September 2022

CMDh/368/2017, Rev.7

RMS Validation Checklist for Human Medicinal Products in DCP

|  |  |
| --- | --- |
| **THIS APPLICATION WAS CHECKED BY** | |
| RMS |  |
| Date |  |
| Contact/unit responsible for validation: |  |
| Telephone: |  |
| E-mail: |  |
|  |  |

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| --- | --- | --- | --- |
| **IDENTIFICATION** | | | |
| Date of receipt |  | | |
| D-14 |  | | |
| Name of the medicinal product in the RMS |  | | |
| Procedure number |  | | |
| National reference number (if applicable) |  | | |
| Applicant |  | | |
| Active Substance |  | | |
| Procedure number duplicates |  | | |
| Technical validation | | | |
|  | YES | NO, REQUESTED | NO |
| Technically Valid |  |  |  |

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| 1. **Extension** **Application** | |
| Yes No | |
| In case of EA:  Reason: | qualitative change in Active substance not defined as a new active substance  change of bioavailability  change of pharmacokinetics  change or addition of a new strength / potency  change or addition of a new pharmaceutical form  change or addition of a new route of administration |
| Existing MA in the MS: | Yes No  National MA-No.:  Comments: |
| **Is this application in accordance with the** Guideline on the Categorisation of Extension Applications (EA) versus Variation Applications (V) | Yes No  **Comments:** |

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| --- |
| 1. **LEGAL BASIS OF THE APPLICATION** **(DIRECTIVE 2001/83/EC)** |
| Please duplicate this section if applicable  Article 8(3) application   Article 10(1) Generic application  Article 10(3) Hybrid application   Article 10(4) Similar Biological application  Article 10a Well-Established Use application  Article 10b Fixed Combination application  Article 10c Informed Consent application  Article 16a Traditional Use registration for herbal medicinal products  **Is the use of this legal basis acceptable?** Yes  No  Comments: |
| **Where applicable: Reference Medicinal Product (RefMP)** |
| **Medicinal product which is or has been authorised in accordance with Union provisions in force for not less than 6/8/10 years in the EEA:**  ■ Data exclusivity period for the RefMP has expired? Yes No☐  ■ RefMP based on art. 8(3), 10a, 10b or 10c? Yes No  ■ RefMP authorized in accordance with *Acquis Communautaire*? Yes No  **Medicinal product authorised in the Union/Member State where the application is made or European reference medicinal product (ERP):**  ■ Use of European Reference Product (ERP) in RMS or any of the member states? Yes No  **If yes:**  Minimum information (Annex II) on ERP provided? Yes No  Minimum information (Annex II) on ERP requested? Yes No  Date of request to MS:  ■ RefMP based on art. 8(3), 10a, 10b or 10c? Yes No  ■ RefMP authorized in accordance with *Acquis Communautaire*? Yes No  *Comments*:  ◼ In case of article 10(3): Difference(s) compared to the reference medicinal product:  changes in the active substance(s)  changes in therapeutic indications   change in pharmaceutical form  change in strength (quantitative change to the active substance(s))  change in route of administration  bioequivalence cannot be demonstrated through bioavailability studies  ■ The Medicinal product which is or has been authorised in accordance with Union provisions in force for not less than 6/8/10 years in the EEA, the RefMP in the RMS/CMS(s) and RefMP used for the demonstration of the BE belong to the same GMA?  Yes  NoNot applicable  *Comments*: |

| **MODULE 1** | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CTD module | Appl. Form | Annex |  | Yes | No | No, requested | N/A | Comments |
| 1.0 |  |  | Cover letter  (*current version*) |  |  |  |  |  |
|  | | | Original/scanned signature on Cover letter |  |  |  |  |  |
| 1.2 |  |  | Application form(s) valid  (*current version*) |  |  |  |  |  |
|  | | | Original/scanned signature on Application form(s) |  |  |  |  |  |
| Applicant in the EEA |  |  |  |  |  |
|  |  | 5.1 | Proof of payment |  |  |  |  |  |
|  | 1.4.1 | 5.23 | In case of legal basis art. 8(3) and claim of new active substance annex provided |  |  |  |  |  |
|  | 1.4.7 | 5.2 | In case of legal basis informed consent:  Annex 5.2 present? |  |  |  |  |  |
| 1.5 | 1.4.2 to 1.4.5 |  | Module 1.5.2 provided in case of art. 10(1), 10(3) or 10(4) and Module 1.5.1 provided in case of art. 10a? |  |  |  |  |  |
| 1.7 | 1.2.1 | 5.18 | Has orphan designation been granted?  (If ticked “Yes”: the application must be in the Centralised Procedure) |  |  |  |  |  |
| 1.2.2 |  | Any MP designated as Orphan MP for condition relating to indication proposed in this application? |  |  |  |  |  |
|  | If yes, does the orphan MP has a MA in EU? |  |  |  |  |  |
| If yes, is the MP considered as “similar” to any of the authorised orphan MP? |  |  |  |  |  |
| If ticked **yes above:**  Module 1.7.1 and 1.7.2 completed? |  |  |  |  | <The CMDh template “Module 1.7.1 Similarity report”, see <https://www.hma.eu/human-medicines/cmdh/templates/applications-for-ma.html>, has not been used for Module 1.7.1. The applicant is requested to amend Module 1.7.1 according to this template. The completed template should be submitted in PDF format in Module 1.7.1 and in Word format in the “working documents” folder."> |
| If ticked **no above**:  Module 1.7.1 completed? | ☐ |  | ☐ |  | <The CMDh template “Module 1.7.1 Similarity report”, see <https://www.hma.eu/human-medicines/cmdh/templates/applications-for-ma.html>, has not been used for Module 1.7.1. The applicant is requested to amend Module 1.7.1 according to this template. The completed template should be submitted in PDF format in Module 1.7.1 and in Word format in the “working documents” folder.> |
|  | 1.5.2 |  | Module 1.5.4 Marketing authorisation granted in exceptional circumstances (Should be provided when 1.5.2 is ticked) |  |  |  |  |  |
| 1.5.3 | 1.5.4  **1.5.5**  **1.5.6** |  | Module 1.5.3 Extended Data/Market Exclusivity  (Should be provided when 1.5.4, 1.5.5 or 1.5.6 is ticked) |  |  |  |  |  |
| 1.10 | 1.6 |  | **If ticked**, check 1.6.4 and 1.6.5.  *No need to check 1.6.1, 1.6.2 and 1.6.3.* |  |  |  |  |  |
|  | 1.6.4 |  | **If** Article 30 (PUMA) applies, a copy of the PIP decision must be included. |  |  |  |  |  |
|  | 1.6.5 |  | **If** ticked “**Yes**” the PDCO compliance must be included. |  |  |  |  |  |
| 1.10 | 1.6 |  | **If not ticked**, check 1.6.1, 1.6.2, 1.6.3, 1.6.4 and 1.6.5. |  |  |  |  |  |
|  | 1.6.1 |  | **If ticked “Yes”** and **“Yes”** forpatent or SPC,*check 1.6.2, 1.6.3, 1.6.4, 1.6.5.* |  |  |  |  |  |
|  | 1.6.1 |  | **If** ticked **“Yes** and **“No”** for patent or SPC, check 1.6.4 and1.6.5. |  |  |  |  |  |
|  | 1.6.1 |  | **If** ticked **“No”,** *check* 1.6.3, 1.6.4, 1.6.5. |  |  |  |  |  |
|  | 1.6.2 |  | **If ticked “Yes”** (new indication, pharmaceutical form, strength, route of administration new strength, check 1.6.3, 1.6.4, 1.6.5. |  |  |  |  |  |
|  | 1.6.2 |  | **If ticked “No”** (new indication, pharmaceutical form, strength, route of administration new strength, check 1.6.4 and 1.6.5. |  |  |  |  |  |
|  | 1.6.3 |  | PIP or WAIVER included |  |  |  |  |  |
|  | 1.6.4 |  | **If** Article 30 (PUMA) applies, a copy of the PIP decision must be included. |  |  |  |  |  |
|  | 1.6.5 |  | **If** ticked “**Yes**” PDCO compliance must be included. |  |  |  |  |  |

| **MODULE 1** | | | | | | | | |
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| CTD module | Appl. Form | Annex |  | **Yes** | **No** | **No, requested** | **N/A** | **Comments** |
|  | 2.1.3 |  | ATC code |  |  |  |  |  |
|  | 2.2.4 |  | Presence of medical device (cat. a, b, c, d, e):  **If Yes**, sections 2.2.4.1 to 2.2.4.4 must be filled in. |  |  |  |  |  |
|  | 2.2.5.1 |  | Companion diagnostic:  **If Yes**, sections 2.2.5.2 to 2.2.5.4 must be filled in. |  |  |  |  |  |
|  | 2.4.1 |  | MAH (in RMS) in the EEA2 |  |  |  |  |  |
|  | 2.4.1 | 5.3 | Proof of establishment of the applicant/MAH in the EEA1 |  |  |  |  |  |
|  | 2.4.2 | 5.4 | Signed Letter of authorisation for communication on behalf of the applicant/MAH1 during procedure |  |  |  |  |  |
|  | 2.4.3 | 5.4 | Signed Letter of authorisation for communication on behalf of the applicant/MAH1 after procedure |  |  |  |  |  |
| 1.8 | 2.4.4 |  | QPPV in the EEA3 |  |  |  |  |  |
|  |  | PSMF location in the EEA3 |  |  |  |  |  |
|  | 2.5.1a) |  | Batch release in the EEA or in UK(NI) |  |  |  |  |  |
|  | 5.6  **5.94** | Manufacturing authorisation for all manufactures **OR** EudraGMDP Manufacturing Authorisation/GMP reference1 |  |  |  |  |  |
|  | 2.5.1.2 |  | Batch Control Testing arrangements |  |  |  |  |  |
|  | 5.6 | Manufacturing authorisation for all manufacturers/sites **OR** GMP compliance4 **OR** EudraGMDP Manufacturing Authorisation reference1 |  |  |  |  |  |
|  | 2.5.2 |  | Manufacturer(s) of the medicinal product and site(s) of manufacture |  |  |  |  |  |
|  | 5.6/5.94 | **If site is in the EEA/UK(NI):**  Manufacturing authorisation for all manufactures **OR** EudraGMDP Manufacturing Authorisation reference1 |  |  |  |  |  |
|  | 5.6 | **If site is outside EEA/UK(NI):**  Manufacturing authorisation for all manufacturers **OR** equivalent1 |  |  |  |  |  |
|  | 5.94 | **If site is outside EEA/UK(NI):** GMP certificate **OR** EudraGMDP certificate number |  |  |  |  |  |
|  | 5.94 | **If sterile API**: GMP certificate for sterilisation of the active substance |  |  |  |  |  |
|  | 5.8 | Flow-chart |  |  |  |  |  |
|  | 2.5.3 |  | Manufacturer of the Active Substance |  |  |  |  |  |
|  | 2.5.3 | 5.10 | **If CEP**: Copy of Ph. Eur. Certificate(s) of Suitability1 |  |  |  |  |  |
|  | 2.5.3 | 5.10 | **If ASMF** Letter of Access that covers the correct product(s) and is addressed to the RMS |  |  |  |  |  |
|  | 2.5.3 |  | **If** **ASMF**: Ensure that the RMS has received both  open part, n°:  and  closed part, n°: |  |  |  |  |  |
|  |  |  | **If** **ASMF**: Is the ASMF included in ASMF worksharing procedure?  If yes, EU ASMF number: EU/ASMF/XXXXX |  |  |  |  |  |
|  | 2.5.3 | 5.11 | If ASMF: Confirmation from the manufacturer of the active substance |  |  |  |  |  |
|  | 2.5.3 | 5.224 | QP declaration for each active substance |  |  |  |  |  |
|  |  | 5.20 | EMA certificate for VAMF |  |  |  |  |  |
|  | 2.5.4 |  | Contract companies for clinical trials |  |  |  |  |  |
|  | 2.6.1 |  | Information on composition is in accordance with section 2.2.1 regarding strength and pharmaceutical form |  |  |  |  |  |
|  | 2.6.2 | 5.12 | Ph. Eur. Certificate(s) of suitability for TSE  *(Should correspond with the Application Form)* |  |  |  |  |  |

| **MODULE 1** | | | | | | | | | | | | | | | |
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| CTD module | Appl. Form | Annex | |  | | **Yes** | | **No** | | **No, requested** | **N/A** | | **Comments** | | |
|  | 3.1 | 5.14 | | **If 3.1** is ticked **yes**: Scientific Advice given by CHMP and/or by member state(s) | |  | |  | |  |  | |  | | |
|  | 4.1 | 4.1.1 | | applications for same medicinal product pending in another MS | |  | |  | |  |  | |  | | |
|  |  | 4.1.2 | | Authorisation granted in another MS | |  | |  | |  |  | |  | | |
|  |  | 4.1.3 | | Authorisation refused/suspended/revoked by another MS | |  | |  | |  |  | |  | | |
|  | | 4.2 | 5.15 | If MA authorised for same product in the EEA is ticked, a copy of MA must be included | |  | |  | |  | |  |  | |
|  |  | | If ticked check if the application is acceptable | |  | |  | |  |  | |  | |
|  | 4.3 |  | | Multiple/duplicate applications | |  | |  | |  |  | |  | |
| If yes, is MAA acceptable | |  | |  | |  |  | |  | |
| 1.3.1 |  |  | | Electronic SmPC/label text/package leaflet in CMD(h)/QRD template *(English, pdf format)* | |  | |  | |  |  | |  | | |
| 1.3.1 |  |  | | Electronic SmPC label text/package leaflet in CMD(h)/QRD template *(English, Word format)* | |  | |  | |  |  | |  | | |
| 1.3.2 |  |  | | Mock-ups *(In an official language of the EU)* **OR** justification for absence | |  | |  | |  |  | |  | | |
| 1.3.4 |  |  | | Consultation with Target Patient Groups (*User test/Readability testing*)  **OR** justification for absence | |  | |  | |  |  | |  | | |
| 1.3.6 |  |  | | Braille  **OR** justification for absence | |  | |  | |  |  | |  | | |
| 1.4 |  |  | | Complete Information about the quality experts | |  | |  | |  |  | |  | | |
|  |  |  | | Complete Information about the non-clinical experts | |  | |  | |  |  | |  | | |
|  |  |  | | Complete Information about the clinical experts | |  | |  | |  |  | |  | | |
| 1.6 |  |  | | Environmental Risk Assessment  OR justification for absence | |  | |  | |  |  | |  | | |
| 1.8.1 |  |  | | Summary of PhV system for all MAH submitted? | |  | |  | |  |  | |  | | |
| 1.8.2 |  |  | | Risk Management System/Plan | |  | |  | |  |  | |  | | |
| 1.9 |  |  | | Statement that clinical trials carried outside the EU meet the ethical requirements of Dir 2001/20/EC | |  | |  | |  |  | |  | | |
| Additional data |  |  | | Risk evaluation on potential presence of nitrosamines | |  | |  | |  |  | | <Risk evaluation on potential presence of nitrosamines with underlying documentation should be provided. Filled in “Template for nitrosamine risk evaluation in marketing authorisation applications” should be provided in Module 3.2.P.5.6> | | |

| MODULE 2 | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| CTD  **module** | Overviews/Summaries/Statements | Yes | No | No, requested | N/A | Comments |
| 2.3 | Quality Overall Summary |  |  |  |  |  |
| 2.4 | Non-Clinical Overview |  |  |  |  |  |
| 2.5 | Clinical Overview |  |  |  |  |  |
| 2.6 | Non-Clinical Summary |  |  |  |  |  |
| 2.7 | Clinical Summary |  |  |  |  |  |

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| Module 3 | | | | | | |
| CTD  module | Quality | Yes | No | No, requested | N/A | Comments |
| 3 | M3.2.S |  |  |  |  |  |
| M3.2.P |  |  |  |  |  |
| M3.2.R |  |  |  |  |  |

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| Module 4 | | | | | | |
| CTD  module | Non-Clinical | Yes | No | No, requested | N/A | Comments |
| 4 | Studies/literature data |  |  |  |  |  |

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| Module 5 | | | | | | |
| CTD  module | Clinical | Yes | No | No, requested | N/A | Comments |
| 5 | Studies/literature data |  |  |  |  |  |

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| 1. **Specific NATIONAL REQUIREMENTS  *(cf. “Additional Data requested for New Applications in the MRP and DCP”)*** |
| YES  NO  Comments: |

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| --- |
| **Status of the application** |
| The application is considered valid.  The application is considered valid and the procedure can start, but the issues in section 2 below need to be addressed before day 30.  The application is considered invalid and the procedure cannot start before the issue(s) in section 1 below have been addressed. |

**1. RMS validation issue(s) preventing the procedure from starting**

**2. RMS validation issue(s) not preventing the procedure from starting but which have to be addressed by day 30 of the DC procedure**

**3. Additional information for the applicant**