# TachoSil

## Procedural steps taken and scientific information after the authorisation

| Application number | Scope | Opinion/ Notification [1] issued on | Commission Decision Issued [2] / amended on | Product Information affected [3] | Summary |
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| IB/0121 | B.I.b.z - Change in control of the AS - Other variation | 19/04/2023 | n/a | | |
| II/0117 | Extension of indication to include treatment of children aged 1 month to 18 years for supportive treatment in surgery for improvement of | 23/02/2023 | 24/03/2023 | SmPC, Annex II, Labelling | Please refer to Scientific Discussion 'TachoSil-H-C-505-II-117' |

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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| | haemostasis, to promote tissue sealing and for suture support in vascular surgery where standard techniques are insufficient, based on available bibliographical data, results from study TC-2402-040-SP which compared TachoSil with Surgicel Original as adjunct to primary surgical treatment in both adult and paediatric subjects, and results from Study TC-019-IN; a prospective, uncontrolled study in paediatric subjects. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the product information. Version 0.1 of the RMP has also been submitted.<br><br>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one | | | and PL | |
| II/0119/G | This was an application for a group of variations.<br><br>B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits<br>B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product<br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process | 16/03/2023 | n/a | | |

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| | of the AS<br>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation | | | | |
| IAIN/0120 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 08/02/2023 | n/a | | |
| IB/0118 | B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) | 22/12/2022 | n/a | | |
| IA/0116 | B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised | 03/05/2022 | n/a | | |
| IAIN/0115 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 23/03/2022 | n/a | | |
| IB/0114 | B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process | 23/11/2021 | n/a | | |

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| T/0112 | Transfer of Marketing Authorisation | 24/08/2021 | 15/09/2021 | SmPC, Labelling and PL | |
| IAIN/0113 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 06/08/2021 | n/a | | |
| IB/0111/G | This was an application for a group of variations.<br><br>B.II.z - Quality change - Finished product - Other variation<br>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process | 22/07/2021 | n/a | | |
| IA/0110/G | This was an application for a group of variations.<br><br>B.II.z - Quality change - Finished product - Other variation<br>B.II.z - Quality change - Finished product - Other variation<br>B.II.z - Quality change - Finished product - Other variation | 28/05/2021 | n/a | | |
| IA/0109 | B.II.z - Quality change - Finished product - Other variation | 23/02/2021 | n/a | | |
| IAIN/0108 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier | 19/02/2021 | n/a | | |

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| | of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | | | | |
| PSUSA/10297 /202006 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 14/01/2021 | n/a | | PRAC Recommendation - maintenance |
| IA/0107 | B.II.z - Quality change - Finished product - Other variation | 08/09/2020 | n/a | | |
| IB/0104/G | This was an application for a group of variations.<br><br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS<br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS<br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS | 13/08/2020 | n/a | | |
| IAIN/0105 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 24/07/2020 | n/a | | |
| IB/0101/G | This was an application for a group of variations.<br><br>B.I.a.2.a - Changes in the manufacturing process of | 16/04/2020 | n/a | | |

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| | the AS - Minor change in the manufacturing process of the AS<br>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation | | | | |
| IA/0103/G | This was an application for a group of variations.<br><br>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation<br>B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State | 10/04/2020 | n/a | | |
| IAIN/0102 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 12/03/2020 | n/a | | |
| PSUSA/10297 /201906 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 16/01/2020 | n/a | | PRAC Recommendation - maintenance |
| IA/0100/G | This was an application for a group of variations.<br><br>A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient | 18/12/2019 | n/a | | |

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| | A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient<br>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits<br>B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol | | | | |
| IA/0099 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 06/12/2019 | 16/11/2020 | SmPC, Annex II, Labelling and PL | |
| IA/0097 | B.II.z - Quality change - Finished product - Other variation | 30/08/2019 | n/a | | |
| IB/0096 | B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) | 29/07/2019 | n/a | | |
| IB/0095/G | This was an application for a group of variations.<br><br>B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) | 04/07/2019 | n/a | | |

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| | B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure<br>B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) | | | | |
| IAIN/0094 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 07/05/2019 | n/a | | |
| II/0092 | B.II.h.1.b.1 - Update to the Adventitious Agents Safety Evaluation information - Replacement of obsolete studies related to manufacturing steps and adventitious agents already reported in the dossier - with modifications of risk assessment | 26/04/2019 | n/a | | |
| IA/0093/G | This was an application for a group of variations.<br><br>B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation<br>B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation | 11/03/2019 | n/a | | |
| PSUSA/10297 /201806 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 17/01/2019 | n/a | | PRAC Recommendation - maintenance |
| IA/0091/G | This was an application for a group of variations.<br><br>A.5.b - Administrative change - Change in the name | 20/11/2018 | n/a | | |

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| | and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)<br>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure<br>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure<br>B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation | | | | |
| PSUSA/10297 /201712 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 12/07/2018 | n/a | | Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Evicel in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity. |
| IB/0089 | B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate | 09/07/2018 | n/a | | |
| IA/0088 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 25/05/2018 | 20/05/2019 | SmPC, Labelling and PL | |
| IAIN/0085 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes | 23/01/2018 | n/a | | |

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| | do not affect the properties of the FP | | | | |
| PSUSA/10297 /201706 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 11/01/2018 | n/a | | PRAC Recommendation - maintenance |
| IB/0084/G | This was an application for a group of variations.<br><br>B.I.c.z - Container closure system of the AS - Other variation<br>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier<br>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier | 05/12/2017 | n/a | | |
| IA/0083 | B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method | 30/11/2017 | n/a | | |
| II/0081 | B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol | 16/11/2017 | n/a | | |
| PSUSA/10297 /201612 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 06/07/2017 | n/a | | PRAC Recommendation - maintenance |

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| II/0077/G | This was an application for a group of variations.<br><br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS<br>B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol<br>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation<br>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation<br>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation<br>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation<br>B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line) | 01/06/2017 | n/a | | |
| IAIN/0080 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 28/04/2017 | n/a | | |
| IAIN/0078 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier | 27/02/2017 | n/a | | |

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| | of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | | | | |
| PSUSA/10297 /201606 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 12/01/2017 | n/a | | PRAC Recommendation - maintenance |
| IA/0076/G | This was an application for a group of variations.<br><br>A.7 - Administrative change - Deletion of manufacturing sites<br>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process<br>B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation | 25/11/2016 | n/a | | |
| IA/0075 | A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient | 19/10/2016 | 26/09/2017 | Annex II | |
| IB/0073 | C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation | 19/07/2016 | n/a | | |
| PSUSA/10297 /201512 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 07/07/2016 | n/a | | PRAC Recommendation - maintenance |
| IAIN/0072 | B.V.a.1.d - PMF - Inclusion of a new, updated or | 14/06/2016 | n/a | | |

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| | amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | | | | |
| IB/0071 | B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data | 09/06/2016 | n/a | | |
| IA/0070/G | This was an application for a group of variations.<br><br>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure<br>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure<br>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure<br>B.II.z - Quality change - Finished product - Other variation<br>B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits<br>B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits<br>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the | 31/03/2016 | n/a | | |

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| | dossier) - Deletion of a supplier<br>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier<br>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier<br>B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation | | | | |
| II/0057 | Extension of indication to add the use of Tachosil for supportive sealing of the dura mater to prevent postoperative cerebrospinal leakage following neurological surgery. As a consequence, sections 4.1, 4.4, and 5.1 of the SmPC have been updated. The MAH also took the opportunity to make minor editorial corrections to the SmPC. An updated RMP version 6.1 was agreed during the procedure.<br><br>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one | 25/02/2016 | 30/03/2016 | SmPC and PL | Please refer to the scientific discussion TachoSil EMEA/H/C/000505/II/057 for further information. |
| II/0066/G | This was an application for a group of variations.<br><br>A.7 - Administrative change - Deletion of manufacturing sites<br>B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance | 25/02/2016 | n/a | | |

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| | which may have a significant impact on the medicinal product and is not related to a protocol | | | | |
| IAIN/0068/G | This was an application for a group of variations.<br><br>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation<br>C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority | 22/02/2016 | 30/03/2016 | SmPC, Annex II, Labelling and PL | |
| II/0065 | Update of section 4.8 of the SmPC in order to include safety information regarding immunogenicity based on data from study TC-2402-040-SP, a clinical trial in hepatic surgery, and to update the existing ADR table in line with cumulative post-marketing experience. The Package Leaflet has been updated accordingly.<br>In addition, the MAH took the opportunity to make very minor consequential changes to the 'method of administration' in section 4.2 of the SmPC and to implement minor editorial changes in the SmPC, labelling and Package Leaflet.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 04/02/2016 | 30/03/2016 | SmPC, Labelling and PL | In a clinical trial with TachoSil in hepatic surgery, in which patients were investigated for the development of antibodies, 26% of the 96 patients tested and treated with TachoSil developed antibodies to equine collagen. The equine collagen antibodies that developed in some patients after TachoSil use were not reactive with human collagen. One patient developed antibodies to human fibrinogen. There were no adverse events attributable to the development of human fibrinogen or equine collagen antibodies.<br>There is very limited clinical data available regarding re-exposure to TachoSil. Two subjects have been re-exposed in a clinical trial and have not reported any immune-mediated adverse events; however, their antibody status to collagen or fibrinogen is unknown.<br><br>In addition, the text from the current SmPC was modified in section 4.8 to include the following ADRs reported in the post-marketing setting: Anaphylactic shock, |

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| | | | | | Hypersensitivity and Thrombosis. However, the ADR pyrexia appears to be related to surgical procedure rather than the current product and has been removed from the list of ADRs. |
| IAIN/0067 | C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location | 28/01/2016 | n/a | | |
| PSUSA/10297 /201506 | Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin | 14/01/2016 | n/a | | PRAC Recommendation - maintenance |
| II/0061 | B.I.d.1.a.3 - Stability of AS - Change in the re-test period/storage period - Extension of storage period of a biological/immunological AS not in accordance with an approved stability protocol | 17/09/2015 | n/a | | |
| N/0063 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 07/08/2015 | 18/09/2015 | PL | |
| IAIN/0062 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 27/07/2015 | n/a | | |
| PSUSA/1627/ 201412 | Periodic Safety Update EU Single assessment - human fibrinogen, human thrombin (all pharmaceutical dose forms except for sealant matrix) | 09/07/2015 | n/a | | PRAC Recommendation - maintenance |

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| IAIN/0060 | C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location | 20/05/2015 | n/a | | |
| IB/0059 | B.II.b.2.z - Change to importer, batch release arrangements and quality control testing of the FP - Other variation | 30/04/2015 | n/a | | |
| PSUSA/1627/ 201406 | Periodic Safety Update EU Single assessment - human fibrinogen, human thrombin (all pharmaceutical dose forms except for sealant matrix) | 09/01/2015 | n/a | | PRAC Recommendation - maintenance |
| II/0052 | To introduce a new pre-rolled presentation of TachoSil.<br>Minor adjustments to the manufacturing process to pre-roll and pack the sponge have been implemented.<br>The MAH takes this opportunity to align annex II with the QRD template and amend the standard terms used for the route of administration from "Local use" to "Epilesional use" and the pharmaceutical form from "Medicated sponge" to "Sealant matrix".<br><br>B.II.a.2.z - Change in the shape or dimensions of the pharmaceutical form - Other variation | 25/09/2014 | 18/09/2015 | SmPC, Annex II, Labelling and PL | To introduce a new pre-rolled presentation of TachoSil.<br>Minor adjustments to the manufacturing process to pre-roll and pack the sponge have been implemented.<br>The MAH takes this opportunity to align annex II with the QRD template and amend the standard terms used for the route of administration from "Local use" to "Epilesional use" and the pharmaceutical form from "Medicated sponge" to "Sealant matrix". |
| IB/0054/G | This was an application for a group of variations.<br><br>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting | 13/06/2014 | n/a | | |

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| | material/intermediate/reagent - Other variation<br>B.I.a.3.z - Change in batch size (including batch size ranges) of AS or intermediate - Other variation<br>B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method | | | | |
| IAIN/0053 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 28/03/2014 | n/a | | |
| IB/0051 | B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data | 09/12/2013 | n/a | | |
| N/0049 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 06/12/2013 | 21/03/2014 | PL | |
| IB/0050/G | This was an application for a group of variations.<br><br>B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits<br>B.I.a.3.z - Change in batch size (including batch size ranges) of AS or intermediate - Other variation | 25/11/2013 | n/a | | |

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| IB/0047/G | This was an application for a group of variations.<br><br>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation<br>B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) | 22/05/2013 | n/a | | |
| IAIN/0048/G | This was an application for a group of variations.<br><br>A.1 - Administrative change - Change in the name and/or address of the MAH<br>A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release<br>A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release) | 22/04/2013 | 21/03/2014 | SmPC, Annex II, Labelling and PL | |
| IAIN/0046 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 04/02/2013 | n/a | | |
| IB/0045 | B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a | 19/12/2012 | n/a | | |

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| | re-test period/storage period supported by real time data | | | | |
| IB/0044 | B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line) | 19/12/2012 | n/a | | |
| IB/0043/G | This was an application for a group of variations.<br><br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS<br>B.I.a.4.f - Change to in-process tests or limits applied during the manufacture of the AS - Addition or replacement of an in-process test as a result of a safety or quality issue<br>B.I.a.3.z - Change in batch size (including batch size ranges) of AS or intermediate - Other variation | 12/12/2012 | n/a | | |
| II/0042/G | This was an application for a group of variations.<br><br>Grouped changes related to the manufacturing process of Fibrinogen Active Substance<br><br>B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS<br>B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion | 15/11/2012 | n/a | | |

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| | of a non-significant in-process test<br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS | | | | |
| II/0041 | Update of section 5.2 of the SmPC in order to add information based on results from pre-clinical toxicity studies and post-marketing data related to the resorption of Tachosil. Sections 4.3 and 5.2 have been updated as well to contraindicate intravascular application of Tachosil in line with the core SmPC for fibrin sealants.<br>Furthermore, the PI is being brought in line with the latest QRD template version 8.1<br><br>C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data | 15/11/2012 | 18/12/2012 | SmPC, Annex II, Labelling and PL | In animal studies, TachoSil biodegrades after administration to a wound surface with few remnants left after 13 weeks. Complete degradation of TachoSil was seen in some animals 12 months after its administration to a liver wound, whereas small remnants were still observed in others. The degradation was associated with infiltration of granulocytes and formation of resorptive granulation tissue encapsulating the degraded remnants of TachoSil. No evidence of local intolerability has been observed in animal studies.<br>From the experience in humans there have been isolated cases where remnants were observed as coincidental findings with no signs of functional impairment.<br>Section 5.2 of the SmPC has been updated to include the above information and to clarify previous statement that Tachosil should not be applied intravascularly.<br>In addition, in order to bring Tachosil's SmPC in line with the core SmPC for fibrin sealants, section 4.3 of the SmPC has been updated as well to contraindicate intravascular application of Tachosil. |
| IAIN/0040 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 30/05/2012 | n/a | | |

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| IB/0038 | B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method | 29/05/2012 | n/a | | |
| IA/0039 | B.I.c.3.a - Change in test procedure for the immediate packaging of the AS - Minor changes to an approved test procedure | 16/05/2012 | n/a | | |
| IA/0037 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 03/09/2011 | n/a | | |
| N/0033 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 25/07/2011 | n/a | PL | |
| IA/0034 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 30/05/2011 | n/a | | |
| IA/0032 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 19/04/2011 | n/a | | |

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| N/0031 | 'The MAH applied to update the text 'MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS' in the labelling text. The sub-headline word 'POLYSTYRENE' has been replaced by 'POLYETHYLENE TEREPHTHALATE''<br><br>Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 30/11/2010 | n/a | Labelling | |
| IA/0030 | B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 27/08/2010 | n/a | | |
| IB/0029/G | This was an application for a group of variations.<br><br>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure<br>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)<br>B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter<br>B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation<br>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure | 12/07/2010 | n/a | | |

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| | (including replacement or addition) | | | | |
| II/0026 | Addition of a manufacturing site responsible for primary and secondary packaging of Tachosil. Change in the primary packaging materials of the finished product .<br><br>Quality changes | 20/05/2010 | 01/07/2010 | SmPC and PL | |
| II/0027 | To update the manufacturing procedure for the active substances fibrinogen and thrombin, including the addition of a new manufacturing site for fibrinogen<br><br>Quality changes | 20/05/2010 | 27/05/2010 | | |
| II/0025 | Additional manufacturing area.<br><br>Quality changes | 20/05/2010 | 27/05/2010 | | |
| IA/0028 | To submit the 2nd step of the annual update of the PMF 2009.<br><br>B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP | 19/05/2010 | n/a | | |
| 2PMF/0024 | Inclusion of the updated or amended Plasma Master File (CSL Behring EMEA/H/PMF/000001/04) in the | 18/06/2009 | n/a | | |

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| | marketing authorisation dossier | | | | |
| R/0023 | Renewal of the marketing authorisation. | 19/02/2009 | 30/04/2009 | SmPC, Labelling and PL | |
| II/0019 | Extension of indication<br><br>Extension of Indication | 18/12/2008 | 10/02/2009 | SmPC, Annex II and PL | Extension of indication to promote tissue sealing, and for suture support in vascular surgery. Subsequently, changes to sections 4.1, 4.4, 4.8 and 5.1 of the SPC have been made. The Package Leaflet has been updated accordingly. Annex II has been updated to include the agreed version of the EU RMP (version 3.0).<br><br>Please refer to Scientific Discussion TachoSil-H-C-505-II-19. |
| MF/0022 | 2PMF (2nd step of PMF certification procedure) | 08/08/2008 | n/a | | |
| MF/0021 | 2PMF (2nd step of PMF certification procedure) | 26/06/2008 | n/a | | |
| N/0020 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 16/05/2008 | n/a | PL | |
| II/0018 | To upscale and upgrade the production process, the filling and packaging procedure of Haemocomplettan (human fibrinogen)<br><br>Change(s) to the manufacturing process for the active substance | 21/02/2008 | 25/02/2008 | | |
| N/0017 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 26/11/2007 | n/a | PL | |

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| MF/0014 | 2PMF (2nd step of PMF certification procedure) | 30/07/2007 | n/a | | |
| N/0016 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 27/07/2007 | n/a | PL | |
| IA/0015 | IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.) | 26/07/2007 | n/a | Annex II | |
| II/0012 | Change(s) to the manufacturing process for the active substance | 26/04/2007 | 02/05/2007 | | |
| IA/0011 | IA_06_a_Change in ATC code: Medicinal products for human use | 08/11/2006 | n/a | SmPC, Annex II, Labelling and PL | |
| II/0009 | Quality changes | 27/07/2006 | 03/08/2006 | | |
| MF/0010 | 2PMF (2nd step of PMF certification procedure) | 10/07/2006 | n/a | | |
| II/0006 | Extension of Indication<br>Update of Summary of Product Characteristics and Package Leaflet | 26/01/2006 | 28/02/2006 | SmPC and PL | Please refer to the Scientific Discussion: TachoSil-H-505-II-06. |
| MF/0008 | 2PMF (2nd step of PMF certification procedure) | 25/01/2006 | n/a | | |
| II/0007 | Update of or change(s) to the pharmaceutical documentation | 13/10/2005 | 20/10/2005 | | |
| IA/0004 | IA_25_b_01_Change to comply with Ph. - compliance with EU Ph. update - active substance | 09/12/2004 | n/a | | |

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| IA/0003 | IA_28_Change in any part of primary packaging material not in contact with finished product | 18/11/2004 | n/a | | |
| IA/0002 | IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.) | 29/10/2004 | n/a | Annex II | |
| IA/0001 | IA_09_Deletion of manufacturing site | 29/10/2004 | n/a | Annex II | |