eunethta

EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

JCA timelines

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List of abbreviations

European Commission	EC
CHMP	Committee for Medicinal Products for Human Use
CTD	Common Technical Document
EMA	European Medicines Agency
HOG	Hands-on group
HTA CG	Health Technology Assessment Coordination Group
HTAR	Health Technology Assessment Regulation
JCA	Joint Clinical Assessment
LoQ	List of Questions
LoOI	List of Outstanding Issues
PICO	Population, Intervention, Comparators, Outcomes

1 Introduction

This document is a living document aiming to capture the discussion in the HOG on timelines for JCAs. So far, the document is only referring to JCA of medicinal products as it takes the EMA procedure into account. It should be noted any changes that might result from the revision of the pharma legislation have not been considered to date. The timelines for the assessment of medical devices will be discussed later.

The HTAR stipulates only two milestones of the JCA process. For medicinal products the deadline for submission of the dossier shall be at the latest 45 days prior to the envisaged date of the CHMP opinion (Art. 10 [1]). Furthermore, the JCA reports shall be endorsed by the HTA Coordination Group (HTA CG) no later than 30 days following the adoption of a European Commission (EC) decision granting a marketing authorisation (Art. 11 [1a]).

General assumptions for the timelines of JCA for medicinal products are explained below. In summary, they are:

- The timelines are based on an assumed standard regulatory process, built on the average duration of the process steps (as communicated by EMA)
- The timelines only include the major procedural steps, and not the individual sub-steps required for this.
- The JCA timelines only cover JCA procedures without a relevant change between the indication claimed by the Health Technology Developer (HTD)
  - In case major deviations between claimed indication and approved indication exist, the JCA procedure has to be stopped and re-started at a later time point
- Different timelines apply for initial marketing authorisation procedures (new chemical entities), and Type II variations and accelerated regulatory procedures
- The JCA report cannot be finalized before a positive CHMP opinion is available

The timelines are based on an assumed standard regulatory process as communicated by EMA, which is built on the average duration of the steps of the process. This also allows a more standardised and predictable planning of the JCA process for all parties involved. The document thus uses a presentation of the assumed standard EMA procedure as a starting point.

In addition, a standard procedure including timelines for the JCA is suggested. This partly builds on timelines that have been discussed in deliverables from EUnetHTA 21 (e.g. in the scoping guidance). This JCA procedure will be further refined taking the ongoing discussions on the JCA methods and processes into account.

For the different regulatory procedures specific scenarios for JCAs are discussed. These are so far:

1) For new chemical entities (in regular regulatory assessment procedures): start of JCA process 2 months after submission of the regulatory dossier to the European Medicines Agency (EMA) aiming to finish the process 30 days after the EC decision for approval
2) For new indications of already approved medicinal products (Type II variation) and for accelerated regulatory assessment procedures of new chemical entities: start of JCA process at the point of submission of the regulatory dossier to EMA aiming to finish the process 30 days after the EC decision for approval

General assumptions

The HTAR requires that the JCA procedure is conducted partly in parallel to the regulatory assessment by EMA. At the same time, the final outcome of the regulatory assessment can have a relevant impact on the JCA, specifically, the final approved indication will influence the PICO question(s) of the JCA.

The timelines discussed in this document only cover JCA procedures without a relevant change between the indication claimed by the Health Technology Developer (HTD) in the submission to EMA and the approved indication. The HOG assumes that this will be the majority of procedures. Therefore, a process, which is optimised for this situation should be developed.

Major deviations between claimed indication and approved indication

For cases in which there are substantial changes between the claimed indication and the approved indication (e.g. with regard to the population for which a drug is approved), there might be the need to change the PICO questions for the assessment. In these cases additional steps to address these changes in the PICO and thus the submission dossier and JCA report will be necessary. For this situation, the EUnetHTA 21 HOG recommends that the JCA procedure may be paused and re-started after appropriate action has been taken as the time available to address this may be insufficient. A procedure for these cases will be defined separately.

Major deviations from the standard EMA procedure timelines

The timelines of the EMA standard procedure used in this document might be prolonged, e.g. when clock stop durations are longer than the assumed 90 (after the List of Questions (LoQ)) plus 30 days (after the List of Outstanding Issues (LoOI)). Information of the HTA CG (incl. it's subgroups) on deviations from standard timelines will be ensured by regular communication between EMA and the HTA CG.

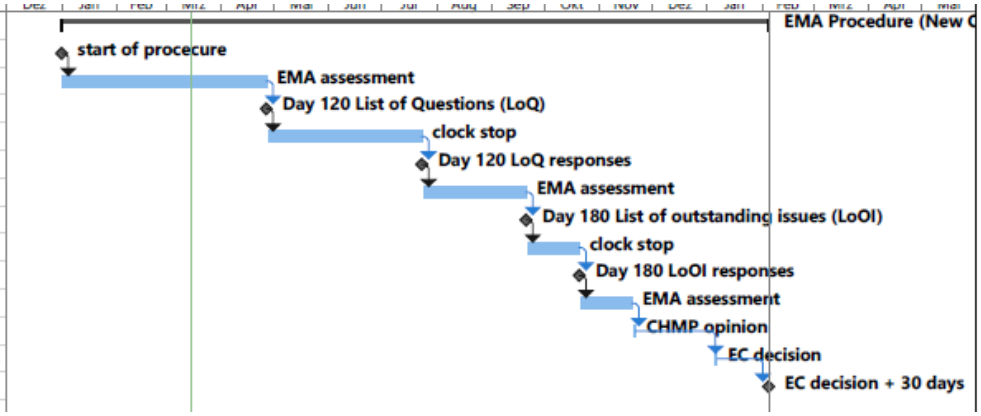
Irrespective of changes in EMA timelines, the final JCA report should only be endorsed after the final CHMP opinion is available to allow for a check of the claimed indication versus the finally approved indication. Therefore, in case of prolonged timelines between submission to EMA and the CHMP opinion, the JCA procedure might be interrupted after the finalisation the

JCA report by the assessment team, i.e. before the review by the HTA CG. The procedure would be resumed once a date for the CHMP opinion becomes available.

2 Timelines for a standard EMA procedure

The depiction of a standard EMA procedure presented below uses assumed EMA review times and minimum durations of clock stops (3 months for Day 120 LoQ clock stop and 1 month for Day 180 LoOI clock stop). These assumptions were reconciled with EMA.

EMA Procedure (New Chemical Entity, standard procedure	414 Tage?	Son 01.01.23	Son 04.02.24
start of procecure	0 Tage	Son 01.01.23	Son 01.01.23
EMA assessment	120 Tage	Son 01.01.23	Mit 26.04.23
Day 120 List of Questions (LoQ)	0 Tage	Mit 26.04.23	Mit 26.04.23
clock stop	90 Tage	Don 27.04.23	Son 23.07.23
Day 120 LoQ responses	0 Tage	Son 23.07.23	Son 23.07.23
EMA assessment	60 Tage	Mon 24.07.23	Mit 20.09.23
Day 180 List of outstanding issues (LoOI)	0 Tage	Mit 20.09.23	Mit 20.09.23
clock stop	30 Tage	Don 21.09.23	Fre 20.10.23
Day 180 LoOI responses	0 Tage	Fre 20.10.23	Fre 20.10.23
EMA assessment	30 Tage	Sam 21.10.23	Son 19.11.23
CHMP opinion	1 Tag	Mon 20.11.23	Die 21.11.23
EC decision	1 Tag	Fre 05.01.24	Sam 06.01.24
EC decision + 30 days	0 Tage	Son 04.02.24	Son 04.02.24



* days are calendar days

Figure 1: Assumed standard regulatory assessment procedure at EMA (new chemical entity)

Important dates (assuming start of procedure on 1.1.2023)

EMA procedure
Start of procedure: 01.01.2023
Day 120 list of questions: 26.04.2023
Day 180 List of outstanding issues: 20.09.2023
CHMP opinion: 20.11.2023

3 Timelines for a standard JCA procedure

The timelines presented in this chapter are set up by using MS Project and are in calendar days. The timelines only present the major procedural steps, and not the individual sub-steps required for this.

3.1 Overview of scenarios 1 and 2 of the JCA procedure

Scenario 1

Scenario 1 is planned for the assessment of new chemical entities (NCE) in regular EMA assessment procedures. NCEs will be the majority of assessments in the beginning of the JCA after 12 January 2025 because new indications (Type II variations) will only be assessed after a JCA report is available for a given medicinal product (HTAR Art. 7 [1b]).

In scenario 1 the JCA procedure will start 2 months after submission of the regulatory dossier to EMA and will be finalised with the endorsement of the JCA report by the HTA CG no later than 30 days after the EC decision for approval.

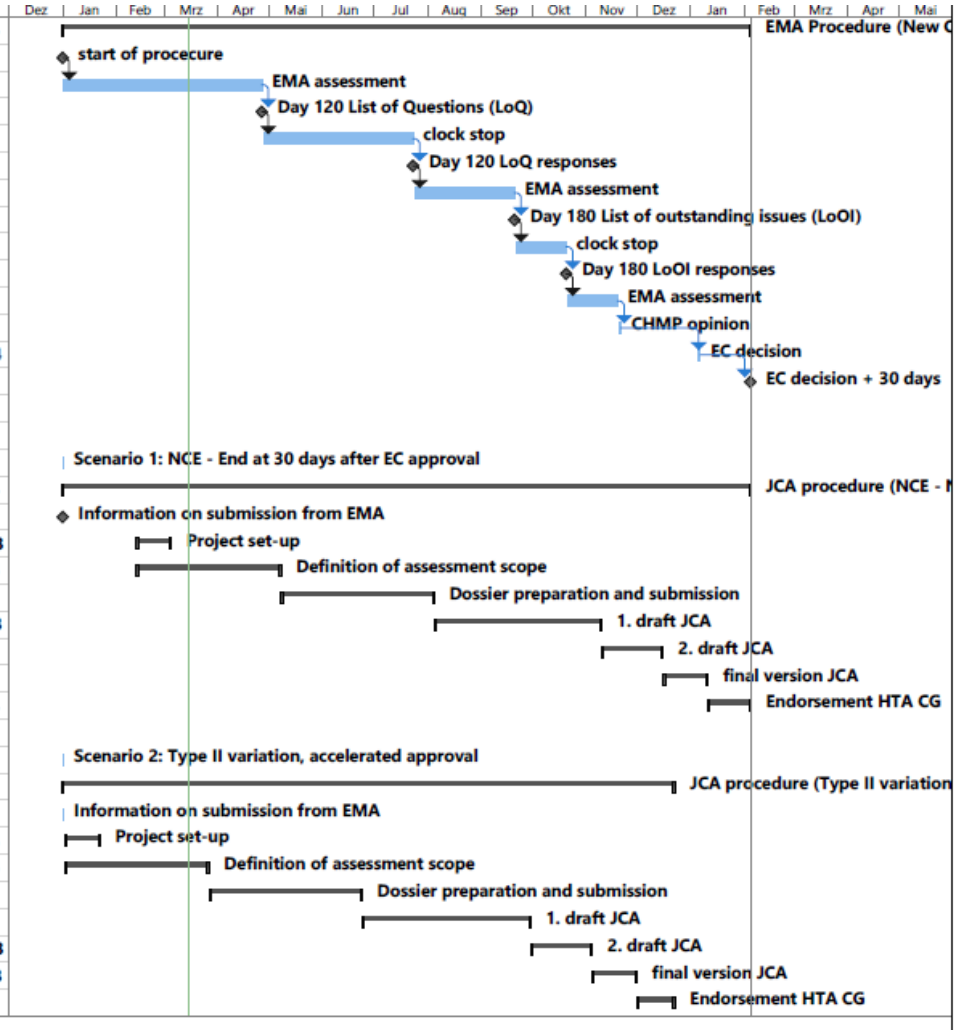
At the point of submission of the regulatory submission dossier (the Common Technical Document, CTD) to EMA, the information on the drug to be assessed and on the claimed indication is available and shall be transmitted to the HTA CG secretariat. In addition, the Clinical Overview (Section 2.5 of the CTD) shall be provided by EMA to enable a better understanding of the claimed indication. Furthermore, information on the type of regulatory procedure and properties (e.g. standard, accelerated, conditional, orphan, exceptions circumstances, PRIME designation) shall be provided. Please see Scenario 2 for the procedure in case of a type II variation or an accelerated approval procedure.

Scenario 2

Scenario 2 could be used for the JCA of new indications of already approved drugs (Type II variations) and in cases of accelerated approval. An earlier start of the JCA process is recommended in these cases because EMA’s standard timelines for these processes are shorter than for the regular assessment of NCEs.

In scenario 2 the JCA procedure starts at the point of submission of the regulatory dossier to EMA. At this point the information on the drug to be assessed and on the claimed indication is available and shall be transmitted to the HTA CG secretariat. In addition, the Clinical Overview (Section 2.5 of the CTD) shall be provided by EMA to enable a better understanding of the claimed indication. The transmission of this information would start the set-up of the project and the scoping process. Assuming the currently planned durations of the JCA steps, this would result in a JCA report being available before EC approval in a standard EMA procedure. However, it is assumed that in the cases included in scenario 2 the EMA procedure might be shorter than the assumed standard procedure.

EMA Procedure (New Chemical Entity, standard procedure	**414 Tage?**	**Son 01.01.23**	**Son 04.02.24**
start of procecure	0 Tage	Son 01.01.23	Son 01.01.23
EMA assessment	120 Tage	Son 01.01.23	Mit 26.04.23
Day 120 List of Questions (LoQ)	0 Tage	Mit 26.04.23	Mit 26.04.23
clock stop	90 Tage	Don 27.04.23	Son 23.07.23
Day 120 LoQ responses	0 Tage	Son 23.07.23	Son 23.07.23
EMA assessment	60 Tage	Mon 24.07.23	Mit 20.09.23
Day 180 List of outstanding issues (LoOI)	0 Tage	Mit 20.09.23	Mit 20.09.23
clock stop	30 Tage	Don 21.09.23	Fre 20.10.23
Day 180 LoOI responses	0 Tage	Fre 20.10.23	Fre 20.10.23
EMA assessment	30 Tage	Sam 21.10.23	Son 19.11.23
CHMP opinion	1 Tag	Mon 20.11.23	Die 21.11.23
EC decision	1 Tag	Fre 05.01.24	Sam 06.01.24
EC decision + 30 days	0 Tage	Son 04.02.24	Son 04.02.24
Scenario 1: NCE - End at 30 days after EC approval	1 Tag?	Son 01.01.23	Son 01.01.23
JCA procedure (NCE - New Chemical Entity)	**414 Tage**	**Son 01.01.23**	**Son 04.02.24**
Information on submission from EMA	0 Tage	Son 01.01.23	Son 01.01.23
Project set-up	**20 Tage**	**Mon 13.02.23**	**Sam 04.03.23**
Definition of assessment scope	**86 Tage**	**Mon 13.02.23**	**Son 07.05.23**
Dossier preparation and submission	**91 Tage**	**Mon 08.05.23**	**Fre 04.08.23**
1. draft JCA	**100 Tage**	**Sam 05.08.23**	**Don 09.11.23**
2. draft JCA	**36 Tage**	**Fre 10.11.23**	**Fre 15.12.23**
final version JCA	**26 Tage**	**Sam 16.12.23**	**Mit 10.01.24**
Endorsement HTA CG	**25 Tage**	**Don 11.01.24**	**Son 04.02.24**
Scenario 2: Type II variation, accelerated approval	1 Tag?	Son 01.01.23	Son 01.01.23
JCA procedure (Type II variation, accelerated approval)	**368 Tage**	**Son 01.01.23**	**Fre 22.12.23**
Information on submission from EMA	1 Tag	Son 01.01.23	Son 01.01.23
Project set-up	**20 Tage**	**Mon 02.01.23**	**Son 22.01.23**
Definition of assessment scope	**86 Tage**	**Mon 02.01.23**	**Son 26.03.23**
Dossier preparation and submission	**91 Tage**	**Mon 27.03.23**	**Fre 23.06.23**
1. draft JCA	**100 Tage**	**Sam 24.06.23**	**Fre 29.09.23**
2. draft JCA	**36 Tage**	**Sam 30.09.23**	**Sam 04.11.23**
final version JCA	**26 Tage**	**Son 05.11.23**	**Don 30.11.23**
Endorsement HTA CG	**22 Tage**	**Fre 01.12.23**	**Fre 22.12.23**



* days are calendar days

Figure 2: Overview of EMA and JCA procedures

The following table provides an overview of important milestones of the standard EMA procedure and the two JCA scenarios (with 1.1.2023 as the assumed regulatory submission date).

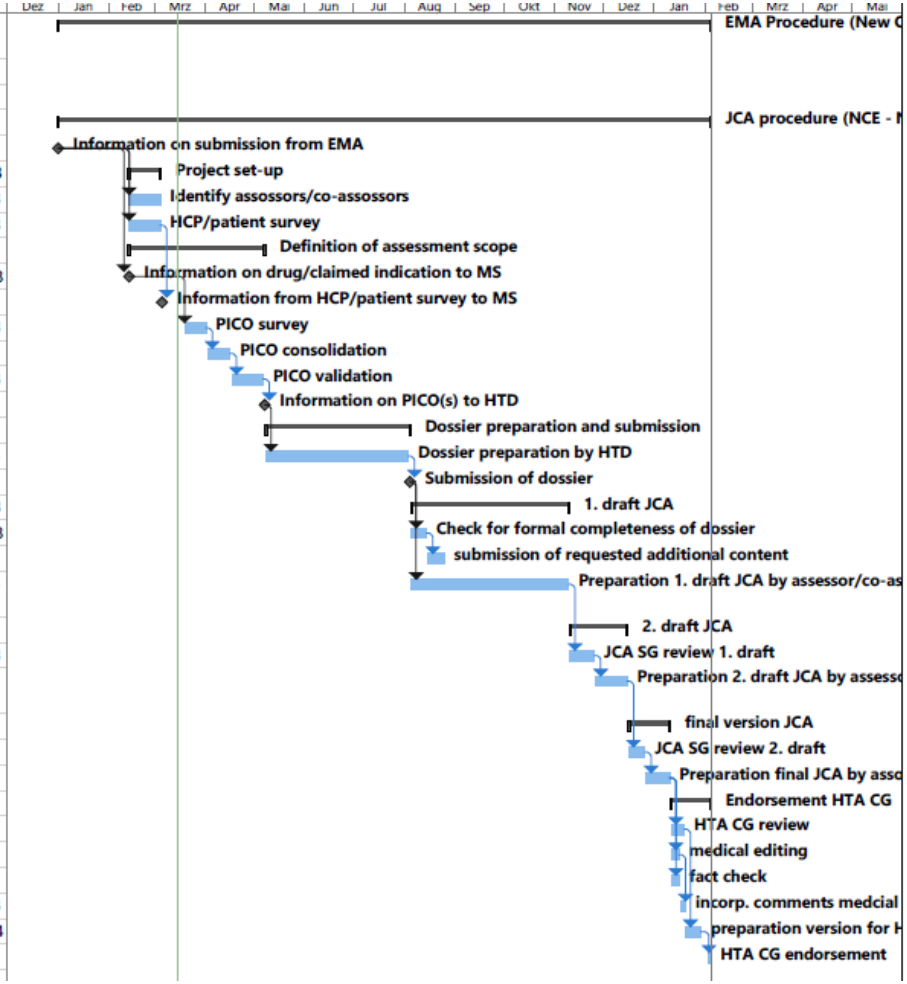
Standard EMA procedure	**JCA scenario 1 (NCE)**	**JCA scenario 2 (Type II variation, accelerated approval)**
Start of procedure: 01.01.2023	Start of procedure: 18.02.2023	Start of procedure: 01.01.2023
Day 120 list of questions: 26.04.2023	Assessment scope available: 07.05.2023	Assessment scope available: 26.03.2023
Day 180 List of outstanding issues: 20.09.2023	Dossier submission 04.08.2023	Dossier submission 23.06.2023
CHMP opinion: 20.11.2023	1. draft JCA: 09.11.2023	1. draft JCA: 29.09.2023
EC approval: 05.01.2024	2. draft JCA: 15.12.2023	2. draft JCA: 04.11.2023
	Final version JCA: 10.01.2024	Final version JCA: 30.11.2023
	Endorsement by HTA CG: 04.02.2024	Endorsement by HTA CG: 22.12.2023

3.2 Granular presentation of scenario 1 and 2

The following graphs provide more granular process steps and their duration for both scenario 1 and scenario 2. The individual steps of both scenarios are identical, however, due to differences in the start of the JCA procedure, the dates at which the assessment steps are finalised differ between the scenarios.

This process is a first suggestion based on the information currently available. The duration of the different process steps might be adjusted. Further steps might be added and the granularity of the process might be extended (e.g. by defining more granular steps for the preparation of the 1. draft JCA report).

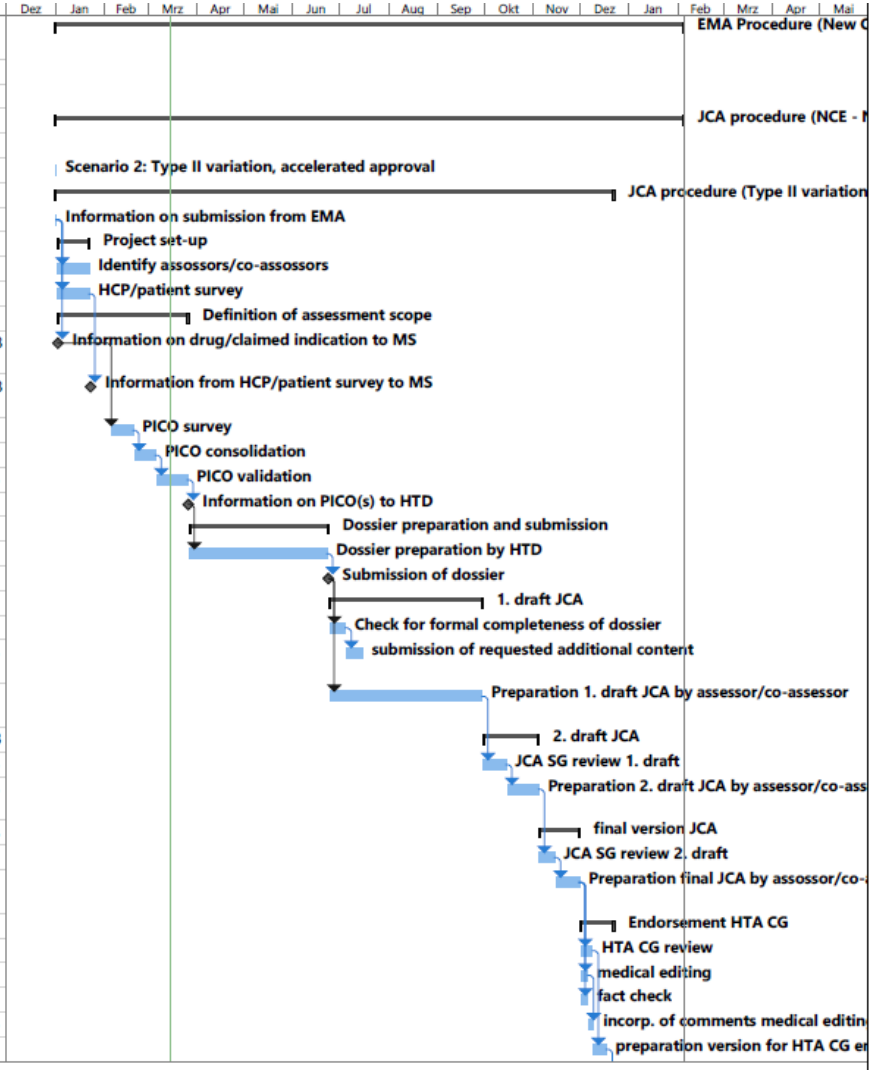
EMA Procedure (New Chemical Entity, standard procedure)	**414 Tage?**	**Son 01.01.23**	**Son 04.02.24**
JCA procedure (NCE - New Chemical Entity)	**414 Tage**	**Son 01.01.23**	**Son 04.02.24**
Information on submission from EMA	0 Tage	Son 01.01.23	Son 01.01.23
Project set-up	**20 Tage**	**Mon 13.02.23**	**Sam 04.03.23**
Identify assossors/co-assossors	20 Tage	Mon 13.02.23	Sam 04.03.23
HCP/patient survey	20 Tage	Mon 13.02.23	Sam 04.03.23
Definition of assessment scope	**86 Tage**	**Mon 13.02.23**	**Son 07.05.23**
Information on drug/claimed indication to MS	0 Tage	Mon 13.02.23	Mon 13.02.23
Information from HCP/patient survey to MS	0 Tage	Son 05.03.23	Son 05.03.23
PICO survey	14 Tage	Son 19.03.23	Sam 01.04.23
PICO consolidation	14 Tage	Son 02.04.23	Son 16.04.23
PICO validation	20 Tage	Mon 17.04.23	Sam 06.05.23
Information on PICO(s) to HTD	0 Tage	Son 07.05.23	Son 07.05.23
Dossier preparation and submission	**91 Tage**	**Mon 08.05.23**	**Fre 04.08.23**
Dossier preparation by HTD	90 Tage	Mon 08.05.23	Don 03.08.23
Submission of dossier	0 Tage	Fre 04.08.23	Fre 04.08.23
1. draft JCA	**100 Tage**	**Sam 05.08.23**	**Don 09.11.23**
Check for formal completeness of dossier	10 Tage	Sam 05.08.23	Mon 14.08.23
submission of requested additional content	10 Tage	Die 15.08.23	Fre 25.08.23
Preparation 1. draft JCA by assessor/co-assessor	100 Tage	Sam 05.08.23	Don 09.11.23
2. draft JCA	**36 Tage**	**Fre 10.11.23**	**Fre 15.12.23**
JCA SG review 1. draft	15 Tage	Fre 10.11.23	Sam 25.11.23
Preparation 2. draft JCA by assessor/co-assessor	20 Tage	Son 26.11.23	Fre 15.12.23
final version JCA	**26 Tage**	**Sam 16.12.23**	**Mit 10.01.24**
JCA SG review 2. draft	10 Tage	Sam 16.12.23	Die 26.12.23
Preparation final JCA by assossor/co-assossor	15 Tage	Mit 27.12.23	Mit 10.01.24
Endorsement HTA CG	**25 Tage**	**Don 11.01.24**	**Son 04.02.24**
HTA CG review	8 Tage	Don 11.01.24	Fre 19.01.24
medical editing	5 Tage	Don 11.01.24	Die 16.01.24
fact check	5 Tage	Don 11.01.24	Die 16.01.24
incorp. comments medcial editing/fact check	3 Tage	Mit 17.01.24	Sam 20.01.24
preparation version for HTA CG endorsement	10 Tage	Sam 20.01.24	Mon 29.01.24
HTA CG endorsement	1 Tag	Sam 03.02.24	Son 04.02.24



* days are calendar days

Figure 3: Granular structure of the JCA procedure - Scenario 1 for standard procedure of NCEs

EMA Procedure (New Chemical Entity, standard procedure)	**414 Tage?**	**Son 01.01.23**	**Son 04.02.24**
JCA procedure (NCE - New Chemical Entity)	**414 Tage**	**Son 01.01.23**	**Son 04.02.24**
Scenario 2: Type II variation, accelerated approval	1 Tag?	Son 01.01.23	Son 01.01.23
JCA procedure (Type II variation, accelerated approval)	**368 Tage**	**Son 01.01.23**	**Fre 22.12.23**
Information on submission from EMA	1 Tag	Son 01.01.23	Son 01.01.23
Project set-up	**20 Tage**	**Mon 02.01.23**	**Son 22.01.23**
Identify assessors/co-assessors	20 Tage	Mon 02.01.23	Son 22.01.23
HCP/patient survey	20 Tage	Mon 02.01.23	Son 22.01.23
Definition of assessment scope	**86 Tage**	**Mon 02.01.23**	**Son 26.03.23**
Information on drug/claimed indication to MS	0 Tage	Mon 02.01.23	Mon 02.01.23
Information from HCP/patient survey to MS	0 Tage	Mon 23.01.23	Mon 23.01.23
PICO survey	14 Tage	Son 05.02.23	Son 19.02.23
PICO consolidation	14 Tage	Mon 20.02.23	Son 05.03.23
PICO validation	20 Tage	Mon 06.03.23	Sam 25.03.23
Information on PICO(s) to HTD	0 Tage	Son 26.03.23	Son 26.03.23
Dossier preparation and submission	**91 Tage**	**Mon 27.03.23**	**Fre 23.06.23**
Dossier preparation by HTD	90 Tage	Mon 27.03.23	Don 22.06.23
Submission of dossier	0 Tage	Fre 23.06.23	Fre 23.06.23
1. draft JCA	**100 Tage**	**Sam 24.06.23**	**Fre 29.09.23**
Check for formal completeness of dossier	10 Tage	Sam 24.06.23	Die 04.07.23
submission of requested additional content	10 Tage	Mit 05.07.23	Sam 15.07.23
Preparation 1. draft JCA by assessor/co-assessor	100 Tage	Sam 24.06.23	Fre 29.09.23
2. draft JCA	**36 Tage**	**Sam 30.09.23**	**Sam 04.11.23**
JCA SG review 1. draft	15 Tage	Sam 30.09.23	Sam 14.10.23
Preparation 2. draft JCA by assessor/co-assessor	20 Tage	Son 15.10.23	Sam 04.11.23
final version JCA	**26 Tage**	**Son 05.11.23**	**Don 30.11.23**
JCA SG review 2. draft	10 Tage	Son 05.11.23	Die 14.11.23
Preparation final JCA by assessor/co-assessor	15 Tage	Mit 15.11.23	Don 30.11.23
Endorsement HTA CG	**22 Tage**	**Fre 01.12.23**	**Fre 22.12.23**
HTA CG review	8 Tage	Fre 01.12.23	Fre 08.12.23
medical editing	5 Tage	Fre 01.12.23	Die 05.12.23
fact check	5 Tage	Fre 01.12.23	Die 05.12.23
incorp. of comments medical editing/fact check	3 Tage	Mit 06.12.23	Sam 09.12.23
preparation version for HTA CG endorsement	8 Tage	Sam 09.12.23	Son 17.12.23



* days are calendar days

Figure 4: Granular structure of the JCA procedure - Scenario 2 for Type II variations and accelerated approval

4 Recommendations

Evaluation of timelines

EUnetHTA 21 recommends the timelines suggested are evaluated after a few JCA have been conducted under the HTAR, to assess the feasibility of the timelines and adjust them if and where needed. However, once a JCA is started, procedures and timelines should not be amended to ensure predictability for the HTD and assessors.

Develop process to deal with major deviations in claimed indication

As explained in Chapter 1, EUnetHTA 21 recommends in cases of a major deviation that the JCA procedure may be paused and re-started after appropriate action has been taken as the time available to address this may be insufficient. It is recommended that a process is developed how to deal with major deviations, for examplebetween the claimed indication and approved indication, including a clock-stop in the JCA process. This could be considered in the Implementing Act.

Timeline calculation tool

It is critical that timelines are consistent between different JCA, and are procedurally fair to all parties involved. To ease the workload of the Secretariat, it is recommended a tool (e.g. MS Project) is used in which a timetable is created that automatically creates a schedule with dates for new JCA productions. As the timelines only present the major procedural steps, and not the individual sub-steps required for this, it is recommended the Secretariat includes these sub-steps in the to be created calculation tool (e.g. sending of reminders, forwarding draft versions etc.)

The timelines presented in this document are based on calendar days. When setting up an automated calculation tool, e.g. in MS Project, it is desirable that weekend days can be avoided. However, it should not lead to differences in time available to parties between the JCA reports. It could be considered to start the procedure on a standard weekday, so that for some shorter tasks (e.g. factual accuracy check) the process does not include a weekend day. However, as there are several tasks of a short duration, weekend days cannot always be avoided. Therefore, it could be considered to allow some flexibility for these tasks or to extend the duration of these task to accommodate for the weekend days included.

Appendix A Additional graphical presentations

If required