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SCIENCE MEDICINES HEALTH

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Dear Drs Rägo and Lindquist,

Conditions for the transfer of data between EMA and WHO/UMC for the implementation of Article 28c (1), 2nd paragraph of Regulation (EC) No 726/2004

Following our collaboration through teleconferences, we are pleased to summarise the modalities and conditions for the implementation of Article 28c (1), 2nd paragraph of Regulation (EC) No 726/2004 as amended by Regulation (EU) No 1235/2010.

Legal reference

Article 28c(1), 2nd paragraph of Regulation (EC) No 726/2004 as amended in 2010 states that: *"The Agency shall make available promptly all suspected adverse reaction reports occurring in the Union to the World Health Organization"*.

In practice, this making available of European Union (EU) adverse reaction reports to the World Health Organization (WHO) will occur with a transfer of data from the EudraVigilance database (EV) to the VigiBase database held by the Uppsala Monitoring Centre (UMC), given that the UMC is the Foundation WHO Collaborating Centre for International Drug Monitoring.

Modalities and conditions

The following modalities and conditions apply to our making available EU adverse reaction reports to VigiBase, further referred to as "the data transfer":

- The data fields provided are those in accordance with the annex of this letter (and this will also be reflected in the revised EV access policy).
- Data stored in EV may be considered personal data within the meaning of EU data protection legislation, as individual case safety reports (ICSRs) reported to EV contain potentially identifiable data concerning the health of data subjects. By communication of a memorandum dated 16 November 2014, the EMA was informed by the legal counsel acting on behalf of the UMC that in

accordance with the Swedish Data Protection Acts (i.e. SFS 1998:204), Section 4 the UMC as a foundation established in Sweden is to be considered a "data controller" subject to the obligations provided for by the Swedish Data Protection Acts and under the supervision of the Swedish Data Protection Board (*"Datainspektionen"*). By means of accepting the modalities and conditions of this letter, the UMC provides a written assurance to the EMA that the data transferred from EV to VigiBase controlled by the UMC will be processed in accordance with Swedish data protection law and copies of the relevant documentation concerning the notification of the processing by the UMC under Section 39 or Section 36 of the Swedish Data Protection Acts as applicable are duly provided to the EMA.

- The UMC will take adequate measures for secure data storage and the protection of personal data. The data will be used for the sole purpose of carrying out the pharmacovigilance activities of the WHO Programme on International Drug Monitoring, and the UMC will make no onward transfer of the data and will not attempt or allow and/or procure third parties to re-identify data subjects from the pseudonymised data sets. The UMC will make publicly available only anonymised information concerning adverse reactions from VigiBase.
- The data will be provided electronically in ICH-E2B(R3) format and the EV schema reference will be provided in XML files.
- The files will be sent via a restful API established at the level of the UMC, provided that this fulfils the EMA's technical and IT data security requirements, as long as those requirements are in compliance with EU laws and regulations.
  - Under these conditions, the EMA will transfer the data daily five days after data receipt by EV or at the latest the following Friday of each week (or the subsequent working day at the EMA, should the Friday be an EMA holiday).
  - The message sender identifier "EVHUMAN" will be entered in the E2B(R3) fields N.1.3 & N.2.r.2 and message receiver identifier "UMCWHO" will be entered in the E2B(R3) N.1.4 & N.2.r.3.
- All versions of the ICSRs received from European Economic Area (EEA) countries will be provided to the UMC, including data as received by EV. Therefore the data will be sent with drug information as provided rather than as recoded by the EMA. The UMC will recode the data with their own drug dictionary. As some of the ICSR data may include either EV drug dictionary codes or ISO IDMP codes, the EMA will make available, upon ad hoc request by the UMC, the necessary data content required to identify the medicinal product. The UMC may indicate in future that they prefer receiving re-coded drug information from EV.
- The ICSRs will be provided to the UMC before the EMA has removed duplicated cases; however the EMA will provide in addition the master case report of each ICSR.
- It is foreseen that a period of testing will be carried out before the official exchange of information starts, to ensure that the data are provided in a format that can be used by the UMC. Therefore technical issues should not occur on a frequent basis in the operational phase.
- If issues with the data exchanged are subsequently found in the operational phase, the EV Helpdesk should be the first contact point for the UMC. Likewise, the EMA will notify any technical difficulty or delay in transfer to the UMC as soon as possible and keep the UMC updated on the progress addressing the difficulty until the problem is solved.
- The above conditions are subject to regular review, given potential changes in health data security, policies and regulation. The first review date will occur in two years' time, unless an event occurs which necessitates earlier review. Any review will include setting the date for the following review. The UMC undertakes to inform immediately the EMA of any event or change in its operation of the

VigiBase database that could have an effect on the UMC's capacity to meet its obligations set out in this letter or that could impact on the EMA's data transfer.

We will be grateful for your review and written acceptance of above modalities and conditions.

The EMA will agree with you a start date for the data transfer, following your written acceptance and the successful audit of the EV functionality. While Regulation (EC) No 726/2004 as amended in 2010 came into force on 1 July 2012, the new provision concerning the making available of EU adverse reaction reports to the WHO only applies following successful audit and release of enhanced functionalities of EV in accordance with Article 24(2) of this Regulation. The EMA will also agree a timeframe with the EEA national competent authorities when they should stop sending ICSRs to the UMC.

We thank you for your collaboration throughout the development phase of above modalities and conditions and look forward to continued collaboration,

Andreas Pott
Deputy Executive Director

Annex: Data fields

ICH/EU E2B(R3) Data Elements in line with EU ISCR Implementation Guide		
ICH/EU	**ICSR ICH E2B(R3) Element Reference**	**DATA ELEMENT NAME**
ICH	**N.1 ICH ICSR Transmission Identification (batch wrapper)**	
ICH	N.1.1	Types of Message in batch
ICH_CSV	N.1.1.CSV	Types of Message in batch Code system version
ICH	N.1.2	Batch Number
ICH	N.1.3	Batch Sender Identifier
ICH	N.1.4	Batch Receiver Identifier
ICH	N.1.5	Date of Batch Transmission
ICH	**N.2.r ICH ICSR Message Header (message wrapper) (repeat as necessary)**	
ICH	N.2.r.1	Message Identifier
ICH	N.2.r.2	Message Sender Identifier
ICH	N.2.r.3	Message Receiver Identifier
ICH	N.2.r.4	Date of Message Creation
ICH	**C.1 Identification of the Case Safety Report**	
ICH	C.1.1	Sender's (case) Safety Report Unique Identifier
ICH	C.1.2	Date of Creation
ICH	C.1.3	Type of Report
ICH_CSV	C.1.3.CSV	Type of Report Code system version
ICH	C.1.4	Date Report Was First Received from Source
ICH	C.1.5	Date of Most Recent Information for This Report
ICH	**C.1.6.1.r Identification of the Case Safety Report**	
ICH	C.1.8.1	Worldwide Unique Case Identification
ICH	C.1.8.2	First Sender of This Case
ICH_CSV	C.1.8.2.CSV	First Sender of This Case Code system version

ICH	C.1.9.1	Other Case Identifiers in Previous Transmissions
ICH	**C.1.9.1.r Source(s) of the Case Identifier(s) (repeat as necessary)**	
ICH	C.1.9.1.r.1	Source(s) of the Case Identifier
ICH	C.1.9.1.r.2	Case Identifier(s)
ICH	**C.1.10.r Identification Number of the Report Which Is Linked to This Report (repeat as necessary)**	
ICH	C.1.10.r	Identification Number of the Report Which Is Linked to This Report
ICH	C.1.11.1	Report Nullification / Amendment
ICH_CSV	C.1.11.1.CSV	Report Nullification / Amendment Code system version
ICH	C.1.11.2	Reason for Nullification / Amendment
ICH	**C.2.r Primary Source(s) of Information (repeat as necessary)**	
ICH	C.2.r.3	Reporter's Country Code
ICH	C.2.r.4	Qualification
ICH_CSV	C.2.r.4.CSV	Qualification Code system version
ICH	C.2.r.5	Primary Source for Regulatory Purposes
ICH	**C.3 Information on Sender of Case Safety Report**	
ICH	C.3.1	Sender Type
ICH_CSV	C.3.1.CSV	Sender Type Code system version
ICH	C.3.2	Sender's organisation
ICH	**C.4.r Literature Reference(s) (repeat as necessary)**	
ICH	C.4.r.1	Literature Reference(s)
ICH	**C.5 Study Identification**	
ICH	**C.5.1.r Study Registration (repeat as necessary)**	
ICH	C.5.1.r.1	Study Registration Number
ICH	C.5.2	Study Name
ICH	C.5.3	Sponsor Study Number
ICH	C.5.4	Study Type Where Reaction(s) / Event(s) Were Observed
ICH_CSV	C.5.4.CSV	Study Type Where Reaction(s) / Event(s) Were Observed Code system version

ICH	D. Patient Characteristics	
ICH	**D.2 Age Information**	
ICH	D.2.2a	Age at Time of Onset of Reaction / Event (number)
ICH	D.2.2b	Age at Time of Onset of Reaction / Event (unit)
ICH	D.2.3	Patient Age Group (as per reporter)
ICH_CSV	D.2.3.CSV	Patient Age Group (as per reporter) Code system version
ICH	D.5	Sex
ICH	D.6	Last Menstrual Period Date
ICH	**D.7.1.r Structured Information on Relevant Medical History (repeat as necessary)**	
ICH	D.9.1	Date of Death
ICH	**D.9.2.r Reported Cause(s) of Death (repeat as necessary)**	
ICH	D.9.2.r.1a	MedDRA Version for Reported Cause(s) of Death
ICH	D.9.2.r.1b	Reported Cause(s) of Death (MedDRA code)
ICH	D.9.3	Was Autopsy Done?
ICH	**D.9.4.r Autopsy-determined Cause(s) of Death (repeat as necessary)**	
ICH	D.9.4.r.1a	MedDRA Version for Autopsy-determined Cause(s) of Death
ICH	D.9.4.r.1b	Autopsy-determined Cause(s) of Death (MedDRA code)
ICH	**D.10 For a Parent-Child / Foetus Report, Information Concerning The Parent**	
ICH	D.10.2.2a	Age of Parent (number)
ICH	D.10.2.2b	Age of Parent (unit)
ICH	D.10.3	Last Menstrual Period Date of Parent
ICH	D.10.6	Sex of Parent
ICH	**E.i Reaction(s)/Event(s) (repeat as necessary)**	
ICH	E.i.2.1a	MedDRA Version for Reaction / Event
ICH	E.i.2.1b	Reaction / Event (MedDRA code)
ICH	E.i.3.1	Term Highlighted by the Reporter

ICH_CSV	E.i.3.1.CSV	Term Highlighted by the Reporter Code system version
ICH	E.i.3.2a	Results in Death
ICH	E.i.3.2b	Life Threatening
ICH	E.i.3.2c	Caused / Prolonged Hospitalisation
ICH	E.i.3.2d	Disabling / Incapacitating
ICH	E.i.3.2e	Congenital Anomaly / Birth Defect
ICH	E.i.3.2f	Other Medically Important Condition
ICH	E.i.4	Date of Start of Reaction / Event
ICH	E.i.5	Date of End of Reaction / Event
ICH	E.i.6a	Duration of Reaction / Event (number)
ICH	E.i.6b	Duration of Reaction / Event (unit)
ICH	E.i.7	Outcome of Reaction / Event at the Time of Last Observation
ICH_CSV	E.i.7.CSV	Outcome of Reaction / Event at the Time of Last Observation Code system version
ICH	E.i.8	Medical Confirmation by Healthcare Professional
ICH	E.i.9	Identification of the Country Where the Reaction / Event Occurred
ICH	**G.k Drug(s) Information (repeat as necessary)**	
ICH	G.k.1	Characterisation of Drug Role
ICH_CSV	G.k.1.CSV	Characterisation of Drug Role Code system version
ICH	G.k.2.1.1a	MPID Version Date / Number
ICH	G.k.2.1.1b	Medicinal Product Identifier (MPID)
ICH	G.k.2.1.2a	PhPID Version Date/Number
ICH	G.k.2.1.2b	Pharmaceutical Product Identifier (PhPID)
ICH	G.k.2.2	Medicinal Product Name as Reported by the Primary Source
EU	G.k.2.2.EU.1	Name part - Invented name
EU	G.k.2.2.EU.2	Name part - Scientific name
EU	G.k.2.2.EU.3	Name part - Trademark name
EU	G.k.2.2.EU.4	Name part - Strength name

EU	G.k.2.2.EU.5	Name part - Form name
EU	G.k.2.2.EU.6	Name part - Container name
EU	G.k.2.2.EU.7	Name part - Device name
EU	G.k.2.2.EU.8	Name part - Intended use name
EU	**G.k.2.2.EU.9 Device component (repeat as necessary)**	
EU	G.k.2.2.EU.9.r.1	Device Component name (free text)
EU	G.k.2.2.EU.9.r.2	Device Component TermID version Date/Number
EU	G.k.2.2.EU.9.r.3	Device Component TermID
EU	G.k.2.2.EU.9.r.4	Device serial number
ICH	**G.k.2.3 Substance / Specified Substance Identifier and Strength (repeat as necessary)**	
ICH	G.k.2.3.r.1	Substance / Specified Substance Name
ICH	G.k.2.3.r.2a	Substance/Specified Substance TermID Version Date/Number
ICH	G.k.2.3.r.2b	Substance/Specified Substance TermID
ICH	G.k.2.3.r.3a	Strength (number)
ICH	G.k.2.3.r.3b	Strength (unit)
ICH	G.k.2.4	Identification of the Country Where the Drug Was Obtained
ICH	G.k.3.1	Authorisation / Application Number
ICH	G.k.3.3	Name of Holder / Applicant
ICH	**G.k.4.r Dosage and Relevant Information (repeat as necessary)**	
ICH	G.k.4.r.1a	Dose (number)
ICH	G.k.4.r.1b	Dose (unit)
ICH	G.k.4.r.2	Number of Units in the Interval
ICH	G.k.4.r.3	Definition of the Time Interval Unit
ICH	G.k.4.r.4	Date and Time of Start of Drug
ICH	G.k.4.r.5	Date and Time of Last Administration
ICH	G.k.4.r.6a	Duration of Drug Administration (number)
ICH	G.k.4.r.6b	Duration of Drug Administration (unit)
ICH	G.k.4.r.8	Dosage Text
ICH	G.k.4.r.9.1	Pharmaceutical Dose Form (free text)

ICH	G.k.4.r.9.2a	Pharmaceutical Dose Form TermID Version Date/Number
ICH	G.k.4.r.9.2b	Pharmaceutical Dose Form TermID
ICH	G.k.4.r.10.1	Route of Administration (free text)
ICH	G.k.4.r.10.2a	Route of Administration TermID Version Date / Number
ICH	G.k.4.r.10.2b	Route of Administration TermID
ICH	G.k.4.r.11.1	Parent Route of Administration (free text)
ICH	G.k.4.r.11.2a	Parent Route of Administration TermID Version Date / Number
ICH	G.k.4.r.11.2b	Parent Route of Administration TermID
ICH	G.k.5a	Cumulative Dose to First Reaction (number)
ICH	G.k.5b	Cumulative Dose to First Reaction (unit)
ICH	G.k.6a	Gestation Period at Time of Exposure (number)
ICH	G.k.6b	Gestation Period at Time of Exposure (unit)
ICH	**G.k.7.r Indication for Use in Case (repeat as necessary)**	
ICH	G.k.7.r.2a	MedDRA Version for Indication
ICH	G.k.7.r.2b	Indication (MedDRA code)
ICH	G.k.8	Action(s) Taken with Drug
ICH_CSV	G.k.8.CSV	Action(s) Taken with Drug code system version
ICH	**G.k.9.i Drug-reaction(s) / Event(s) Matrix (repeat as necessary)**	
ICH	G.k.9.i.1	Reaction(s) / Event(s) Assessed
ICH	G.k.9.i.2.r.1	Source of Assessment
EU	G.k.9.i.2.r.1.EU.1	EU Source of Assessment
EU_CSV	G.k.9.i.2.r.1.EU.1.CSV	EU Source of Assessment Code system version
ICH	G.k.9.i.2.r.2	Method of Assessment
EU	G.k.9.i.2.r.2.EU.1	EU Method of Assessment
EU_CSV	G.k.9.i.2.r.2.EU.1.CSV	EU Method of Assessment Code system version
ICH	G.k.9.i.2.r.3	Result of Assessment
EU	G.k.9.i.2.r.3.EU.1	EU Result of Assessment
EU_CSV	G.k.9.i.2.r.3.EU.1.CSV	EU Result of Assessment Code system version

ICH	G.k.9.i.3.1a	Time Interval between Beginning of Drug Administration and Start of Reaction / Event (number)
ICH	G.k.9.i.3.1b	Time Interval between Beginning of Drug Administration and Start of Reaction / Event (unit)
ICH	G.k.9.i.3.2a	Time Interval between Last Dose of Drug and Start of Reaction / Event (number)
ICH	G.k.9.i.3.2b	Time Interval between Last Dose of Drug and Start of Reaction / Event (unit)
ICH	G.k.9.i.4	Did Reaction Recur on Re-administration?
ICH_CSV	G.k.9.i.4.CSV	Did Reaction Recur on Re-administration? Code system version
ICH	**G.k.10.r Additional Information on Drug (repeat as necessary)**	
ICH	G.k.10.r	Additional Information on Drug (coded)