The European Association Medical Devices - Notified Bodies

Team-NB Position Paper

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Changes to companion diagnostic devices under the IVDR, Annex IX, section 5.2 that require prior approval by a notified body.

1. Introduction

According to Annex IX (5.2 ((f)) of IVDR 2017/746, manufacturers shall inform notified bodies before making a change to a companion diagnostic device that affects the performance and/or the intended use and/or the suitability of the device in relation to the medicinal product concerned.

The notified body shall assess the planned changes and decide whether the planned changes require a new conformity assessment or whether they could be addressed by means of a supplement to the EU technical documentation assessment certificate.

In the latter case, the notified body shall assess the changes and determine if the opinion of the medicinal products authority consulted is required.

2. Scope

This position paper aims to provide guidance on the interpretation used by notified bodies to identify changes affecting the performance, suitability, or intended use of a companion diagnostic device that necessitate consultation with medicinal product authorities.

There are two scenarios for the consultations:

An initial consultation as per IVDR Annex IX, Sections 5.2(c), (d), and (e), or

A follow-up consultation as per IVDR Annex IX, Section 5.2(f)

Details on the consultation process can be found on the EMA's homepage (Medical Devices | European Medicines Agency (EMA)) or through the relevant competent authority for medicinal products in the EU/EEA.

The manufacturer is responsible for determining whether a change requires a consultation with the medicinal products authority and must be able to justify their decision if they conclude that a consultation is not required. The justification must be documented and made available to the competent authorities upon request.

A change requiring consultation with the medicinal products authority should generally be considered a change reportable to the notified body. When a change is likely to affect the design or

intended purpose of the device, its reportability must be assessed, with supporting evidence documenting the conclusion of the assessment. If the change is identified as reportable prior to approval, this document provides a flowchart in the Annex to determine whether consultation with the medicinal products authority is required.

1. Notified Body assessment of changes' significance in accordance with IVDR Article 110(3) in relation to Companion Diagnostic Products

Companion Diagnostic Legacy Devices under IVDR Article 110(3), as per definition in MDCG 2022-8, section II as "*devices for which a declaration of conformity was drawn up prior to 26 May 2022 in accordance with the IVDD and for which the conformity assessment procedure pursuant to the IVDR (contrary to the IVDD) requires the involvement of a notified body*. These devices are subject to the same restrictions regarding significant changes as other Legacy devices. Significant changes to the design or intended purpose of these legacy devices will lead to the loss of their legacy status as defined in MDCG 2022-6. Consequently, a new IVDR conformity assessment involving a notified body and a consultation with the medicinal products authority would then be required.

2. Notified Body assessment of reportable changes to a Companion Diagnostic

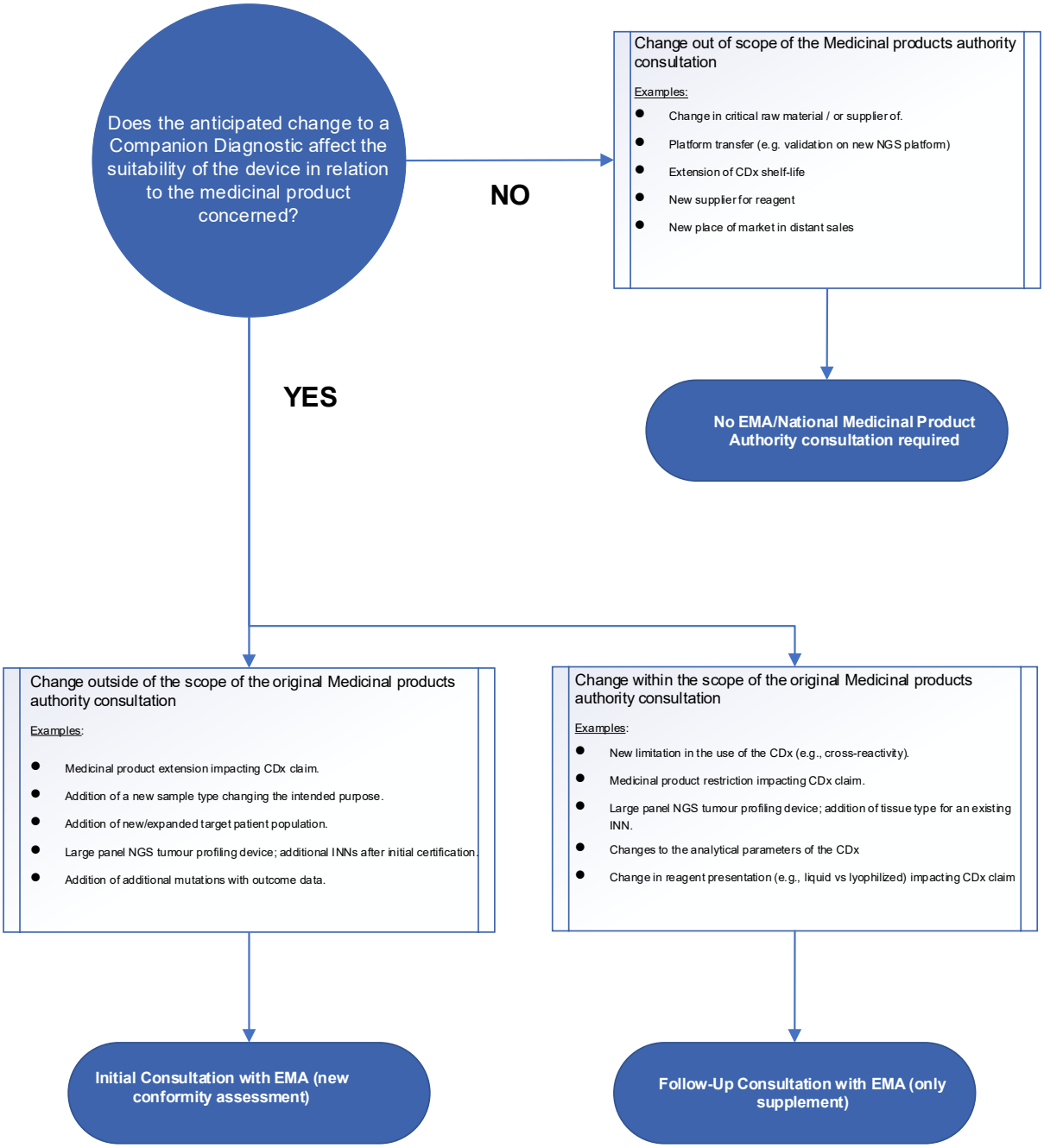
The flowchart below outlines the decision-making steps for determining whether a reportable change to a Companion Diagnostic Product requires medicinal products authority consultation, and whether this would involve a follow-on or an initial consultation. The examples provided in the flowchart are for illustrative (representative) purposes only. Final determinations regarding the impact of the change on the suitability of the device for the corresponding medicinal product can only be made following a detailed evaluation of each individual case. The examples presented in the chart reflect the shared understanding of stakeholders from notified bodies and the Medicinal Product Authorities (EMA or relevant medicinal products competent authority in EU/EEA countries).

ANNEX

The main chart categorizes reportable changes to a companion diagnostic (CDx) that require prior approval into two primary scenarios:

1. Changes outside the scope of the original medicinal product authority consultation.
2. Changes within the scope of the original medicinal product authority consultation.

A third group consists of changes that do not affect the suitability of the device for the medicinal product concerned. Such changes can be considered as entirely outside the scope of consultation with the medicinal product authority.


Does the anticipated change to a Companion Diagnostic affect the suitability of the device in relation to the medicinal product concerned?
NO
Change out of scope of the Medicinal products authority consultation
Examples:
Change in critical raw material / or supplier of.
Platform transfer (e.g. validation on new NGS platform)
Extension of CDx shelf-life
New supplier for reagent
New place of market in distant sales
No EMA/National Medicinal Product Authority consultation required
YES
Change outside of the scope of the original Medicinal products authority consultation
Examples:
Medicinal product extension impacting CDx claim.
Addition of a new sample type changing the intended purpose.
Addition of new/expanded target patient population.
Large panel NGS tumour profiling device; additional INNs after initial certification.
Addition of additional mutations with outcome data.
Change within the scope of the original Medicinal products authority consultation
Examples:
New limitation in the use of the CDx (e.g., cross-reactivity).
Medicinal product restriction impacting CDx claim.
Large panel NGS tumour profiling device; addition of tissue type for an existing INN.
Changes to the analytical parameters of the CDx
Change in reagent presentation (e.g., liquid vs lyophilized) impacting CDx claim
Initial Consultation with EMA (new conformity assessment)
Follow-Up Consultation with EMA (only supplement)