FEDRA

Spanish Pharmacovigilance Database

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FEDRA: Spanish PhV Database

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Legislative Framework

Spanish Law 29/2006 of 29 July on guarantees and rational use of Medicinal Products and Medical Devices, Title II, Chapter VI

SPANISH ROYAL DECREE 1344/2007, of 11 October, regulating pharmacovigilance of Medicinal Products for Human use → **"Questions and Answers on Electronic Transmission"**

-Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004, amending Directive 2001/83/EC on the Community Code relating to Medicinal Products for Human use.

-Regulation (EC) No 726/2004

-Volume 9 A-Guidelines on Pharmacovigilance for Medicinal Products for Human Use (prepared by the European Commission)

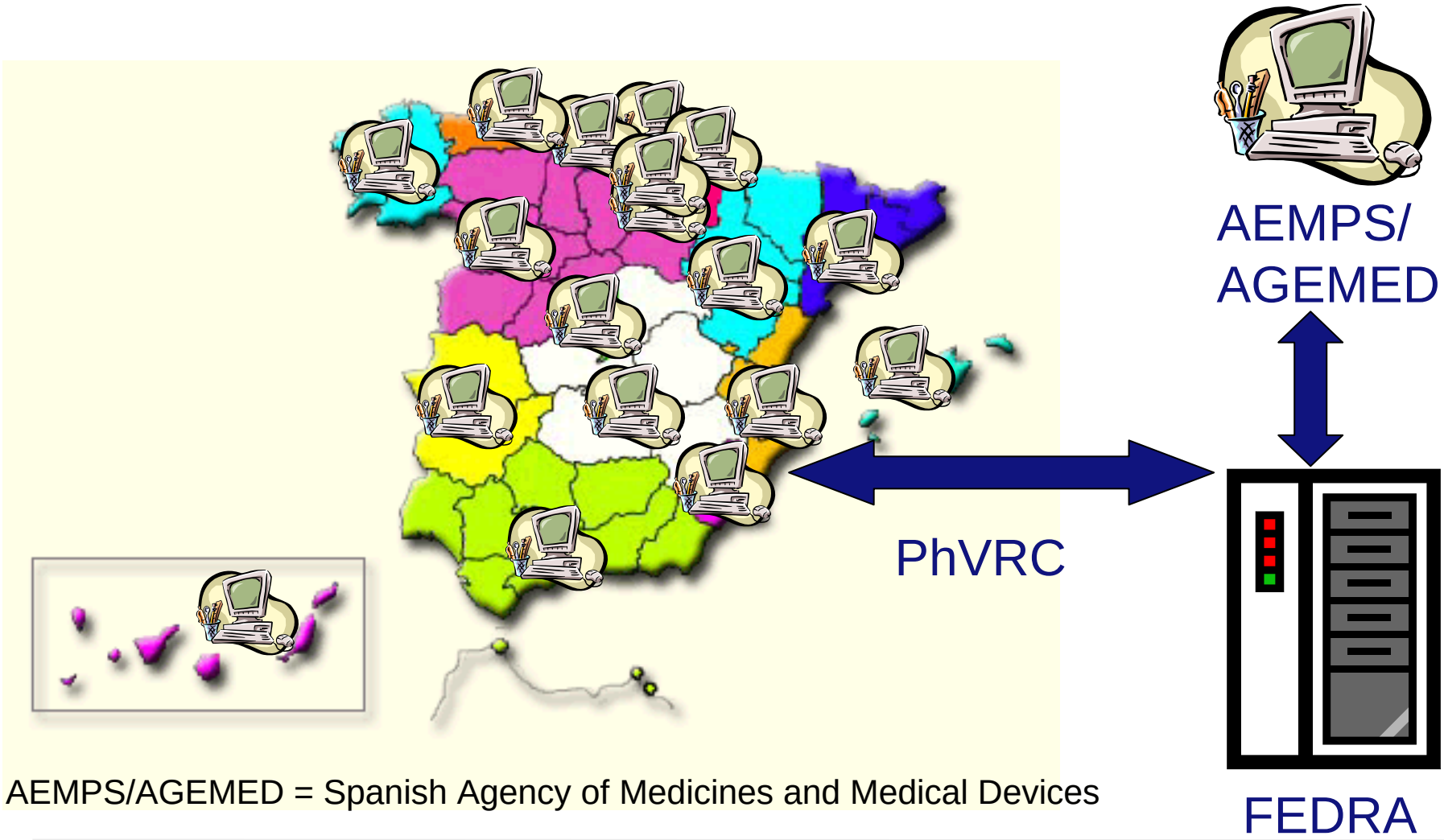
Legislative Framework

- **RD 1344/2007**
  - Updates and adapts to current IT technologies the Spanish Pharmacovigilance System for medicinal products for Human Use (SEFV-H).
  - Includes the requirement for electronic reporting of adverse reactions between the different agents (Pharmaceutical Industry, National Agencies and EMEA).

Legislative Framework

- **RD 1344/2007**
  - Establishes the **agents** who participate in the SEFV-H, as well as the **obligations** of each of the agents involved in this activity.
  - MAHs should record and report serious ICSRs occurring in **Spain** to the Pharmacovigilance Regional Centre where the Healthcare Professional (HP) reporting the case practices.
  - The Pharmacovigilance regional centres (17 PhVRC within Spain) shall record any ICSRs in the database (FEDRA) of the Spanish Pharmacovigilance System.

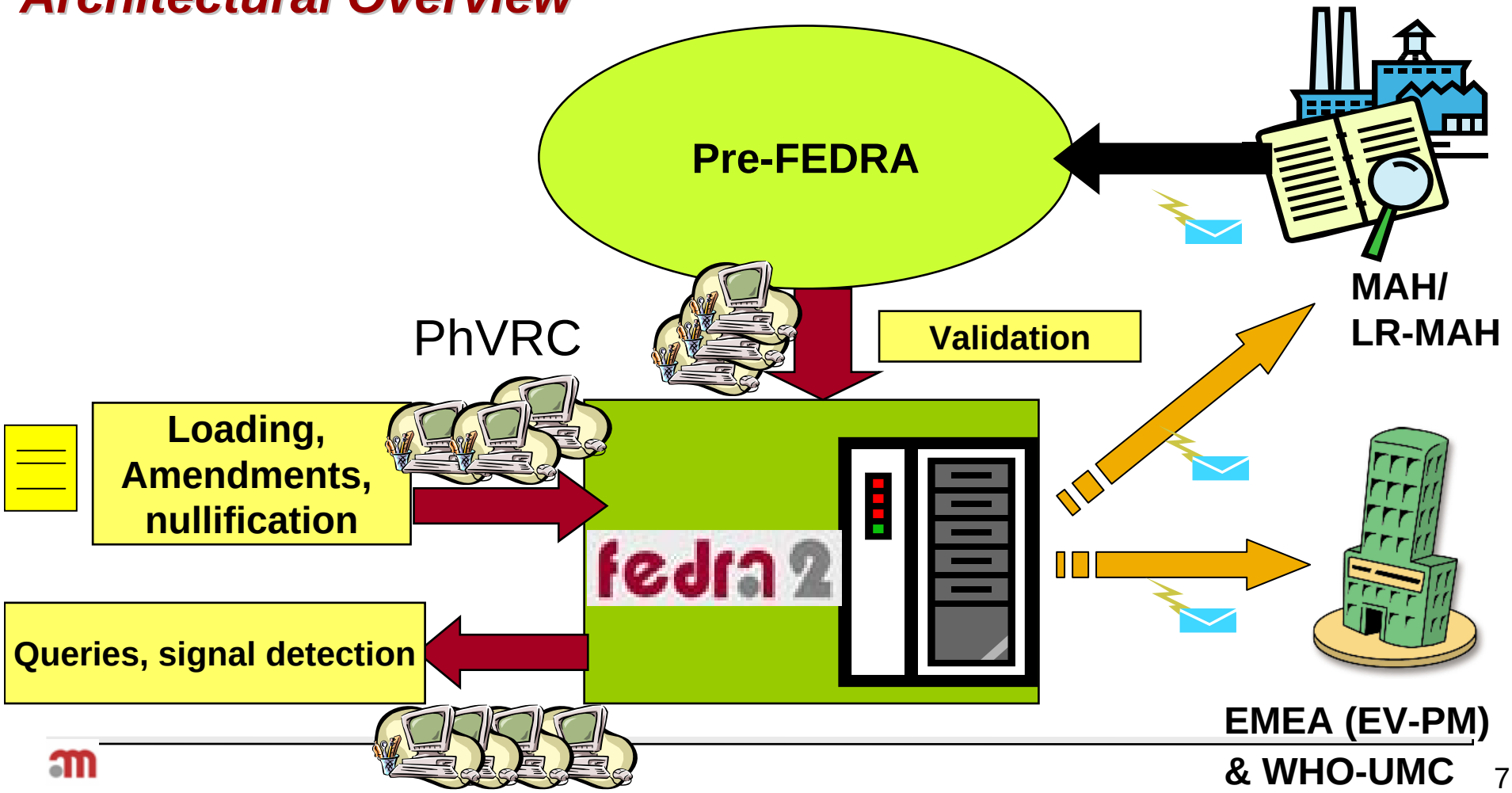
Legislative Framework



AEMPS/AGEMED = Spanish Agency of Medicines and Medical Devices

FEDRA: meeting new requirements

Architectural Overview



FEDRA: meeting new requirements

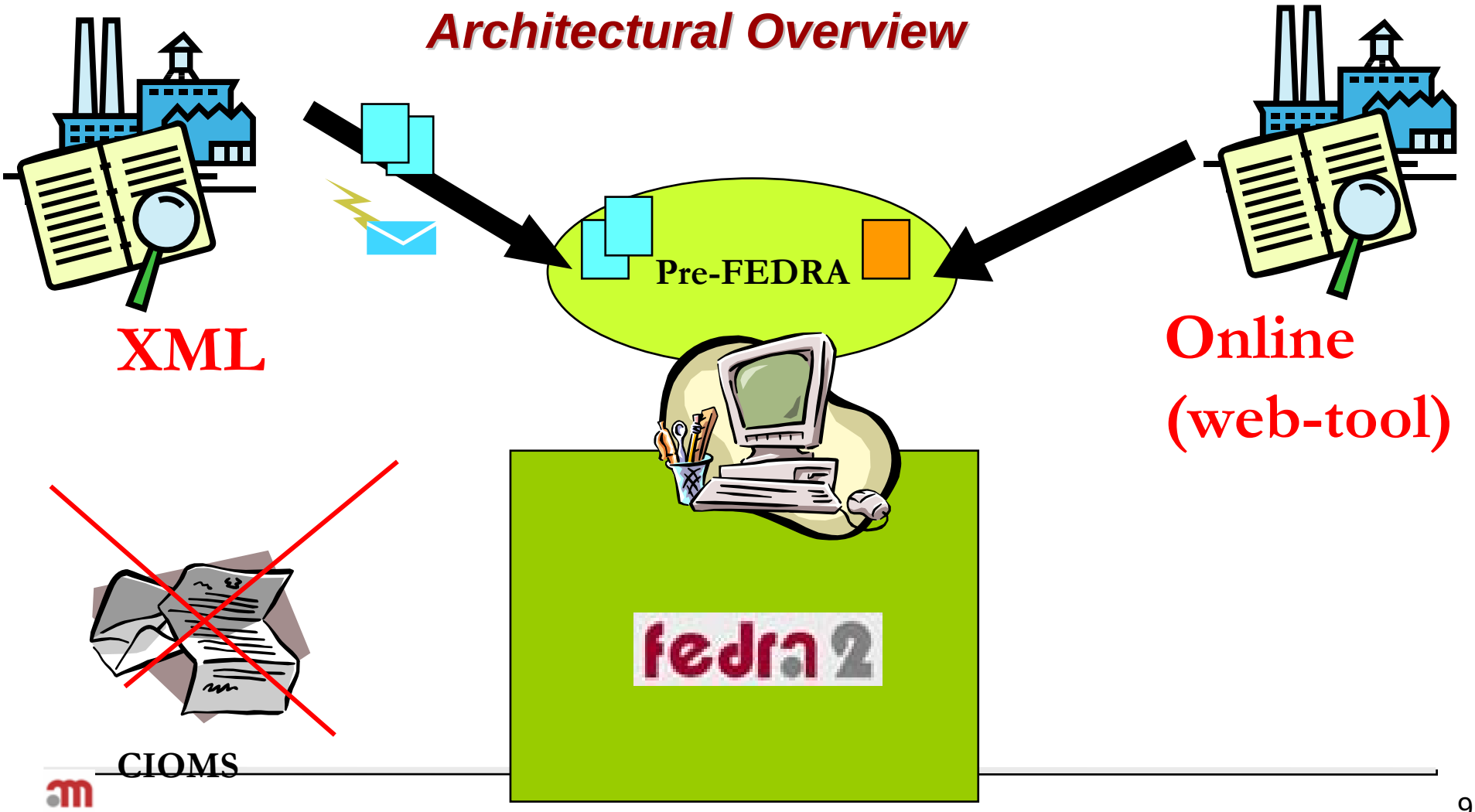
Architectural Overview

AGEMED offers two possibilities for electronic transmission of post-marketing ICSRs occurring in Spain:

- **XML transmission**: you need to register with the EMEA Central Database (EudraVigilance) and hold a valid ID-profile to start testing with AGEMED

- **Online access**: A web-tool allows loading of ICSRs in FEDRA.

FEDRA: meeting new requirements

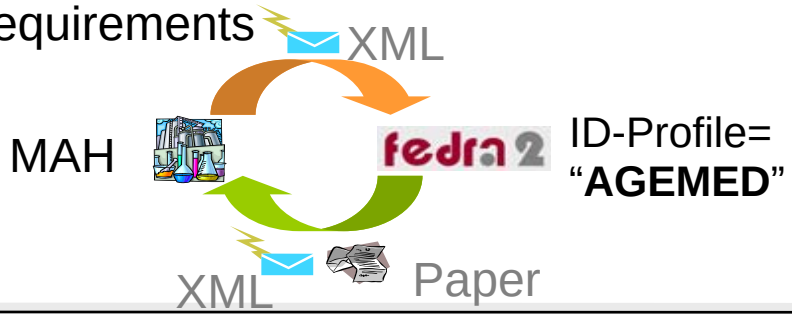


FEDRA: meeting new requirements

XML

Features

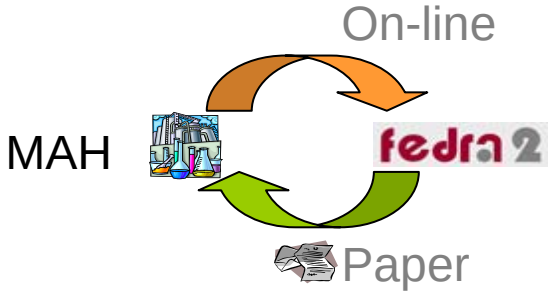
- E-transmission of ICSRs
- The database delivers ICSRs to the concerned PhVRC
- An ID-Profile is mandatory. EMEA manages ID profiles
- Acknowledgments should be regularly monitored to deal with warnings or errors
- Must fulfil local Spanish requirements



ONLINE

Features

- Web-tool that allows MAH / LRMAH data entry of ICSRs in Pre-FEDRA.
- The database delivers ICSRs to the concerned PhVRC
- Internet access, AGEMED web-site.
- User guide available in the web.
- Free of charge
- Must fulfil local Spanish requirements

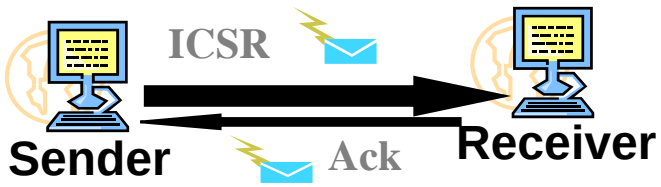


FEDRA: meeting new requirements

XML

Requirements

- Must hold an ID-profile.
- Must perform a test with AGEMED before production phase (as done with EV Test)
- An application form should be submitted to request testing on e-transmission with AGEMED:
  - Fax or e-mail to PhV Div.



ON-LINE

Requirements

- Technical requirements (ADSL, Windows-XP, MS-Explorer 6.0).
- A digital certificate issued by Spain (FNMT) is required
- An application form should be submitted to request users for FEDRA online data entry:
  - Fax or e-mail to PhV Div.

FEDRA: meeting new requirements

XML

Disadvantages

- More investment
- Human Resources should be allocated to manage safety messages, acknowledgments, errors and warnings, etc

Aimed primarily at:

- MAHs/LR-MAHs with large volume of ICSRs.
- MAHs with Medicinal products authorised outside Spain, therefore transmitting ICSRs to different NCAs (ES, IT, UK, FR, PT, …)

ON-LINE

Disadvantages

- Does not allow sending ICSRs to receivers other than AGEMED.
- Does not allow users to recover initial information, therefore when loading a follow up report, you will need to enter every field again.

Aimed primarily at:

- MAHs/LR-MAHs with very small volume of ICSRs.
- MAHs with Medicinal products authorised ONLY in Spain

FEDRA: meeting new requirements

Compliance with new standards

- **From 2002, a project to adapt FEDRA to new ICH standards E2B (M) , M1 (MedDRA) y M2 has been carried out**

- **Migration of 135.000 ICSRs (from 1984 to August, 2007) from:**
  - **WHO-ART>>> MedDRA**
  - **ICD-9-CM>>> MedDRA**

- **Addition of MedDRA to FEDRA (version 11.0, March, 2008)**

FEDRA: meeting new requirements

Compliance with new standards

Allows the e-transmission of MAH reports:

1. **Spontaneous ICSRs from the health professionals (representatives sales network).**
2. **ICSRs from Post-authorization studies**
3. **ICSRs from biomedical journals**
4. **ICSRs from individual compassionate use (e.g. misoprostol)**
5. **ICSRs from foreign medicinal products authorised by AGEMED (e.g. mefloquine)**

FEDRA: meeting new requirements

Compliance with new standards

Does not allow the e-transmission of MAH reports:

- **Clinical trials (SUSARs) related to either control or concomitant use**
- **For information on SUSARs, please follow instructions available in our website:**
  - **Clinical trial Section (Area de Ensayos Clínicos – see info dated 20-05-2008 at www.agemed.es)**
  - **Questions and answers document for e-transmission of ICSRs**

FEDRA: meeting new requirements

Training activities

- **Seminars with pharmacovigilance regional centres (PhVRC):**
  - **March 2004: MedDRA and FEDRA 2.0**
  - **2nd, 31st October 2007: FEDRA 2.0**
  - **26th, February 2008: Validation form pre-FEDRA**

- **Data Entry test with FEDRA 2.0:**
  - **Training for PhVRC Pharmacovigilance staff during 2007**
  - **All users from PhVRC must perform some exercises monitored by AGEMED in order to obtain a user profile.**

- MedDRA:
  - **PhVRC Pharmacovigilance staff: Data entry, data retrieval, and SMQ.**
  - **MAH: Two courses were hold in Madrid on 3 June, and 1 July 2008**

- **Course in EudraVigilance:**
  - **Barcelona: December 05 and January 06**
  - **Madrid: Jan and March 06. Next sessions 3-5 Nov 08, 16-18 Mar 09**

FEDRA: meeting new requirements

Information to MAHs

- **Communications about e-transmission (*):**
  - **July 27th, 2004**
  - **November 24th, 2005 (update on February, 2006)**
  - **August 29th, 2007 (version 3, December 2007)**
  - **September 24th, 2007 (updates the previous from November 2005)**
  - **May 19th, 2008 “Questions and answers for e-submission”**

- **Information day (*):**
  - **April 29th, 2005 about e-transmission.**
  - **November 29th, 2007 about Royal Decree 1344/2007**

(*) available at www.agemed.es

FEDRA: meeting new requirements

FEDRA: meeting new requirements

HUMAN MEDICINES

	INSTRUCTIONS	ONLINE SERVICE	ELECTRONIC CERTIFICATE
Registry of medicinal products	RAEFAR - Registry of Medicinal Products and Medicinal Plants Instructions for electronic submission eCTD/NEES Pilot Phase	raefar	Required
	Submission of the date of placing into market of the first lot/batch	https://sinaem.agemed.es/feccomer/	No Required
	Annual marketing plan (yes/no)	Not available till second half 2008	No Required
Farmacovigilance	Electronic ADR's Submission	fedra 2	Required
Clinical Tri	EudraCT numbers for clinical Trials	udra CT	No Required
	EudraCT european database of clinical trial	EudraCT	No Required
	Foreign Medicines I	//sinaem4.agemed.es/mex	Optional
	Hemoderivates mar	//sinaem4.agemed.es/hemoderivados	Optional
	Authorised Medicin	//sinaem4.agemed.es/consaem	No Required

Electronic ADR's submission information

Access to FEDRA

FEDRA: meeting new requirements

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agencia española de medicamentos y productos sanitarios

Activity | Citizens | Human health professionals | Veterinary health professionals | Industry

Farmacovigilancia Humana >

Transmisión electrónica de sospechas de reacciones adversas de medicamentos de uso humano / Electronic transmission on suspected adverse reactions with human use medicines

La transmisión electrónica de los casos de sospechas de reacciones adversas a medicamentos comercializados permitirá el intercambio ágil de información entre la Industria farmacéutica y las Autoridades competentes. Este proceso se enmarca en el reciente Real Decreto 1344/2007 de farmacovigilancia de medicamentos de uso humano, junto con la puesta en funcionamiento de FEDRA 2.0, base de datos del Sistema Español de Farmacovigilancia Humana (SEFV-H).

- Manual usuario de carga online / Online data entry User's Manual
- Formularios de solicitud / Application forms
- Instrucciones sobre transmisión electrónica / Instructions on electronic transmission
- Preguntas y respuestas sobre transmisión electrónica / Questions and Answers on electronic transmission
- Jornadas, cursos, seminarios sobre transmisión electrónica / Conferences and Seminars on electronic transmission
- Contacto / Contact: fvicsr@agemed.es

FEDRA functionalities

- FEDRA is located in a secure environment (SSL) within the portal SINAEM of the AGEMED/AEMPS. To access the portal a digital certificate, an user name and a password are needed. To obtain the permission of access a formal request signed by the manager (MAH, Regional Centre, AEMPS) is required.

FEDRA functionalities

- Maintaining local master files
- Approval Process: Enables to define the user profile.
- Audit Process: A registry of the actions done by every user.
- Maintaining dictionaries:
  - **Products**: For products that are not included in the medicinal product database of the AEMPS (RAEFAR).
  - **Medical Journals**: The name of the publications that have been reported to SEFV-H are included in FEDRA, and allows querying.
  - **Business Groups**: allocation of transmission type (XML, web-tool), companies that are part of the group, responsible person for pharmacovigilance, ID profile for the XML transmission.
  - **National Responsible for Pharmacovigilance in Spain**: Contact details.

FEDRA functionalities

- ICSRs:
  - **Queries and reports**: Allows consultations in real-time to all ICSRs loaded in FEDRA. Medicines are coded which allows controlled searches by both active substances and trade names. ADR can be found using and combining different categories of MedDRA, including SMQs. Additionally, there are approximately another 40 fields available to make queries, such as: date in which the ICSR is loaded, seriousness criteria, the outcome of the ADR, indication of the drug, etc.
  - **MedDRA categories**: To make standard queries with MedDRA. Equivalent to a local SMQ.
  - **Requested ICSRs**: It allows viewing different outputs of the consultations. Three current possibilities: “Excel format” with most of the data, a detailed form in “Word format”, or a line listing in “Word format”.
  - **Maintenance**: Allows loading, amendment or nullification of ICSRs.

FEDRA functionalities

- Submitting data:
  - EV-PM (EMEA): Sending weekly ICSR via XML (approx 120 ICSRs).
  - Expedited reporting to the MAHs: sending weekly (approx 80 ICSRs) via XML or paper (depending on MAH profile).
  - Ad hoc requests of information by MAHs other than expedited ICSRs.
  - Conversion of external number: equivalence between the internal and external ICSR number.
  - Transmission's management: XML control. Viewing XML and acknowledgements that are sent or received at AGEMED.
  - WHO: Periodically all ICSRs are sent to the WHO Collaborating Centre in Uppsala (SE).

FEDRA functionalities

- Access to Pre-FEDRA (ICSRs sent electronically by MAHs): Each Regional Centre has access only to those ICSRs that should be evaluated by them. AGEMED has access to all ICSR in Pre-FEDRA. The Regional Centres can generate a document which contained every field on the ICSR. They can save it on their computers or print it. The system includes a tool for detection of follow-ups or possible duplicates in FEDRA. Regional Centres validate the ICSRs and load it into FEDRA.

- ICSRs pending : The Regional Centres have access to ICSR which have not yet been loaded. Until the process is concluded, the ICSR does not become part of FEDRA. The AGEMED have access to all pending notifications.

FEDRA functionalities

Output reports:

- Output reports for queries: The user can choose among the following options:
  - Excel format with most fields included in the database
  - Detailed individual information of every ICSR in Word format.
  - Line-listing of ICSRs in Word format (limited number of fields)

- Display of cases sent by the industry available in Pre-FEDRA: Report in a Word document

Current status and lessons learned

Current status and lessons learned

- Currently in a transitional period for ICSR e-submission with MAHs
- Test of XML is ongoing.
- Deadline for e-submission compliance – December 31st, 2008
- Exchange of ICSRs:
  - XML
  - On-line
  - Paper (CIOMS): only for MAH that have not as yet carried out the test

Current status and lessons learned

Current status and lessons learned

- **Beginning of activities of the pharmacovigilance regional centres (PhVRCs):**
  - **Load and querying, from August 1st, 2007**

- **E-transmission of ICSRs in XML format to EMEA:**
  - **Weekly from 08-08-07**
  - **Back-log (27,427 ICSRs) concluded in August 2008.**
  - **Total: 4.100 ICSRs loaded by 20-05-08:**
    - **1.921 from yellow card**
    - **1.578 from industry (MAH)**
    - **132 from both (yellow card+ MAHs)**
    - **32 from literature reviews from PhVRCs**
    - **460 studies from health professionals (APEAS, CMBD, Emergencies,..)**

- **Weekly transmission to the industry from new database (FEDRA) from August 8th, 2007**
  - **Since June, 2008 also in XML for the companies that have successfully passed the test with AGEMED**

Current status and lessons learned

XML:

- **Received submission for tests**
  - **119 applications:**
    - **93 transmission and reception of XML**
    - **26 only for transmission**

- **Gathered experience:**
  - **High degree of collaboration**
  - **Spanish requirements in the tests**
  - **Removal of accents and “Ñ” letter**
  - **Error correction and improvement of the system**

Current status and lessons learned

On-line:

- **FEDRA users of Industry profile**
  - **110 users**
- **Pharmaceutical companies (MAHs):**
  - **66 companies**
- **Gathered experience:**
  - **Tool that it is easy to use**
  - **Problem when loading all the information in the follow-ups**

Current status and lessons learned

E-transmission:

- **Regular Information exchange between AGEMED and MAHs**
- **Availability of all the information on the web**
- **Translation of the majority of the documentation into English**
- **E-mail address to solve doubts:**

fvicsr@agemed.es

Current status and lessons learned

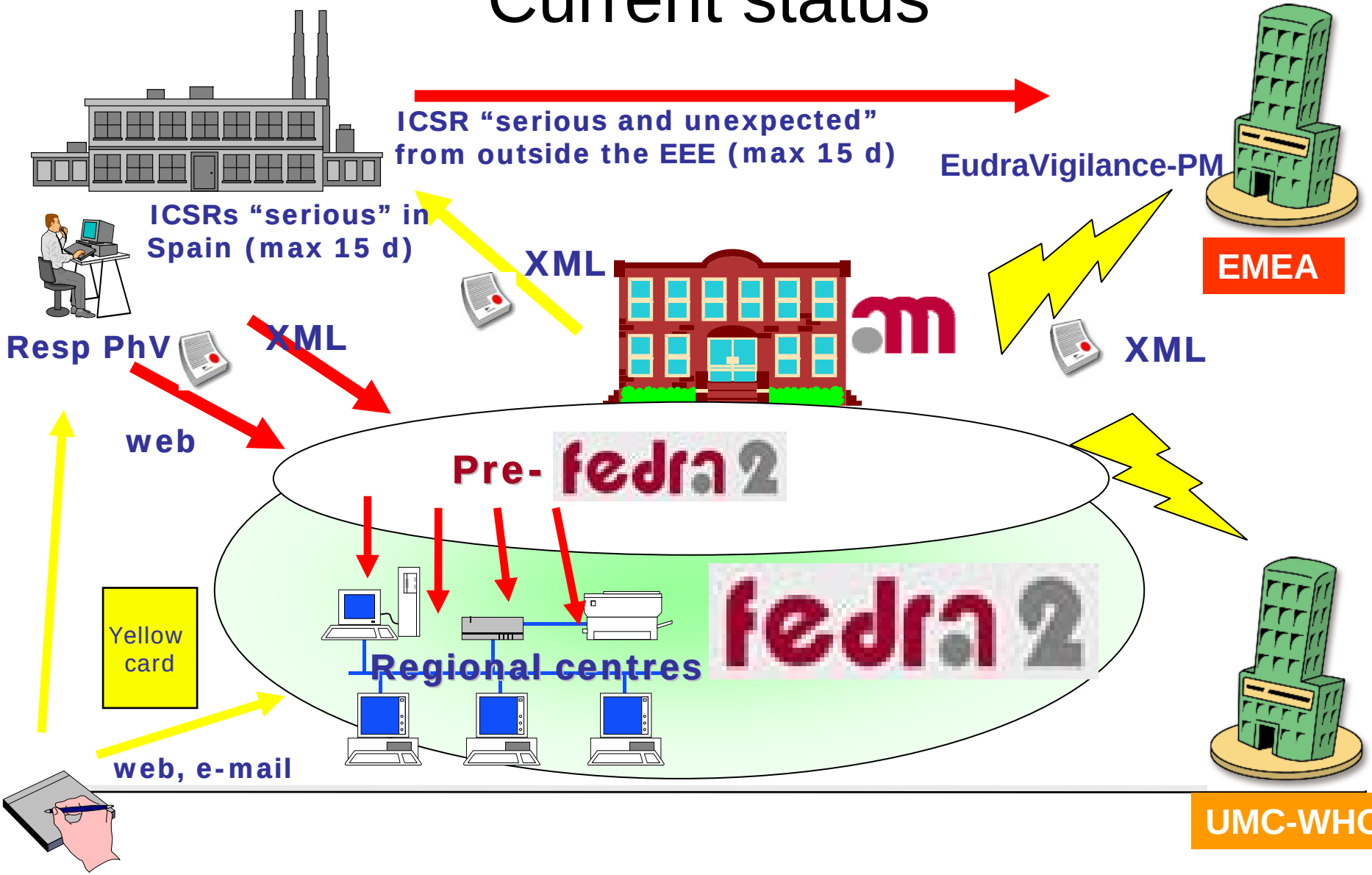
Following steps:

- **Improve graphical outputs: Annual reports, drug-reaction report.**
- **Automatic signal detection.**
- **E-submission to Uppsala Monitoring Centre (WHO).**

MINISTERIO DE SANIDAD Y CONSUMO

agencia española de medicamentos y productos sanitarios

Current status



Useful links

- **Royal Decree 1344/2007, of 11 October, regulating pharmacovigilance of medicinal products for human use** (http://www.agemed.es/actividad/legislacion/espana/docs/RD1344_2007-ingles.pdf).
- **Information day about Royal Decree 1344/2007** (http://www.agemed.es/actividad/legislacion/espana/docs/rd1344_farmacovig.pps)
- **Electronic transmission on suspected adverse reactions with human use medicines** (http://www.agemed.es/indFarma/farmacovigHumana/transmi-electronica.htm)
- **Information day April 29th, 2005 about e-transmission.**
  - http://www.agemed.es/indFarma/docs/transmision-e-RAM-mayo08.pdf
  - http://www.agemed.es/indFarma/docs/carga-online-mayo08.pdf
  - http://www.agemed.es/indFarma/docs/calendario-mayo08.pdf
- **Questions and Answers on Electronic Transmission** (http://www.agemed.es/indFarma/docs/QA_FVICSR.pdf).
- **Spanish local Requirements** http://www.agemed.es/actividad/documentos/infoInteres/docs/NI_XML_v2_Ingles.pdf