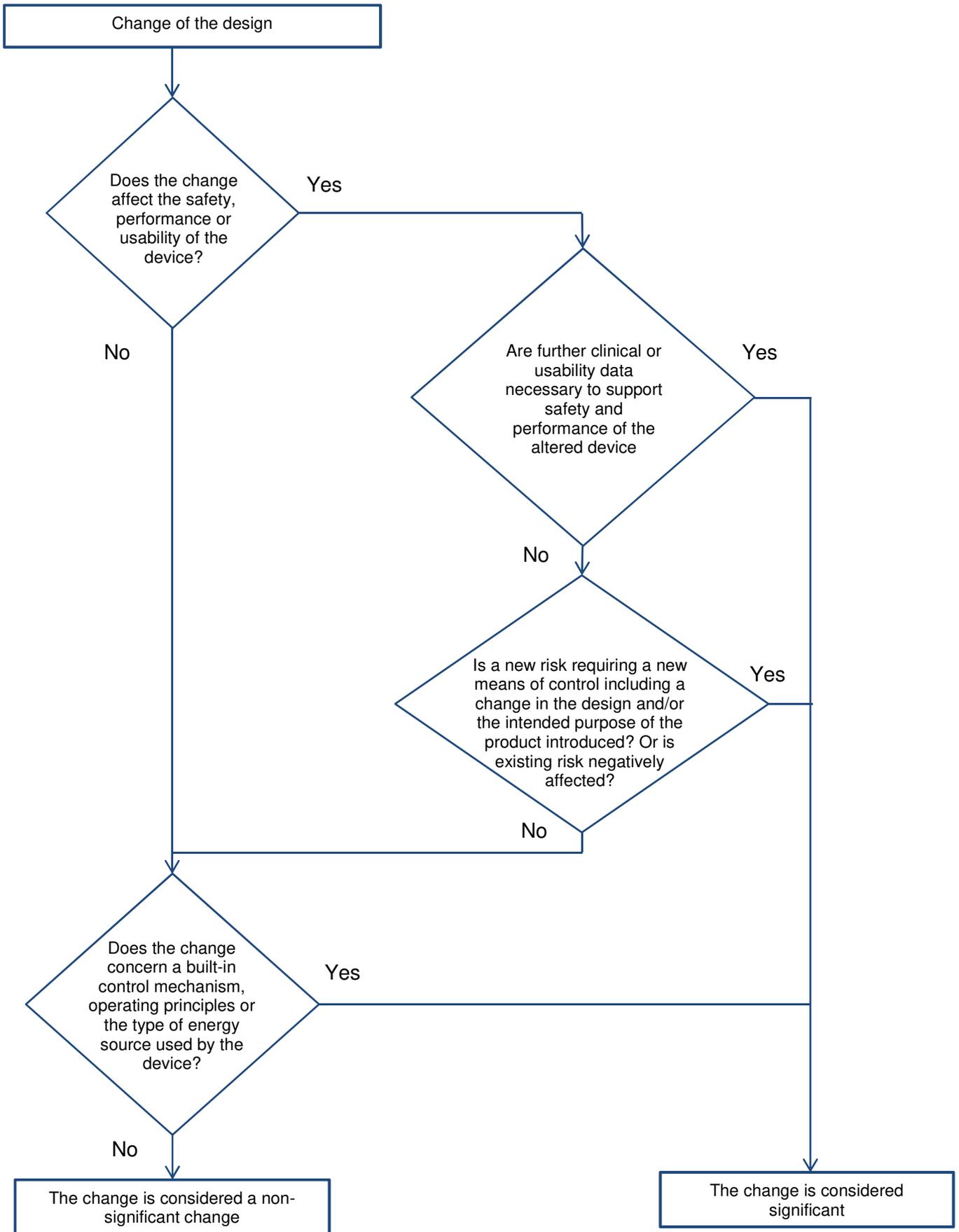
- a safety update (e.g. an improvement related to cyber security) ;
- a new non-medical functionality, a new feature that does not modify the software structure or responsible for medical functionality;
- Appearance of the user interface.

## 7 – Annex: Flowchart for decision-making

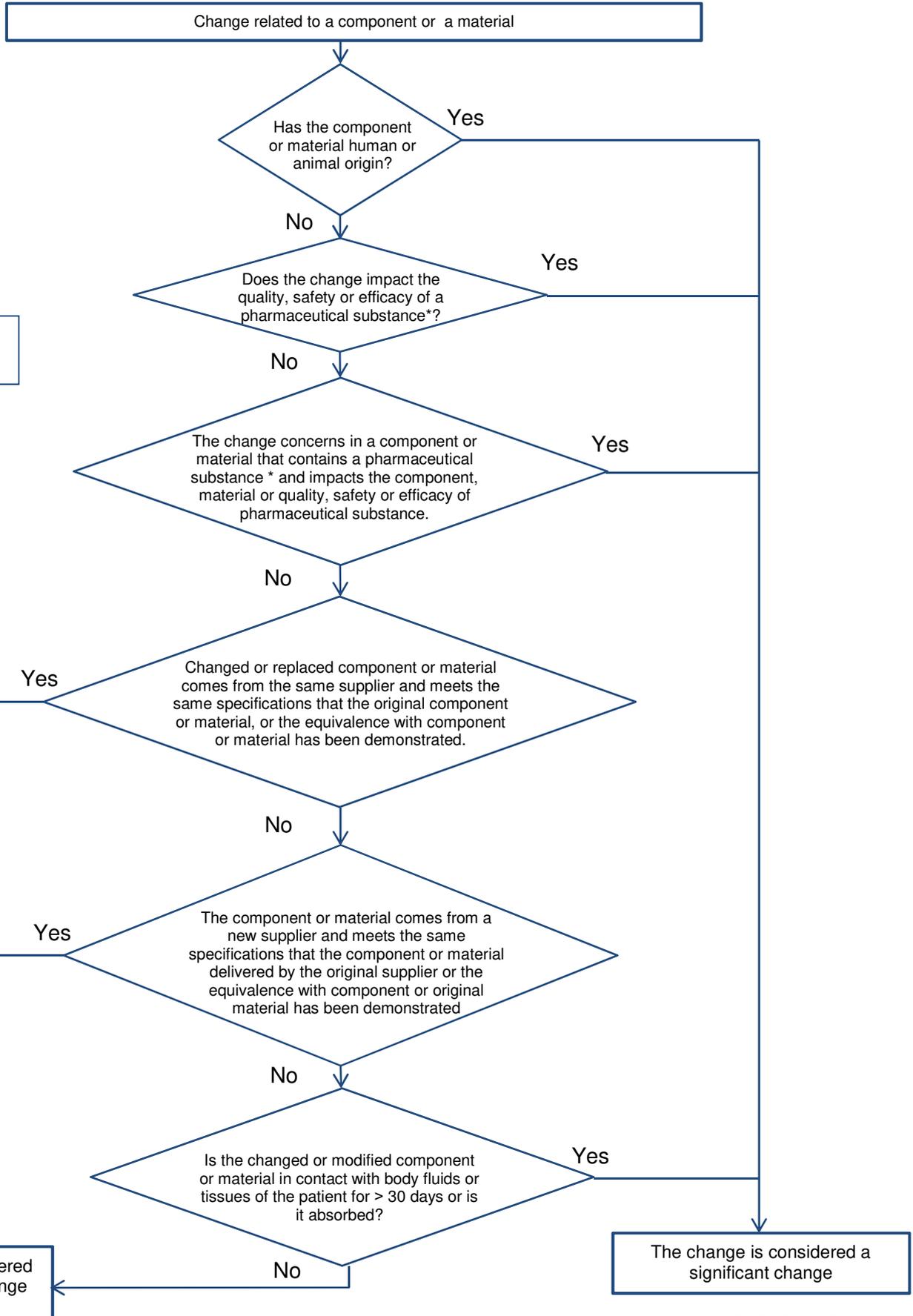
### Flowchart n°1: Significant changes in intended purpose



**Flowchart n°2: Significant changes in the design**

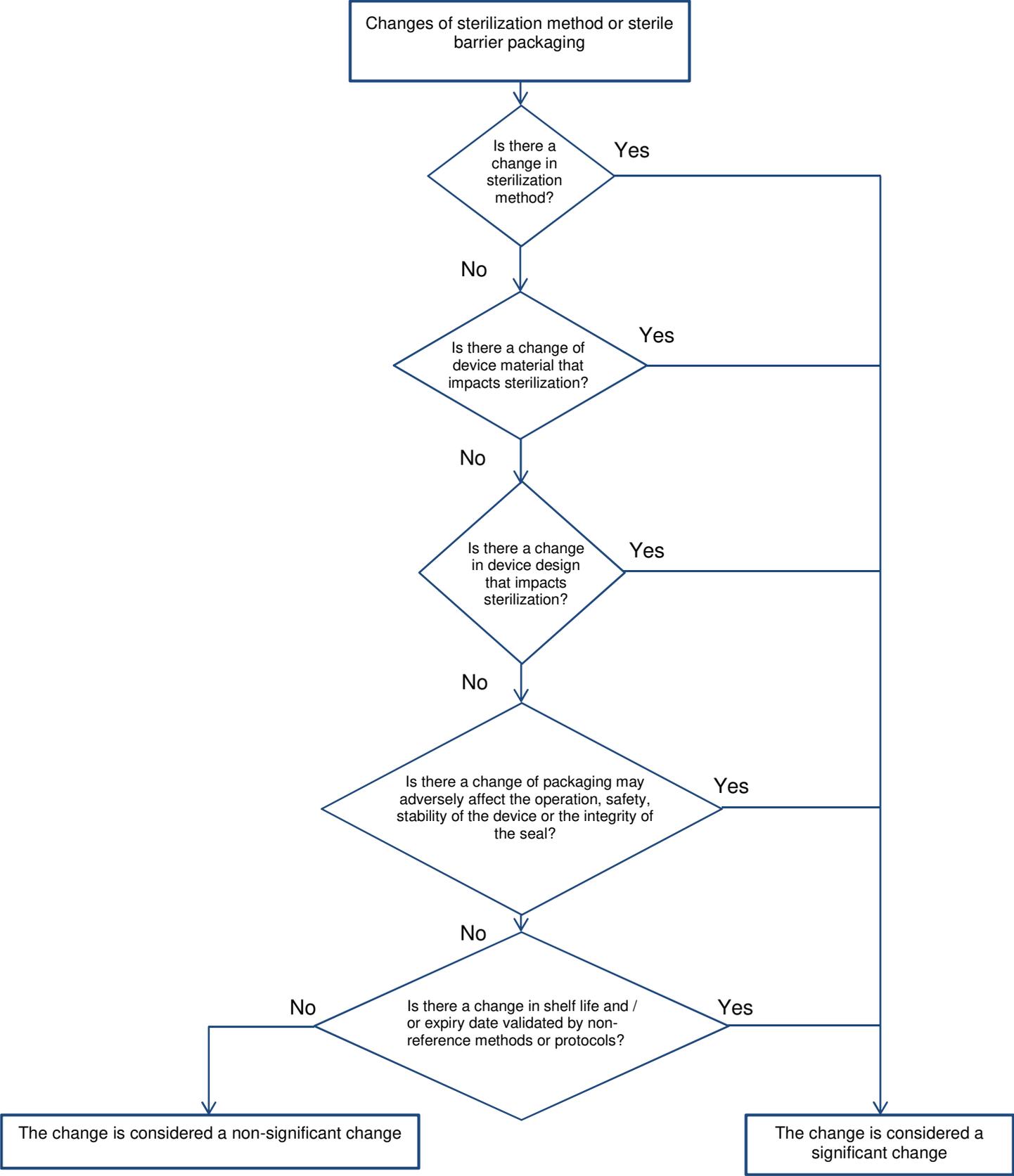


**Flowchart n°3: Significant changes in the design - Changes of a component or a Material**



\* Refer to the definition of a pharmaceutical substance mentioned in section 6b

**Diagramme 4: Significant changes in the design – Changes of sterilization method or packaging design with impact to the sterilisation**



**Diagramme 5 : Significant changes in the design – Software changes**

