

Electronic exchanges of individual case safety reports (ICSRs) with Afssaps

Information for pharmaceutical companies
June 2009. To replace the document published in October 2008.

Introduction

This document concerns the electronic transmission of adverse drug reaction (ADR) case reports occurring after the marketing authorisation, in accordance with the regulations in force: Regulation No. 726/2004, modified Directive 2001/83/EC, article R. 5121-171 and R. 5121-152 of the French public health code (decree No. 2007-1860 of 26 December 2007).

The transmission of suspected, unexpected and serious adverse reactions (SUSARs) occurring within the framework of interventional clinical trials, is not dealt with in this document.

All marketing authorisation holders situated in the European Economic Area are responsible for setting up a system which provides for the electronic transmission to the health authorities of observations of adverse reactions occurring after the entry of medicines on the market, in accordance with the ICH and Community guidelines.

**As such, the pharmacovigilance department of Afssaps has been equipped with a new software package which conforms to the international standards for electronic exchanges on pharmacovigilance Individual Case Safety Reports (ICSRs).*

This application will be able to issue and receive ICSRs in the form of XML files conforming to ICH E2B(R2), M1 and M2(M) (DTD version 2.1) guidelines.

The global operation of the EudraVigilance electronic exchanges community and the terms and conditions of registration within this community are set out in detail on the Internet site of the European EudraVigilance database (<http://eudravigilance.emea.europa.eu>).

The Afssaps application will use the routing functionalities of the EudraVigilance gateway (EV ESTR1 Gateway) (<http://eudravigilance.emea.europa.eu/human/evGatewayu01.asp>). This gateway will enable ICSRs to be exchanged in both directions between pharmaceutical companies and health authorities, without the case reports being loaded in the EudraVigilance European database. This gateway will also enable pharmaceutical companies and health authorities to load case reports in the European database when the latter is the recipient of the messages.

A) Information for pharmaceutical companies which already transmit or which are capable of transmitting to Eudravigilance (EV)

A-1 Transitory dispositions for the transmission to Afssaps of serious adverse reactions occurring in France

For pharmaceutical companies which **already transmit to EV** observations of serious adverse reactions as well as any transmission of infectious agents occurring in France (resulting from spontaneous reporting after the marketing authorisation, or through a Temporary Authorisation for Use (TAU), or during non interventional studies), transmission by fax and/or letter, in the form of CIOMS-I forms to the Afssaps' pharmacovigilance department can be avoided. The pharmacovigilance department will query the EV database daily to extract and evaluate these cases transmitted by pharmaceutical companies to EV, thereby making it possible to continue the watch activity over all cases reported in France.

Pharmaceutical companies which **are capable of transmitting to EV** may adopt the same methods and no longer send reports of serious adverse reactions occurring in France by fax and/or letter.

These reports of serious adverse reactions will be transmitted without delay and at the latest within 15 days following their receipt by the entity responsible for placing the medicinal product on the market..

This phase will be transitory and followed by the definitive phase which will enable pharmaceutical companies to transmit electronically directly to Afssaps (as described in the introduction to this document *). Afssaps will then be responsible for the electronic retransmission to EMEA (via the EudraVigilance database).

The Receiver ID for this transitory phase is: **EVHUMAN**; the Receiver ID for the definitive phase will be: AFSSAPS.

A-2 Definitive conditions for the transmission to Afssaps of ADRs occurring outside France with a product which has a marketing authorisation in France or which is available in France through a temporary authorisation for use

ADRs from EEA excluding France

When France is designated as Reference Member State (RMS) in connection with the registration of a product according to the decentralised procedure or the mutual recognition procedure, or when a product is available in France through a TAU, ADRs as well as any transmission of infectious agents associated with this medicine or product and occurring in any other State of the European Economic Area will be made available to Afssaps through the intermediary of the EV-PM module of the EudraVigilance European database, according to current procedures in occurrence countries. In order to avoid duplicate reporting to EV, the MAH should determinate for each European Member state if domestic cases are being reported to EudraVigilance by the local National Competent Authority (NCA). If they are already reported by the local NCA or the local MAH, no additional transmission is necessary.

These transmission dispositions for such reports are definitive and transmission by fax and/or letter is no longer necessary.

ADRs from third countries (outside the EEA)

Serious and unexpected ADRs as well as any transmission of infectious agents occurring in the territory of third countries, that is to say, outside the European Economic Area, will be made available to Afssaps through the intermediary of the EV-PM module of the EudraVigilance European database (Receiver ID: **EVHUMAN**).

These serious and unexpected ADRs will be transmitted without delay and at the latest within 15 days following their receipt by the MAH.

However, in accordance with the guidelines of Volume 9A, all ADRs (expected or otherwise) may be transmitted electronically to EudraVigilance.

These transmission dispositions for such reports are definitive and transmission by fax and/or letter is no longer necessary.

Technical specifications

The validation rules (business rules) are those used by the EudraVigilance system (Doc. Ref. EMEA/H/20665/04/Final).

The MedDRA terms used must derive from the latest published version of this terminology. The lowest level terms (LLTs) must also be "current" in this latest version. The notion of latest published version must conform to the recommendations of the MSSO (MedDRA Maintenance and Support Services Organization) and the EudraVigilance Expert Working Group of EMEA.

Languages accepted by Afssaps within the framework of the electronic transmission of ICSRs are French and English.

For cases occurring in France: the drug causality assessment according to the French method of imputability must be included in the ICSRs in section B.4.k.18 (Relatedness of drug to reaction(s)/event(s)) of the E2B message. The method used (B.4.k.18.3) must be marked "FRENCH IMPUTABILITY METHOD" and the result (B.4.k.18.4) indicated in "CxSyBz" format (where x, y and z represent the chronological, semiological and bibliographic imputability scores respectively).

Specific situations

- For literature reports, it is recommended to send by fax or letter the full article attached with the referencing number of the case report
- These rules do not modify the current transmission procedures to the regional pharmacovigilance centre responsible for a national survey .

B) Information for pharmaceutical companies which are not yet able to transmit to Eudravigilance

A system enabling electronic transmission to EV must be set up in order to be brought into compliance with the regulations in force.

In the meantime, the adverse effects listed below will be transmitted to the pharmacovigilance department of Afssaps without delay and at the latest within 15 days following their receipt by the MAH, by fax and/or by letter, in the form of CIOMS-I forms :

- Serious ADRs as well as any transmission of infectious agents occurring in France, resulting from spontaneous reporting after the product becomes available on the market, or through a TAU, or during non interventional studies
- Serious and unexpected ADRs as well as any transmission of infectious agents occurring in the territory of third countries, that is to say, outside the European Economic Area
- And where France is designated as the Reference Member State within the framework of registration of a product according to the decentralised procedure or the mutual recognition procedure, or when a product is available in France through a TAU, serious ADRs and the transmission of infectious agents which are liable to be due to that medicine or product and which occur in any other State of the European Economic Area,

C) Information for all

Reports of serious adverse reactions notified to afssaps by health professionals via the network of regional pharmacovigilance centres (crpv) and the national pharmacovigilance database have been transmitted electronically by Afssaps since 20 November 2005 to EMEA (*via* the EudraVigilance database) and by letter (electronically in future) to the marketing body (in the case of drugs identified as suspect or interacting), without delay and at the latest within 15 days following receipt of this information. This system has not been modified. It should be noted that these reports must not be retransmitted by the pharmaceutical companies to EV in order to avoid duplication.

These conditions are applicable on publication but not before informing Afssaps by letter :

- Of the ID used within the framework of transmission to Eudravigilance
- And of the date of interruption of the transmission of serious adverse effects by letter and/or fax

to the following address:

Dr Carmen Kreft-Jais – Pharmacovigilance Department
143, boulevard Anatole France – 93285 Saint Denis Cedex
The subject heading of this letter will be: electronic transmission of SAEs.

For information, please send an e-mail to : pharmacovigilance@afssaps.sante.fr