swissmedic

# Information sheet

## MB Guidance for Industry on the electronic exchange of ICSRs in E2B (R3) format through B2B gateway

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|---|---|
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| **1.1** | **04.09.2024** | | **Chapter 6.3: Deletion of field C.2.r.3 from the list of masked fields for export** | **bop, gem, stt, zma** |
| **1.0** | **26.08.2024** | | **New document** | **bop, gem, isi, sgu, stt, zma** |

# 1 Introduction

This guidance is intended to assist marketing authorisation holders (MAHs) in preparing the electronic transmission of Individual Case Safety Reports (ICSRs) in pharmacovigilance in E2B(R3) format. This document discusses general issues related to the electronic transmission of ICSRs with the goal of achieving common standards for a successful electronic exchange of ICSRs with Swissmedic.

Swissmedic supports the electronic transmission of ICSRs. In developing its electronic reporting systems Swissmedic has the ability to generate and receive electronic reports that comply with the ICH standards.

The electronic reporting requirements apply to all MAHs which have ICH-E2B compliant pharmacovigilance systems.

To make these ICH standards and electronic case reporting more useful and compliant with changing pharmacovigilance practices, a new version referred to as ICH E2B(R3) was finalised in July 2013.

ICH agreed to use the International Organization for Standardization (ISO) Individual Case Safety Report (ICSR) standard ISO EN 27953-2 to meet the reporting requirements for E2B(R3):

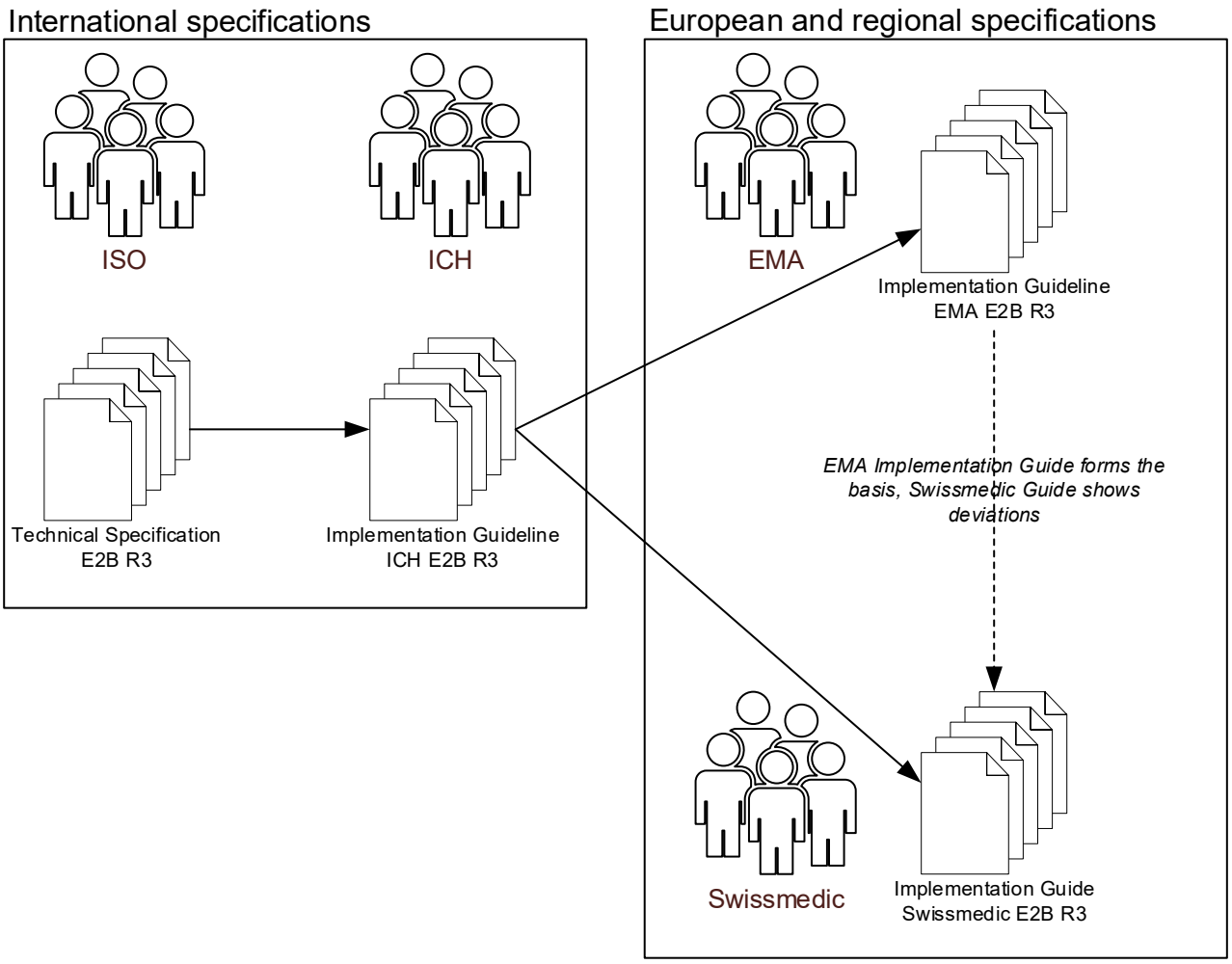
- ISO/HL7 27953-2:2011 - Health informatics — Individual case safety reports (ICSRs) in pharmacovigilance — Part 2: Human pharmaceutical reporting requirements for ICSR

Swissmedic has started the changeover of the reporting process for ICSRs from E2B(R2) to E2B(R3). The transition will be implemented in a step-by-step process to convert all MAHs which already submit ICSRs via the gateway to the new format. The changeover to E2B(R3) in Switzerland will be adapted as far as possible to the recommendations and procedures of the European Medicines Agency with regard to data elements and message specifications (see 11.2 Relevant documents). Differences in the requirements between the EMA and Swissmedic will be addressed in chapter 5 of this document.

This guidance also specifies the technical requirements and the process of transmission of Safety and Acknowledgement Messages through the B2B gateway and describes the obligations that stakeholders must adhere to in this process to ensure successful electronic communication. The Electronic Data Interchange (EDI) process is based on the electronic exchange of a Safety Message between a Sender and a Receiver. The Acknowledgement Message confirms the receipt and the outcome of the validation of a Safety Message and completes the EDI process.

For companies which do not fulfil the conditions for introducing an exchange of ICSRs via the B2B gateway, the electronic reporting system ElViS (Electronic Vigilance System) will be retained in the medium term. You can find further details about ElViS on the Swissmedic website (Reporting/submitting suspected adverse drug reactions by pharmaceutical companies (swissmedic.ch)).

## 2 Context of the standards




## 3 Goal

This guideline describes the requirements for MAHs to participate in the new E2B(R3) electronic exchange of ICSR between Swissmedic and MAHs (bidirectional) and provides guidance on the technical and procedural standards applied by Swissmedic.

## 4 Scope

MAHs are obliged by law to submit certain ICSRs (relating to human medicines) to Swissmedic, and Swissmedic forwards ICSRs received from other sources to the MAH concerned. The scope of this guideline covers Swissmedic and all MAHs for medicinal products and therapeutic biologicals for human use marketed in Switzerland (for reports from Liechtenstein, please refer to the corresponding FAQ on the Swissmedic website: FAQs: General Pharmacovigilance (swissmedic.ch)). It currently refers only to ICSRs from the post-authorisation phase.

# 5 General principles / information

The following table summarises relevant deviations from EMA business rules when post-marketing ICSRs are submitted to Swissmedic via the B2B gateway in E2B(R3) format.

## 5.1 Deviations

| EU Individual Case Safety Report (ICSR) Implementation Guide | **Europe** | **Switzerland** |
|---|---|---|
| Page 5 | EudraVigilance (EV)<br>Reports can be submitted only electronically | Swissmedic Drug Safety System<br>Reports can be submitted only electronically<br><br>Exception: marketing authorisation holders (MAHs) based outside Switzerland: Reporting/submitting suspected adverse drug reactions by pharmaceutical companies (swissmedic.ch) |
| Page 7 | EV Post-Authorisation and Clinical Trial Module | Only Post-Authorisation<br><br>Currently no Clinical Trial Module (SUSARs from notified studies are reported to KLV) |
| Page 8 | Notification periods 15 days (serious) or 90 days (non-serious | Notification periods 15 days (serious) or 60 days (non-serious) |
| Page 9 | Message Flow in the EU Network | No Message Flow in the EU Network |
| Page 13 | EVWEB and WEB Trader | ElViS is an alternative to the B2B gateway for the exchange of ISCRs between MAH and Swissmedic |
| Page 14 | Registration and test process for gateway users | Specific registration and test process for gateway users |
| Page 24 | Data exchange between EV and national authorities | No data exchange with other authorities |
| Page 26 | SUSARs from clinical studies are documented in the Clinical Trial Module of EV. | SUSARs from notified clinical studies are reported to the Clinical Trials Division. No documentation in the Swissmedic drug safety system. |

| | | |
|---|---|---|
| Page 29 | Literature monitoring for selected substances | Literature monitoring is the responsibility of the marketing authorisation holder. |
| Page 29 & 99 | Duplicates: master case procedure | Duplicates: Swissmedic's procedure for duplicates will be published at a later date. |
| Page 38 | Causality assessment is not mandatory for post-authorisation ICSRs | For requirements regarding the medical assessment of ICSRs see relevant FAQ on Swissmedic website |
| General deviation: several different pages in the guide | One ICH ICSR batch can contain one or more safety reports (ICSRs). | One ICH ICSR batch can contain only one safety report (ICSRs). |

## 5.2 Electronic exchange / reporting of ICSRs

Electronic transmission of ICSRs is a two-way process which affects only the reporting mechanism. The legal reporting requirement does not change (see TPA Art. 58, 59 and TPO Art. 61-66). According to the legislation, MAHs are required to submit the following Individual Case Safety Reports (ICSRs), also referred to as safety reports, to Swissmedic:

- all Swiss spontaneous serious ICSRs and non-serious unexpected ICSRs (including ICSRs from observational / non-interventional studies, PASS, registries, compassionate use, etc.)
- abuse
- medication errors and “near misses” on an individual basis with a focus on possible risk minimisation
- lack of efficacy according to the respective FAQ on the Swissmedic website; FAQs: General Pharmacovigilance (swissmedic.ch)

This note for guidance does not currently address:

- SUSARs (suspected unexpected serious adverse reactions reports) from Interventional Clinical Trials notified to Swissmedic.

To be valid for reporting to Swissmedic, an ICSR must fulfil four minimum reporting criteria: an identifiable reporter, an identifiable patient, a reaction and a suspected medicinal product.

The complete information for an ICSR that is available to the sender should be reported in the structured fields and in the narrative. Any supporting information related to the case must be sufficiently described within the ICSR and should be listed in section C.1.6.1.r.1 (document list), C.4.r./C.4.r.1 (literature reference) or the narrative (H/H.1). See chapter 11.2.
In addition, whenever more recent important information on an individual case is submitted (e.g. follow-up information, ICSR highlighted for nullification), the complete (entire) information on the case must be provided and not just partial information, e.g. changes or updates.
For those ICSRs that are highlighted for nullification (‘Report nullification’, C.1.11.1, set to ‘nullified’) the reasons for nullification must also be indicated (C.1.11.2), see chapter 11.2.

For ICSRs arising from literature, the adequate/correct reference must be placed in the section C.4.r./C.4.r.1 (literature reference). The article itself should be attached as a document to the ICSR (see chapter 5.3).

## 5.3 Attachments

In order to provide supplemental information, the sender of an ICSR can attach documents to the ICSR message itself. Attachments are provided as in-line data transmitted using the encapsulated data type.
The main use of this data element will be to provide literature articles (see chapter 5.2). Please note that for marketing authorisation holders which send ICSRs in R3 format it is mandatory to send literature articles as additional documents to ICSR message itself via the gateway. Please refrain in this scenario from sending literature articles via mail.
Other documents made available by a primary source (e.g. autopsy reports, ECG strips, chest X-rays or photographs, etc.) can also be attached using the same method. However, additional documents should not be routinely attached to ICSRs but only at the request of the receiver on a case-by-case basis or where the correct medical interpretation of the ICSR can only be made with access to the attachment(s).

| Supported file types | File type | Media type (values) |
|---|---|---|
| PDF | Portable Document Format | application/pdf |
| JPEG/JPG | Joint Photographic Experts Group | image/jpeg |
| TXT | Text file | text/plain |
| RTF | Rich text file | text/rtf |
| TIFF/TIF | Tagged Image File Format | image/tiff |
| HTML | HyperText Markup Language | text/html |
| Doc | Word document | application/msword |
| Docx | Office Open XML (ISO/IEC 29500) word-processing | application/vnd.openxmlformats-officedocument.wordprocessingml.document |
| XLS | Excel document | application/vnd.ms-excel |
| XLSX | Office Open XML (ISO/IEC 29500) spreadsheet | application/vnd.openxmlformats-officedocument.spreadsheetml.sheet |
| DICOM | Digital Imaging and Communications in Medicine | application/dicom |

## 5.4 Use of nullflavor flags

| Nullflavor flag - Exceptions to ICH E2B(R3) data element | Description |
|---|---|
| C.2.r.4 - Qualification | The reporter qualification is mandatory for all reporters, the use of a nullflavor is not permitted |
| C.4.r.1 - Literature reference(s) | For a report to be considered as a literature report the literature reference must be provided, the use of a nullflavor is not permitted |
| G.k.4.r.7 - Batch / lot number | The nullflavors “UNK” and “ASKU” should be provided for each reported suspect or interacting drug if no information is available |

In addition, there are data elements in the ICH E2B(R3) Implementation Guide that foresee the use of the nullflavor “MSK”, which indicates to the receiver of an ICSR that the (initial) sender holds this information but is/was unable to send it due to data protection / privacy reasons. It is acknowledged that for certain data elements that can identify an individual, such as the Patient (name or initials) (D.1 ICH E2B(R3)) or the Date of Birth (D.2.1 ICH E2B(R3)), the “MSK” flag can be appropriate (see chapter 6.3). However, in other E2B(R3) data elements use of the “MSK” flag is not considered valid for use in the EU and Switzerland as those data elements would not lead to the direct identification of an individual. The exceptions to ICH E2B(R3) Implementation Guide are detailed in the table below.

| **Nullflavor “MSK” flag - Exceptions to the ICH E2B(R3) Implementation Guide ICH E2B(R3) data element code** | **ICH E2B(R3) data element description** |
|---|---|
| D.5 | Patient Sex |
| D.6 | Patient Last Menstrual Period Date |
| D.7.1.r.2 | Medical History Start Date |
| D.7.1.r.3 | Medical History Continuing |
| D.7.1.r.4 | Medical History End Date |
| D.7.2 | Text for Relevant Medical History and Concurrent Conditions (not including reaction / event) |
| D.8.r.4 | Relevant Past Drug History Start Date |
| D.8.r.5 | Relevant Past Drug History End Date |
| D.9.1 | Date of Death |
| D.10.3 | Last Menstrual Period Date of Parent |
| D.10.6 | Sex of Parent |
| D.10.7.1.r.2 | Relevant Medical History and Concurrent Conditions of Parent Start Date |
| D.10.7.1.r.3 | Relevant Medical History and Concurrent Conditions of Parent Continuing |
| D.10.7.1.r.4 | Relevant Medical History and Concurrent Conditions of Parent End Date |
| D.10.8.r.4 | Relevant Past Drug History of Parent Start Date |
| D.10.8.r.5 | Relevant Past Drug History of Parent End Date |
| E.i.4 | Date of Start of Reaction / Event |
| E.i.5 | Date of End of Reaction / Event |
| G.k.4.r.4 | Date and Time of Start of Drug |
| G.k.4.r.5 | Date and Time of Last Administration |

## 5.5 Important notes

MAHs are advised to reduce the number of follow-ups to a minimum; only new and medically relevant information such as outcome, alternative medical conditions, other suspect drugs, results of performed investigations or any other data with an impact on causality should trigger follow-up information. Ideally, an initial case should be followed by one follow-up when the case is closed.

Further information on the current reporting obligations can be found on the Swissmedic homepage under FAQs on General Pharmacovigilance: FAQs: General Pharmacovigilance (swissmedic.ch)

### 5.6 The Swissmedic PV system and EMA guidelines

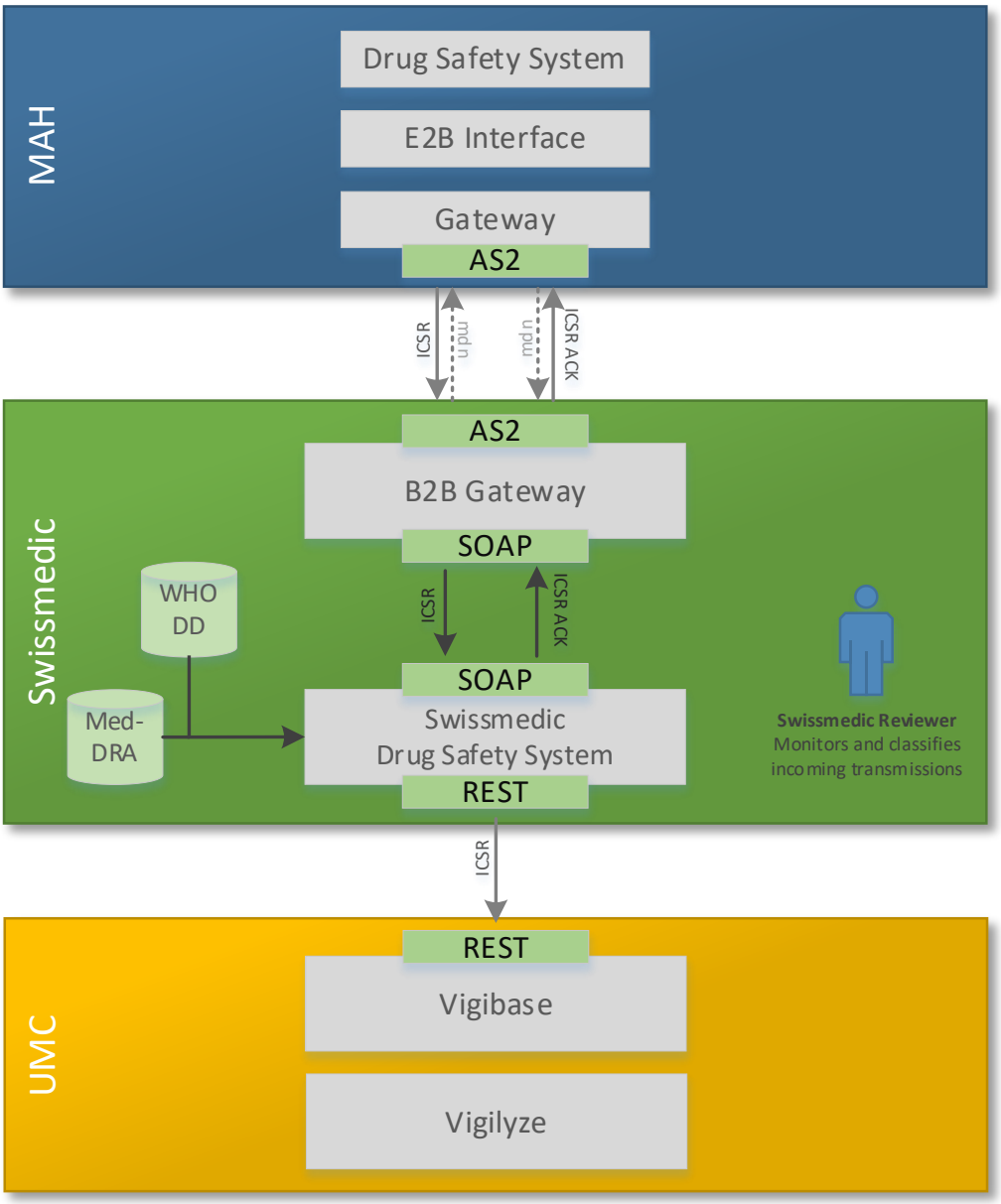
The Swissmedic drug safety system is designed on top of the E2B format with the aim of being E2B(R3) compatible. Therefore no major difficulties regarding E2B interpretation are expected. Safety and acknowledgement messages must follow the content and format of the respective EMA guidelines:

- E2B (R3) Step 5 Electronic transmission of individual case safety reports (ICSRs) - data elements and message specification - implementation guide (europa.eu) see chapter 11.2
- EU Individual Case Safety Report (ICSR)1 Implementation Guide (europa.eu), see chapter 11.2
- The XSD schema location for ICSRs, see chapter 11.2

## 6 Processing of safety reports (ICSRs)

The Swissmedic drug safety system has the ability to generate and receive electronic reports that comply with the ICH standards as detailed in E2B (M). The following chapter describes the processing and management of safety reports and some important standard procedures.

## 6.1 PV system overview



## 6.2 Import

It is important that MAHs comply with the checks listed below when submitting electronic ICSRs to ensure that reports are not automatically rejected (negative ACK log) by the system.

1. In the first step the drug safety system checks whether:
   - the incoming file is a valid xml file (as defined by W3C)
   - the safety message is in accordance with the EMA ICSR Schema Files (XSD), see chapter 11.2.
   - the sender information is complete (the fields “sender information”, “sender organisation” and “sender identifier”).

2. In the second step the drug safety system checks each safety report for:
   - field lengths
   - lexicon / dictionary values
   - a missing safety report ID
   - the worldwide unique number (report rejected if it is missing or if both authority numb and company numb are filled in)
   - a missing report type.

The Swissmedic PV system accepts MedDRA terminology and WHO Drug Dictionaries.

## 6.3 Export

The Swissmedic drug safety system uses MedDRA terminology (e.g. for indications, reactions, etc).

In order to be able to comply with the revised EMA business rules for preparing and processing ICSRs, a validation tool based on the EMA business rules is implemented in the Swissmedic system (see chapter 11.2).
The exported files are checked against the EMA business rules (see chapter 11.2). Some fields, however, cannot be validated or are not relevant.

The table below outlines these exceptions:

| E2B(R3) - Field | Name | Comments |
|---|---|---|
| N.1.1 | Type of Message in batch | Only one message header (N.2.r.) inside a batch wrapper accepted |
| N.1.1.CSV | Type of Message in batch code system version | |
| N.1.2 | Batch Number | |
| N.1.3 | Batch Sender Identifier | |
| N.1.4 | Batch Receiver Identifier | |
| N.1.5 | Date of Batch Transmission | |
| C.5.1.r.1 | Study Registration Number | Not relevant |
| C.5.1.r.2 | Study Registration Country | Not relevant |
| G.k.9.i.2.r.2.EU.1 | EU Method of Assessment | See FAQ on Swissmedic requirements for medical assessments of ICSRs |
| G.k.9.i.2.r.1.EU.1 | EU Source of Assessment | |
| G.k.9.i.2.r.2.E | EU Method of Assessment | |

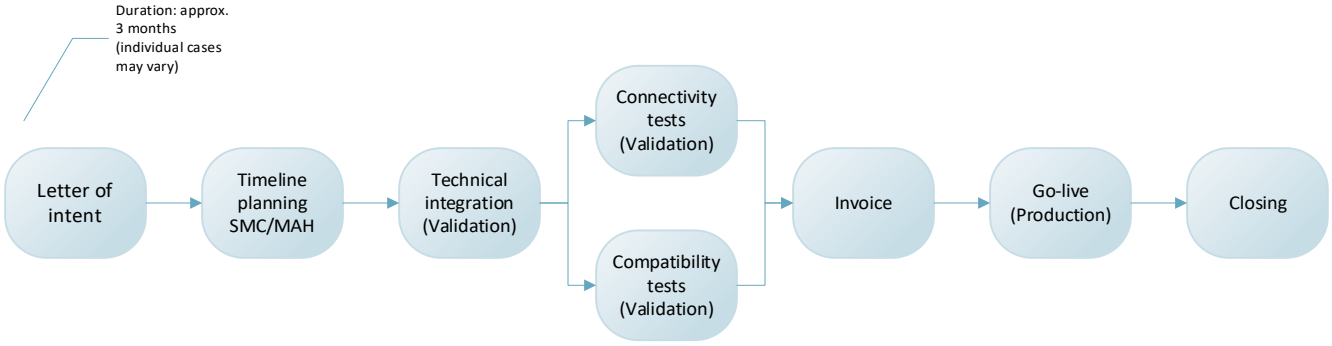
| E2B(R3) - Field | Name | Comments |
|---|---|---|
| U.1 | | |
| G.k.9.i.2.r.3.E<br>U.1 | EU Result of Assessment | |
| N.2.r.3<br>N.2.r.2 | Message Receiver Identifier<br>Message Sender Identifier | The Swissmedic identifier is “SM” for production |
| C.2.r.2.5<br>C.2.r.2.6 | reporterstate<br>reporterpostcode | Not relevant |

The table below contains fields that are masked by Swissmedic in ICSRs sent to the marketing authorisation holder via the B2B gateway.

| Data element | Field name | Nullflavor in ICSRs sent by Swissmedic |
|---|---|---|
| C.2.r.1.1 | Reporter’s Title | Masked |
| C.2.r.1.2 | Reporter’s Given Name | |
| C.2.r.1.3 | Reporter’s Middle Name | |
| C.2.r.1.4 | Reporter’s Family Name | |
| C.2.r.2.1 | Reporter’s Organisation | |
| C.2.r.2.2 | Reporter’s Department | |
| C.2.r.2.3 | Reporter’s Street | |
| C.2.r.2.4 | Reporter’s City | |
| C.2.r.2.5 | Reporter’s State or Province | |
| C.2.r.2.6 | Reporter’s Postcode | |
| C.2.r.2.7 | Reporter’s Telephone | |
| D.1 | Patient (name or initials) | |
| D.1.1.1 | Patient Medical Record Number(s) and Source(s) of the Record Number (GP Medical Record Number) | |
| D.1.1.2 | Patient Medical Record Number(s) and Source(s) of the Record Number (Specialist Record Number) | |
| D.1.1.3 | Patient Medical Record Number(s) and Source(s) of the Record Number (Hospital Record Number) | |
| D.1.1.4 | Patient Medical Record Number(s) and Source(s) of the Record Number (Investigation Number) | |
| D.2.1. | Date of Birth | |
| D.10.2.1 | Parent Identification | |
| D.10.1 | Date of Birth of Parent | |

# 7 Starting electronic submission

Before the electronic transmission of ICSRs can be initiated, MAHs should follow the steps indicated below.




## 7.1 Send letter of intent

A Letter of Intent for the Electronic Transmission of ICSRs must be sent to the PV Specialist (Process Specialist) at Swissmedic (see conditions on www.swissmedic.ch).
The Process Specialist will then contact the MAH to plan a time period for a gateway setup.

## 7.2 Test phase

During the test phase the currently established regulatory reporting mechanism remains unaffected.
It is recommended that the MAH keeps a copy of configuration settings including certificates (public key) used during the test phase to enable the MAH to reconstruct the identical test environment for subsequent testing at a later stage.

### 7.2.1 PV system compatibility test

For the tests the MAH and Swissmedic need to exchange and load the following XML test files into the drug safety system to check whether the E2B structure and the validation rules will work:

- an initial report (including medical and drug history)
- a follow-up report
- a linked parent/child report
- a non-interventional (observational) study report
- a case reported in the literature including the attached literature article
- a nullified / duplicate report

### 7.2.2 B2B gateway connection process

After configuration of the gateways (Swissmedic and MAH), it is necessary to test whether the gateways can communicate (technical layer AS2). The interoperability of the party's gateway with the Swissmedic gateway is tested. Senders may have to adopt hardware, software and data communication configurations to meet the recommended communication standards.
The three steps to connect to the B2B gateway are (1) system integration and test (test environment), (2) system configuration and end to end test between the drug safety systems (test environment) and, finally, (3) system configuration and pilot (productive environment).

### 7.2.3 Exchange certificates

Swissmedic is not mandating any particular software for the electronic communication of ICSRs. If the party's software is fully interoperable with the Swissmedic gateway, then the sender will receive certification from Swissmedic to use it. Swissmedic also needs the public certificate of each participating MAH.

## 7.3 Operational phase

Following successful completion of the operational test phase, the operational phase is initiated when electronic transmission of ICSRs replaces the currently established regulatory transmission between the parties.

## 7.4 What to do in case of system failure

### 7.4.1 Malfunction of the electronic pharmacovigilance system – Swissmedic

When Swissmedic detects a malfunction of the electronic pharmacovigilance system (database and/or gateway), Swissmedic investigates the root cause of the system failure and carries out a preliminary estimation of the expected system downtime within a maximum of 24 hours after detection of the system malfunction. Two scenarios are used:

Scenario B
If system downtime is estimated to be equal to or less than 5 calendar days, Swissmedic informs the respective MAH by e-mail that the electronic pharmacovigilance system is expected to be out of service for a maximum of 5 calendar days and that electronic case submission is delayed. The respective MAH will be informed by a separate e-mail to the same e-mail address once the system is up and running again. The situation is continuously monitored and if after 4 business days it is deemed unlikely that the system will be up and running again after 5 days, the failure is changed to scenario A. Swissmedic uses medical judgement to identify cases deemed critically important for processing under scenario A.

Scenario A
If system downtime is estimated to be more than 5 days, cases fulfilling the Swissmedic criteria for expedited reporting are sent via FileShare in E2B XML file format.

### 7.4.2 Malfunction of the electronic pharmacovigilance system – MAH

When an MAH detects a malfunction of the electronic pharmacovigilance system (database and/or gateway), the MAH investigates the root cause of the system failure and carries out a preliminary estimation of the expected system downtime within a maximum of 24 hours after detection of the system malfunction. Two scenarios are used:

Scenario B
If system downtime is estimated to be equal to or less than 5 calendar days, the MAH informs Swissmedic by e-mail to pvgateway@swissmedic.ch that the electronic pharmacovigilance system is expected to be out of service for a maximum of 5 calendar days and that electronic case submission will include all cases not successfully sent before (ACK log received from Swissmedic). Swissmedic will be informed by a separate e-mail to the same e-mail address once the system is up and running again. The situation is continuously monitored and if after 4 business days it is deemed unlikely that the system will be up and running again after 5 days, the failure is upgraded to scenario A. The MAH uses medical judgement to identify cases deemed critically important for processing under scenario A.

Scenario A
If system downtime is estimated to be more than 5 days, cases fulfilling the Swissmedic criteria for expedited reporting can be sent via FileShare in E2B XML file format. In this case, please contact Swissmedic via pvgateway@swissmedic.ch to initiate the necessary steps for data exchange via this channel. The MAH will assign a provisional case ID and will keep track of this number and provide the worldwide unique case identifier once the primary pharmacovigilance system is up and running again.

## 7.5 Processing and acknowledgement of receipt of ICSRs

The Swissmedic drug safety system performs a basic validation of any incoming ICSRs against the specified XML schema. The sender is responsible for including the correct ICSR message XML header as specified in I.C.3.1. If the sender has not included the correct schema reference in the XML header as indicated in I.C.3.1, the return of an Acknowledgment Message cannot be guaranteed.

- If a parsing error is detected by the Swissmedic drug safety system, the following scenarios may occur:
  If, during the process of parsing the ICSR, the Swissmedic drug safety system can detect a valid sender identifier, an Acknowledgement Message will be created and sent to the sender, listing the detected error. The *Transmission Acknowledgement Code* reported in the data element ICH E2B(R3) ACK.A.4 will be ‘AR’, i.e. no data extracted.

  If, during the process of parsing the ICSR, the Swissmedic drug safety system cannot detect a valid sender identifier, an Acknowledgement Message cannot be created as the sender cannot be identified. In this case no Acknowledgement Message will be returned. Senders of ICSRs should monitor for the absence of a receipt of acknowledgment. In this case contact Swissmedic via pvgateway@swissmedic.ch.
  If the process of parsing the ICSR is successful and the Swissmedic drug safety system cannot detect a valid receiver identifier, an Acknowledgement Message will be created and

sent to the sender, listing the detected error. The *Transmission Acknowledgement Code* reported in the data element ICH E2B(R3) *ACK.A.4* will be 'AR', i.e. no data extracted.

**ACK code AA:** Application Acknowledgement Accept (message successfully processed, no further action)
**ACK code AE:** Application Acknowledgment Error (error detected, error response has additional detail, some ICSR message(s) need further action)
**ACK code AR:** Application Acknowledgment Reject (parsing error, no data extracted, re-send the entire transaction)
The Acknowledgement Message can reflect two different types of transmission acknowledgements at ICSR level:
**ICSR code CA:** Commit Accept (the ICSR message was successfully loaded)
**ICSR code CR:** Commit Reject (the ICSR message contains a fatal error that prevents the ICSR from being loaded)

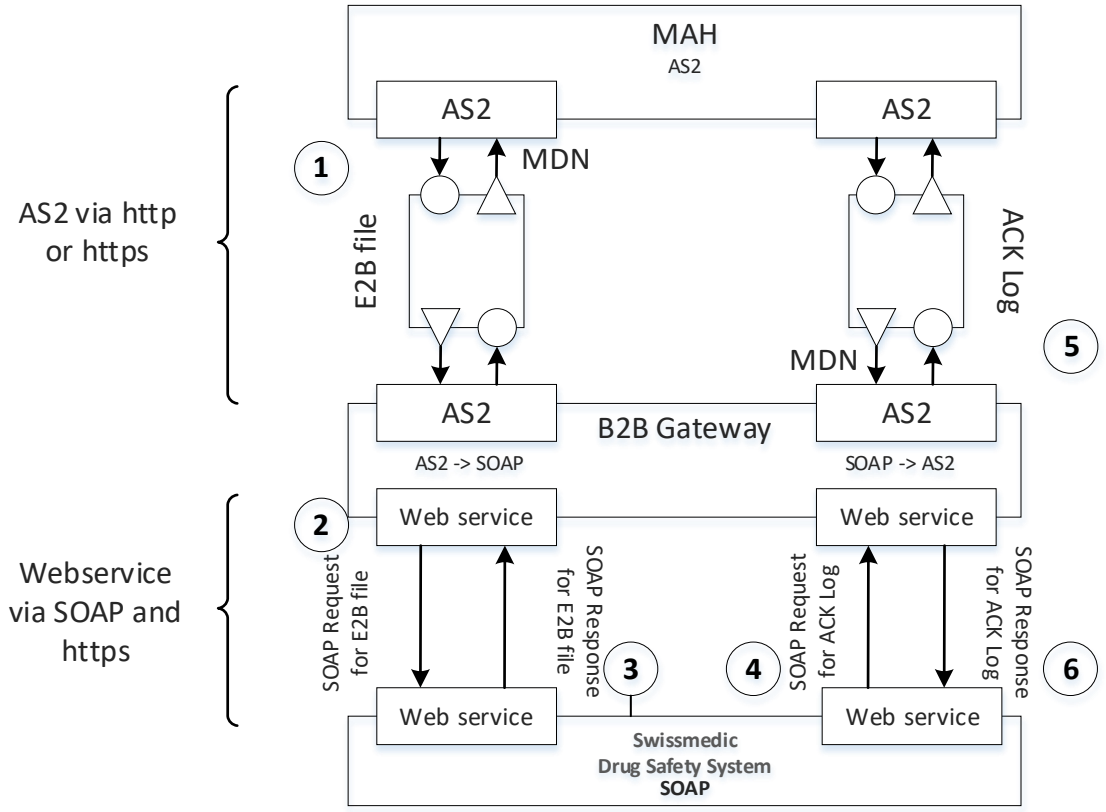
# 8 Description of the Swissmedic gateway

The Swissmedic gateway (IBM DataPower gateway) serves as a security multichannel gateway.

The Swissmedic gateway follows the ICH M2 Gateway Recommendation for the Electronic Transfer of Regulatory Information (see chapter 11.2).

## 8.1 Communication overview and process

### 8.1.1 Process MAH transmits E2B to Swissmedic




**1:** MAH transmits an E2B file to the B2B gateway via HTTP/S per AS2 HTTP interface (AS2 confirms with MDN)

**2:** The B2B gateway forwards the E2B file to the Swissmedic drug safety system via the web service (SOAP request)

**3:** The Swissmedic drug safety system answers via SOAP response to the B2B gateway.

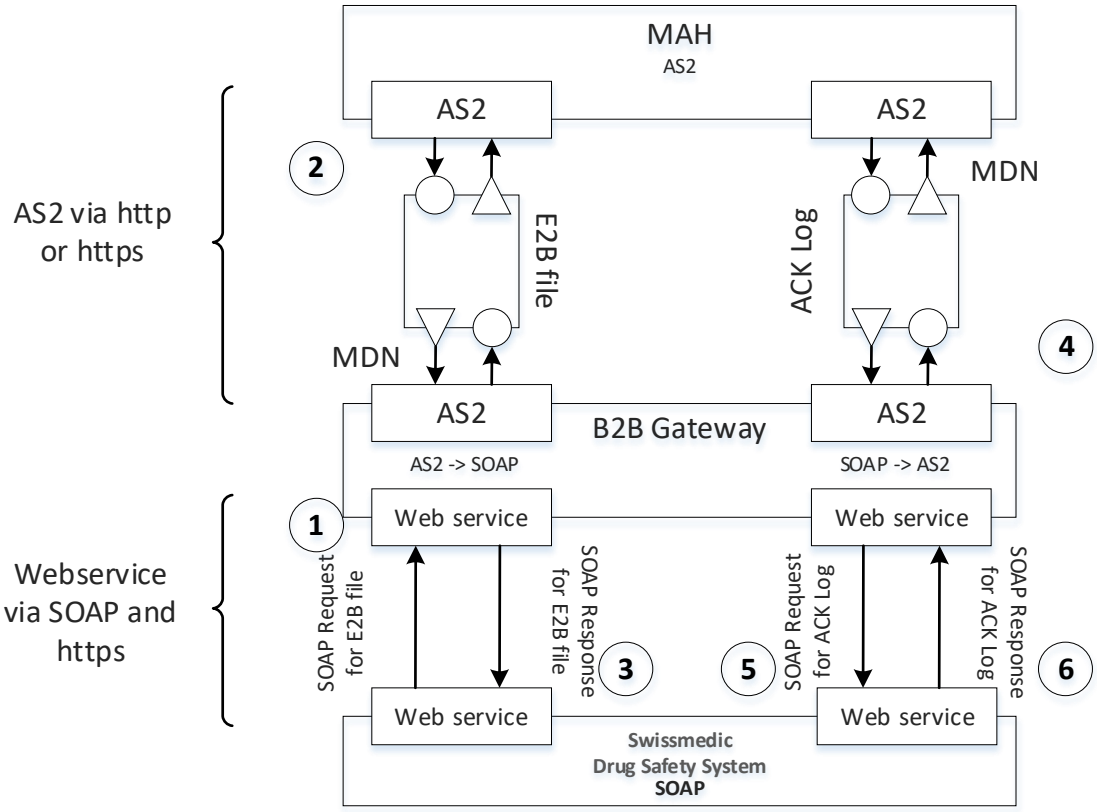
**4:** The Swissmedic drug safety system transmits an ACK log to the B2B gateway via the web service (SOAP request).

**5:** The B2B gateway forwards the ACK log to the respective MAH via HTTP/S per AS2 HTTP interface (AS2 confirms with MDN)

**6:** The B2B gateway answers via SOAP response to the Swissmedic drug safety system.

The B2B gateway stores the MDN temporarily in the file system (90 days). After 90 days the MDN will be stored for 10 years in a storage system.

### 8.1.2 Process Swissmedic transmits E2B to MAH




1. The Swissmedic drug safety system transmits an E2B file to an MAH via web service (SOAP request) to the B2B gateway.
2. The B2B gateway forwards the E2B file to the respective MAH via HTTP/S per AS2 HTTP interface (AS2 confirms with MDN)
3. The B2B gateway answers via SOAP response to the Swissmedic drug safety system
4. The MAH which received the E2B file transmits an ACK log to the B2B gateway via HTTP/S per AS2 HTTP interface (AS2 confirms with MDN)
5. The B2B gateway forwards the ACK log via web service (SOAP request) to the Swissmedic drug safety system
6. The Swissmedic drug safety system answers via SOAP response to the B2B gateway.

The B2B gateway stores the MDN temporarily in the file system. After 90 days the MDN will be stored for 10 years in a storage system.

## 8.2 Additional information

### 8.2.1 Operational requirements for communicating with the Swissmedic gateway

Each party must provide all the equipment, software and services necessary to create, transmit, receive, translate, record and store safety, acknowledgement and MDN messages in compliance with the respective ICH standards and the requirements as defined in this Guidance.

### 8.2.2 Security aspects

To facilitate the secure transmission of safety and acknowledgement messages over the Internet, each party must purchase, install and operate applications that allow for the successful transmission and receipt of encrypted and digitally signed safety and acknowledgement messages via the Swissmedic gateway.
The applications chosen by each party must provide the essential functionality and interoperability as outlined in chapter 6.
Encrypting and digitally signing safety and acknowledgement messages by using certificates provides the parties with assurance about each transaction.

# 9 Information for connecting to the Swissmedic B2B gateway

## 9.1 General information

The following section provides information on the organisational and technical framework of Swissmedic and lists the information MAHs must provide to Swissmedic in order to set up a gateway connection between an MAH and Swissmedic. It also lists the contact persons at Swissmedic.

## 9.2 Swissmedic

| | |
|---|---|
| National Competent Authority address | Swissmedic<br>Hallerstrasse 7<br>3012 Bern<br>Switzerland |
| PV Specialist (Process Specialist) contact | Swissmedic<br>Name: Manuela Zwahlen<br>E-mail: manuela.zwahlen@swissmedic.ch |
| Technical contact | Swissmedic<br>Name: Petya Borissov<br>E-mail: pvgateway@swissmedic.ch |

### 9.2.1 MAH certificate test and production

Please send your certificate to the following e-mail address: pvgateway@swissmedic.ch

**Important: It is not permitted to submit self-signed certificates!**

Note: The provided data will be used to set up a partner configuration on the B2B gateway, e.g. “Require Signature = Yes” means that the B2B gateway will sign messages to the MAH.
Time to Acknowledge: The time that the MAH has to acknowledge receipt of a message via an MDN. After the “Time to Acknowledge” has elapsed, the message will be resent as often as needed at intervals corresponding to the “Time to Acknowledge”.

# 10 Basic conditions

## 10.1 Time frames

The time conditions operate in accordance with the standards used within Switzerland (CET).

## 10.2 Location

The services will be provided within the premises of the respective participant:

- PharmApp Solutions GmbH, Erkrath, Germany
- FOITT, Bern, Switzerland
- Swissmedic, Bern, Switzerland
- MAH, MAH city, MAH country

# 11 Utilities & equipment

## 11.1 Equipment

- Phone
- Functional mail account for B2B gateway Swissmedic: pvgateway@swissmedic.ch
- E-mail client
- Internet portal and current information. The URL will be communicated to all parties during the MAH coordination meeting

## 11.2 Relevant documents

- E2B(R3) ICSR Specification and Related Files: ICH official web site: ICH (accessed 03.01.2024)
- E2B (R3) Step 5 Electronic transmission of individual case safety reports (ICSRs) - data elements and message specification - implementation guide (europa.eu)
- EU Individual Case Safety Report (ICSR)1 Implementation Guide (europa.eu)
- The XSD schema location for ICSRs: http://eudravigilance.ema.europa.eu/XSD/multicacheschemas/MCCI_IN200100UV01.xsd

# 12 Glossary

| | |
|---|---|
| ACK log | Acknowledgment log. Receipt generated automatically by receiver after an E2B has been uploaded to the drug safety system or Vigilance One Ultimate |
| ADR | Adverse Drug Reaction |
| AS2 | Applicability Statement 2 (AS2) |
| E2B | Electronic to Business - ICH standard for electronic transmission of adverse drug reactions in XML format |
| EMA | European Medicines Agency |
| FOITT | Federal Office of Information Technology, Systems and Telecommunication |
| HP QC | Hewlett Packard Quality Centre |
| ICH | International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) |
| ICSR | Individual Case Safety Report |
| Local Company Number | Internal case number of MAH |
| MAH | Marketing Authorisation Holder |
| MAH type 1 | Marketing Authorisation Holder with own gateway |
| MDN | Message Disposition Notification. Standard confirmation of receipt of an AS2 communication |
| NCA | National Competent Authority |
| PASS | Post Authorisation Safety Study |
| PI | Product Information |
| RPVZ | Regional Pharmacovigilance Centre |
| SM/SMC | Swissmedic |
| UMC | Uppsala Monitoring Centre |
| Swissmedic drug safety system | System used by Swissmedic to manage adverse drug reactions |
| WHO | World Health Organization |
| WHO-Art | WHO Adverse Reaction Terminology |
| WHO-Drug | WHO Drug Dictionary |
| XML | Extended mark-up language |