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EUDRAVIGILANCE EXPERT WORKING GROUP

VOLUME 9A IMPLEMENTATION QUESTIONS & ANSWERS

VERSION 1.2

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EXECUTIVE SUMMARY

The EudraVigilance Expert Working Group and the EudraVigilance Steering Committee, in consultation with the CHMP Pharmacovigilance Working Party, have developed a series of Questions and Answers (Q&As) to address frequently asked implementation questions from stakeholders in relation to Volume 9A of the Rules Governing Medicinal Products in the European Union: Pharmacovigilance for Medicinal Products for Human Use.

Q&As:

Document History

Version Number	Date	Description
1.0 1.1 1.2	September 2007 October 2007 December 2007	EudraVigilance Expert Working Group (EV-EWG)
1.0 1.1	November 2007 December 2007	CHMP Pharmacovigilance Working Party (PhVWP)
1.2	February 2008	EudraVigilance Steering Committee (EV-SC)

BACKGROUND

This Q&A document provides conventions for the harmonised interpretation of Volume 9A of the Rules Governing Medicinal Products in the European Union: Pharmacovigilance for Medicinal Products for Human Use. Stakeholders e.g. marketing authorisation holders (MAHs), National Competent Authorities (NCAs), vendors, contract research organisations can submit implementation-related questions to the EudraVigilance Expert Working Group (EV-EWG). Questions can be submitted to eudravigilance@emea.europa.eu.
Answers to these questions are developed by the EV-EWG in consultation with the CHMP PhVWP based on a consensus process.

Questions requiring immediate answers in relation to national requirements should be addressed directly to the appropriate NCAs.

Where reference is made to the ICH E2B(R2) guideline, please note that this was previously referred to as ICH E2B(M) guideline: Maintenance of the Clinical Safety Data Management including Data Elements for Transmission of Individual Case Safety Reports. The tripartite harmonised ICH guideline was finalised as E2B (Step 4) in July 1997 and amended for Maintenance as E2B(R1) on 10 November 2000. Post Step 4 editorial corrections were given on 5 February 2001 (second revision) and the guideline renamed E2B(R2).

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17.12.07	ID: 0001	A literature article describes serious adverse reactions that have been experienced by a large number of patients. How should ICSRs be cross-referenced to the same article?	If a literature article describes up to three patients as referred to in Table 'III.7.A: Example for the reporting of cases originally reported in the worldwide literature referring to more than one patient' of Volume 9A, three ICSRs should be submitted, reporting for each individual patient the adverse reaction(s) and all other available information on the case. In addition, all ICSRs which relate to the same literature article should be cross referenced in the section ICH E2B(R2) field A.1.12 'Identification number of the report which is linked to this report' and the section should be repeated as necessary to cross refer all the three related cases. However, if a literature article describes more than three patients, for each patient an ICSR should be submitted, reporting for each individual patient the adverse reaction(s) and all other available information on the case. For the ICSRs which relate to the same literature article, the cross reference in the section ICH E2B(R2) field A.1.12 'Identification number of the report which is linked to this report' should be conducted as follows: ▪ The first case should be linked to all other cases related to the same article ▪ All the other cases should be only linked to the first one, as in the example below *Example for the reporting of cases originally reported in the worldwide literature referring to a large number of patients* For Case 1 described in the literature article: - ICH E2B(R2) A.1.10.1 'Worldwide Unique Case Identification Number': UK-ORGABC-0001 - ICH E2B(R2) A.1.12 'Linked Report': UK-ORGABC-0002 - ICH E2B(R2) A.1.12 'Linked Report': UK-ORGABC-0003 - ICH E2B(R2) A.1.12 'Linked Report': UK-ORGABC-0004 - ICH E2B(R2) A.1.12 'Linked Report': UK-ORGABC-000N - ICH E2B(R2) A.2.2 'Literature reference(s)': N Engl J Med. 1997;336:309-15. - File name for the copy of literature article to be sent via e-mail to EVLIT@emea.europa.eu: UK-ORGABC-0001.pdf

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			For Case 2 described in the literature article: - ICH E2B(R2) A.1.10.1 'Worldwide Unique Case Identification Number': UK-ORGABC-0002 - ICH E2B(R2) A.1.12 'Linked Report': UK-ORGABC-0001 - ICH E2B(R2) A.2.2 'Literature reference(s)': N Engl J Med. 1997;336:309-15. No copy of the literature article required since the copy was already submitted for case 1. For Case N described in the literature article: - ICH E2B(R2) A.1.10.1 'Worldwide Unique Case Identification Number': UK-ORGABC-000N - ICH E2B(R2) A.1.12 'Linked Report': UK-ORGABC-0001 - ICH E2B(R2) A.2.2 'Literature reference(s)': N Engl J Med. 1997;336:309-15. No copy of the literature article required since the copy was already submitted for case 1.
17.12.07	ID: 0002	Do the Data Privacy rules for 'Patient name or initials' in paper or E2B format applies to submissions to EudraVigilance and NCAs?	The guidance provided in Volume 9A chapter III.5, Section 4 'What to Take into Account for Data Privacy Laws' regarding patient name or initials reads as follows: 'To comply with EU legislation on the protection of individuals with regard to the processing of personal data as referred to in Chapter I.7, Section 7, electronic transmission of ICSRs should operate on the principles of anonymised information, whereby the ICH guidelines should be adhered to as follows: ▪ ICH E2B(R2) field B.1.1 'Patient name or initials': The information should be provided when it is in conformance with the confidentiality requirements. This also applies to medical record number(s) ICH E2B (R2) field (B.1.1.1). If the initials are known to the sender but cannot be transmitted due to data privacy requirements, this field should be populated with 'PRIVACY'. If the initials of the patient are unknown to the sender, this field should be populated with 'UNKNOWN'. The same principles apply for ICH E2B(R2) section A.2 'Primary source(s) of information' and section B.1.10 'For a parent-child/fetus report, information concerning the parent'. The guidance provided in Volume 9A is applicable to: ▪ Submissions to EudraVigilance to both EVHUMAN and EVCTMPROD

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			▪ Submissions to all NCAs in the EEA depending on each NCA's own implementation of the data protection requirements as per national legislation In practice in some EEA countries stakeholders may be asked/permitted to provide patient's initials but in others, where the provision of initials or patient names is not permitted according to national legislation, the provisions as outlined above should be followed (i.e. populate the field with 'PRIVACY'). In this context the data privacy rules interfere with the concept of the 'identifiable patient' because depending on the level of detail of information available on the case, you may be able to identify the patient. That is the reason why some NCAs accept to receive the patient's initials but require deleting them from the forms or the electronic submissions of ICSRs when the cases should be reported outside the country of origin. In order to avoid a high degree of customisation for reporting to each NCA, the rule described in the Volume 9A may therefore be applied in every circumstance.
17.12.07	ID: 0003	How should the fields ICH E2B(R2) B.4.k.2.1 'Proprietary medicinal product name' and ICH E2B(R2) B.4.k.2.2 'Active substance name(s)' in the ICSR be populated, where the active ingredients of a branded medicinal product could be one of two possible generics, depending on the country in which it is marketed?	Where the primary source reported a suspect or interacting branded/proprietary medicinal product name without indicating the active substances of the medicinal product and the proprietary medicinal product could be one of two or more possible generics, which have a different composition depending on the country where the medicinal product is marketed, the ICSR should be populated as follows: ▪ Field ICH E2B(R2) B.4.k.2.1 'Proprietary medicinal product name' should be populated with the proprietary/branded medicinal product name as reported by the primary source. ▪ Field ICH E2B(R2) B.4.k.2.2 'Active substance name(s)' should be completed with those active substances that correspond to the composition of the proprietary/branded medicinal product of the country where the reaction/event occurred (field ICH E2B(R2) A.1.2) or if this is the same, of the country of the primary source, (field ICH E2B(R2) A.1.1). In cases, where information is available on: ▪ The 'Identification of the country where the drug was obtained' (field ICH E2B(R2) B.4.k.2.3), ▪ The 'Authorization/application number' (field ICH E2B(R2) B.4.k.4.1), ▪ The 'Country of authorization/application' (field ICH E2B(R2) B.4.k.4.2) and/or ▪ The 'Batch/lot number' (field ICH E2B(R2) B.4.k.3) The composition with regard to the active substances of the proprietary medicinal product should be provided

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			accordingly. In any cases, the field ICH E2B(R2) B.4.k.2.2 'Active substance name(s)' field needs to be repeated for each active substance.
17.12.07	ID: 0004	How should the fields ICH E2B(R2) B.4.k.2.1 'Proprietary medicinal product name' and ICH E2B(R2) B.4.k.2.2 'Active substance name(s)' in the ICSR be populated, where the active ingredients of a branded medicinal product differ depending on the formulation/presentation marketed?	In case the primary source reports a suspect or interacting branded/proprietary medicinal product name without indicating the formulation/presentation of the product and the proprietary/branded medicinal product can be one of two or more possible formulations/presentations in a country, which have a different composition, the ICSR should be populated as follows: ▪ Field ICH E2B(R2) B.4.k.2.1 'Proprietary medicinal product name' should be populated with the medicinal product name as reported by the primary source. ▪ Field ICH E2B(R2) B.4.k.2.2 'Active substance name(s)' should be completed with those active substances that correspond to the formulation/presentation of the proprietary medicinal product which are in common to all formulations/presentations in the country of authorisation. In situations, where the active substances of a proprietary medicinal product could be one of two possible generics, depending on the country in which it is marketed, the guidance should be followed as provided for question ID: 0003. The ICH E2B(R2) B.4.k.2.2 'Active substance name(s)' field needs to be repeated for each active substance.
17.12.07	ID: 0005	How should the fields ICH E2B(R2) B.4.k.2.1 'Proprietary medicinal product name' and ICH E2B(R2) B.4.k.2.2 'Active substance name(s)' in the ICSR be populated, where the co-medication was reported	Drug information, which is reported as concomitant or interacting medication and which cannot be characterized by the proprietary medicinal product name or by the active substances (e.g. antineoplastic agents), should not be captured in B.4.k.2.1 'Proprietary medicinal product name' and ICH E2B(R2) B.4.k.2.2 'Active substance name(s)'. Instead this information should be provided in field B.5.1 'Case narrative including clinical course, therapeutic measures, outcome and additional relevant information'. The same applies e.g. if a food interaction is reported (e.g. grapefruit juice). As regards the reporting of drug interactions, which includes drug/drug (including biological products), drug/food, drug/device, and drug/alcohol interactions, the coding should be performed in section B.2 'Reactions/Events' in line with the latest version of the ICH-Endorsed Guide for MedDRA Users 'MedDRA

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		as e.g. a class of medicinal products?	Term Selection: Points to Consider'.
17.12.07	ID: 0006	Is it acceptable for MAHs to report all serious adverse drug reactions occurring outside the European Union to all NCAs?	In line with Volume 9A of 'The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Human Use', Chapter III.11 Section 3 'Reporting of all Serious Cases from outside the European Union', MAHs are encouraged to report electronically to EudraVigilance all suspected serious adverse reactions that occur in a third country for all medicinal products authorised in the EU, regardless of the authorisation procedure (national, centralised, decentralised or mutual recognition procedures). As regards the reporting to NCAs, MAHs should follow the requirements as set out in Volume 9A Annex 6.1.3 'Specific Expedited (15-days) Reporting Requirements in Member States for ICSRs from Spontaneous Reporting and Non-Interventional Studies Occurring Outside the EU'.
17.12.07	ID: 0007	Will it be possible to send copy of literature articles via the EudraVigilance Gateway?	Until the revised ICH standards are available, copies of literature articles should be submitted in line with the requirements provided in Volume 9A of 'The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Human Use', Chapter III.7 'Handling of Adverse Reaction Reports Published in the Worldwide Literature'. In the frame of the revision of the ICH E2B(R2) guideline, the requirement to be able to submit electronic copies of literature articles and associate those with the ICSRs concerned have been put forward by the EU and EFPIA.
17.12.07	ID: 0008	Some NCAs request MAHs to nullify a case because they received a report for that patient from a second MAH. How should nullifications be managed?	In Volume 9A, part II 'Guidelines for Competent Authorities and the Agency', chapter II.1 Section 3.3 'Processing Individual Case Safety Reports' the management of duplicates by NCAs is described. It is stated that the NCA should make every effort to ensure that case reports contain sufficient information to identify such duplicates and should liaise with relevant MAHs to facilitate identification of possible duplicate cases. Databases should be reviewed regularly to identify duplicates in accordance with the NCA and Agency procedures. Where e.g. two MAHs may have submitted a report for the same case, after identification, the NCA should merge the duplicates into a single new (or merged) ICSR in accordance with ICH E2B (R2) guidance (see Volume 9A, Chapter III.6 'Nullification of Individual Cases'). Note that in this scenario a nullification of the case is not applicable.

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17.12.07	ID: 0009	How should the retrospective transmission of ICSRs to EudraVigilance be conducted when it may not be possible to differentiate between interventional and non-interventional clinical trials going back to 1995?	The retrospective transmission of ICSRs to EudraVigilance (Post-Authorisation Module) should be conducted in line with the provisions set out in Volume 9A, part Chapter III.11 Section 4'Retrospective Electronic Population of EudraVigilance Post-Authorisation Module'. Where it is not possible for the MAH to differentiate between interventional and non-interventional clinical trials, all cases should be submitted to the EudraVigilance Post-Authorisation Module (EVPM) back to 1 May 2004. According to Directive 2001/20/EC, as of 1st May 2004 all reports arising from interventional clinical trials need to be submitted to the EudraVigilance Clinical Trial Module (EVCTM) and should therefore not be retrospectively submitted to EVPM. As a general principle the Agency should be informed when the retrospective transmission of ICSRs is initiated and what data set will be provided. Furthermore, the Agency should be informed once the retrospective transmission of ICSRs to the EudraVigilance Post-Authorisation Module has been completed successfully.
17.12.07	ID: 0010	How should a MAH handle a case when there is partial confirmation of a consumer case by a health care professional (HCP) .i.e. a consumer reported 5 events but the HCP only confirms 2 of those reported?	Cases initially reported e.g. by a consumer or a lawyer, where at least one adverse event has been medically confirmed should be reported as medically confirmed. The field A.1.14 'Was report medically confirmed if not initially from health care professional' should be set to 'Yes'. In the field ICH E2B(R2) B.5.1 'Case narrative including clinical course, therapeutic measures, outcome and additional relevant information' any relevant information on the medical confirmation of the case should be also included.
17.12.07	ID:0011	In spontaneous reports the primary source often provides the diagnoses as well as signs and symptoms related to adverse reactions in the narrative section of the reporting forms. Should	The coding of diagnoses and provisional diagnoses with signs and symptoms in the ICH E2B(R2) field B.2.i.1 'Reaction/event in MedDRA terminology (Lowest Level Term)' should be performed in line with the latest version of the ICH-Endorsed Guide for MedDRA Users 'MedDRA Term Selection: Points to Consider'. In practice, events, which are typically signs or a symptoms of a diagnosis or a provisional diagnosis reported by a primary source/reporter, should be listed and MedDRA coded in the ICH E2B(R2) section B.2 'Reaction(s)/event(s)' but it is considered sufficient to select a term for only the diagnosis or provisional diagnosis and not for the sign and symptoms.

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		the diagnoses as well as the signs and symptoms be listed in the ICH E2B(R2) section B.2 'Reaction(s)/event(s)' when an ICSR is prepared?	If in the narrative other events have been reported by the primary source, which are not typically signs or symptoms of the primary source's/reporter's diagnosis or provisional diagnosis, and those events are suspected to be adverse reactions, then they should be listed and MedDRA coded in the ICH E2B(R2) section B.2 'Reaction(s)/event(s)'. If no diagnosis is provided by the primary source, all reported signs and symptoms should be listed and MedDRA coded in the ICH E2B(R2) section B.2 'Reaction(s)/event(s)'. In addition, if signs and symptoms are typically part of a diagnosis then the diagnosis can be MedDRA coded in the field ICH E2B(R2) B.5.3 'Sender's diagnosis/syndrome and/or reclassification of the reaction/event'
17.12.07	ID:0012	How should the requirements of Volume 9A regarding the literature reporting and marketing authorisation of medicinal products be interpreted. The question refers to scenario, where the medicinal product source and/or the invented name is not specified and ownership of the product cannot be excluded on the basis of the active substance(s), formulation or route of administration and the MAH. In particular, clarification is needed, if the country where the case occurred	In Volume 9A, Chapter I.4 Section 3.2 'Reports published in the worldwide literature' it is stated: 'if the medicinal product source and /or the invented name is not specified and ownership of the product cannot be excluded on the basis of the active substance, formulation or route of administration, the MAH should assume that it is one of their products the publication refers to, although the report should indicate that the specific product source and the invented name was not identified.' As regards the interpretation of the 'medicinal product source' the MAH may also take the occurrence or the primary source country of the adverse reaction(s) into account to assume that it is one of their products. In practice this means that if in reports published in the world literature the occurrence or the primary source country is provided and the MAH does not have a marketing authorisation in this country, the company does not need to submit these cases. The likelihood to miss reports published in the worldwide literature is negligible compared to the number of potential duplicates submitted for the same case by various companies.

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		can be used to exclude the ownership of the product?	
17.12.07	ID: 0013	As pointed out in Volume 9A, Chapter I. 5 Section 9 'Reporting of Suspected Transmission of Infectious Agents' the requirement to apply MedDRA coding is also relevant to the reporting of cases of suspected transmission of an infectious agent. How should a suspected transmission of an infectious agent via a medicinal product be coded in MedDRA?	The coding of a suspected transmission of an infectious agent via a medicinal product in the ICH E2B(R2) ICSR field B.2.i.1 'Reaction/event in MedDRA terminology (Lowest Level Term)' should be performed in line with the latest version of the ICH-Endorsed Guide for MedDRA Users 'MedDRA Term Selection: Points to Consider'. In accordance with this guide, the following principles apply: If a report of transmission of infectious agent via medicinal product is received, it is considered appropriate to select a term for the transmission i.e. one of the following terms: ▪ **'*Suspected transmission of an infectious agent via a medicinal* product':** choose this term, if there is a suspicion that a transmission via a medicinal product has taken place in the patient. ▪ **'T*ransmission of an infectious agent via a medicinal product*':** choose this term, if there is evidence that the infectious agent has been transmitted via a medicinal product. In addition, if the infectious agent is specified, it is considered appropriate to select the specific infectious agent as a second term. For example: If 'suspected transmission of Hepatitis C via a blood product' is reported, 'Suspected transmission of an infectious agent via a medicinal product' and 'Hepatitis C' should be selected. For electronic reporting such cases should to be classified as serious in the ICH E2B(R2) field A.1.5.1, and the ICH E2B(R2) field A.1.5.2. 'Seriousness criteria' should be set to 'Other medically important condition' (see Volume 9 A, ICH E2B(R2) in Annex 4).

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17.12.07	ID:0014	How should laboratory data be structured in the ICH E2B(R2) B.3 section 'Results of tests and procedures relevant to the investigation of the patient' of the ICSR?	The coding of investigations should be performed in line with the latest version of the ICH-Endorsed Guide for MedDRA Users 'MedDRA Term Selection: Points to Consider'. As described in ICH E2B(R2), the section B.3 'Results of tests and procedures relevant to the investigation of the patient' should capture the tests and procedures performed to diagnose or confirm the reaction/event, including those tests done to investigate (exclude) a non-drug cause, (e.g., serologic tests for infectious hepatitis in suspected drug-induced hepatitis). Both positive and negative results should be reported. While structured information is preferable, provisions have been made to transmit the information as free text in the field ICH E2B(R2) B.3.2. 'Results of tests and procedures relevant to the investigation'. **For example 'Blood glucose increased' should be coded as follows:** The 'Test name' should be provided excluding any reference to the result of the test: ICH E2B(R2) B.3.1c 'Test name': *Blood glucose* The Test result' should be coded separately: ICH E2B(R2) B.3.1d 'Test result': *Increased* The coding <u>should not</u> be as follows: ICH E2B(R2) B.3.1c 'Test name': *Blood glucose increased* ICH E2B(R2) B.3.1d 'Test result': *blank* **For example 'blood glucose 100 mg/l' or 'Blood glucose found to be normal 100 mg/l' should be coded as follows:** ICH E2B(R2) B.3.1c 'Test name': *Blood glucose* ICH E2B(R2) B.3.1d 'Test result': *100* ICH E2B(R2) B.3.1e 'Test unit': *mg/L* ICH E2B(R2) B.3.2 'Results of tests and procedures relevant to the investigation': *Blood glucose found to be normal 100 mg/l*
17.12.07	ID: 0015	What needs to be taken into account in populating the EVMPD as regards	In addition to the information on the EudraVigilance Medicinal Product Dictionary (EVMPD) population, as described in the 'EVMPD training material', specific topics related to vaccines only should be taken into account as follows:

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		vaccines? Which EVMPD field should be populated?	**a.** In accordance with section 1 'Name of the medicinal product' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - The medicinal product name should be entered in the EVMPD field 'Full Presentation Name' - The common name should be entered in the EVMPD field 'Generic Name' i. The 'common name' has been defined in the 'Guideline on pharmaceutical aspects of the product information for human vaccines' (Doc. Ref. EMEA/CPMP/BWP/2758/02). ii. The common name refers to the title of the relevant European Pharmacopoeia monograph, where one exists. In case where there is no European Pharmacopoeia monograph, the stylistics and precedents of European Pharmacopoeia monographs should be observed, including the use of words such as 'live', 'adsorbed' or 'virosome', in parenthesis if relevant. iii. The EVMPD contains a look-up of common names as described in the European Pharmacopoeia, which is systematically updated by the EMEA. iv. If a common name cannot be found in the EVMPD look-up, the MAH/sponsor of clinical trials should contact the EudraVigilance Helpdesk to obtain guidance on how the common name should be presented. **b.** In accordance with section 2 'Qualitative and quantitative composition' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - The vaccine antigen should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Active Ingredient' ii. For each vaccine antigen a separate substance name field should be populated iii. The EVMPD contains a look-up of vaccine antigens, as described in European Pharmacopoeia or authorised in EU SmPCs which is systematically updated by the EMEA. iv. If a vaccine antigen cannot be found in the EVMPD look-up, the MAH/sponsor of clinical trials should contact the EudraVigilance Helpdesk to obtain guidance on how the antigen should be presented - The vaccines adjuvant(s)/adsorbant should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Excipient' ii. The strength/concentration of the vaccine adjuvant(s)/adsorbant is not required iii. For each vaccine adjuvant(s)/adsorbant a separate substance name field should be populated - The vaccine production system should not be entered in the EVMPD, as the dictionary does not currently allow for the association between the individual antigens and their adjuvants/adsorbants or

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			the production system **c.** In accordance with section 6.1 'Excipients' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - Additional vaccine constituents should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Excipient' ii. The strength/concentration of the additional vaccine constituent is not required iii. For each additional vaccine constituent a separate field should be populated Example: SmPC HBVAXPRO SmPC Section 1: 'NAME OF THE MEDICINAL PRODUCT' HBVAXPRO 5 micrograms/0.5 ml Suspension for injection Hepatitis B vaccine (rDNA) SmPC Section 2: 'QUALITATIVE AND QUANTITATIVE COMPOSITION' One dose (0.5 ml) contains: Hepatitis B virus surface antigen, recombinant (HBsAg)* 5.00 micrograms Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al+) * produced from recombinant strain of the yeast Saccharomyces cerevisiae (strain 2150-2-3) For a full list of excipients, see section 6.1 SmPC Section 6.1: 'LIST OF EXCIPIENTS' Sodium chloride Borax Water for injections Example: EVMPD entry for HBVAXPRO

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			Full Presentation Name HBVAXPRO 5 MICROGRAMS/0.5 ML, SUSPENSION FOR INJECTION Product Short Name HBVAXPRO Product Generic Name Hepatitis B vaccine (rDNA) Product Company Name Product Strength Name 5 MICROGRAMS/0.5 ML Product Form Name SUSPENSION FOR INJECTION Package Description 1 VIAL PRD25741 - HBVAXPRO 5 MICROGRAMS/0.5 ML, SUSPENSION FOR INJECTION MAH - AVENTIS PASTEUR MSD, SNC Pharmaceutical Products (1) SUSPENSION FOR INJECTION Drug Routes (1) Drug Ingredients (5) HEPATITIS B SURFACE ANTIGEN (RDNA) - Active Ingredient ALUMINIUM HYDROXYPHOSPHATE SULFATE - Excipient WATER FOR INJECTION - Excipient BORAX - Excipient SODIUM CHLORIDE - Excipient
17.12.07	ID: 0016	What needs to be taken into account in populating the EVMPD as regards insulins? Which EVMPD field should be populated?	In addition to the information on the EudraVigilance Medicinal Product Dictionary (EVMPD) population, as described in the 'EVMPD training material', the following should be taken into account: **a.** In accordance with section 1 'Name of the medicinal product' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - The medicinal product name should be entered in the EVMPD field 'Full Presentation Name' **b.** In accordance with section 2 'Qualitative and quantitative composition' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - The active ingredient should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Active Ingredient' ii. For each active ingredient a separate substance name field should be populated iii. The substance name should be described based on the INN

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			iv. Where no INN is assigned to the insulin, the substance name should be populated with the terms as presented in the EVMPD look-up, which is systematically updated by the EMEA in collaboration with the CHMP BWP. v. If the appropriate insulin cannot be found in the EVMPD look-up, the MAH/sponsor of clinical trials should contact the EudraVigilance Helpdesk to obtain guidance on how the substance name should be presented. • The active ingredient can refer to an 'Insulin Substance(s)', an 'Insulin formulation(s)' or a combination of both **c.** In accordance with section 6.1 'Excipients' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - Excipients should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Excipient' ii. The strength/concentration of the excipient is not required iii. For each excipient a separate substance name field should be populated As regards the characterisation of insulins the following should be taken into account: ▪ 'Insulin Substance' referring to basic insulins, which are not combined with any other particle or molecule. Insulin Substances can be described by the following elements: - Insulin Type: provides information on the final amino acid sequence (i.e. bovine, porcine or human sequence). - Insulin Analogue: provides information whether the insulin has been modified in its amino acid sequence through recombinant technologies. - Insulin Class: provides information on the preparation process (e.g. Recombinant, Semi-synthetic, Non-synthetic). Example: Insulin Human rDNA Insulin Formulation: ▪ 'Insulin Formulation' referring to insulins that have been combined with other molecules or insulins. Insulin Formulations can be described by the following elements: - Physical State: provides information on the physical state of the insulin formulation following completion of the preparation process. - Complexing: provides information on the particles or molecules that have been combined with the insulin (e.g. Insulin Zinc Crystalline).

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			- Onset of action: provides information on the onset of action of the insulin formulation referring to the time interval before the insulin reaches the bloodstream and initiates the lowering of the blood glucose (e.g. Insulin fast acting). - Duration of action: provides information on how long the insulin is lowering the blood glucose. Example: Insulin Isophane Example 1: SmPC ACTRAPID (Insulin Medicinal Product containing an Insulin Substance) SmPC Section 1: 'NAME OF THE MEDICINAL PRODUCT' Actrapid 40 IU/ml Solution for injection in a vial SmPC Section 2: 'QUALITATIVE AND QUANTITATIVE COMPOSITION' Insulin human, rDNA (produced by recombinant DNA technology in Saccharomyces cerevisiae). 1 ml contains 40 IU of insulin human (…) For a full list of excipients, see section 6.1 SmPC Section 6.1: 'LIST OF EXCIPIENTS' Zinc chloride Glycerol Metacresol Sodium hydroxide or/and hydrochloric acid (for pH adjustment) Water for injections Example: EVMPD entry for ACTRAPID

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			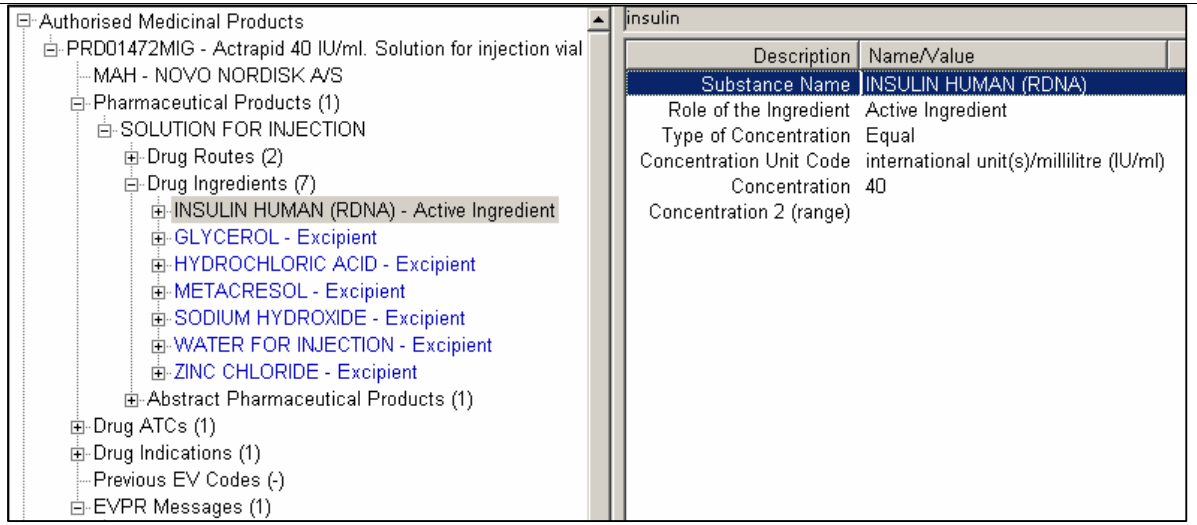 Example 2: SmPC INSULATARD (Insulin Medicinal Product containing an Insulin Formulation) SmPC Section 1: 'NAME OF THE MEDICINAL PRODUCT' Insulatard 40 IU/ml Suspension for injection in a vial SmPC Section 2: 'QUALITATIVE AND QUANTITATIVE COMPOSITION' Insulin human, rDNA (produced by recombinant DNA technology in Saccharomyces cerevisiae). 1 ml contains 40 IU of insulin human (…) Insulatard is a suspension of isophane (NPH) insulin For excipients, see Section 6.1 List of excipients. SmPC Section 6.1: 'LIST OF EXCIPIENTS' Zinc chloride

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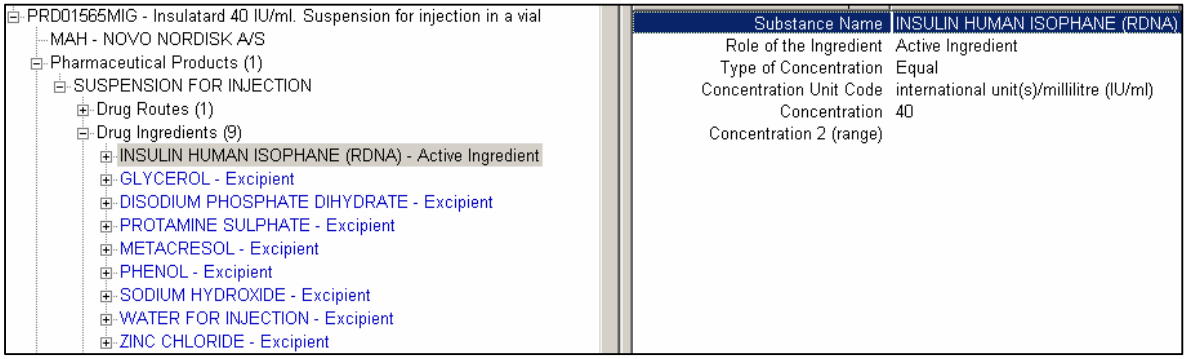
			Glycerol Metacresol Phenol Disodium phosphate dihydrate Sodium hydroxide or/and hydrochloric acid (for pH adjustment) Protamine sulphate Water for injections Example: EVMPD entry for INSULATARD  Example 3: SmPC MIXTARD (Insulin Medicinal Product containing combination of insulin substance and/or formulation) SmPC Section 1: ‘NAME OF THE MEDICINAL PRODUCT’ Mixtard 30, 40 IU/ml Suspension for injection in a vial SmPC Section 2: ‘QUALITATIVE AND QUANTITATIVE COMPOSITION’ Insulin human, rDNA (produced by recombinant DNA technology in Saccharomyces cerevisiae). 1 ml contains 40 IU of insulin human (…)

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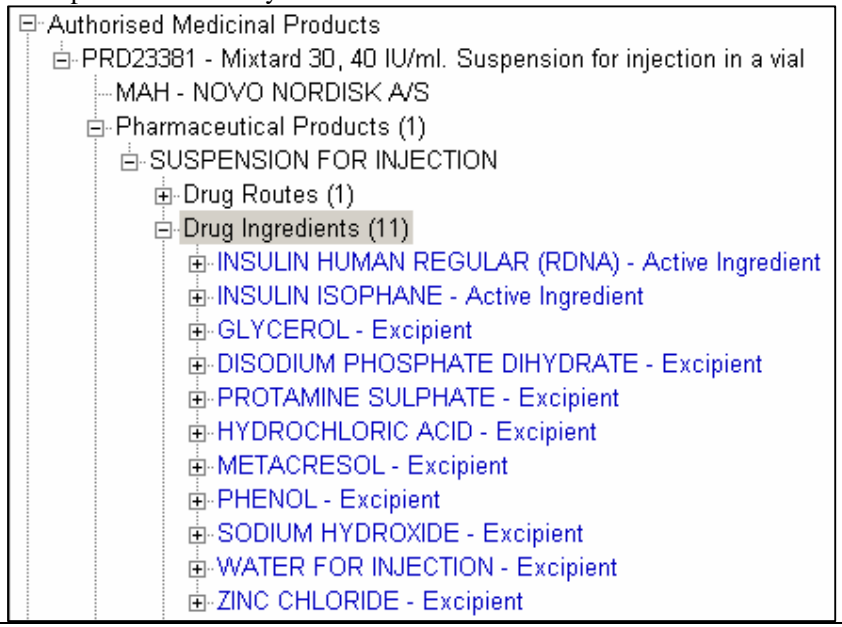
			Mixtard is a mixture of dissolved insulin and isophane (NPH) insulin. Mixtard 30 consists of 30% dissolved insulin and 70% isophane insulin. SmPC Section 6.1: 'LIST OF EXCIPIENTS' Zinc chloride Glycerol Metacresol Phenol Disodium phosphate dihydrate Sodium hydroxide or/and hydrochloric acid (for pH adjustment) Protamine sulphate Water for injections Example: EVMPD entry for MIXTARD 

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	ID: 0017	What needs to be taken into account in populating the EVMPD as regards radioactive compounds? Which EVMPD field should be populated?	In addition to the information on the EudraVigilance Medicinal Product Dictionary (EVMPD) population, as described in the 'EVMPD training material', specific topics related to radioactive compounds only should be taken into account as follows: **a.** In accordance with section 1 'Name of the medicinal product' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - The medicinal product name should be entered in the EVMPD field 'Full Presentation Name' **b.** In accordance with section 2 'Qualitative and quantitative composition' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - The active ingredient should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Active Ingredient' ii. For each active ingredient a separate substance name field should be populated iii. The substance name should be described based on the INN iv. Where no INN is assigned to the radioactive compound, the substance name should refer to the title of the relevant European Pharmacopoeia monograph, where one exists as followed: Example: European Pharmacopoeia monograph: Technetium 99mTc succimer injection EVMPD should be populated with Technetium (99mTc) succimer v. In cases where there is no European Pharmacopoeia monograph, the stylistics and precedents of European Pharmacopoeia monographs should be observed. vi. The substance name should be structured based on the following elements and the order of the elements should be followed: - Radionuclide - Isotope number - Element symbol - Carrier agent name vii. The EVMPD contains a look-up of titles of the monograph for radioactive compounds, as described in European Pharmacopoeia, which is systematically updated by the EMEA. viii. If an appropriate term cannot be found in the EVMPD look-up, the MAH/sponsor of clinical trials should contact the EudraVigilance Helpdesk to obtain guidance on how the common name should be presented.

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			c. In accordance with section 6.1 'Excipients' of the Summary of Product Characteristics (SmPC): - Excipients should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Excipient' ii. The strength/concentration of the excipient is not required iii. For each excipient a separate substance name field should be populated Example: SmPC CARDIOLITE® **CARDIOLITE®**, Sections 1, 2 and 6.1 of SmPC: Section 1. NAME OF THE MEDICINAL PRODUCT **CARDIOLITE®,** Kit for the preparation of **Technetium Tc-99m Sestamibi**. Section 2. QUALITATIVE AND QUANTITATIVE COMPOSITION 1 vial contains Active ingredients Tetrakis (2-methoxy isobutyl isonitrile) Copper (I) Tetrafluoroborate 1.0 mg Stannous chloride dihydrate 0.075 mg L-Cysteine hydrochloride monohydrate 1.0 mg Section 6.1. LIST OF EXCIPIENTS Sodium citrate dihydrate Mannitol Example: EVMPD entry for Technetium Tc-99m Sestamibi

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			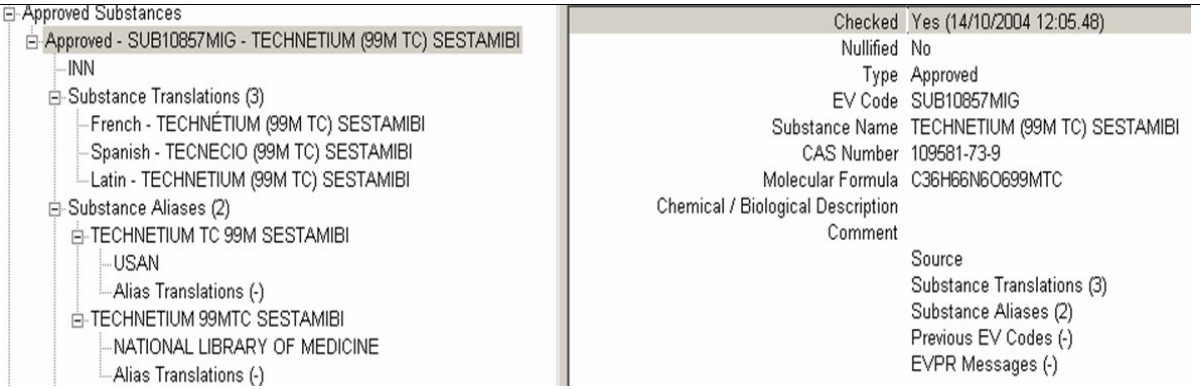 Example: EVMPD entry for Technetium (99mTc) Sestamibi

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			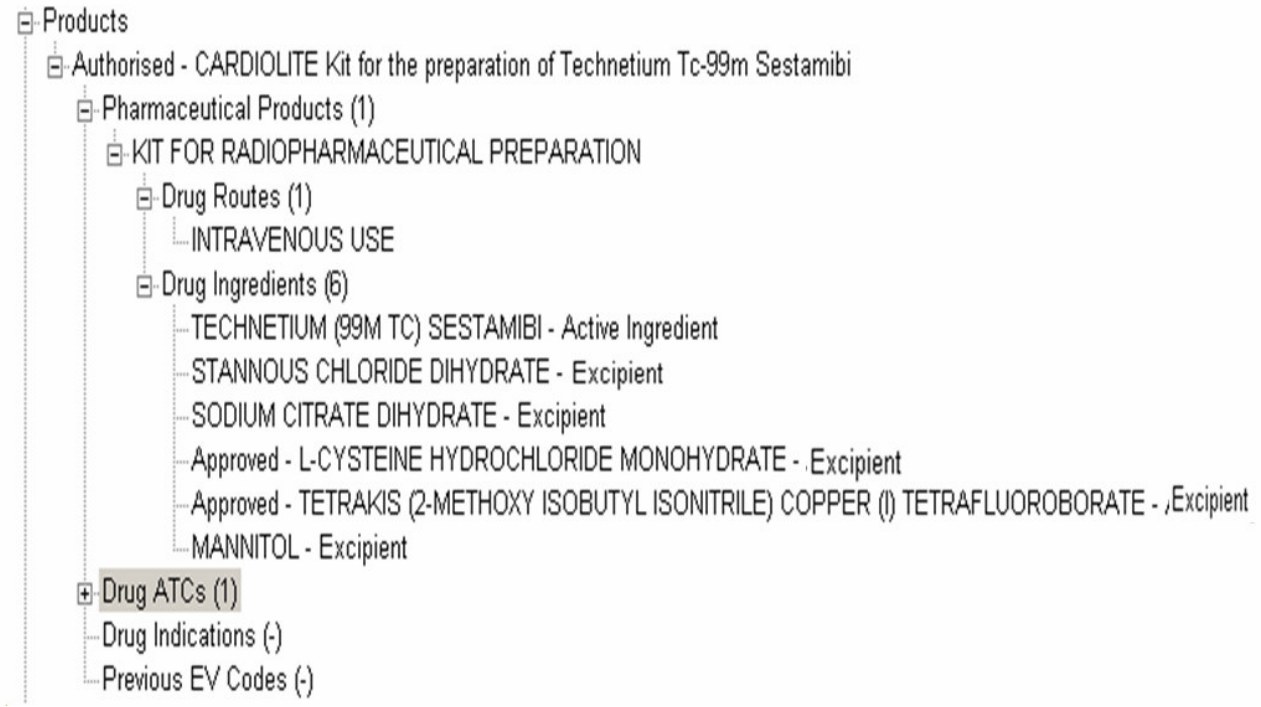 Example: EVMPD entry for CARDIOLITE®
	ID: 0018	What needs to be taken into account in populating the EVMPD as regards immunoglobulins? Which EVMPD field should be populated?	In addition to the information on the EudraVigilance Medicinal Product Dictionary (EVMPD) population, as described in the 'EVMPD training material', specific topics related to immunoglobulins only should be taken into account as follows: **a.** In accordance with section 1 'Name of the medicinal product' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - The medicinal product name should be entered in the EVMPD field 'Full Presentation Name'

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			b. In accordance with section 2 'Qualitative and quantitative composition' of the Summary of Product Characteristics (SmPC) or the Clinical Trial Application Form: - The active ingredient should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Active Ingredient' ii. For each active ingredient a separate substance name field should be populated iii. The common name should be described based on the INN iv. Where no INN is assigned to the immunoglobulin, the common name should refer to the title of the relevant European Pharmacopoeia monograph, where one exists. In cases where there is no European Pharmacopoeia monograph, the stylistics and precedents of European Pharmacopoeia monographs should be observed. v. The common name should be structured based on the following elements and the order of the elements should be followed: - Extractive origin - Targeted antigen - Immnoglobulin - Intended use acronym (optional)* *The Intended use acronym refers to the abbreviation for the route of administration when stated in the reference source. For example, the EU Ph. comprises two distinct monographs for Human Normal Immunoglobulin: 1. Human Normal Immunoglobulin 2. Human Normal Immunoglobulin for intravenous administration These entries should be entered in the EVMPD as: 1. Human Normal Immunoglobulin 2. Human Normal Immunoglobulin (IV) vi. The EVMPD contains a look-up of titles of the monograph for immunoglobulins, as described in European Pharmacopoeia, which is systematically updated by the EMEA in collaboration with the CHMP BWP. vii. If an appropriate term cannot be found in the EVMPD look-up, the MAH/sponsor of clinical trials should contact the EudraVigilance Helpdesk to obtain guidance on how the common name should be presented.

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			c. In accordance with section 6.1 'Excipients' of the Summary of Product Characteristics (SmPC): - Excipients should be entered in the EVMPD field 'Drug Ingredient' i. The EVMPD field 'Role of Ingredient' should be set to 'Excipient' ii. The strength/concentration of the excipient is not required iii. For each excipient a separate field should be populated Example: SmPC RHOPHYLAC® **RHOPHYLAC®,** Sections 1, 2 and 6.1 of SmPC: Section 1. NAME OF THE MEDICINAL PRODUCT **RHOPHYLAC®** 300 micrograms / 2 ml, solution for injection in pre-filled syringe Section 2. QUALITATIVE AND QUANTITATIVE COMPOSITION **Human Anti-D immunoglobulin** Each 2 ml solution in pre-filled syringe contains: Human anti-D immunoglobulin 1500 IU (300 micrograms) Corresponding to a concentration of 750 IU (150 micrograms) per ml The product contains a maximum of 30 mg/ml of human plasma proteins of which 10 mg/ml is human albumin as stabiliser. At least 95 % of the other plasma proteins are IgG. Rhophylac contains not more than 5 micrograms/ml IgA. For a full list of excipients, see section 6.1 Section 6.1. LIST OF EXCIPIENTS Human albumin Glycine Sodium chloride

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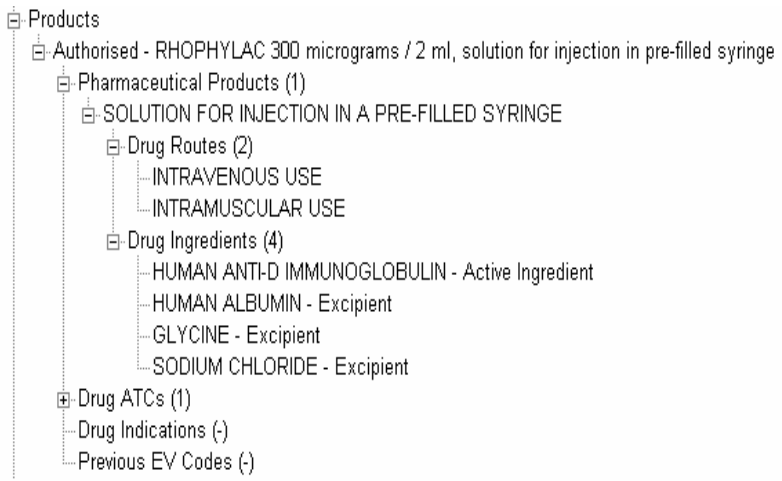
			Example: EVMPD entry for RHOPHYLAC®  Example: EVMPD entry for Human Anti-D Immunoglobulin

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