|  |  |
| --- | --- |
| **Form** | |
| **Variations and extensions HAM** | |
| **Identification number:** | ZL300\_00\_003 |
| **Version:** | 18.1 |
| **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 extension(s) or if a new authorisation no. results. Fields with unchanged content can be left blank.*  *Applications for additional indications and extensions must always state the* ***active substance(s)*** *and the* ***area of application*** *being requested.* | | |
| **Active substance(s):** ……  *(Published on receipt of the application)* | | |
| **Pharmaceutical form:** …… | | |
| **If applicable, reference medicinal product:** …… | | |
| **Authorisation no. of the reference medicinal product:** …… | | |
| **If applicable, name of the foreign comparator product:** …… | | |
| **Indications:** ……  *(In the case of additional indication:* ***requested*** *indication; or, in the case of extensions, the area of application requested or authorised, with details (e.g. administration route newly applied for))*  *(Published on receipt of the application)* | | |
| **Pharmacotherapeutic group** | **ATC code:** ……  *(If affected by variation)* | **IT No.:** ……  *(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.  For antivenins please use only the form *New authorisation variation antivenin* | | |
| **Dispensing category**  Select an option. | | |

**To be completed additionally for known substances and biosimilars – 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) or comparability study (biosimilar) | yes | no |  |

|  |  |
| --- | --- |
| **Information on the foreign comparator product** | |
| Name of the foreign comparator product: | …… |
| Name and address of the authorisation holder abroad: | …… |
| Country of authorisation: | …… |
| Authorisation no.: | …… |
| LOT: | …… |
| 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, town/city: | …… |
| Telephone: | …… |
| E-mail: | …… |

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

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

# Special procedures / Status

|  |  |  |
| --- | --- | --- |
|  | Use of fast-track authorisation procedure1 | Official decision on: …… |
|  | Use of procedure with prior notification1 | Notified on: …… |
|  | Use of temporary authorisation1 | Official decision on: …… |
|  | 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 |  |
|  | Orphan Drug Status | Granted on, date: …… |
| *1Prior approval / granting by Swissmedic required.* | | |

# Additional forms to be submitted

*For variation and/or extension applications, the following modified 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 " and the "Overview of documents to be submitted " table.*

|  |
| --- |
| Does the variation / extension affect the entries in the *Manufacturer information* form?  yes, the *Manufacturer information* formis 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* |

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

|  |
| --- |
| Is a paediatric investigation plan required for this application according to the guidance document *Paediatric investigation plan*?  yes, the *Paediatric investigation plan* form is enclosed  no |

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

|  |
| --- |
| Does the variation / extension affect the entries in the form *Confirmation regarding substances from GMO =*?  yes, the form *Confirmation regarding substances from GMO* is enclosed.  no |

|  |
| --- |
| Does this concern  1) a Type II variation as per Art. 13 TPA  or  2) an application for an extension, an additional indication or a dosage recommendation, and has the application been submitted to a foreign authority?  yes, the *Status of authorisation applications abroad* form is enclosed  no |

|  |
| --- |
| Does the variation / extension affect the entries in the *Declaration of radiopharmaceuticals* form?  yes, the *Declaration of radiopharmaceuticals* form is enclosed  no |

|  |
| --- |
| Is a Drug Master File used?  yes, the form *DMF* is enclosed  no |

|  |
| --- |
| Are clinical trials (including bioequivalence trials) of human medicinal products enclosed with the application?  yes, the completed EMA "GCP inspections template" is enclosed  no |
|  |
| Is a QR code being added to or modified in the medicinal product information and/or on the packaging?  yes, the form *Mobile technologies* is enclosed  no |

# Further information

## Placing on the market

|  |  |
| --- | --- |
|  | Intended for placing on the Swiss market\* |
|  | Intended for export only\* |
|  | n.a. |

\* Concerns changes to the authorisation type or newly requested authorisation type in the case of authorisation extensions, resulting in a new authorisation number or dosage strength number.

Remarks: ……

## 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 |
| Are you requesting the 10-year document protection for purely paediatric use on approval of the new dosage form (Art. 11*b* para. 3 TPA)? | yes1 | no | n.a. |
| Once the indication extension is approved, do you wish to request 15-year document protection for important medicinal products for rare diseases (*Orphan Drugs* Art. 11b para. 4 TPA)? | yes1 | no | n/a |
| *1 Reasons must be provided for requesting the extension of document protection, and their source cited.* | | | |

## 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 trial 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 medical service logging |
|  | Data from patient registers (e.g. disease and product registers) |
|  | Data from digital healthcare technologies in non-research environments |
|  | 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 Module(s): | …… | |
| Excipient(s): | …… | see Module(s): | …… | |
| Others: | …… | see Module(s): | …… | |
| *2 The particles have at least one dimension on the nanoscale (1-1000nm) 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. | |

## Combination products

|  |  |  |
| --- | --- | --- |
| Will a combination product (medicinal product with medical device component) now be submitted along with this application? | yes  *🡪 Question a) to c)* | no |
| Is a modification to a medical device component in an existing combination product being applied for that influences the safety and performance requirements or the use of the component in accordance with its intended purpose? | yes *🡪 Questions a) to c)* | no |
| 1. Is it an **integral** combination product and is the medical device component an integral part of the combination (physically inseparable, *integral*)?  yes  no | | |
| 1. Is it an **integral** combination product with the medical device component enclosed in the packaging (use-specific non-separability, *co-packaged*)?  yes  no | | |
| 1. Is it a **non-integral** combination product with the medical device component **not** enclosed in the packaging, but referred to for combined use (*referenced)*?  yes  no | | |

## 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 6.7 of the Guidance document *Variations and extensions HMP*). |
|  | Yes (please complete table below) |

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

# Consents and confirmations

## Completeness of the 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 applicant 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 evaluation of the differences between the test medicinal product and the notified medicinal product is enclosed *(see under Module 1, m1.5.3).*  n/a |

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

|  |
| --- |
| The applicant confirms that the medicinal product information conforms to the currently published texts of the Information for healthcare professionals and Patient information for the reference medicinal product …… (name of reference medicinal product) / reference preparation …… (name of reference preparation) dated …… (month/year), apart from any deviations permitted by TPLRO.  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 TPLO.  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 most recent 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 of the Consortium

|  |
| --- |
| The applicant permits Swissmedic and, where necessary, the Federal Expert Committee on Radiopharmaceuticals to share the assessment reports that it draws up on this medicinal product within the framework of collaboration with partner authorities of the International Regulators Consortium (Therapeutic Goods Administration of Australia, Health Products and Food Branch of Canada and Health Sciences Authority of Singapore and Medicines and Healthcare Products Regulatory Authority of the UK), based on [existing agreements](https://www.swissmedic.ch/swissmedic/en/home/about-us/international-collaboration/multilateral-co-operation-with-international-organisations---ini/multilateral-co-operation-with-international-organisations---ini.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.  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.  *internal: SAP entry* |

## Exchange of information with partner authorities, international organisations and Swiss federal offices for medicinal products with Covid-19 indications

In the case of new/changed indications or dosage recommendations for medicines with Covid-19 indications the applicant consents – while observing the usual confidentiality rules – to Swissmedic exchanging information on the application documentation and assessment results in the context of its cooperation with Swiss federal offices (e.g. FOPH), international partner authorities (e.g. EMA and FDA) and international organisations (e.g. WHO).  Yes  No  n/a

The applicant acknowledges that, under Art. 24e of Ordinance 3 on Measures to Combat the Coronavirus (COVID-19 Ordinance 3; SR 818.101.24), Swissmedic is authorised to notify such information to the federal agencies named in Art. 12 para. 1 COVID-19 Ordinance 3.  Yes  n/a

## Exchanging information within Project Orbis

|  |
| --- |
| The applicant consents to Swissmedic and, where necessary, the Federal Expert Commission for Radiopharmaceuticals (ECRP) exchanging information on application documentation and assessment results with its partner authorities the *U.S. Food and Drug Administration* (U.S. FDA), the *Therapeutic Goods Administration of Australia* (TGA), the *Health Products and Food Branch of Canada* (Health Canada), the *Health Sciences Authority of Singapore* (HSA), the UK *Medicines and Healthcare Products Regulatory Agency* (MHRA), the Brazilian *Agência Nacional de Vigilância Sanitária* (ANVISA) and the Israeli *Ministry of Health – Pharmaceutical Division* (MOH) in order to evaluate additional indications that are assessed within Project Orbis (see guidance document *Project Orbis*).  Yes  No  n/a |

## Information sharing in the context of processing risk evaluations on nitrosamine impurities

The applicant permits Swissmedic to share with international partner authorities assessments drawn up by Swissmedic on nitrosamine impurities in a medicinal product within the scope of participation in the Nitrosamine Strategic Group (NISG) and the Nitrosamine Technical Working Group (NITWG) for the purpose of sharing information and as support for forming opinions. This exchange is 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>). Swissmedic is thus authorised to provide its assessments to partner authorities1. The decision regarding an authorisation is made independently of any information sharing with Swissmedic.

Agreement of authorisation holder  yes  no

DMF holder's consent (cf. FO DMF, part B)

1 These assessments may contain confidential data, such as personal data, business secrets and both positive and negative evaluations with regard to the assessment of an authorisation.

## Disclosure of documentation as part of the MAGHP Light procedure

|  |
| --- |
| The applicant wishes to share the application documentation for the new, proposed indication with the following authorities1 as part of the MAGHP Light procedure:  ……  Option 1: The applicant itself provides the authorisation dossier to the specified authorities directly. Swissmedic will disclose the assessment reports and correspondence (including information for healthcare professionals)2 after the procedure has been completed. At the authorisation holder's request, Swissmedic will establish contact with the authorities in question.  yes  no  n/a  Option 2: Swissmedic will provide both the application dossier submitted and the assessment reports and correspondence (including information for healthcare professionals)2 to the specified authorities after the procedure has been completed.  yes  no  n/a  For information on the conditions and the process, please see the [*MAGHP Procedure*](https://www.swissmedic.ch/dam/swissmedic/de/dokumente/stab/networking/maghp_procedure.pdf.download.pdf/maghp_procedure.pdf) guidance document.  1 The focus is on countries in sub-Saharan Africa.  2 The Swissmedic documents may contain confidential data such as personal data, business secrets and both positive and negative evaluations with regard to the assessment of an authorisation. Note that other requirements may apply to the handling of confidential data in other countries than in Switzerland.  *Internal: [yes] report to Stakeholder Engagement* |

## Dispatch of Assessment Report for Applicants (ARA)

|  |  |  |  |
| --- | --- | --- | --- |
| Will a request to **view the Assessment Report for Applicants** when the decision is opened be submitted simultaneously with this application? Assessment Reports for Applicants are issued for extensions, 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 the 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

A. Regulatory changes

A.2 b)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.2 b)** | | **Change in the name of the medicinal product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | |  |  | 2 | 5042 |
|  | | **Documentation** | | | |
|  | 1. | Not applicable to Switzerland. | | | |
|  | 2. | 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** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | | Date of implementation: …… | 1, 2 | 1, 2, 3 | 5043# |
| IB\* | |  | 1, 2 | 1, 2, 3 | 5503 |
|  | | **Conditions** | | | |
|  | 1. | The active substance or excipient must remain the same. | | | |
|  | 2. | Not applicable to Switzerland. | | | |
|  | | **Documentation** | | | |
|  | 1. | Proof of inclusion in the WHO ATC/DDD 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 Note for Guidance on Quality of (traditional) Herbal Medicinal Products and with the EMA Guideline on declaration of herbal substances and herbal preparations in (traditional) herbal medicinal products. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |
|  | 3. | *Full declaration* form with correspondingly changed names. | | | |

\*If the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

A.4

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.4** | | **Change in the name and/or address of a DMF holder, manufacturing site (if applicable also of the quality control testing sites) of the active substance or any starting material, reagent or intermediate used in the manufacture of the active substance, where the approved documentation does not include a Ph. Eur. Certificate of Suitability (CEP), or in those of the manufacturer of a novel excipient (where specified in the dossier)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | | Date of implementation: …… | 1 | 1, 2, 3 | 5044#Z |
| IB\* | |  | 1 | 1, 2, 3 | 5504 |
|  | | **Conditions** | | | |
|  | 1. | The manufacturing site and all 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. | In case of change in the name of the DMF holder, an updated Letter of Access. | | | |
| n/a |  | Justification: | | | |

\*If the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

A.5

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.5** | | **Change in the name and/or address of a manufacturer of the finished product (including batch release and quality control sites)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | The activities for which the manufacturer is responsible also include batch releases.  Date of implementation: …… | 1 | 1, 2 | 5045#Z |
| IB\* |  | 1 | 1, 2 | 5505 |
| IA | b) | Batch releases are not included in the activities for which the manufacturer is responsible.  Date of implementation: …… | 1 | 1, 2 | 5046#Z |
| IB\* |  | 1 | 1, 2 | 5506 |
|  | | **Conditions** | | | |
|  | 1. | The manufacturing location and all manufacturing steps remain unchanged. | | | |
|  | | **Documentation** | | | |
|  | 1. | A copy of the revised establishment licence (if one exists) or 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 and, if applicable, revised product information and/or packaging texts. | | | |

\*If the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

A.6

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.6** | | **Change in ATC code** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | | Date of implementation: …… | 1 | 1, 2 | 5047 |
| IB\* | |  | 1 | 1, 2 | 5507 |
|  | | **Conditions** | | | |
|  | 1. | Change following granting or amendment to the ATC code by the WHO. | | | |
|  | | **Documentation** | | | |
|  | 1. | Proof of inclusion in the ATC/DDD Index, or copy of the ATC code list. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |

\*If more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

A.7

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **A.7** | | **Deletion of sites for the manufacture of an active substance, intermediate or finished products, for packaging, for quality control, for batch release or of sites of suppliers/manufacturers of a starting material, reagent or excipient (provided these are listed in the dossier Module 3)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | | Date of implementation: …… | 1, 2 | 1, 2 | 5048# |
| IB\* | |  |  | 1,2 | 5508 |
|  | | **Conditions** | | | |
|  | 1. | At least one previously authorised site performing the same functions as the site affected by the deletion should remain. | | | |
|  | 2. | The deletion is not attributable to critical deficiencies concerning manufacturing. | | | |
|  | | **Documentation** | | | |
|  | 1. | Comparison of present and proposed sites. | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form, if applicable. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **A.8** | | **Change to date of the audit to verify GMP compliance of the active substance manufacturer** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | | Date of implementation: …… |  | 1 | 5049# |
| IB\* | |  |  | 1 | 5509 |
|  | | **Documentation** | | | |
|  | 1. | Written confirmation from the manufacturer of the finished product stating verification of compliance of the manufacturer of the active substance with the principles and guidelines of good manufacturing practices. | | | |

\*If more than 12 months have elapsed between the date of implementation and date of submission of the variation.

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

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| **A.100** | | **Change in the product information and/or packaging texts without the submission of scientific data** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | New design (corporate identity)  Implementation date: …… | 1, 2 | 1 | 5754# |
| IB | b) | Other changes |  | 1 | 5050 |
|  | | **Conditions** | | | |
|  | 1. | If a new design (corporate identity), the first pack has been submitted as a regulatory change A.100 b) type IB and approved. | | | |
|  | 2. | The application ID number of the type IB variation (first pack with new design, A.100 b)) is specified under “Scope/justification for the change”. | | | |
|  | | **Documentation** | | | |
|  | 1. | Revised product information and/or packaging texts. | | | |

\*If condition is not fulfilled, or there is more than one month between the implementation date and the date when the type IAIN variation was submitted.

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| **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

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| **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 product information and/or packaging text or a quality change)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | a) | With variation of the packaging code. | 1, 2, 3, 4, 5 | 1, 2, 3 | 5051 |
| IAIN | b) | Without variation of the packaging code. | 1, 2, 4, 5 | 1, 2, 3 | 5052# |
| IB\* |  |  | 1, 2, 3 | 5510 |
|  | | **Conditions** | | | |
|  | 1. | In the event of a change to the 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 product information and/or packaging texts: The product information texts (information for healthcare professionals and/or patient information) 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 resulted 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 product information, the most recently approved version of the information for healthcare professionals and/or patient information for the basic product, with corrections for the name of the medicinal product, authorisation number and marketing authorisation holder, or the 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 or alternatively for a variation requiring notification (types IA, IAIN and IB) that concerns the basic product, a copy of the Swissmedic Portal entry on the conclusion of the submission or the invoice should be submitted. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II.

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

A.102

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| **A.102** | | **New and/or modified pack size** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | |  | 1, 2, 3, 4, 5 | 1, 2 | 5053 |
|  | | **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 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. Chapter 3.1, is allowed for foodstuffs, satisfies the general requirements of Ph. Eur. for containers (Chapters 1.3 and 3.2), brief description of the composition, etc.). | | | |
| n/a |  | Justification: | | | |

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

A.103

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| **A.103** | | **Omission of a pack size** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | | Date of implementation: …… | 1 | 1 | 5054# |
| IB\* | |  |  | 1 | 5511 |
|  | | **Conditions** | | | |
|  | 1. | The dosage strength remains the same, and the dosage recommendation remains valid for implementation. | | | |
|  | | **Documentation** | | | |
|  | 1. | Revised product information and/or packaging texts. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

A.104

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| **A.104** | | **Conversion of a main authorisation to an export licence** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | |  |  | 1 | 5055 |
|  | | **Documentation** | | | |
|  | 1. | Revised product information (new: basic information). | | | |

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

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| **A.105** | | **Conversion of an export licence to a main authorisation** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | |  |  | 1 | 5056 |
|  | | **Documentation** | | | |
|  | 1. | Revised product information and/or packaging texts. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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A.106

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| **A.106** | | **Conversion of the authorisation of a co-marketing medicinal product to independent authorisation (basic product)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | |  | 1 | 1, 2, 3 | 5057 |
|  | | **Conditions** | | | |
|  | 1. | No new scientific data are submitted. | | | |
|  | | **Documentation** | | | |
|  | 1. | Submission of a complete identical set of documentation. 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 was 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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A.107

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| **A.107** | | **Conversion of the authorisation from an independent authorisation (basic product) to co-marketing medicinal product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | |  | 1, 2 | 1 | 5058 |
|  | | **Conditions** | | | |
|  | 1. | No new scientific data are submitted. | | | |
|  | 2. | Application A.106 is submitted simultaneously (i.e. within one week). | | | |
|  | | **Documentation** | | | |
|  | 1. | Module 1, as for new submission for a co-marketing medicinal product. | | | |

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

A.109

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| **A.109** | | **Implementation of the new requirements in accordance with the revised TPLRO** Revision of the product information / packaging texts, including full declaration, warnings according to Annex 3a TPLRO | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | |  |  | 1, 2 | 5618FK |
|  | | **Documentation** | | | |
|  | 1. | Revised product information and/or packaging texts. | | | |
|  | 2. | Form *Full declaration.* | | | |

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

A.z. Other regulatory change

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| --- | --- | --- | --- | --- |
| **A.z** | **Other regulatory change** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | Date of implementation: …… |  |  | 5488# |
| IA | Date of implementation: …… |  |  | 5487# |
| IB |  |  |  | 5060 |
| II |  |  |  | 5489 |

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

B. Quality changes

B.I. Active substance

B.I.a) Manufacture

B.I.a.1

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| --- | --- | --- | --- | --- | --- |
| **B.I.a.1** | | **Change in the manufacturer of a starting material, reagent or intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control testing sites) of an active substance, where no Ph. Eur. Certificate of Suitability is part of the approved dossier** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer  Date of implementation: …… | 1, 2, 3 | 1, 2, 3, 4, 5, 6, 7, 8 | 5061#Q |
| IB\* |  |  | 1, 2, 3, 4, 5, 6, 7, 8 | 5512 |
| II | b) | Introduction of a manufacturer of the active substance supported by a DMF |  |  | 5062 |
| II | c) | The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions, which may have a potential to change important quality characteristics of the active substance, such as qualitative and/or quantitative impurity profile requiring qualification, or physico-chemical properties impacting on bioavailability |  |  | 5063 |
| II | d) | New manufacturer of material for which an assessment is required of viral safety and/or TSE risk |  |  | 5064 |
| II | e) | The change relates to a biological active substance or a starting material, reagent or intermediate used in the manufacture of a biological or immunological finished product |  |  | 5065 |
| IA | f) | Changes to the quality control site for the active substance: replacement or addition of a site where batch control or testing takes place  Date of implementation: …… | 2, 4 | 1, 5 | 5066#Q |
| IB\* |  |  | 1, 5 | 5513 |
| II | g) | Introduction of a new manufacturer of the active substance that is not supported by a DMF and that requires significant update to the relevant active substance section of the dossier |  |  | 5067 |
| IB | h) | Addition of an alternative sterilisation site for the active substance using a Ph. Eur. method |  | 1, 2, 4, 5, 8 | 5068 |
| IA | i) | Introduction of a new site of micronisation  Date of implementation: …… | 2, 5 | 1, 4, 5, 6 | 5069#Q |
| IB\* |  |  | 1, 4, 5, 6 | 5514 |
| II | j) | Changes to the quality control site for a biological active substance: replacement or addition of a site where batch control or testing including a biological or immunological / immunochemical method takes place |  |  | 5070 |
| IB | k) | New storage site of Master Cell Bank and/or Working Cell Bank |  | 1, 5 | 5071 |
| IB | z) | Other change |  |  | 5757 |
| IAIN | Date of implementation: …… |  |  | 5755Q |
| IA | Date of implementation: …… |  |  | 5756Q |
| II |  |  |  | 5758 |
|  | | **Conditions** | | | |
|  | 1. | For starting materials and reagents, the specifications (including in process controls, methods of analysis of all materials), are identical to those already approved. For intermediates and active substances, the specifications (including in process controls, methods of analysis of all materials), method of preparation (including batch size) and detailed route of synthesis are identical to those already approved. | | | |
|  | 2. | The active substance is neither a biological or immunological substance nor sterile. | | | |
|  | 3. | Where materials of human or animal origin are used in the manufacturing process, the manufacturer does not use any new supplier for which assessment is required of viral safety or of compliance with the current "Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products". | | | |
| n/a |  | Justification: | | | |
|  | 4. | Method transfer from the old to the new site has been successfully completed. | | | |
|  | 5. | The particle size specification of the active substance and the corresponding analytical method remain the same. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form, if applicable. | | | |
|  | 2. | A declaration from the marketing authorisation holder or DMF Holder stating that the synthetic route (or in the case of herbal medicinal products, where appropriate the manufacturing method and the processing of herbal drug), quality control procedures and specifications of the active substance and of the starting material, reagent or intermediate used in the manufacturing process of the active substance are the same as those already approved. | | | |
|  | 3. | Either a TSE Ph. Eur. Certificate of Suitability for any new source of material or, where applicable, documentary evidence that the specific source of the TSE risk material complies with the current "Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products" and an updated *Substances of Animal and Human Origin* form. | | | |
| n/a |  | Justification: | | | |
|  | 4. | Batch analysis data (in the form of a comparative table) for at least two batches (minimum pilot scale) of the active substance from the current and proposed manufacturers or sites. | | | |
|  | 5. | Comparison of present and proposed manufacturer. | | | |
|  | 6. | Completed and signed form *Declaration by the Responsible Person for foreign manufacturers*, if applicable. | | | |
| n/a |  | Justification: | | | |
|  | 7. | If applicable, a commitment by the active substance manufacturer to inform the marketing authorisation holder of any changes to the manufacturing process, specifications or test procedures of the active substance. | | | |
| n/a |  | Justification: | | | |
|  | 8. | Proof that the site's GMP compliance has been verified, if applicable (only if the change concerns the active substance manufacturer). | | | |
| ☐ n/a |  | Justification: | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.I.a.2

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| **B.I.a.2** | | **Changes in the manufacturing process of the active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Minor change in the manufacturing process of the active substance  Date of implementation: …… | 1, 2, 3, 4, 5, 6, 7 | 1, 2, 3 | 5072Q |
| IB\* |  |  | 1, 2, 3 | 5515 |
| II | b) | Substantial change to the manufacturing process of the active substance which may have a significant impact on the quality, safety or efficacy of the finished product. |  |  | 5073 |
| II | c) | The change relates to a biological or immunological substance or the use of a different chemically derived substance in the manufacture of a biological or immunological substance, which may have a significant impact on the quality, safety and efficacy of the finished product and is not related to a protocol |  |  | 5074 |
| II | d) | The change relates to a herbal medicinal product and there is a change to one of the following: manufacturing route or production |  |  | 5075 |
| IB | e) | Minor change to the restricted part of the DMF |  | 1, 2, 3, 4 | 5076 |
| IB | z) | Other change |  |  | 5761 |
| IAIN | Date of implementation: …… |  |  | 5759Q |
| IA | Date of implementation: …… |  |  | 5760Q |
| II |  |  |  | 5762 |
|  | | **Conditions** | | | |
|  | 1. | No adverse change in the qualitative or quantitative impurity profile or in physico-chemical properties. | | | |
|  | 2. | The synthetic route remains the same, i.e. intermediates remain the same, and no new reagents, catalysts or solvents are used in the process. In the case of herbal medicinal products, the production of the herbal substance and the manufacturing route of the active substance remain the same. | | | |
|  | 3. | The specifications of the active substance or intermediates remain the same. | | | |
|  | 4. | The change is fully described in the applicant’s part of the DMF, if applicable. | | | |
| n/a |  | Justification: | | | |
|  | 5. | The active substance is not a biological or immunological substance. | | | |
|  | 6. | The change does not relate to the manufacturing route or the production of a herbal medicinal product. | | | |
|  | 7. | The change does not relate to a restricted part of the DMF. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier and of the approved DMF, if applicable, including a comparison of the present process and the proposed process. | | | |
|  | 2. | Batch analysis data (in the form of a comparative table) for at least two batches (minimum pilot scale) of the active substance that were manufactured according to the currently approved and proposed manufacturing processes. | | | |
|  | 3. | A copy of the approved specifications of the active substance. | | | |
|  | 4. | A declaration from the marketing authorisation holder or the DMF holder stating that there is no change in qualitative and quantitative impurity profile or in physico-chemical properties, that the synthetic route remains the same and that the specifications of the active substance or intermediates are unchanged. | | | |
| Note on B.I.a.2.b: For chemical active substances, this refers to substantial changes to the synthetic route or manufacturing conditions which may have a potential to change important quality characteristics of the active substance, such as the qualitative and/or quantitative impurity profile requiring qualification, or physico-chemical properties impacting on bioavailability. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.I.a.3

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| --- | --- | --- | --- | --- | --- |
| **B.I.a.3** | | **Change in batch size (incl. batch size range) of the active substance or any intermediate used in the manufacture of an active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Up to 10-fold increase compared to the originally approved batch size  Date of implementation: …… | 1, 2, 3, 4, 6, 7, 8 | 1, 2, 5 | 5077Q |
| IB\* |  |  | 1, 2, 5 | 5516 |
| IA | b) | Downscaling down to 10-fold  Date of implementation: …… | 1, 2, 3, 4, 5 | 1, 2, 5 | 5078Q |
| IB\* |  |  | 1, 2, 5 | 5517 |
| II | c) | The change requires assessment of the comparability of a biological or immunological active substance |  |  | 5079 |
| IB | d) | More than 10-fold increase compared to the originally approved batch size |  | 1, 2, 3, 4 | 5080 |
| IB | e) | The scale for a biological or immunological active substance is increased or decreased without any change in the manufacturing process (e.g. duplication of the production lines) |  | 1, 2, 3, 4 | 5081 |
| IB | z) | Other change |  |  | 5765 |
| IAIN | Date of implementation: …… |  |  | 5763Q |
| IA | Date of implementation: …… |  |  | 5764Q |
| II |  |  |  | 5766 |
|  | | **Conditions** | | | |
|  | 1. | Any changes to the manufacturing methods are only those necessitated by scale-up or downscaling, e.g. use of different-sized equipment. | | | |
|  | 2. | Test results of at least two batches according to the specifications should be available for the proposed batch size | | | |
|  | 3. | The product is not a biological or immunological medicinal product. | | | |
|  | 4. | The change does not adversely affect the reproducibility of the process. | | | |
|  | 5. | The change should not be the result of unexpected events arising during manufacture or because of stability concerns. | | | |
|  | 6. | The specifications of the active substance or intermediates remain unchanged. | | | |
|  | 7. | The active substance is not sterile. | | | |
|  | 8. | The batch size is within the 10-fold range of the batch size foreseen when the marketing authorisation was granted, or following a subsequent change not agreed as a Type IA variation. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | The batch numbers of the tested batches having the proposed batch size. | | | |
|  | 3. | Batch analysis data (in the form of a comparative table) for a minimum of one production batch of the active substance or intermediate as appropriate, manufactured to both the currently approved and the proposed sizes. Batch data on the next two full production batches should be made available upon request and reported by the marketing authorisation holder if outside specification (with proposed action). | | | |
|  | 4. | A copy of the approved specifications of the active substance or intermediate. | | | |
|  | 5. | A declaration from the marketing authorisation holder or the DMF holder stating that the changes to the manufacturing methods are only those necessitated by scale-up or downscaling, e.g. use of different-sized equipment, that the change does not adversely affect the reproducibility of the process, that it is not the result of unexpected events arising during manufacture or because of stability concerns, and that the specifications of the active substance / intermediates remain the same. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **Present** | **Proposed** |
| …… | …… |

B.I.a.4

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.I.a.4** | | **Change to in-process tests or limits applied during the manufacture of the active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Tightening of in-process limits  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5082Q |
| IB\* |  |  | 1, 2 | 5518 |
| IA | b) | Addition of a new in-process test and limits  Date of implementation: …… | 1, 2, 5, 6 | 1, 2, 3, 4, 6 | 5083Q |
| IB\* |  |  | 1, 2, 3, 4, 6 | 5519 |
| IA | c) | Deletion of a non-significant in-process test  Date of implementation: …… | 1, 2, 7 | 1, 2, 5 | 5084Q |
| IB\* |  |  | 1, 2, 5 | 5520 |
| II | d) | Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the active substance |  |  | 5085 |
| II | e) | Deletion of an in-process test which may have a significant effect on the overall quality of the active substance |  |  | 5086 |
| IB | f) | Addition or replacement of an in-process test as a result of a safety or quality issue |  | 1, 2, 3, 4, 6 | 5087 |
| IB | z) | Other change |  |  | 5769 |
| IAIN | Date of implementation: …… |  |  | 5767Q |
| IA | Date of implementation: …… |  |  | 5768Q |
| II |  |  |  | 5770 |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure). | | | |
|  | 2. | The change does not result from unexpected events arising during manufacture e.g. new unqualified impurity or change in total impurity limits. | | | |
|  | 3. | Any change should be within the range of currently approved limits. | | | |
|  | 4. | The test procedure remains the same, or changes to the test procedure are minor. | | | |
|  | 5. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | 6. | The new test method is neither a biological, immunological or immunochemical method or a method using a biological reagent for a biological active substance (does not include standard pharmacopoeial microbiological methods). | | | |
|  | 7. | The specification parameter does not concern a critical parameter, e.g. assay, impurities (unless a particular solvent is definitely not used in the manufacture of the active substance), any critical physical characteristics, e.g. particle size, bulk or tapped density, identity test, water content, any request for changing the frequency of testing. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of current and proposed in-process tests. | | | |
|  | 3. | Details of any new non-pharmacopoeial analytical method and validation data, where relevant. | | | |
| n/a |  | Justification: | | | |
|  | 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 marketing authorisation holder or the DMF holder showing that the in-process tests are non-significant, or that the in-process tests are obsolete. | | | |
|  | 6. | Justification from the MAH or DMF holder for the new in-process tests and limits. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.I.a.5** | | **Changes to the active substance of a seasonal, pre-pandemic or pandemic vaccine against human influenza or against SARS-CoV-2** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | a) | Replacement of the strain(s) in a seasonal, pre-pandemic or a pandemic vaccine against human influenza |  |  | 5088 |
| II | b) | Changes associated with changes to the active substance of a human SARS-CoV-2 vaccine, including the exchange or addition of a serotype, strain, antigen or coding region or a combination of serotype, strain, antigen or coding region |  |  | 5967 |
| IB | z) | Other change |  |  | 5773 |
| IAIN | Date of implementation: …… |  |  | 5771Q |
| IA | Date of implementation: …… |  |  | 5772Q |
| II |  |  |  | 5774 |

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

B.I.b.1

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| **B.I.b.1** | | **Change in the specification parameters and/or limits of an active substance, starting material, intermediate or reagent used in the manufacturing process of the active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | Tightening of specification limits for medicinal products subject to Official Control Authority Batch Release  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5089Q |
| IB\* |  |  | 1, 2 | 5521 |
| IA | b) | Tightening of specification limits  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5090Q |
| IB\* |  |  | 1, 2 | 5522 |
| IA | c) | Addition of a new specification parameter with its corresponding test method  Date of implementation: …… | 1, 2, 5, 6, 7 | 1, 2, 3, 4, 5, 7 | 5091Q |
| IB\* |  |  | 1, 2, 3, 4, 5, 7 | 5523 |
| IA | d) | Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)  Date of implementation: …… | 1, 2, 8 | 1, 2, 6 | 5092Q |
| IB\* |  |  | 1, 2, 6 | 5524 |
| II | e) | Deletion of a specification parameter which may have a significant effect on the overall quality of the active substance and/or the finished product |  |  | 5093 |
| II | f) | Change outside the approved specifications limits range for the active substance |  |  | 5094 |
| II | g) | Widening of the approved specifications limits for starting materials or intermediates, which may have a significant effect on the overall quality of the active substance and/or the finished product |  |  | 5095 |
| IB | h) | Addition or replacement (excluding biological or immunological substances) of a specification parameter with its corresponding test method as a result of a safety or quality issue |  | 1, 2, 3, 4, 5, 7 | 5096 |
| IB | i) | Where there is no monograph in the European Pharmacopoeia or the Pharmacopoeia Helvetica for an active substance, a change in specification from in-house to a non-official pharmacopoeia or a pharmacopoeia of a third country |  | 1, 2, 3, 4, 5, 7 | 5097 |
| IB | z) | Other change |  |  | 5777 |
| IAIN | Date of implementation: …… |  |  | 5775Q |
| IA | Date of implementation: …… |  |  | 5776Q |
| II |  |  |  | 5778 |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure). | | | |
|  | 2. | The change does not result from unexpected events arising during manufacture e.g. new unqualified impurity or change in total impurity limits. | | | |
|  | 3. | Any change should be within the range of currently approved limits. | | | |
|  | 4. | The test procedure remains the same, or changes to the test procedure are minor. | | | |
|  | 5. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | 6. | The test method is not a biological, immunological or immunochemical method or a method using a biological reagent for a biological active substance (does not include standard pharmacopoeial microbiological methods). | | | |
|  | 7. | For any material, the change does not concern a genotoxic impurity. If the change involves the final active substance, other than for residual solvents which must be in line with ICH limits, the specifications for new impurities should be in line with Ph. Eur. or Pharmacopoeia Helvetica. | | | |
|  | 8. | The specification parameter does not concern a critical parameter, e.g. assay, impurities (unless a particular solvent is definitely not used in the manufacture of the active substance), any critical physical characteristics, e.g. particle size, bulk or tapped density, identity test, water content, any request for skip testing. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of current and proposed specifications. | | | |
|  | 3. | Details of the new analytical method and validation data, where relevant. | | | |
|  | 4. | Batch analysis data for two production batches (three production batches for biologicals, unless otherwise justified) of the relevant substance for all specification parameters. | | | |
|  | 5. | Where appropriate, comparative dissolution profile data for the finished product on at least one pilot batch containing the active substance complying with the current and proposed specifications. For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
| n/a |  | Justification: | | | |
|  | 6. | Justification or risk assessment from the marketing authorisation holder or the DMF holder showing that the parameter is non-significant, or that it is obsolete. | | | |
|  | 7. | Justification from the marketing authorisation holder or DMF holder for the new specification parameter and the limits. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.I.b.2** | | **Change in the test procedure for active substance or for a starting material, an intermediate or a reagent used in the manufacturing process of an active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Minor changes to an approved test procedure  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5098Q |
| IB\* |  |  | 1, 2 | 5525 |
| IA | b) | Deletion of a test procedure for the active substance or a starting material, reagent or intermediate, if an alternative test procedure is already authorised.  Date of implementation: …… | 7 | 1 | 5099Q |
| IB\* |  |  | 1 | 5526 |
| IA | c) | Other changes to a test procedure (including replacement or addition) for a reagent which does not have a significant effect on the overall quality of the active substance  Date of implementation: …… | 1, 2, 3, 5, 6 | 1, 2 | 5100Q |
| IB\* |  |  | 1, 2 | 5527 |
| II | d) | Substantial change to, or replacement of, a biological, immunological or immunochemical test method or a method using a biological reagent for a biological active substance |  |  | 5101 |
| IB | e) | Other changes to a test procedure (including replacement or addition) for the active substance or a starting material or intermediate |  | 1, 2 | 5102 |
| IB | z) | Other change |  |  | 5781 |
| IAIN | Date of implementation: …… |  |  | 5779Q |
| IA | Date of implementation: …… |  |  | 5780Q |
| II |  |  |  | 5782 |
|  | | **Conditions** | | | |
|  | 1. | Appropriate validation studies have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the previously approved test procedure. | | | |
| n/a |  | Justification: | | | |
|  | 2. | No changes have been made to the total impurity limits, and no new unqualified impurities have been detected. | | | |
|  | 3. | The analytical method essentially remains the same (e.g. a change in column length or temperature, but not a different type of column or method). | | | |
|  | 4. | The test method is not a biological, immunological or immunochemical method or a method using a biological reagent for a biological active substance (does not include standard pharmacopoeial microbiological methods). | | | |
|  | 5. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| ☐ n/a |  | Justification: | | | |
|  | 6. | The active substance is not a biological or immunological substance. | | | |
|  | 7. | An alternative test procedure is already authorised for the specification parameter, and this procedure has not been added through IA/IAIN notification. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the 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 analysis results showing that the current test and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new test procedure. | | | |
| n/a |  | Justification: | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.I.c.1

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| **B.I.c.1** | | **Change in immediate packaging of the active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Qualitative and/or quantitative composition  Date of implementation: …… | 1, 2, 3 | 1, 2, 3, 4, 6 | 5103Q |
| IB\* |  |  | 1, 2, 3, 4, 6 | 5528 |
| II | b) | Qualitative and/or quantitative composition for sterile and non-frozen biological or immunological active substances |  |  | 5104 |
| IB | c) | Liquid active substances (non-sterile) |  | 1, 2, 3, 5, 6 | 5105 |
| IB | z) | Other change |  |  | 5785 |
| IAIN | Date of implementation: …… |  |  | 5783Q |
| IA | Date of implementation: …… |  |  | 5784Q |
| II |  |  |  | 5786 |
|  | | **Conditions** | | | |
|  | 1. | The proposed packaging material is at least equivalent to the approved material in respect of its relevant properties. | | | |
|  | 2. | Relevant stability studies have been started under ICH conditions, relevant stability parameters have been assessed in at least two pilot scale or industrial scale batches, and at least three months satisfactory stability data are at the disposal of the applicant at the time of implementation. However, if the proposed packaging is more resistant than the existing packaging, the three months’ stability data do not yet have to be available. These studies must be finalised, and the data will be provided immediately to Swissmedic if outside specifications or potentially outside specifications at the end of the shelf-life or retest period (with proposed action). | | | |
|  | 3. | Sterile, liquid and biological or immunological active substances are excluded. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Appropriate data on the new packaging (e.g. comparative data on permeability e.g. for O2, CO2 moisture), including a confirmation that the material complies with relevant pharmacopoeial requirements or legislation on materials and articles intended to come into contact with food (requirements of the Consumer Goods Ordinance; SR 817.023.21). | | | |
|  | 3. | Where appropriate, proof must be provided 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 relevant pharmacopoeia requirements or legislation on materials and articles intended to come into contact with food (requirements of the Consumer Goods Ordinance; SR 817.023.21). | | | |
| n/a |  | Justification: | | | |
|  | 4. | A declaration from the marketing authorisation holder or the DMF holder stating that the required stability studies have been started under ICH conditions (with indication of the batch numbers concerned) and that, as relevant, the required minimum satisfactory stability data were at the disposal of the applicant at the time of implementation and that the available data did not indicate a problem. It should also be confirmed that the studies will be finalised and that data will be provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). | | | |
|  | 5. | The results of stability studies that have been carried out under ICH 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 provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved retest period (with proposed action). | | | |
|  | 6. | If applicable, comparison of the current and proposed immediate packaging specifications. | | | |
| n/a |  | Justification: | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.I.c.2** | | **Change in the specification parameters and/or limits of the immediate packaging of the active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Tightening of specification limits  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5106Q |
| IB\* |  |  | 1, 2 | 5529 |
| IA | b) | Addition of a new specification parameter with its corresponding test method  Date of implementation: …… | 1, 2, 5 | 1, 2, 3, 4, 6 | 5107Q |
| IB\* |  |  | 1, 2, 3, 4, 6 | 5530 |
| IA | c) | Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)  Date of implementation: …… | 1, 2 | 1, 2, 5 | 5108Q |
| IB\* |  |  | 1, 2, 5 | 5531 |
| IB | d) | Addition or replacement of a specification parameter as a result of a safety or quality issue |  | 1, 2, 3, 4, 6 | 5109 |
| IB | z) | Other change |  |  | 5789 |
| IAIN | Date of implementation: …… |  |  | 5787Q |
| IA | Date of implementation: …… |  |  | 5788Q |
| II |  |  |  | 5790 |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure) unless it has been previously assessed and agreed as part of a follow-up measure. | | | |
|  | 2. | The change does not result from unexpected events arising during manufacture of the packaging material or during storage of the active substance. | | | |
|  | 3. | Any change should be within the range of currently approved limits. | | | |
|  | 4. | The test procedure remains the same, or changes to the test procedure are minor. | | | |
|  | 5. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of current and proposed specifications. | | | |
|  | 3. | Details of the new analytical method and validation data, where relevant. | | | |
|  | 4. | Batch analysis data on two batches of the immediate packaging for all specification parameters. | | | |
|  | 5. | Justification or risk assessment from the marketing authorisation holder or the DMF holder showing that the parameter is non-significant, or that it is obsolete. | | | |
|  | 6. | Justification from the marketing authorisation holder or DMF holder for the new specification parameter and the limits. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.I.c.3** | | **Change in test procedure for the immediate packaging of the active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Minor changes to an approved test procedure  Date of implementation: …… | 1, 2, 3 | 1, 2 | 5110Q |
| IB\* |  |  | 1, 2 | 5532 |
| IA | b) | Other changes to a test procedure (including replacement or addition)  Date of implementation: …… | 1, 3, 4 | 1, 2 | 5111Q |
| IB\* |  |  | 1, 2 | 5533 |
| IA | c) | Deletion of a test procedure if an alternative test procedure is already authorised  Date of implementation: …… | 5 | 1 | 5112Q |
| IB\* |  |  | 1 | 5534 |
| IB | z) | Other change |  |  | 5793 |
| IAIN | Date of implementation: …… |  |  | 5791Q |
| IA | Date of implementation: …… |  |  | 5792Q |
| II |  |  |  | 5794 |
|  | | **Conditions** | | | |
|  | 1. | Appropriate validation studies have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the previously approved test procedure. | | | |
| n/a |  | Justification: | | | |
|  | 2. | The analytical method essentially remains the same (e.g. a change in column length or temperature, but not a different type of column or method). | | | |
|  | 3. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | 4. | The active substance / finished product is not a biological or immunological substance. | | | |
|  | 5. | There is still a test procedure registered for the specification parameter, and this procedure has not been added through IA/IAIN notification. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a description of the analytical method and a summary of the validation data. | | | |
|  | 2. | Comparative validation results or, if justified, comparative analysis results showing that the current test and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new test procedure. | | | |
| n/a |  | Justification: | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.I.d) Stability

B.I.d.1

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| **B.I.d.1** | | **Change in the retest period/storage period or storage conditions of the active substance where no Ph. Eur. Certificate of Suitability (CEP) covering the retest period is part of the approved dossier** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | Retest period or storage period |  |  |  |
| IA | 1. | Reduction  Date of implementation: …… | 1 | 1, 2, 3 | 5113Q |
| IB\* |  |  | 1, 2, 3 | 5535 |
| II | 2. | Extension of the retest period based on extrapolation of stability data not in accordance with ICH guidelines (not applicable for biological or immunological active substances) |  |  | 5114 |
| II | 3. | Extension of storage period of a biological or immunological active substance not in accordance with an approved stability protocol |  |  | 5115 |
| IB | 4. | Extension or introduction of a retest period or storage period supported by real time data |  | 1, 2, 3 | 5116 |
|  | b) | Storage conditions |  |  |  |
| IA | 1. | Change to more restrictive storage conditions of the active substance  Date of implementation: …… | 1 | 1, 2, 3 | 5117Q |
| IB\* |  |  | 1, 2, 3 | 5536 |
| II | 2. | Change in storage conditions of biological or immunological active substances, when the stability studies have not been performed in accordance with a currently approved stability protocol |  |  | 5118 |
| IB | 3. | Change in storage conditions of the active substance |  | 1, 2, 3 | 5119 |
| IA | c) | Change to an approved stability protocol  Date of implementation: …… | 1, 2 | 1, 4 | 5120Q |
| IB\* |  |  | 1, 4 | 5537 |
| IB | z) | Other change |  |  | 5797 |
| IAIN | Date of implementation: …… |  |  | 5795Q |
| IA | Date of implementation: …… |  |  | 5796Q |
| II |  |  |  | 5798 |
|  | | **Conditions** | | | |
|  | 1. | The change should not be the result of unexpected events arising during manufacture or because of stability concerns. | | | |
|  | 2. | The changes do not concern a widening of the acceptance criteria in the parameters tested, a removal of stability indicating parameters or a reduction in the frequency of testing. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. This 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 requested retest period or requested storage conditions. | | | |
|  | 2. | Confirmation that stability studies have been done to the currently approved protocol. The studies must show that the agreed relevant specifications are still met. | | | |
|  | 3. | Copy of approved specifications of the active substance. | | | |
|  | 4. | Justification for the proposed changes. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** |
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| **Present** | **Proposed** |
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B.I.e) Design space and post approval change management protocol

B.I.e.1

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| **B.I.e.1** | | **Introduction of a new design space or extension of an approved design space for the active substance, concerning:** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | a) | One unit operation in the manufacturing process of the active substance including the resulting in-process controls and/or test procedures |  | 1, 2, 3 | 5121 |
| II | b) | Test procedures for starting materials / reagents / intermediates and/or the active substance |  | 1, 2, 3 | 5122 |
| IB | z) | Other change |  |  | 5801 |
| IAIN | Date of implementation: …… |  |  | 5799Q |
| IA | Date of implementation: …… |  |  | 5800Q |
| II |  |  |  | 5802 |
|  | | **Documentation** | | | |
|  | 1. | The design space has been developed in accordance with the relevant international scientific guidelines. Results from product, process and analytical development studies (e.g. interaction of the different parameters forming the design space have to be studied, including risk assessment and multivariate studies, as appropriate) demonstrating where relevant that a systematic mechanistic understanding of material attributes and process parameters to the critical quality attributes of the active substance has been achieved. | | | |
|  | 2. | Description of the design space in tabular format, including the variables (material attributes and process parameters, as appropriate) and their proposed ranges. | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier. | | | |

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

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| **B.I.e.2** | | **Introduction of a post approval change management protocol related to the active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II |  |  |  | 1, 2, 3 | 5123 |
| IB | z) | Other change |  |  | 5805 |
| IAIN | Date of implementation: …… |  |  | 5803Q |
| IA | Date of implementation: …… |  |  | 5804Q |
| II |  |  |  | 5806 |
|  | | **Documentation** | | | |
|  | 1. | Detailed description for the proposed change. | | | |
|  | 2. | Change management protocol related to the active substance. | | | |
|  | 3. | 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.I.e.3

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| **B.I.e.3** | | **Deletion of an approved change management protocol related to the active substance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN |  | Date of implementation: …… | 1 | 1, 2 | 5124Q |
| IB\* |  |  | 1, 2 | 5538 |
| IB | z) | Other change |  |  | 5809 |
| IAIN | Date of implementation: …… |  |  | 5807Q |
| IA | Date of implementation: …… |  |  | 5808Q |
| II |  |  |  | 5810 |
|  | | **Conditions** | | | |
|  | 1. | The deletion of the approved change management protocol related to the active substance is not due to unexpected events or to out-of-specification results during the implementation of the changes described in the protocol and does not have any effect on the already approved information in the dossier. | | | |
|  | | **Documentation** | | | |
|  | 1. | Justification for the proposed deletion. | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.I.e.4** | | **Changes to an approved change management protocol** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | a) | Major changes to an approved change management protocol |  |  | 5125 |
| IB | b) | Minor changes to an approved change management protocol that do not change the strategy defined in the protocol |  | 1 | 5126 |
| IB | z) | Other change |  |  | 5813 |
| IAIN | Date of implementation: …… |  |  | 5811Q |
| IA | Date of implementation: …… |  |  | 5812Q |
| II |  |  |  | 5814 |
|  | | **Documentation** | | | |
|  | 1. | Declaration that any change should be within the range of currently approved limits. In addition, declaration that an assessment of comparability is not required for biological or immunological medicinal products. | | | |

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

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| **B.I.e.5** | | **Implementation of changes foreseen in an approved change management protocol** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | The implementation of the change requires no further supportive data  Date of implementation: …… | 1 | 1, 2, 4 | 5127Q |
| IB\* |  |  | 1, 2, 4 | 5539 |
| IB | b) | The implementation of the change requires further supportive data |  | 1, 2, 3, 4 | 5128 |
| IB | c) | Implementation of a change for a biological/immunological medicinal product |  | 1, 2, 3, 4, 5 | 5129 |
| IB | z) | Other change |  |  | 5817 |
| IAIN | Date of implementation: …… |  |  | 5815Q |
| IA | Date of implementation: …… |  |  | 5816Q |
| II |  |  |  | 5818 |
|  | | **Conditions** | | | |
|  | 1. | The proposed change has been performed fully in line with the approved change management protocol. | | | |
|  | | **Documentation** | | | |
|  | 1. | Reference to the approved change management protocol. | | | |
|  | 2. | Declaration that the change is in accordance with the approved change management protocol and that the study results meet the acceptance criteria specified in the protocol. In addition, declaration that an assessment of comparability is not required for biological or immunological medicinal products. | | | |
|  | 3. | Results of the studies performed in accordance with the approved change management protocol. | | | |
|  | 4. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 5. | Copy of approved specifications of the active substance. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.I.z. Other quality change to active ingredient

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| **B.I.z** | **Other quality change to active ingredient** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | Date of implementation: …… |  |  | 5819Q |
| IA | Date of implementation: …… |  |  | 5820Q |
| IB |  |  |  | 5821 |
| II |  |  |  | 5822 |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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B.II. Finished product

B.II.a) Description and composition

B.II.a.1

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| **B.II.a.1** | | **Change or addition of imprints, bossing or other markings including replacement or addition of inks used for product marking** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | Changes in imprints, bossing or other markings  Date of implementation: …… | 1, 2, 3, 4, 5 | 1, 2 | 5130Q |
| IB\* |  |  | 1, 2 | 5540 |
| IB | b) | Changes in scoring/break lines intended to divide into equal doses |  | 1, 2, 3 | 5131 |
| IB | z) | Other change |  |  | 5825 |
| IAIN | Date of implementation: …… |  |  | 5823Q |
| IA | Date of implementation: …… |  |  | 5824Q |
| II |  |  |  | 5826 |
|  | | **Conditions** | | | |
|  | 1. | Finished product release and end of shelf-life specifications have not been changed (except for appearance) | | | |
|  | 2. | Any ink must comply with the relevant pharmaceutical legislation. | | | |
|  | 3. | The scoring/break lines are not intended to divide into equal doses. | | | |
|  | 4. | Any product markings used to differentiate dosage strengths should not be completely deleted. | | | |
|  | 5. | If the change also involves a co-marketing medicinal product, the change (e.g. imprint/bossing) must be compatible with the co-marketing medicinal product, see guidance document *Authorisation of co-marketing medicinal products.* | | | |
| n/a |  | Justification: | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a detailed drawing or written description of the current and new appearance, and including revised product information and/or packaging texts as appropriate. | | | |
|  | 2. | Not applicable to Switzerland. | | | |
|  | 3. | Results of the appropriate Ph. Eur. tests demonstrating equivalence in characteristics / correct dosing. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as a type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.a.2** | | **Change in the shape or dimensions of the pharmaceutical form** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | Immediate-release tablets, capsules, suppositories and pessaries  Date of implementation: …… | 1, 2, 3, 4 | 1, 4 | 5132# |
| IB\* |  |  | 1, 4 | 5541 |
| IB | b) | Gastro-resistant, modified or prolonged-release pharmaceutical forms and scored tablets intended to be divided into equal doses |  | 1, 2, 3, 4, 5 | 5133 |
| II | c) | Addition of a new kit for a radiopharmaceutical preparation with another fill volume |  |  | 5134 |
| IB | z) | Other change |  |  | 5829 |
| IAIN | Date of implementation: …… |  |  | 5827Q |
| IA | Date of implementation: …… |  |  | 5828Q |
| II |  |  |  | 5830 |
|  | | **Conditions** | | | |
|  | 1. | If appropriate, the dissolution profile of the reformulated product is comparable to the old one. For herbal medicinal products, where dissolution testing may not be feasible, the disintegration time of the new product compared to the old one. | | | |
| n/a |  | Justification: | | | |
|  | 2. | Release and end of shelf-life specifications of the finished product have not been changed (except for dimensions). | | | |
|  | 3. | The qualitative or quantitative composition and mean mass remain unchanged. | | | |
|  | 4. | The change does not relate to a scored tablet that is intended to be divided into equal doses. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a detailed drawing of the current and proposed situation, and including revised product information and/or packaging texts as appropriate. | | | |
|  | 2. | Comparative dissolution data on at least one pilot batch of the current and proposed dimensions (no significant differences regarding comparability see the relevant guidance on bioavailability. For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
|  | 3. | Justification for not submitting a new bioequivalence study according to the relevant guidance on bioavailability. | | | |
|  | 4. | Not applicable to Switzerland. | | | |
|  | 5. | Results of the appropriate Ph. Eur. tests demonstrating equivalence in characteristics / correct dosing. | | | |
| Note on B.II.a.2.c: Applicants are reminded that any changes to the dosage strength of the medicinal product requires the submission of an extension application. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.a.3** | | **Changes in the composition (excipients) of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | Changes in components of the flavouring or colouring system |  |  |  |
| IAIN | 1. | Addition, deletion or replacement  Date of implementation: …… | 1, 2, 3, 4, 5, 6, 7, 9, 11 | 1, 2, 4, 5, 6 | 5135Q |
| IB\* |  |  | 1, 2, 4, 5, 6 | 5542 |
| IA | 2. | Increase or reduction  Date of implementation: …… | 1, 2, 3, 4, 11 | 1, 2, 4 | 5136Q |
| IB\* |  |  | 1, 2, 4 | 5543 |
|  | 3. | Not applicable for human medicinal products. |  |  |  |
|  | b) | Other excipients |  |  |  |
| IA | 1. | Any minor adjustment of the quantitative composition of the finished product with respect to excipients  Date of implementation: …… | 1, 2, 4, 8, 9, 10 | 1, 2, 7 | 5138Q |
| IB\* |  |  | 1, 2, 7 | 5544 |
| II | 2. | Qualitative or quantitative changes in one or more excipients that may have a significant impact on the safety, quality or efficacy of the finished product |  |  | 5139 |
| II | 3. | Change that relates to a biological or immunological product |  |  | 5140 |
| II | 4. | Any new excipient that includes the use of materials of human or animal origin for which assessment is required of viral safety data or TSE risk |  |  | 5141 |
| II | 5. | Change that is supported by a bioequivalence study |  |  | 5142 |
| IB | 6. | Replacement of a single excipient with a comparable excipient with the same functional characteristics and at a similar level |  | 1, 3, 4, 5, 6, 7, 8, 9, 10 | 5143 |
| IB | z) | Other change |  |  | 5833 |
| IAIN | Date of implementation: …… |  |  | 5831Q |
| IA | Date of implementation: …… |  |  | 5832Q |
| II |  |  |  | 5834 |
|  | | **Conditions** | | | |
|  | 1. | No change in functional characteristics of the pharmaceutical form, e.g. disintegration time, dissolution profile. | | | |
|  | 2. | Any minor adjustment to the formulation to maintain the total weight should be made by an excipient which currently makes up a major part of the finished product formulation. | | | |
|  | 3. | The finished product specification has only been updated in respect of appearance / odour / taste and if relevant, deletion of an identification test. | | | |
|  | 4. | Stability studies have been started under ICH conditions (with indication of batch numbers) and relevant stability parameters have been assessed in at least two pilot scale or industrial scale batches and at least three months satisfactory stability data are at the disposal of the applicant (at time of implementation for type IA and at time of notification for type IB variations) and that the stability profile is similar to the currently registered situation. Confirmation has been provided that these studies will be finalised and that data will be provided immediately to Swissmedic if outside specifications or potentially outside specification at the end of the approved shelf-life (with proposed action). In addition, where relevant, photostability testing has been performed. | | | |
|  | 5. | Any new proposed components comply with the relevant food legislation. e.g. Food Additives Ordinance (FoodAO; SR 817.022.31), Flavourings Ordinance (SR 817.022.41). | | | |
|  | 6. | Any new component does not include the use of materials of human or animal origin for which assessment is required of viral safety data or compliance with the current "Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products". | | | |
|  | 7. | Where applicable, the change does not affect the differentiation between dosage strengths and does not have a negative impact on taste acceptability for paediatric formulations. | | | |
|  | 8. | The dissolution profile of the new finished product determined on a minimum of two pilot scale batches is comparable to the old one (no significant differences regarding comparability, see the relevant guidance on bioavailability). For herbal medicinal products where dissolution testing may not be feasible, the disintegration time of the new product is comparable to the old one. | | | |
|  | 9. | The change is not the result of stability issues and/or should not result in potential safety concerns i.e. differentiation between dosage strengths. | | | |
|  | 10. | The product is not a biological or immunological medicinal product. | | | |
|  | 11. | Not applicable for human medicinal products. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including identification method for any new colouring agent, where relevant, and including revised product information and packaging texts and *Full declaration* form as appropriate. | | | |
|  | 2. | A declaration stating that the required stability studies have been started under ICH conditions (with indication of the batch numbers concerned) and that, as relevant, the required minimum satisfactory stability data were at the disposal of the applicant at the time of implementation and that the available data did not indicate a problem. It should also be confirmed that the studies will be finalised and that data will be provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). | | | |
|  | 3. | The results of stability studies that have been carried out under ICH 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 provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). | | | |
|  | 4. | Not applicable to Switzerland. | | | |
|  | 5. | Either a TSE Ph. Eur. Certificate of Suitability for any new source of material derived from animals susceptible to TSE risk or, where applicable, documentary evidence that the specific source of the TSE risk material (including substances used in the manufacture of the active substance/excipient) complies with the current "Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products". The following information should be included for each such material: Name of manufacturer, species and tissues from which the material is a derivative, country of origin of the source animals and its use. In addition, an updated *Substances of animal or human origin* form. | | | |
| n/a |  | Justification: | | | |
|  | 6. | Data to demonstrate that the new excipient does not interfere with the finished product specification test methods, if appropriate. | | | |
| n/a |  | Justification: | | | |
|  | 7. | Justification for the change/choice of excipients etc. must be given by appropriate pharmaceutical development (including stability aspects and antimicrobial preservation where appropriate). | | | |
|  | 8. | For solid pharmaceutical forms, comparative dissolution profile data on at least two pilot scale batches of the finished product in the new and old composition. For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
|  | 9. | Justification for not submitting a new bioequivalence study according to the current guidance on bioequivalence. | | | |
|  | 10. | Not applicable for human medicinal products. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.a.4** | | **Change in coating weight of oral pharmaceutical forms or change in weight of capsule shells** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Solid oral pharmaceutical forms  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5144# |
| IB\* |  |  | 1, 2 | 5545 |
| II | b) | Gastro-resistant, modified- or prolonged-release pharmaceutical forms where the coating is a critical factor for the release mechanism |  |  | 5145 |
| IB | z) | Other change |  |  | 5837 |
| IAIN | Date of implementation: …… |  |  | 5835Q |
| IA | Date of implementation: …… |  |  | 5836Q |
| II |  |  |  | 5838 |
|  | | **Conditions** | | | |
|  | 1. | The dissolution profile of the new product determined on a minimum of two pilot scale batches is comparable to the old one. For herbal medicinal products where dissolution testing may not be feasible, the disintegration time of the new product is comparable to the old one. | | | |
|  | 2. | The coating is not a critical factor for the release mechanism. | | | |
|  | 3. | The finished product specification has only been updated in respect of weight and dimensions, if applicable. | | | |
| n/a |  | Justification: | | | |
|  | 4. | Stability studies in accordance with ICH conditions have been started with at least two pilot scale or industrial scale batches and at least three months satisfactory stability data are at the disposal of the applicant at the time of implementation and confirmation that these studies will be finalised. Data will be provided immediately to Swissmedic if outside specifications or potentially outside specifications at the end of the approved shelf-life (with proposed action). | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | A declaration stating that the required stability studies have been started under ICH conditions (with indication of the batch numbers concerned) and that, as relevant, the required minimum satisfactory stability data were at the disposal of the applicant at the time of implementation and that the available data did not indicate a problem. It should also be confirmed that the studies will be finalised and that data will be provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). In addition, where relevant, photostability testing has been performed. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.a.5** | | **Change in concentration of a single-dose, total use parenteral product, where the amount of active substance per unit dose (i.e. the strength) remains the same** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II |  |  |  |  | 5146 |
| IB | z) | Other change |  |  | 5841 |
| IAIN | Date of implementation: …… |  |  | 5839Q |
| IA | Date of implementation: …… |  |  | 5840Q |
| II |  |  |  | 5842 |

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

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| **B.II.a.6** | | **Deletion of the solvent / diluent container from the pack** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB |  |  |  | 1, 2 | 5147 |
| IB | z) | Other change |  |  | 5845 |
| IAIN | Date of implementation: …… |  |  | 5843Q |
| IA | Date of implementation: …… |  |  | 5844Q |
| II |  |  |  | 5846 |
|  | | **Documentation** | | | |
|  | 1. | Justification for the deletion, including a statement regarding alternative means to obtain the solvent or diluent as required for the safe and effective use of the medicinal product. | | | |
|  | 2. | Revised 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.II.b) Manufacture

B.II.b.1

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| **B.II.b.1** | | **Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | Secondary packaging site  Date of implementation: …… | 1, 2 | 1, 3, 8 | 5148#Z |
| IB\* |  |  | 1, 3, 8 | 5546 |
| IAIN | b) | Primary packaging site  Date of implementation: …… | 1, 2, 3, 4, 5 | 1, 2, 3, 4, 8, 9 | 5149#Z |
| IB\* |  |  | 1, 2, 3, 4, 8, 9 | 5547 |
| II | c) | 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 |  |  | 5150 |
| II | d) | Site which requires an initial or product-specific inspection |  |  | 5151 |
| IB | e) | 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 | 5152 |
| IB | f) | 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 | 5153 |
| IB | z) | Other change |  |  | 5849 |
| IAIN | Date of implementation: …… |  |  | 5847Q |
| IA | Date of implementation: …… |  |  | 5848Q |
| II |  |  |  | 5850 |
|  | | **Conditions** | | | |
|  | 1. | The site is GMP compliant. | | | |
|  | 2. | Site appropriately authorised (to manufacture the pharmaceutical form or product concerned). | | | |
|  | 3. | The product is not a sterile product. | | | |
|  | 4. | Where relevant, for instance for suspensions and emulsions, validation scheme is available, or validation of the manufacture at the new site has been successfully carried out according to the current protocol with at least three production scale batches. | | | |
| n/a |  | Justification: | | | |
|  | 5. | The product is not a biological or immunological medicinal product. | | | |
|  | | **Documentation** | | | |
|  | 1. | Proof that the manufacturer's GMP compliance has been verified. | | | |
|  | 2. | Where relevant, the batch numbers, corresponding batch size and the manufacturing date of batches (≥3) used in the validation study should be indicated and the validation data presented, or validation protocol (scheme) submitted. | | | |
| n/a |  | Justification: | | | |
|  | 3. | Comparison of present and proposed sites. | | | |
|  | 4. | Copy of approved release and end-of-shelf-life specifications if relevant. | | | |
| n/a |  | Justification: | | | |
|  | 5. | Batch analysis data on one production batch and two pilot-scale batches simulating the commercial production process (or two production batches) and comparative data on the last three batches from the previous site. Batch data on the next two production batches should be available on request or reported if outside specifications (with proposed action). | | | |
|  | 6. | For semisolid and liquid formulations in which the active substance is present in non-dissolved form, appropriate validation data, including microscopic imaging of particle size distribution and morphology or any other appropriate imaging technique. | | | |
| n/a |  | Justification: | | | |
|  | 7. | Completed and signed form *Declaration by the Responsible Person for foreign manufacturers*, if applicable. | | | |
|  | 8. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form. | | | |
|  | 9. | If the manufacturing site and the primary packaging site are different, conditions of transport and bulk storage should be specified and validated. | | | |
| n/a |  | Justification: | | | |
| Note:  The guidance document *GMP compliance by foreign manufacturers* should be consulted for the GMP requirements for foreign manufacturers. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.II.b.2

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| **B.II.b.2** | | **Change to batch release arrangements and quality control testing of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Replacement or addition of a site where batch control or testing (quality control) takes place  Date of implementation: …… | 2, 3, 4, 5 | 1, 2, 5 | 5154#Z |
| IB\* |  |  | 1, 2, 5 | 5548 |
| II | b) | Replacement or addition of a site where batch control or testing (quality control) takes place for a biological or immunological product and any of the test methods performed at the site is a biological or immunological method |  |  | 5155 |
|  | c) | Replacement or addition of a manufacturer responsible for batch release |  |  |  |
| IAIN | 1. | Not including batch control or testing (quality control)  Date of implementation: …… | 1, 2, 5 | 1, 2, 3, 4, 5 | 5156#Z |
| IB\* |  |  | 1, 2, 3, 4, 5 | 5549 |
| IAIN | 2. | Including batch control or testing (quality control)  Date of implementation: …… | 1, 2, 3, 4, 5 | 1, 2, 3, 4, 5 | 5157#Z |
| IB\* |  |  | 1, 2, 3, 4, 5 | 5550 |
| II | 3. | Including batch control or testing (quality control) for a biological or immunological finished product and any of the test methods performed at that site is a biological, immunological or immunochemical method |  |  | 5158 |
| IB | z) | Other change |  |  | 5853 |
| IAIN | Date of implementation: …… |  |  | 5851Q |
| IA | Date of implementation: …… |  |  | 5852Q |
| II |  |  |  | 5854 |
|  | | **Conditions** | | | |
|  | 1. | Not applicable to Switzerland. | | | |
|  | 2. | The site is appropriately authorised. | | | |
|  | 3. | The product is not a biological or immunological medicinal product. | | | |
|  | 4. | Method transfer from the old to the new site or new test laboratory has been successfully completed. | | | |
|  | 5. | Not applicable to Switzerland. | | | |
|  | | **Documentation** | | | |
|  | 1. | Proof that the manufacturer's or testing laboratory's GMP compliance has been verified. | | | |
|  | 2. | Comparison of present and proposed sites. | | | |
|  | 3. | Not applicable to Switzerland. | | | |
|  | 4. | Not applicable to Switzerland. | | | |
|  | 5. | Amendment of the relevant section(s) of the dossier, including the updated *Manufacturer information* form and, if applicable, revised product information and/or packaging texts. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.II.b.3

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| **B.II.b.3** | | **Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Minor change in the manufacturing process  Date of implementation: …… | 1, 2, 3, 4, 5, 6, 7 | 1, 2, 3, 4, 5, 6, 7, 8 | 5159Q |
| IB\* |  |  | 1, 2, 3, 4, 5, 6, 7, 8 | 5551 |
| II | b) | Substantial changes to the manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product |  |  | 5160 |
| II | c) | The product is a biological or immunological finished product and the change requires an assessment of comparability |  |  | 5161 |
| II | d) | Introduction of a non-standard terminal sterilisation method |  |  | 5162 |
| II | e) | Introduction or increase in the overage used for the active substance |  |  | 5163 |
| IB | f) | Minor change in the manufacturing process of an aqueous oral suspension |  | 1, 2, 4, 6, 7, 8 | 5164 |
| IB | z) | Other change |  |  | 5857 |
| IAIN | Date of implementation: …… |  |  | 5855Q |
| IA | Date of implementation: …… |  |  | 5856Q |
| II |  |  |  | 5858 |
|  | | **Conditions** | | | |
|  | 1. | No change in qualitative and quantitative impurity profile or in physico-chemical properties. | | | |
|  | 2. | Either the change relates to an immediate-release solid oral pharmaceutical form or oral solution, and the medicinal product concerned is not a biological or immunological or herbal medicinal product;  or the change relates to process parameters that, in the context of a previous assessment, have been considered to have no impact on the quality of the finished product (regardless of the type of product and/or pharmaceutical form). | | | |
|  | 3. | The manufacturing principle including the single manufacturing steps remain the same (e.g. processing intermediates), and there are no changes to any manufacturing solvent used in the process. | | | |
|  | 4. | The currently registered process has to be controlled by relevant in-process controls, and no changes (widening or deletion of limits) are required for these in-process controls. | | | |
|  | 5. | The specifications of the finished product or intermediates are unchanged. | | | |
|  | 6. | The new process must lead to an identical product regarding all aspects of quality, safety and efficacy. | | | |
|  | 7. | Relevant stability studies in accordance with the ICH conditions have been started with at least one pilot scale or industrial scale batch and at least three months stability data are at the disposal of the applicant. It should also be confirmed that these studies will be finalised and that the data will be provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a direct comparison of the present process and the proposed manufacturing 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. | | | |
| n/a |  | Justification: | | | |
|  | 3. | For solid pharmaceutical forms: dissolution profile data of one representative production batch and comparative data of the last three batches from the previous manufacturing process; data on the next two full production batches should be available on request or reported if outside specification (with proposed action). For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
| n/a |  | Justification: | | | |
|  | 4. | Justification for not submitting a new bioequivalence study according to the relevant guidance on bioavailability. | | | |
|  | 5. | For changes to process parameters that have been considered to have no impact on the quality of the finished product, declaration to this effect reached in the context of the previously approved risk assessment. | | | |
| n/a |  | Justification: | | | |
|  | 6. | Copy of approved release and end-of-shelf-life specifications. | | | |
|  | 7. | Batch analysis data (in a comparative tabulated format) for a minimum of one batch manufactured to both the currently approved and the proposed process. Batch data on the next two production batches should be available on request and reported if outside specifications (with proposed action). | | | |
|  | 8. | Declaration that relevant stability studies have been started under ICH conditions, as appropriate, (with indication of the batch numbers concerned) and relevant stability parameters have been assessed in at least one pilot scale or industrial scale batch and at least three months satisfactory stability data are at the disposal of the applicant at time of notification and that the stability profile is similar to the currently registered situation. Confirmation should be provided that these studies will be finalised and that data will be provided immediately to Swissmedic if outside specifications or potentially outside specification at the end of the approved shelf-life (with proposed action). | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.b.4** | | **Change in the batch size (including batch size range) of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Up to 10-fold increase compared to the originally approved batch size  Date of implementation: …… | 1, 2, 3, 4, 5, 7 | 1, 4 | 5165Q |
| ☐ IB\* |  |  | 1, 4 | 5552 |
| IA | b) | Downscaling down to 10-fold  Date of implementation: …… | 1, 2, 3, 4, 5, 6 | 1, 4 | 5166Q |
| ☐ IB\* |  |  | 1, 4 | 5553 |
| II | c) | 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 |  |  | 5167 |
| II | d) | The change relates to all other pharmaceutical forms manufactured by a complex manufacturing process |  |  | 5168 |
| IB | e) | More than 10-fold increase compared to the originally approved batch size for immediate-release oral pharmaceutical forms |  | 1, 2, 3, 4, 5, 6 | 5169 |
| IB | f) | The scale for a biological or immunological medicinal product is increased or decreased without any change in the manufacturing process (e.g. duplication of the production lines) |  | 1, 2, 3, 4, 5, 6 | 5170 |
| IB | z) | Other change |  |  | 5861 |
| IAIN | Date of implementation: …… |  |  | 5859Q |
| IA | Date of implementation: …… |  |  | 5860Q |
| II |  |  |  | 5862 |
|  | | **Conditions** | | | |
|  | 1. | The change does not affect the reproducibility and/or consistency of the product. | | | |
|  | 2. | The change relates to conventional immediate-release oral pharmaceutical forms or non-sterile liquid pharmaceutical forms. | | | |
|  | 3. | Any changes to the manufacturing methods and/or to the in-process controls are only those necessitated by the change in batch-size, e.g. use of different sized equipment of the same type. | | | |
|  | 4. | Validation scheme is available, or validation of the manufacture has been successfully carried out according to the current protocol with at least three batches at the proposed new batch size in accordance with the relevant guidelines. | | | |
|  | 5. | The product is not a biological or immunological medicinal product. | | | |
|  | 6. | The change should not be the result of unexpected events arising during manufacture or because of stability concerns. | | | |
|  | 7. | The batch size is within the 10-fold range of the batch size foreseen when the marketing authorisation was granted, or following a subsequent change not agreed as a Type IA variation. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Batch analysis data (in a comparative tabulated format) for a minimum of one production batch manufactured in both the currently approved and the proposed batch sizes. Batch data on the next two full production batches should be made available upon request and reported by the marketing authorisation holder if outside specification (with proposed action). | | | |
|  | 3. | Copy of approved release and end-of-shelf-life specifications. | | | |
|  | 4. | Where relevant, the batch numbers, corresponding batch size and the manufacturing date of batches (≥3) used in the validation study should be indicated or the validation protocol (scheme) be submitted. | | | |
|  | 5. | The validation results should be provided. | | | |
|  | 6. | The results of stability studies that have been carried out under ICH 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 provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). For biological or immunological medicinal products: a declaration that an assessment of comparability is not required. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.b.5** | | **Change to in-process tests or limits applied during the manufacture of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Tightening of in-process limits  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5171Q |
| IB\* |  |  | 1, 2 | 5554 |
| IA | b) | Addition of new in-process tests and limits  Date of implementation: …… | 1, 2, 5, 6 | 1, 2, 3, 4, 5, 7 | 5172Q |
| IB\* |  |  | 1, 2, 3, 4, 5, 7 | 5555 |
| IA | c) | Deletion of a non-significant in-process test  Date of implementation: …… | 1, 2, 7 | 1, 2, 6 | 5173Q |
| IB\* |  |  | 1, 2, 6 | 5556 |
| II | d) | Deletion of an in-process test which may have a significant effect on the overall quality of the finished product |  |  | 5174 |
| II | e) | Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the finished product |  |  | 5175 |
| IB | f) | Addition or replacement of an in-process test as a result of a safety or quality issue |  | 1, 2, 3, 4, 5, 7 | 5176 |
| IB | z) | Other change |  |  | 5865 |
| IAIN | Date of implementation: …… |  |  | 5863Q |
| IA | Date of implementation: …… |  |  | 5864Q |
| II |  |  |  | 5866 |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure). | | | |
|  | 2. | The change does not result from unexpected events arising during manufacture e.g. new unqualified impurity or change in total impurity limits. | | | |
|  | 3. | Any change should be within the range of currently approved limits. | | | |
|  | 4. | The test procedure remains the same, or changes to the test procedure are minor. | | | |
|  | 5. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | 6. | The new test method is not a biological, immunological or immunochemical method or a method using a biological reagent for a biological active substance (does not include standard pharmacopoeial microbiological methods). | | | |
|  | 7. | The in-process test does not concern the control of a critical parameter, e.g. assay, impurities (unless a particular solvent is definitely not used in the manufacture of the active substance), any critical physical characteristics (particle size, bulk or tapped density...), identity test (unless there is a suitable alternative control already present), microbiological control (unless not required for the particular pharmaceutical form). | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of current and proposed in-process tests and limits. | | | |
|  | 3. | Details of any new analytical method and validation data, where relevant. | | | |
|  | 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 on at least one pilot batch manufactured using the current and new in-process tests. For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
| n/a |  | Justification: | | | |
|  | 6. | Justification or risk assessment showing that the in-process test is non-significant or that it is obsolete. | | | |
|  | 7. | Justification of the new in-process tests and limits. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.II.c) Control of excipients

B.II.c.1

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| **B.II.c.1** | | **Change in the specification parameters and/or limits of an excipient** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Tightening of specification limits  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5177Q |
| IB\* |  |  | 1, 2 | 5557 |
| IA | b) | Addition of a new specification parameter with its corresponding test method  Date of implementation: …… | 1, 2, 5, 6, 7 | 1, 2, 3, 4, 6, 8 | 5178Q |
| IB\* |  |  | 1, 2, 3, 4, 6, 8 | 5558 |
| IA | c) | Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)  Date of implementation: …… | 1, 2, 8 | 1, 2, 7 | 5179Q |
| IB\* |  |  | 1, 2, 7 | 5559 |
| II | d) | Change outside the approved specifications limits range |  |  | 5180 |
| II | e) | Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product |  |  | 5181 |
| IB | f) | Addition or replacement (excluding biological or immunological products) of a specification parameter with its corresponding test method, as a result of a safety or quality issue |  | 1, 2, 3, 4, 5, 6, 8 | 5182 |
| IB | g) | Where there is no monograph in the European Pharmacopoeia or the Pharmacopoeia Helvetica for the excipient, a change in specification from in-house to a non-official pharmacopoeia or a pharmacopoeia of a third country |  | 1, 2, 3, 4, 5, 6, 8 | 5183 |
| IB | z) | Other change |  |  | 5869 |
| IAIN | Date of implementation: …… |  |  | 5867Q |
| IA | Date of implementation: …… |  |  | 5868Q |
| II |  |  |  | 5870 |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure). | | | |
|  | 2. | The change does not result from unexpected events arising during manufacture e.g. new unqualified impurity or change in total impurity limits. | | | |
|  | 3. | Any change should be within the range of currently approved limits. | | | |
|  | 4. | The test procedure remains the same, or changes to the test procedure are minor. | | | |
|  | 5. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | 6. | The test method is neither a biological/immunological/immunochemical method nor a method using a biological reagent (does not include standard pharmacopoeial microbiological methods). | | | |
|  | 7. | The change does not concern a genotoxic impurity. | | | |
|  | 8. | The specification parameter does not concern the control of a critical parameter, e.g. impurities (unless a particular solvent is definitely not used in the manufacture of the excipient), any critical physical characteristics (particle size, bulk or tapped density...), identity test (unless there is a suitable alternative control already present), microbiological control (unless not required for the particular pharmaceutical form). | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of current and proposed specifications. | | | |
|  | 3. | Details of any new analytical method and validation data, where relevant. | | | |
|  | 4. | Batch analysis data for two production batches (three production batches for biological excipients) of the excipient for all specification parameters. | | | |
|  | 5. | Where appropriate, comparative dissolution profile data for the finished product on at least one pilot batch containing the excipient complying with the current and proposed specifications. For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
| n/a |  | Justification: | | | |
|  | 6. | If appropriate, justification for not submitting a new bioequivalence study according to the relevant guidance on bioavailabilitys). | | | |
| n/a |  | Justification: | | | |
|  | 7. | Justification or risk assessment showing that the parameter is non-significant or that it is obsolete. | | | |
|  | 8. | Justification of the new specification parameter and the limits. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.c.2** | | **Change in test procedures for an excipient** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Minor changes to an approved test procedure  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5184 |
| IB\* |  |  | 1, 2 | 5560 |
| IA | b) | Deletion of a test procedure if an alternative test procedure is already authorised  Date of implementation: …… | 5 | 1 | 5185 |
| IB\* |  |  | 1 | 5561 |
| II | c) | Substantial change to, or replacement of, a biological, immunological or immunochemical test method or a method using a biological reagent |  |  | 5186 |
| IB | d) | Other changes to a test procedure (including replacement or addition) |  | 1, 2 | 5187 |
| IB | z) | Other change |  |  | 5873 |
| IAIN | Date of implementation: …… |  |  | 5871Q |
| IA | Date of implementation: …… |  |  | 5872Q |
| II |  |  |  | 5874 |
|  | | **Conditions** | | | |
|  | 1. | Appropriate validation studies have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the previously approved test procedure. | | | |
| n/a |  | Justification: | | | |
|  | 2. | No changes have been made to the total impurity limits, and no new unqualified impurities have been detected. | | | |
|  | 3. | The analytical method essentially remains the same (e.g. a change in column length or temperature, but not a different type of column or method). | | | |
|  | 4. | The test method is not a biological, immunological or immunochemical method or a method using a biological reagent (does not include standard pharmacopoeial microbiological methods). | | | |
|  | 5. | An alternative test procedure is already authorised for the specification parameter, and this procedure has not been added through IA/IAIN notification. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the 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 analysis results showing that the current test and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new test procedure. | | | |
| n/a |  | Justification: | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.c.3** | | **Change in source of an excipient or reagent with TSE risk** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | From TSE risk material to material of vegetable or synthetic origin |  |  |  |
| IA | 1. | For excipients or reagents not used in the manufacture of a biological or immunological active substance or in a biological or immunological medicinal product  Date of implementation: …… | 1 | 1 | 5188 |
| IB\* |  |  | 1 | 5562 |
| IB | 2. | For excipients or reagents used in the manufacture of a biological or immunological active substance or in a biological or immunological medicinal product |  | 1, 2 | 5189 |
| II | b) | Change or introduction of a TSE risk material, or replacement of a TSE risk material from a different TSE risk material, not covered by a TSE certificate of suitability |  |  | 5190 |
| IB | z) | Other change |  |  | 5877 |
| IAIN | Date of implementation: …… |  |  | 5875Q |
| IA | Date of implementation: …… |  |  | 5876Q |
| II |  |  |  | 5878 |
|  | | **Conditions** | | | |
|  | 1. | Excipient and finished product release and end of shelf-life specifications remain the same. | | | |
|  | | **Documentation** | | | |
|  | 1. | Declaration from the manufacturer or the marketing authorisation holder of the material that it is purely of vegetable or synthetic origin. | | | |
|  | 2. | Study of equivalence of the materials and the impact on production of the final material and impact on behaviour (e.g. dissolution characteristics) of the finished product. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** | |
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B.II.c.4

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| **B.II.c.4** | | **Change in synthesis or recovery of a non-pharmacopoeial excipient (when described in the dossier Module 3) or a novel excipient** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Minor change in synthesis or recovery of a non-pharmacopoeial excipient or a novel excipient  Date of implementation: …… | 1, 2 | 1, 2, 3, 4 | 5191 |
| IB\* |  |  | 1, 2, 3, 4 | 5563 |
| II | b) | The specifications are affected or there is a change in the physico-chemical properties of the excipient which may affect the quality of the finished product. |  |  | 5192 |
| II | c) | The excipient is a biological or immunological substance |  |  | 5193 |
| IB | z) | Other change |  |  | 5881 |
| IAIN | Date of implementation: …… |  |  | 5879Q |
| IA | Date of implementation: …… |  |  | 5880Q |
| II |  |  |  | 5882 |
|  | | **Conditions** | | | |
|  | 1. | The synthetic route and specifications are identical and there is no change in the qualitative and quantitative impurity profile (excluding residual solvents, provided they are controlled in accordance with ICH limits), or in physico-chemical properties. | | | |
|  | 2. | Adjuvants are excluded. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Batch analysis data (in the form of a comparative table) for at least two batches (minimum pilot scale) of the excipient that were manufactured according to the currently approved and proposed processes. | | | |
|  | 3. | Where appropriate, comparative dissolution profile data for the finished product on at least two batches (minimum pilot scale). For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
| n/a |  | Justification: | | | |
|  | 4. | Copy of approved and new (if applicable) specifications of the excipient. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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B.II.d) Control of finished product

B.II.d.1

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| **B.II.d.1** | | **Change in the specification parameters and/or limits of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Tightening of specification limits  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5194Q |
| IB\* |  |  | 1, 2 | 5564 |
| IAIN | b) | Tightening of specification limits for medicinal products subject to Official Control Authority Batch Release  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5195Q |
| IB\* |  |  | 1, 2 | 5565 |
| IA | c) | Addition of a new specification parameter with its corresponding test method  Date of implementation: …… | 1, 2, 5, 6, 7 | 1, 2, 3, 4, 5, 7 | 5196Q |
| IB\* |  |  | 1, 2, 3, 4, 5, 7 | 5566 |
| IA | d) | Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter such as odour and taste or identification test for a colouring or flavouring material)  Date of implementation: …… | 1, 2, 9 | 1, 2, 6 | 5197Q |
| IB\* |  |  | 1, 2, 6 | 5567 |
| II | e) | Change outside the approved specifications limits range |  |  | 5198 |
| II | f) | Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product |  |  | 5199 |
| IB | g) | Addition or replacement (excluding biological or immunological products) of a specification parameter with its corresponding test method as a result of a safety or quality issue |  | 1, 2, 3, 4, 5, 7 | 5200 |
| IAIN | h) | Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the finished product (1)  Date of implementation: …… | 1, 2, 3, 4, 7, 8 | 1, 2 | 5201Q |
| IB\* |  |  | 1, 2 | 5568 |
| IAIN | i) | Ph. Eur. 2.9.40 Uniformity of dosage units is introduced to replace the currently registered method, either Ph. Eur. 2.9.5 (Uniformity of mass) or Ph. Eur. 2.9.6 (Uniformity of content)  Date of implementation: …… | 1, 2, 10 | 1, 2, 4 | 5202Q |
| IB\* |  |  | 1, 2, 4 | 5569 |
| IB | z) | Other change |  |  | 5885 |
| IAIN | Date of implementation: …… |  |  | 5883Q |
| IA | Date of implementation: …… |  |  | 5884Q |
| II |  |  |  | 5886 |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure), unless the supporting documentation has been already assessed and approved within another procedure. | | | |
|  | 2. | The change does not result from unexpected events arising during manufacture e.g. new unqualified impurity or change in total impurity limits. | | | |
|  | 3. | Any change should be within the range of currently approved limits. | | | |
|  | 4. | The test procedure remains the same, or changes to the test procedure are minor. | | | |
|  | 5. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | 6. | The test method is not a biological, immunological or immunochemical method or a method using a biological reagent for a biological active substance. | | | |
|  | 7. | The change does not concern any impurities (including genotoxic impurities) or dissolution. | | | |
|  | 8. | The change concerns the updating of the microbial control limits to be in line with the current Pharmacopoeia, and the currently registered microbial control limits (present situation) are in line with the pre-January 2008 (non-harmonised) situation and does not include any additional specified controls over the Pharmacopoeia requirements for the particular pharmaceutical form and the proposed controls are in line with the harmonised monograph. | | | |
|  | 9. | The specification parameter or proposal for the specific pharmaceutical form does not concern a critical parameter for example: assay, impurities (unless a particular solvent is definitely not used in the manufacture of the finished product), any critical physical characteristics (hardness or friability for uncoated tablets, dimensions), a test that is required for the particular pharmaceutical form in accordance with the general notices of the Ph. Eur. or any request for skip testing. | | | |
|  | 10. | The proposed control is fully in line with Table 2.9.40.-1 of the Ph. Eur. monograph 2.9.40 and does not include the alternative proposal for testing uniformity of dosage units by mass variation instead of content uniformity when the latter is specified in Table 2.9.40.-1. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of current and proposed specifications. | | | |
|  | 3. | Details of any new analytical method and validation data, where relevant. | | | |
|  | 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 on at least one pilot batch complying with the current and proposed specifications. For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
| n/a |  | Justification: | | | |
|  | 6. | Justification or risk assessment showing that the parameter is non-significant or that it is obsolete. | | | |
|  | 7. | Justification of the new specification parameter and the limits. | | | |
| 1 Note: There is no need to notify Swissmedic of an updated monograph in the European Pharmacopoeia or the Pharmacopoeia Helvetica in the case that reference is made to the “current edition” in the dossier of an authorised medicinal product. This variation therefore applies to cases where no reference to the updated monograph of the pharmacopoeia was contained in the dossier and the variation is made to make reference to the updated version. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.II.d.2

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| **B.II.d.2** | | **Change in test procedure for the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Minor changes to an approved test procedure  Date of implementation: …… | 1, 2, 3, 4, | 1, 2 | 5203Q |
| IB\* |  |  | 1, 2 | 5570 |
| IA | b) | Deletion of a test procedure if an alternative test procedure is already authorised  Date of implementation: …… | 4 | 1 | 5204Q |
| IB\* |  |  | 1 | 5571 |
| II | c) | 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 preparation not covered by an approved protocol |  |  | 5205 |
| IB | d) | Other changes to a test procedure (including replacement or addition) |  | 1, 2 | 5206 |
| IA | e) | Update of the test procedure to comply with the updated general monograph in the Ph. Eur.  Date of implementation: …… | 2, 3, 4, 5 | 1 | 5207Q |
| IB\* |  |  | 1 | 5572 |
| IA | f) | To reflect compliance with the Ph. Eur. and remove reference to the outdated internal test method and test method number (1)  Date of implementation: …… | 2, 3, 4, 5 | 1 | 5208Q |
| IB\* |  |  | 1 | 5573 |
| IB | z) | Other change |  |  | 5889 |
| IAIN | Date of implementation: …… |  |  | 5887Q |
| IA | Date of implementation: …… |  |  | 5888Q |
| II |  |  |  | 5890 |
|  | | **Conditions** | | | |
|  | 1. | Appropriate validation studies have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the previously approved test procedure. | | | |
| n/a |  | Justification: | | | |
|  | 2. | No changes have been made to the total impurity limits, and no new unqualified impurities have been detected. | | | |
|  | 3. | The analytical method essentially remains the same (e.g. a change in column length or temperature, but not a different type of column or method). | | | |
|  | 4. | The test method is not a biological, immunological or immunochemical method or a method using a biological reagent (does not include standard pharmacopoeial microbiological methods). | | | |
|  | 5. | The registered test procedure already refers to the general monograph of the Ph. Eur., and any changes are minor in nature and require update of the technical dossier. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the 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 analysis results showing that the current test and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new test procedure. | | | |
| n/a |  | Justification: | | | |
| 1 Note: There is no need to notify Swissmedic of an updated monograph of the European Pharmacopoeia in the case that reference is made to the “current edition” in the dossier of an authorised medicinal product. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** |
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| **Present** | **Proposed** |
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B.II.d.3

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| **B.II.d.3** | | **Variations related to the introduction of real-time release or parametric release in the manufacture of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II |  |  |  |  | 5209 |
| IB | z) | Other change |  |  | 5893 |
| IAIN | Date of implementation: …… |  |  | 5891Q |
| IA | Date of implementation: …… |  |  | 5892Q |
| II |  |  |  | 5894 |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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B.II.e) Container closure system

B.II.e.1

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| **B.II.e.1** | | **Change in immediate packaging of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | Qualitative and quantitative composition |  |  |  |
| IA | 1. | Solid pharmaceutical forms  Date of implementation: …… | 1, 2, 3 | 1, 2, 3, 4, 6 | 5210# |
| IB\* |  |  | 1, 2, 3, 4, 6 | 5574 |
| IB | 2. | Semi-solid and non-sterile liquid pharmaceutical forms |  | 1, 2, 3, 5, 6 | 5211 |
| II | 3. | Sterile medicinal products and biological or immunological medicinal products |  |  | 5212 |
| II | 4. | The change relates to a less protective pack where there are associated changes in storage conditions and/or a reduction in shelf-life. |  |  | 5213 |
|  | b) | Change in type of container or addition of a new container |  |  |  |
| IB | 1. | Solid, semi-solid and non-sterile liquid pharmaceutical forms |  | 1, 2, 3, 5, 6, 7 | 5214 |
| II | 2. | Sterile medicinal products and biological or immunological medicinal products |  |  | 5215 |
| IA | 3. | Deletion of an immediate packaging container that does not lead to the complete deletion of a strength or pharmaceutical form  Date of implementation: …… | 4 | 1, 8 | 5216# |
| IB\* |  |  | 1, 8 | 5575 |
| IB | z) | Other change |  |  | 5897 |
| IAIN | Date of implementation: …… |  |  | 5895Q |
| IA | Date of implementation: …… |  |  | 5896Q |
| II |  |  |  | 5898 |
|  | | **Conditions** | | | |
|  | 1. | The change only concerns the same packaging/container type (e.g. blister to blister). | | | |
|  | 2. | The proposed packaging material must be at least equivalent to the approved material in respect of its relevant properties. | | | |
|  | 3. | Relevant stability studies have been started under ICH conditions, relevant stability parameters have been assessed in at least two pilot scale or industrial scale batches, and at least three months satisfactory stability data are at the disposal of the applicant at the time of implementation. However, if the proposed packaging is more resistant than the existing packaging (e.g. thicker blister packaging), the three months’ stability data do not yet have to be available. These studies must be finalised and the data will be provided immediately to Swissmedic if outside specifications or potentially outside specifications at the end of the approved shelf-life (with proposed action). | | | |
|  | 4. | The remaining product presentations must be adequate for the dosing instructions and treatment duration as mentioned in the information for healthcare professionals. | | | |
|  | | **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. for O2, CO2, moisture). | | | |
|  | 3. | Where appropriate, proof must be provided 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 relevant pharmacopoeia requirements or legislation on materials and articles intended to come into contact with food (requirements of the Consumer Goods Ordinance; SR 817.023.21). | | | |
|  | 4. | A declaration stating that the required stability studies have been started under ICH conditions (with indication of the batch numbers concerned) and that, as relevant, the required minimum satisfactory stability data were at the disposal of the applicant at the time of implementation and that the available data did not indicate a problem. It should also be confirmed that the studies will be finalised and that data will be provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). | | | |
|  | 5. | The results of stability studies that have been carried out under ICH 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 provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). | | | |
|  | 6. | If applicable, comparison of the current and proposed immediate packaging specifications. | | | |
| n/a |  | Justification: | | | |
|  | 7. | Not applicable to Switzerland. | | | |
|  | 8. | Declaration that the remaining pack sizes are consistent with the dosing instructions and duration of treatment as approved in the information for healthcare professionals and are adequate. | | | |
| Note on B.II.e.1.b: Applicants are reminded that any change which results in a “new pharmaceutical form” requires the submission of an extension application. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.II.e.2

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| **B.II.e.2** | | **Change in the specification parameters and/or limits of the immediate packaging of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Tightening of specification limits  Date of implementation: …… | 1, 2, 3, 4 | 1, 2 | 5217Q |
| IB\* |  |  | 1, 2 | 5576 |
| IA | b) | Addition of a new specification parameter with its corresponding test method  Date of implementation: …… | 1, 2, 5 | 1, 2, 3, 4, 6 | 5218Q |
| IB\* |  |  | 1, 2, 3, 4, 6 | 5577 |
| IA | c) | Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)  Date of implementation: …… | 1, 2 | 1, 2, 5 | 5219Q |
| IB\* |  |  | 1, 2, 5 | 5578 |
| IB | d) | Addition or replacement of a specification parameter as a result of a safety or quality issue |  | 1, 2, 3, 4, 6 | 5220 |
| IB | z) | Other change |  |  | 5901 |
| IAIN | Date of implementation: …… |  |  | 5899Q |
| IA | Date of implementation: …… |  |  | 5900Q |
| II |  |  |  | 5902 |
|  | | **Conditions** | | | |
|  | 1. | The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure). | | | |
|  | 2. | The change does not result from unexpected events arising during manufacture. | | | |
|  | 3. | Any change should be within the range of currently approved limits. | | | |
|  | 4. | The test procedure remains the same, or changes to the test procedure are minor. | | | |
|  | 5. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of current and proposed specifications. | | | |
|  | 3. | Details of the new analytical method and validation data, where relevant. | | | |
|  | 4. | Batch analysis data on two batches of the immediate packaging for all specification parameters. | | | |
|  | 5. | Justification or risk assessment showing that the parameter is non-significant or that it is obsolete. | | | |
|  | 6. | Justification of the new specification parameter and the limits. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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| **Scope / justification for the change** | |
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| **Present** | **Proposed** |
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B.II.e.3

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| **B.II.e.3** | | **Change in test procedure for the immediate packaging of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Minor changes to an approved test procedure  Date of implementation: …… | 1, 2, 3 | 1, 2 | 5221Q |
| IB\* |  |  | 1, 2 | 5579 |
| IA | b) | Other changes to a test procedure (including replacement or addition)  Date of implementation: …… | 1, 3, 4 | 1, 2 | 5222Q |
| IB\* |  |  | 1, 2 | 5580 |
| IA | c) | Deletion of a test procedure if an alternative test procedure is already authorised  Date of implementation: …… | 5 | 1 | 5223Q |
| IB\* |  |  | 1 | 5581 |
| IB | z) | Other change |  |  | 5905 |
| IAIN | Date of implementation: …… |  |  | 5903Q |
| IA | Date of implementation: …… |  |  | 5904Q |
| II |  |  |  | 5906 |
|  | | **Conditions** | | | |
|  | 1. | Appropriate validation studies have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the previously approved test procedure. | | | |
| n/a |  | Justification: | | | |
|  | 2. | The analytical method essentially remains the same (e.g. a change in column length or temperature, but not a different type of column or method). | | | |
|  | 3. | Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. | | | |
| n/a |  | Justification: | | | |
|  | 4. | The active substance / finished product is not a biological or immunological substance. | | | |
|  | 5. | An alternative test procedure is already authorised for the specification parameter, and this procedure has not been added through IA/IAIN notification. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including a description of the analytical method and a summary of the validation data. | | | |
|  | 2. | Comparative validation results or, if justified, comparative analysis results showing that the current test and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new test procedure. | | | |
| n/a |  | Justification: | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.e.4** | | **Change in shape or dimensions of the container or closure (immediate packaging)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Non-sterile medicinal products  Date of implementation: …… | 1, 2, 3 | 1, 2, 4 | 5224# |
| IB\* |  |  | 1, 2, 4 | 5582 |
| II | b) | The change in shape or dimensions concerns a fundamental part of the packaging material, which may have a significant impact on the administration, use, safety or stability of the finished product |  |  | 5225 |
| IB | c) | Sterile medicinal products |  | 1, 2, 3, 4 | 5226 |
| IB | z) | Other change |  |  | 5909 |
| IAIN | Date of implementation: …… |  |  | 5907Q |
| IA | Date of implementation: …… |  |  | 5908Q |
| II |  |  |  | 5910 |
|  | | **Conditions** | | | |
|  | 1. | No change in the qualitative or quantitative composition of the container. | | | |
|  | 2. | The change does not concern a fundamental part of the packaging material, which affects the delivery, use, safety or stability of the finished product. | | | |
|  | 3. | In case of a change in the headspace or a change in the surface/volume ratio, stability studies in accordance with the relevant guidelines have been started and relevant stability parameters have been assessed in at least two pilot scale (three for biological or immunological medicinal products) or industrial scale batches and at least three months (six months for biological or immunological medicinal products) stability data are at the disposal of the applicant. It should also be confirmed that these studies will be finalised and that the data will be provided immediately to Swissmedic if outside specifications, or potentially outside specifications, at the end of the approved shelf-life (with proposed action). | | | |
| n/a |  | Justification: | | | |
|  | | **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 as appropriate. | | | |
|  | 2. | Not applicable to Switzerland. | | | |
|  | 3. | Revalidation studies have been performed in case of sterile products terminally sterilised. The batch numbers of the batches used in the revalidation studies should be indicated, where applicable. | | | |
| n/a |  | Justification: | | | |
|  | 4. | In case of a change in the headspace or a change in the surface/volume ratio, a declaration that the required stability studies have been started under ICH conditions (with indication of the batch numbers concerned) and that, as relevant, the required minimum satisfactory stability data were at the disposal of the applicant at time of implementation for a type IA variation and time of submission of a type IB variation, and that the available data did not indicate a problem. Confirmation has been provided that these studies will be finalised and that data will be provided immediately to Swissmedic if outside specifications or potentially outside specification at the end of the approved shelf-life (with proposed action). | | | |
| n/a |  | Justification: | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

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| **B.II.e.5** | | **Change in pack size of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | Change in the number of units (e.g. tablets, ampoules) in a pack | This change should be submitted as a regulatory change A.102 | | |
|  | 1. | Change within the range of the currently approved pack sizes |
|  | 2. | Change outside the range of the currently approved pack sizes |
|  | b) | Deletion of pack size(s) | This change should be submitted as a regulatory change A.103 | | |
| II | c) | Change in the fill weight or fill volume of sterile multidose (or single-dose, partial use) parenteral medicinal products, including biological or immunological parenteral medicinal products. |  |  | 5227 |
| IB | d) | Change in the fill weight or fill volume of non-parenteral multi-dose (or single-dose, partial use) products |  | 1, 2, 3 | 5228 |
| IB | z) | Other change |  |  | 5913 |
| IAIN | Date of implementation: …… |  |  | 5911Q |
| IA | Date of implementation: …… |  |  | 5912Q |
| II |  |  |  | 5914 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including revised product information and/or packaging texts as appropriate. | | | |
|  | 2. | Justification for the new/remaining pack-size, showing that the new/remaining size is consistent with the dosing instructions and duration of treatment as approved in the information for healthcare professionals. | | | |
|  | 3. | Declaration that stability studies will be conducted in accordance with the relevant guidelines for products where stability parameters could be affected. Data to be reported only if outside specifications (with proposed action). | | | |
| Note on B.II.e.5.c) and d): Applicants are reminded that any changes to the dosage strength of the medicinal product require the submission of an extension application. | | | | | |

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

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| **B.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))** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | Change that affects the product information and/or packaging texts  Date of implementation: …… | 1 | 1 | 5229# |
| IB\* |  |  | 1 | 5583 |
| IA | b) | Change that does not affect the product information and/or packaging texts  Date of implementation: …… | 1 | 1 | 5230Q |
| IB\* |  |  | 1 | 5584 |
| IB | z) | Other change |  |  | 5917 |
| IAIN | Date of implementation: …… |  |  | 5915Q |
| IA | Date of implementation: …… |  |  | 5916Q |
| II |  |  |  | 5918 |
|  | | **Conditions** | | | |
|  | 1. | The change does not concern a part of the packaging material, which affects the delivery, use, safety or stability of the finished product. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including revised product information and/or packaging texts as appropriate. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.II.e.7

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| --- | --- | --- | --- | --- | --- |
| **B.II.e.7** | | **Change in supplier of packaging components or devices (when mentioned in the dossier Module 3)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IA | a) | Deletion of a supplier  Date of implementation: …… | 1 | 1 | 5231Q |
| IB\* |  |  | 1 | 5585 |
| IA | b) | Replacement or addition of a supplier  Date of implementation: …… | 1, 2, 3, 4 | 1, 2, 3 | 5232Q |
| IB\* |  |  | 1, 2, 3 | 5586 |
| II | c) | Any change to suppliers of spacer devices for metered dose inhalers |  |  | 5233 |
| IB | z) | Other change |  |  | 5921 |
| IAIN | Date of implementation: …… |  |  | 5919Q |
| IA | Date of implementation: …… |  |  | 5920Q |
| II |  |  |  | 5922 |
|  | | **Conditions** | | | |
|  | 1. | No deletion of packaging components or devices. | | | |
|  | 2. | The qualitative and quantitative composition of the packaging components / device and design specifications remain the same. | | | |
|  | 3. | The specifications and quality control method are at least equivalent. | | | |
|  | 4. | The sterilisation method and conditions remain the same, if applicable. | | | |
| n/a |  | Justification: | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | For devices for medicinal products, proof of CE marking. | | | |
|  | 3. | Comparison of current and proposed specifications, if applicable. | | | |
| n/a |  | Justification: | | | |

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

B.II.f) Stability

B.II.f.1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.II.f.1** | | **Change in the shelf-life or storage conditions of the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | Reduction of the shelf-life of the finished product |  |  |  |
| IAIN | 1. | As packaged for sale  Date of implementation: …… | 1 | 1, 2, 3 | 5234# |
| IB\* |  |  | 1, 2, 3 | 5587 |
| IAIN | 2. | After first opening  Date of implementation: …… | 1 | 1, 2, 3 | 5235Q |
| IB\* |  |  | 1, 2, 3 | 5588 |
| IAIN | 3. | After dilution or reconstitution  Date of implementation: …… | 1 | 1, 2, 3 | 5236# |
| IB\* |  |  | 1, 2, 3 | 5589 |
|  | b) | Extension of the shelf-life of the finished product |  |  |  |
| IB | 1. | As packaged for sale (supported by real time data) |  | 1, 2, 3 | 5237 |
| IB | 2. | After first opening (supported by real time data) |  | 1, 2, 3 | 5238 |
| IB | 3. | After dilution or reconstitution (supported by real time data) |  | 1, 2, 3 | 5239 |
| II | 4. | Extension of the shelf-life based on extrapolation of stability data not in accordance with ICH VICH guidelines1 |  |  | 5240 |
| IB | 5. | Extension of the shelf-life of a biological or immunological medicinal product in accordance with an approved stability protocol. |  | 1, 2, 3 | 5241 |
| II | c) | Change in storage conditions for biological or immunological medicinal products, when the stability studies have not been performed in accordance with an approved stability protocol |  |  | 5242 |
| IB | d) | Change in storage conditions of the finished product or the diluted / reconstituted product |  | 1, 2, 3 | 5243 |
| IA | e) | Change to an approved stability protocol  Date of implementation: …… | 1, 2 | 1, 4 | 5244Q |
| IB\* |  |  | 1, 4 | 5590 |
| IB | z) | Other change |  |  | 5925 |
| IAIN | Date of implementation: …… |  |  | 5923Q |
| IA | Date of implementation: …… |  |  | 5924Q |
| II |  |  |  | 5926 |
|  | | **Conditions** | | | |
|  | 1. | The change should not be the result of unexpected events arising during manufacture or because of stability concerns. | | | |
|  | 2. | The change does not concern a widening of the acceptance criteria in the parameters tested, a removal of stability indicating parameters or a reduction in the frequency of testing. | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. This must contain results of appropriate real-time stability studies (covering the entire shelf-life) conducted in accordance with the relevant stability guidelines on at least two pilot scale batches2 of the finished product in the authorised packaging material and/or after first opening or reconstitution. Where applicable, results of appropriate microbiological testing should be included. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |
| n/a |  | Justification: | | | |
|  | 3. | Copy of approved end of shelf-life finished product specification and where applicable, specifications after dilution/reconstitution or first opening. | | | |
|  | 4. | Justification for the proposed changes. | | | |
| 1 Note: extrapolation not applicable for biological or immunological medicinal products  2 Pilot scale batches can be accepted with a commitment to verify the shelf-life on production scale batches. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.II.g) Design space and post approval change management protocol

B.II.g.1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.II.g.1** | | **Introduction of a new design space or extension of an approved design space for the finished product, concerning:** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | a) | One or more unit operations in the manufacturing process of the finished product including the resulting in-process controls and/or test procedures |  | 1, 2, 3 | 5245 |
| II | b) | Test procedures for excipients / intermediates and/or the finished product |  | 1, 2, 3 | 5246 |
| IB | z) | Other change |  |  | 5929 |
| IAIN | Date of implementation: …… |  |  | 5927Q |
| IA | Date of implementation: …… |  |  | 5928Q |
| II |  |  |  | 5930 |
|  | | **Documentation** | | | |
|  | 1. | Results from product and process development studies (including risk assessment and multivariate studies, as appropriate) demonstrating that a systematic mechanistic understanding of material attributes and process parameters to 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, as appropriate) and their proposed ranges. | | | |
|  | 3. | 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.II.g.2

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| **B.II.g.2** | | **Introduction of a post approval change management protocol related to the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II |  |  |  | 1, 2, 3 | 5247 |
| IB | z) | Other change |  |  | 5933 |
| IAIN | Date of implementation: …… |  |  | 5931Q |
| IA | Date of implementation: …… |  |  | 5932Q |
| II |  |  |  | 5934 |
|  | | **Documentation** | | | |
|  | 1. | Detailed description for the proposed change. | | | |
|  | 2. | Change management protocol related to the finished product. | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier. | | | |

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| **Scope / justification for the change** | |
| …… | |
| **Present** | **Proposed** |
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B.II.g.3

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| **B.II.g.3** | | **Deletion of an approved change management protocol related to the finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN |  | Date of implementation: …… | 1 | 1, 2 | 5248Q |
| IB\* |  |  | 1, 2 | 5591 |
| IB | z) | Other change |  |  | 5937 |
| IAIN | Date of implementation: …… |  |  | 5935Q |
| IA | Date of implementation: …… |  |  | 5936Q |
| II |  |  |  | 5938 |
|  | | **Conditions** | | | |
|  | 1. | The deletion of the approved change management protocol related to the finished product is not a result of unexpected events or out of specification results during the implementation of the changes described in the protocol and does not have any effect on the already approved information in the dossier. | | | |
|  | | **Documentation** | | | |
|  | 1. | Justification for the proposed deletion. | | | |
|  | 2. | Amendment of the relevant section(s) of the dossier. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.II.g.4

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| --- | --- | --- | --- | --- | --- |
| **B.II.g.4** | | **Changes to an approved change management protocol** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | a) | Major changes to an approved change management protocol |  |  | 5249 |
| IB | b) | Minor changes to an approved change management protocol that do not change the strategy defined in the protocol |  | 1 | 5250 |
| IB | z) | Other change |  |  | 5941 |
| IAIN | Date of implementation: …… |  |  | 5939Q |
| IA | Date of implementation: …… |  |  | 5940Q |
| II |  |  |  | 5942 |
|  | | **Documentation** | | | |
|  | 1. | Declaration that any change should be within the range of currently approved limits. In addition, declaration that an assessment of comparability is not required for biological or immunological medicinal products. | | | |

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

B.II.g.5

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| **B.II.g.5** | | **Implementation of changes foreseen in an approved change management protocol** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | The implementation of the change requires no further supportive data  Date of implementation: …… | 1 | 1, 2, 4 | 5251Q |
| IB\* |  |  | 1, 2, 4 | 5592 |
| IB | b) | The implementation of the change requires further supportive data |  | 1, 2, 3, 4 | 5252 |
| IB | c) | Implementation of a change for a biological/immunological medicinal product |  | 1, 2, 3, 4, 5 | 5253 |
| IB | z) | Other change |  |  | 5945 |
| IAIN | Date of implementation: …… |  |  | 5943Q |
| IA | Date of implementation: …… |  |  | 5944Q |
| II |  |  |  | 5946 |
|  | | **Conditions** | | | |
|  | 1. | The proposed change has been performed fully in line with the approved change management protocol, which requires its immediate notification following implementation. | | | |
|  | | **Documentation** | | | |
|  | 1. | Reference to the approved change management protocol. | | | |
|  | 2. | Declaration that the change is in accordance with the approved change management protocol and that the study results meet the acceptance criteria specified in the protocol. In addition, declaration that an assessment of comparability is not required for biological or immunological medicinal products. | | | |
|  | 3. | Results of the studies performed in accordance with the approved change management protocol. | | | |
|  | 4. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 5. | Copy of approved specifications of the finished product. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.II.h Adventitious Agents Safety

B.II.h.1

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| **B.II.h.1** | | **Update to the "Adventitious Agents Safety Evaluation" information in section 3.2.A.2** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | a) | Studies related to manufacturing steps investigated for the first time for one or more adventitious agents |  |  | 5254 |
|  | b) | Replacement of obsolete studies related to manufacturing steps and adventitious agents already reported in the dossier: |  |  |  |
| II | 1. | With modification of the risk assessment |  |  | 5255 |
| IB | 2. | Without modification of the risk assessment |  | 1, 2, 3 | 5256 |
| IB | z) | Other change |  |  | 5949 |
| IAIN | Date of implementation: …… |  |  | 5947Q |
| IA | Date of implementation: …… |  |  | 5948Q |
| II |  |  |  | 5950 |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier including the introduction of the new studies to investigate the capability of manufacturing steps to inactivate/reduce adventitious agents. | | | |
|  | 2. | Justification that the studies do not modify the risk assessment. | | | |
|  | 3. | Revised product information and/or packaging texts, where applicable. | | | |

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

B.II.z. Other quality change to finished product

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| --- | --- | --- | --- | --- |
| **B.II.z** | **Other quality change to finished product** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | Date of implementation: …… |  |  | 5951Q |
| IA | Date of implementation: …… |  |  | 5952Q |
| IB |  |  |  | 5953 |
| II |  |  |  | 5954 |

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

B.III. CEP/TSE/Monographs

B.III.1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.III.1** | | **Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: for an active substance, for a starting material used in the manufacturing process of the active substance, reagent, intermediate product or for an excipient** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph |  |  |  |
| IAIN | 1. | New certificate from an already approved manufacturer  Date of implementation: …… | 1, 2, 3, 4, 5, 8, 11 | 1, 2, 3, 4 | 5257Q |
| IB\* |  |  | 1, 2, 3, 4 | 5593 |
| IA | 2. | Updated certificate from an already approved manufacturer  Date of implementation: …… | 1, 2, 3, 4, 8 | 1, 2, 3, 4, 5 | 5258Q |
| IB\* |  |  | 1, 2, 3, 4, 5 | 5594 |
| IAIN | 3. | New certificate from a new manufacturer (replacement or addition)  Date of implementation: …… | 1, 2, 3, 4, 5, 8, 11 | 1, 2, 3, 4, 5 | 5259#Q |
| IB\* |  |  | 1, 2, 3, 4, 5 | 5595 |
| IA | 4. | Deletion of certificates (if multiple certificates exist for a material)  Date of implementation: …… | 10 | 3 | 5260#Q |
| IB\* |  |  | 3 | 5596 |
| IB | 5. | New certificate for a non-sterile active substance that is to be used in a sterile medicinal product, where water is used in the last steps of the synthesis and the material is not claimed to be endotoxin free |  | 1, 2, 3, 4, 5, 6 | 5261 |
|  | b) | European Pharmacopoeial TSE Certificate of suitability for an active substance, a starting material, a reagent, an intermediate or an excipient |  |  |  |
| IAIN | 1. | New certificate for an active substance from a new or an already approved manufacturer  Date of implementation: …… | 3, 5, 6, 11 | 1, 2, 3, 4 | 5262Q |
| IB\* |  |  | 1, 2, 3, 4 | 5597 |
| IA | 2. | New certificate for a starting material, reagent, intermediate or excipient from a new or an already approved manufacturer  Date of implementation: …… | 3, 6, 9 | 1, 2, 3, 4 | 5263 |
| IB\* |  |  | 1, 2, 3, 4 | 5598 |
| IA | 3. | Updated certificate from an already approved manufacturer  Date of implementation: …… | 7, 9 | 1, 2, 3, 4 | 5264 |
| IB\* |  |  | 1, 2, 3, 4 | 5599 |
| IA | 4. | Deletion of certificates (if multiple certificates exist for a material)  Date of implementation: …… | 10 | 3 | 5265 |
| IB\* |  |  | 3 | 5600 |
| II | 5. | New/updated certificate from an already-approved/new manufacturer using materials of human or animal origin for which an assessment of the risk with respect to potential contamination with adventitious agents is required |  |  | 5266 |
| IB | z) | Other change |  |  | 5957 |
| IAIN | Date of implementation: …… |  |  | 55955Q |
| IA | Date of implementation: …… |  |  | 5956Q |
| II |  |  |  | 5958 |
|  | | **Conditions** | | | |
|  | 1. | The finished product release and end of shelf-life specifications remain the same. | | | |
|  | 2. | Unchanged (excluding tightening) additional (to Ph. Eur.) specifications for impurities (excluding residual solvents, provided they are in compliance with ICH requirements) and product-specific requirements (e.g. particle size distribution or polymorphic form), if applicable. | | | |
|  | 3. | The manufacturing process of the active substance, starting material, reagent or intermediate does not include the use of materials of human or animal origin for which an assessment of viral safety data is required. | | | |
|  | 4. | For active substances only: the active substance will be tested immediately prior to use if no retest period is included in the Ph. Eur. Certificate of Suitability, or if data to support a retest period is not already provided in the dossier. | | | |
| n/a |  | Justification: | | | |
|  | 5. | The active substance / starting material, reagent or intermediate / excipient is not sterile. | | | |
|  | 6. | Not applicable for human medicinal products. | | | |
|  | 7. | Not applicable for human medicinal products. | | | |
|  | 8. | For herbal preparations: the manufacturing route, physical form, extraction solvent and drug extract ratio (DER) should remain the same. | | | |
| n/a |  | Justification: | | | |
|  | 9. | If gelatine manufactured from bones is to be used in a medicinal product for parenteral use, it should only be manufactured in compliance with the relevant country requirements. | | | |
| n/a |  | Justification: | | | |
|  | 10. | At least one manufacturer for the same material remains in the dossier. | | | |
|  | 11. | If the active substance is a not a sterile substance but is to be used in a sterile medicinal product then, according to the European Pharmacopoeial Certificate of Suitability (CEP), it must not use water during the last steps of the synthesis. If water is used during the last steps of the synthesis, the active substance must also be declared to be free from bacterial endotoxins. | | | |
| n/a |  | Justification: | | | |
|  | | **Documentation** | | | |
|  | 1. | Copy of the current (updated) Ph. Eur. Certificate of Suitability. | | | |
|  | 2. | If a manufacturing site is added, a comparison of present and proposed manufacturers. | | | |
| n/a |  | Justification: | | | |
|  | 3. | Amendment of the relevant section(s) of the dossier (presented in the CTD format) including the updated *Manufacturer information* form, if applicable. | | | |
|  | 4. | Where applicable, a document providing information of any materials falling 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 those used in the manufacture of the active substance/excipient). The following information should be included for each such material: Name of manufacturer, species and tissues from which the material is a derivative, country of origin of the source animals and its use. In addition an updated *Substances of Animal or Human Origin* form. | | | |
| n/a |  | Justification: | | | |
|  | 5. | For a new active substance manufacturer: Completed and signed form *Declaration by the Responsible Person for foreign manufacturers* and proof that the site's GMP compliance has been verified. | | | |
| n/a |  | Justification: | | | |
|  | 6. | Suitable evidence to confirm compliance of the water used in the final steps of the synthesis of the active substance with the corresponding requirements on quality of water for pharmaceutical use. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.III.2

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.III.2** | | **Change to comply with Pharmacopoeia Europaea or Pharmacopoeia Helvetica** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | Change of specifications of a former non-EU Pharmacopoeial substance to fully comply with the Pharmacopoeia Europaea or Pharmacopoeia Helvetica |  |  |  |
| IAIN | 1. | Active substance.  Date of implementation: …… | 1, 2, 3, 4, 5 | 1, 2, 3, 4 | 5267Q |
| IB\* |  |  | 1, 2, 3, 4 | 5601 |
| IA | 2. | Excipient / active substance starting material.  Date of implementation: …… | 1, 2, 4 | 1, 2, 3, 4 | 5268Q |
| IB\* |  |  | 1, 2, 3, 4 | 5602 |
| IA | b) | Change to comply with an update of the relevant monograph of the Pharmacopoeia Europaea or Pharmacopoeia Helvetica  Date of implementation: …… | 1, 2, 4, 5 | 1, 2, 3, 4 | 5269Q |
| IB\* |  |  | 1, 2, 3, 4 | 5603 |
| IA | c) | Change in specifications from the Pharmacopoeia Helvetica to the Pharmacopoeia Europaea  Date of implementation: …… | 1, 4, 5 | 1, 2, 3, 4 | 5270Q |
| IB\* |  |  | 1, 2, 3, 4 | 5604 |
| IB | z) | Other change |  |  | 5961 |
| IAIN | Date of implementation: …… |  |  | 5959Q |
| IA | Date of implementation: …… |  |  | 5960Q |
| II |  |  |  | 5962 |
|  | | **Conditions** | | | |
|  | 1. | The change is made exclusively to fully comply with the pharmacopoeia. All the tests in the specification (with the exception of any additional tests) need to correspond to the pharmacopoeial standard after the change. | | | |
|  | 2. | Additional specifications to the pharmacopoeia for product-specific properties are unchanged (e.g. particle size distribution, polymorphic form or e.g. bioassays, aggregates). | | | |
|  | 3. | No significant changes in the qualitative and quantitative impurities profile unless the specifications are tightened. | | | |
|  | 4. | Additional validation of a new or changed pharmacopoeial method is not required. | | | |
|  | 5. | For herbal preparations: the manufacturing route, physical form, extraction solvent and drug extract ratio (DER) should remain the same. | | | |
| n/a |  | Justification: | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of current and proposed specifications. | | | |
|  | 3. | Batch analysis data (in a comparative tabulated format) for two production batches of the relevant substance for all tests in the new specification and additionally, where appropriate, comparative dissolution profile data for the finished product on at least one pilot batch. For herbal medicinal products, comparative disintegration data may be acceptable. | | | |
|  | 4. | Data to demonstrate the suitability of the monograph to control the substance, e.g. a comparison of the potential impurities with those listed in the monograph. | | | |
| Note: There is no need to notify Swissmedic of an updated monograph of the European Pharmacopoeia or Pharmacopoeia Helvetica in the case that reference is made to the ‘current edition’ in the dossier of an authorised medicinal product. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.IV. Medical devices

B.IV.1

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| --- | --- | --- | --- | --- | --- |
| **B.IV.1** | | **Change of a measuring or administration device** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
|  | a) | Addition or replacement of a device which is not an integral part of the primary packaging. |  |  |  |
| IAIN | 1. | Device with CE marking  Date of implementation: …… | 1, 2, 3, 6, 7 | 1, 2, 4 | 5271# |
| IB\* |  |  | 1, 2, 4 | 5605 |
|  | 2. | Not applicable for human medicinal products. |  |  |  |
| II | 3. | Spacer device for metered dose inhalers or other devices which may have a significant impact on the delivery of the active substance in the product (e.g. nebuliser). |  |  | 5273 |
| IAIN | b) | Deletion of a device.  Date of implementation: …… | 4, 5 | 1, 5 | 5274# |
| IB\* |  |  | 1, 5 | 5606 |
| II | c) | Addition or replacement of a device which is an integral part of the primary packaging. |  |  | 5275 |
| IB | z) | Other change |  |  | 5965 |
| IAIN | Date of implementation: …… |  |  | 5963Q |
| IA | Date of implementation: …… |  |  | 5964Q |
| II |  |  |  | 5966 |
|  | | **Conditions** | | | |
|  | 1. | The proposed measuring or administration device must accurately deliver the required dose for the product concerned in line with the approved dosage instructions, and the results of corresponding studies are available. | | | |
|  | 2. | The new device is compatible with the medicinal product. | | | |
|  | 3. | The change does not lead to substantial amendments of the product information and/or packaging texts. | | | |
|  | 4. | The medicinal product can still be accurately delivered. | | | |
|  | 5. | Not applicable for human medicinal products. | | | |
|  | 6. | The medical device is not used as a solvent of the medicinal product. | | | |
|  | 7. | If a measuring function is intended, the CE marking should also cover the measuring function. | | | |
| n/a |  | Justification: | | | |
|  | | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier, including description, detailed drawing and composition of the device material and supplier where appropriate, and including revised product information and/or packaging texts as appropriate. | | | |
|  | 2. | Proof of CE marking and, if a measuring function is intended, the proof of CE marking should also include the 4-digit notified body number. | | | |
|  | 3. | Not applicable for human medicinal products. | | | |
|  | 4. | Not applicable to Switzerland. | | | |
|  | 5. | Justification for the deletion of the device. | | | |
| Note on B.IV.1.c: Applicants are reminded that any change which results in a “new pharmaceutical form” requires the submission of an extension application. | | | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

B.z. Other quality changes

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B.z** | | **Other quality change** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN |  | Date of implementation: …… |  |  | 5490Q |
| IA |  | Date of implementation: …… |  |  | 5491Q |
| IB |  |  |  |  | 5285 |
| II |  |  |  |  | 5286 |

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

C. Safety, efficacy and pharmacovigilance changes

C.I.

C.I.1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **C.I.1** | | **Change in the product information and/or packaging texts intended to implement the outcome of a Swissmedic administrative procedure:** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | The medicinal product is covered by the defined scope of the procedure.  Date of implementation: …… | 1 | 1, 2, 3 | 5287# |
| IB\* |  |  | 1, 2, 3 | 5613 |
| IB | b) | 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 is required to be submitted by the marketing authorisation holder. |  | 1, 2, 3 | 5288 |
| II | c) | 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 marketing authorisation holder. |  | 1, 3 | 5289 |
|  | | **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. | Attached to the variation application is a reference to the relevant official decision together with the product information and/or packaging texts. | | | |
|  | 2. | Declaration that the proposed product information and/or packaging texts are identical, in the sections concerned, to the corresponding texts attached to the official decision. | | | |
|  | 3. | Revised product information and/or packaging texts. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

C.I.2

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **C.I.2** | | **Change in the product information and/or packaging texts for a medicinal product with a known active substance with/without innovation, biosimilar or preparation for parallel import following assessment of the same change for the reference medicinal product / reference preparation** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | Implementation of one or more changes for which no new additional data is required to be submitted by the marketing authorisation holder.  Date of implementation: …… | 1, 2 | 1, 2 | 5290# |
| IB\* |  |  | 1, 2 | 5614 |
| II | b) | Implementation of one or more changes which require to be substantiated by the submission of new additional data (e.g. comparability) by the marketing authorisation holder. |  |  | 5291 |
|  | | **Conditions** | | | |
|  | 1. | The product information for the medicinal product is identical, in the sections affected by the change, to that for the reference medicinal product / reference preparation. | | | |
|  | 2. | If applicable, passages for the reference medicinal product / reference preparation connected with document protection are deleted (in Track Changes mode). | | | |
| n/a |  | Justification: | | | |
|  | | **Documentation** | | | |
|  | 1. | Not applicable to Switzerland. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

C.I.3

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **C.I.3** | | **Change in the 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)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | Implementation of the wording agreed with Swissmedic  Date of implementation: …… | 1 | 1, 2 | 5292# |
| IB\* |  |  | 1, 2 | 5615 |
| II | b) | Implementation of one or more changes that require to be substantiated by the submission of new additional data by the marketing authorisation holder |  | 2 | 5293 |
|  | | **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 should be attached to the variation application. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

C.I.4

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **C.I.4** | **Change in the product information and/or packaging texts due to new quality, preclinical, clinical or pharmacovigilance data[[2]](#footnote-2)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II |  |  |  | 5294 |

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

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

C.I.5

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **C.I.5** | | **Change in the dispensing category** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | a) | For a medicinal product with a known active substance without innovation or a biosimilar after an approved change in the legal category for the reference product |  | 2 | 5295 |
| II | b) | For all other medicinal products |  | 1, 2 | 5296 |
|  | | **Documentation** | | | |
|  | 1. | Scientific documentation. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |

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

C.I.6

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **C.I.6** | | **Change to therapeutic indication(s)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | a) | Addition of a new therapeutic indication or modification of an approved one. |  | 1, 2, 3, 4 | 5297  6276 |
| IB | b) | Deletion of a therapeutic indication |  | 4 | 5298 |
|  | | **Documentation** | | | |
|  | 1. | Quality: If applicable, supplemented Section 3.2.P together with a change index and tabular comparison. | | | |
| n/a |  | Justification: | | | |
|  | 2. | Preclinical:   * Section 2.4 supplemented with critical, safety-related points. * Benefit/risk analysis for the new indication. As a rule, new experimental trials must be submitted for newly identified risks or extension of the duration of use. These should be summarised accordingly in Section 2.6 and the studies incorporated in Module 4. If new populations are involved, specific non-clinical studies and corresponding dose-finding studies should be considered. * An Environmental Risk Assessment (ERA) must be submitted, as an additional indication is likely to have a substantial impact on the environment. If no ERA is submitted, reasons for this must be stated. | | | |
|  | 3. | Clinical: Studies on efficacy and safety for the new indication(s)   * Pharmacokinetic studies (PK) (Sections 5.3.1 and 5.3.3) (if applicable), for example * Investigation of PK in specific populations that were not investigated for the primary indication (Section 5.3.3.3). * Investigation of PK in patients for the new proposed indication(s) (Section 5.3.3.2) (e.g. if the organ system for which the product's new indication is intended is difference from the primary organ systems treated with the product). * additional interaction studies on population kinetics (Section 5.3.3.5). * Pharmacodynamic (PD) studies (Section 5.3.4) * Investigation of the mechanism of action in the new proposed indication(s). * PK/PD analyses to determine the effective concentration where appropriate. * Studies on efficacy and safety (Section 5.3.5) * Dose-finding studies or appropriate justification as to why the dosage to date is also appropriate for the new indication(s). * Studies on the efficacy and safety of the new proposed indications, including specific, indication-related studies, e.g. long-term studies. * Pooled analysis of the Phase III (and Phase II) data where appropriate.   If the new indication is linked to a new dosage strength and/or dosage recommendation, see also the requirements for documentation on C.I.101 *Change in the product information and/or packaging texts due to new dosage recommendation data* and/or on extension 2.c) *Change or addition of a dosage strength/potency.* | | | |
|  | 4. | Revised product information. | | | |

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

C.I.7

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| --- | --- | --- | --- | --- | --- |
| **C.I.7** | | **Deletion** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | a) | A pharmaceutical form |  | 1, 2 | 5299 |
| IB | b) | A dosage strength |  | 1, 2 | 5300 |
|  | | **Documentation** | | | |
|  | 1. | Declaration that the remaining product presentations conform to the dosage instructions and treatment duration included in the information for healthcare professionals. [[3]](#footnote-3) | | | |
| n/a |  | Reason: | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |
| n/a |  | Reason: | | | |

4 or, as the case may be, the dosage instruction can be met using the remaining dosage strengths; or that the deletion is clinically justifiable.

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

C.I.12

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **C.I.12** | | **Inclusion or deletion of the black triangle and inclusion or deletion of explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN[[4]](#footnote-4) | | Date of implementation: …… | 1 | 1, 2 | 5301# |
| IB\* | |  |  | 1, 2 | 5616 |
|  | | **Conditions** | | | |
|  | 1. | The medicinal product is included in, or deleted from, the list of medicinal products that are subject to additional monitoring. | | | |
|  | | **Documentation** | | | |
|  | 1. | A reference to the list of medicinal products that are subject to additional monitoring is attached to the variation application. | | | |
|  | 2. | Revised product information and/or packaging texts. | | | |

\*If one of the conditions is not met and the variation is not specifically listed as type II, or if more than 12 months (type IA) or more than 1 month (type IAIN) have/has elapsed between the date of implementation and date of submission of the variation.

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

C.I.13

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| --- | --- | --- | --- | --- |
| **C.I.13** | **Other variations relating to safety, efficacy and pharmacovigilance that require the submission of studies to Swissmedic** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II |  |  |  | 5302 |

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

C.I.100

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **C.I.100** | **Safety-related change in the product information and/or packaging texts due to new quality, preclinical, clinical or pharmacovigilance data** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II |  |  |  | 5303 |

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

C.I.101

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **C.I.101** | | **Change in the product information and/or packaging texts due to new dosage recommendation data** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | |  |  | 1, 2, 3 | 5304 |
|  | | **Documentation** | | | |
|  | 1. | Quality: If applicable, supplemented Section 3.2.P together with a change index and tabular comparison. | | | |
| n/a |  | Justification: | | | |
|  | 2. | Preclinical:   * Section 2.4 supplemented with critical, safety-related points. * Benefit/risk analysis relating to the new dosage recommendation, taking particular account of the safety margins. | | | |
| n/a |  | Reason: | | | |
|  | 3. | Clinical:   * The requirements depend on the type of variation. Normally, corresponding studies on efficacy and safety (Section 5.3.5) should be submitted, including specific studies depending on the indication, e.g. long-term studies. For higher dosages, the focus must be on safety, whereas for lower dosages it must be on efficacy. Additional data on safety pharmacology may also be required, in particular for doses higher than those previously recommended. * If the only change concerns the dosing interval, PK bridging or PD bridging may be sufficient. | | | |

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

C.I.102

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| --- | --- | --- | --- | --- | --- |
| **C.I.102** | | **Expansion of the document protection for additional indications** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| II | |  | 1, 2, 3 | 1 | 5305 |
|  | | **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 was submitted. | | | |
|  | 3. | The new indication is supported by comprehensive clinical trials. | | | |
|  |  | **Documentation** | | | |
|  | 1. | Conclusive proof 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** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

C.I.103

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **C.I.103** | | **Document protection for purely paediatric use** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | |  | 1, 2, 3 |  | 5306 |
|  | | **Conditions** | | | |
|  | 1. | The medicinal product is specifically and exclusively intended for paediatric use. | | | |
|  | 2. | Document protection has not yet been granted for any other medicinal product authorised by Swissmedic with the same active substance for the same specific paediatric use. | | | |
|  | 3. | The studies submitted for authorisation conform to the approved paediatric investigation plan according to Article 54a TPA, and all measures for the proposed population from the paediatric investigation plan are fulfilled. | | | |

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

C.I.104

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| --- | --- | --- | --- | --- | --- |
| **C.I.104** | | **Document protection for important medicinal products for rare diseases (ODS)** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB | |  | 1, 2 |  | 5307 |
|  |  | **Conditions** | | | |
|  | 1. | The medicinal product has been granted Orphan Drug 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** | |
| …… | |
| **Present** | **Proposed** |
| …… | …… |

C.I.z. Other change relating to safety, efficacy or pharmacovigilance

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **C.I.z** | **Other change relating to safety, efficacy or pharmacovigilance** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | Date of implementation: …… |  |  | 5493# |
| IA | Date of implementation: …… |  |  | 5492# |
| IB |  |  |  | 5308 |
| II |  |  |  | 5494 |

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

X. Changes to PMF

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **X.** | | **Changes to PMF**  Changes to PMF with Annual Update PMF (5331)  Changes to PMF without Annual Update PMF | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IAIN | a) | Type IAIN (according to EU D. PMF/VAMF) | 1 | 1, 2 | 5315#Q |
| IA | b) | Type IA (according to EU D. PMF/VAMF) | 1 | 1, 2 | 5316#Q |
| IB | c) | Type IB (according to EU D. PMF/VAMF) | 1 | 1, 2 | 5317 |
|  | d) | Type II (according to EU B.V.a.1 PMF/VAMF or D. PMF/VAMF) |  |  |  |
| II | 1. | First-time inclusion of a new Plasma Master File (EU B.V.a.1 a) |  | 1 | 5318 |
| II | 2. | Other type II variation (EU D. PMF/VAMF) | 1 | 1, 2 | 5319 |
|  |  | **Conditions** | | | |
|  | 1. | The application for each PMF for one or more PMF changes is submitted according to the highest category according to the classification in the European Guideline under "B.V.a.1 PMF/VAMF" or "D. PMF/VAMF". | | | |
|  |  | **Documentation** | | | |
|  | 1. | Amendment of the relevant section(s) of the dossier. | | | |
|  | 2. | Comparison of currently approved situation and proposed changes. | | | |

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

Y. Change in the reduced dossier for complementary medicines

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Y.1** | | **Change in the reduced dossier** | **Conditions to be fulfilled** | **Documentation to be submitted** | SAP no. |
| IB |  |  | 1 | 1 | 5320 |
|  | | **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** |
| …… | …… |

Z. Extensions

|  |  |  |  |
| --- | --- | --- | --- |
| **1.** | | **Change in the 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. | 5029 |
|  | b) | Replacement by a different isomer, a different mixture of isomers, of a mixture by an isolated isomer (e.g. racemate by a single enantiomer), where the efficacy/safety characteristics are not significantly different. | 5030 |
|  | c) | Replacement of a biological active substance with one of a slightly different molecular structure where the efficacy/safety characteristics are not significantly different, with the exception of:   * changes to the active substance of a seasonal, pre-pandemic or pandemic vaccine against human influenza, * exchange or addition of a serotype, strain, antigen or coding region or a combination of serotype, strain, antigen or coding region of a human SARS-CoV-2 vaccine. | 5031 |
|  | 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. | 5032 |
|  | e) | A new ligand or coupling mechanism for a radiopharmaceutical, where the efficacy/safety characteristics are not significantly different. | 5033 |
|  | 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. | 5034 |
| **2.** |  | **Change in dosage strength, pharmaceutical form or administration route:** |  |
|  | a) | Change of bioavailability. | 5035 |
|  | b) | Change of pharmacokinetics, e.g. change in rate of release. | 5036 |
|  | c) | Change or addition of a dosage strength/potency. | 5037 |
|  | d) | Change or addition of a pharmaceutical form. | 5038 |
|  | e) | Change or addition of a route of administration.[[5]](#footnote-5) | 5039 |
| **3.** |  | Not applicable for human medicinal products. |  |
| **4.** |  | **Other authorisation extension:** e.g. reclassification of active substance to excipient or deletion of active substance | 5968 |

Change history

| **Version** | **Change** | **sig** |
| --- | --- | --- |
| 18.1 | Section 5.1 – Clarification regarding which boxes to check and when.  Section 5.9 – Clarification regarding delayed implementation time limit. | stb |
| 18.0 | Section 5.1: Option n.a. added.  New section 5.9 “Delayed implementation”:  Applicant clarifies how variations will be implemented according to section 6.7 of the Guidance document *Variations and Extensions HAM*.  Deletion of the suffix HMV4 in referenced specification documents. | stb |
| 17.0 | New section 5.1 Placing on the market:The applicant should indicate whether the line extension is intended for placing on the Swiss market or only for export.  Numbering of subsequent subsections in section 5 changed. | stb |
| 16.0 | New section 5.3 “Real world evidence”: Details on RWE must now be entered in application submissions | dts |
| 15.1 | Section 4: possibility of adding a QR code to the medicinal product information and/or packaging | ski, sab |
| 15.0 | Section 3: Additions due to extended scope of temporary authorisation – new temporary additional indications and clarification of wording.  Section 5.6: Combination products: Clarification of concepts.  Section 6.8: Deletion of the sentence *Swissmedic informs the authorisation holder in writing if Assessment Reports are shared.* | stb, nma, spb, na |
| 14.0 | Addition of section 6.11 “Information sharing in the context of processing risk evaluations on nitrosamine impurities” for the purpose of obtaining the agreement of the applicant. The numbering of the subsequent sections 6.11 to 6.13 has changed as a result to 6.12 to 6.14.  Deletion of “n.a.” in section 6.8.  Changes regarding internal information (replacement of Q with # in “SAP. no.” column). | stb, vy, grs |
| 13.0 | Adaptation due to revision of Annex 7 TPLRO (incl. various clarifications regarding conditions and documentation) | stb |
| 12.0 | Adaptation due to separation of the changes for veterinary medicinal products and those for human medicinal products (revision of VMP regulations)  Insertion of new SAP numbers for the z variations, B.I.a.5.b) and authorisation extension no. 4 (for internal purposes) | stb |
| 11.0 | Mention of the Federal Expert Commission for Radiopharmaceuticals (ECRP) in Access Consortium and Orbis applications (sections 6.8 and 6.10) and naming of the Israeli *Ministry of Health (MOH) – Pharmaceutical Division* in Orbis applications (section 6.10) for the purpose of obtaining consent to sharing information. | ski, stb |
| 10.0 | Addition to section 1 “Basic information"  Addition in section 5.2 “Extended document protection” (in the case of new dosage form (auth. extension) for purely paediatric use), further explanation in section 5.6 and additional authorisation extension 4 “Other authorisation extension”. | stb |
| 9.0 | Amendments on the inclusion of a type II change – *Modifications to the active substance in approved COVID-19 vaccines relating to new SARS-CoV-2 variants* – in B.I.a.5 (Changes in quality) and Z (Extensions)  Clarification in A.101 on the required documentation (3.)  Change to wording in section 6.9 (Exchange of information for medicinal products with COVID-19 indications | stb, vy |
| 8.0 | Explanation at “area of application” under 1. Basic information  Explanations at A.3, A.4, A.5, A.6, A.107 | stb |
| 7.0 | New section 6.10: Exchanging information within Project Orbis  Section 6.13: Letter elements / texts in English 🡪 change to wording.  B.I.a.1: Clarification under Documentation 8. | dts, stb |
| 6.2 | Inclusion of MHRA as a new Access Consortium Partner (section 6.8, page 6) and  Correction to footnote numbering on page 102 | stb |
| 6.1 | New section 6.9 inserted: Declaration of consent re Covid-19 MP | dts |
| 6.0 | Addition to section 6.9: Disclosure of documentation as part of the MAGHP Light procedure | ze |
| 5.0 | Review owing to revision of Annex 7 MPLO plus various clarifications, e.g.:   * Section 5.2: Extended document protection: 15 years for IE with ODS and note that the application must be accompanied by reasons and the source indicated. * Section 6.10: Letter elements/English texts: asking companies whether this is possible. | stb |
| 4.0 | Various clarifications, including:   * Section 5.6 Combination products: * Information only required if changes are made through a variation or authorisation extension * A.100: additional condition: “The application ID number of the type IB variation (1st pack with new design) is specified under “Scope / justification for the change”.” * A.101: Documentation requirement no. 1 expanded. * A.106: 2 documentation requirements expanded: * “Confirmation that the documentation submitted is identical to that for the basic product (including any additional material that was approved in the meantime)” and * “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.” * C.I.6: -Preclinical documentation requirement expanded for additional indications: * “An Environmental Risk Assessment (ERA) must be submitted, as an additional indication is likely to have a substantial impact on the environment. If no ERA is submitted, reasons for this must be stated.” * C.I.102: Adaptation of formulation in connection with document protection: * New: use “expansion” rather than “extension”. | stb |
| 3.0 | New variation A.100, type IAIN: Implementation of the design change can be notified as of the second pack in the form of an A.100, type IAIN. This should be done after the first pack in the new design (corporate identity) has been submitted as a regulatory change A.100 type IB and approved.  “It must not be an essential medicinal product” no longer a condition for regulatory change A.104 conversion of a main authorisation to an export licence.  Various clarifications, including:   * Applications for (an) additional indication(s) and extensions must always state the active substance(s) and the area of application being requested. * If clinical trials (including bioequivalence trials) are enclosed with the application, a completed EMA “GCP inspections template” must always be sent to Swissmedic. * When applying for extensions, applicants must specify whether or not they are also applying for extended 10-year document protection. * Where applications involve co-marketing medicinal products and the Information for healthcare professionals and Patient information are affected, applicants have to confirm that these match the texts for the basic product. * What information Swissmedic expects for “Currently approved – Requested” when medicinal product information has been changed (sections A.100, A.109, C.I.1, C.I.3, C.I.4, C.I.13. C.I.100 and C.I.z, date of revision: A.101 and C.I.2) * A.106 and A.107: Condition associated with “No scientific data are submitted” specified in greater detail. * Linguistic clarification regarding the submission of the form *Status of authorisation applications abroad* HMV4 * New chapter 5.5 and 5.6 inserted | stb, vy |
| 2.3 | Clarification of entries under Part 1  Clarification of entries under Part 6.3 Confirmation of identity for the bioavailability study  Clarification in Part C.I.101 Change in the product information and/or packaging texts due to new dosage recommendation data  Clarification in Part X Changes to PMF | fg, nma  stb, wer |
| 2.2 | Explanation regarding the indication  Amendment A.101: Modified the type of change from plural into singular.  Column SAP-no: Amendment of the codings.  Basic information: Deletion of the eCTD-Sequence-Nr. | fg, lac  stb  wja  dts |
| 2.1 | Further clarification regarding the variations of the section A.101: changes to the product information and/or packaging texts.  Chapter 4, Additional forms to be submitted: Explanation regarding the list of forms to be submitted in addition. Consult the Overview *documents to be submitted HMV4*.  B.III.1: Addition for documentation No. 5: For a new active substance manufacturer, proof that the site's GMP compliance has been verified. | stb, ze |
| 2.0 | With regard to the templates under “C. Variations relating to safety, efficacy and pharmacovigilance”, a variation classed as “Other variation” can now only be submitted using template C.I.z.  Explanations relating to template A.4 and the templates under “B. Changes in quality”. | stb |
| 1.2 | Addition of medicinal product categories in the drop-down menu. | dts |
| 1.1 | Further clarification regarding the submission of the form *Status of authorisation applications abroad HMV4* | ze |
| 1.0 | Implementation of TPO4 | wer |

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. [↑](#footnote-ref-2)
3. [↑](#footnote-ref-3)
4. This variation covers the situation where the inclusion or deletion of the black triangle or explanatory statements is not done as part of another procedure (e.g. a renewal or variation procedure connected with the medicinal product information). [↑](#footnote-ref-4)
5. For parenteral administration, it is necessary to distinguish between intra-arterial, intravenous, intramuscular, subcutaneous and other routes. [↑](#footnote-ref-5)