|  |  |  |
| --- | --- | --- |
| **Form** | | |
| **Variations TAM** | | |
| **Identification number:** | ZL300\_00\_004 |
| **Version:** | 5.1 |
| **Valid from:** | 15.10.2023 |

# Basic information[[1]](#footnote-1)

|  |  |  |
| --- | --- | --- |
| **External reference (Company Reference):** …… | | |
| **Authorisation no.:** | | |
| **Basic company dossier no.:**  *(Only for sample quality documentation for Asian MP. For variations relating to basic company dossiers or master dossiers, submit only the form New authorisation variation in notification procedure KPTPO).* | | |
| **Name of medicinal product:** …… | | |
| *The following information is required only if it is modified / new as a result of the requested variation(s) or if a new authorisation no. results. Fields with unchanged content can be left blank.*  *Applications for additional indications, change in the active substance, dosage strength, pharmaceutical form, administration route or food-producing target species must always state the* ***active substance(s)*** *and the short form of the* ***area of application*** *being requested. Both are published on receipt and conclusion of the application.* | | |
| **Active substance(s):** ……  *(Published on receipt of the application)* | | |
| **Pharmaceutical form:** …… | | |
| **If applicable, Swiss reference medicinal product:** …… | | |
| **Authorisation no. of the Swiss reference medicinal product:** …… | | |
| **If applicable, name of the foreign comparator product:** …… | | |
| **Short form of the area of application incl. target species:** ……  *(Enter the currently approved short form of the area of application (see publication* [*Extended list of veterinary medicines*](https://www.swissmedic.ch/dam/swissmedic/de/dokumente/internetlisten/erweiterte_tam.xlsx.download.xlsx/Erweiterte_Arzneimittelliste%20TAM.xlsx) *on the Swissmedic website). If the short-form wording of the area of application changes due to an application (e.g. in a new target species), a* ***new*** *short form of the area of application should be applied for and listed here. (For example: For systemic treatment of fleas in cats.)* | | |
|  | **ATCvet code:** ……  *(If affected by variation)* |  |
| **Dosage strength(s)** | **Primary container**  *(e.g. blister pack)* | **Secondary container**  *(All pack sizes including hospital packs)* |
| …… | …… | …… |
| …… | …… | …… |
| …… | …… | …… |
| …… | …… | …… |
| …… | …… | …… |
| **Product category**  Select an option. | | |
| **Dispensing category**  Select an option. | | |

**To be completed additionally for known active substances – where change is relevant**  n.a.

|  |  |  |  |
| --- | --- | --- | --- |
| **Information on the Swiss reference medicinal product** | | | |
| Name of the Swiss reference medicinal product: | …… | | |
| Swissmedic authorisation no.: | …… | | |
| Used in bioequivalence study (KAS) | yes | no |  |

|  |  |
| --- | --- |
| **Information on the foreign comparator product**  (For applications according to Art. 13 TPA: if applicable, foreign original product with which comparability was studied abroad; For applications according to Art. 14 para. 1 letter abis TPA: foreign medicinal product on which authorisation in Switzerland is based and from which the product information is being adopted) | |
| Name of the foreign comparator product: | …… |
| Name and address of the authorisation holder abroad: | …… |
| Country of authorisation: | …… |
| Authorisation no.: | …… |
| For Art. 13 TPA: LOT: | …… |
| For Art. 13 TPA: EXP: | …… |
| Reference country / Reference source / Address: (wholesale / pharmacy) | …… |

# Addresses

## Marketing authorisation holder

|  |  |
| --- | --- |
| Company name: | …… |
| Addition: | …… |
| Street / no.: | …… |
| Postcode, town / city: | …… |
| Telephone: | …… |
| E-mail: | …… |

## Address for correspondence (if not the same as 2.1)

|  |  |
| --- | --- |
| Company name: | …… |
| Addition: | …… |
| Street / no.: | …… |
| P.O. Box: | …… |
| Postcode, place: | …… |
| Telephone: | …… |
| E-mail: | …… |

## Legal representative (if not the same as 2.1)

|  |  |
| --- | --- |
| Last name: | …… |
| Addition: | …… |
| Street / no.: | …… |
| P.O. Box: | …… |
| Postcode, place: | …… |
| Telephone: | …… |
| **Does Swissmedic already possess the power of attorney?**  yes  no, the power of attorney is enclosed with this application (including original signature) | |

# Special procedures / Status

|  |  |  |
| --- | --- | --- |
|  | Application for use of procedure according to Art. 13 TPA  The form *Information for application Art.13 TPA* is enclosed (compulsory). |  |
|  | Herbal medicinal product with traditional use |  |
|  | Herbal medicinal product with well established use |  |
| ☐ | Application for use of procedure according to Art. 14 para. 1 letter abis TPA |  |
|  | Application for use of procedure according to Art. 14 para. 1 letter ater TPA |  |
|  | Application for use of procedure according to Art. 14 para. 1 letter aquater TPA |  |
|  | Application for use of procedure according to Art. 14 para. 1 letter cbis TPA |  |
|  | MUMS status | Granted on, date: …… |

# Additional forms to be submitted

*For variation applications, the following additional forms should be submitted if the application requires modification / updating or first submission of the corresponding form.*

The list is not exhaustive. Please also consult the guidance document *Formal requirements*.

|  |
| --- |
| Does the variation affect the entries in the *Manufacturer information* form?  yes, the *Manufacturer information* form is enclosed.  no  A *Declaration by the Responsible Person for foreign manufacturers* form should be submitted for each proposed foreign manufacturer 🡪 Guidance document *GMP compliance by foreign manufacturers of active substances and/or ready-to-use medicinal products* |

|  |
| --- |
| Does the variation affect the entries in the *Full declaration* form?  yes, the *Full declaration* form is enclosed  no |

|  |
| --- |
| Does the variation affect the entries in the *Substances of animal and human origin* form?  yes, the *Substances of animal and human origin* form is enclosed.  no |

|  |
| --- |
| Does this concern   1. a variation with assessment according to Art. 13 TPA   or   1. a *change in active substance, dosage strength, pharmaceutical form, administration route, food-producing target species*, additional indication or dosage recommendation   and has the application at any time been submitted to a foreign authority?  yes, the *Status of authorisation applications abroad* is enclosed  no |

|  |
| --- |
| Does the variation affect a Drug Master File?  yes, the *DMF* form is enclosed  no |
|  |
| Is a QR code being added to or modified in the medicinal product information and/or on the packaging?  yes, the completed *Mobile technologies* form is enclosedi  no |

# Further information

## Company meetings

|  |  |  |
| --- | --- | --- |
| Was a company meeting conducted for this application? | | |
| Presubmission Meeting | no | Yes, date: ……  Application ID: …… |
| Scientific Advice Meeting | no | Yes, date: ……  Application ID: …… |

## Extended document protection

|  |  |  |  |
| --- | --- | --- | --- |
| Does your application for a new indication also include an application for extended 10-year document protection on the grounds of significant clinical benefit over existing treatments (Art. 11*b* para. 2 TPA and Art. 30 para. 3 TPO)? | yes1 | no | n.a. |
| Does your application for a new indication also include an application for 15-year document protection for important medicinal products for rare diseases (*MUMS*, Art. 11*b* para. 4 TPA)? | yes1 | no | n.a. |
| *1 Reasons for requesting the extension of document protection should be given in the cover letter.* | | | |

## Real world evidence

|  |  |  |
| --- | --- | --- |
| Does the application include real world evidence (RWE) in support of the proof of safety and efficacy? | yes | no |

If so:

Study design (please check all appropriate boxes):

|  |  |
| --- | --- |
|  | Randomised controlled study with pragmatic elements |
|  | Study designs that use real world data (RWD) to supplement the control arm |
|  | Single-arm study that uses RWD in an external control arm |
|  | Non-interventional (observational) study |
|  | Other study design (please provide details): …… |

Other comments on the study design: ……

RWD sources (please check all appropriate boxes)

|  |  |
| --- | --- |
|  | Data from electronic patient records |
|  | Data from digital healthcare technologies |
|  | Data from production systems (incl. precision livestock farming) |
|  | Data from surveillance programmes (disease surveillance, lab data) |
|  | Other data sources (e.g. questionnaires) which could provide information on state of health (please provide details): …… |

Other comments on the RWD sources: ……

## Nanoparticles

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Does this application involve changes to the medicinal product in respect of synthetic nanoparticles2? | | | yes | no |
| if yes:  Which component(s) of the medicinal product is/are involved? | | | | |
| Active substance(s): | …… | See Part II, section: | …… | |
| Excipient(s): | …… | See Part II, section: | …… | |
| Others: | …… | See Part II, section: | …… | |
| *2 The particles have at least one dimension on the nanoscale (1-1000 nm) plus a function and/or mode of action based on nanotechnology characteristics.* | | | | |

## Blood or blood components

|  |  |  |
| --- | --- | --- |
| Will blood or blood components continue to be used for the manufacture of the medicinal product? | yes | no |
| Will blood or blood components be newly used for the manufacture of the medicinal product? | yes | no |

## Narcotics

|  |  |  |
| --- | --- | --- |
| Does the medicinal product contain a narcotic substance? | yes | no |
| 🡪 If yes, the narcotic substance is classified as list | Select an option. | |

## Delayed implementation

|  |  |
| --- | --- |
|  | No, the variation   * has already been implemented, or * takes place with production of the next batch or next reprinting of packaging elements (within one year of approval at the latest), or * must be implemented more quickly (e.g. in the case of safety-relevant changes) and is decided accordingly when Swissmedic completes the variation application (see section 6.2.6 of the Guidance document *Variations VMP*). |
|  | Yes, please complete the table below |

|  |  |  |
| --- | --- | --- |
| Variation concerned | Time limit | Reason |
|  |  |  |
|  |  |  |
|  |  |  |

# Consents and confirmations

## Completeness of scientific documentation and compliance with formal requirements

|  |
| --- |
| The applicant confirms that all existing data that are relevant for evaluating the quality, safety and efficacy of the medicinal product have been submitted and that the application documents satisfy the requirements of the guidance document *Formal requirements* and the *Overview of documents to be submitted*.  yes  The present application relates solely to the variations applied for with this form. Any other variations contained in the documentation are excluded from the review. |

## eDok confirmation of identity (paper-based applications with eDok copy)

|  |
| --- |
| The applicant confirms that the electronic copy and the paper documentation are complete and identical. We hereby consent to the review being conducted by Swissmedic exclusively on the basis of the electronic documents.  yes  n/a |

## Confirmation of identity for the bioavailability study

|  |
| --- |
| The applicant confirms that the test medicinal product used in the bioavailability study is identical to the medicinal product notified to Swissmedic.  yes *(no additional documents need to be submitted).*  no, a description and an evaluation of the differences between the test medicinal product and the medicinal product submitted for authorisation are enclosed*.*  n/a |

## Conformity of the Information for healthcare professionals and package leaflet with the reference medicinal product for KAS without innovation

|  |
| --- |
| The applicant confirms that the medicinal product information conforms to the currently published text of the Information for healthcare professionals and package leaflet for the reference medicinal product …… (name of reference medicinal product) dated …… (month/year) with the exception of the deviations, which are clearly marked as such.  yes  n/a |

## Conformity of the Information for healthcare professionals and package leaflet with the basic product for co-marketing medicinal products

|  |
| --- |
| The applicant confirms that the medicinal product information conforms to the text of the Information for healthcare professionals and package leaflet most recently approved by Swissmedic for the basic product ...... (name of basic product) dated ...... (month/year) and that the only deviations are permitted by the TPLRO.  yes  n/a |

## For variations to the medicinal product information

|  |
| --- |
| The applicant confirms that all variations, including those that are still pending with Swissmedic, are clearly marked as such. Pending variations submitted with other applications are marked in a different colour and carry the ID of the application in question; alternatively, the omission of the pending variations is justified1. The rest of the text dated (**month/year**) corresponds to the latest version of the approved text or the variation notified to and not contested by the Agency (completed on**(day/month/year)**.  yes  n/a  1 Pending variations should only be added to the medicinal product information if it is expected that they will be approved at the same time as the application in question or before the application in question is completed. |

## Packaging material / laser colour prints

|  |
| --- |
| The applicant confirms that the enclosed laser colour prints for the above-mentioned product are completely identical to the original print of the packaging materials in terms of both text and graphic design.  yes  n/a |

## Sharing information with partner authorities

|  |
| --- |
| The applicant permits Swissmedic to share the Assessment Reports that it draws up on this medicinal product within the framework of the collaboration with partner authorities (Ireland: HPRA / Health Products Regulatory Authority; Canada: Health Canada; Austria: AGES / Agency for Health and Food Safety; Germany: BVL / Federal Office of Consumer Protection and Food Safety; Netherlands: CBG/MEB / College ter Beordeling van Geneesmiddelen/Medicines evaluation board; United Kingdom: VMD / Veterinary Medicines Directorate) based on [existing agreements](https://www.swissmedic.ch/swissmedic/en/home/about-us/international-collaboration/bilateral-collaboration-with-partner-authorities/agreements-on-information-exchange.html) for the purpose of sharing information and as support for forming opinions. Swissmedic is thus authorised to provide its Assessment Reports to partner authorities on request1. The decision regarding an authorisation is made independently of any information sharing with Swissmedic. Swissmedic informs the authorisation holder in writing if Assessment Reports are shared.  yes  no  1 These Assessment Reports may contain confidential data, such as personal data, business secrets and both positive and negative evaluations with regard to the assessment of an authorisation. |

## Dispatch of Public Assessment Report

|  |  |  |  |
| --- | --- | --- | --- |
| Will a request to **view the Public Assessment Report** when the decision is opened be submitted simultaneously with this application? Public Assessment Reports are issued for changes in the active substance, dosage strength, pharmaceutical form, administration route, for new or modified target species, new or modified therapeutic indications and new or modified dosage recommendations. | yes | no | n.a. |

## Letter elements / English-language texts

|  |  |  |
| --- | --- | --- |
| The applicant agrees that some parts of Swissmedic’s correspondence (e.g. in the List of Questions) may be written in English. If the response is “no”, all texts will be sent in the correspondence language. | yes | no |

# Signature

|  |  |  |  |
| --- | --- | --- | --- |
| **All the entries made in this form and in additional forms enclosed with the application are certified to be complete and accurate:**  *(company stamp of the applicant – optional)*  ……  ……  …… | | | |
| *Authorised signatory* | | *Other responsibilities (optional signature)* | |
| Place, date: ……  Signature: …………………………….. | | Place, date: ……  Signature: …………………………….. | |
| Last name: | …… | Last name: | …… |
| First name: | …… | First name: | …… |
| Position: | …… | Position: | …… |
| Telephone: | …… |  | |
| E-mail: | …… |
|  | | | |
| **The application must be sent to** | | **For enquiries contact** | |
| Swissmedic  Swiss Agency for Therapeutic Products  Operational Support Services  Hallerstrasse 7  3012 Bern | | Telephone +41 58 462 02 11  Fax +41 58 462 02 12  E-mail Anfragen@swissmedic.ch | |

**Formal requirements:**

* List of variations: Pages with variation templates that are not the subject of the application must be deleted prior to submission to Swissmedic. If this is not done, Swissmedic will raise a formal objection to the application.

See guidance document *Formal requirements*.

# List of variations

## Variations that do not require assessment (sections A - C)

A. Administrative changes

A.1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.1** | | **Change in the name, address or contact information of the following persons or departments:**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| b) | | Manufacturer or supplier of the active substance, starting material, reagent or intermediate used to manufacture the active substance, or quality control site (where stated in the dossier), if the approved dossier does not contain a Ph. Eur. Certificate of Suitability (CEP). | 1 | 1, 2 | 6213 |
| c) | | DMF holder | 2 | 1, 2, 3 | 6214 |
| d) | | Manufacturer of a new excipient (if named in the dossier) | 2 | 1, 2 | 6215 |
| e) | | Manufacturer of the finished product (including batch release or quality control sites) | 2 | 1, 2 | 6216 |
|  | | **Conditions** | | | |
|  | 1. | The manufacturing or quality control site and all manufacturing operations must remain the same. | | | |
|  | 2. | The manufacturing site and the individual manufacturing operations must remain the same. | | | |
|  | | **Documentation** | | | |
|  | 1. | An official document showing the new name and/or the new address. | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form, if applicable. | | | |
|  | 3. | An updated Letter of Access. | | | |
| n/a |  | Justification: | | | |

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

A.2

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.2** | | **Change in the name of the veterinary medicinal product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | 1 | 6217 |
|  | | **Documentation** | | | |
|  | 1. | Revised product information and/or packaging texts. | | | |

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

A.3

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.3** | | **Change in the name of the active substance or of an excipient**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1, 2, 3 | 6218 |
|  | | **Conditions** | | | |
|  | 1. | The substance must remain the same. | | | |
|  | | **Documentation** | | | |
|  | 1. | Proof of inclusion in the WHO ATCvet Index or copy of the INN List; if applicable, proof of conformity of the change with the pharmacopoeia; for herbal medicinal products, a declaration to the effect that the name is in accordance with the EMA Guideline on quality of herbal medicinal products/traditional herbal medicinal products and with the EMA Guideline on declaration of herbal substances and herbal preparations in herbal medicinal products/traditional herbal medicinal products. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |
|  | 3. | *Full declaration* form with correspondingly changed names. | | | |

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

A.4

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.4** | | **Change in the Anatomical Therapeutic Chemical veterinary code (ATCvet code)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1, 2 | 6219 |
|  | | **Conditions** | | | |
|  | 1. | The change may not be introduced until the Index of the ATCvet code has been modified. | | | |
|  | | **Documentation** | | | |
|  | 1. | Proof of inclusion in the ATCvet Index or copy of the ATCvet code list. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

A.100

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.100** | | **Change in the product information and/or packaging texts without the submission of scientific data**  **New design (corporate identity)**  **Date of implementation: ……** | **Conditions to be fulfilled**  1, 2 | **Documentation to be submitted**  1 | SAP no.  6269 |
|  | | **Conditions** | | | |
|  | 1. | If a new design (corporate identity), the first pack has been submitted as an E.100 change and approved. | | | |
|  | 2. | The application ID of the E.100 change (first pack with new design) is specified under “Scope / Justification for the change”. | | | |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| Change in medicinal product information: - *(no details necessary)*  …… | Change in medicinal product information: List of affected sections  …… |

A.101

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.101** | | **Adaptation of a co-marketing medicinal product to ensure alignment with the basic product (for example in the event of a change in the medicinal product information and/or packaging texts or a change of quality), without a change to the packaging code**  **Date of implementation:** | **Conditions to be fulfilled**  1, 2, 3, 4, 5 | **Documentation to be submitted**  1, 2, 3 | SAP no.  6270 |
|  | | **Conditions** | | | |
|  | 1. | In the event of changes to the medicinal product information and/or packaging texts: The modified / new text passages for the basic product will be taken over unchanged. | | | |
| n/a |  | Justification: | | | |
|  | 2. | In the event of changes to the medicinal product information and/or packaging texts: The medicinal product information texts (Information for healthcare professionals and/or package leaflet) and their translations required by therapeutic products legislation will be uploaded to the Swissmedic publication platform and released (exception: export licence). | | | |
| n/a |  | Justification: | | | |
|  | 3. | The change in the basic product did not result in a change to the packaging code. | | | |
|  | 4. | Based on the duty of the authorisation holder of the basic product to notify changes that need to be taken over to the authorisation holder of the co-marketing medicinal product, the latter submits the respective change within 30 days of approval being granted for the basic product. | | | |
|  | 5. | The change to the co-marketing medicinal product is implemented simultaneously with the change to the basic product. | | | |
|  | | **Documentation** | | | |
|  | 1. | In the case of a change to the medicinal product information, the most recently approved version of the Information for healthcare professionals and/or package leaflet for the basic product, with corrections for the name of the medicinal product, authorisation number, date of first authorisation and date of latest renewal, and marketing authorisation holder, or the medicinal product information for the co-marketing medicinal product with the most recently approved changes to the basic product in track changes mode, should be submitted. | | | |
| n/a |  | Justification: | | | |
|  | 2. | If appropriate, relevant updated forms (e.g. *Full declaration* form, *Manufacturer information* form). | | | |
| n/a |  | Justification: | | | |
|  | 3. | The copy of the Swissmedic approval letter for the basic product must be submitted. For a variation of the basic product without an approval letter, a copy of the Swissmedic receipt of confirmation or a print-out of the relevant Swissmedic Portal entry should be submitted instead of the copy of the approval letter. | | | |
|  |  |  | | | |

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| Change in the medicinal product information: Current date of revision  …… | Change in the medicinal product information: New date of revision  …… |

A.z Other administrative change that does not require assessment

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **A.z.** | **Other administrative change that does not require assessment**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6220 |

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

B. Quality changes

B.1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.1** | | **Change in the name, address or contact information of a supplier of a packaging component or a device that is part of the finished product (if mentioned in the dossier)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1 | 6221 |
|  | | **Conditions** | | | |
|  | 1. | The manufacturing site must remain the same. | | | |
|  | | **Documentation** | | | |
|  | 1. | If applicable, amendment of the relevant section(s) of the dossier. | | | |

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

B.2

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.2** | | **Change in the nomenclature(1) of the material for the primary packaging of the finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 |  | 6222 |
|  | | **Conditions** | | | |
|  | 1. | The change may not be introduced until the name of the container has been changed in the Standard Terms database on the website of the European Directorate for the Quality of Medicines & HealthCare (EDQM). | | | |

(1) According to the Standard Terms of the EDQM, the system of names and terms published by the European Directorate for the Quality of Medicines & HealthCare (EDQM) for authorisation applications.

|  |  |
| --- | --- |
| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

B.3

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.3** | | **Deletion**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6223 |
| a) | | of manufacturing sites (including for an active substance, intermediate or finished product), a packaging site, a manufacturer responsible for batch release, a batch control site or the site of a supplier of a starting material for an active substance, reagent or excipient (provided these are mentioned in the dossier) | 1, 2 | 1, 2 |  |
| b) | | of a process for the manufacture of the active substance or finished product, including an intermediate that is used to manufacture the finished product, if an alternative has already been authorised | 1, 3 | 2 |  |
| c) | | of a non-significant in-process test during the manufacture of the active substance (e.g. deletion of an outdated in-process test) | 4, 5 | 1, 2 |  |
| d) | | of a non-significant specification parameter (e.g. deletion of an outdated parameter)  - for an active substance;  - for a starting material;  - for an intermediate or reagent used in the manufacture of the active substance. | 4, 5 | 1, 2 |  |
| e) | | of a test procedure  - for the active substance or a starting material, reagent or intermediate of the active substance;  - for the primary packaging of the active substance;  - for an excipient or the finished product;  - for the primary packaging of the finished product. | 6 | 2 |  |
| f) | | of an authorised container for unfilled products, an authorised final container (including the packaging of an active substance) or an approved primary packaging of the finished product that does not result in the complete deletion of a dosage strength or pharmaceutical form | 7 | 2 |  |
| g) | | of a non-significant specification parameter (e.g. deletion of an outdated parameter) from the specification parameters or limits for the primary packaging of the active substance or the finished product | 8, 9 | 1, 2 |  |
| h) | | of an approved change management protocol concerning the active substance or the finished product | 10 | 2 |  |
| i) | | of a component or components of the system of flavouring or colouring agents | 11, 12 | 2 |  |
| j) | | of a solvent or diluent container from the pack | 13 | 3, 4 |  |
| k) | | of a non-significant in-process test during the manufacture of the finished product (e.g. deletion of an outdated test) | 4, 5 | 1, 2 |  |
| l) | | of details of the frequency of testing by the manufacturer of the finished product of an excipient or an active substance or of packaging material for the primary packaging of an active substance or the finished product, provided that this is mentioned in the dossier |  | 2 |  |
| m) | | of a non-significant specification parameter (e.g. deletion of an outdated parameter) from the specification parameters or limits for an excipient | 4, 5 | 2 |  |
| n) | | of a non-significant specification parameter (e.g. deletion of an outdated parameter such as odour or taste or an identity test for a colouring or flavouring agent) from the specification parameters or limits for the finished product | 4, 5 | 1, 2 |  |
| o) | | of a dosing or administration device | 14 | 2 |  |
| p) | | of a non-significant specification parameter (e.g. deletion of an outdated parameter) for a dosing or administration device | 4, 9 | 1, 2 |  |
| q) | | of a test procedure for a dosing or administration device | 6 | 2 |  |
| r) | | of a/of pack size(s) of the finished product | 15 | 4 |  |
| s) | | of a supplier of packaging components or devices (provided that this is mentioned in the dossier) | 16 | 2 |  |
| t) | | of Ph. Eur. Certificates of Suitability (CEP)  - for an active substance;  - for a starting material, reagent or intermediate that is used in the manufacture of the active substance;  - for an excipient. | 17 | 2 |  |
| u) | | of Ph. Eur. Certificates of Suitability (CEP) for Transmissible Spongiform Encephalopathy (TSE)  - for an active substance;  - for a starting material, reagent or intermediate for an active substance;  - for an excipient. | 17 | 2 |  |
| v) | | of a pharmaceutical form or dosage strength | 18 | 4 |  |
|  | | **Conditions** | | | |
|  | 1. | The deletion must not be due to critical deficiencies concerning manufacturing. | | | |
|  | 2. | At least one previously authorised site/manufacturer performing the same functions as the site(s)/manufacturer(s) affected by the deletion must remain. | | | |
|  | 3. | The finished product, the active substance, the intermediates or the materials used to manufacture the finished product must still comply with the approved specifications. | | | |
|  | 4. | The change must not be due to an obligation or an unexpected event during manufacture. | | | |
|  | 5. | The change must not concern a critical in-process test / a critical specification parameter / a critical parameter and must not have the potential to adversely affect the identity, quality, purity, potency or physical properties of the active substance/finished product or the starting material, intermediate or reagent used in the manufacture of the active substance/finished product. | | | |
|  | 6. | An alternative test procedure must already have been authorised. | | | |
|  | 7. | If appropriate, the remaining product presentations must conform to the dosage instructions and treatment duration defined in the Information for healthcare professionals. | | | |
|  | 8. | The change must not be due to an obligation or an unexpected event during manufacture of the primary packaging material and storage of the active substance or finished product. | | | |
|  | 9. | The change must neither concern a critical parameter nor have the potential to adversely affect the identity or quality of the primary packaging or the dosing or administration device. | | | |
|  | 10. | The change must not be due to an expected event or to out-of-specification results during the implementation of the changes described in the protocol. | | | |
|  | 11. | The change must not apply to a biological or immunological medicinal product. | | | |
|  | 12. | The change must not have the potential to adversely affect the identity, strength, quality, purity, potency, safety or efficacy of the finished product. | | | |
|  | 13. | The pharmaceutical form must remain the same. There must be suitable alternative products to provide the solvent or diluent required for safe and effective use. | | | |
|  | 14. | The change must not adversely affect the dispensing, use or safety of the finished product. | | | |
|  | 15. | The remaining pack sizes must correspond to the dosage and treatment duration approved in the Information for healthcare professionals. | | | |
|  | 16. | The change must not involve the deletion of packaging components or devices. | | | |
|  | 17. | At least one manufacturer of the named substance must still be named in the dossier. | | | |
|  | 18. | The remaining form(s) or strength(s) must be suitable for enabling exact dosing of the medicinal product and the treatment duration without several pharmaceutical forms (e.g. several pipettes or tablets) or unauthorised divided doses (e.g. half-tablets that have not yet been authorised) being used. | | | |
|  | | **Documentation** | | | |
|  | 1. | Comparison of present and proposed (sites/specifications/test procedures, etc.) | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form, if applicable. | | | |
|  | 3. | Justification for the deletion | | | |
|  | 4. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.4

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| **B.4** | | **Change in the production site or storage of active substances for which the approved dossier does not contain a Ph. Eur. Certificate of Suitability (CEP) for an active substance (including starting material, reagent or intermediate)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6224 |
| a) | | Change in the manufacture of the active substance (including relevant quality control sites) | 1, 2, 3, 4, 5 | 1, 2, 3 |  |
| b) | | Changes in the regulations for quality control of an active substance: Replacement or addition of a site for batch control or testing of the active substance | 1, 2, 6 | 1 |  |
| c) | | Introduction of a new micronisation site for the manufacturer of the active substance (including relevant quality control sites) | 1, 2, 7, 8 | 1, 2, 3, 4 |  |
| d) | | New site for storage of the master cell bank and/or the working cell banks for the manufacturer of an active substance, reagent or intermediate used in the manufacture of the active substance or in the active substance itself | 1, 9 | 1 |  |
|  | | **Conditions** | | | |
|  | 1. | For starting materials and reagents, the specifications (including in-process tests, methods of analysis for all materials) must be identical to those that have already been approved. For intermediates and active substances, the specifications (including in-process tests, methods of analysis for all materials), the method of preparation (including batch size) and detailed route of synthesis must be identical to those that have already been approved. | | | |
|  | 2. | The change must not apply to a sterile active substance or a biological or immunological substance. | | | |
|  | 3. | The change must not apply to a herbal substance or a herbal preparation in a herbal medicinal product. | | | |
|  | 4. | The new manufacturer must be part of the same pharmaceutical group as the currently authorised manufacturer. | | | |
|  | 5. | The change must not have the potential to adversely affect the identity, quality, purity, potency or physical properties of the active substance or the starting material, intermediate or reagent used in the manufacture of the active substance. | | | |
|  | 6. | Method transfer from the old to the new site has been successfully completed. | | | |
|  | 7. | The change must not cause any adverse change in the physical and chemical properties. | | | |
|  | 8. | The particle size specification of the active substance and the corresponding analytical method must remain the same. | | | |
|  | 9. | No changes may be made to the storage conditions, stability or specifications. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form, if applicable. | | | |
|  | 2. | Completed and signed *Declaration by the Responsible Person for foreign manufacturers* form, if applicable. | | | |
|  | 3. | Proof that the site’s GMP compliance has been verified, if applicable (only if the change concerns the active substance manufacturer). | | | |
|  | 4. | If applicable, amendment of the relevant section(s) of the dossier (comparative batch data for the present and new sites). | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.5

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| **B.5** | | **Shortening of the retest period or storage period (stability) where the approved dossier does not contain a Ph. Eur. Certificate of Suitability (CEP) covering the retest period**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1 | 6225 |
|  | | **Conditions** | | | |
|  | 1. | The change must not be the result of unexpected events arising during manufacture or to stability concerns. | | | |
|  | | **Documentation** | | | |
|  | 1. | If appropriate, amendment of the relevant section(s) of the dossier, including the specifications and confirmation of stability. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.6

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| **B.6** | | **Change to more restrictive storage conditions**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6226 |
| a) | | for the reference standard (if mentioned in the dossier) | 1 | 1 |  |
| ☐ b) | | for the active substance | 1 | 1 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not be the result of unexpected events arising during manufacture or to stability concerns. | | | |
|  | | **Documentation** | | | |
|  | 1. | If appropriate, amendment of the relevant section(s) of the dossier, including the specifications and confirmation of stability. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.7

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| **B.7** | | **Change in an approved stability protocol for an active substance (including starting material, reagent or intermediate)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1 | 6227 |
|  | | **Conditions** | | | |
|  | 1. | The change must not be the result of unexpected events arising during manufacture or to stability concerns. | | | |
|  | 2. | The change must not have the potential to adversely affect the identity, strength, quality, purity, potency or the physical properties of the active substance. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including the results of appropriate real-time stability studies. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.8

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| **B.8**  ☐ | | **Implementation of changes foreseen for the active substance in an approved change management protocol**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1 | 6228 |
|  | | **Conditions** | | | |
|  | 1. | The change must conform to the approved change management protocol, and the results of the studies performed must show that the acceptance criteria stated in the protocol are fulfilled. | | | |
|  | 2. | No further supporting data for the change management protocol are required to implement the change. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.9

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| **B.9** | | **Change in the batch size (including batch size ranges) of active substances or intermediates used in the manufacture of an active substance**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6229 |
| a) | | Up to a ten-fold increase compared to the originally approved batch size | 1, 2, 3, 4, 5 | 1 |  |
| b) | | Downscaling by at most a factor of ten | 1, 2, 3, 4 | 1 |  |
| c) | | More than a ten-fold increase compared to the originally approved batch size | 1, 2, 3, 4, 5, 6, 7, 8 | 1 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not apply to a sterile active substance or a biological or immunological substance. | | | |
|  | 2. | The change must not adversely affect the reproducibility of the process. | | | |
|  | 3. | The change must not be the result of unexpected events arising during manufacture or of stability concerns. | | | |
|  | 4. | Any changes to the manufacturing methods are only those necessitated by scale-up or downscaling of the production scale, e.g. use of different-sized equipment. The tested batches must be of the proposed batch size. | | | |
|  | 5. | The active substance and all intermediates, reagents, catalysts or solvents must still comply with the authorised specifications. | | | |
|  | 6. | The intermediates, reagents, catalysts or solvents used in the process must remain unchanged. | | | |
|  | 7. | The change must not adversely affect the qualitative and quantitative impurity profile, the potency or the physical and chemical properties of the active substance. | | | |
|  | 8. | The change must not refer to the restricted part of the DMF. | | | |
|  | | **Documentation** | | | |
|  | 1. | If appropriate, amendment of the relevant section(s) of the dossier, including the batch data. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.10

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| **B.10** | | **Change to in-process tests or limits applied during the manufacture of the active substance**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6230 |
| a) | | Tightening of in-process limits | 1, 2, 3 | 1, 2 |  |
| b) | | Addition of a new in-process test with limits | 1, 2, 4, 5 | 1, 2 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not be a consequence of a commitment from previous assessments to review specification limits. | | | |
|  | 2. | The change must not be the result of unexpected events arising during manufacture, e.g. a new unqualified impurity or a change in the limits for total impurities. | | | |
|  | 3. | The change must be within the range of currently approved limits. The test procedure must remain the same, or changes must be minor. | | | |
|  | 4. | New test methods must not involve a novel non-standard technique or a standard technique used in a novel way. | | | |
|  | 5. | The new test method must be neither a biological, immunological or immunochemical method nor a method that uses a biological reagent for a biological active substance (does not include standard microbiological methods in the pharmacopoeia). | | | |
|  | | **Documentation** | | | |
|  | 1. | If appropriate, amendment of the relevant section(s) of the dossier for the new test method, validation and batch data. | | | |
|  | 2. | Table comparing the present and new in-process tests and limits. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.11

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| **B.11** | | **Change in the specification parameters or limits for an active substance or a starting material, intermediate or reagent used in the manufacture of an active substance or for the primary packaging of the active substance**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6207 |
| a) | | Tightening of the specification limits for veterinary medicinal products subject to official batch release testing | 1, 2, 3, 4 | 1, 2 |  |
| b) | | Tightening of the specification limits for an active substance or a starting material, intermediate or reagent used to manufacture an active substance | 1, 2, 3, 4 | 1, 2 |  |
| c) | | Tightening of the specification limits for the primary packaging of the active substance | 1, 2, 3 | 1, 2 |  |
| d) | | Addition of a new specification parameter with the corresponding test method to the specification | 1, 2, 3, 5, 6, 7 | 2, 3 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not be the result of unexpected events arising during manufacture (e.g. a new unqualified impurity or a change in the limits for total impurities). | | | |
|  | 2. | The change must not be a consequence of a commitment (undertaken, for example, during the authorisation procedure or a variation procedure) from previous assessments to review specification limits. | | | |
|  | 3. | The test procedure must remain the same, or changes must be minor. | | | |
|  | 4. | The change must be within the range of currently approved limits. | | | |
|  | 5. | The new test method must not be a novel non-standard technique or a standard technique that is being used in a novel way. | | | |
|  | 6. | The new test method must be neither a biological, immunological or immunochemical method nor a method that uses a biological reagent for a biological active substance (does not include standard microbiological methods in the pharmacopoeia). | | | |
|  | 7. | The change must not concern a genotoxic impurity. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Table comparing the present and new specification parameters and limits. | | | |
|  | 3. | If appropriate, amendment of the relevant section(s) of the dossier for the new method, validation and batch data. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.12

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| **B.12** | | **Minor changes**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6231 |
| a) | | to an approved test procedure   * for an active substance; * for the finished product; * for the primary packaging of the active substance or the finished product; * for a dosing or administration device. | 1, 2, 3, 4 | 1 |  |
| b) | | to an approved test procedure   * for a starting material, reagent or intermediate that is used in the manufacture of the active substance; * for an excipient | 1, 2, 3, 4 | 2 |  |
| c) | | to an approved test procedure for an in-process test   * for an active substance; * for the finished product. | 1, 2, 3, 4 | 3 |  |
| d) | | in the process used to manufacture an active substance | 5, 6, 7, 8 | 3 |  |
| e) | | in the synthesis or recovery of an excipient not listed in the Ph. Eur. or Ph. Helv. (if described in the dossier) or of a new excipient | 9, 10 | 4 |  |
| f) | | in an in-process limit range for the finished product | 11, 12 | 3, 5 |  |
| g) | | in an approved change management protocol for the active substance that has no impact on the strategy described in the protocol | 13, 14, 15, 16 | 3 |  |
|  | | **Conditions** | | | |
|  | 1. | The test method must be neither a biological, immunological or immunochemical method nor a method that uses a biological reagent for a biological active substance. | | | |
|  | 2. | Appropriate validation studies must have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the previous test procedure. | | | |
|  | 3. | No changes may have been made to the total impurity limits, and no new unqualified impurities may have been found. | | | |
|  | 4. | The analytical method must remain unchanged (e.g. different column length or temperature, but not a different column type or method). | | | |
|  | 5. | The change must not apply to a biological or immunological active substance. | | | |
|  | 6. | The change must not concern the geographical origin, manufacturing route or production of a herbal medicinal product. | | | |
|  | 7. | The change must concern solely a solid oral pharmaceutical form or an oral solution and must not adversely affect the qualitative and quantitative impurity profile or the physical and chemical properties. | | | |
|  | 8. | The active substance and all intermediates, reagents, catalysts or solvents must still comply with the authorised specifications. The change must not refer to the restricted part of the DMF. The manufacturing operations must remain the same. | | | |
|  | 9. | The excipients and all intermediates, reagents, catalysts, solvents or in-process tests must still comply with the authorised specifications (e.g. the qualitative and quantitative impurity profile). Adjuvants and preservatives are excluded from the scope of this entry. | | | |
|  | 10. | Synthetic routes and specifications must be identical and there must be no change in the physical and chemical properties. | | | |
|  | 11. | The change must not be the result of unexpected events arising during manufacture or to stability concerns. | | | |
|  | 12. | The change must not concern an in-process test that is also part of the release specification for the finished product, and the new in-process limit range must be within the approved release limit. | | | |
|  | 13. | The intermediates, reagents, catalysts or solvents used in the process must remain unchanged. The active substance and all intermediates, reagents, catalysts or solvents must still comply with the authorised specifications. There must be no adverse change in the qualitative and quantitative impurity profile or the physical and chemical properties. The change must not refer to the restricted part of the DMF. | | | |
|  | 14. | The changes must be within the range of the currently approved limits. | | | |
|  | 15. | This change may only be made for biological products if comparability is not required. | | | |
|  | 16. | Changes concerning the geographical origin, manufacturing route or production of a herbal substance or herbal preparation of a herbal medicinal product are exempted. | | | |
|  | | **Documentation** | | | |
|  | 1. | If appropriate, amendment of the relevant section(s) of the dossier and the comparative validation data. | | | |
|  | 2. | If appropriate, amendment of the relevant section(s) of the dossier and the comparative data. | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 4. | If appropriate, amendment of the relevant section(s) of the dossier for batch data, comparative data and specifications. | | | |
|  | 5. | Table comparing the present and new in-process limits | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.13

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| **B.13** | | **Change to a test procedure (including replacement or addition) for a reagent used in the manufacture of the active substance or the primary packaging of the active substance**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6232 |
| a) | | for a reagent that does not have a tangible effect on the overall quality of the active substance | 1, 2, 3, 4 | 1 |  |
| b) | | for the primary packaging of the active substance | 1, 2, 5 | 1, 2 |  |
|  | | **Conditions** | | | |
|  | 1. | The new test method must not be a novel non-standard technique or a standard technique that is being used in a novel way. | | | |
|  | 2. | The active substance must not be a biological or immunological substance. | | | |
|  | 3. | No changes may have been made to the total impurity limits, and no new unqualified impurities may have been found. | | | |
|  | 4. | The analytical method must remain unchanged (e.g. different column length or temperature, but not a different column type or method). Appropriate validation studies must have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the previous test procedure. | | | |
|  | 5. | If the change involves the replacement of a method, this must not be a consequence of a commitment (undertaken, for example, during the authorisation procedure or a variation procedure) from previous assessments to review specification limits. | | | |
|  | | **Documentation** | | | |
|  | 1. | If applicable, amendment of the relevant section(s) of the dossier for comparative validation data. | | | |
|  | 2. | A document containing comparative validation results or, in justified cases, comparative analytical results showing that the present and the new test method are equivalent. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.14

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| **B.14** | | **Change in the qualitative or quantitative composition of the primary packaging of the active substance**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1, 2 | 6233 |
|  | | **Conditions** | | | |
|  | 1. | Sterile or liquid formulations or biological or immunological active substances are excluded. | | | |
|  | 2. | The new packaging material must be at least equivalent to the approved material in terms of its relevant properties and there must be no interactions between contents and packaging material. Stability studies in accordance with the currently approved stability protocol and the VICH guidelines must have been started; relevant stability parameters must have been assessed in at least two pilot scale or industrial scale batches, and the applicant must be able to submit at least three months of satisfactory stability data. The stability profile must be similar to the currently authorised situation. However, if the new packaging is more resistant than the existing packaging, the three-month stability data do not have to be available yet. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including the confirmation of stability. | | | |
|  | 2. | If the new packaging is more resistant than the existing packaging, the studies that have just been started must be finalised. Swissmedic must be informed immediately of any unexpected results (OOS results) during the study using the form “Notification of quality defects”. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.15

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| **B.15** | | **Addition to or change in a calendar pack for an authorised pack size**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 |  | 6234 |
|  | | **Conditions** | | | |
|  | 1. | The material of the primary packaging must be the same. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.16

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| **B.16** | | **Change or addition of imprints, bossing or other markings including replacement or addition of inks used for marking of the finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4 | 1 | 6188 |
|  | | **Conditions** | | | |
|  | 1. | The change must not adversely affect the dispensing, use or safety of the finished product. | | | |
|  | 2. | The specifications for the release of the medicinal product and stability must be the same except for appearance. | | | |
|  | 3. | The ink must comply with the relevant requirements of the pharmaceutical legislation. | | | |
|  | 4. | The change must not involve a scored tablet intended for division into equal doses. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.17

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| **B.17** | | **Change in the shape or dimensions of the pharmaceutical form for immediate-release tablets, capsules, suppositories and pessaries**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4 | 1 | 6235 |
|  | | **Conditions** | | | |
|  | 1. | The dissolution profile of the finished product must be the same. For herbal medicinal products, where dissolution testing may not be feasible, the new disintegration time of the product must be comparable to the existing one. | | | |
|  | 2. | The release and stability specifications of the finished product must not have changed. | | | |
|  | 3. | The qualitative or quantitative composition and mean mass must remain unchanged. | | | |
|  | 4. | The change must not involve a scored tablet intended for division into equal doses. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.18

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| **B.18** | | **Change(s) in the composition (excipients) of a non-sterile finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6236 |
| a) | | Increase or reduction of a component or components of the system of flavouring or colouring agents | 1, 2, 3, 4, 5, 6, 7 | 1 |  |
| b) | | Any minor adjustment of the quantitative composition of the finished product with respect to excipients | 1, 2, 3, 4, 5, 8, 9 | 1, 2 |  |
| c) | | Addition or replacement of a component or components of the system of flavouring or colouring agents | 1, 2, 3, 4, 5, 8, 9, 10 | 1, 2 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not apply to a biological or immunological medicinal product. | | | |
|  | 2. | The change must not have the potential to adversely affect the identity, strength, quality, purity, potency, physical properties, safety or efficacy of the finished product. | | | |
|  | 3. | Stability studies in accordance with the currently approved stability protocol and the VICH guidelines must have been started; relevant stability parameters must have been assessed in at least two pilot scale or industrial scale batches, and the applicant must be able to submit at least three months of satisfactory stability data. The stability profile must be similar to the currently authorised situation. | | | |
|  | 4. | The quantitative change(s) must not differ from the existing concentration of the component by more than +/-10%. | | | |
|  | 5. | The functional characteristics of the pharmaceutical form (e.g. disintegration time, dissolution profile) must not change. | | | |
|  | 6. | The finished product specification must only have been changed in respect of appearance, odour or taste (if applicable, deletion of an identification test). | | | |
|  | 7. | For orally administered veterinary medicinal products, the change must not adversely affect consumption by the target species. | | | |
|  | 8. | For solid pharmaceutical forms, the dissolution profile of the modified finished product must be determined using at least two pilot scale batches and must be comparable to the existing dissolution profile. There must be no significant differences in comparability. For herbal medicinal products, where dissolution testing may not be feasible, the disintegration time of the modified finished product must be comparable to the existing one. | | | |
|  | 9. | The change must not be the result of stability issues and must not result in potential safety concerns, e.g. differentiation between dosage strengths. | | | |
|  | 10. | For veterinary medicinal products for species used to produce food, proof that excipient residues in animal tissue are harmless according to the current state of science and technology or justification of why the excipient has no pharmacological effect at the dose administered to the target animal. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including the confirmation of stability. | | | |
|  | 2. | Either a TSE Ph. Eur. Certificate of Suitability (CEP) for any new component derived from animals susceptible to TSE risk or, if applicable, documentary evidence for all substances within the scope of the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (including substances used in the manufacture of the active substance/excipient). The following information is required for these substances: name of manufacturer, species and tissues from which the material is derived, country of origin of the source animals and its use. In addition, an updated *Substances of animal and human origin* form. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.19

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| **B.19** | | **Change in coating weight of oral pharmaceutical forms or change in weight of capsule shells for a solid oral pharmaceutical form**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4, 5 | 1 | 6237 |
|  | | **Conditions** | | | |
|  | 1. | The change must not be the result of stability issues and must not result in potential safety concerns (e.g. differentiation between dosage strengths). | | | |
|  | 2. | The coating must not be a critical factor for the release mechanism, and the change must not affect uptake by the target species. | | | |
|  | 3. | The finished product specification must only have been updated in respect of weight and dimensions, if applicable. | | | |
|  | 4. | The dissolution profile of the modified finished product must be determined using at least two pilot scale batches and must be comparable to the existing dissolution profile. For herbal medicinal products, where dissolution testing may not be feasible, the disintegration time of the modified product must be comparable to the existing one. | | | |
|  | 5. | Relevant stability studies in accordance with the VICH guidelines must have been started, and relevant stability parameters must have been assessed in at least two pilot scale or industrial scale batches; in addition, the applicant must be able to submit at least three months of satisfactory stability data at the time of implementation. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including the confirmation of stability. | | | |

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| **Scope / justification for the change** | |
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B.20

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| **B.20** | | **Replacement or addition of a primary packaging site for a non-sterile finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4, 5 | 1, 2 | 6238 |
|  | | **Conditions** | | | |
|  | 1. | The change must not apply to a biological or immunological medicinal product. | | | |
|  | 2. | The site must be appropriately authorised (to manufacture the pharmaceutical form or medicinal product concerned). | | | |
|  | 3. | Where relevant, a validation plan must be available, or confirmation that manufacture at the new site has been successfully carried out according to the current protocol with at least three production scale batches. | | | |
|  | 4. | If manufacture and primary packaging take place at two different sites, the conditions for transport and bulk storage must be specified and validated. | | | |
|  | 5. | The site is GMP-compliant. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Proof that the manufacturer’s GMP compliance has been verified. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.21

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| **B.21** | | **Replacement or addition of a secondary packaging site for a finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1, 2 | 6239 |
|  | | **Conditions** | | | |
|  | 1. | The site is GMP-compliant. | | | |
|  | 2. | The site must be appropriately authorised (to manufacture the pharmaceutical form or medicinal product concerned). | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form and, if applicable, revised medicinal product information and/or packaging texts. | | | |
|  | 2. | Evidence that the manufacturer’s GMP compliance has been verified. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.22

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| **B.22** | | **Replacement or addition of a site for batch control and quality control (batch testing) of a finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4 | 1, 2 | 6189 |
|  | | **Conditions** | | | |
|  | 1. | The site is GMP-compliant. | | | |
|  | 2. | The site must be appropriately authorised (to manufacture the pharmaceutical form or medicinal product concerned). | | | |
|  | 3. | The change must not apply to a biological or immunological medicinal product. | | | |
|  | 4. | Method transfer from the old to the new site must have been successfully completed. | | | |
|  | | **Documentation** | | | |
|  | 1. | Evidence that the manufacturer’s GMP compliance has been verified. | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form and, if applicable, revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.24

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| **B.24** | | **Replacement or addition of a manufacturer responsible for batch release, including batch control or testing of a non-sterile finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4 | 1, 2 | 6240 |
|  | | **Conditions** | | | |
|  | 1. | The site is GMP-compliant. | | | |
|  | 2. | The site must be appropriately authorised (to manufacture the pharmaceutical form or medicinal product concerned). | | | |
|  | 3. | The change must not apply to a biological or immunological medicinal product. | | | |
|  | 4. | Method transfer from the old to the new site must have been successfully completed. | | | |
|  | | **Documentation** | | | |
|  | 1. | Evidence that the manufacturer’s GMP compliance has been verified. | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form and, if applicable, revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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B.25

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| **B.25** | | **Change in the packaging material for unfilled products (bulk products or intermediates) that does not come into contact with the formulation of the unfilled product (including replacement or addition)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1 | 6190 |
|  | | **Conditions** | | | |
|  | 1. | The manufacturing operations must remain the same. The finished product, intermediates and in-process tests during manufacture of the finished product must still comply with the authorised specifications. | | | |
|  | 2. | The secondary packaging must not play a functional role in the stability of the bulk product, or if it does play such a role it must not provide less protection than the authorised packaging. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
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B.26

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| **B.26** | | **Change in the batch size (including batch size range) of the finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6241 |
| a) | | Up to a ten-fold increase compared to the originally approved batch size for immediate-release oral pharmaceutical forms or non-sterile liquid pharmaceutical forms | 1, 2, 3 | 1, 2 |  |
| b) | | Up to a ten-fold increase compared to the originally approved batch size for the pharmaceutical form “medical gas” | 1, 2, 3 | 1, 2 |  |
| c) | | Downscaling by at most a factor of ten compared to the originally approved batch size for immediate-release oral pharmaceutical forms or non-sterile liquid pharmaceutical forms | 1, 2, 3 | 1, 2 |  |
| d) | | Downscaling by at most a factor of ten for the pharmaceutical form “medical gas” | 1, 2, 3 | 1, 2 |  |
| e) | | More than a ten-fold increase compared to the originally approved batch size for an immediate-release oral solid pharmaceutical form | 1, 2, 3 | 1, 2, 3 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not apply to a biological or immunological medicinal product. | | | |
|  | 2. | The change must not be the result of unexpected events arising during manufacture or to stability concerns. The change must not affect the reproducibility or consistency of the product. | | | |
|  | 3. | Any changes to the manufacturing method or the in-process tests must only be those necessitated by the change in batch size, e.g. use of different-sized equipment. A validation plan must be available, or validation of manufacture must have been carried out with at least three batches of the new batch size and according to the relevant guidelines. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | If applicable, the batch numbers, corresponding batch size and date of manufacture of the batches used in the validation study (3) must be stated and the validation data or the validation protocol (scheme) must be submitted. | | | |
|  | 3. | Three-month stability data for at least one pilot batch under VICH conditions. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.27

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| **B.27** | | **Change to in-process tests or limits performed or applied during manufacture of the finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6242 |
| a) | | Tightening of in-process limits | 1, 2, 3, 4 | 1, 2 |  |
| b) | | Addition of new in-process tests with limits | 1, 2, 5, 6 | 1, 3 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not be due to an obligation or an unexpected event arising during manufacture. | | | |
|  | 2. | The change must not have the potential to adversely affect the identity, strength, quality, purity, potency or physical properties of the finished product, intermediates or materials used during manufacture. | | | |
|  | 3. | The change must be within the range of currently approved limits. | | | |
|  | 4. | The test procedure must remain the same, or changes must be minor. | | | |
|  | 5. | New test methods must not involve a novel non-standard technique or a standard technique used in a novel way. | | | |
|  | 6. | The new test method must be neither a biological, immunological or immunochemical method nor a method that uses a biological reagent for a biological active substance (does not include standard microbiological methods in the pharmacopoeia). | | | |
|  | | **Documentation** | | | |
|  | 1. | Table comparing the present and new in-process tests with limits. | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 3. | If appropriate, amendment of the relevant section(s) of the dossier for method and validation, batch data and relevant comparative data. | | | |

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| **Scope / justification for the change** | |
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B.28

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| **B.28** | | **Change in the specification parameters or limits for an excipient**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6243 |
| a) | | Tightening of specification limits | 1, 2, 3 | 1 |  |
| b) | | Addition of a new specification parameter with the corresponding test method to the specification | 1, 2, 4, 5, 6 | 2 |  |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the authorisation procedure or during a variation procedure). | | | |
|  | 2. | The change must not be the result of unexpected events arising during manufacture, e.g. a new unqualified impurity or a change in the limits for total impurities. | | | |
|  | 3. | The change must be within the range of currently approved limits. The test procedure must remain the same, or changes must be minor. | | | |
|  | 4. | New test methods must not involve a novel non-standard technique or a standard technique used in a novel way. | | | |
|  | 5. | The new test method must be neither a biological, immunological or immunochemical method nor a method that uses a biological reagent for a biological active substance (does not include standard microbiological methods in the pharmacopoeia). | | | |
|  | 6. | The change must not concern a genotoxic impurity. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier with details of the test method, if appropriate with validation data, batch data and relevant comparative data. | | | |

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| **Scope / justification for the change** | |
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B.29

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| **B.29** | | **Change in the source of an excipient or reagent presenting a TSE risk to material of plant or synthetic origin**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1, 2 | 6244 |
|  | | **Conditions** | | | |
|  | 1. | The release and stability specifications for the excipient and the finished product must remain the same. | | | |
|  | 2. | The change must not involve excipients or reagents used in the manufacture of a biological or immunological active substance or a biological or immunological medicinal product. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Declaration by the manufacturer or the authorisation holder stating that the material is of purely plant or synthetic origin. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.30

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| **B.30** | | **Change in the specification parameters or limits of the finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6245 |
| a) | | Tightening of the specification limits | 1, 2, 3, 4 | 1, 2 |  |
| b) | | Tightening of the specification limits for finished products subject to official batch release testing | 1, 2, 3, 4 | 1, 2 |  |
| c) | | Addition of a new specification parameter with the corresponding test method | 1, 2, 5, 6, 7 | 1, 2, 3 |  |
| d) | | Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the relevant finished product | 1, 2, 3, 4, 7 | 1, 2 |  |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the authorisation procedure or during a variation procedure) provided the accompanying documentation was not previously assessed and approved in the context of another procedure. | | | |
|  | 2. | The change must not be the result of unexpected events arising during manufacture, e.g. a new unqualified impurity or a change in the limits for total impurities. | | | |
|  | 3. | The change must be within the range of currently approved limits. | | | |
|  | 4. | The test procedure must remain the same, or changes must be minor. | | | |
|  | 5. | New test methods must not involve a novel non-standard technique or a standard technique used in a novel way. | | | |
|  | 6. | The test method must be neither a biological, immunological or immunochemical method nor a method that uses a biological reagent for a biological active substance (does not include standard microbiological methods in the pharmacopoeia). | | | |
|  | 7. | The change must not affect impurities (including genotoxic impurities) or dissolution. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Table comparing the present and new specification parameters and limits. | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier with details of the test method, if appropriate with validation data, batch data and relevant comparative data. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.31

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| **B.31** | | **Uniformity of dosage units (Ph. Eur. 2.9.40) is introduced to replace the currently authorised method**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1, 2 | 6191 |
|  | | **Conditions** | | | |
|  | 1. | The change must correspond to the changes in Ph. Eur. 2.9.5 (Uniformity of mass) and Ph. Eur. 2.9.6 (Uniformity of content). | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Table comparing the present and new specification parameters and limits. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.32

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| **B.32** | | **Change in the specification parameters or limits of the finished product to describe the appearance of the finished product more accurately**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1, 2 | 6192 |
|  | | **Conditions** | | | |
|  | 1. | The change must not be the result of unexpected events arising during manufacture or testing of the finished product. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Table comparing the present and new specification parameters and limits. | | | |

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| **Scope / justification for the change** | |
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B.33

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| **B.33** | | **Change in the test procedure for the finished product to comply with the Ph. Eur.**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6246 |
| a) | | Updating of the test procedure to the updated general monograph in the Ph. Eur. | 1, 2, 3 | 1 |  |
| b) | | Updating of the test procedure to confirm compliance with the Ph. Eur. and removal of the reference to the obsolete internal test method and test method number. | 1, 2, 3 | 1 |  |
|  | | **Conditions** | | | |
|  | 1. | The changes must not affect the total impurity limits, and no new unqualified impurities may have been found. | | | |
|  | 2. | The analytical method must remain unchanged (e.g. different column length or temperature, but not a different column type or method). | | | |
|  | 3. | The test method must be neither a biological, immunological or immunochemical method nor a method that uses a biological reagent for a biological active substance (does not include standard microbiological methods in the pharmacopoeia). | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier (if appropriate, a description of the analytical method, a summary of the validation data and revised specifications for impurities). | | | |

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| **Scope / justification for the change** | |
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B.34

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| **B.34** | | **Change in the qualitative and quantitative composition of the primary packaging of a solid pharmaceutical form of a finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4 | 1, 2 | 6247 |
|  | | **Conditions** | | | |
|  | 1. | The change must only affect the same type of packaging or container (e.g. from blister to blister). | | | |
|  | 2. | The finished product must not be sterile. The change must not adversely affect the dispensing, use, safety or stability of the finished product. | | | |
|  | 3. | Relevant stability studies in accordance with the VICH guidelines must have been started, and relevant stability parameters must have been assessed in at least two pilot scale or industrial scale batches; in addition, the applicant must be able to submit at least three months of satisfactory stability data at the time of implementation. However, if the proposed packaging is more resistant than the existing packaging, the three-month stability data do not have to be available yet. | | | |
|  | 4. | The new packaging material must be at least equivalent to the approved material in terms of its relevant properties. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | If appropriate, table comparing the present and new specifications of the primary packaging, permeability data and interactions. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.35

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| **B.35** | | **Change in the specification parameters or limits for the primary packaging of the finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6248 |
| a) | | Tightening of specification limits | 1, 2, 3, 4 | 1 |  |
| b) | | Addition of a new specification parameter with the corresponding test method to the specification | 1, 2, 5 | 1, 2 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the authorisation procedure or during a variation procedure). | | | |
|  | 2. | The change must not be the result of unexpected events arising during manufacture. | | | |
|  | 3. | The change must be within the range of currently approved limits. | | | |
|  | 4. | The test procedure must remain the same, or changes must be minor. | | | |
|  | 5. | New test methods must not involve a novel non-standard technique or a standard technique used in a novel way. | | | |
|  | | **Documentation** | | | |
|  | 1. | Table comparing the present and new specifications or limits. | | | |
|  | 2. | If appropriate, amendment of the relevant section(s) of the dossier for the method and validation and batch data. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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B.36

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| **B.36** | | **Change in the test procedure for the primary packaging of the finished product (including replacement or addition)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3 | 1 | 6249 |
|  | | **Conditions** | | | |
|  | 1. | The change must not apply to a biological or immunological medicinal product. | | | |
|  | 2. | Appropriate validation studies must have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the previous test procedure. | | | |
|  | 3. | New test methods must not involve a novel non-standard technique or a standard technique used in a novel way. | | | |
|  | | **Documentation** | | | |
|  | 1. | If appropriate, amendment of the relevant section(s) of the dossier for the method and validation and batch data. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.37

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| **B.37** | | **Change in the shape or dimensions of the container or closure (primary packaging) of a non-sterile finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3 | 1 | 6250 |
|  | | **Conditions** | | | |
|  | 1. | The change must not involve any part of the packaging material that affects the dispensing, administration, safety or stability of the finished product. | | | |
|  | 2. | The change must not affect the qualitative or quantitative composition of the container. | | | |
|  | 3. | If the head space or the surface/volume ratio is changed, stability studies in accordance with the relevant guidelines must have been started, relevant stability parameters must have been assessed in at least two pilot scale or industrial scale batches, and the applicant must submit stability data for at least three months. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.38

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| **B.38** | | **Change in pack size (change in the number of doses, e.g. tablets, ampoules, etc. in a pack) within the range of the currently approved pack sizes**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1 | 6251 |
|  | | **Conditions** | | | |
|  | 1. | The new pack size must be consistent with the dosing instructions and treatment duration approved in the Information for healthcare professionals. | | | |
|  | 2. | The material of the primary packaging must be the same. | | | |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.39

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| **B.39** | | **Change in any part of the primary packaging material not in contact with the finished product formulation (such as change in colour of flip-off caps due to a different plastic being used, change in colour of colour code rings on ampoules or different needle shield)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1 | 6252 |
|  | | **Conditions** | | | |
|  | 1. | The change must not involve any part of the packaging material that affects the dispensing, administration, safety or stability of the finished product. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Revised medicinal product information and/or packaging texts if affected by the change. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.40

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| **B.40** | | **Replacement or addition of a supplier of packaging components or devices (if mentioned in the dossier)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1 | 6193 |
|  | | **Conditions** | | | |
|  | 1. | The qualitative and quantitative composition of the packaging component or device and the specification must remain the same. The change must not have the potential to adversely affect the identity, quality or purity of the packaging component or device. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.41

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| **B.41** | | **Change in the storage period or an approved stability protocol for the finished product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6253 |
| a) | | Reduction of the storage period of the finished product as packaged for sale, after first opening or after dilution or reconstitution | 1 | 1, 2 |  |
| b) | | Change in an approved stability protocol | 1, 2, 3 | 1 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must not be the result of unexpected events arising during manufacture or to stability concerns. | | | |
|  | 2. | The change must not have the potential to adversely affect the identity, strength, quality, purity, potency or the physical properties of the finished product. | | | |
|  | 3. | The change must not involve a widening of the acceptance criteria in the parameters tested, the deletion of stability-indicating parameters or a reduction in the frequency of testing. | | | |
|  | 4. |  | | | |
|  | 5. |  | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Revised medicinal product information and/or packaging texts if affected by the change | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.42

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| **B.42** | | **Implementation of changes foreseen for the finished product in an approved change management protocol**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 |  | 6194 |
|  | | **Conditions** | | | |
|  | 1. | The change must conform to the approved change management protocol, and the results of the studies performed must show that the acceptance criteria stated in the protocol are fulfilled. | | | |
|  | 2. | No further supporting data for the change management protocol are required to implement the change. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.43

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| **B.43** | | **Editorial changes to Part II of the dossier if it is not possible to incorporate them into Part II of a pending procedure**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | 1 | 6195 |
|  | | **Documentation** | | | |
|  | 1. | Table comparing the changes in the dossier | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.44

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| **B.44** | | **Submission of a new or updated Ph. Eur. Certificate of Suitability (CEP) for an approved manufacturer for a non-sterile:**   * **active substance;** * **starting material, reagent or intermediate that is used in the manufacture of the active substance;** * **excipient**   **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4 | 1, 2 | 6254 |
|  | | **Conditions** | | | |
|  | 1. | The release and stability specifications for the finished product must remain the same. | | | |
|  | 2. | The change must not have the potential to adversely affect the identity, quality, purity, potency or physical properties of the active substance or the starting material, reagent or intermediate used in the manufacture of the active substance or excipient. | | | |
|  | 3. | No materials of human or animal origin may be used in the manufacture of the active substance, starting material, reagent, intermediate or excipient. | | | |
|  | 4. | For a herbal substance or a herbal preparation in a herbal medicinal product: the manufacturing route, physical form, extraction solvent and drug extract ratio (DER) must remain the same. | | | |
|  | | **Documentation** | | | |
|  | 1. | If appropriate, amendment of the relevant section(s) of the dossier, including a copy of the updated Ph. Eur. Certificate of Suitability (CEP) and, if appropriate, the updated *Manufacturer information* form. If appropriate, completed and signed *Declaration by the Responsible Person for foreign manufacturers* form and evidence that the site's GMP compliance has been verified. | | | |
|  | 2. | If applicable: evidence for all substances within the scope of the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (including substances used in the manufacture of the active substance or excipient). The following information is required for these substances: name of manufacturer, species and tissues from which the material is derived, country of origin of the source animals and its use. In addition an updated *Substances of animal and human origin* form. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.45

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| **B.45** | | **Submission of a new Ph. Eur. Certificate of Suitability (CEP) for a new manufacturer for a non-sterile:**   * **active substance;** * **starting material, reagent or intermediate that is used in the manufacture of the active substance;** * **excipient.**   **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4 | 1, 2, 3 | 6255 |
|  | | **Conditions** | | | |
|  | 1. | The release and stability specifications for the finished product must remain the same. | | | |
|  | 2. | The change must not have the potential to adversely affect the identity, quality, purity, potency or physical properties of the active substance or the starting material, reagent or intermediate used to manufacture the active substance or excipient. | | | |
|  | 3. | No materials of human or animal origin may be used in the manufacture of the active substance, starting material, reagent, intermediate or excipient. | | | |
|  | 4. | For a herbal substance or a herbal preparation in a herbal medicinal product: the manufacturing route, physical form, extraction solvent and drug extract ratio (DER) must remain the same. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a copy of the updated Ph. Eur. Certificate of Suitability (CEP) and, if appropriate, the updated *Manufacturer information* form. | | | |
|  | 2. | If applicable: evidence for all substances within the scope of the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (including substances used in the manufacture of the active substance or excipient). The following information is required for these substances: name of manufacturer, species and tissues from which the material is derived, country of origin of the source animals and its use. In addition an updated *Substances of animal and human origin* form. | | | |
|  | 3. | Completed and signed *Declaration by the Responsible Person for foreign manufacturers* form and evidence that the site's GMP compliance has been verified. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.46

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| **B.46** | | **Submission of a new or updated TSE Ph. Eur. Certificate of Suitability (CEP) for a non-sterile:**   * **active substance;** * **starting material, reagent or intermediate that is used in the manufacture of the active substance;** * **excipient**   **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1, 2 | 6256 |
|  | | **Conditions** | | | |
|  | 1. | The change must not have the potential to adversely affect the identity, quality, purity, potency or physical properties of the active substance or the starting material, reagent, intermediate or excipient used to manufacture the active substance or excipient. | | | |
|  | 2. | The change must not affect the risk of contamination by extraneous agents (i.e. no change in the country of origin). | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a copy of the updated Ph. Eur. Certificate of Suitability (CEP) and, if appropriate, the updated *Manufacturer information* form. | | | |
|  | 2. | If applicable: evidence for all substances within the scope of the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (including substances used in the manufacture of the active substance or excipient). The following information is required for these substances: name of manufacturer, species and tissues from which the material is derived, country of origin of the source animals and its use. In addition, an updated *Substances of animal and human origin* form. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.47

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| **B.47** | | **Change to comply with the Ph. Eur. or the Ph. Helv.**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6257 |
| a) | | Change in specifications for a previously non-Ph. Eur. active substance, excipient or starting material for an active substance to fully comply with the Ph. Eur. or the Ph. Helv. | 1, 2, 3, 4, 5 | 1, 2, 3 |  |
| b) | | Change to comply with an update of the relevant monograph of the Ph. Eur. or the Ph. Helv. | 1, 2, 3, 4 | 1, 2 |  |
| c) | | Change in specifications when transitioning from the Ph. Helv. to the Ph. Eur. | 1, 2, 3 | 1, 2, 3 |  |
| d) | | Change to confirm compliance with the Ph. Eur. by deleting the reference to the internal test method and the number of this test method. | 1, 2, 3 | 1, 2 |  |
|  | | **Conditions** | | | |
|  | 1. | The change must be made exclusively to comply fully with the pharmacopoeia. All the tests foreseen in the specification (apart from additional tests) must conform to the standard described in the pharmacopoeia after they have been changed. | | | |
|  | 2. | Further validation of a new or modified pharmacopoeial method is not required. | | | |
|  | 3. | For a herbal substance or a herbal preparation in a herbal medicinal product: the manufacturing route, physical form, extraction solvent and drug extract ratio (DER) must remain the same. | | | |
|  | 4. | Additional pharmacopoeial specifications for product-specific characteristics must remain unchanged (e.g. particle size distribution, polymorphic form, bioassays or aggregates). | | | |
|  | 5. | The change must not involve any substantial changes in the qualitative and quantitative impurities profile unless the specifications are tightened. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | If appropriate, table comparing the present and new specifications. | | | |
|  | 3. | Batch data and data demonstrating the suitability of the monograph for controlling the substance. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.48

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| **B.48** | | **Addition or replacement of a measuring or administration device which is not part of the primary packaging**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2, 3, 4, 5 | 1 | 6258 |
|  | | **Conditions** | | | |
|  | 1. | The change must not adversely affect the dispensing, use, safety or stability of the finished product. | | | |
|  | 2. | The change must only apply to a device with CE marking. | | | |
|  | 3. | The new measuring or administration device must accurately deliver the required dose for the product concerned in line with the approved dosage instructions; the results of corresponding studies must be available. | | | |
|  | 4. | The new device must be compatible with the veterinary medicinal product. | | | |
|  | 5. | The change must not result in substantial changes to the medicinal product information. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
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B.49

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| **B.49** | | **Change in the specification parameters or limits of a measuring or administration device**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6259 |
| a) | | Tightening of specification limits | 1, 2, 3, 4 | 1, 2 |  |
| b) | | Addition of a new specification parameter with the corresponding test method to the specification | 1, 2, 5 | 1, 3 |  |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the authorisation procedure or during a variation procedure) provided the accompanying documentation was not previously assessed and approved in the context of another procedure. | | | |
|  | 2. | The change must not be the result of unexpected events arising during manufacture. | | | |
|  | 3. | The change must be within the range of currently approved limits. | | | |
|  | 4. | The test method must remain the same, or changes must be minor. | | | |
|  | 5. | New test methods must not involve a novel non-standard technique or a standard technique used in a novel way. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Table comparing the present and new specification parameters and limits. | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier for the method and validation and batch data. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.50

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| **B.50** | | **Change in the test procedure (including replacement or addition) for a measuring or administration device**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1 | 6260 |
|  | | **Conditions** | | | |
|  | 1. | Appropriate validation studies must have been performed in accordance with the relevant guidelines and show that the updated test method is at least equivalent to the previous test procedure. | | | |
|  | 2. | New test methods must not involve a novel non-standard technique or a standard technique used in a novel way. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier for the method and validation and batch data. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.z Other quality change that does not require assessment

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| **B.z** | **Other quality change that does not require assessment**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6196 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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C. Safety, efficacy and pharmacovigilance changes

C.1

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| **C.1** | **Change(s) in the name, address or contact information of the qualified person for pharmacovigilance**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6261 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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C.3

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| **C.3** | | **Change in the medicinal product information and/or packaging texts for a medicinal product with a known active substance with/without innovation or preparation for parallel import following assessment of the same change for the reference medicinal product**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1 | 6262 |
|  | | **Conditions** | | | |
|  | 1. | This change only applies if no new or additional data are required for assessment. | | | |
|  | 2. | The proposed changes in the Information for healthcare professionals, labelling or package leaflet must be identical to the changes that have been approved for the reference medicinal product. | | | |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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C.4

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| **C.4** | | **Change in the medicinal product information and/or packaging texts intended to implement the outcome of a Swissmedic administrative procedure, including risk management measures**  **Implementation of the wording agreed with Swissmedic**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1, 2 | 6263 |
|  | | **Conditions** | | | |
|  | 1. | The wording required by Swissmedic is implemented with the variation, but the submission of additional information and/or further assessment is not required. | | | |
|  | | **Documentation** | | | |
|  | 1. | A reference to the relevant official decision must be attached to the variation application. | | | |
|  | 2. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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C.5

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| **C.5** | **Change in the site at which the pharmacovigilance system master file is located**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | 1 | 6264 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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C.6

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| **C.6** | | **Introduction of a summary of the pharmacovigilance system master file or changes in this summary that have not already been submitted with another application**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | 1 | 6264 |
|  | | **Documentation** | | | |
|  | 1. | Summary of the pharmacovigilance system master file | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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C.7

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| **C.7** | | **Introduction of requirements and conditions relating to an authorisation or changes in these requirements and conditions, including the risk management plan**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1 | 6265 |
|  | | **Conditions** | | | |
|  | 1. | The wording must be restricted to the wording agreed with the competent authority or Swissmedic. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
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C.8

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| **C.8** | | **Implementation of changes in the Information for healthcare professionals that have not already been submitted with another application**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1, 2 | 1 | 6263 |
|  | | **Conditions** | | | |
|  | 1. | This change only applies if no new or additional data are required for assessment. The changes must not adversely affect the quality, safety or efficacy of the product. | | | |
|  | 2. | The changes must be minor and must agree with the information in the current Information for healthcare professionals. | | | |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

C.9

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| **C.9** | | **Editorial changes to the Information for healthcare professionals, labelling or package leaflet if they cannot be incorporated into a pending procedure**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| 1 | 1 | 6266 |
|  | | **Conditions** | | | |
|  | 1. | The changes must not adversely affect the quality, safety or efficacy of the medicinal product. | | | |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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C.10

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| **C.10** | | **Changes to the labelling or the package leaflet which are not connected with the Information for healthcare professionals**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6267 |
| a) | | Not applicable to Switzerland |  |  |  |
| b) | | Other changes | 1, 2, 3 |  |  |
| c) | | Inclusion of adhesive traceability labels in or on the secondary packaging | 4 |  |  |
|  | | **Conditions** | | | |
|  | 1. | The changes must be minor and must agree with the information in the current Information for healthcare professionals. | | | |
|  | 2. | The change must not involve the introduction of new batch release sites. | | | |
|  | 3. | Changes must not be made for advertising purposes and must not have an adverse effect on the readability of the product information. | | | |
|  | 4. | The addition must not have an adverse effect on the readability of the product information. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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C.z Other change relating to safety, efficacy and/or pharmacovigilance that does not require assessment

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| **C.z** | **Other change relating to safety, efficacy and/or pharmacovigilance that does not require assessment**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  |  | 6268 |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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D. Changes in the dossier section on the vaccine antigen master file (VAMF)

D.

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| **D** | | **Changes in the dossier section on the vaccine antigen master file (VAMF)**  **Date of implementation: ……** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no.  6187 |
| D.1 | | Changes to the name, address or contact details of the holder of the VAMF certification for biological products | 1 | 1 |  | |
| D.2 | | Inclusion of an already certified VAMF in the authorisation dossier for a veterinary medicinal product. (VAMF – procedure in a second step) | 2 | 1 |  | |
|  | | **Conditions** | | | |
|  | 1. | The marketing authorisation holder must remain the same legal person. | | | |
|  | 2. | Changes must not adversely affect the properties of the finished product. | | | |
|  |  | **Documentation** | | | |
|  | 1. | If applicable, amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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## Changes that require assessment (sections E – Y)

E. Administrative changes

E.1

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| --- | --- | --- | --- | --- | --- |
| **E.1** | | **Change to date of the audit to verify GMP compliance of the active substance manufacturer** | **Documentation to be submitted** | **Time limit** | SAP no. |
| 1 | Reduced | 6208 |
|  | | **Documentation** | | | |
|  | 1. | Written confirmation from the manufacturer of the finished product that compliance of the manufacturer of the active substance with the principles and guidelines of Good Manufacturing Practice has been verified. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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E.100

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| **E.100** | | **Change in the medicinal product information and/or packaging texts without the submission of scientific data** | **Documentation to be submitted** | **Time limit** | SAP no. |
| 1 | Reduced | 6209 |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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E.101

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| --- | --- | --- | --- | --- | --- |
| **E.101** | | **Conversion of a main authorisation to an export licence** | **Documentation to be submitted** | **Time limit** | SAP no. |
| 1 | Reduced | 6210 |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information (new: basic information). | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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E.102

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| **E.102** | | **Conversion of an export licence to a main authorisation** | **Documentation to be submitted** | **Time limit** | SAP no. |
| 1 | Reduced | 6211 |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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E.103

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| **E.103** | | **Conversion of the authorisation of a co-marketing medicinal product to independent authorisation (basic product)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| 1, 2, 3 | Reduced | 5975 |
| **Documentation** | | | |
|  | 1. | Submission of a complete identical set of documentation (containing no new scientific data!). If the existing basic medicinal product dispenses with authorisation, its documentation can also be transcribed to the existing co-marketing medicinal product. | | | |
|  | 2. | Confirmation that the documentation submitted is identical to that for the basic product (including any additional material that may have been approved in the meantime). | | | |
|  | 3. | Confirmation that the authorisation holder has at its disposal all the documents it requires to fulfil its healthcare-related responsibilities, and accepts all the obligations associated with the authorisation of a stand-alone medicinal product. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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E.104

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| **E.104** | | **Conversion of the authorisation from an independent authorisation (basic product) to a co-marketing medicinal product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| 1, 2 | Reduced | 5976 |
|  | | **Documentation** | | | |
|  | 1. | Part I, as for a new submission for a co-marketing medicinal product (no new scientific data!) | | | |
|  | 2. | The E.103 application | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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E.105

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| **E.105** | | **Adaptation of a co-marketing medicinal product to ensure alignment with the basic product (for example in the event of a change in the medicinal product information and/or packaging texts or a change of quality) with a change to the packaging code** | **Conditions to be fulfilled**  1, 2 ,3, 4, 5 | **Documentation to be submitted**  1, 2, 3 | **Time limit**  Reduced | SAP no.  5977 |
|  | | **Conditions** | | | | |
|  | 1. | In the event of a change to the medicinal product information and/or packaging texts: The modified / new text passages for the basic product will be taken over unchanged. | | | | |
| n/a |  | Justification: | | | | |
|  | 2. | In the event of a change to the medicinal information and/or packaging texts: The medicinal product information texts (Information for healthcare professionals and/or package leaflet) and their translations required by therapeutic products legislation will be uploaded to the Swissmedic publication platform and released (exception: export licence). | | | | |
| n/a |  | Justification: | | | | |
|  | 3. | The change resulted in a change to the packaging code of the basic product. | | | | |
|  | 4. | Based on the duty of the authorisation holder of the basic product to notify changes that need to be taken over to the authorisation holder of the co-marketing medicinal product, the latter submits the respective change within 30 days of approval being granted for the basic product. | | | | |
|  | 5. | The change to the co-marketing medicinal product is implemented simultaneously with the change to the basic product. | | | | |
|  | | **Documentation** | | | | |
|  | 1. | In the case of a change to the medicinal product information, the most recently approved version of the Information for healthcare professionals and/or package leaflet for the basic product, with corrections of the name of the medicinal product, authorisation number and marketing authorisation holder, or the medicinal product information for the co-marketing medicinal product with the most recently approved changes to the basic product in track changes mode, should be submitted. | | | | |
| n/a |  | Justification: | | | | |
|  | 2. | If appropriate, relevant updated forms (e.g. *Full declaration* form, *Manufacturer information* form). | | | | |
| n/a |  | Justification: | | | | |
|  | 3. | The copy of the Swissmedic approval letter for the basic product must be submitted. For a variation of the basic product without an approval letter, a copy of the Swissmedic receipt of confirmation or a print-out of the relevant Swissmedic Portal entry should be submitted instead of the copy of the approval letter. | | | | |
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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| Change in medicinal product information: Current date of revision  …… | …… |

E.106

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| **E.106** | | **Implementation of the new requirements in accordance with the revised TPLRO (as of 1.1.2019)**Revision of the veterinary medicinal product information / packaging materials to EU format including full declaration in accordance with Annex 6 TPLRO | **Documentation to be submitted** | **Time limit** | SAP no. |
| 1, 2, 3 | Standard | 6272 |
|  | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |
|  | 2. | *Full declaration* form | | | |
|  | 3. | Documentation of statements proposed in addition to the medicinal product information approved by Swissmedic. | | | |
| n/a |  | Justification: | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| *no details necessary*  …… | no details necessary  …… |

E.107

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| **E.107** | | **New and/or modified pack sizes** | **Conditions to be fulfilled** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | 1, 2 ,3, 4, 5 | 1, 2 | Reduced | 5978 |
|  | | **Conditions** | | | | |
|  | 1. | No scientific data are submitted. | | | | |
|  | 2. | Declaration that the new pack size is appropriate and consistent with the approved dosage regimen and duration of treatment stated in the Information for healthcare professionals. | | | | |
|  | 3. | If the additional pack size is a free sample pack, a "Free sample" label in at least two official languages must be clearly visible and permanently affixed to the pack. | | | | |
|  | 4. | Sample packs must also be manufactured according to the rules of Good Manufacturing Practice (GMP). | | | | |
|  | 5. | Sample packs of non-prescription medicinal products may contain a maximum of one daily dosage. | | | | |
|  | | **Documentation** | | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | | |
|  | 2. | If applicable, information on the primary packaging material used for sample packs if this is not identical to the packaging of the authorised product (material is described in Ph. Eur. 3.1, is permitted for foodstuffs, satisfies the general requirements of the Ph. Eur. for containers (Chapters 1.3 and 3.2), brief description of the composition, etc.). | | | | |
| n/ a |  |  | | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
| *no details necessary*  …… | no details necessary  …… |

E.z Other administrative change that requires assessment

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| **E.z** | **Other administrative change that requires assessment** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) |  |  | Reduced | 5979 |
| b) |  |  | Standard | 5980 |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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F. Quality changes

F.I Active substance

F.I.a) Manufacture

F.I.a.1

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| --- | --- | --- | --- | --- | --- |
| **F.I.a.1** | | **Change in the manufacturer of a starting material, reagent or intermediate used in the manufacture of an active substance, or change in the manufacturer (including where relevant quality control testing sites) of an active substance, where the approved dossier does not contain a Ph. Eur. Certificate of Suitability (CEP)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Addition of a manufacturer of the active substance supported by a DMF |  | Standard | 5981 |
| b) | | The proposed manufacturer uses a substantially different synthesis route or manufacturing conditions which may have the potential to modify important quality traits of the active substance, such as the qualitative and/or quantitative impurity profile requiring qualification, or physical and chemical properties that affect bioavailability |  | Standard | 5982 |
| c) | | New manufacturer of material for which assessment is required of viral safety and/or TSE risk |  | Standard | 5983 |
| d) | | The change involves a biological active substance or a starting material, reagent or intermediate used in the manufacture of a biological or immunological finished product |  | Standard | 5984 |
| e) | | Addition of a new manufacturer of the active substance that is not supported by a DMF and requires a significant update of the active substance section of the documentation |  | Standard | 5985 |
| f) | | Addition of an alternative sterilisation site for the active substance using a Ph. Eur. method | 1, 2, 3, 4 | Reduced | 5986 |
| g) | | Changes to the quality control site for a biological active substance: Replacement or addition of a site at which batch control or testing including a biological, immunological or immunochemical method takes place |  | Standard | 5987 |
| z) | | Other change |  | Reduced | 5988 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form, if applicable. | | | |
|  | 2. | A declaration by the authorisation holder/DMF holder that the synthesis route (or for herbal medicines, if applicable, the manufacturing method, geographical origin and processing of the herbal drug), the quality control procedures and the specifications for the active substance or the starting material, reagent or intermediate used in the manufacture of the active substance are identical to the procedures and specifications that have already been approved. | | | |
|  | 3. | Batch analysis data (in the form of a comparative table) from at least two batches (on at least pilot scale) of the active substance from the present and proposed manufacturer or site. | | | |
|  | 4. | Comparison of present and proposed manufacturer. | | | |
|  | 5. | Evidence that the site’s GMP compliance has been verified, if applicable (only if the change concerns the active substance manufacturer). | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.I.a.2

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| --- | --- | --- | --- | --- | --- |
| **F.I.a.2** | | **Changes in the manufacturing process for the active substance** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Substantial change in the manufacturing process for the active substance that could have a considerable impact on the quality, safety or efficacy of the finished product |  | Standard | 5989 |
| b) | | The change involves a biological or immunological substance or the use of another substance obtained chemically for the manufacture of a biological or immunological substance that could have a considerable impact on the quality, safety and efficacy of the finished product and is not related to a protocol |  | Standard | 5990 |
| c) | | The change involves a herbal medicinal product and there is a change to one of the following: geographical origin, manufacturing route or production |  | Standard | 5991 |
| d) | | Minor change to the restricted part of the DMF | 1, 2, 3, 4 | Reduced | 5992 |
| z) | | Other change |  | Reduced | 5993 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier and, if applicable, the updated DMF, including a comparison of the present and the proposed manufacturing process. | | | |
|  | 2. | Batch analysis data (in the form of a comparative table) from at least two batches (on at least pilot scale) manufactured using the present and the proposed manufacturing processes. | | | |
|  | 3. | A copy of the approved specifications for the active substance. | | | |
|  | 4. | A declaration by the authorisation holder or the DMF holder that there is no change in the qualitative and quantitative impurity profile or the physical and chemical properties, that the synthesis route remains the same and that the specifications for the active substance or the intermediates remain unchanged. | | | |

Note on F.I.a.2.a): For chemical active substances, this refers to substantial changes to the synthesis route or the manufacturing conditions which may have the potential to modify important quality characteristics of the active substance, such as the qualitative and/or quantitative impurity profile requiring qualification, or physical and chemical properties impacting bioavailability.

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| **Scope / justification for the change** | | |
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| **Present** | **Proposed** |
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F.I.a.3

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| **F.I.a.3** | | **Change in batch size (including batch size range) of the active substance or any intermediate used in the manufacture of an active substance** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | The change requires assessment of the comparability of a biological or immunological active substance |  | Standard | 5994 |
| b) | | The batch size for a biological or immunological active substance is increased or decreased without any change to the manufacturing process (e.g. duplication of the production lines) | 1, 2, 3, 4 | Reduced | 5995 |
| z) | | Other change |  | Reduced | 5996 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | The batch number of the tested batches with the proposed batch size. | | | |
|  | 3. | Batch analysis data (in the form of a comparative table) for at least one production scale batch of the active substance or intermediate manufactured in both the present and the proposed batch sizes. Batch data for the next two full production batches must be submitted on request; they must bereported by the authorisation holder if out of specification (with proposed corrective action). | | | |
|  | 4. | A copy of the approved specifications for the active substance or intermediate. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.I.a.4

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| **F.I.a.4** | | **Change to in-process tests or limits applied during the manufacture of the active substance** | **Documentation to be submitted** | **Time limit** | SAP no. | |
| a) | | Widening of the approved in-process limits that could have a significant effect on the overall quality of the active substance |  | Standard | 5997 | |
| b) | | Deletion of an in-process test that could have a significant effect on the overall quality of the active substance |  | Standard | 5998 | |
| c) | | Addition or replacement of an in-process test as a result of a safety or quality issue | 1, 2, 3, 4, 5 | Reduced | 5999 | |
| z) | | Other change |  | Reduced | 6000 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of present and proposed in-process tests. | | | |
|  | 3. | Details of any new non-pharmacopoeial analytical methods and validation data, if applicable. | | | |
|  | 4. | Batch analysis data for two production batches (three production batches for biologicals, unless otherwise justified) of the active substance for all specification parameters. | | | |
|  | 5. | Justification or risk assessment from the authorisation holder or the DMF holder for the new in-process tests. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.I.b) Control of the active substance

F.I.b.1

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| **F.I..b.1** | | **Change in the specification parameters and/or limits of an active substance or a starting material, intermediate or reagent used in the manufacture of an active substance** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Deletion of a specification parameter that could have a significant effect on the overall quality of the active substance and/or the finished product |  | Standard | 6001 |
| b) | | Change outside the approved specification limits range for the active substance |  | Standard | 6002 |
| c) | | Widening of the approved specification limits for starting materials or intermediates that could have a significant effect on the overall quality of the active substance and/or the finished product |  | Standard | 6003 |
| d) | | Addition or replacement (except for biological or immunological substances) of a specification parameter with the corresponding test method as a result of a safety or quality issue | 1, 2, 3, 4, 5, 6 | Reduced | 6004 |
| e) | | Where there is no monograph in the Ph. or the Ph. Helv. for an active substance, a change in specification from in-house to an unofficial pharmacopoeia or a pharmacopoeia of a third country | 1, 2, 3, 4, 5, 6 | Reduced | 6005 |
| f) | | Deletion from the dossier of details of the extent of testing by the finished product manufacturer on receipt of the active substance 1) |  | Reduced | 6006 |
| g) | | Reduction of the testing frequency of a test parameter from routine to occasional testing (skip testing) or complete elimination |  | Reduced | 6007 |
| z) | | Other change |  | Reduced | 6008 |
|  | | **Documentation** |  |  |  |
|  | 1. | Amendment of the relevant section(s) of the dossier. |  |  |  |
|  | 2. | Comparison of present and proposed specifications. | | | |
|  | 3. | Details of new analytical methods and, if applicable, validation data. | | | |
|  | 4. | Batch analysis data for two production batches (three production batches for biologicals, unless otherwise justified) of the active substance for all specification parameters. | | | |
|  | 5. | If applicable, comparative dissolution profiles of the finished product from at least one pilot scale batch with the active substance that complies with the present and the proposed specifications. Comparative disintegration data may also be acceptable for herbal medicinal products. | | | |
|  | 6. | Justification of the new specification parameter and limits by the authorisation holder or the DMF holder. | | | |

1) The information on the extent of testing by the finished product manufacturer on receipt of the active substance should be deleted from the dossier since this is considered to be a GMP issue.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.I.b.2

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| **F.I.b.2** | | **Change in test method for an active substance or for a starting material, intermediate or reagent used in the manufacture of an active substance** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Substantial change in or replacement of a biological, immunological or immunochemical test method or a method in which a biological reagent is used for a biological active substance |  | Standard | 6009 |
| b) | | Other changes in a test method (including replacement or addition) for the active substance or a starting material or intermediate | 1, 2 | Reduced | 6010 |
| z) | | Other change |  | Reduced | 6011 |
|  | | **Documentation** |  | |  |
|  | 1. | Amended relevant section(s) of the dossier, including a description of the analytical method, a summary of the validation data and, if applicable, revised specifications for impurities. | | | |
|  | 2. | Comparative validation results or, if justified, comparative analytical results showing that the present and proposed test methods are equivalent. This requirement is not applicable if a new test method is being added. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.I.c) Container closure system

F.I.c.1

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| **F.I.c.1** | | **Change in the primary packaging of the active substance** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Qualitative and/or quantitative composition for sterile and non-frozen biological or immunological active substances |  | Standard | 6012 |
| b) | | Liquid active substances (non-sterile) | 1, 2, 3, 4, 5 | Reduced | 6013 |
| z) | | Other change |  | Reduced | 6014 |
|  | | **Documentation** |  | |  |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Appropriate data on the new packaging (e.g. comparative permeability data for O2, CO2, moisture), including confirmation that the material complies with the relevant pharmacopoeial requirements or the provisions of the Food Contact Materials Ordinance (SR 817.023.21). | | | |
|  | 3. | If appropriate, evidence must be provided that no interaction between the contents and the packaging material occurs (e.g. no migration of components of the proposed material into the contents and no loss of components of the product into the pack); in addition, confirmation that the material complies with the relevant pharmacopoeial requirements or the provisions of the Food Contact Materials Ordinance (SR 817.023.21). | | | |
|  | 4. | The results of stability studies that have been carried out under VICH conditions, on the relevant stability parameters, on at least two pilot or production scale batches, covering a minimum period of three months, and confirmation that these studies will be finalised, and that data will be submitted to Swissmedic without delay if out of specification or potentially out of specification at the end of the retest period (with proposed corrective action). | | | |
|  | 5. | If applicable, a comparison of the present and proposed primary packaging specifications. | | | |

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| **Scope / justification for the change** | |
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F.I.c.2

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| **F.I.c.2** | | **Change in the specification parameters and/or limits for the primary packaging of the active substance** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Addition or replacement of a specification parameter as a result of a safety or quality issue |  | Reduced | 6015 |
| z) | | Other change |  | Reduced | 6016 |
|  | | **Documentation** |  | |  |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of present and proposed specifications. | | | |
|  | 3. | Details of the new analytical method and, if applicable, validation data. | | | |
|  | 4. | Batch analysis data for two batches of the primary packaging for all specification parameters. | | | |
|  | 5. | Justification of the new specification parameter and the limits by the authorisation holder or the DMF holder. | | | |

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| **Scope / justification for the change** | |
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F.I.c.3

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| **F.I.c.3** | **Change in test method for the primary packaging of the active substance** | **Documentation to be submitted** | **Time limit** | SAP no. |
| z) | Other change |  | Reduced | 6017 |

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| **Scope / justification for the change** | |
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F.I.d) Stability

F.I.d.1

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| **F.I.d.1** | | **Change in the retest period or storage period of the active substance if the approved dossier does not contain a Ph. Eur. Certificate of Suitability (CEP) covering the retest period** | | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Extension of the retest period based on extrapolation of stability data that do not comply with the VICH guidelines (not applicable to biological or immunological active substances) | |  | Standard | 6018 |
| b) | | Extension of the storage period of a biological or immunological active substance that does not comply with an approved stability testing plan | |  | Standard | 6019 |
| c) | | Extension or addition of a retest period or storage period supported by real-time data | | 1, 2, 3 | Reduced | 6020 |
|  | | **Documentation** |  | | |  |
|  | 1. | Amendment of the relevant section(s) of the dossier. The relevant sections must contain results of appropriate real-time stability studies conducted in accordance with the relevant stability guidelines on at least two (three for biological medicinal products) pilot or production scale batches of the active substance in the authorised packaging material and covering the duration of the proposed retest period or proposed storage conditions. | | | | |
|  | 2. | Confirmation that the stability studies were conducted according to the currently approved protocol; the studies must show that the agreed relevant specifications are still met. | | | | |
|  | 3. | Copy of the approved specifications for the active substance. | | | | |

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| **Scope / justification for the change** | |
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F.I.d.2

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| **F.I.d.2** | | **Change in the storage conditions for the active substance if the approved dossier does not contain a Ph. Eur. Certificate of Suitability (CEP) covering the retest period** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Change in storage conditions for biological or immunological active substances if the stability studies have not been performed in accordance with the currently approved stability protocol |  | Standard | 6021 |
| b) | | Change in storage conditions for the active substance / reference standard | 1, 2, 3 | Reduced | 6022 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. The relevant sections must contain the results of appropriate real-time stability studies conducted in accordance with the relevant stability guidelines on at least two (three for biological medicinal products) pilot or production scale batches of the active substance in the authorised packaging material and covering the duration of the proposed retest period or proposed storage conditions. | | | |
|  | 2. | Confirmation that the stability studies were conducted according to the currently approved protocol; the studies must show that the agreed relevant specifications are still met. | | | |
|  | 3. | Copy of the approved specifications for the active substance. | | | |

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| **Scope / justification for the change** | |
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F.I.d.z

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| **F.I.d.z** | **Other change to section F.I.d** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Reduced | 6023 |

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| **Scope / justification for the change** | |
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F.I.e) Design space and post-approval change management protocol

F.I.e.1

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| **F.I.e.1** | | **Introduction of a new design space or extension of an approved design space for the active substance, concerning:** | | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | A manufacturing operation for the active substance including the resulting in-process tests and/or test methods | | 1, 2, 3 | Standard | 6024 |
| b) | | Test methods for starting materials / reagents / intermediates and/or the active substance | | 1, 2, 3 | Standard | 6025 |
|  | | **Documentation** |  | | |  |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |  |
|  | 2. | The design space was developed in accordance with the relevant international scientific guidelines. The results of product, process and analytical development studies (e.g. interaction of the different parameters forming the design space must be studied, including risk assessment and multivariate studies, if appropriate) demonstrate that a systematic mechanistic understanding of material attributes and process parameters for the critical quality traits of the active substance has been achieved. | | | |  |
|  | 3. | Description of the design space in tabular format, including the variables (material attributes and process parameters, if relevant) and their proposed ranges. | | | | |

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| **Scope / justification for the change** | |
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F.I.e.2

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| **F.I.e.2** | | **Changes to an approved change management protocol related to the active substance** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Introduction of a post-approval change management protocol related to the active substance | 1, 2, 3 | Standard | 6026 |
| b) | | Major changes in an approved change management protocol |  | Standard | 6027 |
| c.1) | | Implementation of proposed changes in an approved change management protocol requiring further supporting data | 4, 5, 6 | Reduced | 6028 |
| c.2) | | Implementation of proposed changes in an approved change management protocol for a biological or immunological medicinal product | 4, 5, 6, 7 | Reduced | 6029 |
|  | | **Documentation** | | | |
|  | 1. | Detailed description of the proposed change. | | | |
|  | 2. | Change management protocol for the active substance. | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 4. | Reference to the approved change management protocol. | | | | |
|  | 5. | Declaration that the change has been implemented in accordance with the approved change management protocol and that the study results comply with the acceptance criteria in the protocol; in addition, a declaration that a comparability evaluation is not required for biological or immunological medicinal products. | | | | |
|  | 6. | Results of studies performed in accordance with the approved change management protocol. | | | | |
|  | 7. | Copy of the approved specifications for the active substance. | | | | |

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| **Scope / justification for the change** | |
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F.I.e.z

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| **F.I.e.z** | Other change **to section F.I.e** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Reduced | 6030 |

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| **Scope / justification for the change** | |
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F.I.f) Other changes to the active substance

F.I.f.1

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| **F.I.f.1** | **Substantial changes to the amended version of the DMF or in the active substance part of the dossier** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6031 |

Note: Amendments to the active substance part of the dossier or the DMF can in principle be submitted as a multiple application, with the process being determined by the longest time limit. However, if the number of changes exceeds a certain number, it is recommended to submit them not as a multiple application but as a single category F.I.f.1 variation.

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| **Scope / justification for the change** | |
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F.II. Finished product

F.II.a) Description and composition

F.II.a.1

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| **F.II.a.1** | | **Change in or addition of imprints, bossing or other markings including replacement or addition of inks used for product marking** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Changes in scoring/break lines intended to divide into equal doses | 1, 2 | Reduced | 6032 |
| z) | | Other change |  | Reduced | 6033 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a detailed drawing or written description of the present and new appearance, and including revised medicinal product information and/or packaging texts if appropriate. | | | | |
|  | 2. | Results of the appropriate Ph. Eur. tests demonstrating equivalence of characteristics / correct dosing. | | | | |

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| **Scope / justification for the change** | |
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F.II.a.2

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| **F.II.a.2** | | **Change in the shape or dimensions of the pharmaceutical form** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Gastric-coated, modified or prolonged-release pharmaceutical forms and scored tablets intended to be divided into equal doses | 1, 2, 3, 4 | Reduced | 6034 |
| b) | | Addition of a new kit for a radiopharmaceutical preparation with a different fill volume |  | Standard | 6035 |
| z) | | Other change |  | Reduced | 6036 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a detailed drawing of the present and proposed situation and, if appropriate, revised medical product information and/or packaging texts. | | | |
|  | 2. | Comparative dissolution profiles of at least one pilot batch of the present and proposed dimensions (no significant difference regarding comparability, see the relevant guidance on bioavailability (human or veterinary medicinal products)). Comparative disintegration data may also be sufficient for herbal medicinal products. | | | |
|  | 3. | Justification for not submitting a new bioequivalence study according to the relevant guidance on bioavailability / bioequivalence. | | | |
|  | 4. | Results of the appropriate Ph. Eur. tests demonstrating equivalence of characteristics / correct dosing. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.II.a.3

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| **F.II.a.3** | | **Changes in the composition (excipients) of the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Changes in components of the flavouring or colouring system |  |  |  |
| 1) | | Biological veterinary medicinal products for oral use in which the colouring or flavouring agent is important for uptake by the target species |  | Standard | 6037 |
| b) | | Other excipients |  |  |  |
| 1) | | Qualitative or quantitative changes in one or more excipients that may have a significant effect on the safety, quality or efficacy of the finished product |  | Standard | 6038 |
| 2) | | Changes in a biological or immunological finished product |  | Standard | 6039 |
| 3) | | Any new excipient that includes the use of materials of human or animal origin for which assessment of viral safety data or TSE risk is required |  | Standard | 6040 |
| 4) | | Change that is supported by a bioequivalence study |  | Standard | 6041 |
| 5) | | Replacement of a single excipient with a comparable excipient with the same functional characteristics and in a similar quantity | 1, 2, 3, 4, 5, 6, 7, 8 | Reduced | 6042 |
| z) | | Other change |  | Reduced | 6043 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a method to determine the identity of new colouring agents, if appropriate, and revised medicinal product information and packaging texts and the *Full declaration* form, if appropriate. | | | |
|  | 2. | The results of stability studies that have been carried out under VICH conditions, on the relevant stability parameters, on at least two pilot or industrial scale batches, covering a minimum period of three months, and confirmation that these studies will be finalised, and that data will be submitted to Swissmedic without delay if out of specification or potentially out of specification at the end of the approved storage period (with proposed corrective action). | | | |
|  | 3. | Either a Ph. Eur. Certificate of TSE Suitability (CEP) for each new substance originating from animals with a risk of TSE or, if applicable, proof for all substances within the scope of the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (including substances used in the manufacture of the active substance/excipient). The following information must be included for each of these materials: name of manufacturer, species and tissues from which the material is derived, country of origin of the source animals and its use. In addition, an updated *Substances of animal and human origin* form. | | | |
|  | 4. | If applicable, data to demonstrate that the new excipient does not interfere with the finished product specification test methods. | | | |
|  | 5. | Justification for the change/choice of excipients, etc. must be provided through appropriate pharmaceutical development (including stability aspects and antimicrobial preservation if applicable). | | | |
|  | 6. | For solid pharmaceutical forms, comparative dissolution profile data for at least two pilot scale batches of the finished product in the old and new composition. Comparative disintegration data may also be acceptable for herbal medicinal products. | | | |
|  | 7. | Justification for not submitting a new bioequivalence study according to the current guidance on bioequivalence. | | | |
|  | 8. | For veterinary medicinal products intended for use in food-producing species, evidence that excipient residues in animal tissues are harmless according to the state of the art in science and technology, or reason why the excipient has no pharmacological activity at the dose administered to the target animal. | | | |

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| **Scope / justification for the change** | |
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F.II.a.4

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| **F.II.a.4** | **Change in the shape or dimensions of the pharmaceutical form** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | Gastric-coated, modified or extended release pharmaceutical forms in which the coating is a major factor in the release mechanism |  | Standard | 6044 |
| z) | Other change |  | Reduced | 6045 |

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| **Scope / justification for the change** | |
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F.II.a.5

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| **F.II.a.5** | **Change in concentration of a single-dose, total-use parenteral, where the amount of active substance per unit dose (i.e. the strength) remains the same** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6046 |

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| **Scope / justification for the change** | |
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F.II.a.z

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| **F.II.a.z** | Other change **to section F.II.a** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Reduced | 6047 |

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| **Scope / justification for the change** | |
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F.II.b) Manufacture

F.II.b.1

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| **F.II.b.1** | | **Replacement or addition of a manufacturing site for part or all of the manufacturing process for the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Site where any manufacturing operations take place, except batch release, batch control (quality control) and secondary packaging, for biological or immunological medicinal products, or for pharmaceutical forms manufactured by complex manufacturing processes |  | Standard | 6048 |
| b) | | Site which requires an initial inspection or product-specific inspection |  | Standard | 6049 |
| c) | | Site where any manufacturing operations take place, except batch-release, batch control (quality control), primary and secondary packaging, for non-sterile medicinal products | 1, 2, 3, 4, 5, 6, 7, 8, 9 | Reduced | 6050 |
| d) | | Site where any manufacturing operations take place, except batch release, batch control (quality control) and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological or immunological medicinal products | 1, 2, 3, 4, 5, 6, 7, 8 | Reduced | 6051 |
| e) | | Change in the supplier of components for sterilised primary containers used for aseptically manufactured veterinary medicinal products |  | Reduced | 6052 |
| z) | | Other change |  | Reduced | 6053 |
|  | | **Documentation** | | | |
|  | 1. | Evidence that the manufacturer’s GMP compliance has been verified. | | | |
|  | 2. | Where necessary, the batch numbers, corresponding batch size and manufacturing date of the batches (≥3) used in the validation study and the validation data or validation protocol (scheme) must be submitted. | | | |
|  | 3. | Comparison of present and proposed sites. | | | |
|  | 4. | A copy of the approved release and storage period specifications. | | | |
|  | 5. | Batch analysis data for one production batch and two pilot scale batches manufactured using the commercial manufacturing process (or two production batches) and comparative data for the last three batches from the current site. Batch data for the next two production batches should be available on request or submitted if out of specification (with proposed corrective action). | | | |
|  | 6. | For semi-solid and liquid formulations in which the active substance is present in non-dissolved form, appropriate validation data, including a microscopic image of particle size distribution and morphology or any other appropriate imaging technique. | | | |
|  | 7. | Completed and signed *Declaration by the Responsible Person for foreign manufacturers* form. | | | |
|  | 8. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form. | | | |
|  | 9. | If manufacture and primary packaging take place at two different sites, the conditions for transporting and storing the bulk product must be specified and validated. | | | |

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| **Scope / justification for the change** | |
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F.II.b.2

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| **F.II.b.2** | **Change to the site where batch release and quality control testing of the finished product take place** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | Replacement or addition of a site where batch control and testing (quality control) take place |  |  |  |
| 1) | Replacement or addition of a site where batch control and testing (quality control) take place for a biological or immunological product and any of the test methods performed at the site is a biological or immunological method |  | Standard | 6054 |
| b) | Replacement or addition of a manufacturer responsible for batch release |  |  |  | |
| 1) | Including batch control or testing (quality control) of a biological or immunological finished product, where any of the test methods performed at the site is a biological, immunological or immunochemical method |  | Standard | 6056 | |
| z) | Other change |  | Reduced | 6057 | |

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| **Scope / justification for the change** | |
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F.II.b.3

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| **F.II.b.3** | | **Change in the manufacturing process for the finished product, including an intermediate used in the manufacture of the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Minor change in the manufacturing process | 1, 2, 3, 4, 5, 6, 7, 8 | Reduced | 6058 |
| b) | | Substantial changes in the manufacturing process that may have a significant effect on the quality, safety and efficacy of the finished product |  | Standard | 6059 |
| c) | | The product is a biological or immunological finished product and the change requires an assessment of comparability |  | Standard | 6060 |
| d) | | Introduction of a non-standard terminal sterilisation method |  | Standard | 6061 |
| e) | | Introduction or increase in the overage used for the active substance |  | Standard | 6062 |
| f) | | Minor change in the manufacturing process of an aqueous oral suspension | 1, 2, 4, 6, 7, 8 | Reduced | 6063 |
| g) | | Change in sterile filtration from clean room class A/B to clean room class C |  | Standard | 6064 |
| h) | | Change in holding time of an intermediate or bulk product (if applicable) |  | Reduced | 6065 |
| i) | | Minor change in the manufacturing process of a sterile finished product after filling into the primary container |  | Reduced | 6066 |
| z) | | Other change |  | Reduced | 6067 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a comparison of the present manufacturing process and the proposed process. | | | |
|  | 2. | For semi-solid and liquid medicinal products in which the active substance is present in non-dissolved form: appropriate validation of the change including microscopic imaging of particles to check for visible changes in morphology and comparative size distribution data obtained by an appropriate method. | | | |
|  | 3. | For solid pharmaceutical forms: dissolution profile data for one representative production batch and comparative data for the last three batches from the present manufacturing process; data for the next two production batches should be available on request or submitted if out of specification (with proposed corrective action). For herbal medicinal products comparative disintegration data may be acceptable. | | | |
|  | 4. | Justification for not submitting a new bioequivalence study according to the relevant guidance on bioavailability. | | | |
|  | 5. | For changes to process parameters that are considered to have no impact on the quality of the finished product, a declaration to this effect reached in the context of the previously approved risk assessment. | | | |
|  | 6. | A copy of the approved release and storage period specifications. | | | |
|  | 7. | Batch analysis data (in the form of a comparative table) for a minimum of one batch manufactured using the present process and one using the proposed process. Batch data for the next two production batches should be available on request and submitted if out of specification (with proposed corrective action). | | | |
|  | 8. | A declaration that relevant stability studies have been started under VICH conditions (stating the batch numbers concerned), that relevant stability parameters have been assessed in at least one pilot scale or industrial scale batch, that the applicant has at least three months of satisfactory stability data at the time of notification and that the stability profile is similar to the present situation. Confirmation that these studies will be finalised and that data will be submitted to Swissmedic without delay if out of specification or potentially out of specification at the end of the storage period (with proposed corrective action). | | | |

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| **Scope / justification for the change** | |
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F.II.b.4

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| **F.II.b.4** | | **Change in the batch size (including batch size range) of the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | The change requires assessment of the comparability of a biological or immunological medicinal product, or the change in batch size requires a new bioequivalence study |  | Standard | 6068 |
| b) | | The change involves all other pharmaceutical forms manufactured using a complex manufacturing process |  | Standard | 6069 |
| c) | | More than ten-fold increase compared to the originally approved batch size for rapid-release oral pharmaceutical forms | 1, 2, 3, 4, 5, 6 | Reduced | 6070 |
| d) | | The batch size for a biological or immunological medicinal product is being increased or decreased without any change in the manufacturing process (e.g. duplication of the production lines) | 1, 2, 3, 4, 5, 6 | Reduced | 6071 |
| z) | | Other change |  | Reduced | 6072 |
|  | | **Documentation** |  | |  |
|  | 1. | Amended relevant section(s) of the dossier | | | |
|  | 2. | Batch analysis data (in the form of a comparative table) for at least one production batch manufactured in both the present and the proposed batch size. Batch data for the next two full production batches must be made available upon request and reported by the authorisation holder if out of specification (with proposed corrective action). | | | |
|  | 3. | A copy of the approved release and storage period specifications. | | | |
|  | 4. | Where necessary, the batch numbers, corresponding batch size and manufacturing date of the batches (≥3) used in the validation study must be indicated or the validation protocol (scheme) must be submitted. | | | |
|  | 5. | The validation results are available. | | | |
|  | 6. | The results of stability studies that have been carried out under VICH conditions, on the relevant stability parameters, on at least one pilot or industrial scale batch, covering a minimum period of three months, and confirmation that these studies will be finalised, and that data will be submitted to Swissmedic without delay if out of specification or potentially out of specification at the end of the approved storage period (with proposed corrective action). For biological or immunological medicinal products: a declaration that an assessment of comparability is not required. | | | |

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F.II.b.5

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| **F.II.b.5** | | **Change to in-process tests or limits applied during the manufacture of the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Deletion of an in-process test that could have a significant effect on the overall quality of the finished product |  | Standard | 6073 |
| b) | | Widening of the approved in-process test limits that could have a significant effect on the overall quality of the finished product |  | Standard | 6074 |
| c) | | Addition or replacement of an in-process test as a result of a safety or quality issue | 1, 2, 3, 4, 5, 6 | Reduced | 6075 |
| z) | | Other change |  | Reduced | 6076 |
|  | | **Documentation** | | | |
|  | 1. | Amended relevant section(s) of the dossier | | | |
|  | 2. | Comparison of present and proposed in-process tests and limits. | | | |
|  | 3. | Details of the new analytical methods and validation data, if applicable. | | | |
|  | 4. | Batch analysis data for two production batches (three production batches for biologicals, unless otherwise justified) of the finished product for all specification parameters. | | | |
|  | 5. | Where appropriate, comparative dissolution profile data for the finished product from at least one pilot scale batch containing the active substance manufactured using the present and new in-process tests. For herbal medicinal products, comparative disintegration data are also sufficient. | | | |
|  | 6. | Justification for the new in-process tests and limits. | | | |

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| **Scope / justification for the change** | |
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F.II.c) Control of excipients

F.II.c.1

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| **F.II.c.1** | | **Change in specification parameters and/or limits for an excipient** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Change outside the approved specification limits range |  | Standard | 6077 |
| b) | | Deletion of a specification parameter that may have a significant effect on the overall quality of the finished product |  | Standard | 6078 |
| c) | | Addition or replacement (excluding biological or immunological products) of a specification parameter with the corresponding test method as a result of a safety or quality issue | 1, 2, 3, 4, 5, 6, 7 | Reduced | 6079 |
| d) | | Where there is no monograph in the Ph. Eur. or the Ph. Helv. for an excipient, a change in specification from in-house to an unofficial pharmacopoeia or a pharmacopoeia of a third country | 1, 2, 3, 4, 5, 6, 7 | Reduced | 6080 |
| z) | | Other change |  | Reduced | 6081 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of present and proposed specifications. | | | |
|  | 3. | Details of the new analytical method and, if applicable, validation data. | | | |
|  | 4. | Batch analysis data from two production batches of the excipient for all specification parameters (or three production batches for biological excipients). | | | |
|  | 5. | Where applicable, comparative dissolution profile data for the finished product on at least one pilot batch containing the excipient complying with the current and proposed specifications. Comparative disintegration data may be sufficient for herbal medicinal products. | | | |
|  | 6. | If applicable, justification for not submitting a new bioequivalence study according to the relevant guidance on bioavailability/bioequivalence. | | | |
|  | 7. | Justification of the new specification parameter and limits. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.II.c.2

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| **F.II.c.2** | | **Change in the test methods for an excipient** | | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Substantial change in or replacement of a biological, immunological or immunochemical test method or a method involving a biological reagent | |  | Standard | 6082 |
| b) | | Other changes in a test method (including replacement or addition) | | 1, 2 | Reduced | 6083 |
| z) | | Other change | |  | Reduced | 6084 |
|  | | **Documentation** |  | | |  |
|  | 1. | Amended relevant section(s) of the dossier, including a description of the analytical method, a summary of the validation data and, if applicable, revised specifications for impurities. | | | | |
|  | 2. | Comparative validation results or, if justified, comparative analytical results showing that the present and proposed test methods are equivalent. This requirement is not applicable if a new test method is being added. | | | | |

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| **Scope / justification for the change** | |
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F.II.c.3

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| **F.II.c.3** | | **Change in the source of an excipient or reagent with TSE risk** | **Documentation to be submitted** | **Time limit** | SAP no. | |
| a) | | For excipients or reagents used in the manufacture of a biological or immunological active substance or a biological or immunological medicinal product | 1, 2 | Reduced | 6085 | |
| b) | | Change in or addition of a TSE risk material, or replacement of a TSE risk material by a different TSE risk material not covered by a TSE Ph. Eur. Certificate of Suitability (CEP) |  | Standard | 6086 | |
| z) | | Other change |  | Reduced | 6087 | |
|  | | **Documentation** | | | |
|  | 1. | Declaration from the manufacturer or the authorisation holder of the material that it is of purely plant or synthetic origin. | | | | |
|  | 2. | Study of equivalence of the materials and the impact on manufacture of the final material and on the behaviour (e.g. dissolution characteristics) of the finished product. | | | | |

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F.II.c.4

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| **F.II.c.4** | **Change in synthesis or recovery of a non-pharmacopoeial excipient (if described in the dossier) or a novel excipient** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | The specifications are affected or there is a change in the physical and chemical properties of the excipient which may affect the quality of the finished product |  | Standard | 6088 |
| b) | The excipient is a biological or immunological substance. |  | Standard | 6089 |
| z) | Other change |  | Reduced | 6090 |

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| **Scope / justification for the change** | |
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F.II.d) Control of the finished product

F.II.d.1

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| **F.II.d.1** | | **Change in the specification parameters and/or limits for the finished product** | **Documentation to be submitted** | | **Time limit** | SAP no. |
| a) | | Change outside the approved specification limits range |  | | Standard | 6091 |
| b) | | Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product |  | | Standard | 6092 |
| c) | | Addition or replacement (excluding biological or immunological products) of a specification parameter with the corresponding test method as a result of a safety or quality issue | 1, 2, 3, 4, 5, 6 | Reduced | | 6093 |
| d) | | Reduction of the testing frequency of a test parameter from routine to occasional testing (skip testing) or complete elimination (microbial testing of the finished product) |  | | Reduced | 6094 |
| z) | | Other change |  | | Reduced | 6095 |
|  | | **Documentation** | | | | |
|  | 1. | Amended relevant section(s) of the dossier | | | | |
|  | 2. | Comparison of present and proposed specifications. | | | | |
|  | 3. | Details of the new analytical method and, if applicable, validation data. | | | | |
|  | 4. | Batch analysis data for two production batches (three production batches for biologicals, unless otherwise justified) of the finished product for all specification parameters. | | | | |
|  | 5. | If applicable, comparative dissolution profile for the finished product on at least one pilot batch complying with the present and proposed specifications. For herbal medicinal products, comparative disintegration data are also sufficient. | | | | |
|  | 6. | Justification of the new specification parameter and limits. | | | | |

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| **Scope / justification for the change** | |
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F.II.d.2

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| **F.II.d.2** | | **Change in the test method for the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Substantial change to, or replacement of, a biological, immunological or immunochemical test method or a method using a biological reagent or replacement of a biological reference substance not covered by an approved protocol |  | Standard | 6096 |
| b) | | Other changes to a test method (including replacement or addition) | 1, 2 | Reduced | 6097 |
| c) | | Replacement of a biological or immunological reference preparation (e.g. reference vaccine batch or reference serum batch) in an immunological or immunochemical test method that may have a significant effect on the quality of the medicinal product (e.g. estimation of potency). |  | Standard | 6098 |
| z) | | Other change |  | Reduced | 6099 |
|  | | **Documentation** |  | |  |
|  | 1. | Amended relevant section(s) of the dossier, including a description of the analytical method, a summary of the validation data and, if applicable, revised specifications for impurities. | | | |
|  | 2. | Comparative validation results or, if justified, comparative analytical results showing that the present and proposed test procedures are equivalent. This requirement is not applicable if a new test method is being added. | | | |

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F.II.d.3

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| **F.II.d.3** | **Changes related to the addition of real-time release or parametric release in the manufacture of the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6100 |

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| **Scope / justification for the change** | |
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F.II.e) Container closure system

F.II.e.1

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| **F.II.e.1** | | **Changes to the primary packaging of the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Qualitative and quantitative composition |  |  |  |
| 1) | | Semi-solid and non-sterile liquid pharmaceutical forms | 1, 2, 3, 4, 5 | Reduced | 6101 |
| 2) | | Sterile medicinal products and biological or immunological medicinal products |  | Standard | 6102 |
| 3) | | The change relates to a less protective pack where there are associated changes in storage conditions and/or a reduction of the storage period |  | Standard | 6103 |
| b) | | Change in type of container or addition of a new container |  |  |  |
| 1) | | Solid, semi-solid and non-sterile liquid pharmaceutical forms | 1, 2, 3, 4, 5 | Reduced | 6104 |
| 2) | | Sterile medicinal products and biological or immunological medicinal products |  | Standard | 6105 |
| z) | | Other change |  | Reduced | 6106 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including revised product information and/or packaging texts as appropriate. | | | |
|  | 2. | Appropriate data on the new packaging (comparative data on permeability e.g. to O2, CO2, moisture). | | | |
|  | 3. | If applicable, evidence that no interaction between the content and the packaging material occurs (e.g. no migration of components of the proposed material into the content and no loss of components of the product into the pack), including confirmation that the material complies with the relevant pharmacopoeial requirements or the provisions of the Food Contact Materials Ordinance (SR 817.023.21). | | | |
|  | 4. | The results of stability studies that have been carried out under VICH conditions, on the relevant stability parameters, on at least two pilot or industrial scale batches, covering a minimum period of three months, and confirmation that these studies will be finalised, and that data will be submitted to Swissmedic without delay if out of specification or potentially out of specification at the end of the approved storage period (with proposed corrective action). | | | |
|  | 5. | If applicable, a comparison of the present and proposed primary packaging specifications. | | | |

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| **Scope / justification for the change** | |
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F.II.e.2

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| **F.II.e.2** | | **Change in the specification parameters and/or limits for the primary packaging of the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Addition or replacement of a specification parameter as a result of a safety or quality issue | 1, 2, 3, 4, 5 | Reduced | 6107 |
| z) | | Other change |  | Reduced | 6108 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of present and proposed specifications. | | | |
|  | 3. | Details of the new analytical method and, if applicable, validation data. | | | |
|  | 4. | Batch analysis data for two batches of the primary packaging for all specification parameters. | | | |
|  | 5. | Justification of the new specification parameter and limits. | | | |

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| **Scope / justification for the change** | |
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F.II.e.3

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| **F.II.e.3** | **Change in the test method for the primary packaging of the finished product** | | **Documentation to be submitted** | **Time limit** | SAP no. |
| z) | Other change |  | | Reduced | 6109 |

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| **Scope / justification for the change** | |
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F.II.e.4

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| **F.II.e.4** | | **Change in shape or dimensions of the container or the closure (primary packaging)** | | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | The change in shape or dimensions involves a fundamental part of the packaging material and may have a significant effect on the administration, use, safety or stability of the finished product | |  | Standard | 6110 |
| b) | | Sterile medicinal products |  | 1, 2, 3 | Reduced | 6111 |
| z) | | Other change | |  | Reduced | 6112 |
|  | | **Documentation** |  | | |  |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a description, detailed drawing and composition of the container closure material, and including revised product information and/or packaging texts if applicable. | | | | |
|  | 2. | Revalidation studies have been performed for terminally sterilised sterile products. The batch numbers of the batches used in the revalidation studies must be stated, if applicable. | | | | |
|  | 3. | If the head space or the surface/volume ratio changes, a declaration that the required stability studies have been started under VICH conditions (stating the batch numbers concerned) and that, where relevant, the required minimum satisfactory stability data were available to the applicant at the time of implementation of a type IA variation or the time of submission of a type IB variation, and that the available data did not indicate a problem. Confirmation that these studies will be finalised and that data will be submitted without delay to Swissmedic if out of specification or potentially out of specification at the end of the approved storage period (with proposed corrective action). | | | | |

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| **Scope / justification for the change** | |
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F.II.e.5

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| **F.II.e.5** | | **Change in the pack size of the finished product** | | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Change in the number of units (e.g. tablets, ampoules) in a pack outside the range of the currently approved pack sizes | | 1, 2, 3 | Reduced | 6113 |
| b) | | Change in the fill weight or fill volume of sterile multi-dose (or single-dose, partial use) parenteral medicinal products, including biological, immunological and parenteral medicinal products | |  | Standard | 6114 |
| c) | | Change in the fill weight or fill volume of non-parenteral multi-dose (or single-dose, partial use) medicinal products |  | 1, 2, 3 | Reduced | 6115 |
| z) | | Other change | |  | Reduced | 6116 |
|  | | **Documentation** |  | | |  |
|  | 1. | Amendment of the relevant section(s) of the dossier, including revised medicinal product information and/or packaging texts if applicable. | | | | |
|  | 2. | Justification for the new/remaining pack size, showing that the new/remaining size is consistent with the dosing instructions and treatment duration as approved in the Information for healthcare professionals. | | | | |
|  | 3. | Declaration that stability studies will be conducted in accordance with the relevant guidance for products where stability parameters could be affected. Data to be reported only if they are out of specification (with proposed corrective action). | | | | |

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F.II.e.6

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| **F.II.e.6** | **Change in any part of the (primary) packaging material not in contact with the finished product formulation (such as colour of flip-off caps, colour code rings on ampoules, change of needle shield (different plastic used), etc.)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| z) | Other change |  | Reduced | 6117 |

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| **Scope / justification for the change** | |
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F.II.e.7

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| **F.II.e.7** | **Change in supplier of packaging components or administration devices (when mentioned in the dossier)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | Any change to suppliers of spacer devices for metered dose inhalers |  | Standard | 6118 |
| z) | Other change |  | Reduced | 6119 |

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| **Scope / justification for the change** | |
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F.II.f) Stability

F.II.f.1

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| **F.II.f.1** | | **Change in the storage period or storage conditions of the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Extension of the storage period of the finished product |  |  |  |
| 1) | | As packaged for sale (supported by real-time data) | 1, 2, 3 | Reduced | 6120 |
| 2) | | After first opening (supported by real-time data) | 1, 2, 3 | Reduced | 6121 |
| 3) | | After dilution or reconstitution (supported by real-time data) | 1, 2, 3 | Reduced | 6122 |
| 4) | | Extension of the storage period based on extrapolation of stability data not in accordance with IVCH guidelines1 |  | Standard | 6123 |
| 5) | | Extension of the storage period of a biological or immunological medicinal product in accordance with an approved stability protocol | 1, 2, 3 | Reduced | 6124 |
| b) | | Change in storage conditions for biological or immunological medicinal products if the stability studies have not been performed in accordance with the currently approved stability protocol |  | Standard | 6125 |
| c) | | Change in storage conditions for the finished product or the diluted / reconstituted product | 1, 2, 3 | Reduced | 6126 |
| z) | | Other change |  | Reduced | 6127 |
|  | | **Documentation** | | | |
|  | 1. | Amended relevant section(s) of the dossier. The relevant sections must contain results of appropriate real-time stability studies (covering the entire storage period) conducted in accordance with the relevant stability guidance on at least two pilot scale batches2 of the finished product in the authorised packaging material and/or after first opening or reconstitution. If applicable, results of appropriate microbiological testing must be submitted.  2 Pilot scale batches can be accepted with a commitment to verify the storage period with production scale batches. | | | |
|  | 2. | Revised medicinal product information and/or packaging texts. | | | |
|  | 3. | Copy of the approved end-of-storage period specifications of the finished product and, if applicable, specifications after dilution/reconstitution or first opening. | | | |

1 Note: Extrapolation cannot be used for biological or immunological medicinal products.

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| **Scope / justification for the change** | |
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F.II.g) Design space and post-approval change management protocol

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| **F.II.g.1** | | **Addition of a new design space or extension of an approved design space for the finished product, concerning:** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | One or more unit operations in the manufacturing process for the finished product including the resulting in-process tests and/or test methods | 1, 2, 3 | Standard | 6128 |
| b) | | Test methods for excipients / intermediates and/or the finished product | 1, 2, 3 | Standard | 6129 |
|  | | **Documentation** | | | |
|  | 1. | Results from product and process development studies (including risk assessment and multivariate studies, if applicable) demonstrating that a systematic mechanistic understanding of material attributes and process parameters for the critical quality attributes of the finished product has been achieved. | | | |
|  | 2. | Description of the design space in tabular format, including the variables (material attributes and process parameters, if relevant) and their proposed ranges. | | | |
|  | 3. | Amended relevant section(s) of the dossier | | | |

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F.II.g.2

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| **F.II.g.2** | | **Changes in or introduction/implementation of a post-approval change management protocol related to the finished product** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Addition of a post-approval change management protocol related to the finished product | 1, 2, 3 | Standard | 6130 |
| b) | | Changes in an approved change management protocol |  |  |  |
| 1) | | Major changes in an approved change management protocol |  | Standard | 6131 |
| 2) | | Minor changes in an approved change management protocol that do not affect the strategy described in the protocol | 4 | Reduced | 6132 |
| c) | | Implementation of changes foreseen in an approved change management protocol |  |  |  |
| 1) | | Implementation of the change requires further supporting data | 3, 5, 6, 7 | Reduced | 6133 |
| 2) | | Implementation of the change for a biological or immunological medicinal product | 3, 5, 6, 7, 8 | Reduced | 6134 |
|  | | **Documentation** | | | |
|  | 1. | Detailed description of the proposed change. | | | |
|  | 2. | Change management protocol for the finished product. | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 4. | A declaration that all changes are within the currently approved limits; in addition, a declaration that a comparability evaluation is not required for biological or immunological medicinal products. | | | |
|  | 5. | Reference to the approved change management protocol. | | | |
|  | 6. | Declaration that the change has been implemented in accordance with the approved change management protocol and that the study results comply with the acceptance criteria in the protocol; in addition, a declaration that a comparability evaluation is not required for biological or immunological medicinal products. | | | |
|  | 7. | Results of studies performed in accordance with the approved change management protocol. | | | |
|  | 8. | Copy of the approved specifications for the finished product. | | | |

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| **Scope / justification for the change** | |
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F.II.g.z

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| **F.II.g.z** | Other change **to section F.II.g** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Reduced | 6135 |

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| **Scope / justification for the change** | |
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F.III. CEP/TSE/monographs

F.III.1

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| **F.III.1** | | **Submission of a new or updated Ph. Eur. Certificate of Suitability (CEP) or deletion of a Ph. Eur. Certificate of Suitability (CEP) for an active substance, for a starting material used to manufacture an active substance, for a reagent, for an intermediate or for an excipient** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Ph. Eur. Certificate of Suitability (CEP) according to the relevant Ph. Eur. monograph |  |  |  |
| 1) | | New certificate for a non-sterile active substance that is to be used in a sterile medicinal product, where water is used in the final steps of the synthesis and the material is not claimed to be endotoxin-free | 1, 2, 3, 4, 5, 6 | Reduced | 6136 |
| b) | | TSE Ph. Eur. Certificate of Suitability (CEP) for an active substance, starting material, reagent, intermediate or excipient |  |  |  |
| 1) | | New/updated certificate for an approved/new manufacturer using materials of human or animal origin for which an assessment of the risk of potential contamination with adventitious agents is required |  | Standard | 6138 |
| z) | | Other change |  | Reduced | 6139 |
|  | | **Documentation** | | | |
|  | 1. | A copy of the valid (updated) Ph. Eur. Certificate of Suitability (CEP) | | | |
|  | 2. | If the change involves an additional manufacturing site, a comparison of present and proposed manufacturers. | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier and the updated *Manufacturer information* form, if applicable. | | | |
|  | 4. | If relevant: evidence for all substances within the scope of the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (including substances used in the manufacture of the active substance or excipient). The following information should be included for each of these materials: name of manufacturer, species and tissues from which the material is derived, country of origin of the source animals and its use. In addition, an updated *Substances of animal and human origin* form. | | | |
|  | 5. | For a new active substance manufacturer: completed and signed *Declaration by the Responsible Person for foreign manufacturers* form and evidence that the site’s GMP compliance has been verified. | | | |
|  | 6. | Suitable evidence to confirm compliance of the water used in the final steps of the active substance synthesis with the corresponding quality requirements for water for pharmaceutical use. | | | |

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| **Scope / justification for the change** | |
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F.III.2

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| **F.III.2** | **Change to comply with the Ph. Eur. or the Ph. Helv.** | **Documentation to be submitted** | **Time limit** | SAP no. |
| z) | Other change |  | Reduced | 6140 |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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F.IV. Medical devices

F.IV.1

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| --- | --- | --- | --- | --- | --- |
| **F.IV.1** | | **Change in a measuring or administration device** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Addition or replacement of a device which is not an integral part of the primary packaging |  |  |  |
| 1) | | Device without CE marking | 1, 2, 3 | Reduced | 6141 |
| 2) | | Spacer device for metered dose inhalers or other devices which may have a significant effect on the delivery of the active substance in the product (e.g. nebulisers) |  | Standard | 6142 |
| ☐ b) | | Addition or replacement of a device which is an integral part of the primary packaging |  | Standard | 6143 |
| z) | | Other change |  | Reduced | 6144 |
|  | | **Documentation** |  | |  |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a description, detailed drawing and composition of the device material and supplier if appropriate, and including revised product information and/or packaging texts if appropriate. | | | |
|  | 2. | Data to demonstrate the accuracy, precision and compatibility of the device. | | | |
|  | 3. | A sample of the new device | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.IV.2

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| **F.IV.2** | | **Change in the specification parameters and/or limits for a measuring or administration device** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Widening of the approved specification limits with a significant effect on the overall quality of the device |  | Standard | 6197 |
| b) | | Deletion of a specification parameter with a significant effect on the overall quality of the device |  | Standard | 6198 |
| c) | | Addition of a specification parameter as a result of a safety or quality issue | 1, 2, 3, 4, 5 | Reduced | 6199 |
| z) | | Other change |  | Reduced | 6200 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of present and proposed specifications. | | | |
|  | 3. | Details of any new analytical method and summary of the validation data. | | | |
|  | 4. | Batch analysis data for two production batches for all tests in the new specification. | | | |
|  | 5. | Justification of the new specification parameter and limits. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.IV.3

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| **F.IV.3** | **Change in the test method for a measuring or administration device** | **Documentation to be submitted** | **Time limit** | SAP no. |
| z) | Other change |  | Reduced | 6201 |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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F.V. Change to an authorisation due to another regulatory procedure

F.V.a) VAMF/PTMF

F.V.a.1

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| --- | --- | --- | --- | --- | --- |
| **F.V.a.1** | | **Inclusion of a new, updated or revised vaccine antigen master file (VAMF) in the authorisation documentation for a medicinal product. (VAMF second step of the procedure)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | First-time inclusion of a new vaccine antigen master file |  | Standard | 6181 |
| b) | | Inclusion of an updated/revised vaccine antigen master file, if the changes have an impact on the properties of the finished product | 1, 2 ,3, 4 | Standard | 6182 |
|  | | **Documentation** | | | |
|  | 1. | Declaration that the VAMF certificate and the evaluation report are applicable in full to the authorised product, that the VAMF holder has transferred the VAMF certificate, the evaluation report and the VAMF dossier to the marketing authorisation holder (if the VAMF holder is not the marketing authorisation holder) and that the VAMF certificate and the evaluation report replace the previous VAMF documentation for this authorisation. | | | |
|  | 2. | VAMF certificate and evaluation report. | | | |
|  | 3. | An expert statement, in which all changes associated with the certified VAMF are listed and in which all possible effects on the finished product are evaluated, including product-specific risk assessments. | | | |
|  | 4. | Comparison of the previously approved and the requested VAMF EMA certificate (code number). If applicable, the application for authorisation must also clearly list all other VAMFs to which the medicinal product refers, even if these are not part of the application. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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F.V.a.2

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| **F.V.a.1** | **Inclusion of a new, updated or revised platform technology master file (PTMF) in the authorisation documentation for a medicinal product. (PTMF second step of the procedure)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | First-time inclusion of a new PTMF |  | Standard | 6183 |
| b) | Inclusion of an updated/revised PTMF, if the changes have an impact on the properties of the finished product |  | Standard | 6184 |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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F.z Other quality change that requires assessment

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| --- | --- | --- | --- | --- |
| **F.z** | **Other quality change that requires assessment** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) |  |  | Reduced | 6202 |
| b) |  |  | Standard | 6203 |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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G. Changes relating to safety, efficacy and pharmacovigilance

G.I.1

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| --- | --- | --- | --- | --- | --- |
| **G.I.1** | | **Change in the medicinal product information and/or packaging texts intended to implement the outcome of a Swissmedic administrative procedure** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | The medicinal product is not covered by the defined scope of the procedure, but the change implements the outcome of the procedure and no new additional data need to be submitted by the authorisation holder. | 1, 2, 3 | Reduced | 6204 |
| b) | | The medicinal product is not covered by the defined scope of the procedure, but the change implements the outcome of the procedure with new additional data submitted by the authorisation holder. | 1, 3 | Standard | 6205 |
| z) | | Other change |  | Reduced | 6206 |
|  | | **Documentation** | | | |
|  | 1. | Attached to the variation application is a reference to the relevant official decision together with the medicinal product information and/or packaging texts. | | | |
|  | 2. | Declaration that the proposed medicinal product information and/or packaging texts are identical, in the sections concerned, to the corresponding texts attached to the official decision. | | | |
|  | 3. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.2

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| **G.I.2** | **Change in the medicinal product information and/or packaging texts for a medicinal product with a known active substance with/without innovation, or a preparation for parallel import after an assessment of the same change in the reference medicinal product / reference preparation** | | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | Implementation of one or more changes which need to be substantiated by the submission of new additional data (e.g. comparability) by the authorisation holder | | 1 | Standard | 6145 |
| b) | Not applicable to Switzerland | |  |  |  |
| z) | Other change | |  | Reduced | 6146 |
|  | **Documentation** | | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.3

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| **G.I.3** | | | **Change in the medicinal product information and/or packaging texts intended to implement the outcome of a Swissmedic procedure concerning Periodic Safety Update Reports (PSUR) or Post-Authorisation Safety Studies (PASS)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | | Implementation of one or more changes that need to be substantiated by the submission of new additional data by the authorisation holder | 1 | Standard | 6147 |
| b) | | | Implementation of the wording agreed with Swissmedic, which requires an additional minor assessment | 1 | Reduced | 6148 |
|  | | | **Documentation** | | | |
|  | 1. | Revised medicinal product information and/or packaging texts. | | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.4

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| **G.I.4** | **Change in the medicinal product information and/or packaging texts due to new quality, preclinical, clinical or pharmacovigilance data1** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6149 |

1 G.I.101 applies to changes in the medicinal product information and/or packaging texts due to new dosage recommendation data.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.6

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| **G.I.6** | | **Change in the dispensing category** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | For a medicinal product with a known active substance without innovation after an approved change in the dispensing category of the reference product | 2 | Reduced | 6150 |
| b) | | For all other medicinal products | 1, 2 | Standard | 6151 |
|  | | **Documentation** | | | |
|  | 1. | Scientific documentation. | | | |
|  | 2. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.7

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| **G.I.7** | **Change to therapeutic indication(s)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | Addition of a new therapeutic indication or modification of an approved one |  | Standard | 6152 |
| b) | Deletion of a therapeutic indication |  | Reduced | 6153 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.8

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| **G.I.8** | **Addition of requirements and conditions relating to an authorisation or changes in these requirements and conditions, including the risk management plan** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | Addition of a change/changes which require(s) the authorisation holder to submit new data, necessitating significant assessment. 1) |  | Standard | 6154 |
| b) | Addition of a risk management plan |  | Standard | 6155 |

1) This change applies if the only change added affects the authorisation requirements and/or obligations, including the risk management plan and authorisation requirements and obligations in special circumstances.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.9

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| G.I.9 | **Other change relating to safety, efficacy and pharmacovigilance that requires assessment, i.e. additional clinical and preclinical studies, including BE studies, must be submitted** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6156 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.10

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| **G.I.10** | **Change or addition of a non-food producing target species (pet)** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6157 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.11

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| **G.I.11** | | **Deletion of a target species (pet or livestock)** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) | | Deletion as a result of a safety issue | 1 | Standard | 6158 |
| b) | | Deletion not resulting from a safety issue | 1, 2 | Reduced | 6159 |
|  | | **Documentation** | | | |
|  | 1. | Justification for deletion of the target species. | | | |
|  | 2. | Revised medicinal product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.12

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| **G.I.12** | **Change to the waiting time for a veterinary medicinal product** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6160 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.13

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| **G.I.13** | **Changes relating to replacement or addition of a serotype, strain or antigen or a combination of serotypes, strains or antigens for a veterinary vaccine on the basis of authorisation documentation on several strains.** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6185 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.14

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| **G.I.14** | **Changes relating to replacement of a strain for a veterinary vaccine against equine influenza.** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6186 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.15

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| **G.I.15** | **Changes to the labelling or the package leaflet which are not related to the medicinal product information** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Reduced | 6161 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.16

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| **G.I.16** | **Clarification of the temperature of the medicinal product during use (Information for healthcare professionals section 4.9; package leaflet section 8) to ensure correct use** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Reduced | 6162 |

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| **Scope / justification for the change** | |
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| **Present** | **Requested** |
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G.I.100

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| **G.I.100** | **Safety-related change in the medicinal product information and/or packaging texts due to new quality, preclinical, clinical or pharmacovigilance data** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | according to guidance document *Time limits for safety-relevant variations with assessment VMP* | 6163 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.101

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| **G.I.101** | **Change in the medicinal product information and/or packaging texts as a result of new dosage recommendation data** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  |  |  | Standard | 6164 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.102

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| **G.I.102** | | **Extension of the document protection for additional indications** | **Conditions to be fulfilled** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  | |  | 1, 2, 3 | 1 | Standard | 6165 |
|  | | **Conditions** | | | | |
|  | 1. | This involves a new indication with a document protection period of three years. | | | | |
|  | 2. | The new indication provides significant clinical benefit compared to existing treatments at the time when the application for extended document protection is submitted. | | | | |
|  | 3. | The new indication is supported by comprehensive clinical trials. | | | | |
|  |  | **Documentation** | | | | |
|  | 1. | Conclusive evidence that a significant therapeutic improvement exists. It can be demonstrated, on the basis of comprehensive clinical trial data, that the benefit-risk profile in an indication is significantly improved compared to the existing therapeutic options. | | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.103

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| **G.I.103** | | **Document protection for important medicinal products for rare diseases (MUMS)** | **Conditions to be fulfilled** | **Time limit** | SAP no. |
|  | |  | 1, 2 | Reduced | 6166 |
|  | | **Conditions** | | | |
|  | 1. | The medicinal product has been granted Orphan Drug or MUMS status by Swissmedic. | | | |
|  | 2. | Document protection has not yet been granted for any other medicinal product authorised by Swissmedic with the same active substance for the same use. | | | |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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G.I.z Other change relating to safety, efficacy or pharmacovigilance that requires assessment

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| --- | --- | --- | --- | --- |
| **G.I.z** | **Other change relating to safety, efficacy or pharmacovigilance that requires assessment** | **Documentation to be submitted** | **Time limit** | SAP no. |
| a) |  |  | Reduced | 6167 |
| b) |  |  | Standard | 6168 |

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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I. Change in active substance, dosage strength, pharmaceutical form, administration route or food-producing target species1)

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| --- | --- | --- | --- |
| **I.I.1** | | **Change in active substance** | SAP no. |
|  | a) | Replacement of a chemical active substance by a different salt/ester complex/derivative with the same therapeutic moiety, where the efficacy/safety characteristics are not significantly different. | 6169 |
|  | b) | Replacement by a different isomer or a different mixture of isomers, or replacement of a mixture by an isolated isomer (e.g. a racemate by an individual enantiomer), where the efficacy/safety characteristics are not significantly different. | 6170 |
|  | c) | Replacement of a biological active substance by one with a slightly different molecular structure, where the efficacy/safety characteristics are not significantly different. | 6171 |
|  | d) | Modification of the vector used to produce the antigen or the source material, including a new master cell bank from a different source, where the efficacy/safety characteristics are not significantly different. | 6172 |
|  | e) | A new ligand or coupling mechanism for a radiopharmaceutical, where the efficacy/safety characteristics are not significantly different. | 6173 |
|  | f) | Major change to the extraction solvent or the ratio of herbal drug to herbal drug preparation, where the efficacy/safety characteristics are not significantly different. | 6174 |
| **I.II.1** | | **Change in dosage strength, pharmaceutical form or administration route** |  |
|  | c) | Change or addition of a dosage strength | 6175 |
|  | d) | Modification or addition of a pharmaceutical form | 6176 |
|  | e) | Change or addition of an administration route.[[2]](#footnote-2) | 6177 |
| **I.III.1** | | **Change or addition of a food-producing target species (livestock)** | 6178 |
| **I.IV.1** | | **Other change to section I:** e.g. reclassification from active substance to excipient or deletion of active substance | 6179 |

1) “Time line Standard” applies to all the changes listed in this section (cf. guidance document *Variations VMP*).  
All relevant full applications received by Swissmedic – before 28 January 2022, applications for extension of authorisation – are published in accordance with Art. 68 para. 1 let. a TPO.

Y. Change in the reduced dossier for complementary medicines

Y.100

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| **Y.100** | | **Change in the reduced dossier** | **Conditions to be fulfilled** | **Documentation to be submitted** | **Time limit** | SAP no. |
|  | |  | 1 | 1 | Reduced | 6180 |
|  | | **Conditions** | | | | |
|  | 1. | See Complementary and Phytotherapeutic Products Ordinance (KPTPO) | | | | |
|  | | **Documentation** | | | | |
|  | 1. | See KPTPO Annex 3 | | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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Change history

| **Version** | **Change** | **sig** |
| --- | --- | --- |
| 5.1 | Section 5.7 – Clarification regarding delayed implementation deadline | stb |
| 5.0 | New section 5.7 “Delayed implementation”: Applicant clarifies how variations will be implemented according to section 6.2 of the Guidance document *Variations VMP*.  Deletion of the suffix HMV4 in referenced specification documents / other editorial corrections. | fg/ps |
| 4.0 | New section 5.3 “Real world evidence”: Details on RWE must now be entered in application submissions | dts |
| 3.1 | Update due to the possibility of adding a QR code to the medicinal product information and/or packaging; addition of the VMD in section 6.8. | ski, lac |
| 3.0 | Catalogue of variations with assessment included according to EU catalogue; updates relating to the inclusion of immunologics; chapter 1: simplification of details concerning indication; chapter 6.8 updated | fg/ps/lac/stb |
| 2.0 | Several minor changes | fg |
| 1.1 | Adaptation of the checkbox | fg |
| 1.0 | New form as a result of the new structure of Variations VMP (early revision of the VMP regulations) | fg/ps |

1. For collective applications, the basic information should be reproduced based on the number of medicinal products concerned and stated accordingly. [↑](#footnote-ref-1)
2. For parenteral administration, a distinction must be made between intra-arterial, intravenous, intramuscular, subcutaneous and other administration routes. [↑](#footnote-ref-2)