SIXTH FRAMEWORK PROGRAMME

Horizontal Research Activities involving SMEs

CO-OPERATIVE RESEARCH PROJECT

Contract Number:

COOP-CT-2006-33016

MED-EPHV PROJECT

"Learning and Practicing Pharmacovigilance in the Mediterranean countries of the EU"

Final Project Activity Report

Due date of Deliverable: 15 February 2009

Actual Submission date: 31 March 2009

Period covered: from 1 September 2006 to 31 December 2008

Start date of project: 1 September 2006

Duration: 28 months

Project coordinator name: Oreste Salvaggio

Project coordinator organisation name: Gruppo S LAB S.r.l.

Date of preparation: 15 March 2009

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1. Preamble

Annex 2 to the EC Contract – Article II.7 – Reports and deliverables states:
In addition to the documents referred to in paragraph 2 of this Article for the last period, the *consortium* shall submit the following final reports to the *Commission* after the end of the *project*:

a) a final activity report covering all the work, objectives, results and conclusions, and the final *plan for using and disseminating the knowledge*, including a summary of all these aspects……

Therefore the scope of this Final Activity Report is to present in a concise way the most important aspects of the Med-ePHV project, and of the results achieved. More details can be found in the Interim Report covering the activities of the first year of the project and in the Activity Report for the second reporting period (from month 13 to month 28), that describes all activities, results achieved and planned actions for the future.
More detailed information is included in the 27 contractual deliverables, which have been duly submitted to the EC.

In addition a Publishable Executive Summary of the Projects and of its results has been included at the beginning of this Final Activity Report.

2. Publishable executive summary

Med-ePHV is a co-operative research project co-financed by the European Commission through the Sixth EU Framework Programme for Research and Technological Development.

The signed research contract has a budget of € 1,315,840, with a Commission contribution of € 804,420.

The project started on September 1st 2006 and had an initial duration of 24 months, subsequently extended four additional months, until December 31st, 2008.

2.1 Background

Pharmacovigilance consists in identifying collecting and analysing the adverse reactions to medicines following their market authorization; it is an essential practice to safeguard public health and is intended to minimise risks.

The recognition and notification of Adverse Drug Reactions (ADRs) is a complex task requiring knowledge and expertise from health professionals.

The complexity of ADRs recognition and notification is at the origin of the current poor delivery of notifications, in terms of both quality and quantity, to the central medicines authorities (national and European Agency).

In addition the limited pharmacovigilance support provided, in terms of knowledge dissemination and technical systems, to health practitioners and patients contributes significantly to the scarce production of ADRs recognitions and notifications in the periphery of the health systems and of the market authorization holders networks.

All parties recognize it but in particular the EU pharmaceutical regulators underline that pharmacovigilance is an essential tool in order to ensure public health in the Union.

The new pharmaceutical legislation proposed by the EC in 2001 and modified in the final adoption following the amendment of the European Parliament stresses the importance of pharmacovigilance by enforcing ADRs notification (Council Regulation No. 726/2004).

2.2 Project Objectives

The Med-ePHV project was intended to research and develop an innovative approach to the EU pharmacovigilance practice by designing and implementing a pharmacovigilance co-operative e-learning system specifically addressing the needs and profile of health practitioners and patients of Southern Europe (Mediterranean countries).

The system will permit to learn and practice adverse drug reactions notification at the peripheral edge of the pharmacovigilance systems.

These objectives that have been set by the Med-ePHV Consortium were to be achieved through:

Development of pharmacovigilance e-learning courses and tutoring schemes in line with the latest EU legislation and adapted to the specific national implementation schemes and directed to health professionals of France Italy and Spain.

Test and validation of the e-learning modules by a representative sample of health practitioners and by selected Pharmaceutical industry representatives.

Study and design of a co-operative environment as the central component of an application grid accessible to LHAs, MAHs and health professionals, to be implemented upon satisfactorily completion of the project.

Upon completion of the project the participating SMEs intend to commercially exploit the e-learning modules in their respective countries and to establish cooperation agreements in other Mediterranean countries, which have similar business interest and needs.

The Med-ePHV approach is based on the modelling of the pharmacovigilance practice, allowing to deliver a suite of software solutions and network based integration services capable to support an efficient ADRs recognition and notification. The grid-based services will include:

An e-learning system focused on pharmacovigilance science and regulation which will be developed, tested and validated during the project with the active support of three levels of end-users (the SMEs, the Health practitioners and the Pharmaceutical industry).

A knowledge based notification module compliant with ADRs standardization (ICH M2).

An integration and cooperation environment providing on-line, Internet based portal type of services.

2.3 Med-ePHV consortium members

The project has been set up around three specialised European Small and Medium Enterprises (SMEs) based in Italy, France and Spain.

The necessary research and technological development (RTD) assistance is provided by five public and private research institutions located in Italy, France, Spain and Belgium. The RTD performers have been selected to cover the same geographical areas of the SMEs (with the exception of EFGCP which has a pan-European coverage of the Health sector), since they must have a direct knowledge of the national medical environment and in particular of the pharmacovigilance rules.

In the following section we provide a brief description of the Med-ePHV consortium members.

2.3.1 SME Partners

The project coordination is assigned to an Italian SME: **Gruppo S Lab S.p.a.** (**GS**) which has appointed Mr. Oreste Salvaggio and Mrs. Roberta Fabrizi as the overall Project Coordinator and Project Manager respectively.

GS is an Italian SME with recognized experience as supplier of a wide range of services to the industry and Public Administration in the field of Information & Communication Technology (ICT).

Headquartered in Reggio Emilia, since 1994 GS has been operating with offices located in several Italian northern regions.

GS has developed the software for ADRs recognition and notification and integrated it with the e-learning platform within the Med-ePHV grid.

AriSoft Editorial (**AS**) is a Spanish company with more than ten years experience in the e-learning field. It's focused on the dissemination of educative contents developed either by the company, or by other firms and institutions belonging to different education and training sectors. One of the key business sectors for AS is the education for health professionals. AS main role is to select and adapt the e-learning platform to the Med-ePHV requirements. The person in charge for the project is Mr. Carlos Arias Rodríguez, General Manager of AS.

Pasteur Mediavita (**PMV**) is a spin-off of the Pasteur Institute, but independent French SME, specialised in publishing, consulting, training and communication in the field of health.

PMV has specific skills in the acquisition, management and updating of medical and scientific contents. PMV develops training schemes tailor-made for the needs of health professionals acting around the patient. The person in charge for the project is Anne-Sophie Godón, President and responsible for consulting services.
Unfortunately PMV has changed its business focus and priorities during the final stage of the project, with a consequent reduction in its contribution to the project results.

2.3.2 RTD Performers

The **University of Pavia** (**UNIPV**) is one of the oldest Universities and the second oldest faculty of Medicine in Italy. More than 50 Clinical Divisions are performing research in the biomedical field and have been involved in several European projects. UNIPV has brought to the Med-ePHV project all the learning methods to support the development of e-learning on pharmacovigilance assuring correct and ethical information of both doctors and patients. The person in charge for the project is Mrs. Maria Giovanna Ruberto, Associate Professor of Bioethics.

Tecnofarmaci (**TF**) S.C.p.A. is a research and training company established by 19 Italian and international pharmaceutical companies with the aim to set up a link between the academic research and the emerging demands of industries. TF participation to the Med-ePHV project is related to its well established expertise in the field of pharmaceutical training. TF has led the development of the ADRs notification pilot and supported testing and validation activities. The person in charge for the project is Dr. Sabrina Bozzoli.

INSERM's vocation is to promote health for all. This French Institute is presently running more than 100 clinical trials and has extensive experience in monitoring ADRs and training of investigators on how to report adverse reactions. The specific objective and role of INSERM in the Med-ePHV project has been to customize the e-learning modules and ADRs reporting system to the specific rules and requirements of the French Health system. ISERM has also contributed to the development of a user friendly and easy system which may stimulate and permit to the health professionals to correctly report ADRs. The person in charge for the project is Dr. Jacques Demotes-Mainard.

The Spanish Institute of Pharmacoepidemiology (IFE) is an interdisciplinary centre of the **University of Valladolid** (**UVA**) devoted to the investigation about drugs safety and their effects on the population. This Institute currently collaborates with the Spanish Medicines Agency with the EMEA and with the Uppsala Monitoring Centre (WHO). Within the Med-ePHV project UVA has been responsible of the WPs focused on the development of the models for ADRs recognition and notification, in structuring the pilot e-learning program and modules and in leading the validation effort in Spain. The person in charge for the project is Dr. Alfonso Carvajal García-Pando, Professor of Pharmacology and Head of the Institute of Pharmacoepidemiology.

The **European Forum for Good Clinical Practice** (**EFGCP**) is a pan-European non-profit organisation, based in Brussels, devoted to promoting the interests of patients in clinical research through the development of European ethical and scientific standards. As part of its contribution to the project, EFGCP has brought a global vision of pharmacovigilance within Europe. One of the project missions of EFGCP has been to offer a more effective dissemination of the project's results to European end-users such as patients, commercial and non-commercial research bodies and regulatory authorities. The person in charge for the project is Dr. Jean-Pierre Tassignon.

2.4 European benefits and impacts

Recognizing that at present, in the target EU Mediterranean countries a comprehensive pharmacovigilance e-learning service that addresses the new EU legislation, does not exist, the Med-ePHV consortium believes that the potential impact of the project in France, Italy and Spain will certainly be highly positive for public health and represents an unmatched business opportunity for the SMEs.

The Med-ePHV project development phase has produced as pilot applications a number of models for knowledge representation and for cognition implemented as on-line, Internet based software products.

The expected end-users of these services, which will be offered in the respective markets by the participating SMEs, are of three distinct levels: a) the health practitioners, LHAs and MAHs staff; b) the pharmaceutical industries and c) the SMEs that will exploit the e-learning services.

The Consortium partners and the Sponsoring institutions believe that the suite of pharmacovigilance services to be provided by Med-ePHV could be of great importance for orphan drugs and bio-medicines, which represent an increasing market.

It is quite clear that the Med-ePHV project addresses one very important public health issue of the EU, especially where the performance of the pharmacovigilance is far from being optimal. An efficient EU pharmacovigilance system could also indirectly provide strong support to the solution of other recent issues such as the monitoring of bio terrorism and the increasing appearance of adverse reactions in young people to tattoo colours and body piercing practices.

2.5 Activities accomplished during the project development phase.

Concerning the consortium management activities, the Project Coordinator has implemented the Intranet based Med-ePHV Communication and Cooperation platform, not only for the purpose of sharing project related documents and deliverables between partners, but also for loading and testing the on-line ADR notification software and e-learning modules. A Project Master Document has been approved and adopted by all partners together with common cost control procedures and tools. A project risk analysis has been conducted and a project risk management plan put in place to promptly address unexpected threats, and allowing the undertaking of any needed remedial actions.

Five Project Steering Committee Meetings have been held as planned.

Concerning the RTD and innovation activities, the SME partners with the support of RTD Performers have conducted a detailed analysis of the pharmacovigilance business process, identifying the current pharmaceutical legislation of the EU as implemented in France, Italy and Spain. Overall the main achievements of these project activities are: a) the comparative analysis of the implementation of this business process in the EU and in particular in the three Mediterranean countries and b) the identification of the requirements for an improved pharmacovigilance business process.

The design work performed prior to the implementation of the e-learning pilot applications has covered the following main lines:

Definition of cognitive models for the design of advanced e-learning schemes. These models have been based on a detailed map of the medical, pharmacological and genetic issues at the origin of the adverse drug reactions and on the different types of actors that operate at the peripheral edge of the pharmacovigilance systems.

Definition of the knowledge base representations and the inference mechanisms needed to support the identification of ADRs, focusing on the established standard model for ADRs notification (ICHM2) as implemented in Italy, France and Spain.

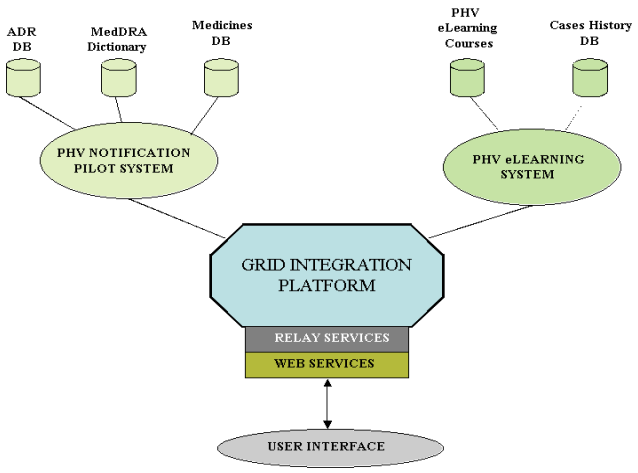
The selection of representative case histories to be included in the ADRs recognition module.

The implementation phase, based on the Med-ePHV system design, has been satisfactorily accomplished and the French, Italian and Spanish pilot systems tested and validated by a representative samples of selected end-users. The implementation phase of the e-learning pilot system included:

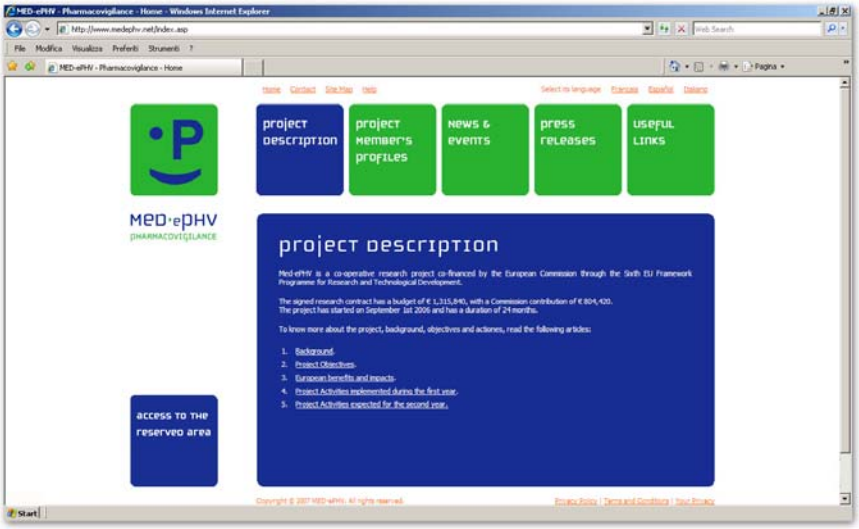
Setting-up of the on-line ADR recognition and notification pilot following the rules prescribed by the ICHs standard, integrated with all the available notes/improvements from the quoted sources. The integration has also covered all those taxonomies which were considered to be more beneficial for didactic purpose. The DRUPAL open-source platform satisfactorily used for the Med-ePHV Intranet, has been chosen also for developing the ADRs software.

Setting-up of the on-line e-learning modules using the MOODLE open-source platform. The modules that have been implemented cover a complete in-depth pharmacovigilance training program in the three languages. The system permits to automatically extract and package the modules to fit the specific learning needs of the target categories of end-users. The modules include learning tests based on questionnaires and automatic rating system of the answers.

Design of a state-of-the-art grid middleware to be shared among the SME partners during the commercial exploitation phase. The resources that Med-ePHV integrates are a Learning Management System (LMS) and a Grid Middleware. These two elements are based on Web and Grid Services respectively.
The following diagram shows how the Med-ePHV system components have been integrated within the Grid platform.



Promotion of the Med-ePHV project and dissemination of the achieved results in the three countries and at EU level have played an important role since the start of the project. Partners of the Consortium have been active in presenting the Med-ePHV project with articles and at conferences in their respective countries, following a pre-established plan jointly developed by the SME and RTD partners. The Med-ePHV web site (www.medephv.net) is the mirror of the project and point of access to the on-line services.



3 Objectives

3.1 Overall Project Objectives

The Med-ePHV project proposes a new approach to pharmacovigilance practice in the EU by addressing the recognition and notification of the adverse drug reactions caused in patients by the use of medicines.

Ongoing pharmacovigilance practice at the periphery of public and private health systems is lacking a finalized expertise in both health practitioners and patients and so far it is not sufficiently supported by appropriate information and communication services and software applications. It is a fact that in the EU countries of the Mediterranean area health practitioners have a need to learn and practice pharmacovigilance, but there is no systematic training programme for on-line learning and practicing pharmacovigilance. The objective of the Med-ePHV project is to fill this gap by having prestigious RTD institutions of France, Italy and Spain, providing the necessary research to develop innovative tools and internet based on-line e-learning services to support pharmacovigilance practice and to train the interested parties.

The project will focus on the medical population and institutions involved in pharmacovigilance in France, Italy and Spain. Upon satisfactory completion, testing and validation of the project results, the consortium partners intend expand their business to all the EU Mediterranean regions and to other countries which have language affinity.

3.2 Scientific and technical objectives

To develop e-learning courses and tutoring scheme directed specifically to health practitioners focused on pharmacovigilance science and regulation.

  - Real Adverse Drug Reactions (ADRs) case histories will be integrated in the training modules.
  - The e-learning modules, will be tested and validated during the project with the active support of three levels of end-users (the SMEs, the Health practitioners and the Pharmaceutical industry belonging to the three target Mediterranean countries).

- To develop on-line ADRs notification and reporting models to be used for training purpose, complying with the established international standards (ICH M2) and in agreement with the ongoing practices of the European Agency (EMEA) and following the practices and official forms of the National Authorities of the three target countries, responsible for pharmacovigilance.

- Study and design of a co-operative environment as the central component of a transnational application grid, initially covering the three target countries, and shared by Local Health Authorities (LHAs), Market Authorisation Holders (MAHs) and health practitioners. The objective is to establish a pharmacovigilance focused virtual community.

3.3 Economic objectives

- By addressing a need by the medical community to comply with regulatory requirements about Pharmacovigilance and in particular ADR's notification obligation, the SME's partners will develop a new e-learning business opportunity, using jointly developed training modules.
- The on-line based e-learning services will be made available and exploited using a jointly developed and shared application grid. The grid will be designed in such a way to be easily expandable, with the objective of limiting the initial investment and allow adaptation to expected future growth in the number of on-line users within the three countries, from other potential Mediterranean countries and other countries with language affinity (e.g., South America, North Africa, etc.).
- The training materials developed during the project for e-learning application, must be easily adaptable for other training methods (e.g. Multimedia interactive CD/DVD, Personal Digital Assistant application (PDA), Residential training in Hospitals, etc.). The SME's partners will own exploitation rights for the training modules in their respective language and will be able to package them in line with specific customers needs.
- Post-project cooperation between SME's and RTD partners will be maintained and will be economically beneficial also for the RTD organisations, which will be requested to provide support as remote e-learning tutors, to develop new exams/tests, update the courses with new ADR's case histories or to impart residential courses.
- The creation of the joint transnational application grid, will allow to the partners to expand their business opportunities, by offering existing applications outside their country to the other partners, or to develop new applications compatible with the joint grip platform.
- By using the joint application grid, set-up investment cost, operation, upgrade and maintenance cost will be shared, with consequent economical advantage for the SME's partners.

3.4 Social objectives

- The Med-ePHV development is not only an appealing business opportunity for the SMEs but also brings a contribution to the important social issue of public health in the context of the safe use of medicines.
- The project clearly points out the priority given to education and training as part of the objective of developing the European Union as an advanced knowledge society, with sustainable development, more and better jobs and greater social cohesion.

- Through the on-line e-learning system. there is also the general aim of facilitating knowledge access for everyone in order to combat social exclusion, whether it is due to particular needs, a disability, age or illness.

3.5 EC policy objectives

On July 2004, the **European Commission** adopted ambitious proposals for the new generation of programmes in the field of education and culture as part of a bigger package on the new financial perspectives for the 2007-2013 period.

Among this objective the Med-ePHV project, clearly addresses:

- **e-learning services**
  The project clearly points out the priority given to education and training as part of the objective of developing the European Union as an advanced knowledge society, with sustainable development, more and better jobs and greater social cohesion. It will also contribute to the development of education and training systems in Europe (through innovative pilot projects) and to the emergence of a Single European Knowledge Area (through focus on mobility of people).
- **e-health services**
  Continuing Medical Education (CME) is part of Continuing Professional Development (CPD), is addressed to medical doctors. CME is or will shortly be a legal requirement in the majority of EU countries. The Med-ePHV project will provide to European health practitioners an on-line on-demand service, helping them to continue their professional development, by filling knowledge gaps and keeping knowledge updated with latest scientific findings.

4 Deliverables and milestones

The following contractual deliverables were scheduled to be completed:

4.1 Work Package 01 – Project Management

D01: Kick-off Meeting Report
Status Complete
Meeting was held in Reggio Emilia on September 8th, 2006.
Minutes after review and approval were issued on September 27th, 2006.

D02: Project Presentation
Status Complete
A MS Power Point slides presentation of the Med-ePHV project has been produced and issued on September 30th, 2007.

D03: Communication based project control and reporting system
Status Complete
The document describing the project control and reporting system has been produced and issued on November 30th, 2006.

D04: Project Intranet and cooperation tools
Status Complete
The specification requirement document for the project Intranet and cooperation tools, has been produced and issued on November 30th, 2006. Intranet is operating with all functions. Cost reporting tool has been finalised and implemented.

D05: Project Master Document (PMD)
Status Complete
The Project Master Document has been produced and released on November 30th, 2007.

D06: Project Steering Committee Meeting Report
Status Complete
PSC meeting was held in Levallois-Perret (Paris) on February 5th 2007.
Minutes after review and approval were issued on February 20th, 2007.

D12: Project Steering Committee Meeting Report
Status Complete
PSC meeting was held in Milan on July 19th, 2007.
Minutes after review and approval were issued on August 7th, 2007.

D17: Project Steering Committee Meeting Report

Status Completed

The project Steering Committee meeting was held in Turin (Italy) on January 16th, 2008.

Minutes after review and approval were issued on February 25th, 2008.

D23: Project Steering Committee Meeting Report

Status Completed

PSC meeting was held in Milan on November 19th, 2008.

Minutes after review and approval were issued on November 21st, 2008.

4.2 Work Package 02 – Business Process Requirements

D07: Report on business process requirements

Status Complete

The business process requirements document has been produced and its conclusions discussed during a workshop held in Paris, on February 5th, 2007 in conjunction with the Project Steering Committee meeting. The report has been finalised and issued on April 15th, 2007.

4.3 Work Package 03 – Study of Med-ePHV Learning Models

D09: Report on reference and specific cognitive models

Status Complete

The Report on reference and specific cognitive models has been produced and its conclusions discussed during a workshop held in Milan, on July 19th, 2007 in conjunction with the Project Steering Committee meeting. The report has been finalised and issued on August 8th, 2007.

D10: Report on Med-ePHV Learning Models

Status Complete

The scope of the work to be performed and the outline of the Report on reference and specific cognitive models, has been discussed during a specific workshop held in Valladolid on June 14-15th, 2007 and subsequently reviewed again in draft version during a workshop held in Milan, on July 19th, 2007 in conjunction with the Project Steering Committee meeting. The report has been finalised and issued on October 10th, 2007.

4.4 Work Package 04 – Study of ADRs Recognition and Notification

D11: Report on Med-ePHV notification and recognition

Status Complete

Outline of the report has been discussed during a workshop held in Milan, on July 19th, 2007 in conjunction with the Project Steering Committee meeting.

The report has been finalised and issued on October 15th, 2007.

D13: Report on implementation guidelines

Status Complete

The draft version of the Report on implementation guidelines, has been discussed during a specific workshop held in Paris on September 26th, 2007. The report has been finalised and issued on October 15th, 2007.

4.5 Work Package 05 - Development of ADRs notification pilot

D15 Design of the software for ADR notification and recognition

Status Complete

The draft version of the Report on design of the software for ADR notification and recognition, has been discussed during a specific workshop held in Turin on January 17th, 2008. The report has been finalised and issued on April 2nd, 2008.

D19 Pilot ADRs Notification-Recognition Software

Status Complete

The first version of the Pilot for ADR notification and recognition, has been issued on April 8, 2008 and issued on October 9, 2008. Final release has taken place after the workshop review held in Milan on November 4th 2008.

4.6 Work Package 06 - Development of Med-ePHV e-learning pilot

D16 Med-ePHV Pilot e-learning Software

Status Complete

The draft version of the Pilot e-learning software has been discussed during a specific workshop held in Turin on January 17th, 2008. and has been finally released on April 1, 2008

D20 Report on the Med-ePHV e-learning Pilot

Status Complete

The first release of draft version of the report on the e-learning Pilot was issued on April 10, 2008. The final version has been released on November 18, 2008 after review and discussion during the workshop held in Milan on November 5th 2008.

4.7 Work Package 07 - Design of the Med-ePHV Grid

D18 Report on Med-ePHV Grid Architecture and Resources Integration

Status Complete

The draft version of the report on the Med-ePHV Grid Architecture and Resources Integration was issued on April 8, 2008. The final version has been released after completion of the internal review process on July 2, 2008.

D21 Report on Web Services and User Interface

Status Complete

The draft version of the Report on Web Services and User Interface was issued on November 11, 2008. The final version has been released after completion of the internal review process on February 18, 2009.

4.8 Work Package 08 - Testing and Validation

D24 Report on Testing and Validation addressing the three levels of target end-users

Status Complete

The draft version of the Report on Testing and Validation addressing the three levels of target end-users was issued on November 11, 2008. The final version has been released after completion of the internal review process on March 31, 2009.

4.9 Work Package 09 - Promotion and Dissemination

D02 Project Presentation

Status Complete

Presentation on the project as official executive summary of the Med-ePHV project and as A ms power Point slide presentation for meetings, conferences and workshops were prepared and issued on September 30th, 2007.

D08 Demonstration of Med-ePHV web site

Status Complete

The specification requirement document for the project web site has been produced and issued on March 15, 2007. The Internet domain medephv.com has been registered and the project web page has been opened to the public and disseminated to the main search engines.

An update of the web page content has been performed in October 2007, October 2008 and January 2009.

D14: Med-ePHV Plan for using and disseminating knowledge

Status Complete.

A draft dissemination plan was first produced at the end of the first year. It has been finalised after the PSC has decided the list of specific events and media where to present and promote the Med-ePHV project and e-learning services.

The Dissemination Plan has been released after completion of the internal review process on November 13th, 2007.

D22 Med-ePHV Exploitation Business Plan

Status Complete

The principles of the Med-ePHV Exploitation Business Plan were discussed and agreed upon among the Consortium partners during the PSC meeting held in Milan on November 4, 2008. The final version has been issued upon completion of the internal review process on March 31, 2009.

D25 Report on Med-ePHV web site contents

Status Complete

The final version of the Report on Med-ePHV web site contents has been issued upon completion of the internal review process on March 31, 2009.

D26 Final Plan for using and disseminating knowledge

Status Complete

The final version of the Plan for using and disseminating knowledge has been issued upon completion of the internal review process on March 31, 2009.

D27 Report on IPR management and copyright application

Status Complete

The final version of the Report on IPR management and copyright application has been issued upon completion of the internal review process on March 31, 2009.

4.9.1 Summary of overall progress at the end of the project:

The estimated percentages of project accomplishment as compared to targets for the entire 28 months period, detailed for each work package are as follows:

WP01	**100%**	**Target**	**100%**
WP02	**100%**	**Target**	**100%**
WP03	**100%**	**Target**	**100%**
WP04	**100%**	**Target**	**100%**
WP05	**100%**	**Target**	**100%**
WP06	**100%**	**Target**	**100%**
WP07	**100%**	**Target**	**100%**
WP08	**90%**	**Target**	**100%**
WP09	**90%**	**Target**	**100%**

All deliverables have been issued even if with some delay.

During the last Project Steering Committee meeting held at the beginning of November 2008 in Milan, it was decided that it wouldn't make sense to run the full (external) test and validation process of the French, Italian and Spanish e-learning modules in parallel. A better approach would have been to first test and validate the Spanish modules, which were in a more advanced stage. The comments and other inputs to the common sections collected as a result of the Spanish test and validation, after a lesson learned analysis, would then be used to modify and improve the French and Italian modules. The improved French and Italian e-learning modules will then undergo a smaller scale (internal) test and validation process. While this approach was followed by INSERM in the case of the French module due to the unavailability of the French SME partner to support a full validation, in the case of the Italian module UNIPV succeeded in having the e-learning modules tested (externally) by more than 150 health professionals. To complete the validation process the comments received will have to be analyzed and the needed changes and improvements introduced in the final version. For this reason WP08 has been given a percentage of accomplishment of 90%.

In the case of the Promotion and Dissemination WP09, the level of accomplishment has also been equal to 90% essentially due to reduced activity in France (again caused by the unavailability of the French SME partner to support the action) and the postponement of a large Med-ePHV communication event in Italy which had been prepared and scheduled by CIRM for the last quarter of 2008. Unfortunately Prof. Nicola Fabris, who was organizing this event together with UNIPV, suffered a fatal illness that did not allow him to accomplish this objective before his sudden death that occurred at the beginning of January 2009. The Med-ePHV communication event that had to be postponed has now been rescheduled as follows:

- On March 31, 2009 a meeting of the Lombardy Region Working Group on Pharmacovigilance, sponsored by UNIPV, will be held in the CIRM facilities in Milan, with the specific objective of reviewing the Med-ePHV e-learning systems and in particular the Italian modules.
- During the same meeting the Working Group will decide to include Med-ePHV in the international congress that has been scheduled to take place in Rome for the autumn of 2009. This event will be sponsored by UNIPV and Federfarma.

All presentation materials to be used for the Working Group meeting and for the communication event have been prepared within the scope of WP09 and are available for supporting these dissemination activities.

5. Work Package Progress at the end of the project

5.1 Work Package 01 – Project Management

Project Management activity has been more intensive than expected especially during the second period of the project and has required additional administrative and coordination effort.

The following events have required more dedicated effort by the project coordinator.

The SME Spanish partner JB had to leave the project at the end of 2006, due to lack of human resources to be dedicated to the project activities. After EC approval, JB has been replaced effective January 1, 2007 by the Spanish SME AS. The Contract with the EC, budget distribution and the Consortium Agreement (CA) had to be amended accordingly to reflect that change.

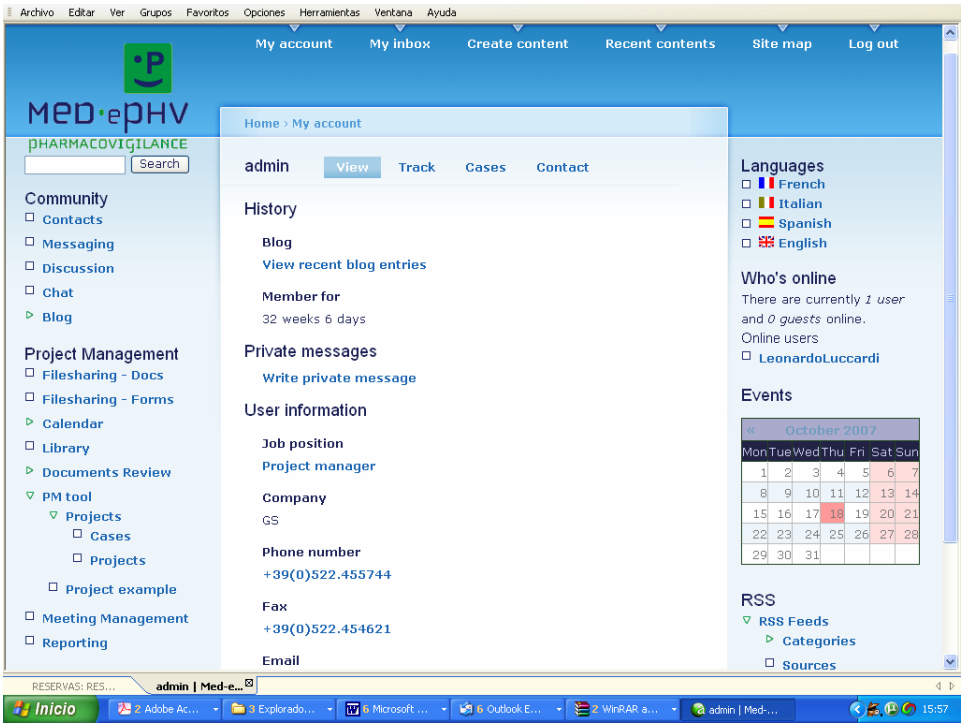
The French SME partner PMV was declared in the status of bankruptcy by the Commercial Court of Paris on March 13, 2008. However the project coordinator had no knowledge of this issue until the beginning of May 2008, when he received an official notification by the bankruptcy official receiver appointed by the Court, MJA-Selafa, which was only interested in collecting the outstanding EC contribution and offered no cooperation at all in the resolution of the administrative obligations, deriving from their participation as partner in the EC Contract. The coordinator, in an attempt to resolve the open administrative issues, even visited MJA-Selafa in Paris where he held a meeting with the officer in charge of the PMV liquidation. Nevertheless the agreed upon actions that MJA-Selafa had committed to undertake during the meeting had no follow-up and this in-spite of several expediting messages and telephone calls by the coordinator.

In order to complete the project the PSC decided to reassign the work previously allocated to PMV to the other SME partners and to a lesser extent to the French RTD partner (INSERM). The work-scope and associated budget transfer has required a new revision of the Annex 1 to the EC Contract to be prepared and submitted to the EC as an Amendment to the Contract. Considering that the PMV inactivity had caused a chain of delays also to the interfacing activities of the other project partners, the request for Contract Amendment also included a four months extension of the project duration. The Contract Amendment was approved by the EC on October 2, 2008. Again a new revision of the CA had to be made to reflect work and budget redistribution.

The kick-off meeting and four periodical Project Steering Committee (PSC) meetings have been held as planned. To improve cost effectiveness, whenever possible, technical workshops were combined with the PSC meetings.

An internal procedure defining the requirements of cost collection and reporting in accordance with EC rules, has been prepared, issued to all partners and discussed during the PSC meeting held in Milan on July 19th, 2007.

A communication based project control and reporting system was defined and implemented through the project Intranet platform (see entry page below).



Project reports; updated GANTT charts and task reports have been regularly uploaded by the co-ordinator the Intranet platform, which has been regularly maintained and updated. Partners training and indoctrination on cost reporting, the use of project procedures and Intranet, has been done during the plenary meetings (kick off and PSC's).

A project Risk Assessment using the Semi-Quantitative Analysis Tool (SQUAT) methodology, developed in the frame of an EC funded FP4 Innovation Project, has been conducted with the support of an external consultant (LTBC), experienced in risk management and co-developer of the SQUAT methodology.

WP Leaders under the guidance of the analyst have conducted a systematic analysis of the work involved in each individual WP task, identifying which ones of the project pre-selected risk categories (budget / cost, schedule, product & technology) where applicable to the WP tasks.

Having analysed the 9 WP's, comprising a total of individual 49 tasks, for 15 of them one of more of the risk areas had been identified as being applicable.

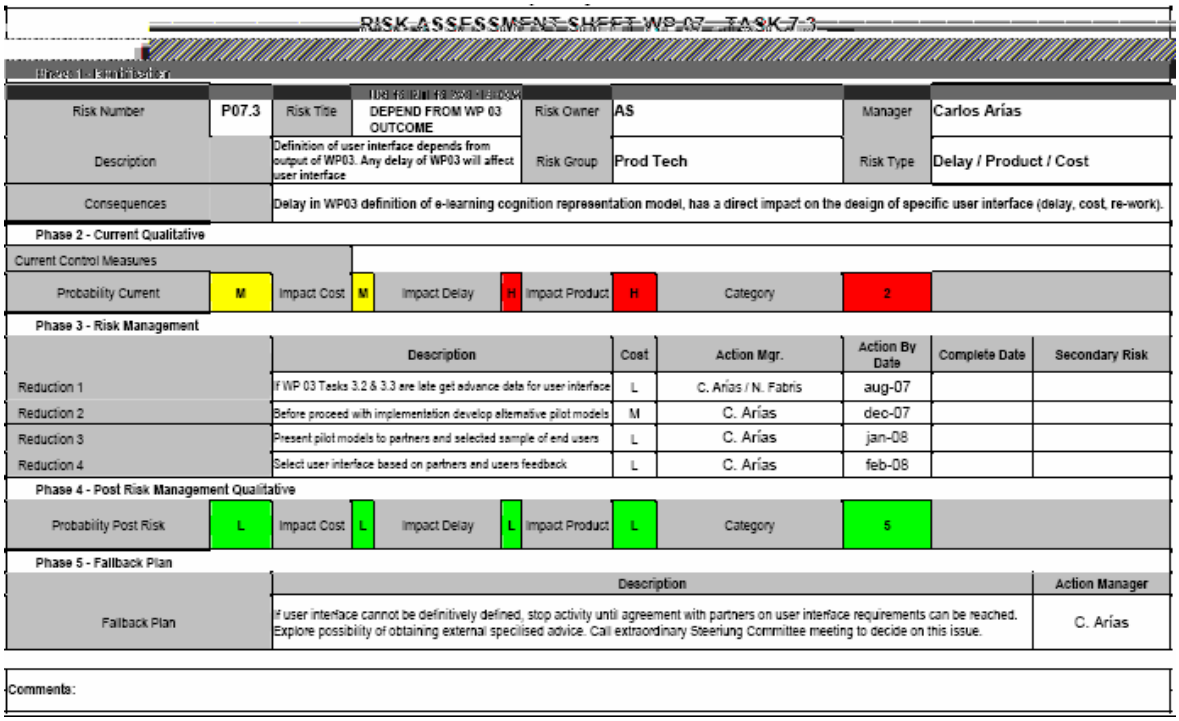
Of these two (2) had been screened as having a "low" risk potential, eight (8) with "medium" risk impact and five (5) with "high" risk impact.

Risk management process had then been defined for those WP tasks which had a "medium" or "high" risk impact.

A total of 41 possible Risk Reduction measure were identified that, if duly implemented would bring all identified risks to "low" level (category Nº 5).

The following table shows an example of a risk assessment sheet conducted for WP07 – Task 7.3. It can be seen how an identified risk (lack of external cooperation for testing and

validation) is mitigated by proper definition and implementation of risk reduction measures.



RISK ASSESSMENT SHEET WP 07 TASK 7.3

Risk Number	P07.3	Risk Title	DEPEND FROM WP 03 OUTCOME	Risk Owner	AS	Manager	Carlos Arias
Description		Definition of user interface depends from output of WP03. Any delay of WP03 will affect user interface		Risk Group	Prod Tech	Risk Type	Delay / Product / Cost
Consequences		Delay in WP03 definition of e-learning cognition representation model, has a direct impact on the design of specific user interface (delay, cost, re-work).					

Phase 2 - Current Qualitative

Current Control Measures									
Probability Current	M	Impact Cost	M	Impact Delay	H	Impact Product	H	Category	2

Phase 3 - Risk Management

	Description	Cost	Action Mgr.	Action By Date	Complete Date	Secondary Risk
Reduction 1	If WP 03 Tasks 3.2 & 3.3 are late get advance data for user interface	L	C. Arias / N. Fabris	aug-07		
Reduction 2	Before proceed with implementation develop alternative pilot models	M	C. Arias	dec-07		
Reduction 3	Present pilot models to partners and selected sample of end users	L	C. Arias	jan-08		
Reduction 4	Select user interface based on partners and users feedback	L	C. Arias	feb-08		

Phase 4 - Post Risk Management Qualitative

Probability Post Risk	L	Impact Cost	L	Impact Delay	L	Impact Product	L	Category	5

Phase 5 - Fallback Plan

	Description	Action Manager
Fallback Plan	If user interface cannot be definitively defined, stop activity until agreement with partners on user interface requirements can be reached. Explore possibility of obtaining external specilised advice. Call extraordinary Steering Committee meeting to decide on this issue.	C. Arias

Comments:

The next table is showing a summary of all the risks identified for the different work-packages and tasks and the expected situation after implementation of risk-management measures.

PHASE 1- RISK IDENTIFICATION				PHASE 2 - CURRENT QUALITATIVE					PHASE 3 RISK MANAGEMENT		PHASE 4 - POST RISK MGMT QUALITATIVE				
RISK #	RISK GROUP	RISK TITLE	RISK OWNER	PROB.	IMPACTS 1	IMPACTS 2	IMPACTS 3	CAT.	N° of RR's	NEXT ACTION DATE	PROB.	IMPACTS 1	IMPACTS 2	IMPACTS 3	CAT.
H01.7	Human Res.	Lack of H.R. to undertake risk mgmt.	GS - O. Salvaggio	H	M	M	M	2	4		M	L	L	L	5
E03.2	Ext. Depend.	Need ext. cooperation to define user needs	UNIPV - Ruberto / Fabris	M	L	M	H	2	3		L	L	L	L	5
E03.3	Ext. Depend.	Need ext. Coop to define validation guidelines	UNIPV - Ruberto / Fabris	M	M	M	H	2	4		L	L	L	L	5
E04.1	Ext. Depend.	Lack of support from Agency or other centers	UVA - A. Carvajal	M	L	M	M	4	3		L	Nil	L	L	5
E04.2	Ext. Depend.	Needed ref docs are proprietary information	UVA - A. Carvajal	M	M	L	M	4	2		L	L	L	L	5
H04.3	Human Res.	Lack H.R. to do work or lack partners support	UVA - A. Carvajal	M	M	M	M	4	3		L	L	M	L	5
P07.1	Product / Tech.	Grid definition needs interface with ext provider	AS - C. Arias	M	M	M	M	4	4		L	L	L	L	5
P07.3	Product / Tech.	User interface requirenment depend from WP03	AS - C. Arias	M	M	H	H	2	4		L	L	L	L	5
E08.1	Ext. Depend.	Need ext. coop. to test & validate modules	INSERM . J. Demotes	M	L	M	M	4	3		L	Nil	L	L	5
E08.2	Ext. Depend.	Need ext. coop. to test & validate user interface	INSERM . J. Demotes	M	M	M	M	4	3		L	L	L	L	5
E09.3	Ext. Depend.	Dissemination mat's not ready when needed	AS - C. Arias	M	M	M	Nil	4	4		L	L	L	Nil	5
E09.4	Ext. Depend.	Limited attendance to events and workshops	AS - C. Arias	M	M	L	Nil	4	3		L	L	L	Nil	5
P09.6	Product / Tech.	Product IPR not protected	AS - C. Arias	M	H	L	Nil	2	1		L	L	L	Nil	5

The SQUAT Risk Management procedure and detailed assessment results have been documented in the "Med-ePHV Project Risk Management" report attached as Annex 1, to this Project Activity Report of the first year.
The project Risk Assessment analysis conducted during the first period has been re-visited to find possible solutions/remedies to the consequences on the project of the unexpected PMV bankruptcy and in particular to the WP's where PMV had a significant role.

Intermediate and Final Project Activity Reports and Management Reports have been issued according with EC Contract requirements even if with some small delay.

5.2 Work Package 02 – Business Process Requirements

A comparative analysis of the implementation of the pharmacovigilance business process, as established in the current pharmaceutical EU and participating countries legislation, has been conducted with the objective of identifying and modelling the business requirements for the project.

The Med-ePHV improved pharmacovigilance process has been designed focusing mainly at the health system periphery, where adverse events are generated by health professionals in collaboration with Local Health Administrations (LHAs) and Market Authorisation Holders (MAHs.).

The current EU pharmacovigilance system is organised with functions, responsibilities and accountability shared between the Members States competent authorities, the European Commission and the European Medicines Agency (EMEA). The latter has the overall responsibility of coordinating the pharmacovigilance activities of the Member States.

The EMEA also collects data from pharmaceutical companies and the Member States and manages a community pharmacovigilance data base.

The review that the Consortium has made, has revealed that at national level, the pharmacovigilance systems presents similar organisations in the 3 countries involved in the project.

In France, the national pharmacovigilance system is based on a network of 31 regional centres able to provide localised support to the health professionals and a National Commission at the French Agency for the Sanitary Safety of Health Products (AFSSAPS) that centralises and evaluates all the information.

In Italy, the system is also based on a national network of Pharmacovigilance and on a coordinating centre, the Italian Drug Agency (Agenzia Italiana del Farmaco (AIFA). AIFA coordinates the national telematic Network that interconnects all health structures, regions and pharmaceutical companies.

In Spain, the system is based on 17 regional centres depending on regional authorities and on the Spanish Medicine and Health Products Agency acting as a coordinating centre.

The three national central organisations, AFSSAPS, the Spanish Medicine and Health Products Agency and the Agenzia Italiana del Farmaco are collaborating with EMEA and with WHO.

Concerning specialised training for pharmacovigilance professionals, several courses including bachelor's or master's degrees were available in the three countries, but usually there was not an officially established learning framework for pharmacovigilance.

For the health professionals, pharmacovigilance training existed as seminars for doctors and nurses. E-learning courses were only available in Spain but are not specific.

As a result of the analysis, a work-shop was held where it has been concluded that for the development of the Med-ePHV learning tools for health professionals, the following key aspects were common to the target end-users of the three participating countries and would need to be taken into account:

Adults learning substantially differs from that of younger people education and requires a different approach for content and teaching methodology.

Health professionals have very little spare time to be devoted to education and training

The education often requires to be addressed to a working team and not only to a single health professional.

Training materials can be common (except for national legislation), but must be written and made available in the three languages (French, Italian and Spanish), with the exception of reference materials (case studies) which could be kept in the original language.

The Med-ePHV Business Process Requirements, defined as a result of the study have been included in the relevant report (D07), and had been the basis for the design of the Med-ePHV system.

5.3 Work Package 03 – Study of Med-ePHV Learning Models

The scope of this work-package is key to the success of the entire project, in that it studies specifically the learning process in pharmacovigilance, in view of defining cognitive models useful for the design of advanced e-learning schemas.

The definition of the above cognitive models is based on a detailed map of the medical, pharmacological and genetic issues at the origin of adverse drug reactions (ADRs).

The study which has been performed, addresses the design of the specific learning profiles that are needed by the different type of actors that operate at the peripheral edge of the pharmacovigilance systems, i.e. health practitioners, LHAs and MAHs.

The study considers pharmacovigilance for e-learning purposes from both the viewpoint of the biomedical science and the EU regulatory framework, including its implemented at national level.

The study has been conducted following a pre-established logical sequence, implying the following tasks:

Task 3.1 and 3.2 Aimed to find which are the reference cognitive model to be used to organize biomedical and pharmacological issues for a reference actor of the pharmacovigilance business process.

The study has analysed the cognitive models for the activities of instruction and formation that have been in use since the middle of the last century, discussing the different theories developed to understand how to teach young people in school of all orders.

Then it has been analysed how these theories have been applied to adult learning, recognizing that adult learners require different methodologies, in order to adapt the instructional systems used in ordinary schools. to the experience reached as a result of the professional activity. In essence, how from a pedagogical teaching systems we must pass

to a new approach of androgogical learning systems, adding to the teaching capacities the motivation, attention, relevance, confidence and satisfaction that the learners in adult age require.

The third step was to transfer this knowledge to the new learning technologies, i.e. e-learning and on-line formation, that can foster continuous professional development as an alternative to the traditional class-room, face-to-face education method. The online formation takes into account the possibility of individual learning as well as collaborative learning, i.e. the exchange of personal experiences, or group interaction.

The last activity of this task has been dedicated to examine how these principles have been translated into the health sector. The professionals of the health sector are the most recent category having accepted the idea that professionals have to learn also in adult age. The concept of CPD (Continuous Professional Development), already in place since decades in other professions, has only reached the medical area very recently. It is a fact that CME (Continuous Medical Education) only started at the beginning of this century in the majority of the European Union Member States. Moreover, not in all of them CME is mandatory for medical doctors and only in one is mandatory also for other categories of health professionals.

This analysis has also provided information on how CME is being delivered, generally by face-to-face courses, more rarely by online formation, and how the credits for formation has been recognized and used for a re-certification of professionals.

In order to give valuable inputs for deciding the reference models for different categories of users, the study includes suggestions obtained from external sources, which have given more than specific indication for future definitions of the Med-ePHV model.

The Med-ePHV Report on reference and specific cognitive models (D09) has been produced and its conclusions discussed during a workshop held in Milan, on July 19th, 2007 in conjunction with the Project Steering Committee meeting.

The results of the study on cognitive models have been used as an input for the subsequent design phase of the e-learning courses on pharmacovigilance.

Task 3.3 and 3.4 The activities undertaken have been aimed at defining the design principle for the e-learning courses on pharmacovigilance, in line with the specific cognitive models identified in D09, by taking into account the state of the art of the standardization for e-learning cognition representation in medical education.

The study has identified that, the constructive approach seems to be the most promising for adult learning. Constructivism is a philosophy of learning founded on the assumption that, by reflecting on their experiences, learners construct their own understanding of the world they live in; thus, knowledge would be constructed through the interaction of learners with their environment.

The constructivist teacher provides tools such as problem-solving and inquiry-based learning activities with which learners formulate and test their ideas, draw conclusions and inferences, and pool and convey their knowledge in a collaborative learning environment. Constructivism transforms the student from a passive recipient of information to an active participant in the learning process.

On this basis, it has been decided that the Med-ePHV e-learning system would follow constructivism principles.

In the specific case of medical education directed to health professionals the ADDIE instructional design model was also taken into account to build the Med-ePHV e-learning modules, implying the following sequence of logical learning steps: Analysis, Design, Development, Implementation, and Evaluation.

Considering that the Med-ePHV e-learning system is targeting adults learners, the development of the learning model, should address the fact that health professionals learn by relating new learning to past experiences, by linking learning to specific needs, and by practically applying learning; this is because e-learning suits with their needs. Thus, Med-ePHV interactive learning approach shifts the focus from a passive, teacher-centred model to one that is active and learner-centred.

Some key factors of success for e-learning have been identified: Initial evaluation allowing potential modification of the training; easy-to-use, interactive, real life situation; short modules; final evaluation with different procedures to test knowledge acquisition.

It has been concluded that the e-learning model which best fits the needs for teaching pharmacovigilance and to encourage reporting to health professionals, presumably the main users, is an asynchronous online model which at the same time fulfils some requirements referred to materials (contents), teachers (facilitators), students (users organization) and environment (virtual spaces). Ideally, it should be an interaction not only with the e-learning disposal material but with the facilitator (if possible) and among users (chats, forum). Self-evaluation is an essential part of the Med-ePHV model.

As to the pharmacovigilance e-learning programme the following main topics have been identified for inclusion in the training modules subsequently developed in WP 04:

Part I. Introduction and general concepts

Safety of medicines

Definitions of terms used in Pharmacovigilance

Methods in pharmacovigilance.

Clinical and epidemiological approaches. Pharmacoepidemiology.

Spontaneous Reporting

Causality in pharmacovigilance

Signal generations in pharmacovigilance

Pharmacovigilance in pharmaceutical companies

Pharmacovigilance: Legislation and organisation

Special issues

Part II: Pharmacological approach to adverse drug reactions

Introduction

Classification of adverse drug reactions

Drug metabolism and adverse drug reactions

Interactions. Interactions between drug and disease

Genetic polymorphisms and adverse drug reactions: pharmacogenetic

Part III: Examples, cases histories and exercises

Sources of information on drug adverse reactions

Case studies

Exercises and tests

The Med-ePHV Report on Learning Models (D10) outline has been discussed during a specific workshop held in Valladolid on June 14-15th, 2007 and subsequently reviewed again in draft version during a workshop held in Milan, on July 19th, 2007 in conjunction with the Project Steering Committee meeting. The report has been finalised and issued on October 10th, 2007.

5.4 Work Package 04 – Study of ADRs Recognition and Notification

The scope of this work-package is the definition of knowledge base representation and inference mechanisms to support the generation of Adverse Drug Reactions (ADRs) in crucial pharmacovigilance areas such as innovative new medicines and orphan drugs; the envisaged knowledge bases will refer both to the established standard model for ADRs notification (ICHM2) as implemented in France, Italy and Spain and to the most relevant ADRs recognition schemes validated in the established biomedical and pharmacological science.
Within the objectives of this work-package, there is also to investigate the adoption of case histories for ADRs recognition by evaluating the feasibility of using case based reasoning (CBR) inference for ADRs recognition.

One of the outcomes of this work-package is also the Guidelines for implementation of an on-line notification system, taking into account the specific environment existing in France, Italy and Spain.

The Study of ADRs Recognition and Notification has been conducted following the tasks included in the work-package description and has resulted in two different deliverables, as summarised below.

Task 4.1, 4.2 and 4.3 are intended to develop, starting from the previously defined cognitive and e-learning models, the e-learning objects which are required to build suitable courses for a wide range of potential users.

The pharmacovigilance learning material has been organized in units which present brief and essential information on a particular topic, along with an additional and comprehensive information. For each topic multiple-choice tests have been designed with the objective of assessing the acquired knowledge. Main references from literature, recommended reading and links are also incorporated in the training material. Similarly, several clinical cases are presented with the corresponding questions.

All these materials permit to be assembled in different ways, in accordance with the constructivist approach for learning recommended in D10. Following this approach, whichever way might be chosen by the potential learners, they may start from the main concepts and then go to the clinical cases or conversely they could start facing the cases and then go back to the main concepts and to the additional information. Thus, although in D10 a formal programme was presented in reality it would not exist as such, since several "programmes" may be packaged with the developed learning material, tailor made to fit individual learner needs.

Very detailed multilingual training materials, specifically designed for the profile of the health professional who want to learn or improve his/her knowledge in pharmacovigilance, have been prepared and are included in the Report on Med-ePHV notification and recognition (D11).

The report includes a matrix which allows to package the different subjects to the specific profile of the target users (medical doctor, pharmacist, nurse, etc.), at basic and advanced learning level.

The main topics covered by the training materials that have been developed have been grouped as follows:

a Essential Information
- Safety of medicines
- Pharmacoepidemiology
- Spontaneous Reporting
- Causality in pharmacovigilance
- Signal generations in pharmacovigilance
- Special issues

b) Additional Information
- Pharmacoepidemiology
- Spontaneous Reporting
- Causality in pharmacovigilance
- Signal generations in pharmacovigilance
- Special issues

c) References and recommended reading
- Pharmacoepidemiology
- Spontaneous Reporting
- Causality in pharmacovigilance
- Signal generations in pharmacovigilance
- Special issues

d) Recommended web sites
- Safety of medicines
- Pharmacoepidemiology
- Spontaneous Reporting
- Special issues

e) Clinical cases
- Anemia and Leukopenia caused by drugs
- Cyclosporine induced renal toxicity
- Alopecia caused by Strontium Ranelate
- Other clinical cases

f) Problems and questionnaires

- Pharmacoepidemiology
- Spontaneous Reporting
- Causality in pharmacovigilance
- Signal generations in pharmacovigilance
- Special issues

g) Annexes

Glossary of most common terms used in pharmacovigilance

The Med-ePHV Report on Notification and Recognition (D11) outline has been discussed during a specific workshop held in Valladolid on June 14-15th, 2007 and subsequently reviewed again in draft version during a workshop held in Milan, on July 19th, 2007 in conjunction with the Project Steering Committee meeting. Rev. 1 of the report has been finalised and issued on October 15th, 2007.

Task 4.4 has an objective to develop the Guidelines for implementing the Med-ePHV Notification and Recognition system, taking into account the specific environment existing in France, Italy and Spain.

The Report on Implementation Guidelines (D13) covers a synthesis of the systems used in France, Italy and Spain to collect and analyse ADR's (including how ADR's are statistically treated). The report is based on the survey results provided by the RTD partners of the three countries and the recommendation on how to address this topic within the Med-ePHV pilot, is the result of a specific workshop that was held in Paris on September 26th, 2007.

The conclusions of the workshop, which have been included in the final version of the Report on Implementation Guidelines have been:

There is no online ADR's reporting system in France and Italy. A pilot on-line notification system has been implemented in some of the Spanish autonomous regions. The Med-ePHV project will bring a new service.

The added value of an on-line notification tool in the Med-ePHV project is multiple:

It makes it possible to put into practice what was learned during the training

The use of new technologies allows a contextual assistance (dictionary of definitions, links towards the course, details on the nature of information requested, etc), which facilitates the filling, avoids or reduces the errors of information or reading.

The project will be limited to medicinal products.

The notification tool will be different for the three countries since it will have to reflect the national legislation and notification forms (they are different in the three countries). Only one on-line form per country will be implemented.

As a result of the discussion that took place during the workshop, it was decided to exclude from the project the following subjects:

The integration of the MedDRA dictionary in the notification tool, since coding will continue to be done by the local health authorities by qualified and trained people . The scope of the project stops when a health professional transmits his/her form to the centre

of pharmacovigilance. Nevertheless the MedDRA coding and how information is treated needs to be covered in the corpus of the training programme.

The development of a patient online notification tool (France and Italy) even if it could aim at the formation of patients' associations (official intermediary between the patients and Afssaps in the French project of partnership with patients' and consumers' organizations), is a subject to be covered in the corpus of the training programme.

Consideration should be given to the possibility of direct transmission of the form to the centres of pharmacovigilance.

The on-line notification tool has been conceived with the objective of facilitating the work and the comprehension by the health professionals.

Recommended practical aspects to be implemented were:

- A seizure field by field is recommended. Several fields can be gathered on the same page: e.g. data relating to the patient (age, sex.)

With each stage, an on-line help is proposed. It can take the form of:

- an example
- access to a dictionary allowing to include /understand the definition of a term employed
- a reference towards the corpus of training,
- a closed list of possible answers
- a spelling check tool.

In a more transverse way, the health professional will have access to a list of the "most frequently asked questions".

Upstream, and on a banner page, the professional is brought to make one of the following choices:

- I want to see an example
- I want to print a blank form
- I want to fill a form

After having completed all the fields, the user can visualise his/her duly well filled form and can decide to save a pdf version of it.

The Report on Implementation Guidelines (D13) has been finalised and issued on October 10th, 2007.

5.5 Work Package 05 – Development of ADRs notification pilot

The main scope of this workpackage is the design and implementation of a pilot notification system based on the results of achieved in WP 04, with the objective of demonstrating the feasibility of a knowledge based problem solving system for both ADRs recognition and notification.

The notification component was to be developed by leveraging on the well established international standards and regulations. The design and implementation of the recognition component was evidently more challenging and requiring a more intensive effort and a longer development and validation time.

It must be reminded that the Med-ePHV pilot notification (and recognition) system was intended to be designed and implemented only for training purposes and not for direct production of ADRs.

The design and construction of the pilot notification / recognition system has followed a pre-established logical sequence, implying the following tasks:

Task 5.1 & 5.2 – These two tasks covered first the acquisition of the results of WP 04 and the identification of the necessary information resources (medicines, database, appropriate medical dictionaries, …) specific to the needs of health practicioners in France, Italy and Spain.
As a second step a pilot notification system based on the results of WP 04 needed to be designed. The design included both the software architecture and the necessary knowledge base for ADRs notification and recognition.

The chosen user interface is a web application suitable to any browser supporting Ajax.
In order to properly design the end user level (the focus of Med-ePHV) we have taken into account the following elements:

1. The first level of data collection must be conveniently planned at the initial level of the **authority chain**: i.e. in Italy the ASL (Azienda Sanitaria Locale). The envisaged architecture will give moreover the possibility to the regional pharmacovigilance offices to manage and evaluate the data under their direct responsibility in order to produce analysis of specific regional interest.
2. **ICH M2** Data Model for ADRs reporting, adapted to the Scope of Peripheral Spontaneous Submissions, seeking the simplified data model of the ICH E2B protocol proposed by the responsible authorities : such as the “Scheda Unica” of Italian AIFA
3. In the ADRs Med-ePHV system, we have decided to use the simplified notification schemes prepared by the national responsible authorities, taking into account the medical culture and the characteristic of each pharmaceutical market.
4. Optionally, adding to this synoptic model a simple MedDRA coding, to be performed as automatically as possible via software and involving the health practitioner in a kind of validation process only.

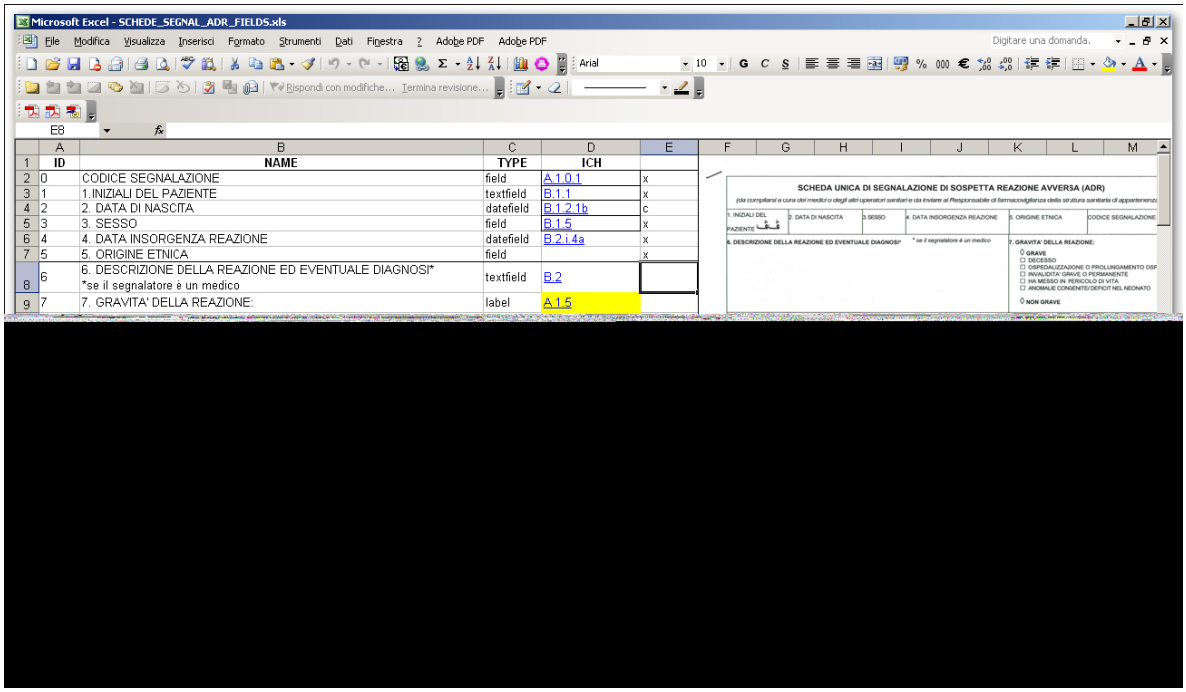
The following scheme shows how the different components integrate and are inter-related.

The application had to conceived in such a manner that would make it possible to support the compilation of the ADRs regional reports by ensuring the following support and validation:

- Support for the correct identification of the medicines involved by validation with respect to the *national database of market authorized medicines*;
- Validation of *patient data* through logical and semantic cross checks;
- *Terminological support* to the suspected ADRs description and eventual patient's diagnosis;
- Comprehensive integration support in the case of suspected ADRs involving the *parallel use of more than one medicine or medicine associated* with nutraceuticals, herbal products or homeopathic products;
- Whenever possible, support the determination of facilitating conditions by access to a known database of such conditions (i.e. access to MedDRA dictionary for users guided coding).

The platform that has been chosen to develop the ADRs software is DRUPAL, as well as the project's intranet.
Drupal is a free and open source modular framework and content management system (CMS) written in the programming language PHP. Drupal, like many modern CMSs, allows the system administrator to organize the content, customize the presentation, automate administrative tasks, and manage site visitors and contributors.
Although there is a sophisticated programming interface, most tasks can be accomplished with little or no programming. Drupal is sometimes described as a "web application framework", as its capabilities extend from content management to enabling a wide range of services and transactions.

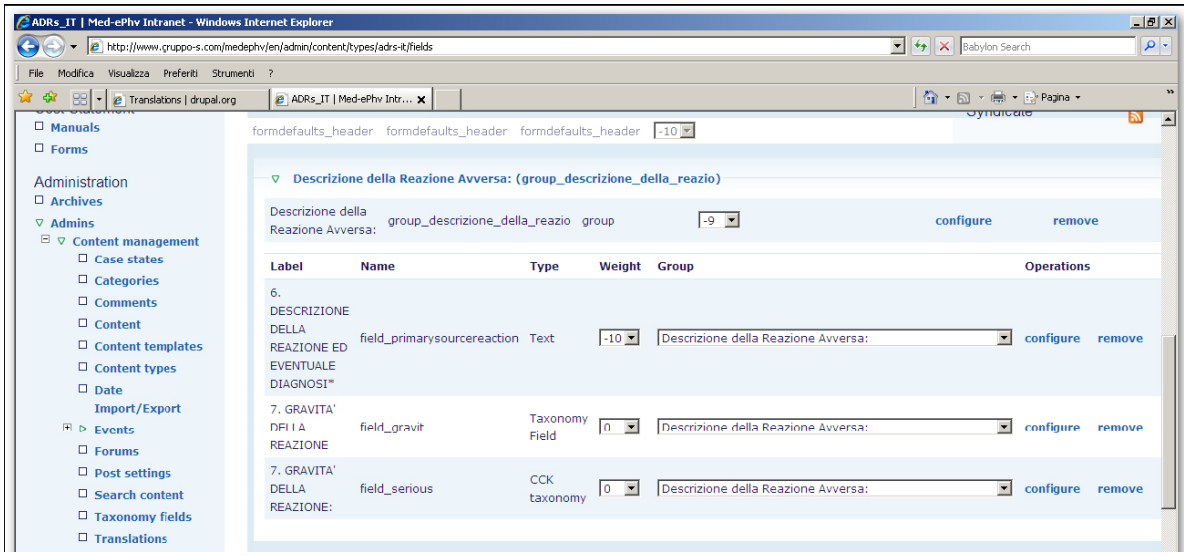
The following images are a sample of screenshots of the pilot implementation as would appear on the user's computer screen:



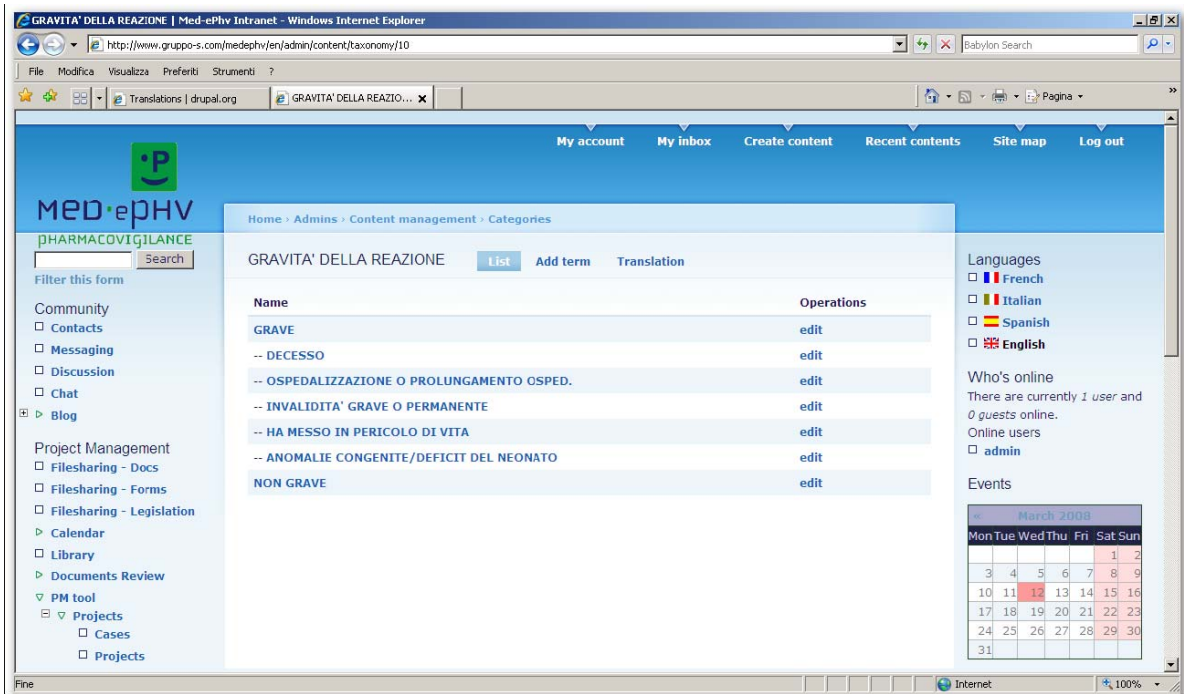
	A	B	C	D	E
1	ID	NAME	TYPE	ICH	
2	0	CODICE SEGNALAZIONE	field	A.1.0.1	x
3	1	1.INIZIALI DEL PAZIENTE	textfield	B.1.1	x
4	2	2. DATA DI NASCITA	datefield	B.1.2.1b	c
5	3	3. SESSO	field	B.1.5	x
6	4	4. DATA INSORGENZA REAZIONE	datefield	B.2.i.4a	x
7	5	5. ORIGINE ETNICA	field		x
8	6	6. DESCRIZIONE DELLA REAZIONE ED EVENTUALE DIAGNOSI* *se il segnalatore è un medico	textfield	B.2	
9	7	7. GRAVITA' DELLA REAZIONE:	label	A.1.5	

Field cross-correlation

Analysis: field cross-correlation between *"Scheda unica di segnalazione di sospetta reazione avversa"* (ADR) and ICH specifications



***"Descrizione della reazione avversa"* (Description of ADR) fieldgroup**



Taxonomy module: *"Gravità della Reazione"* (Seriousness) Vocabulary

The pilot has been first established on the basis of the Italian ADR notification scheme following the rules prescribed by the ICHs standard, integrated with all the available notes/improvements from the quoted sources.
We have also integrated all those taxonomies which were considered to be more beneficial for didactic purpose.
Having completed, tested and validated the Italian model, we have proceeded with the adaptation of the software to the specific requirements of France and Spain. Having benefitted of the experience acquired in the development of the Italian model, this adaptation step has resulted to be a much simpler and quicker task.

Task 5.3 – This task had as an objective the implementation and testing of a pilot for on-line training in ADRs notification and recognition. One specific model was planned to be implemented for each of the three countries (France, Italy and Spain).

To achieve this objective, we have designed an electronic interactive form that mirrors the paper forms currently used in the target countries (France, Italy and Spain), by helping step by step the user to fill them correctly, by means of an user-friendly on-line interface. The electronic form, which fully complies with the applicable national legislation, also creates as an output a form compatible with the ICH standard.

The ADR intelligent reporting application that has been developed within the Med-ePHV project provides a high level of guidance to users who have a limited or inexistent experience in ADR reporting, in such a way that it can deliver a suspect ADR report, that can provide a valid input to the EU pharmacovigilance process. The Med-ePHV intelligent reporting application has been specifically designed by taking into account the specific requirement of the health professionals operating in the three target Mediterranean countries (France, Italy and Spain). Following the indications of the Med-ePHV PSC, the

first pilot has been realized using as a reference, the Italian ADR model. Once tested and validated the Italian version of the intelligent reporting application, it has been adapted to fit the French and Spanish ADR reporting forms and respective national notification requirements.

For the development of the ADRs pilot system we have taken into account the following key points:

1. The **documentation** and its current state of use;
2. The use of a Open Source platform (**Drupal**) and the standards;
3. The use of appropriate data bases and information sources (**taxonomies**);
4. The **legislation** in force;

   The ICH standard ADRs message has been decided by the Med-ePHV Consortium to be the reference standard for the data structure design and implementation for the suspected ADRs reporting.

To make it really possible the use of the tool by end-users with limited or non-existent experience in the recognition and notification of ADRs, we have privileged, for a facilitated compilation of the fields in the form, the use of taxonomies, or even categories and on-line databases. In particular, the following databases have been used in our pilot model:

Clinical tests;
Drugs
Reaction Seriousness
Ethnic origin
Reporter identifier

In addition, in order to correctly define the format of the fields, an analysis was made in the form of a crossroad between the national paper form and the ICH standard. We have also taken into account the results of an extended survey conducted on the current state of the art in ADRs reporting practice.
These are the most relevant advantages which had targeted for our pilot intelligent reporting application:

no limitation in the number of simultaneous on-line users;

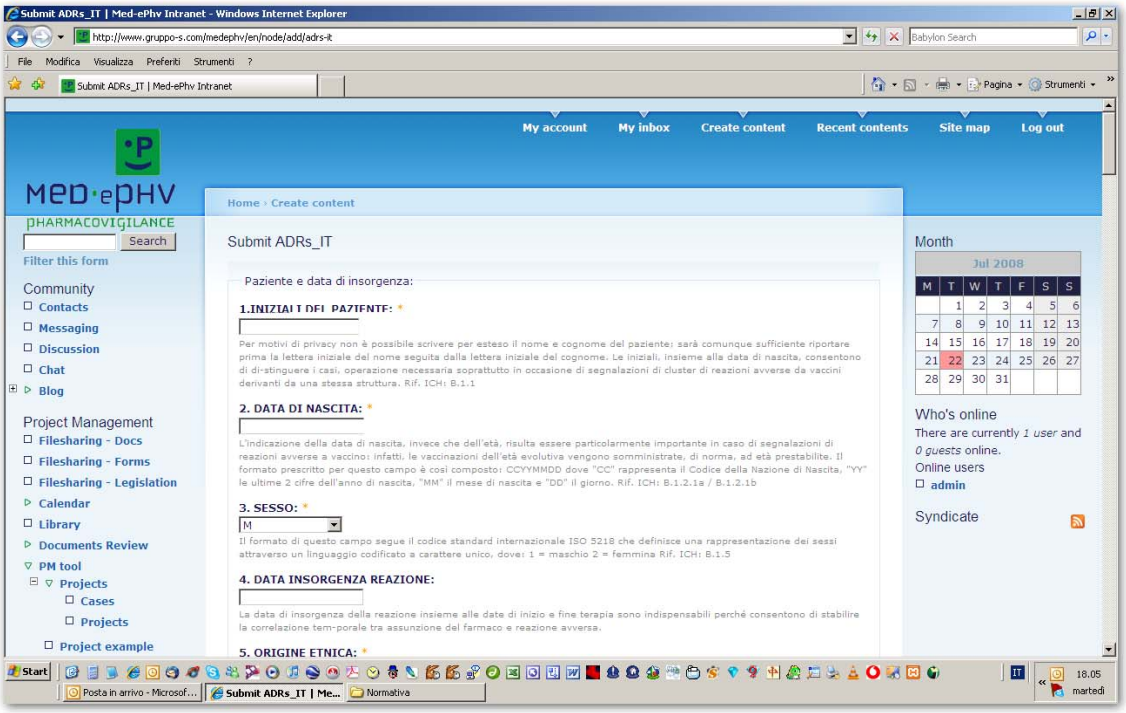
simple and secure ADR reporting in ICH standard;

intelligent management of data fields;

accessibility to a full feature on line guides and help tool.

The entire pilot system for on-line ADR's notification was developed on the Med-ePHV project intranet, which is installed on a DRUPAL Open Source platform consisting of various friendly and versatile modules, developed in PHP, allowing the development and customization of web applications 2.0.

In the next example we show the first pilot implementation developed taking as a model the Italian ADRs form "AIFA_scheda_unica_segnalazione_ADR". The on-line Italian ADRs notification module is displayed to the user as shown below:



The entire content and structure of the Italian version of the ADRs notification and recognition module is described with all details in the project deliverable D 19 - Pilot ADRs Notification-Recognition Software. The French and Spanish versions of the same module, are available in the Med-ePHV Intranet to registered users (including the EC officers in charge of the Med-ePHV Contract).

5.6 Work Package 06 – Development of Med-ePHV e-learning pilot

The scope of this workpackage was the design and implementation of a number of pilot e-learning courses on Pharmacovigilance, based on the specific cognitive models developed in the WP 03.
The e-learning courses would be tailored for the identified category of users and cover the three languages of the participating SMEs (French, Italian and Spanish).

The SME partner AS, responsible for the development and implementation of the Med-ePHV e-learning pilot had conducted a survey of the available software platforms for e-learning application and made a comparison with the objective of selecting the most suitable software for the Med-ePHV system.

As a result of the comparison study, it had been decided to adopt the “Moodle” Open-Source course management system.

The design and construction of the Med-ePHV e-learning pilot system has included the following tasks:

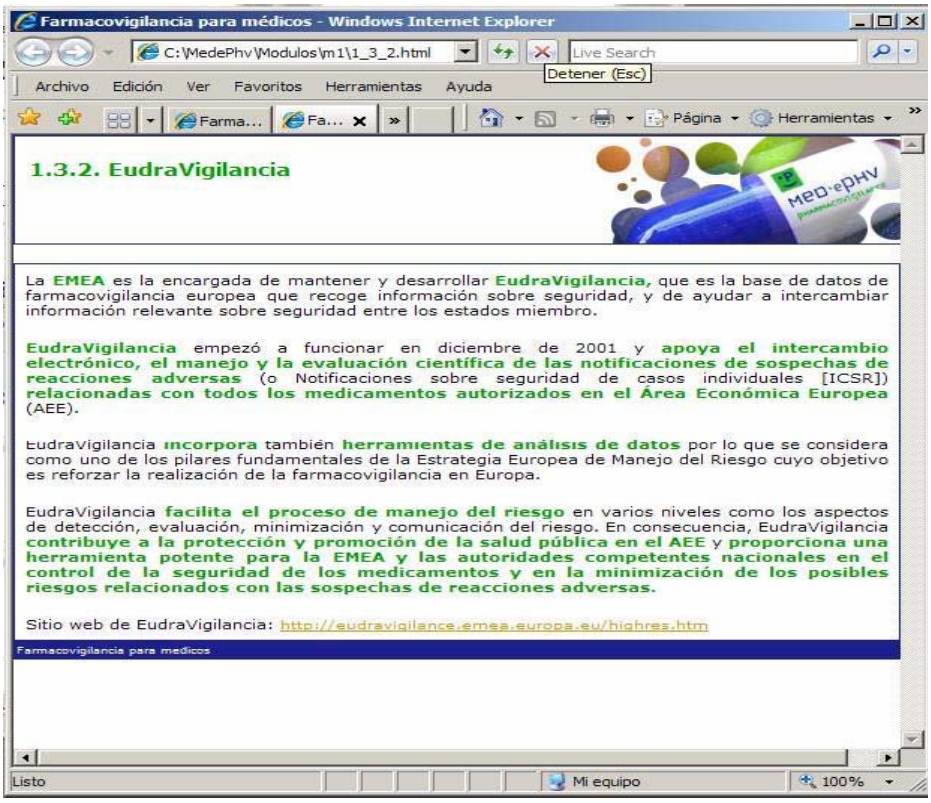
Task 6.1 – An in-depth analysis of how the Med-ePHV cognitive model could be adapted to the Moodle e-learning platform has been made. A matrix of the specific Med-ePHV requirements has been prepared and checked against the Moodle e-learning platform specification.

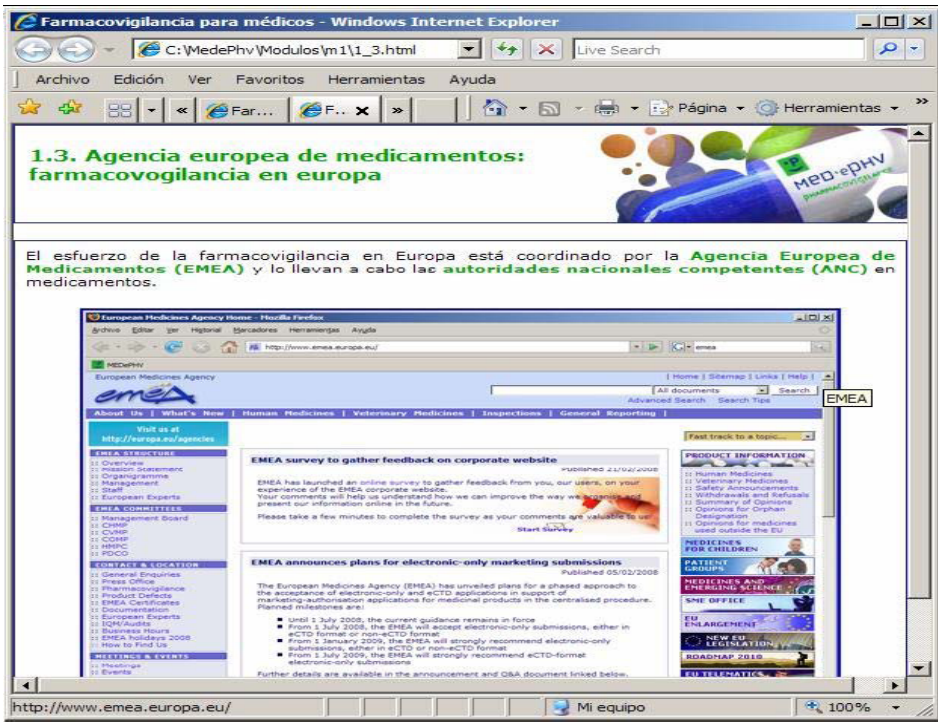
Moodle is a software package for producing internet-based courses and web sites. It´s an ongoing development project designed to support a social constructionist framework of education. Moodle is an active and evolving work in progress.
The project Moodle is based on courses. The word Moodle applies both to the way it was developed, and to the way a student or teacher might approach studying or teaching. Moodle's modular design makes it easy to create new courses, adding content that will engage learners.
Moodle has been chosen because it has got many advantages to achieve the aims of the Med-ePHV project, such as:
Moodle is an Open Source software and the most important advantages for the Med-ePHV project are:

- Med-ePHV project guarantees the right to copy, modify and redistribute the software
- Being an Open Source software, Moodle tends to be more secure, more stable and to develop faster than equivalent closed source software.

Moodle's Open Source nature means that there are far more avenues for support available than is the case for other LMS systems.

In the following screen-prints we are showing examples of how Moodle has been applied in the Med-ePHV e-learning pilot using a modular design approach.





A detailed description of the development of the Med-ePHV e-learning software made through adaptation of the Moodle platform, has been given in the project deliverable D16 - Med-ePHV Pilot e-learning Software.

Task 6.2 & 6.3 – These two tasks were intended to cover, starting from the Cognitive Models developed as a result of WP 03, the development of common courses modules for different user's profile (health practitioners, LHAs and MAH) and the adaptation to the specific end-users requirements of France, Italy and Spain. The modules would subsequently undergo on-line testing within the Consortium.

It must be pointed out that the PSC had decided to develop the most comprehensive courses, from which, in a subsequent phase, certain matters not relevant for less demanding users (eg. Nursery personnel), would be removed to make the course simpler and better oriented to the specific identified user profiles.

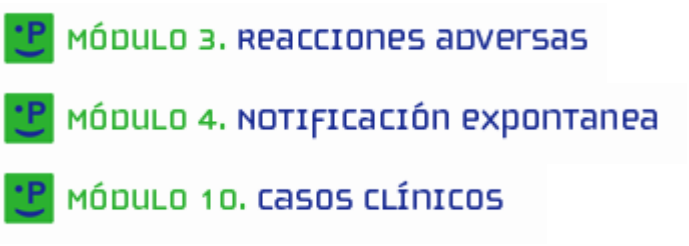
Below we summarize the content of the different modules as designed and packaged for the different profiles of Med-ePHV users (note: the screen images are taken from the Spanish version, which is the first version developed).

BASIC COURSE FOR HEALTH PRACTITIONERS

The aim of this course is that health practitioners can know the main elements that are part of the system of epidemiological vigilance of the adverse reactions and they can inform with the "yellow card" or other equivalent ADR notification form, about the adverse reactions that may appear in their daily lives.

The course is divided up in three modules, module 3 in which the adverse reactions are

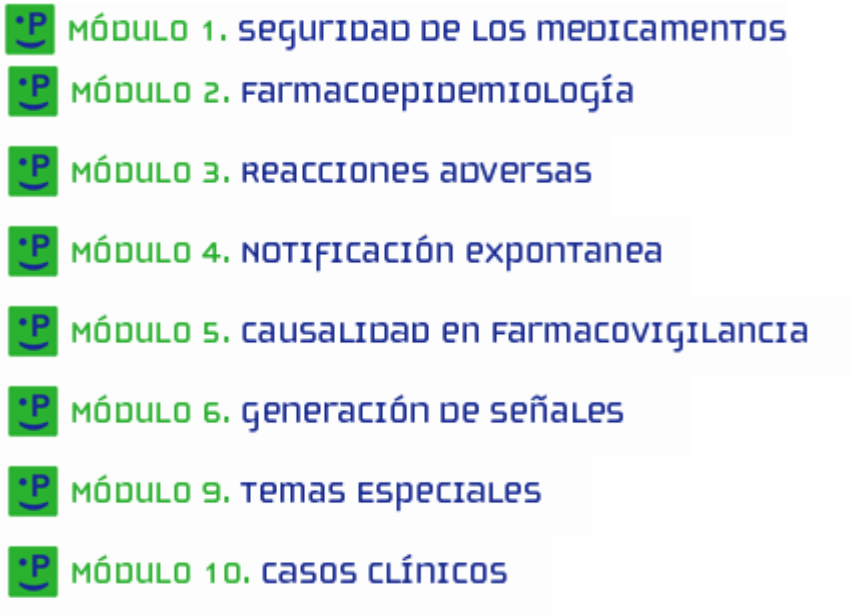
described, module 4 that explains what the spontaneous notification is about, and another one in which some clinical examples are shown:



ADVANCED COURSE FOR HEALTH PRACTITIONERS

The aim of this course is that Health Practitioners of Pharmaceutical Industry can achieve a wide knowledge about everything related with the security of the medicines and their valuation. The limitations of the clinical essays and the necessity of nets of epidemiological vigilance of the adverse reactions will be studied. We will also study the way in which we evaluate the relation of chance between taking of a medicine and the appearance of an adverse reaction, using different algorithms.

The health Practitioners that take part in this course will not only achieve the knowledge to inform about the adverse reactions that may appear in their daily lives but also they will be able to read and understand scientist literature about the security of medicines and value the relation benefit-risk of a certain medication. This course is divided up in eight units:

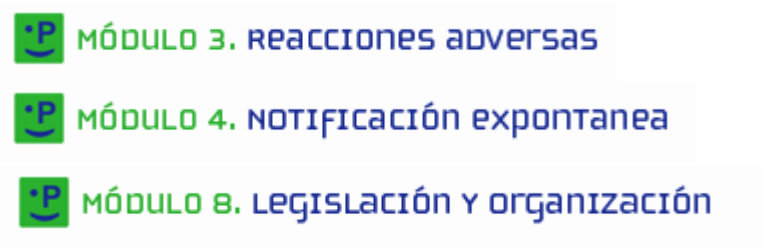


The module about legislation and about pharmacovigilance in the Pharmaceutical Industry are not part of this package. In the unit about “spontaneous notification” there are some references concerning the most important legislation about medicines security.

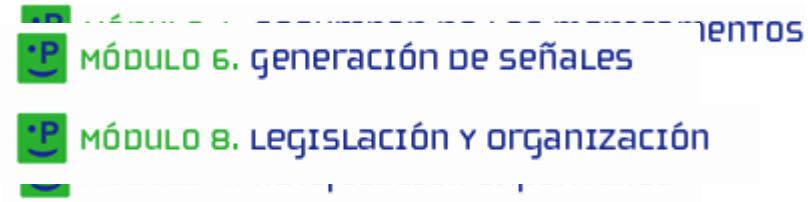
BASIC COURSE FOR HEALTH AUTHORITIES

The aim of this introductory course is that health authorities can know the main elements

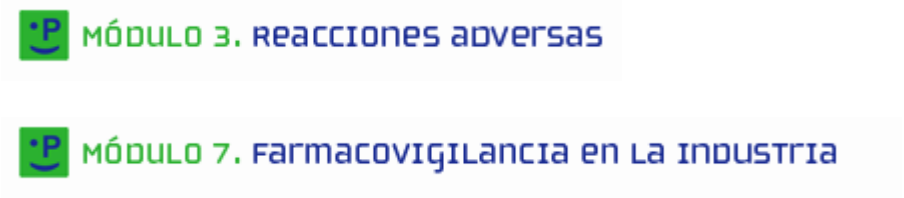
that are part of the system of epidemiological vigilance of the adverse reactions and they can assure the good working of this system.
The course is divided up in three modules, module 3 in which the adverse reactions are described, module 4 that explains what the spontaneous notification is about (using the "yellow card") and another one in which the most important legislation about the subject is explained

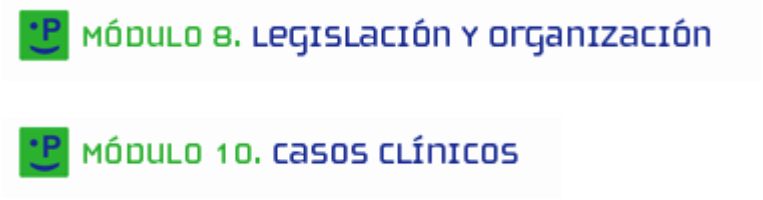


ADVANCED COURSE FOR HEALTH AUTHORITIES
The aim of this course is that Health Authorities achieve a wide knowledge dealing with the security of drugs from the point of view of its organization and working. The course includes five modules, covering "security of medicines", "adverse reactions", "spontaneous notification", "signals generation" and "legislation"



BASIC COURSE FOR PHARMACEUTICAL INDUSTRY
The aim of this course is that Health Practitioners of the Pharmaceutical industry achieve a knowledge of the main elements that are part of the system of epidemiological vigilance of the adverse reactions and they can carry out the tasks about pharmacovigilance.
This course is divided up in four modules, they are about "adverse reactions", "pharmacovigilance in the industry" and the legislation, and in the last module we can see some clinical examples.



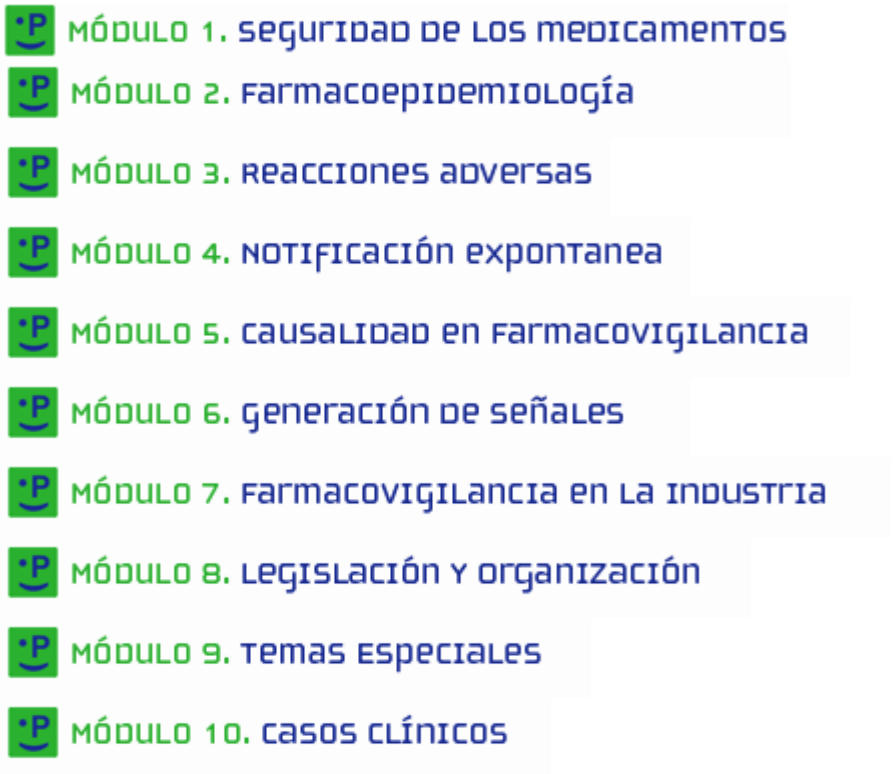


ADVANCED COURSE FOR PHARMACEUTICAL INDUSTRY

The aim of this course is that Health Practitioners of Pharmaceutical Industry can achieve a wide knowledge about everything related with the security of the medicines and their valuation. The limitations of the clinical essays and the necessity of nets of epidemiological vigilance of the adverse reactions will be studied. We will also study the way in which we evaluate the relation of chance between taking of a medicine and the appearance of an adverse reaction, using different algorithms.

The health practitioners that take part in this course will not only achieve the knowledge to inform about the adverse reactions that may appear in their daily lives, but they will be able to read and understand scientist literature about the security of medicines and appreciate the relation benefit-risk of a certain medication. We will stress the design of programs about the management of risks.

These are the modules of the course:



MED-EPHV E-LEARNING PILOT

The first on-line e-learning pilot has been implemented for the Spanish modules.

In the following screen prints we show some examples of the pilot implementation of the Basic Course for Health Authorities.

When the student that in the example has been name Dr. Martinez, wants to enter in the platform of the course he must click on the following link:

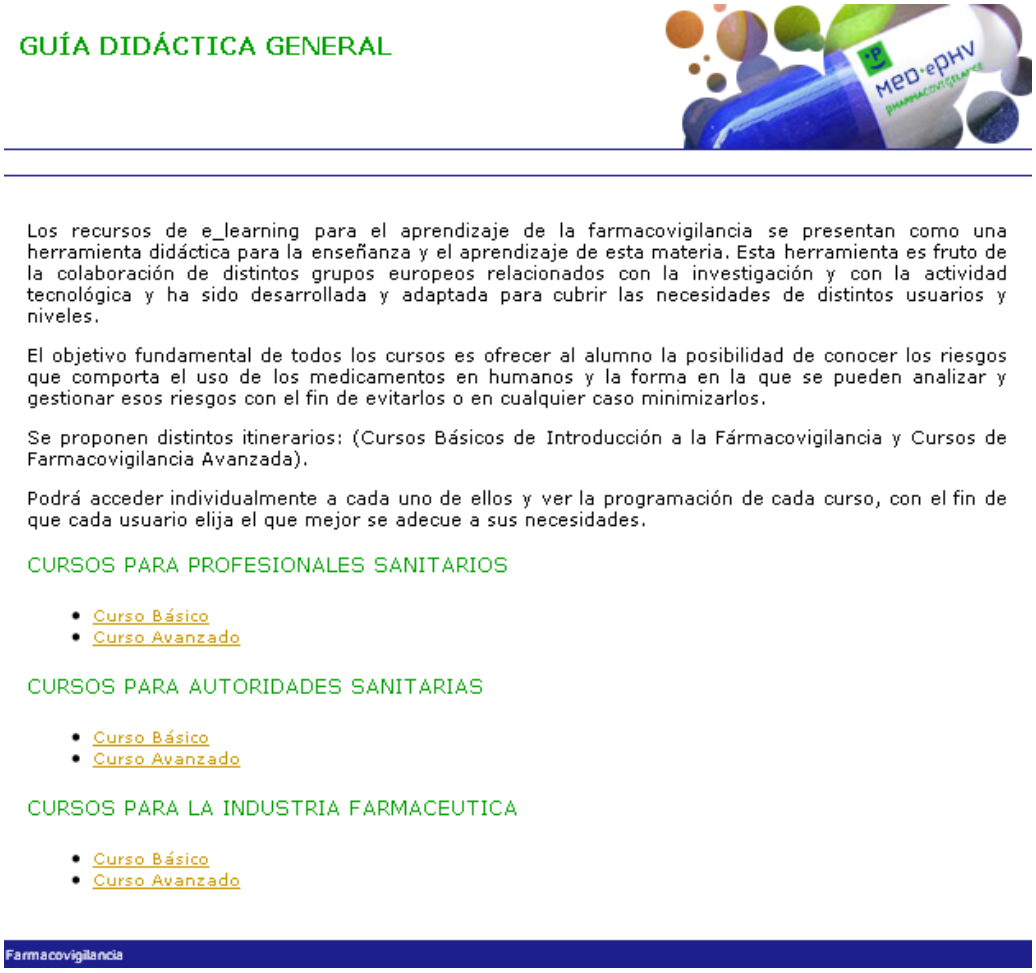
http://www.formacionenlinea.org/medephv/

He will then see the screen below:

When he clicks on "Introduction to the Pharmacovigilance", this page will be displayed asking the user to log-in (user and password are to be input):

Doctor Martinez has his password and he enters in the platform of Med- ePHV to start the development of the course.
Doctor Martinez has just entered in the course and he appears as "registered"

Doctor Martinez enters in the didactic guide to see in a more detailed way the contents of the course that he is going to study, the aims and the modules that are part of this course.



GUÍA DIDÁCTICA GENERAL

Los recursos de e_learning para el aprendizaje de la farmacovigilancia se presentan como una herramienta didáctica para la enseñanza y el aprendizaje de esta materia. Esta herramienta es fruto de la colaboración de distintos grupos europeos relacionados con la investigación y con la actividad tecnológica y ha sido desarrollada y adaptada para cubrir las necesidades de distintos usuarios y niveles.

El objetivo fundamental de todos los cursos es ofrecer al alumno la posibilidad de conocer los riesgos que comporta el uso de los medicamentos en humanos y la forma en la que se pueden analizar y gestionar esos riesgos con el fin de evitarlos o en cualquier caso minimizarlos.

Se proponen distintos itinerarios: (Cursos Básicos de Introducción a la Fármacovigilancia y Cursos de Farmacovigilancia Avanzada).

Podrá acceder individualmente a cada uno de ellos y ver la programación de cada curso, con el fin de que cada usuario elija el que mejor se adecue a sus necesidades.

CURSOS PARA PROFESIONALES SANITARIOS

- Curso Básico
- Curso Avanzado

CURSOS PARA AUTORIDADES SANITARIAS

- Curso Básico
- Curso Avanzado

CURSOS PARA LA INDUSTRIA FARMACEUTICA

- Curso Básico
- Curso Avanzado

Farmacovigilancia

In the didactic guide Doctor Martinez opens a PDF in which he is interested like the one shown below:

GUIA DIDACTICA PARA LAS AUTORIDADES SANIARIAS

CURSO BÁSICO

1. Título:

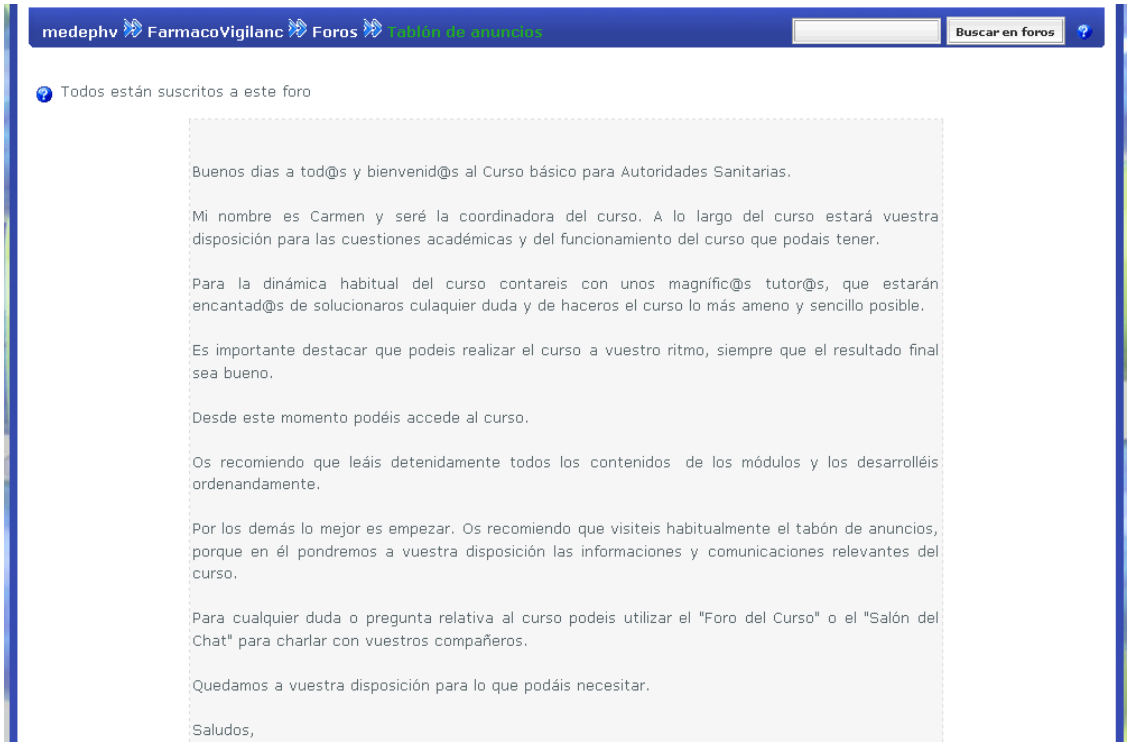
Introducción a la Fármacovigilancia para Autoridades Sanitarias.

2. Descripción:

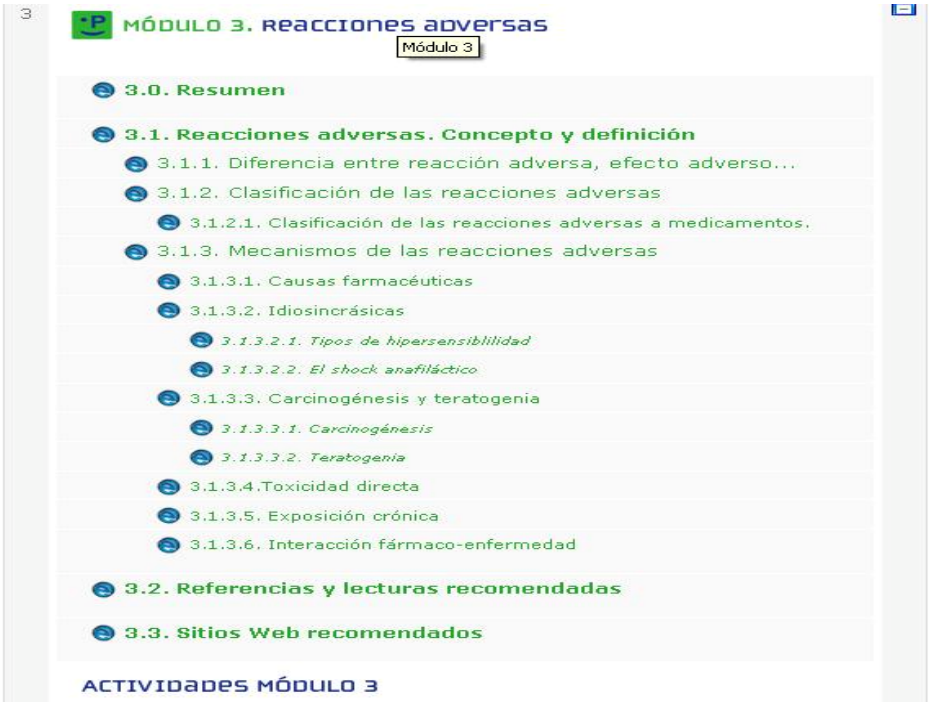
El objetivo fundamental del curso es ofrecer al alumno la posibilidad de conocer los riesgos que comporta el uso de los medicamentos en humanos y la forma en la que se pueden analizar y gestionar esos riesgos con el fin de evitarlos o en cualquier caso minimizarlos.

...

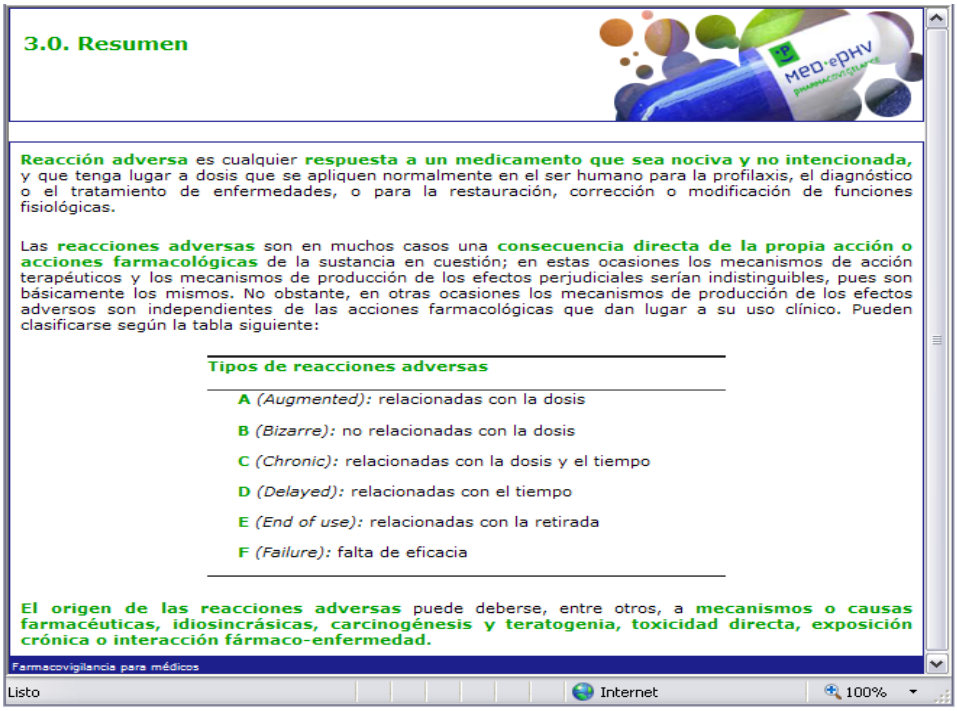
He has already seen all the information about the course that he is going to study and he enters in the notice board to see more interesting information and he reads that the tutor of the course is welcoming the students.

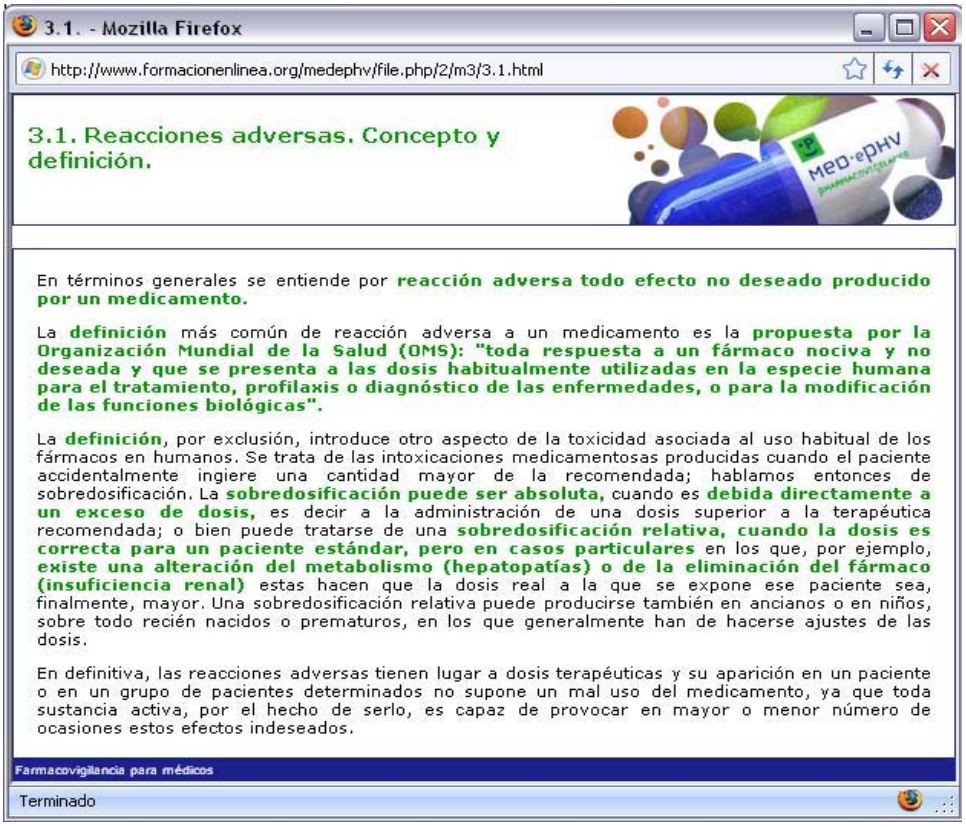


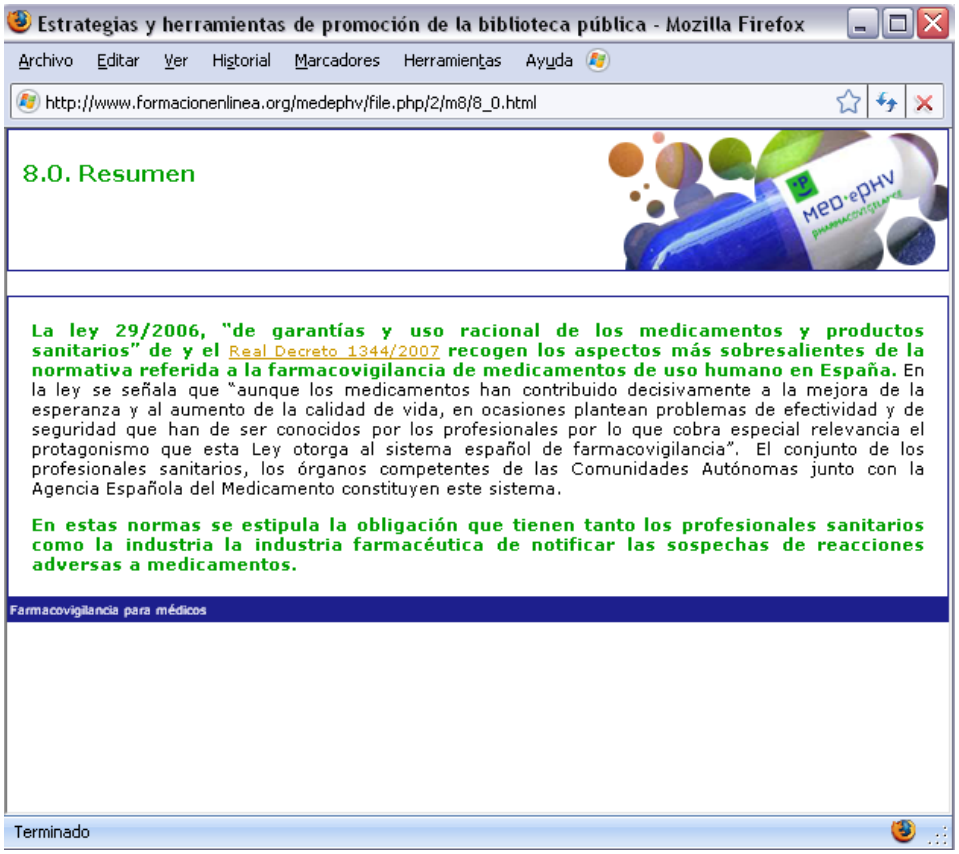
After this, Doctor Martinez gains access to the contents of the module 3 which is the first module of the course he has decided to follow.



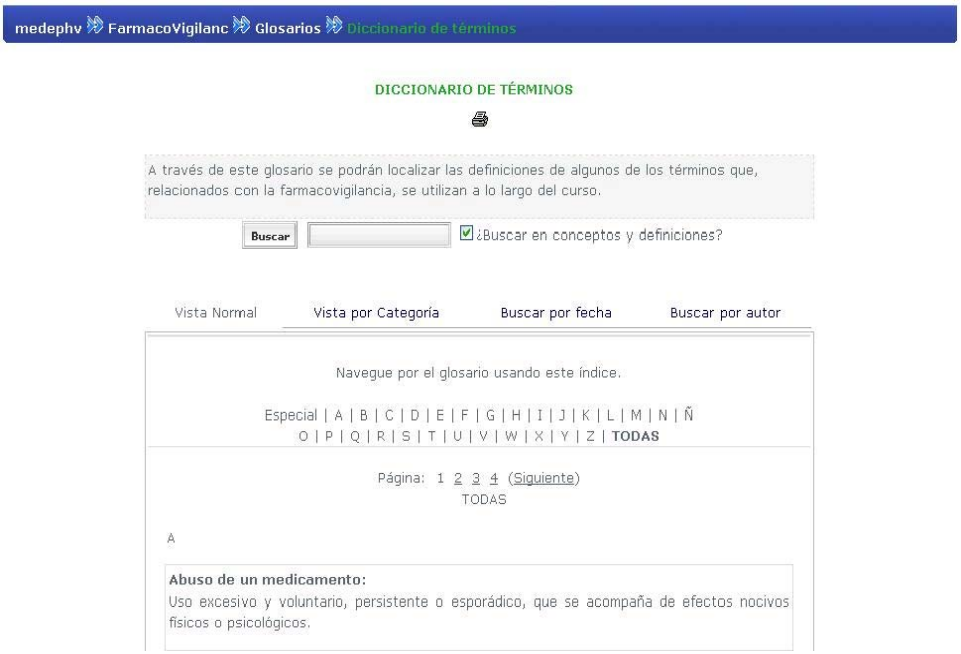
He starts looking at the figure 3.0 summary and the figure 3.1. Adverse reactions of the medicines. All their contents will appear in a detailed way, separated by index cards. After module 3 Doctor Martinez starts to study the other two modules of the basic course for Health Authorities, the module 4 “spontaneous notification” and module 8 “legislation and organization”.





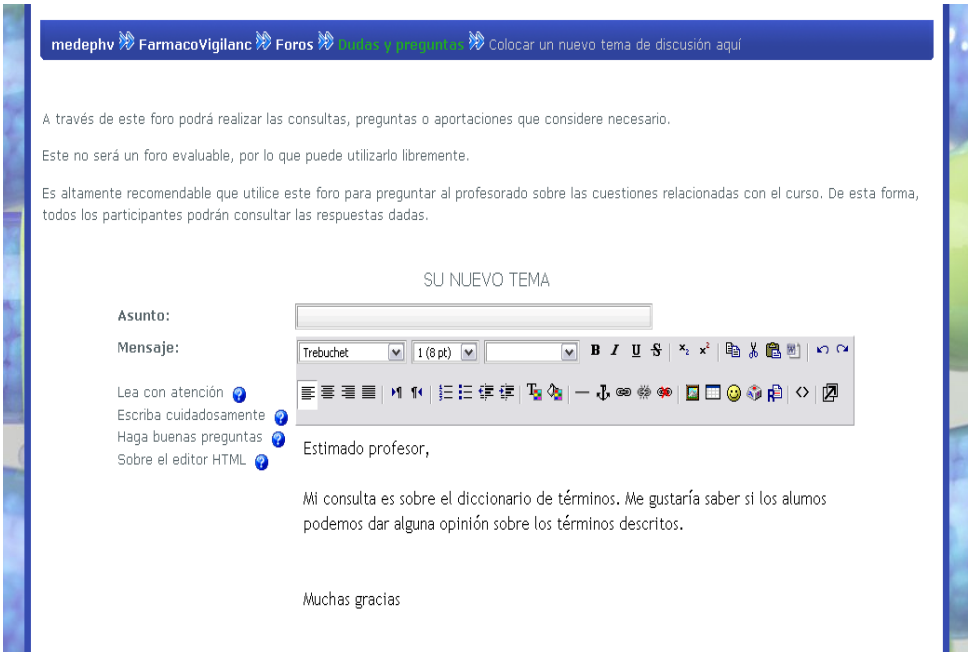


Doctor Martinez has doubts about some definitions that appear in the index cards and he enters in the glossary of definitions of the course. When he reads the definitions there, he understands many more concepts than before.

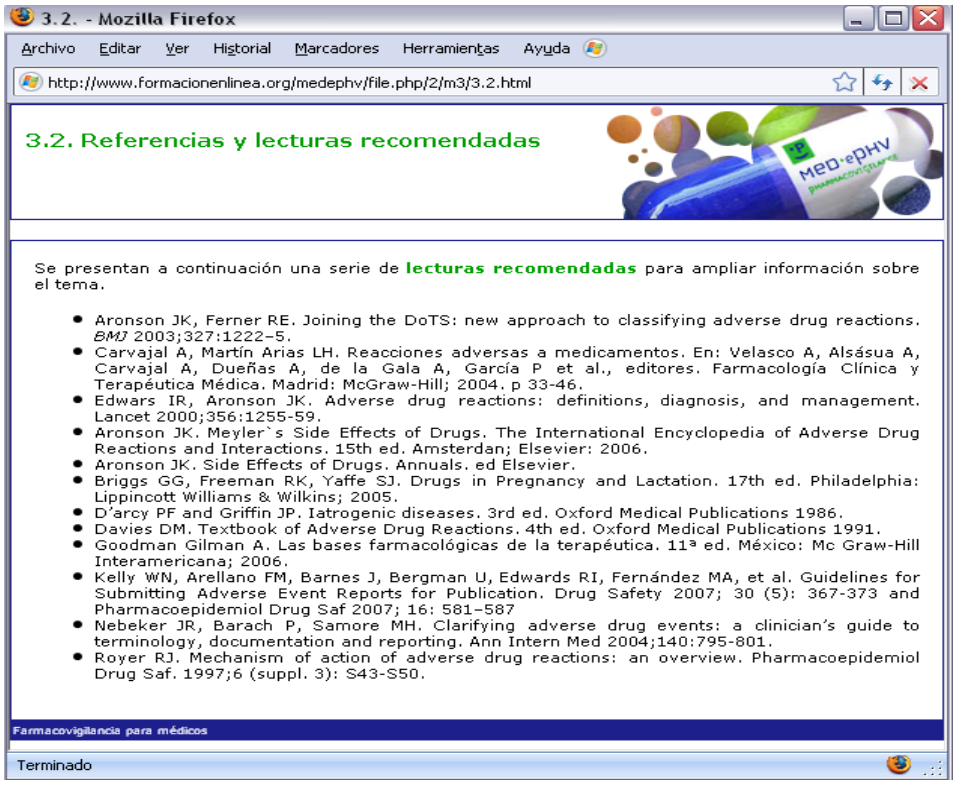


He thinks about some definitions that are important for him and he gets in touch with the teacher, using the forum of the course because he wants to add definitions to the dictionary of the course.

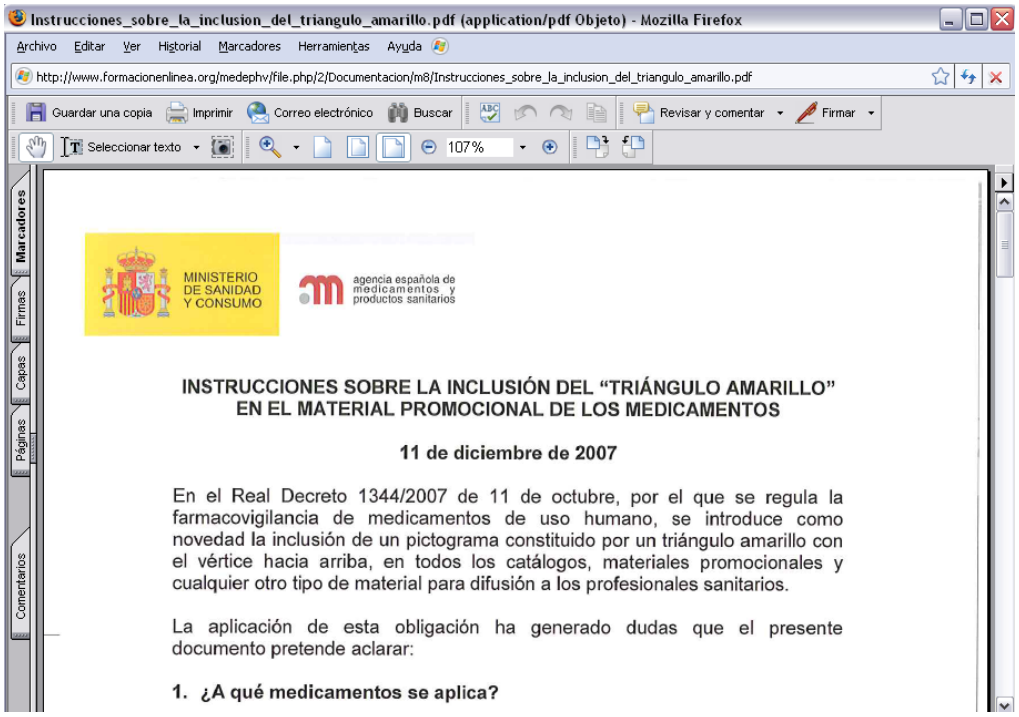
For this reason he enters in the forum and he asks his questions to the teacher:



After studying all the indexcards of the modules 3-4-8 (which are the modules of his course) Doctor Martinez wants to know more about adverse reactions of the medicines. Moreover, he would like to read the most important articles of each module.

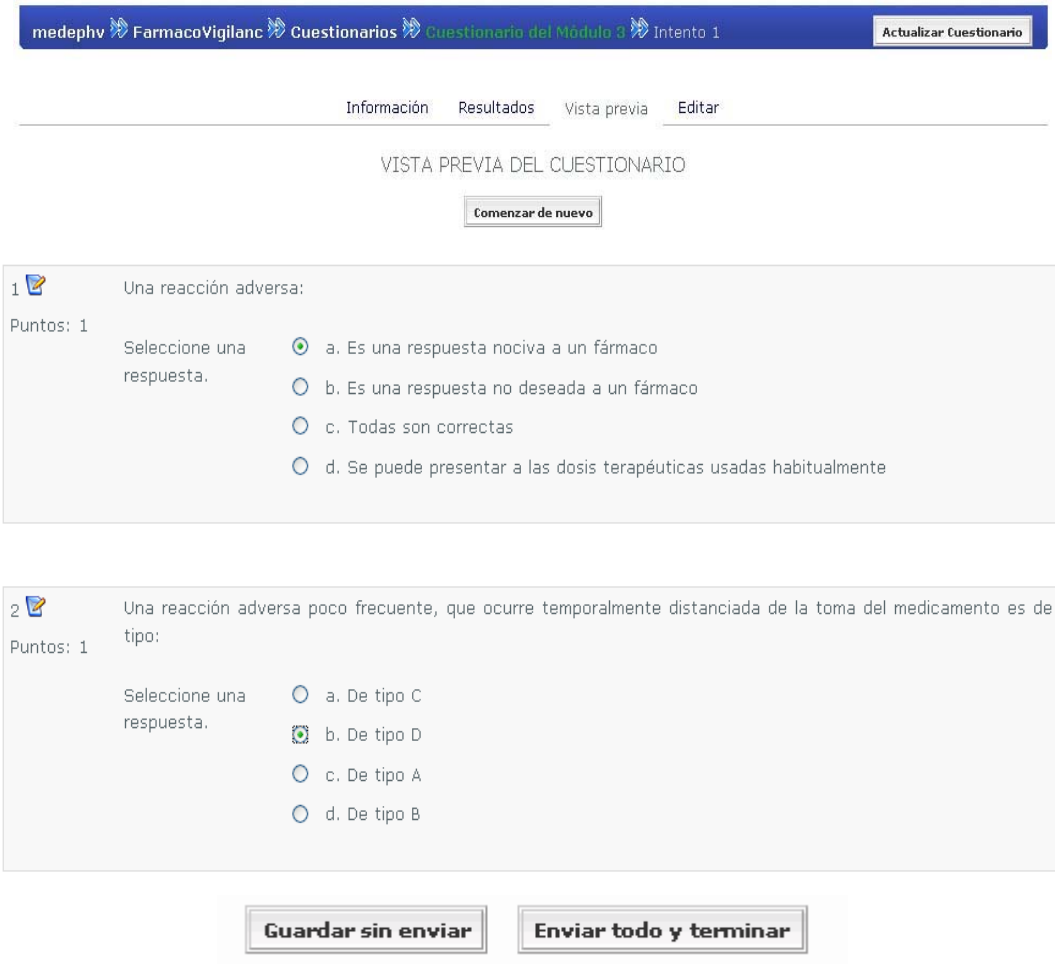


Doctor Martinez then clicks on the title of the articles of his interest in some of the modules. In this example he can study in more depth about the introduction of the yellow triangle in the promotional material of the medicines:



After he has studied all the contents of the modules, Doctor Martinez will complete some questionnaires, to verify the degree of his acquired knowledge.

He starts with the questionnaire of the module 3.



When he has finished with the questionnaires, Doctor Martinez sends his answers to the teachers so that they can correct them and assess him.

He can also record them before sending the answers to the teachers.

Once the tests have been evaluated by the teacher, Doctor Martinez can verify the test to see where he has given the wrong answers.

CUESTIONARIO DEL MÓDULO 3

REVISIÓN DEL INTENTO 1

Comenzado el:	viernes, 31 de octubre de 2008, 09:54
Completado el:	viernes, 31 de octubre de 2008, 09:54
Tiempo empleado:	17 segundos
Puntuación bruta:	2/10 (20 %)
Calificación:	de un máximo de

Continuar

The above are just examples of the main features of the e-learning pilot. There are other useful features that have been implemented to facilitate the communication between student and teacher and among students (peers), such as the "Chat Room".
There is also a "Centre of Documentation and Resources", where students can find some useful sources of specialized information with links to external web sites and pages.

The entire detail description of the content of the e-learning modules and how the pilot is structured is available in the project deliverables D16 - Med-ePHV Pilot e-learning Software and D20 - Report on the Med-ePHV e-learning Pilot.

5.7 Work Package 07 – Design of the Med-ePHV Grid

The objective of this work-package was to study and design the integration of the developed software components and information resources (e-learning courses, medicines database, medical dictionaries) through a state-of-the-art grid middleware to be shared among the SME partners.
With this grid technology the SMEs will be able to act as independent but coordinated suppliers of the involved computational and information resources that can be transparently assembled by the grid middleware in a consistent suite of services. These services will be perceived by the users as a single product capable to serve many clients and thus achieving favourable economies of scale.
The grid design was conceived to be modular and allow gradual expansion with the objective of being able to cope with the expected increase in the number of users.
In this way the SMEs could limit the amount of initial investment required and achieve a significant increase in their competitiveness.

The architecture and design of the Med-ePHV grid and associated web services has been conducted following the WP pre-defined sequence which implied the following tasks:

Task 7.1 – Definition of the Med-ePHV grid architecture and design of the integration tasks including network interface and middleware servers management.

It is a fact that up to now, complex applications which are computationally intensive and handle large data sets have been systematically ignored in the context of e-learning, due mainly to technical feasibility problems and prohibitively high costs. However in the Med-ePHV application that we have envisaged, grid computing can close this gap and enable new types of e learning applications, such as photo-realistic visualisations or complex real-time simulations. Computations and data could be distributed on a grid as soon as desktop computers of learners cannot handle them anymore. This particularly pertains to university environments where the hardware infrastructure already exists, since there are often hundreds of networked computers, ranging from PCs to supercomputers, which most of the time are not working to capacity or even run idle. In Med-ePHV we have decided the creation of *e-learning grids* in which grid computing functionality is integrated into e-learning systems. There are many conceivable

applications for *e-learning grids* that go further beyond the present Med-ePHV application and that the Consortium partners could adopt in the future.

The advantages of the Med-ePHV grid system

Med-ePHV Project is an e-learning related with the health area and the use of the GRID COMPUTING technology has many advantages in this field.

In the past complex applications that required an intensive use of the computing resources, have usually been excluded from e-learning applications because of their high costs and technical difficulties.

However, GRID COMPUTING can solve this problem allowing the development of new uses of new e-learning applications that in the Med-ePHV Project are very important such as the photo-realistic visualizations or complex real-time simulations, these resources could be used by the students of Med-ePHV e-learning, for example, in the future we could use photo-realistic visualizations of a complex model of the human body to study the adverse reaction to drugs graphically. These visualizations in a real time would allow us to see the bones, the muscles and organs in three dimensions, the power that we get with the grid would allow the students to see it from different angles and use the zoom to improve the visualization, it would also allow us the use of the electron microscope into the GRID.

On the other hand, in the Med-ePHV e-learning platform we need to gain admittance in huge medical data bases and medical dictionaries, such as Medra which requires a great deal of resources. For that reason, in order to use all these possibilities, it has been necessary to design a GRID with the following architecture and implementation of resources.

It is necessary to make it as user friendly as possible. The resources that we need to integrate are a Learning Management System (LMS) and a Grid Middleware; these two elements are based on Web and Grid Services respectively.

In the Med-ePHV Project we have chosen the Moodle platform as LMS, this element contains the learning contents which are implemented as web services. The students of the Med-ePHV e-learning will usually use a PC to work with the e-learning platform and all the web services of Moodle can work with web pages so that the learner only needs a Web Browser, at the same time the PC of the student can be used as a resource in the Grid.

For that reason, we define a LMS login service that allows us to integrate the PC as a resource in the Grid. The only software support that a student needs is a Java-enabled Internet Browser to be used together with the LMS and the Grid.

In order to design the architecture and implementation of the resources of Med-ePHV GRID we have tested the GRID in experimental conditions using the virtual software VMWARE. In this way, we get the configuration of GRID based on virtual machines using six computers with the Windows XP operating system and two computers with the Linux operating system.

As a result of our analysis, we have determined that e-learning and learning management systems on the one hand and grid computing on the other, which have been considered and developed separately in the past, can fruitfully be brought together, in particular for applications or learning scenarios where either high computational power is needed or the tool sets on which learning should be done are too expensive to

be given out to each and every learner. Beyond making a case for its feasibility and more importantly, we have outlined in detail the architecture for an e-learning grid which integrates core grid middleware and LMS functionality appropriately. Finally, we have indicated how an e-learning grid could be realized on the basis of suitably designed grid learning objects during the exploitation phase of the Med-ePHV project.
Future issues to be verified during the project exploitation phase will need to be addressed are the recovery protocols that help restore an operational state after an unexpected event of grid failure.

The complete detail description of the Med-ePHV Grid Design can be found in the project deliverables D18 - Med-ePHV Grid Architecture and Resources Integration.

Task 7.2 and 7.3 – These two tasks are complementary and cover the development of the web software under secure protocols to access grid resources (web services) and the design of the user interface.

The expected final result of the Med-ePHv project is the design of a suite of transparent network based services for learning and training in pharmacovigilance, to be implemented by the SME partners after the pilot has been satisfactorily tested and validated and before launching the commercial exploitation phase. The objective is to be able to integrate a number of information and computational resources through an appropriate grid computing middleware.
The envisaged services will be delivered through the emerging broadband Internet to the identified pharmacovigilance users and customers. The SMEs of this project have agreed to create a transnational cooperation agreement to distribute commercial pharmacovigilance services in the EU Mediterranean member states and at a later stage in the associated countries, starting from the pilots developed during the project.
The scope of this WP was to study and design the integration of the developed software components and information resources (e-learning courses, medicines database, medical dictionaries) through a state-of-the-art grid middleware to be shared among the SME partners. With the grid technology that has been chosen in the previous Task of this same WP, the SMEs will be able to act as independent but coordinated suppliers of the involved computational and information resources that can be transparently assembled by the grid middleware in a consistent suite of services. These services will be perceived by the users as a single product capable to serve many clients and thus achieving favorable economies of scale.
Web services are a new way of making applications, especially if what we are trying is using the functions that are available in a net. An example of the Web services that is known to everybody is the e-mail, but in recent times there have been great advances thanks to new technologies such as the XML which is used for the organization of texts and pieces of http information, the Internet convention used by today, Web Browsers.
The software can be divided up in two essential components:

- Applications
- Services.

The applications are programs that require an interaction with the user and they may have any kind of virtual interface. The Web services interact with the applications and others.

Moreover, they are more related to the exchange of pieces of information. Going back to the example of the e-mail, when we use it to receive messages, the mail server is acting as a Service. When the administrator configures the logs of the Server of the e-mail to configure the different choices, is acting as an application.
When we use "interface" it can have two different meanings: one that is an interface between the users and the software (user interface) and other meaning that is an interface between two parts of software (machine interface or web service) and the latter is what we are describing now.
Providing web services interfaces instead of showing only user interface, allows us a bigger flexibility to use the functions of the software.
First, what we have done in order to know the structures of the web services in the Med-ePHV project, was to study what we understand for Web Service. The easiest definition of Web service is any application that we use to access Internet.
We can define the web service as a collection of protocols and standards that are used for exchanging information between the different applications and systems.
Software applications identified by a URI (Uniform Resource Identifier), whose interfaces and bindings are capable of being defined, described, and discovered as XML artifacts; support direct interactions with other software agents using XML-based messages exchanged via Internet-based protocols (This definition is used in the World Wide Web Consortium W3C)
Software that puts up with the interaction between machines using a network, its interface is described in a machine-processable format (WSDL). Other systems interact with the Web Service in the described way in its interface using the indications of SOAP (Simple Object Access Protocol).
Web services are components that are integrated easily with distributed applications normally used by a user in a Web Browser such as Internet Explorer or Mozilla Firefox.
XML is the organization that is in charge of all the following standards:

- SOAP (Simple Object Access Protocol)
- WSDL (Web Services Description Language)
- UDDI (Universal Description and Discovery Protocol)

A Web service is a collection of functions that are considered as a single entity and published in the net for use in conjunction with other programs. Web services are component blocks that create open distributed systems and that allow companies and persons to access to the digital resources that are available worldwide.
The base of Web Services is the adoption of XML for the protocols of the standard Web such as HTTP. This is a very light mechanism of communication in which any programming language, middleware or platform can take part in, easing the interoperability in a great way.
The most popular technologies and ways of work that are more accepted in the industry and that they have been used in the Med-ePHV project to develop the Web-based services are these ones:

- A supplier makes, assembles a Web service using a programming language, middleware and platform of the choice of the supplier.
- The supplier defines the Web service in WSDL (Web Services Description Language) a WSDL document describes a Web service to the other.

- The supplier records the service as UDDI (Universal Description, Discovery and Integration) registers. UDDI allows the developers to publish the Web Services and this allows their software to look for the services offered by others.
- A possible user finds this service when he looks for a register of UDDI.
- The application of the user is joined to the web service and invokes the operations of the service using SOAP (Simple Object Access Protocol). SOAP offers a format of XML to represent parameters and values about HTTP.
- It is generally recognised that SOAP, WSDL and UDDI are suitable entities and that they will provide a base in the future.
- All software developers are working together to establish Web services standards and the technology that has been implemented in the Med-ePHV Project is coherent with this approach.

Basic concepts of Med-ePHV user interface

In the definition of the Med-ePHV user interface we have taken a technical and methodical approach, and conducted a complete study to achieve the objectives. We have studied the performances that may affect the user as a student and that will help him/her to learn better by designing a suitable user interface.

- **Easy use**

  We must assure the easy use of the contents, and so any student can use them in an easy, productive and efficient way. The interaction with the information must be efficient. For this reason, in the Med-ePHV project, the design of the graphic interface and the contents have addressed these requirements:

  - Visible Interface: We have not used invisible elements that must be suspected by the users such as hidden instructions.
  - Suitable selection of the colour to make the access easier for those users with problems in distinguishing colours.
  - Legibility: We have used the colour contrast o f the texts and the bottom and a big enough size of the words so that the contents and the information can be used from the beginning in an easy way.
  - Use of the contents: we have given priority to the productivity of the user and not to graphical skills.
  - Treatment of the user. When the user makes a mistake, the system has to solve it or it must suggest several possible solutions, but it does not remark answers that just inform about the mistake and could confuse the user.
  - Avoid unexpected results, such as broken or non-existent links.
  - We try that the user achieves his objective without a great effort and with the optimum results.
  - The contents are consistent and homogeneous all around the process, although we may think the different areas could have different designs. However, design consistency will make it easier for the user to learn different didactic units.
  - Limitation of interactive elements and of the number of links in a single screen image.

- **Accessibility**

The accessibility will guarantee that people with diminished ability can access to the on-line contents. For the production of the Med-ePHV e-learning contents, we have taken into account the rules marked by the Web Accessibility Initiative (WAI) which is part of World Wide Web Consortium (W3C) that watches over Web accessibility.

System navigation

The way navigation of the contents that has been designed and implemented, follows general rules of efficiency and simplicity enabling to access them in an easy and fast way. The following are the main principles that we have considered:

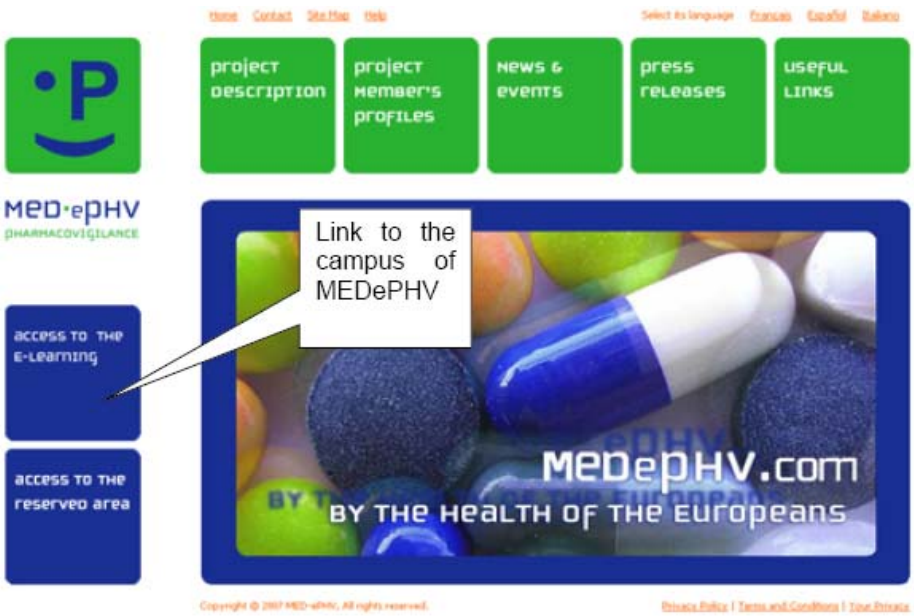
- Definition of styles, the structures and navigation tools are easy and they are aimed to the learning needs of the users.
- The distribution of the contents has made easier the levels of depth and the relationship among them.
- The tool bar has been designed with easy icons and with on-line help access.
- The tool bar is always available and it follows the same rules of the navigation bar.
- The navigation is intuitive for the user with clear direct access.
- Limited, justified and balanced use of the hypertexts. These elements are very useful for on line learning.
- Superfluous links that direct the user to the same contents or elements in the screen have been avoided.
- The sequence navigation is done with arrows that allow the user to move forward and back the pages of contents that are being studied.
- The direct navigation uses the menu that contains the index of contents, didactic units to which the user can access in a direct way using this menu.
- The hipertextual navigation includes access to other elements of the screen in which the user interacts provoking an action of the content.

User interface as implemente in the Med-ePHV e-learning system

The virtual campus of Med-ePHV is based on a Web platform called Moodle (Modular Object Oriented Distance Learning Environment). The access to the Virtual campus is done with a Web navigator. Moodle can work with any virtual navigator, with any operative system (MS-Windows, MacOS, GNU/Linux and others). The recommended navigators are MS-IE 6.0 or Mozilla/Firefox.

To access virtual Campus the student can use the link to the e-learning platform that appears in the lower side of the web www.medephv.com or www.medephv.net, or writing in the navigator in the address bar, www.formacionenlinea.org/medephv.

In the following images we show some screen prints which present the main features of the user interface as implemented in the Med-ePHV on-line virtual campus.



The first screen that we see when we enter in the platform is this one:

This is the entry page to the campus, where we can see on the left the available courses and on the right the user login and the users that have been connected in the last five minutes.

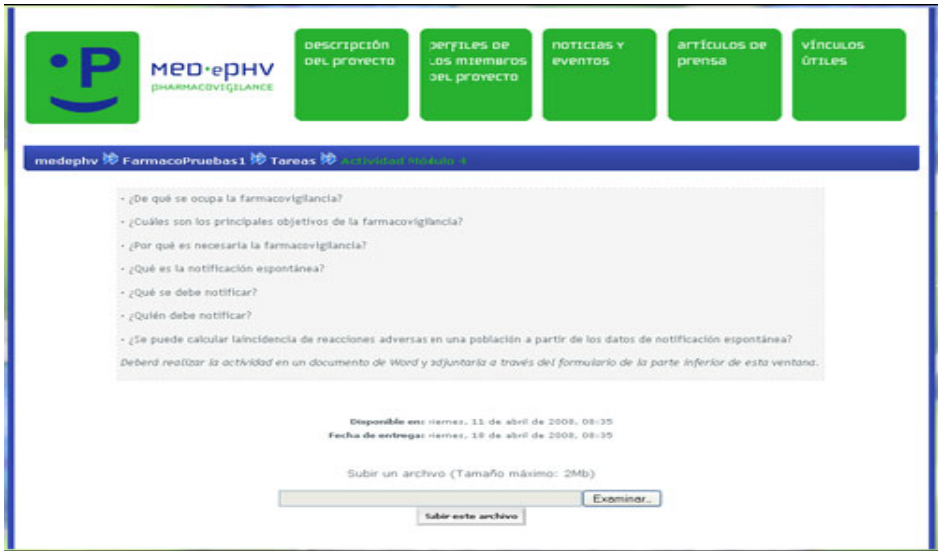
There are resources, identified an icon and are hiperlinks to elements that can be seen, read…and so on. There are many elements that can make up a resource:

- Texts with more or less format
- Web pages internal or external to the virtual campus.
- Enclosed documents in different formats: PDF, doc, ppt, sxw, sxi etc.

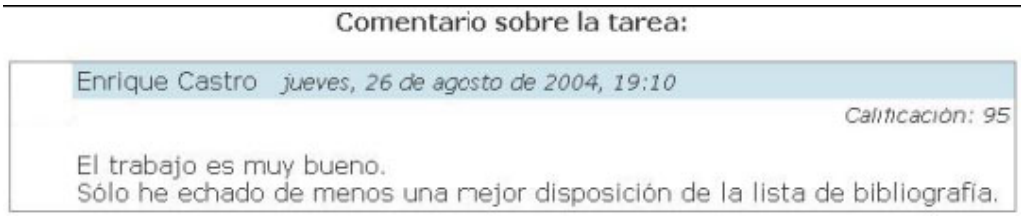
- Image files
- Performed files

Many texts have been designed to be read in the screen, not to be printed. Unlike a conventional library, the Virtual campus is available 24 hours a day, seven days a week. In the following screen-print we show an example of a Resource providing information about the verification of safety during the medicine development phase.

In the following screen-print we show an example of a test. The student will see a short questionnaire that will allow him/ her to handle the job. The system will not allow to send it or alter a date. If many users try to be connected at the same time, the system may be blocked. For this reason the student is instructed not to send the questionnaire at the last moment. Once the file has been sent the task may go on opened and a new version of the questionnaire can be sent. Each version will replace the previous one. The teacher will only see the last version.



The teacher will evaluate it and he will also mark it. If the task is in the virtual campus, the student will be able to see the mark obtained using Internet. When the student clicks on the task, he/ she will see the date of the evaluation, the mark and a comment about the completed task.



Moreover, the Moodle system will automatically send to the student an e-mail when the teacher has completed the evaluation. The student can verify check the mark using the choice “Qualifications” in the “Administration” menu.

Finally the student will be asked to participate on a survey of multiple questions about the course undertaken. This activity is not evaluated.
Its aim is to collect the opinion of the participants in the course about different matters.

The complete detail description of all the features of the Web Services and User Interface can be found in the project deliverables D21 - Med-ePHV Web Services and User Interface

5.8 Work Package 08 – Testing and Validation

The scope of WP08 was the testing and validation of the pharmacovigilance services achieved to verify that:

1) They meet end-users expectations and needs for the three target Mediterranean countries (FR, IT, ES) in terms of content, quality and level of detail.
2) The on-line services are tested by end-users and meet the criteria of being "user-friendly"
3) The quality of the output to the Health Administration and Pharmaceutical Industry meets expectations and represents a substantial improvement over the present situation.

The end objective was to verify if the e-learning modules as designed and implemented are compatible with the on-line exploitation vehicles and can be integrated in the Med-ePHV grid that the SMEs will put in place.

The Testing and Validation process as defined by the partners of the Med-ePHV consortium encompassed three main tasks:

Task 8.1 - Testing and validation of e-learning and ADRs notification components.
Task 8.2 - Testing and validation of integration components and web based user interface.
Task 8.3 - Validation of the complete pharmacovigilance suite of services.

The first step of the testing and validation programme, consisted in the selection of a representative sample of end-users within the medical personnel and possibly pharmaceutical industry. A sample of one-hundred Health practitioners in each of the target countries (FR, IT, ES), was planned to be selected in cooperation between RTD partners and the sponsoring institutions. The three SMEs agreed to test and validate the prototype, internally within their respective organisations (to avoid disclosure to potential competitors).

The scenario of the Med-ePHV partnership and of the organizations involved in the testing and validation process in the three participating countries, can be summarized as follows:

France

In France, INSERM was acting as the local RTD provider and Pasteur Mediavita as the SME partner.
Due to the bankruptcy of Pasteur Mediavita and the decision not to replace the SME partner, due to the proximity of the EC Contract closure, the French RTD partner has had to face a serious and unexpected adverse situation.
Nevertheless, the material developed for the e-learning tool (deliverable D11) was translated into French and adapted to the French specific requirements by INSERM and was available for implementation and on-line testing.
During the PSC meeting held in Milan on November 4-5, 2008, the Consortium Steering Committee decided that the Spanish SME Arisoft SA would undertake the original scope of Pasteur Mediavita as the provider of Internet supported training, also for the French testing process.

Considering the very short remaining time, INSERM started to translate from Spanish to French all the additional information necessary to for the development of the e-platform and started the selection process of a sample of French health practitioners through the collaboration with the French Regional Pharmacovigilance Centre of Poitiers.

These professionals are already working in a network, and are motivated collaborators of the Centre.
The Regional pharmacovigilance centre of Lille has also accepted to collaborate, but with the condition that the sample would be selected only once the e-learning tool will be available on line.
However, despite all INSERM and Arisoft SA efforts, to make all French modules available by the December 31, 2008, it was not possible to upload to the server the complete pilot version of the French e-learning tool, making it accessible on the web on time to complete the full-scale external validation process.
A limited but representative sample of 10 professionals working in a pharmacovigilance department of academic sponsors and clinical project managers based at Inserm in different therapeutic areas tested the tool and the feedback was very similar to that obtained from the wider sample of health professionals in Spain and Italy.
The methodological approach of the course was considered as good or very good and the content of the course considered as well developed and structured by all the "testers". The content of the course was considered as presented in a clear and organised way by all the testers except one who completely disagreed.
All have considered the forum of discussion as useful.
With respect to their professional activities all the "testers" considered the course as very useful or useful except one who considered it as not useful at all.
The part of the course considered as the best designed was the module 2 and the part of the course considered as the best structured is the overall theoretical content of the modules (50%), the clinical cases (30%) and the summary and introduction (20%).
Regarding the e-learning platform the opinion is very heterogeneous with 40% of the testers finding it easy and accessible, 20% accessible with some difficulties, 20% that is requires some effort but it is worth and 20% find it inaccessible and very complicated.
Some of the users proposed to improve the tool by:

- highlighting the section already studied in order to make the progression easier
- creating more links between screens and chapters
- adding a summary of the different definitions
- adding more details on clinical research and notification during clinical trials.

The examples to illustrate the course were found very useful.

One of the users expressed a different opinion and found the e-learning tool too complicated and too detailed for general health professionals and suggested to simplify it. This pilot tool was considered as more targeted to professionals working in the field of pharmacovigilance rather than medical doctors or health professionals.

Italy

Following the successful implementation of WP05 activities ("Development of ADRs notification pilot"), Tecnofarmaci actively contributed to the finalization of WP08 objectives. During the November 4-5, 2008 PSC meeting it was agreed that, in order to gather the Italian health professionals' attitude towards the developed Med-ePHV e-learning tools and to assess their potential needs for improvements, it was necessary to provide them with a common feedback format. TF actively participated in the creation of

the "Users' feedback questionnaire", to be integrated both on the on-line ADRs notification and e-learning tools.
UNIPV held several meetings with health professional organisations, representative from AIFA (Agenzia Italiana per il Farmaco) , Farmindustria and from different health providers (public / university hospitals, local agencies and government agencies) in order to choose the appropriate samples of professionals to be asked to validate the e-learning process and the questionnaire.

For the Italian testing and validation program UNIPV choose to target health professionals, following the suggestions coming out from the meeting previously held. They have been selected carefully in order to comply with different situations as family doctors and institutional (health care system and university) workers. The sample has been considered representative as a first approach, to assess the interest of people who are usual (and institutional) ADR notificators. One of the advantages has been the fact that this population is familiar with the present Italian system and is interested in a different and more useful approach, as the one we are testing.

The e-training tool has been assessed through a sample of 156 Italian health professionals. These professionals were allowed to get access to the Pharmacovigilance e-learning tool for a period of approximately 2 weeks, in order to facilitate the handling of the training materials and of the functioning of the tool.

The e-learning tool has been rated by the selected testing group sample as :
1- 70% as "good" or "very good" with regard to the method
2- 65% as "very good" with regard to the modules contents.
3- 80%. as "good" or "very good" for the organization and clarity of the contents
4- 50% found as useful the debate forums.
Only a few users entered the Med-ePHV forum at this stage, probably because the professionals involved in the test were not familiar with this type of on-line tool. It must be emphasized that a vast majority (80%) of those who filled the questionnaires think that e-learning can be useful to improve their knowledge in this area and this would, in their opinion, improve the present situation of under-reporting of adverse drug reactions. A high percentage (70%) considered the tool as useful and a similar percentage considered it as easy to use.

Approximately 30 open comments were submitted. Most of them were included in the questionnaire, and came from doctors, pharmacists and people involved in institutional health care pharmacovigilance.
In general, the health professionals who have got in contact with the pharmacovigilance e-learning tool and have had the opportunity to enter and assess the different materials felt happy with the possibility of having the e-learning tool, in order to improve their pharmacovigilance knowledge and thus contribute to a better and more frequent reporting.

It is clear that some updating should be made, due to continuous changes in the legislation at national and European levels.

There has been a request by several of the professionals who have participated in the on-line testing to update the e learning tool, taking into consideration additional adverse reactions, such as those associated with the growing usage by the populations of non-medical practices, such as tattoo, piercing, cosmetics and implanted devices.

There has been a general complaint about the difficulty for printing some of the didactic and reference materials. At the moment the only possibility to print these materials is in small parts. So the users asked for the possibility to print the course as a PDF document. The letter font size has been identified as too small and difficult to read for some of the materials.
In general most of the health professionals that have participated in the on-line testing of the ADR recognition tool and e-learning modules considered that the content of the two Med-ePHV components is correct and suitable for the intended professional use.

Spain

In Spain, the Instituto de Farmacoepidemiologia de la Universidad de Valladolid (UVA) was acting as the RTD partner, and Arisoft SA, as the local SME. Both Spanish partners have developed a pharmacovigilance e-learning tool, and managed successfully the internet portal access to the training program for testing and validation by a selected sample of health professionals.

In order to get a high quality and representative sample, the selection in Spain was not let to the hazard of randomization, or to a representative health professional group in a determined geographical area .
The first criterion to obtain the population who would act as assessors in this ratification test was to target exclusively health professionals (doctors, pharmacists, and nurses), keeping in mind that, at first, the Spanish UVA was specifically interested on those who had the profile defined as “usual (frequent) ADR notificators”. The advantage of this population is that they already know about the Spanish program of spontaneous notification “Sistema de la tarjeta amarilla”, and have used it at least more than once in their professional activity.
We have to notice that this first target, because of its high level of qualification and capacity of criticism was able to provide a major and qualified feed-back about the pilot training course, and can be considered to be formed by a group of experts.
Another criterion we tried to achieve is that the majority of the participants is motivated by the pharmacovigilance and receptive to the method of e-learning. Because of this observation, the condition was that the participants had to agree to undertake the course on a voluntary basis. Their only reward was to get the access to the content of the e-training course, in addition to the possibility of helping to improve it.

The sample was obtained by sending an e-mail to approximately 150 “notificators”, who were regular and motivated collaborators of the Regional Pharmacovigilance Centre of Castille and Leon in Spain. Most of them were doctors, pharmacists, and nurses.

The training course was also proposed to the “family” doctors network in the East area de Atencion Primaria in Valladolid.

In order to diversify and complete the sample, a search for volunteers was conducted also within the Spanish internet forum "Foro de Atencion Farmaceutica". The participants of the forum seemed to be an interesting sample, as they are health professionals accustomed to argue on topics of their therapeutic daily practice through internet, and therefore we estimated them to be motivated over an "on-line" distant method, such as the e-learning method.

Several other professionals of different autonomous centres of the Spanish Pharmacovigilance System were also requested to share their opinion and comments about the training course. It was felt that their high level knowledge of the topic, would enhance the criticism, as compared to the others participants in the testing and validation process.

Finally, the e-training tool was assessed through a sample of 160 health professionals.
These professionals were allowed to get access to the Pharmacovigilance e-learning tool for a period of approximately 4 weeks, permitting them to get used to handling of the training materials and to the functioning of the tool.

In general, the pharmacovigilance e-learning tool has been highly rated by the selected testing group sample. With regard to the method, 80% of the responses considered it as "good" or "very good". The contents were similarly considered by 82% of the responses. The organization and clarity of the contents were found "good" or "very good" by 70%. Debate forums were found as useful by 53%. It should be pointed out that only a few users entered these forums at this stage; it was probably due to the fact that users were not encouraged by teachers with comments or by suggestions to do that – for the testing we do not considered teachers to be involved in tutorials-. It must be emphasized that 84% of those who filled the questionnaires think that pharmacovigilance e-learning is useful to improve knowledge upon this subject and thus improving reporting of adverse drug reactions. A high percentage considered useful and commented the tool (72%) and a similar percentage considered it as easy to use.
The module M2, treating about *Pharmacoepidemiology* and the clinical cases were regarded as the best designed (annex 3). Small "letter type size" was regarded as a drawback, and was pointed out by 48% of the respondents. Lack of adaptation to different users was pointed out by 42%.

Approximately 30 open comments were sent. Most of them were included in the questionnaire, and came from doctors, pharmacists and nursing personnel.
In general, the health professionals who have got in contact with the pharmacovigilance e-learning tool and have had the opportunity to enter and assess the different materials feel happy with the possibility of having the e-learning tool, in order to improve their pharmacovigilance knowledge and thus contribute to a better and more frequent reporting.

Nursing personnel has considered some modules as too extensive; similarly, this profile of health personnel considered the clinical cases as difficult.
Some minor errors have been found in different modules, they can be easily amended.

Like in the Italian testing users have indicated that documents' printing is difficult and the letter font size has been identified as too small and difficult to read for some of the materials.

Overall Test and Validation results

In the overall we have noticed that all participants in the on-line testing and validation process of the Med-ePHV pilot, have been very enthusiastic to collaborate, and found the tool as useful.

For a better understanding of some critics, it should be taken into account that the pharmacovigilance e-learning tool has three possible itineraries with two levels of difficulty for each one. During the testing process, all professionals have had access to all contents in order for us to gather and "centralize" whatever problems that will be found by the testers. It should be considered the possibility to develop an ad-hoc, less demanding, itinerary specifically targeting nursing personnel.

The content should be updated when necessary. The majority of detected errors are easy to amend, and will be rectified.

Some technical improvements should be made regarding the accessibility, and it is important to have a friendly reading material, easy to print.

The testing and validation process that has been conducted on the pilot system, gave us a very valuable insight upon the pharmacovigilance e-learning platform to be improved.

Upon completion of the testing and validation process, the Spanish version of the training modules will be corrected and improved taking into account the comments collected.

A verification matrix to ensure that all comments have been properly resolved and duly incorporated, will be established and checked within the Consortium by three different persons.

The verification records will be signed following the formal Med-ePHV documents approval process.

The revised training modules will be assigned the status of "ready for external release – version for medical doctors, pharmacists and pharmaceutical industry".

This Spanish version will also be used as the basis for finalizing the French and Italian versions (only for common modules) prior to their finalisation and subsequent launch on the respective markets.

A simplified version of the training modules, adapted to the specific learning needs and professional profile of nursing personnel will be developed during the first quarter of 2009 and undergo a limited testing and validation process, by the same nursing people previously involved in the testing of the full modules and by 10-15 other nursing professional who have not been previously exposed to the training materials testing process.

Once the testing and validation of the Spanish modules for nursing personnel is completed, the French and Italian equivalent will follow the same testing and validation process, as described for the full modules.

The complete detail report with the description of the Test and validation process, the analysis of its results and of the feedback questionnaires can be found in the project deliverables D24 - Report on testing and validation addressing three levels of target end-users

5.9 Work Package 09 – Promotion and Dissemination

The objective of this work-package is to define and implement all those actions, which are required for an effective dissemination of Project results. To meet this objective the consortium strategy for promotion and dissemination of the Med-ePHV e-learning system, has been constructed around the use of both traditional means of dissemination, such as conferences, articles, posters, etc., as well as the publication and the opening of a public Internet web site.

The SME partners have agreed a preliminary Business Plan for the joint exploitation of knowledge products and services developed by the Med-ePHV Consortium along the lines stated in the Consortium Agreement.

The Med-ePHV promotion and dissemination activities, have been segmented in different actions lines and tasks encompassed in WP09, as follows:

Task 9.1 – This task included the preparation of a Project Presentation in the form of:

An official Executive summary of the Med-ePHV project in text format.
A MS Power Point slide presentation for use during meetings, conferences and workshops.
Both presentation were included in deliverable D2, which was finalized and issued on September 30th, 2006.
An updated Publishable Executive Summary covering the entire project duration and its results, is included in Chapter 2 of this Final Activity Report

Task 9.2 – The activities included in this task, covered the design, set-up and maintenance of the project Internet web site for external dissemination.

The Internet domain medephv.com and medephv.net have been registered and the project web site has been opened to the public and disseminated via the main international search engines.
The public website was opened at the beginning of the project and has been regularly updated along the project development phase.
From the web entry page, a link permits to connect to the project private Intranet.

The following image represents the most recent entry page design showing also the Med-ePHV official project logo.

Med-ePHV web home page (English version)

The construction and maintenance of the web site was a task following under the responsibility of the SME partner Arisoft Editorial (AS), while the definition of the web contents and functionality, was a task assigned to the SME partner and project coordinator Gruppo S Lab (GS), that is also responsible for the construction and maintenance of the project private Intranet.

The Web Site content is divided in two main areas:

1. The public area, where every Internet user can find public material concerning the Med-ePHV project.
2. The private area, where only project partners and EC officers can access.

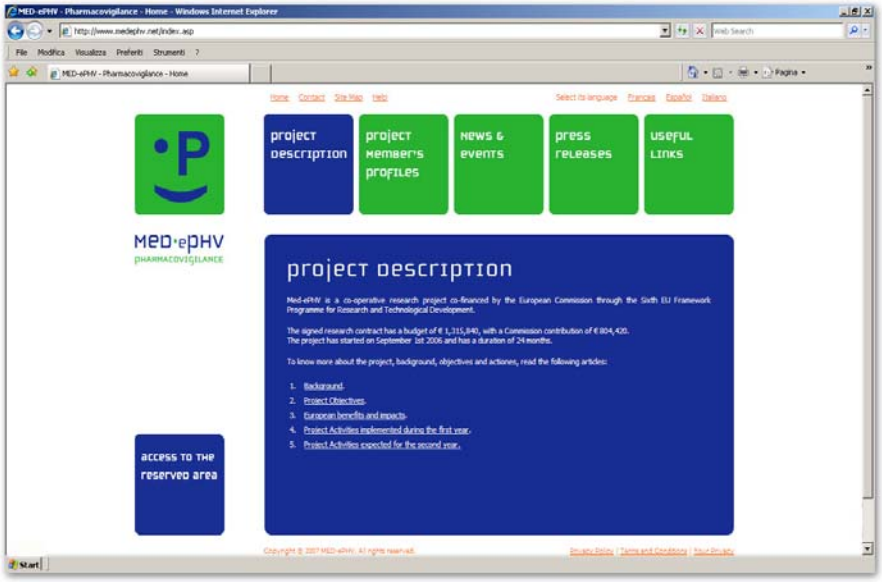
The following is a brief description of the content and graphic design applied.

Web Site public content

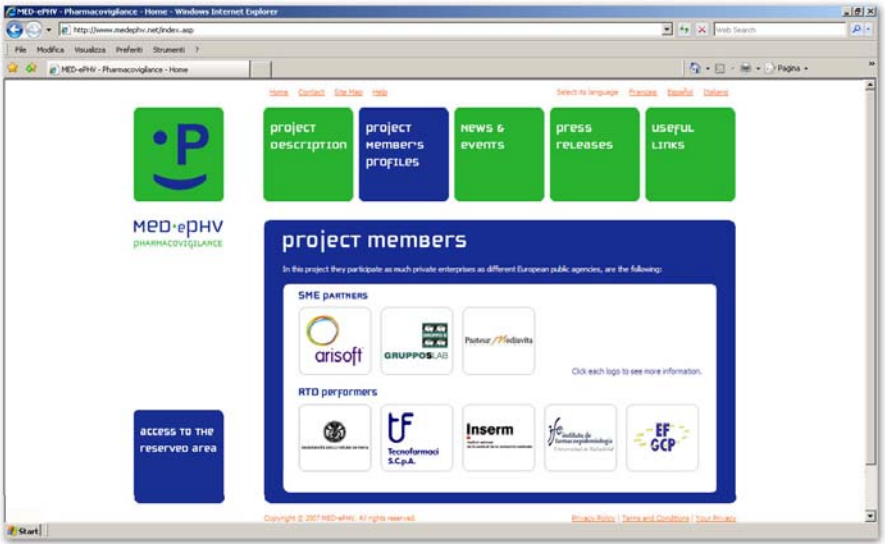
The objective of the public area of the Med-ePHV Web Site is to promote knowledge on the project, its partners and results among the generic Internet users.
For such reason, the content is prepared and published in English as main language, but the contents are also available in French, Spanish and Italian.

The following information are presented in this area:

- **Project Description**: a general description of the project, its scientific and technical objectives. This section is basically “static”: once set up it’s not supposed to change frequently, so it is implemented by using normal HTML pages.

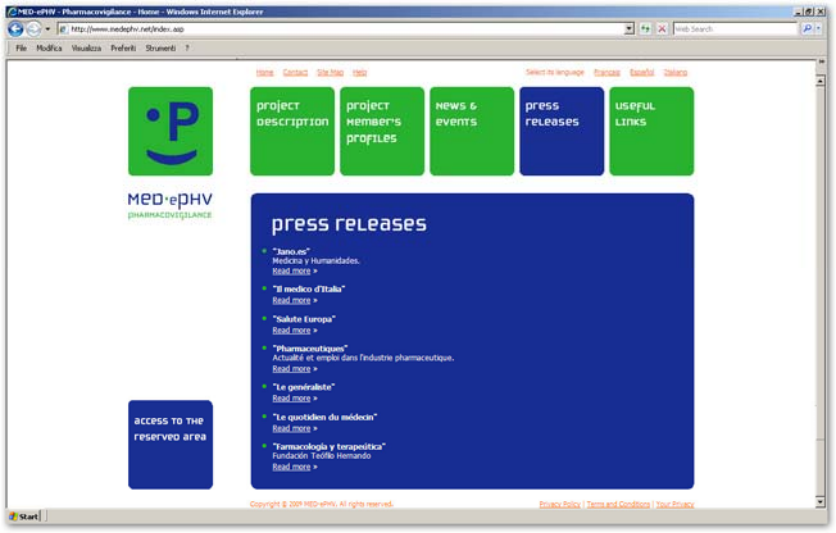


- **Project Member's profiles**: This section shortly presents each member of the project, both SMEs and RTD Performers. The presentation page contains both "official" and project specific role information on the partner.

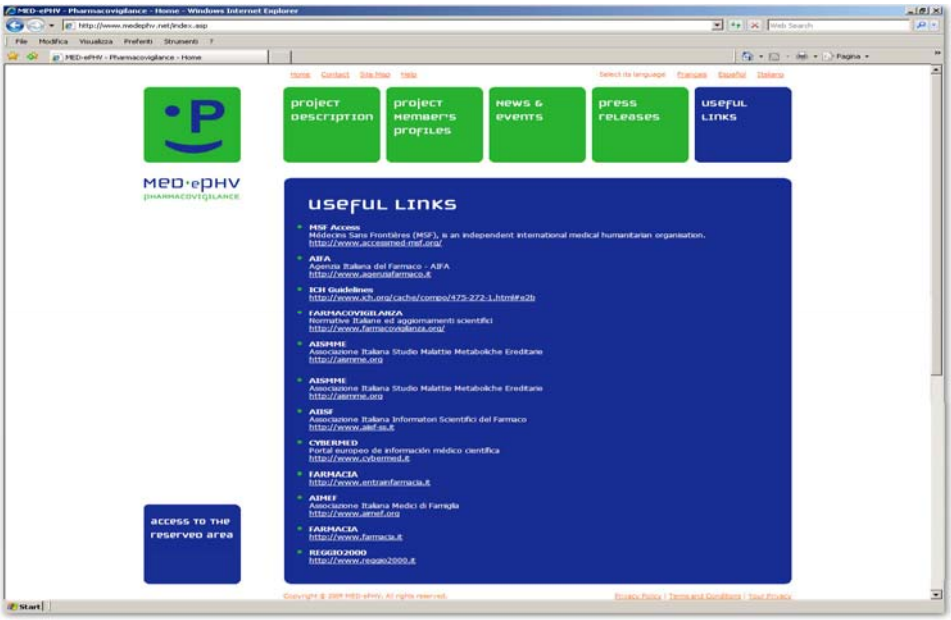


- **News & events**: This part of the website is dedicated to the "publishing" of all key information, published from time to time, that have an impact and mark the evolution of the project. This information covers scientific and technical results, milestones achievements, participation and organization of meetings, etc.
  Since this information has a much "shorter" life cycle, the dynamic publishing of such information is available to administrative users with proper functions in the private area.

- **Press releases**: this section is used to organize a press releases repository. Each article is presented with clear reference to the official source. The administrative functions to be used to publish such information are available in the private area.



- **Useful Links**: In this area there is a collection of useful links to other sites which have a close relation to the project, its objectives, the project partners, the European Commission. The links are classified by the project partners by means of functions available in the private area.



Web Site private area

The Med-ePHV Web Site private area has administrative functions for the publishing activities concerning the public area.

The access to the private area is protected by username and password.

The administrative users are enabled to use publishing functions for the dynamic Web Site contents highlighted in the previous section:

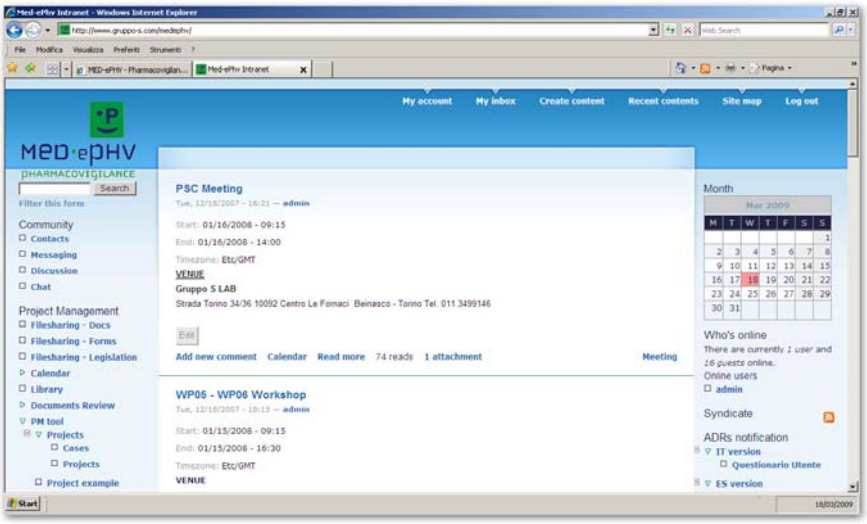
- ✓ News and events
- ✓ Press releases
- ✓ Useful links

Of course, there is also a function for users management, whose access is restricted to the system administrator.

The administrative functions allow administrative users to add, modify, delete and, finally, publish any of the previously mentioned items. It is important to note that only when an item is "published" it becomes visible in the public area.

Each item may have attachments that can be loaded by using the browser. The content of each item is based on HTML, and so it may be arbitrarily formatted.

The following screen print shows the Home page of the Med-ePHV Intranet from were authorized and registered users can have access to the different functions (left column), such as the directory of Contacts, Messaging area, Discussion area, Chat room, Project files repository, etc.



Upon completion of the project development phase, the Intranet discussion tool / Forum, will be relocated to the public web-site and made accessible to registered health operators, who want to exchange and discuss information and experiences in the field of pharmacovigilance. The open Forum will be set up for each of the participating countries and language (French, Italian and Spanish), plus a pan-European Forum in English. Each Forum will be, administered and monitored by one of the Med-ePHV e-learning tutors in each of the three countries. The pan-European Forum will initially be monitored and administered by EFGCP.

The complete detailed description of the public web site and of the project Intranet can be found in the project deliverables D25 - Report on Med-ePHV web site contents.

Task 9.3 and 9.4 – The activities included in these two tasks, covered the preparation of the Med-ePHV Plan for using and disseminating knowledge and its implementation during the project development phase. The first task included also the preparation of diffusion graphic materials: articles, brochures, posters and presentations

The dissemination strategy has been has been first outlined in the Preliminary Plan for using and disseminating knowledge, described in the project deliverable D14. The Plan has been subsequently further refined during the last quarter of the project when, in addition to a detailed list of dissemination related activities geographically distributed at national and international levels, all the materials needed to support the action have been designed and prepared.

In this chapter we are presenting a summary the Med-ePHV dissemination strategy and which have been the main activities undertaken. We are also covering the latest plan which includes the dissemination activities that the Med-ePHV partners have planned to perform after the end of the EC supported phase of the project, when the Med-ePHV system will enter the commercial exploitation phase.

In the research and innovation segment, the Med-ePHV project work plan includes an action on dissemination and promotion. This action is considered of key importance because the Consortium has the perception (corroborated by the initiative taken in the European Parliament) that the awareness for pharmacovigilance requirements is still quite poor at the edge of the EU health systems and that the introduction of new innovative services needs a significant promotional effort. The concept here is based on two tiers:

- First, to contribute to raise the awareness and understanding of pharmacovigilance, and
- Second, to respond at the obstacle of the complexity of the pharmacovigilance practice, by providing efficient and easy-to-use solutions.

The diffusion of project results plays an important role and must be done in the most efficient and cost-effective way.
To meet this objective, both traditional means of diffusion (conferences, articles, brochures, posters, etc.) and the opening of an internet website constituted the main line of action. The dissemination plan assures that the project results reach not only a selected minority group of medical professionals and scientists, but also a wide spectrum of EU citizens, especially in the Mediterranean regions.
The dissemination action that we have envisaged, counts on the support of the national and regional sponsoring public health care and medical institutions who have expressed interest in the project results.

Below we provide a list that summarizes the dissemination activities that have been undertaken during the development phase of the project and the other that are planned for the initial exploitation phase of the Med-ePHV system at national level, within the three target countries and at EU / International level.

<u>Dissemination Actions undertaken during the development phase of the project</u>

Actions undertaken at National level:

1. France

Presentations at Conferences & Workshops:

- **Pharmacovigilance dans 3 pays européens: développement d'un outil de formation en ligne / Projet Med-ePHV** (Pharmacovigilance in 3 European countries: development of an e-learning tool)
  - Workshop of the working group on vigilance and security of trials
  - Date: 31 March 2008
  - Fédération Hospitalière de France, Paris

Direct mailings:

Pharmacovigilance institutions/centres/associations:

- Presentation of the project to the Head of the French Network of Centres of Pharmacovigilance - 21 September 2007

- Presentation of the first draft training module to the Head of the French Network of Centres of Pharmacovigilance - 31 October 2007
- Information on the status of the project and testing phase provided to the Head of the French Network of Centres of Pharmacovigilance - 26 November 2008

Pharmacists:

Presentation of the project to OCP (leading wholesaler in France – www.ocp.fr) performed by Pasteur Mediavita

2. Italy

Articles (scientific journals, newsletter)

- "Con il progetto Med-ePHV parte la farmacovigilanza in Europa", published on the electronic newsletter Sanità News on 20.11.08
- (http://www.sanitanews.it/quotidiano/index4.php?id=44)
- "Progetto Med-ePHV: pillole di farmacovigilanza in Europa", on the waiting publication list of the 'Sole 24 Ore Sanità' journal
- "Med-ePHV: un progetto europeo sulla farmacovigilanza", to be published on the 'Forum PA Sanità' web portal

Presentations at Conferences & Workshops

- Pharmacovigilance Med-ePHV LHA
  - Presentation to the responsible people for PHV in Lombardia
  - Date: 25 May 2007
  - Place: Lombardia

- Congress on "La Sperimentazione Clinica in Italia"
  - Date: 30-31 May 2007
  - Place: Auditorium della Tecnica-Confindustria, Rome
  - Participation

Advertisement & contacts with professional training organisations

Italy has many traditional courses on pharmacovigilance (Master in Milano, Bologna, Roma, Firenze, Siena; various courses and seminars in different Universities) and also an e-learning course, prepared by the Italian Society of Pharmacology (SIF). Med-ePHV has liaised with these institutions making them aware of the availability of the tool and its use.

Contacts were also made with the Federazione Italiana Societá Medico-Scientifiche (FISM), Italy to ensure the distribution of the information to all its members about the Med-ePHV results.

Concerning the dissemination activities in Italy, it must be noted that a large Med-ePHV communication event which had been prepared and scheduled by CIRM for the last quarter of 2008, had to be postponed. Unfortunately Prof. Nicola Fabris, who was organizing this event together with UNIPV, suffered a fatal illness that did not allow him to accomplish this objective before his sudden death that occurred at the beginning

of January 2009. This communication has now been rescheduled and is included in the dissemination plan for the initial exploitation phase.

3. Spain

Presentations at Conferences & Workshops

- **Pharmacovigilance Committee Meeting**
  - Proyecto "Med-ePHV": proyecto internacional de enseñanza de FV a través de Internet
  - Date: 21 June 2007
  - Place: Madrid (Spain)
  - Organiser: Spanish Medicines Agency (Agencia Española de Medicamentos y Productos Sanitarios - AEMPS -)
  - Presentation

- **VIII National Pharmacovigilance Meeting**
  - Med-ePhV project: Learning and practicing Pharmacovigilance in the Mediterranean countries of the European Union
  - Date: 29-30 May 2008
  - Place: Murcia (Spain)
  - Organiser: Spanish Pharmacovigilance System
  - Presentation

- **XXI Congress of the Spanish Society of Clinical Pharmacology**
  - Date: 23-25 October 2008
  - Place: Barcelona
  - Organiser: Spanish Society of Clinical Pharmacology
  - Participation

Direct mailings

Health practitioners - Medical Associations – Pharmaceutical companies

A direct mailing was sent to health professionals (physicians, pharmacists and nurses) in Spain in order to inform them about the project and invite them to participate in the evaluation part. The letter also went to pharmaceutical companies to make them aware of the setting up of the Med-ePHV e-tool.

Actions undertaken at European level:

Articles (scientific journals, newsletter)

- "Med-ePHV: pills of pharmacovigilance in Europe", submitted to http://cordis.europa.eu/wire/ on 27 November 2008 and published on 'CORDIS News and Research Headlines' service: http://cordis.europa.eu/fetch?CALLER=EN_NEWS&ACTION=D&RCN=30390

Brochures

Distribution of informative brochures at the following events gathering European and international participants:

- The EFGCP Annual Conference 2008 on Safety in Clinical Trials - Are We in Jeopardy?
  29-30 January 2008, Résidence Palace, Brussels, Belgium (150 participants)

- EFGCP-ITCC-DIA Conference on Meeting the Challenges of Paediatrics within Oncology Drug Treatment
  25 November 2008, Management Centre Europe, Brussels, Belgium (50 participants)
- The EFGCP Children's Medicines Working Party 4th Annual Conference EU & US Paediatric Legislation: What is Changing in Practice in Paediatric Drug Treatment, Research & Development?
  26 November 2008, Management Centre Europe, Brussels, Belgium (70 participants)
- A Conference on the Impact on Clinical Research of European Legislation ICREL: Results & Discussion
  2 December 2008, Diamant Centre, Brussels, Belgium (270 participants)
  ICREL is a one-year project financed by the European 7th Framework Programme. Under EFGCP's coordination, ECRIN, EORTC, as well as the Hospital Clínic of Barcelona and the Medical University of Vienna collaborate in this project. Its aim is to measure and analyse the direct and indirect impact of the Clinical Trials Directive 2001/20/EC and related legislations in the EU on all categories of clinical research and on the different stakeholders: commercial and non-commercial sponsors, ethics committees and competent authorities.

Liaison with other European Initiatives:
Innovative Medicines Initiative (IMI)
The Innovative Medicines Initiative (IMI) is a unique Public-Private Partnership (PPP) between the pharmaceutical industry represented by the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the European Communities represented by the European Commission. The IMI JU Research Agenda is a multiannual plan. It is based on the Strategic Research Agenda developed by the European Technology Platform on Innovative Medicines which identified principal research bottlenecks in the biopharmaceutical R&D process and sets forth recommendations to overcome these bottlenecks by focusing on four areas among which Education and training to close the existing training gaps in the drug development process.
As stated in the IMI Annual Implementation Plan 2008, including the Scientific Priorities for 2008, one of the 18 calls will specifically focus on pharmacovigilance training programme:

18. Pharmacovigilance training programme

The science of pharmacovigilance is still developing from being traditionally reactive towards a more proactive focus on coordinating and analysing the wealth of data already available in the EU on the use of medicines. This change of focus requires inclusion of disciplines such as advanced epidemiology, biostatistics, drug utilisation, pharmacoepidemiology and use of large automated population-based exposure-outcome databases. There is thus a pressing need to expand the knowledge of pharmacovigilance professionals in both industry and at regulatory agencies in order to support proactive pharmacovigilance and risk management of medicines throughout their life-cycle. An understanding of pharmacovigilance is also needed by e.g. journalists and patient organisations to improve their communication of hazards associated with medicines. Further, development of better methodologies for risk communication is needed. The project will achieve this by customised education and training programmes at three levels: short training courses for journalists, venture capitalists, patients, health care professionals, etc who require a basic understanding of the principles of contemporary pharmacovigilance; Masters level courses for professionals working within pharmaceutical companies and regulatory agencies; and long term programmes in benefit-risk communication.

Duration 5 years
Indicative total in-kind contribution from the EFPIA companies €3.5m.

Therefore it was felt essential to propose the Med-ePHV project outcomes to the future consortium managing the topic and establish fruitful contacts with the partners involved in the 5 IMI Training calls (Call 14 to 18) which will target both specialist and non-specialist audiences throughout Europe.

Dissemination actions planned to be undertaken during the initial exploitation phase of the project (after 31 December 2008)

Actions planned at national level:

1. France

Presentations at Conferences & Workshops

- Presentation at the Fédération Hospitalière de France, Paris by INSERM (date to be confirmed)

Direct mailings of information about the finalised Med-ePHV tool/set-up of web-links to the Med-ePHV website in European Mediterranean countries.

Pharmacovigilance institutions/centres/associations

1. Association Française des Centres Régionaux de PharmacoVigilance
2. Société française de Pharmacologie et de Thérapeutique

Health practitioners – Medical Associations:

1. Ordre national des Pharmaciens
2. Ordre national des médecins
3. MEDicaments à DISpensation PARticulière
4. Association of Health Products Industry Physicians (Association des Médecins des Industries des Produits de Santé)

Competent authorities:

1. Agence française de sécurité sanitaire des produits de santé
2. Ministry of Health

Industry associations:

1. LEEM – Les entreprises du Médicament

Articles (scientific journals, newsletter)

It is proposed to submit an article in French to the following specialised and recognised journals:

- Quotidien du médecin
- Généraliste
- Pharmaceutiques

2. Italy

Direct mailings of information about the finalised Med-ePHV tool/set-up of web-links to the Med-ePHV website

Pharmacovigilance institutions/centres/associations

1. Gruppo Interregionale di Farmacovigilanza
2. Farmacovigilanza
3. Società Italiana di Farmacia Ospedaliera e dei Servizi Farmaceutici delle Azienda Sanitare
4. Italian Society of Pharmacology (Società Italiana di Farmacologia)
5. Consorzio Italiano per la Ricerca in Medicina

Health practitioners - Medical Associations

Competent authorities

1. Agenzia Italiana del Farmaco
2. Italian Ministry of Health

Industry associations

1. Society for Applied Pharmacological Sciences (Società di Scienze Farmacologiche Applicate)
2. Associazione Nazionale dell'industria farmaceutica dell'automedicazione

The communication event which was planned by CIRM and UNIPV for the last quarter of 2008 and had to be cancelled, due to the fatal illness of Prof. Nicola Fabris, has been rescheduled as follows:

- On March 31, 2009 a meeting of the Lombardy Region Working Group on Pharmacovigilance, sponsored by UNIPV, will be held in the CIRM facilities in Milan, with the specific objective of reviewing the Med-ePHV e-learning systems and in particular the Italian modules.
- During the same meeting the Working Group will decide to include Med-ePHV in the international congress that has been scheduled to take place in Rome for the autumn of 2009. This event will be sponsored by UNIPV and Federfarma.

3. Spain

Direct mailings of information about the finalised Med-ePHV tool/set-up of web-links to the Med-ePHV website

Pharmacovigilance institutions/centres/associations

1. Consejo General de Colegios Oficiales de Farmacéuticos and Colegios Oficiales de Farmacéuticos
2. Portalfarma
3. Spanish Clinical Pharmacology Society (Sociedad Española de Farmacología Clínica)
4. Federation of Spanish Medical Scientific Societies (Federación de Asociaciones Científico Médicas Españolas)
5. Sociedad Española de Farmacología
6. Asociación de Medicina de la Industria Farmacéutica en España
7. Asociación Nacional de Especialidades Farmacéuticas Publicitarias

Health practitioners - Medical Associations

1. Catalan Agency for Health Technology Assessment **(**Agència d'Avaluació de Tecnologia i Recerca Mèdiques de Catalunya)

Competent authorities

1. Spanish Agency of Medicines and Medical Devices (Agencia Española de Medicamentos y Productos Sanitários)
2. Ministry of Health

Industry associations:

1. Farmaindustria Foundation (Fundación Farmaindustria)

Universities

1. Catalan Institute of Pharmacology (Fundació Institut Català de Farmacologia)
2. University of Alicante

4. Portugal

Direct mailings of information about the finalised Med-ePHV tool/set-up of web-links to the Med-ePHV website

Pharmacovigilance institutions/centres/associations

1. National Pharmacovigilance Centre
2. Portuguese Pharmacological Society (Sociedade Portuguesa de Farmacologia)

Health practitioners - Medical Associations

Competent authorities

1. National Authority of Medicines and Health Products (Autoridade Nacional do Medicamento e Produtos de Saúde, INFARMED)
2. Ministry of Health

Industry associations

1. Associação Portuguesa da Indústria Farmacêutica (APIFARMA)

Universities

5. Greece

Direct mailings of information about the finalised Med-ePHV tool/set-up of web-links to the Med-ePHV website

Pharmacovigilance institutions/centres/associations

1. Greek Society of Pharmacology

Health practitioners - Medical Associations

Competent authorities

1. National Organization for Medicines (EOF)

2. Ministry of Health

Industry associations

1. Hellenic Association of Pharmaceutical Companies

Actions planned at European level:

Partnerships with organisations/institutions have been carefully inquired and initiated to ensure the dissemination of the Med-ePHV tool via an efficient on-line dissemination in order to obtain a wider coverage, whether at a European or national level, and increase the profile of the project within the pharmacovigilance sector.

Websites (links) & Direct mailings

Pharmacovigilance institutions/centres/associations:

1. European Association for Clinical Pharmacology and Therapeutics
2. The International Society of Pharmacovigilance (ISoP) (Worldwide)
3. EudraPharm
4. EudraVigilance
5. International Pharmaceutical Excipients Council Europe
6. International Association for Pharmaceutical Technology
7. Support in Pharmacovigilance

Health practitioners - Medical Associations

1. European Medical Association
2. International Pharmaceutical Federation (Worldwide)
3. Standing Committee of European Doctors

Competent authorities

1. European Medicines Agency (EMEA) – Pharmacovigilance contact point
2. European Directorate for the Quality of Medicines & HealthCare

Industry associations

1. International Federation of Pharmaceutical Manufacturers & Associations
2. European Federation of Pharmaceutical Industries and Associations
3. pharma.be (Belgium)
4. Association of Clinical Research Professionals

Universities

1. Academy of Pharmaceutical Physicians and Investigators

Others:

1. Centre Belge d Information Pharmacoterapeuthique (Belgium)
2. Belgian Association of Pharmaceutical Physicians (Belgium)
3. Dutch Pharmacovigilance Centre Lareb (The Netherlands)
4. Dutch Medicines Evaluation Board (The Netherlands)
5. Swiss Association of Pharmaceutical Professionals (Switzerland)
6. Swiss Society of Pharmaceutical Medicine (Switzerland)
7. Pharmaceutical Information and Pharmacovigilance Association (United Kingdom)
8. Medicines and Healthcare products Regulatory Agency (United Kingdom)
9. Association of the British Pharmaceutical Industry (United Kingdom)

10. Prescription Medicines Code of Practice Authority (United Kingdom)
11. British Association of Pharmaceutical Physicians (United Kingdom)
12. British Pharmacological Society (United Kingdom)
13. National Institute for Health and Clinical Excellence (United Kingdom)
14. Belgian College of Pharmaceutical Medicine (Belgium)

Brochures
Distribution of informative brochures at the following events gathering European and international participants:

- The EFGCP Annual Conference 2009 on Research Integrity: a European Perspective 27-28 January 2009, Diplomat Hotel, Prague, Czech Republic (125 participants)

The detail report of the Med-ePHV Final Plan for Using and Disseminating Knowledge, with annexed copies of the supporting materials (paper and digital formats), and of the papers presented at conferences or published in the specialized journals and professional magazines, has been submitted as project deliverable D26.

Task 9.5 – This task aimed at the Preparation of the Exploitation Business Plan and has been accomplished at the end of the project development phase.
The Exploitation Business Plan that has been developed by the SME partners of the Consortium, builds over the exploitation strategies for the Med-ePHV system, which had been agreed at the time when the SME's decided to join their forces and invest in this project. The initial exploitation strategy has been refined during the project development phase, taking into account the inputs received from potential users, industry, entities operating in the public health sector and sponsoring institutions.

In this section we present a summary of the Med-ePHV Exploitation Business Plan.

During the last phase of the project, the Consortium developed a network based application grids models to define the **most cost effective platform useful to support a heavy multi-user e-learning programme**.
The target market for the SMEs is represented by Local Health Authorities, Market Authorization Holders, Hospitals, Public and Private Health Organizations, Health education centers, individual doctors, pharmacists and other professionals of the Health sector.

One of the declared objectives of this Project is to try to offer successfully some results as commercial products in the market, and this requires a special effort to disseminate and make known to potential users the results and benefits of the Project. Since the main idea is to address the benefits brought by the MED-EPHV services for European users, the project WP09: Dissemination and Exploitation, shall stimulate the European users to take advantage of the Medical Technologies developed.
This shall be achieved using several available actions such as: Webs on the Internet, medical publications and press releases covering the results achieved in the area of pharmacovigilance, in on-line e-learning and with the ADR's notification tools.

The action for the Dissemination of Project results, has been tailored to the profile of the target users, and is of great importance with respect to mapping this generic solution for other Health segments. A further objective was to present the Project results on public events such as workshops, conferences, not only during the Project development phase, but also during the subsequent commercial exploitation phase.
The Dissemination actions undertaken and planned have been described in the previous chapter of this report.

The Med-ePHV product to be exploited
The scientific and technological solution that has been developed and will be exploited, is based on the establishment within a small computing grid of the following components:

- An e-learning system focused on pharmacovigilance science and regulation developed, tested and validated during the project with the active support of three levels of end-users (the SMEs, the Health practitioners and the Pharmaceutical industry belonging to the three target Mediterranean countries).
- A knowledge based notification module compliant with ADRs standardization (ICH M2).
- An integration and cooperation environment providing portal type of services.

Targeted Market and Customers
The target market for the SMEs is represented by Local Health Authorities, Market Authorization Holders, Hospitals, Public and Private Health Organizations, Health education centers, individual doctors, pharmacists and other professionals of the Health sector.
The Med-ePHV modules will be made accessible not only to health practitioners, that can attend traditional type of seminars and workshops, but also to those health professionals that operate in remote rural locations and cannot leave their patients to attend a pharmacovigilance course in a metropolitan area.
To reach the wide medical population of all the EU Mediterranean regions Med-ePHV has designed and implemented a state-of-the art wide-band grid, which allows to reach and train a large group of health practitioners where they work or at their homes.
In order to improve the current pharmacovigilance practice and meet the goal of Excellence in pharmacovigilance training, which are both key aspects for the safeguard of public health, it was necessary to ensure the following:

- Learning and training services focused on pharmacovigilance science and regulation for health practitioners.
- Knowledge based support to ADRs recognition and notification.
- Use of fully integrated information systems for medicines and ADRs case histories.
- Design of common grid based virtualization services for LHAs, MAHs, health practitioners and patients to establish pharmacovigilance focused virtual communities, leveraging on a state-of-the-art broadband communication and grid computing technology.

The complexity of ADRs recognition and notification is at the origin of the current poor delivery of notifications, in terms of both quality and quantity, to the central pharmaceutical authorities (national and European Agency).
In addition the limited pharmacovigilance support provided, in terms of knowledge dissemination and technical systems, to health practitioners and patients contributes significantly to the scarce production of ADRs recognitions and notifications in the periphery of the health systems and of the market authorization holders networks.
All parties recognize it but in particular the EU pharmaceutical regulators underline that pharmacovigilance is an essential tool in order to ensure public health in the Union.
The pharmaceutical legislation proposed by the EC in 2001 and modified in the final adoption following the amendment of the European Parliament stresses the importance of pharmacovigilance by enforcing ADRs notification (Council Regulation No. 726/2004).
The importance given by regulators to pharmacovigilance will promote the development of the pharmacovigilance practice at the edge of the EU health systems, i.e. at the interface where ADRs recognition and notification takes place.
While central pharmacovigilance systems such as the systems of the national pharmaceutical authorities and of the European Agency (EMEA) are already in place and operational the component that has to provide the data to these systems, i.e. the notification systems in the periphery at the interface between LHA/MAH and health practitioners appears not adequately developed.
The system allows to learn and to practice adverse drug reactions notification at the peripheral edge of the pharmacovigilance systems, i.e. at the interface between Local Health Authorities (LHAs), Market Authorisation Holders (MAHs) and health practitioners and patients.
The size of this market is considerable: concentrating again only on the medical industry, in the EU market, globally, this would encompass for the medical industry alone, a market size of 500,000 to 1,000,000 plants and enterprises that are potential users of an e-learning ADRs notification system like Med-ePHV.

The number of public institutions is in the same order of magnitude if not larger. While national and regional bodies concerned with ADRs management are in the order of thousands, at the local level (IT, ES, FR), are again in the hundreds of thousands in the European Market.

Therefore, the potential market for a system like Med-ePHV is of a considerable size.
AS and GS will be looking for a French partner to undertake the exploitation of the Med-ePHV system in France, since the original French project partner (PMV) is no longer in position to maintain and commercially exploit the product.

Trends in e-learning demand and market
The picture in 2008 about e-learning trends and what is happening in the market was not a clear one.
The most commonly identified trend was a desire for faster and lower cost e-learning.
The *Bersin report* published in November 2008 by Training Magazine, highlighted a reduction in e-learning in large organisations for the first time in the recent years. By

contrast, many commentators felt that 2009 would be a major opportunity for e-learning.
Due to present global recession with consequent general cost cut measures, also Training budgets are being scrutinised carefully along with all other budgets.
Budget cuts do not necessarily mean cuts in training, they mean that training must be delivered in a more flexible way with greater use of technology. Susan Varnadoe, president of Ninth House, says the recession is accelerating a change in training delivery, whereby organisations move from site-based training to a mobile, technology-enabled classroom.

Companies are reacting in different ways to reducing budgets. Some are delaying training, some are switching to e-learning, others are only delivering priority training needs and asking tough questions about the value of each and every training intervention. **In some companies the priorities are training interventions** that have a direct impact on generating revenue.

It is widely recognized that there are evident potential benefits that e-learning can deliver to organisations. In a recent survey conducted by Becta as part of the Next Generation Learning @ Work campaign, one of the conclusions says that "*learning technologies are starting to add some strong value in areas that are becoming increasingly important to organisations in a downturn when efficiency and competitiveness are key*."
The feedback from the survey shows that learning technologies are helping organisations:

- Save time
- Reduce cost
- Implement organisational change
- Improve the rollout of new products and IT systems

It is evident that within this cost-saving trend affecting conventional training, e-learning may find new growth opportunities.
The findings on e-learning expenditure in the coming year were positive in that whilst over 25% expected training budgets as a whole are to reduce, 64% expected the proportion of the overall training budget allocated to e-learning to increase.

64% of 225 respondents believe the % of overall training budget allocated to e-learning will increase

Med-ePHV SME partners objectives

Med-ePHV SME partners have a long-term plan to be in business for themselves and to utilize the specialized business knowledge they have gained.
We have developed business relationships with other key players, such as vendors and distributors of scientific training programs, that they market in both traditional and digitally packaged formats, including via the Internet.

One of the SME partners, Gruppo S, has defined the possibility of developing with the collaboration of the CIRM (Italian consortium of medical research) a series of actions of promotion of the platform, constructing conditions for its exploitation through agreements to be put in place with the Health Authorities of the different Italian regions.

The activity is based on the integration of the instruments that have been developed within the Med-ePHV project, with the FAD tools already present in the training processes of Italian medical practitioners. These practicioners, by attending the Med-ePHV courses might get credits needed to document their individual activities undertaken with the objective of updating their professional knowledge.
The aim is to reach the highest possible number of doctors to concentrate more attention to this topic.
The current market conditions and project standards enable to sell the platform in different training areas, both to direct end users in the medical field and to high education institutions (e.g. universities).
The courses on pharmacovigilance will also be proposed in post-graduate master courses at on Hospital management course to be held at the Politecnico di Torino, addressed to professionals that are involved in the management of Hospitals, Clinics and other public and private Healthcare Centers, The present and medium term status of medical training in Europe is recognised to represent a significant element of national growth and a key element of the plan for European development of skills.

Med-ePHV commercial products and customer support

SME's will handle the full administration and coordination of the sales, as they have the needed expertise and experience to do so, and since they are also responsible for the production and maintenance of the product.

As a commercial product, the results of the Med-ePHV project represent a bundle of two software components (ADRs recognition and notification SW + e-learning platform) that can be licensed together or individually (the framework system and its component screening models); together with consultancy services that can be offered in support of, or by using, the software.

As an optional extension of the consultancy in support of end users, the optional on-site training using components of Med-ePHV e-learning platform can be offered by the project partners, or qualified future distribution and support partners, as a service. This would allow end-users to minimize their investment, training, and long-term maintenance efforts by outsourcing these components to an external service provider.

While this option is conceptually very attractive, and technically and commercially sound, there may be issues of confidentiality that may make it difficult to implement both in the industrial and public administration environment.

The Consortium will continue to exploit the Med-ePHV developments in future projects, and provide continuing support and consultancy on a case by case basis. Research oriented but externally funded projects will try to build on the Med-ePHV components such as the parallel models, sensitivity analysis, and parallel implementation techniques together with the remote client-server execution of models on powerful hardware, triggered by a web-request.

Commercially oriented exploitation and continuing support for end users is foreseen under a number of constructs, currently under discussion, that will involve spin-off companies that can license and then commercially exploit, Med-ePHV developed products in other countries.

Business Organization

Marketing, distribution and sales of the web services will be handled by the SME partners as defined in the business plan, whereby the aim is to:
Promotion of the e-learning courses will also take place through the Web Service.
Constraints on the availability of Med-ePHV infrastructure (massive parallel computers, cluster with fast LAN connections, fast external network connections) are to be expected in most potential applications.
Therefore, the following issues must be addressed:

- simple entry-level configurations
- flexible upgrade options through cluster solutions
- porting to other browser the basic (client) platform or further development of Java clients.

The marketing strategy for Med-ePHV is based on a phased – growth approach.

The initial phase will concentrate on the direct exploitation of the project in Italy, France and Spain. It will focus on the national partners in these three countries and their existing professional contacts and clients.

Since the national partners already operate successfully in this market, no further market analysis seems necessary. The primary mechanism for marketing will be:

- exploitation of existing business contacts of the partners;
- presentations of the e-learning platform by consortium demonstrator at exhibitions, conferences, and technology fares;
- mailings to potential users with personalized follow up;
- as accompanying measures, publications of articles, features, and editorials describing the system in appropriate technical journals;
- continuing use of the Internet as an advertising medium.

The second phase of the business development plan will require identifying strategic partners in various countries. Due to the very important (and comparatively time consuming) consultancy component, and the need for customization to national regulatory frameworks, institutional structures, language, etc., building up a network of local support partners is essential.

5.10 Financial Plan

5.10.1 Pricing

Pricing was discussed within the Consortium. In view of:
The available spending budgets of the above described target groups,
The experience of the SME partners with the e-courses with comparable content (generally priced between 500 and 1500 Euros),
The fact that a web service presents a higher barrier to access information than printed matter since users could only 'read' the contents on a computer,

It was concluded that the price barrier for this particular CD-ROM (a second sub product of the on-line educational materials) would need to be set as low as economically possible.
The e-learning courses should therefore be very competitively priced: between 500 and 1000 Euro, a price considered to be in reach of the target groups and low enough to tempt buyers into immediate purchase. This should warrant broad use and widest possible exposure of the information on the web platform.

During a meeting of the Consortium the price of the product was set to be of 1000 Euro, which is a price level in line the prices of other e-learning courses and attractive enough for a new course not yet available as an Internet product.

5.10.2 Projected revenues

Cost considerations are a major constraints both for public authorities, as well as for medical doctors or industrial enterprises.
Med-ePHV as a product must therefore:

- offer a low-cost entry level configuration
- be easily upgradable if and when more performance is required.

Short Range Plan (6 to 12 months): Initially our advertising and promotion will be done on an entirely personal basis without any budget for paid advertising. We will limit our advertising budget to personal travel expenses in making these presentations and follow-up presentations
Mid Range Plan (12 – 36 months): To establish brand recognition at the retail level, we plan to budget 50% of our sales to joint advertising. We will solicit presentations from local advertising agencies.

Long Range Plan: We plan to aggressively build brand recognition and loyalty by budgeting 100% of sales, which will be allocated between space advertising in medical and pharmaceutical journals, appropriate health related magazines and joint advertising with our customers.

5.10.3 Cash Flow

The exploitation plan that was developed for the web services counts on revenues (net income) from sales of the courses to be used mainly for product maintenance and updates, to cover development and production costs for new versions to be released at a later date. It is expected that the current courses will have a life cycle of three years and thus can be marketed till the end of the year 2011. Whether or not an updated version of the e-courses will be produced will depend on the success of the products in the market and demand.

Each SME partner will handle the full administration and coordination of the sales in their own country, as it has the expertise and experience to do so and since it is also responsible for the production of the courses in its own language and customized to national requirements.

This exploitation and business plan covers the Web Service (server and maintenance of catalogues/software), that will only have yearly server and maintenance costs.

It is impossible to predict the financial turnover of the products with great precision. This because the product is new and unique in its kind and moreover since marketing and sales will be partly experimental by using multiple distribution channels to sell e-learning products, part of them new and not tried before.

The table below provides a first insight in the business plan for the web services. It presents estimates of minimal and expected sales and resulting income for these

products until the end of the year 2011. NB: the expected sales are conservative estimates.

Web Services Sales prognosis for the period 2009-2011 (three years)					
Product price (market in Euro)		1000			
Sales outlet		minimum no of sales	expected no of sales	minimum turnover	expected turnover
Distributors Italy		500	2.000	500.000	2.000.000
Distributors Spain		500	2.000	500.000	2.000.000
Distributors France		300	1.000	100.000	1.000.000
Direct mailing Italy		200	500	200.000	500.000
Direct mailing Spain		200	300	200.000	300.000
Direct mailing France		100	200	100.000	200.000
Prognosis IT over 2 years IT version		700	2.500	700.000	2.500.000
Prognosis ES over 2 years ES version		700	2.300	700.000	2.300.000
Prognosis FR over 2 years FR version		400	1.200	200.000	1.200.000
Total numbers sold and gross income		1.800	6.000	1.600.000	6.000.000
Costs of user support (helpdesk)					30.000
Handling, mailing, administration					5.000
Advertisement					15.000
Net revenues				1.550.000	5.950.000
Use of revenues	%				
Server costs Web Service	5			77.500	297.500
Royalties to third parties	10			155.000	595.000
Software licenses	10			155.000	595.000
To stakeholders	30			465.000	178.500
To trust funds	45			697.500	2.677.5000

The costs for the update web services production is roughly estimated as follows (in Euro):

Activity	personnel	costs
Updating contents	1 man month	5.000
Purchase of new materials (copyrights)		2.000
Meetings, travel costs content partners		5.500
Programming (AS, GS)	2 man months	10.000
Production (AS, GS: 2 versions)		10.000
Total		32.500

The ROI will be reached at the end of the second year of the exploitation phase of the project. This value will be reached without considering the exploitation in the French

and Spanish countries of North Africa to be supported by the European Chamber of European experts (UCEE) that will help guiding this evolution of the business plan.

5.10.4 Other business vehicles pursued by the Consortium

In principle, there are several options in the business strategy for the exploitation of the Med-ePHV e-learning platform and associated side products; they include:

- concentration on a small number of high-profit projects;
- building a support and distribution network capable of supporting a high-volume but relatively low-cost market;
- licensing to national or regional distribution partners or value-added resellers with a minimum direct involvement.
- seek strategic partnerships with established players in the market.

These strategies are of course not mutually exclusive but can be combined and mixed with a geographical discretisation, and evolve depending on market response and first experiences.

For the last point, several initiatives have been started aimed at establishing strategic partnerships with developers of similar systems, among which it's worth mentioning the following:

- initial contacts with Regional Health Authorities
- discussion with MEDRA dictionary owners with the goal of integrating the data bases, and simple screening models from MEDRA in the Med-ePHV ADRs management systems.
- Initial contacts with ORACLE to explore possibilities for integration, since ORACLE ARDs management system and MED-ePHV have complementary capabilities.

The full Med-ePHV Exploitation Business Plan has been submitted as Contract deliverable D22.

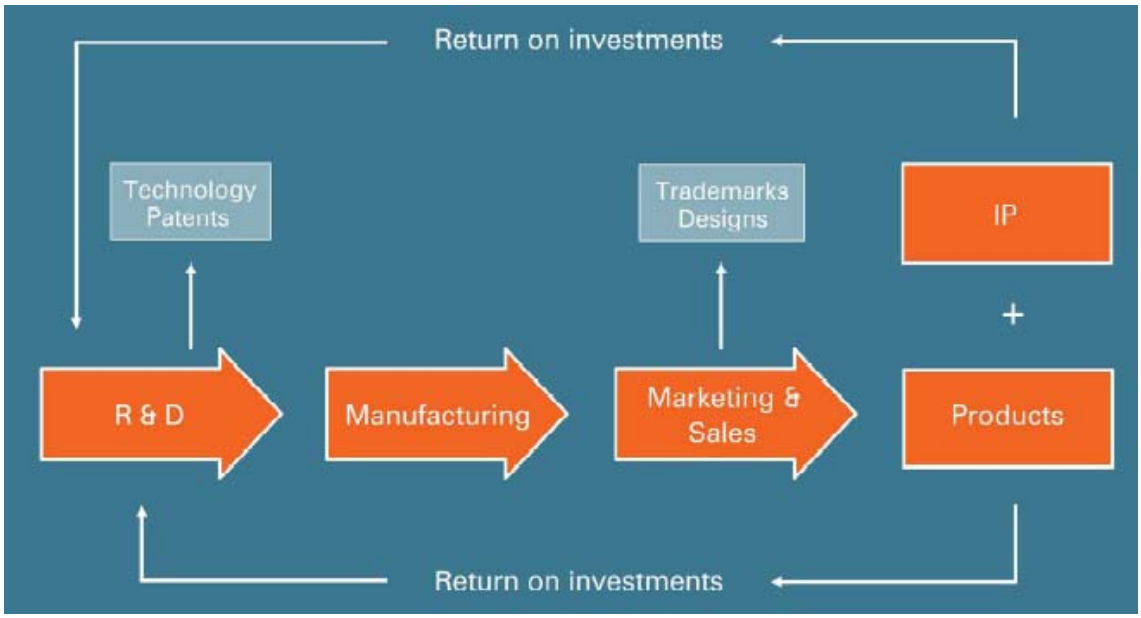
Task 9.6 – IPR management and Copyright application.

IPR coverage of course materials and e-learning platform system software was to be addressed upon completion of testing and validation of the products, before they will be made available outside the consortium for commercial exploitation.

The IPRs generated by the project is shared by the SMEs, following a scheme which has been agreed among them and has been outlined in the Consortium Agreement.
Among the main objectives of the Med-ePHV project there is the dissemination and exploitation of project results.
However due to the nature of the Med-ePHV end product, that is basically an on-line accessible software, it is strategically important that before the product is brought to the market, proper protection means are put in place to prevent unauthorised access or illegal copying of the Med-ePHV software.

To limit the risk of unauthorised access to the on-line modules, measures will be put in place to restrict access to the Med-ePHV server, such as the use of firewall, user login and password and use of secure (https) protocols.
These preventive measures have been defined in the design phase of the project Grid and have been covered in the project Deliverables D18 (Report on Med-ePHV Grid Architecture and Resources Integration) and D21 (Report on Web Services and User Interface).

In this chapter we summarize how the Consortium has been addressing the protection of IPR generated by the Med-ePHV partners, before the e-learning modules and other related proprietary features, are brought to the market. In particular we will describe the Consortium plans for copyrights applications and the preparation of the necessary legal agreements between partners.
The following scheme shows the strategic key role of the protection of the IP of a product that results from a R&D project like Med-ePHV, when the product is brought to the market. The Return on Investment cycle is completely dependent from the possibility of protecting the IP (Patent, Copyright and Trademark) of the product that has been developed.



Background
In the last decade, several new legal instruments have been adopted or proposed to harmonise part of the IPR environment at European level, ranging from a Project for a **Software Patent Directive** to the Directive on the Enforcement of Intellectual Property Rights (2004/48/EC, 29 April 2004).
The legal framework for digital content IPRs in the EU was established by the **Directive on the Harmonisation of Copyright and Related Rights in the Information Society** (2001/29/EC). This addresses the use of technological measures to protect content against illegal use, and calls for voluntary measures by rightholders to protect copyrighted material whilst encouraging the interoperability of different copyright protection systems.

In today's global economy the success of European business and industry depends not only on creativity and inventiveness but also on the effective and profitable transposition of new products and services to the market.
The Intellectual Property Rights (IPRs) systems are an essential tool for enabling business success based on innovation. These **IPRs include patents, trademarks, designs, and copyright**. Much attention has been paid to the role of patents for technological advance, perhaps too much so and at the expense of other forms of IP and IP Rights. Patents undoubtedly are of great importance in today's world of high technology and rapid technological advance. However, patent holding companies often also have a portfolio of the other rights, such as trademarks, designs and copyright, to protect themselves fully.
The importance of collaboration between EU Member States in the creation of a strong and open internal market with its underpinning IPR systems is demonstrated by the operations of the **Office for the Harmonisation in the Internal Market (OHIM)** that delivers EU-wide Trade Marks and Designs and also the European Patent Organisation, a non- EU body the majority of whose members are also EU Member States, that provides a bundle of national patents based on a single application. Industry has made it clear that the patent system needs to be updated to reduce costs and to move towards a single EU system. The above applies to all sizes of business and a great deal of attention is being paid to the rising challenges presented due to globalization.

5.11 Med-ePHV IPR issues

The "Consortium Agreement" defines which are the IPs rights of each partner.
During its preparation, the Coordinator had contacted the EC IPR Help Desk Services in order to clarify how to copyright the Med-ePHV product/services. The procedure for software copyright protection is well known and the Consortium has sufficient information to proceed in this direction.
IPR management is inspired to the most diffused market codes/standards and to the international best practices, establishing also terms such as the liability for possible infringements.
Concerning the ownership of knowledge developed during the project, the SME partners have in principle agreed on the following sharing scheme, as the Med-ePHV project from a business viewpoint has produced these groups of products/services:

1. Med-ePHV Learning Models
2. Med-ePHV ADR Recognition
3. ADRs Notification-Recognition Software
4. Med-ePHV e-learning courses
5. Med-ePHV Grid:
    - ✓ Med-ePHV Grid Architecture basic engineering
    - ✓ Resources Integration
    - ✓ Web Services
    - ✓ User Interface

6. Graphic material for Business Planning support

The Med-ePHV IPR Agreement

Below we reproduce the latest version of the Med-ePHV Consortium IPR Agreement:

"*The CP and project partners agree to regulate their ownership of the IPRs generated by the project.*
(1) The RTDs contractors:

- *Università di Pavia – Dipartimento di Medicina Interna (UNIPV)*
- *Tecnofarmaci – Società Consortile per Azioni – per lo Sviluppo della Ricerca Farmaceutica S.C.p.A. (TF)*
- *Institut National de la Santé et de la Recherche Médicale (INSERM)*
- *Istituto de Farmacoepidemiologìa de la Universidad de Valladolid (UVA)*
- *European Forum for Good Clinical Practice (EFGCP)*

In accordance with the rules of the Cooperative Research are considered as "service providers" with no right to the IPR foreground generated as a result of the project.
The SMEs contractors:

- *Gruppo S Lab S.r.l. (GS)*
- *Arisoft Editorial SA (AS)*
- *Pasteur Mediavita (PMV)*

Have agreed to retain full ownership and rights for all background knowledge and IPR's developed by the individual partner prior to commencement of the Med-ePHV project and jointly share all foreground knowledge and IPR's developed during the execution of the Med-ePHV project.
Each SME contractor shall have exclusive exploitation rights of the Med-ePHV products and services in their respective countries of incorporation and for those countries where the same language is spoken.
The terms of transfer of Med-ePHV products and services to other countries or markets will be agreed on a case-by-case basis by the SMEs contractors, taking into account the role, effort and involvement of the promoting partner.
(2) Concerning confidentiality the Parties have agreed to hold in strict confidence and to not disclose in whole or in part to any third party Confidential Information received from the other Parties. Each Party shall be obliged to keep in strict confidence and to bind all of its employees, consultants, and/or subcontractors to keep in strict confidence all the Confidential Information, both commercial and technical, received directly or indirectly from the other Parties and shall not at any time disclose such information to any third party for any purpose without prior written consent of the other Parties concerned, except this obligation shall not apply to:

- *information which at the time of disclosure is generally available to the public, or*
- *information which after disclosure becomes generally available to the public through no fault of the receiving Party, or*
- *information which the receiving Party can show was in its possession prior to disclosure and which was not acquired directly or indirectly from another Party*

is disclosed to either Party by a third party that is not under an obligation to maintain the confidentiality of the information after such disclosure.

(3) Promptly upon termination of the Agreement and following notification, each Party shall return to the other all Confidential Information received and all other material possessed by or under the control of each Party that was created by such Party and that is related to the Confidential Information.

(4) Each party agrees that all Confidential Information, including tangible information such as drawings, designs, specifications, descriptions, data, samples, software and computer codes, and other material pertaining to Confidential Information and obtained from or through another Party shall remain the property of the Party that has generated such Confidential Information. In addition to the obligation to return Confidential Information upon the termination of the Agreement, each Party agrees to return to the other at any time and upon specific request all Confidential Information received and all existing copies thereof."

After the unfortunate bankruptcy of Pasteur MediaVita, the other SME partners have agreed to undertake and complete the work still to be accomplished by PMV. As a compensation for the additional work scope, the Italian partner (GS) and the Spanish partner (AS) will jointly retain and equally share the IPRs rights for France. These two SME partners intend to license these rights to another French SME, willing to exploit the Med-ePHV system within the territory previously assigned to PMV. The search and selection of the French SME will be made upon conclusion of the project, with the support of the French RTD partner (INSERM).
The commercial terms of the licensing agreement will be agreed upon between the Italian and Spanish SME partners before being negotiated with the candidate French SME.

Copyrights Application
Each SME partner which has the right to ownership and use of **marks and content generated by the project**, will do the registration of these marks and products for its country: GS for Italy, AS for Spain and other Spanish speaking countries.
Concerning France, the registration will be delayed until a suitable French partner or licensee will be found. However until that time, access to the French version of the Med-ePHV system and software will be restricted. Immediately upon the establishment of the exploitation agreement with the French SME partner, and prior to begin the commercial exploitation, the marks and content generated by the project will be registered and protected in France and in other French speaking countries where exploitation is envisaged,
At the time of registration, companies can start to support the commercial distribution of the products using a national web domain, e.g.: “medephv.it” or “medephv.es”…
The conditions of the Allocation Agreement concerning the application of copyright as well as other clauses will be managed by an IPR pool, to be constituted by the legal representatives of the companies, or Oreste Salvaggio for GS and Carlos Arias for AS.

The original website (medephv.com, medephv.net and related links) will be maintained by the respective responsible (AS, GS) in English, in order to promote the work done by

the Consortium. The same level of detail and quality of the communication parameters established for the project will be maintained and assured by the respect of the applicable documentation and communication rules used during the project development phase (eg.: updated version of the Project Master Document, etc.).
The companies before submitting the copyright registration application in their own country will send the relevant documentation to the other member(s) of the IPR pool for review and approval.

The complete detailed report covering all the IPR aspects can be found in the project deliverable D27 - Report on IPR management and copyright application.

6. Deviations from the project work-programme

No major deviation or change of work-scope has occurred until the middle of 2008, as compared to the original work-packages description.

Scope transfer between partners, had to be made as a direct consequence of the French SME partner PMV bankruptcy occurred in March 2008 and that essentially affected the other two SME's (AS and GS), who had to undertake the work activities previously assigned to PMV. The transfer of work scope from PMV to AS and GS has also impacted on the work and budget usage of the RTD partners which were teaming with the SME's in the respective countries.

The work scope re-assignments have been duly covered by the EC Contract Amendment Nº 3, including a revision of the Contract Annex 1, dated July 31, 2008 and approved on October 2, 2008.

The Contract Amendment Nº 3 also included a four months extension of the project duration.

The additional workload imposed on the Spanish and Italian SME and RTD partners, as a result of the PMV bankruptcy and cease of support to the project activities, during a critical time of the project development phase, has caused some activities to be completed later than originally scheduled.

In spite of these delay incidences, the project development phase has been satisfactorily concluded, having practically achieved all the initial stated objectives.

Concerning the final product development, only a few deviations, essentially affecting the full validation of the French version of the e-learning modules, and the postponement of a dissemination event in Italy are worth to be reported.

In the following section we provide more details about non-schedule type of deviations experienced during the second reporting period, that are worth to be mentioned. Minor deviations that had no impact nor altered the outcome of the project have not been recorded in this summary. They are however noted in the relevant project deliverables covering these activities.

6.1 Work Package 08 – Testing and Validation

Task 8.1, 8.2 & 8.3 – The full scale external testing and validation of the of e-learning and ADRs notification components, of the of integration components and web based user interface and of the complete pharmacovigilance suite of services, has been satisfactorily completed in Italy and Spain using a representative sample of more than 150 target users.

In France testing and validation has been conducted using a smaller sample. It will be completed on a larger sample, as soon as a French SME, replacing PMV is found, and in any case, before starting commercial exploitation of the French Med-ePHV e-learning system.

Details of the status of the Med-ePHV system testing and validation can be found in the project deliverable D24.

6.2 Work Package 09 – Promotion and Dissemination

Task 9.4 – Presentations at selected medical and scientific national and international events.

We had less activity in France (again caused by the unavailability of the French SME partner to support the action). Some of the dissemination actions have been postponed until a new SME partner is found for the Med-ePHV system exploitation in France, so that this partner can participate in the events and receive recognition and visibility by potential customers and Health Institutions.

In Italy we were forced to postpone a large Med-ePHV communication event, which had been prepared and scheduled by CIRM for the last quarter of 2008. Unfortunately Prof. Nicola Fabris, who was organizing this event together with UNIPV, suffered a fatal illness that did not allow him to accomplish this objective. The Med-ePHV communication event that had to be postponed has now been rescheduled for the year 2009.

7. Consortium Management

Project Management activity has been more intensive than expected especially during the second period of the project and has required additional administrative and coordination effort.

The following events have required more dedicated effort by the project coordinator.

The SME Spanish partner JB had to leave the project at the end of 2006, due to lack of human resources to be dedicated to the project activities. After EC approval, JB has been replaced effective January 1, 2007 by the Spanish SME AS. The Contract with the EC, budget distribution and the Consortium Agreement (CA) had to be amended accordingly to reflect that change.

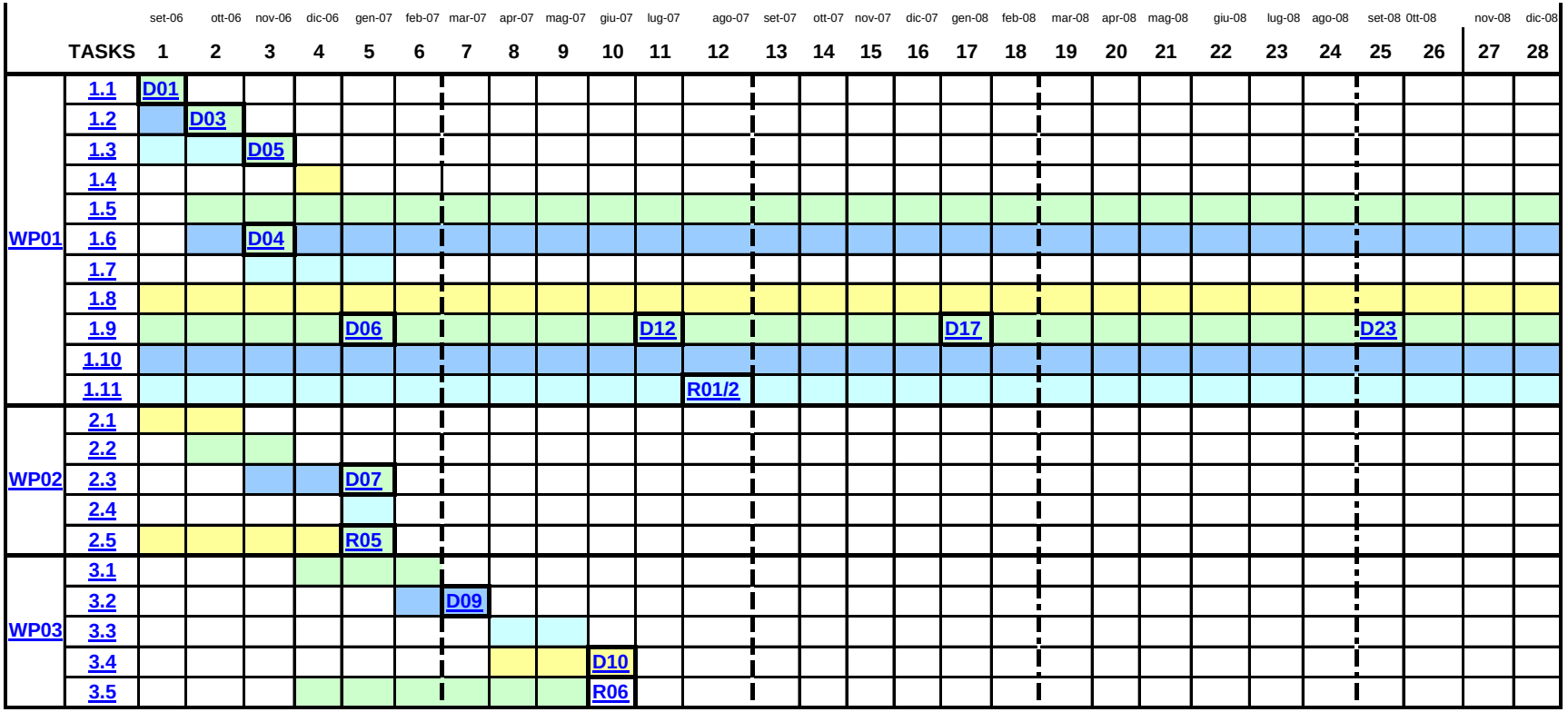
The French SME partner PMV was declared in the status of bankruptcy by the Commercial Court of Paris on March 13, 2008. However the project coordinator had no knowledge of this issue until the beginning of May 2008, when he received an official notification by the bankruptcy official receiver appointed by the Court, MJA-Selafa, which was only interested in collecting the outstanding EC contribution and offered no cooperation at all in the resolution of the administrative obligations, deriving from their participation as partner in the EC Contract. The coordinator, in an attempt to resolve the open administrative held a meeting with MJA-Selafa in Paris. Nevertheless the agreed upon actions that MJA-Selafa had committed to take during the meeting have not been accomplished.

In order to complete the project the PSC decided to reassign the remaining work previously allocated to PMV to the other two SME. The work-scope and associated budget transfer has required a new revision of the Annex 1 to the EC Contract to be prepared and submitted to the EC as an Amendment to the Contract. Considering that the PMV inactivity had caused a chain of delays also to the interfacing activities of the other project partners, the request for Contract Amendment also included a four months extension of the project duration. The Contract Amendment Nº 3 was approved by the EC on October 2, 2008.

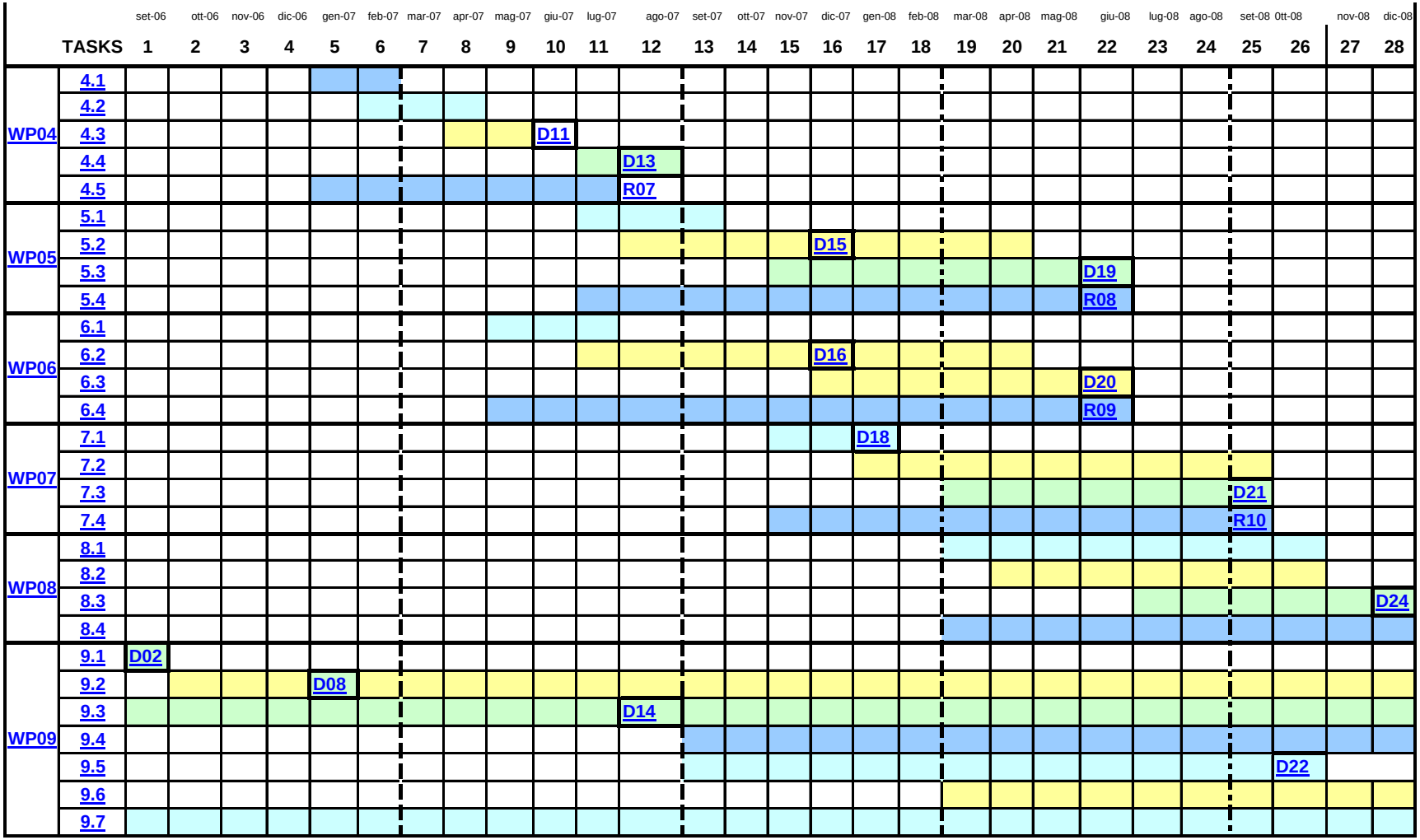
These unexpected events and the associated actions undertaken by the Project Mgr. and Project Coordinator explain the greater expenditure in the Management budget by the Consortium coordinator.

8. Workplanning and Time-table

The attached Project timetable / barchart shows the status of all the work-packages and associated tasks at the end of the project.



Med-ePHV Project



9. Conclusions

Med-ePHV is a co-operative research project co-financed by the European Commission through the Sixth EU Framework Programme for Research and Technological Development.

The EC Contract started on September 1st. 2006 and covered a project with an initial duration of 24 months, subsequently extended during four additional months, until December 31st, 2008.

The Med-ePHV project main objective was to research and develop an innovative approach to the EU pharmacovigilance practice by designing and implementing a pharmacovigilance co-operative e-learning system specifically addressing the needs and profile of health practitioners and patients of Southern Europe (Mediterranean countries).

The envisaged system would have permitted to learn and practice adverse drug reactions notification at the peripheral edge of the pharmacovigilance systems.

The following objectives that had been set by the Med-ePHV Consortium for the project development phase, have been achieved by strictly following the work-programme included in the Annex 1 to the EC Contract:

- Development of pharmacovigilance e-learning courses and tutoring schemes in line with the latest EU legislation and adapted to the specific national implementation schemes and directed to health practitioners of France Italy and Spain.
- Test and validation of the e-learning modules by a representative sample of health professionals and by selected Pharmaceutical industry representatives.
- Study and design of a co-operative environment as the central component of an application grid accessible to LHAs, MAHs and health professionals, to be implemented during the commercial exploitation phase of the project.

The Med-ePHV approach is based on the modelling of the pharmacovigilance practice, allowing to deliver a suite of software solutions and network based integration services capable to support an efficient ADRs recognition and notification. The grid-based services that will be offered by the participating SME in their respective countries include:

- An e-learning system focused on pharmacovigilance science and regulation which has been developed, tested and validated during the project with the active support of three levels of end-users (the SMEs, the Health practitioners and the Pharmaceutical industry).

The participating SMEs intend to commercially exploit the e-learning modules, not only in their respective countries, but also to establish cooperation agreements in other Mediterranean countries, which have similar business interest and needs.

The SME's also intend to establish cooperation agreements with the RTD partners that have cooperated in the development of the project, for future updates of the e-learning modules, for training support and other initiatives in the field of on-line medical education.