The Italian National System of Pharmacovigilance

Management of Pharmacovigilance at AIFA and local level

Pietro Erba

20th November 2015

Agenzia Italiana del Farmaco
AIFA

Public Declaration of transparency/interests*

The view and opinions expressed are those of the individual presenter and should not be attributed to AIFA

Interests in pharmaceutical industry	NO	Current	From 0 to 3 previous years	Over 3 preavious years
DIRECT INTERESTS:				
1.1 Employment with a company: pharmaceutical company in an executive role	X	☐	☐	☐ mandatory
1.2 Employment with a company: in a lead role in the development of a medicinal product	X	☐	☐	☐ mandatory
1.3 Employment with a company: other activities	☐	☐	☐	X optional
2. Consultancy for a company	X	☐	☐	☐ optional
3. Strategic advisory role for a company	X	☐	☐	☐ optional
4. Financial interests	X	☐	☐	☐ optional
5. Ownership of a patent	X	☐	☐	☐ optional
INDIRECT INTERESTS:				
6. Principal investigator	X	☐	☐	☐ optional
7. Investigator	X	☐	☐	☐ optional
8. Grant or other funding	X	☐	☐	☐ optional
9. Family members interests	X	☐	☐	☐ optional

*Pietro Erba, in accordance with the Conflict of Interest Regulations approved by AIFA Board of Directors (25.03.2015) and published on the Official Journal of 15.05.2015 according to EMA policy /626261/2014 on the handling of the conflicts of interest for scientific committee members and experts.

N.B. I am not receiving any compensation

Overview

1. The National Pharmacovigilance System
2. Regional pharmacovigilance funds
3. Italian ADR reporting figures

Directive 2010/84/EU Article 101

DIRECTIVE 2010/84/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 15 December 2010

amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use

(Text with EEA relevance)

1. Member States shall operate a pharmacovigilance system for the fulfilment of their pharmacovigilance tasks and their participation in Union pharmacovigilance activities.

(...)

3. Each Member State shall designate a competent authority for the performance of pharmacovigilance tasks.

Decree 30 April 2015
(Art. 14)

The national pharmacovigilance system

- is headed by AIFA

AIFA – The Italian Medicines Agency

Instituted by Law n. 326/2003

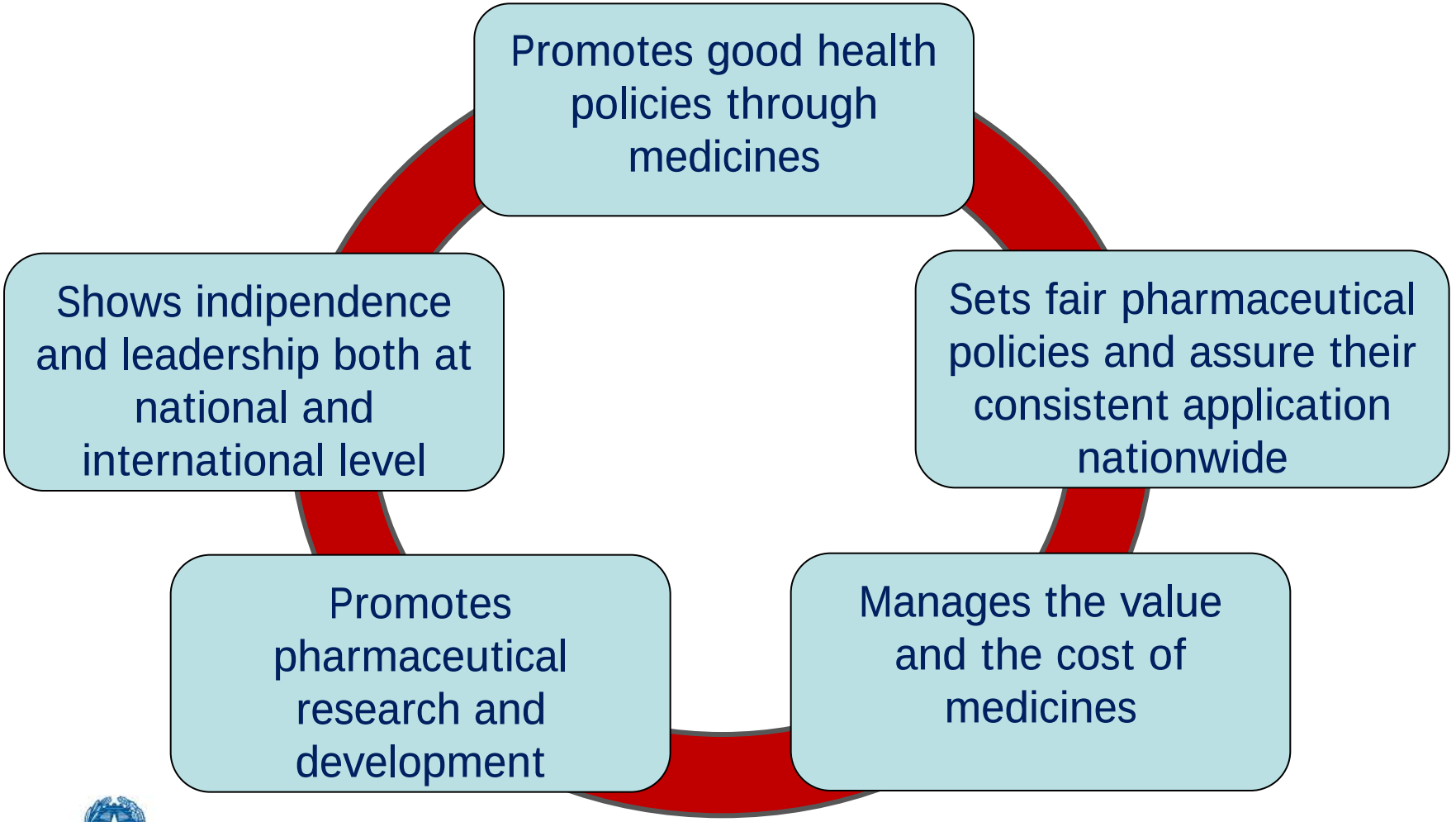
It is a public body operating autonomously, transparently and according to cost-effectiveness criteria;

operates under the direction of the Ministry of Health and under the vigilance of the Ministry of Health and the Ministry of Economy.

AIFA – The mission

- Promote good health through medicines;
- Set fair pharmaceutical policies and assure their consistent application nationwide;
- Manage the value and cost of medicines;
- Promote pharmaceutical research and development;
- Demonstrate independence and leadership both at home and internationally.

The Mission – AIFA



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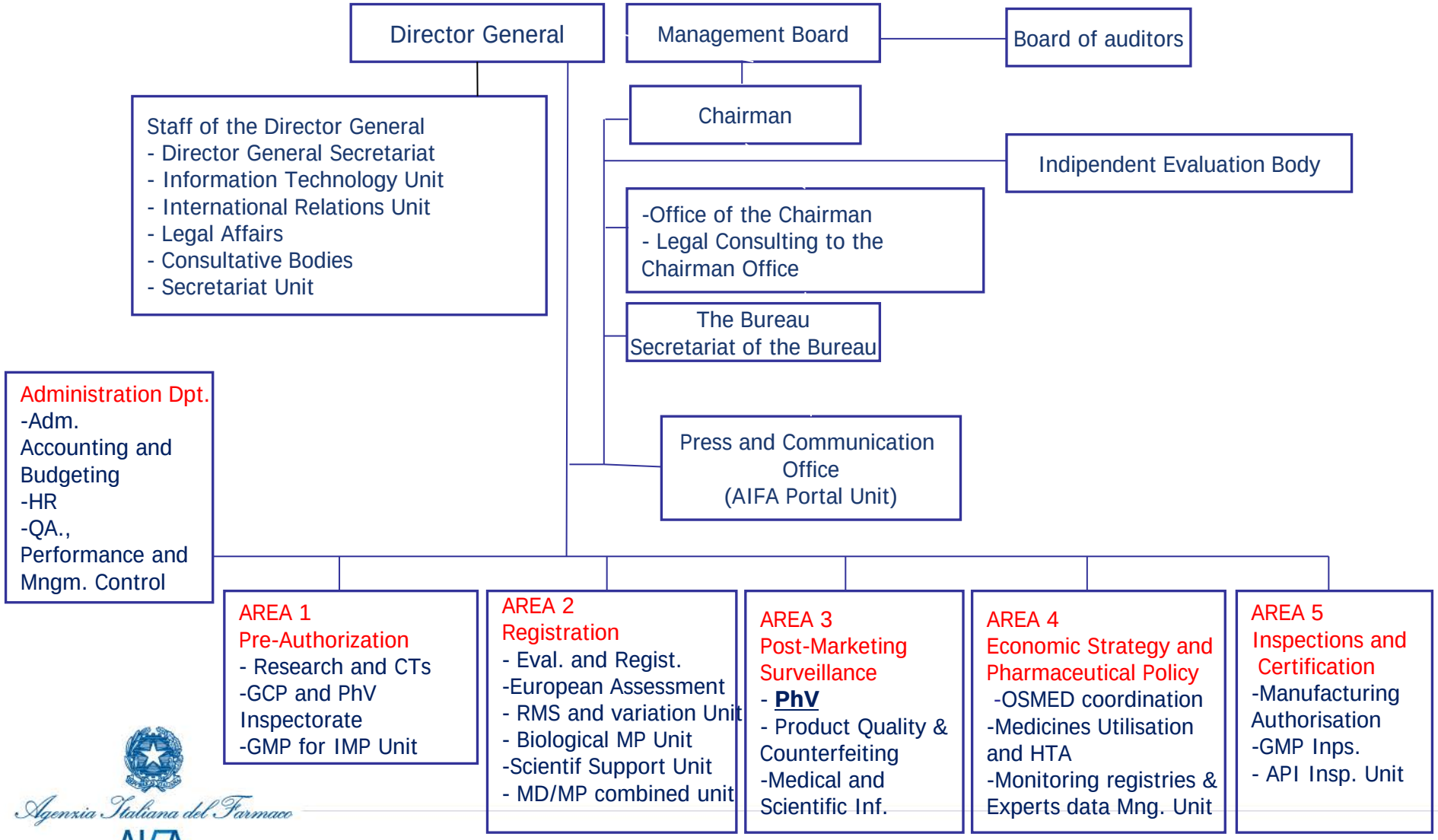
AIFA – Organizational chart 1/2



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AIFA – Organizational chart 2/2

AREA 1
Pre-Authorization
-Research and CTs
-GCP and PhV Inspection
-GMP for IMP Unit

AREA 2
Registration

AREA 3
Post-Marketing Surveillance
-Pharmacovigilance
-Product Quality and Counterfeiting
-Medical and Scientific Information

AREA 4
Economic Strategy and Pharmaceutical Policy

AREA 5
Inspections and Certification

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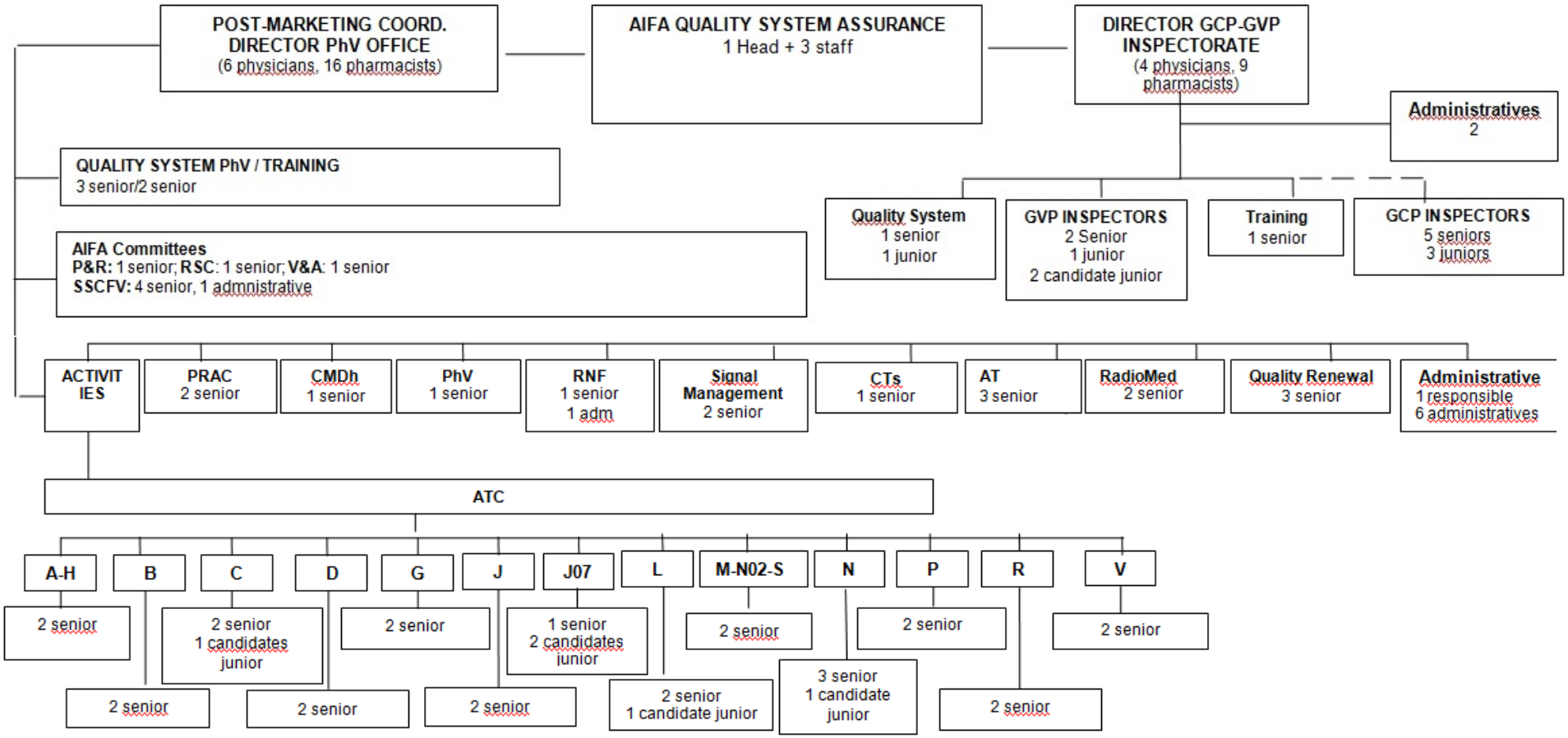
The organizational chart of the PhV Area



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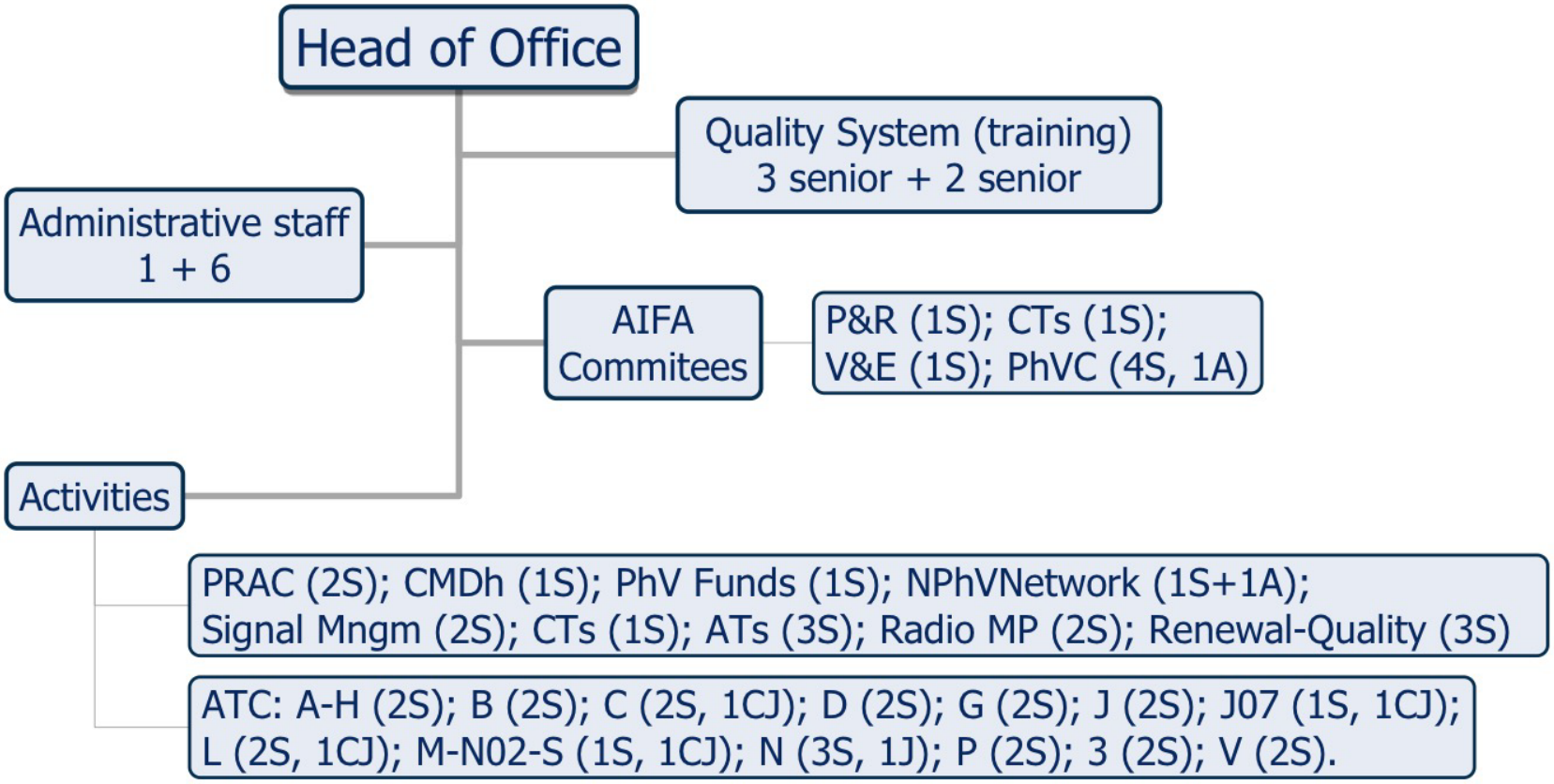
The organizational chart of the PhV Office



Directive 84/2010 Article 101

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(Text with EEA relevance)

1. Member States shall operate a pharmacovigilance system [...]

2. Member States shall, [...], evaluate all information scientifically, consider options for risk minimisation and prevention [...]

3. Each Member State shall designate a competent authority for the performance of pharmacovigilance tasks.

Decree 30 April 2015
(Art. 14)

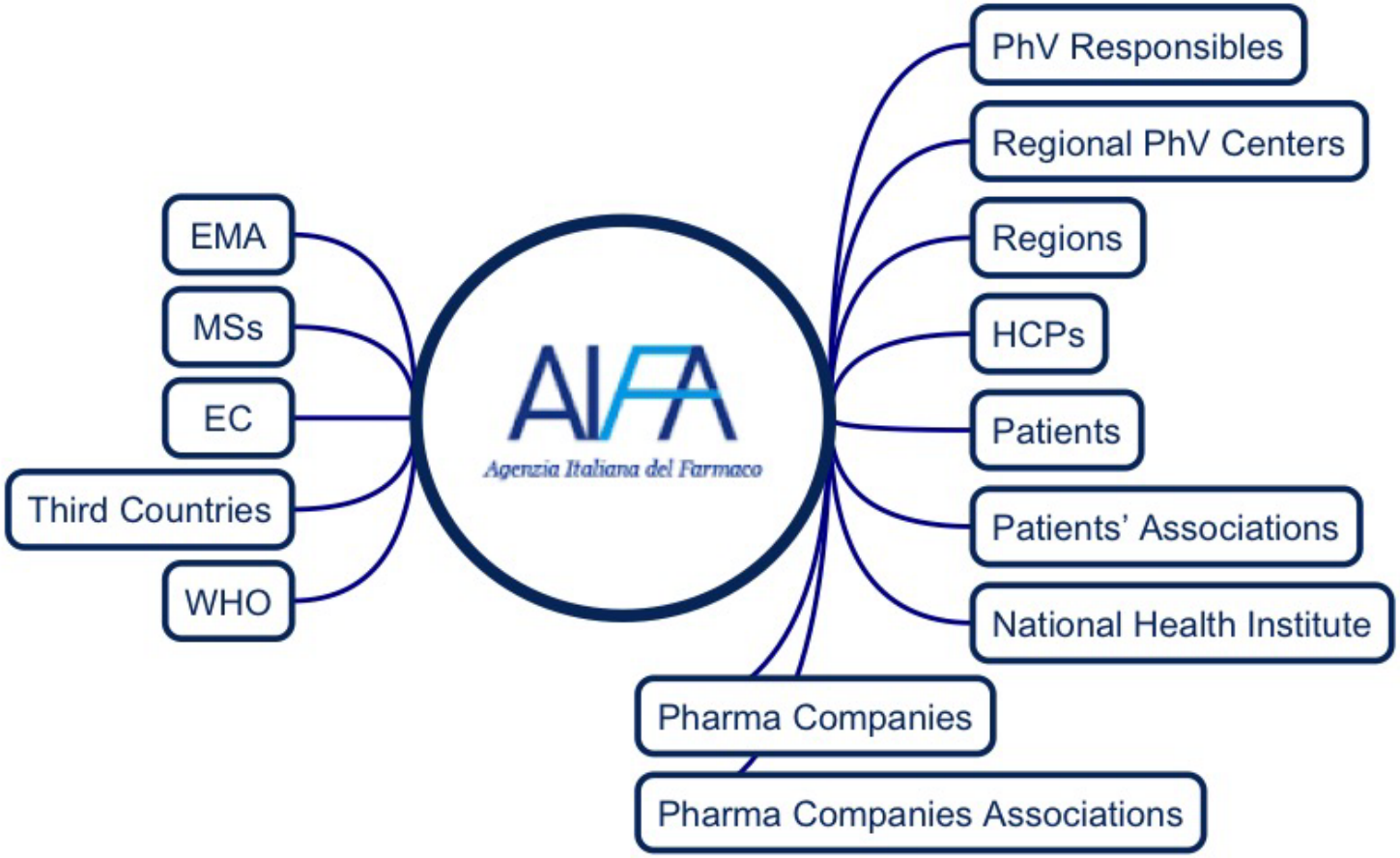
The national pharmacovigilance system

- is headed by AIFA;
- is used to collect information on the risks of medicinal products (ADRs).
- through the NPhV System, AIFA evaluates all information scientifically

and considers options to minimize and prevent risks.

How?

National Pharmacovigilance System



Decree 30 April 2015
(Art. 14)

AIFA's Pharmacovigilance tasks

- Evaluate all the in information in a scientific manner;
- Minimise and prevent the risks;
- Adopt regulatory actions towards MAH;
- Audit the PhV system and regularly report to the EC.

Decree 30 April 2015
(Art. 14)

Regions PhV task's

- Cooperation with AIFA;
- Evaluation and integration of data;
- Dissemination of information to HCPs;
- Regional PhV Centers.

Decree 30 April 2015
(Art. 22)

Obligations of structure and HCPs and subsequent steps due by AIFA

The local health authorities, the hospitals, universities and other similar health care facilities should appoint a person responsible for pharmacovigilance structure [...]

Decree 30 April 2015
(Art. 22)

Tasks of the PhV Responsibles

- Log in in the National PhV Network;
- Register paper reports;
- Validation of elecronic reports;
- Request follow up;
- Information;
- Training.

Decree 30 April 2015
(Art. 22)

Tasks of physicians and other HCPs

- Report asap (max 2 days) the ADRs;
- Follow up as requested.

Reporting flow

From paper reporting form to the network

ADR

As soon as possible

Reporter

- Observes the reaction
- Fills the form
- Provides follow-up
- Provides a clinic assessment in case of serious reaction

7 days

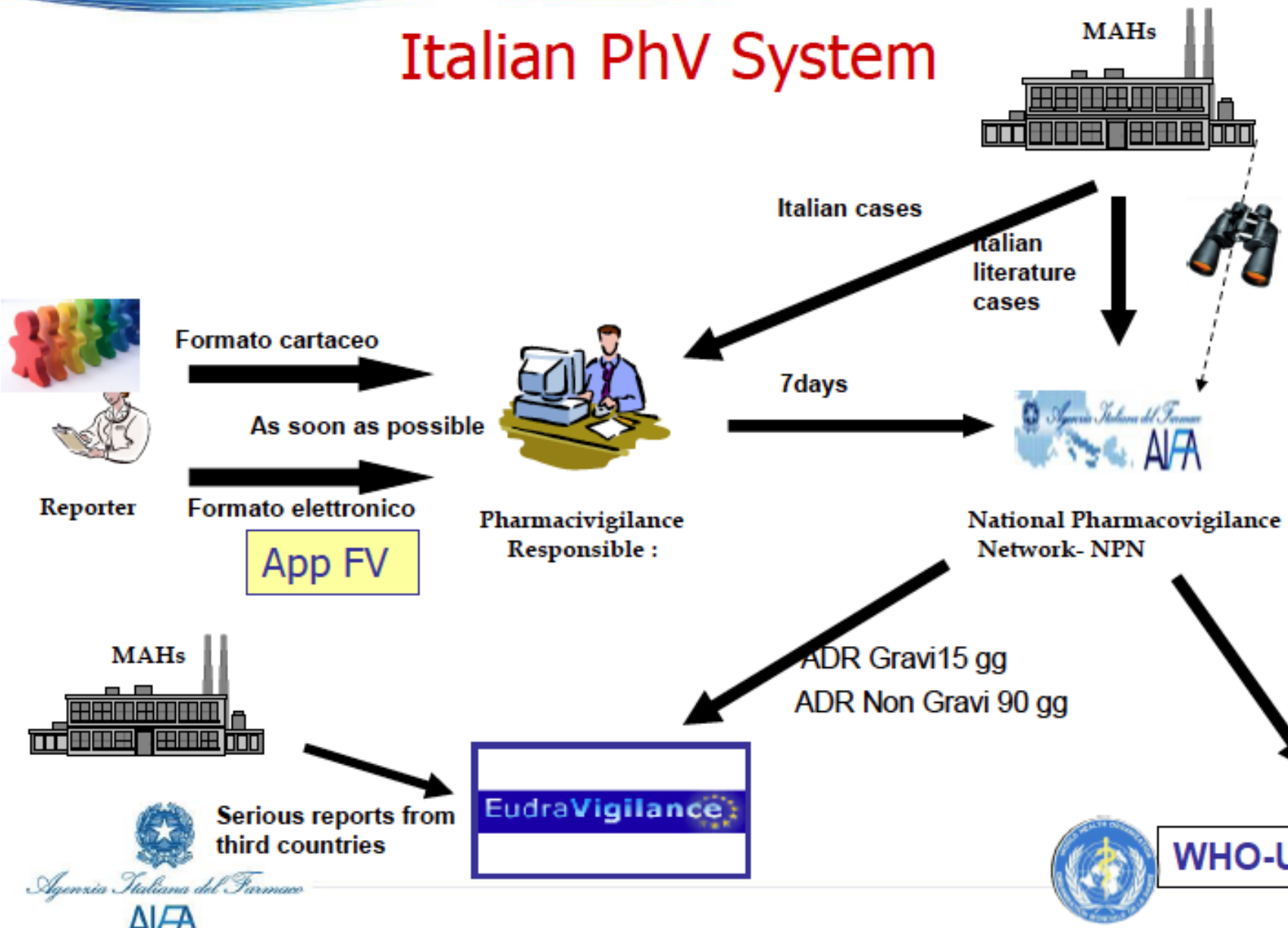
Pharmacovigilance Responsible :

- Checks completness of data
- Codifies and data entry
- Feed-back at reporter

National Pharmacovigilance Network- RNF

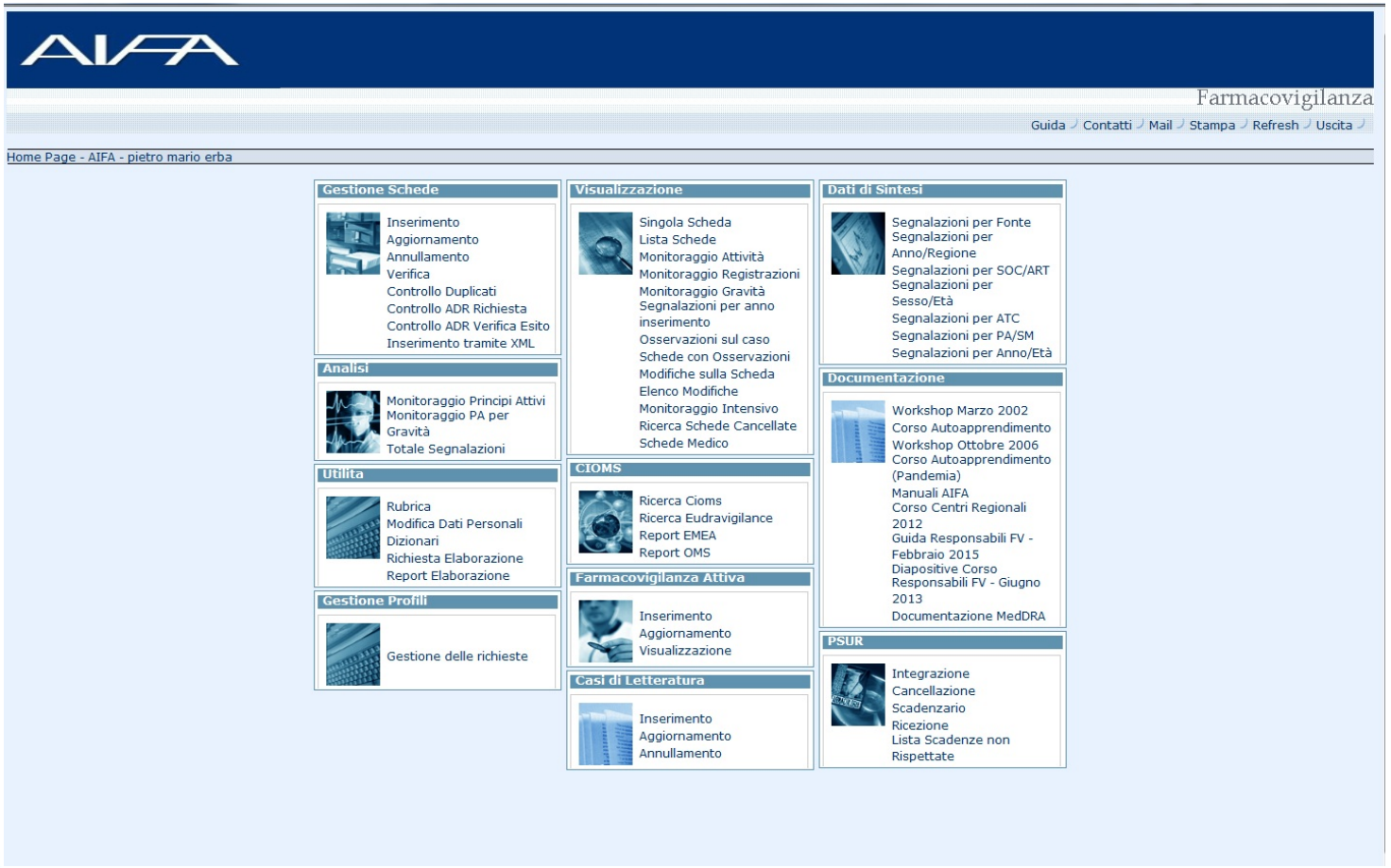
- Patient
- Adverse reaction
- Suspected drug
- Concomitant drug
- Clinical history.
- Other substance used
- Reporter
- Follow up

Italian PhV System



The Italian PhV database – login

The Italian PhV database – home page



Overview

1. The National Pharmacovigilance System

2. Regional pharmacovigilance funds

3. Italian ADR reporting figures

Directive 2010/84/EU Article 102

MSs take all appropriate measures:

- to encourage patients, doctors, pharmacists and other healthcare professionals;
- to report suspected adverse reactions to the national competent authority;
- for these tasks, organisations representing consumers, patients and healthcare professionals may be involved as appropriate.

Regional funds PhV: legal basis

Law n.449 del 27 Dec. 1997 (art.36, c.14)

- Annual allocation of funds to the regions and autonomous provinces for pharmacovigilance initiatives.

Law n.296 del 27 Dec. 2006 – Financial Law 2007- (art.1, c.819)

- Definition of Guidelines for the implementation of a program of active PhV, proposed by the Ministry of Health and ratified by a specific agreement between the Government, Regions and the Autonomous Provinces.
- Use of funds available after signing of appropriate agreements between AIFA and individual regions.

With financial Law 2007

- Activities or projects have been agreed with the regions to use funds for PhV;

- regional funds of PhV are bound to the execution of those activities or projects (signing agreements AIFA-regions).

Objectives of Active PhV programs

- improve knowledge on the benefit/risk profile of drugs after marketing;
- promote the safe and effective use of medicines;
- promote information (independent) and the awareness of HCPs (and patients)
- development and strengthening of regional centers of PhV

Background

- State-Regions Agreement of 18 October 2007: regional funds in 2007;
- State-Regions Agreement of 28 October 2010: regional funds 2008-2009;
- Funds transferred to the Regions 2007-2009: 70 MLN euro.

The agreements define

- Thematic areas
- Types of projects funded
- Procedures for submitting projects
- Mode of distribution and allotment of funds
- Monitoring of financed projects

Evaluation and approval of projects by AIFA

Based on:

- Compliance to the guidelines;
- Scientific relevance;
- Strengh of the methodology;
- feasibility in the regional context;

At the conclusion of the evaluation procedure AIFA announced the final outcome to the Regions and start the administrative procedure for the signing of the Conventions and the supply of funds.

Monitoring of the projects
(Art. 5)

"The regions that receive funding commit to provide AIFA with:

- A biannual report on the progress of each individual project;
- A final report on completion of the projects;
- Availability to attend meetings or conferences organized by AIFA specific.
- In specific cases, AIFA carries out site visits at the regional centers, departments, etc. ”

Monitoring of the projects funded in 2007
(Art. 5 Agreement)

1st phase Feb. 2010: audit on progress

2nd phase Oct. 2013: survey results (scientific articles, abstracts, ...).

95 projects funded:

- 44 projects (45.4% annual)
- 53 multi-year projects (37.1% biannual; 17.5% three-year)

Planned publication on AIFA website.

Agreement State-Regions Oct. 2010
features

- Study of adverse drug reactions (ADR)
- Evaluation of the use of drugs
- Information and training Strengthening of pharmacovigilance Ethics Committees (EC) in clinical trials
- Establishment and maintenance of regional centers of pharmacovigilance (CRFV)

Agreement State-Region Oct. 2010

Provisions

Specific areas of interest:

- Study of ADRs either on the base of analyses of spontaneous reports or conduction of epidemiological studies;
- Evaluation of drug use and promotion of drug appropriateness;
- Drug information and training directed to HCPs to foster spontaneous reporting;
- Strengthening the PhV activities of ethical committees in the context of clinical trials;
- Set up and/or maintenance of Regional Centres.

Type of projects

- "Regional" projects
- "Multiregional" projects with Region leader (Regions with more than 3 million residents have participated in at least two multi-regional projects)

At least one project/activity per Region should referr to specific categories of patients:

- pediatric population
- Elderly population with multiple diseases
- Hospitalised (long-term) patients

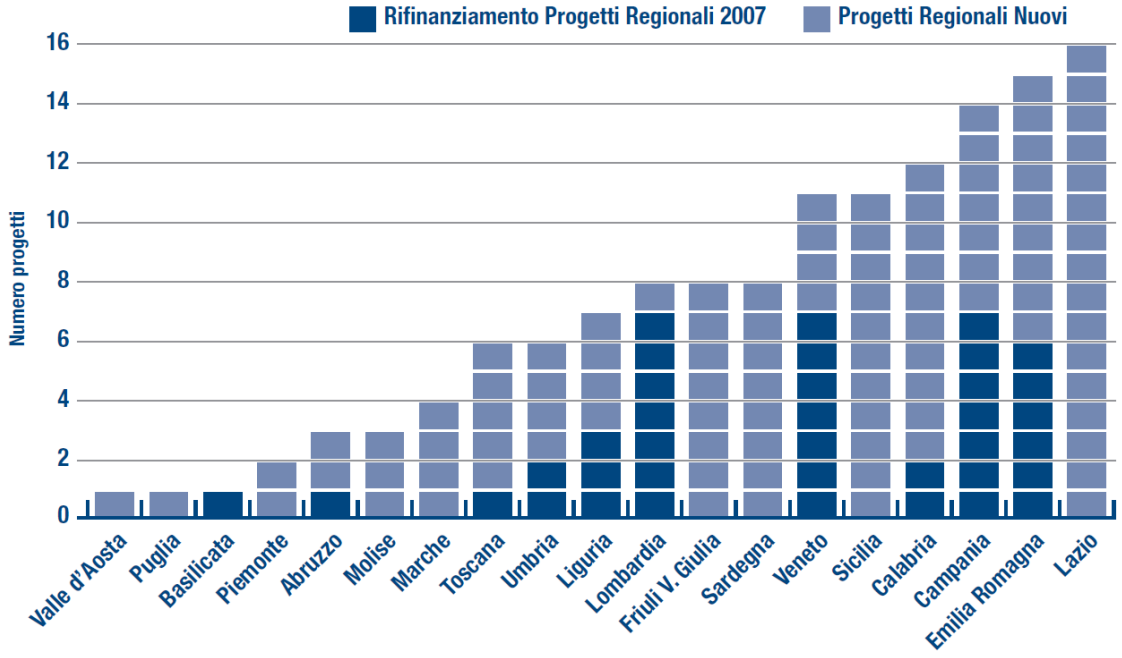
Agreement State-Region (28th Oct. 2010) Regional funds 2008-2009

Report on the program of active PhV funded through Regional funds available for the years 2008 and 2009.

Authors: Trotta F, Alessandro A, Tartaglia L.

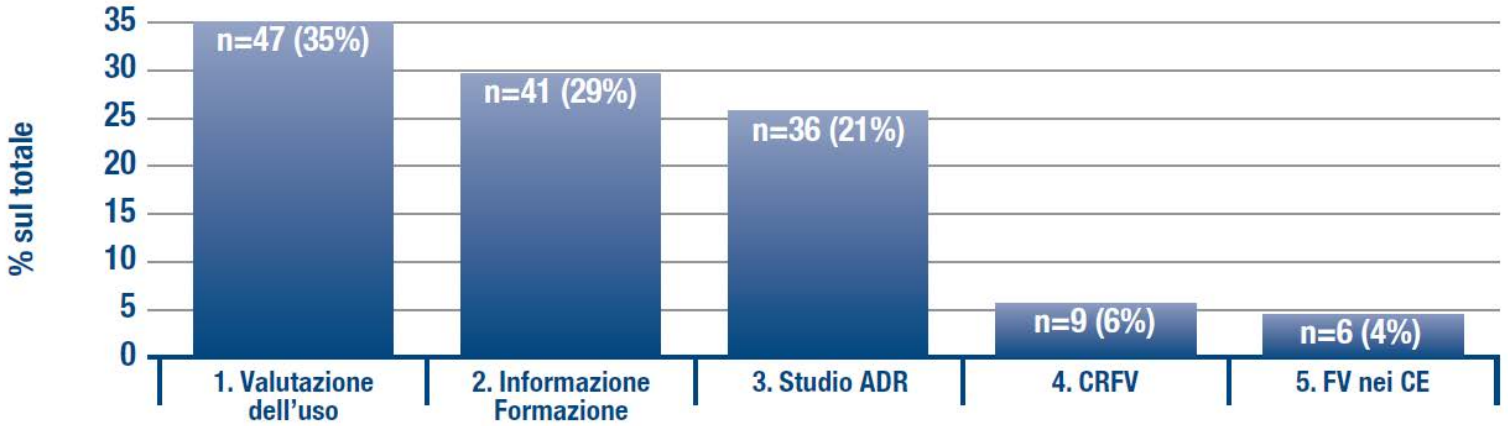
Rome, Italian Medicines Agency; 2013.

Regional distributon of the 139 projects financied through the funds 2008 e 2009*



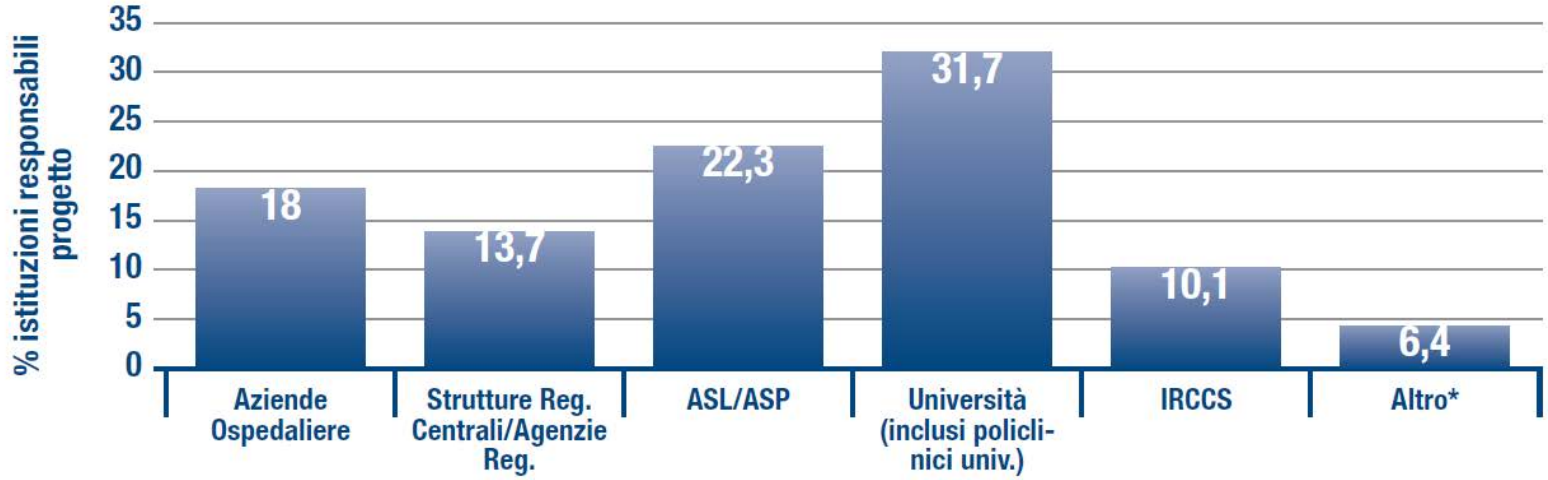
*Le Province autonome di Trento e Bolzano non avanzano richiesta di fondi a seguito della revisione dell'ordinamento finanziario delle Province autonome e dei rapporti finanziari con lo Stato ai sensi dei commi 106-126 dell'art. 2 della Legge n. 191 del 23 dicembre 2009 (finanziaria 2010).

Distribution of Regional projects for specific area (n=139)



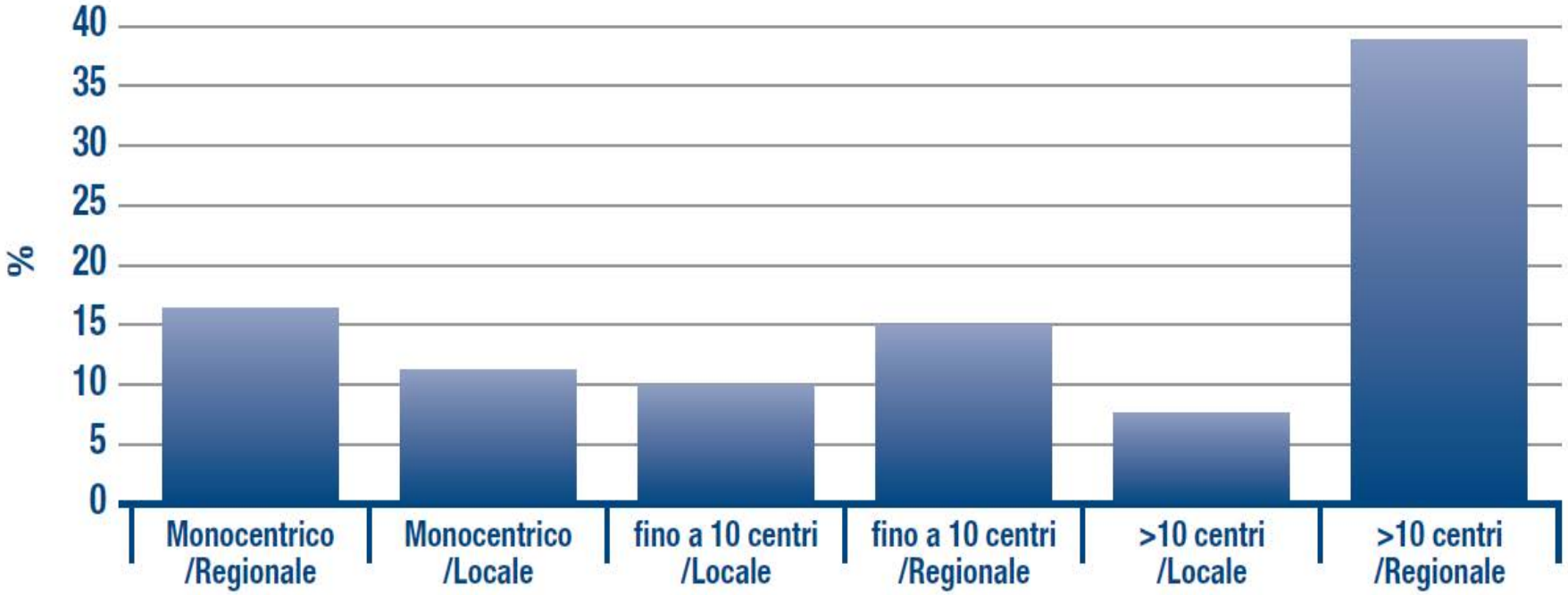
Distribution (%) of the institutions where the scientific leader operates

based on 139 projects

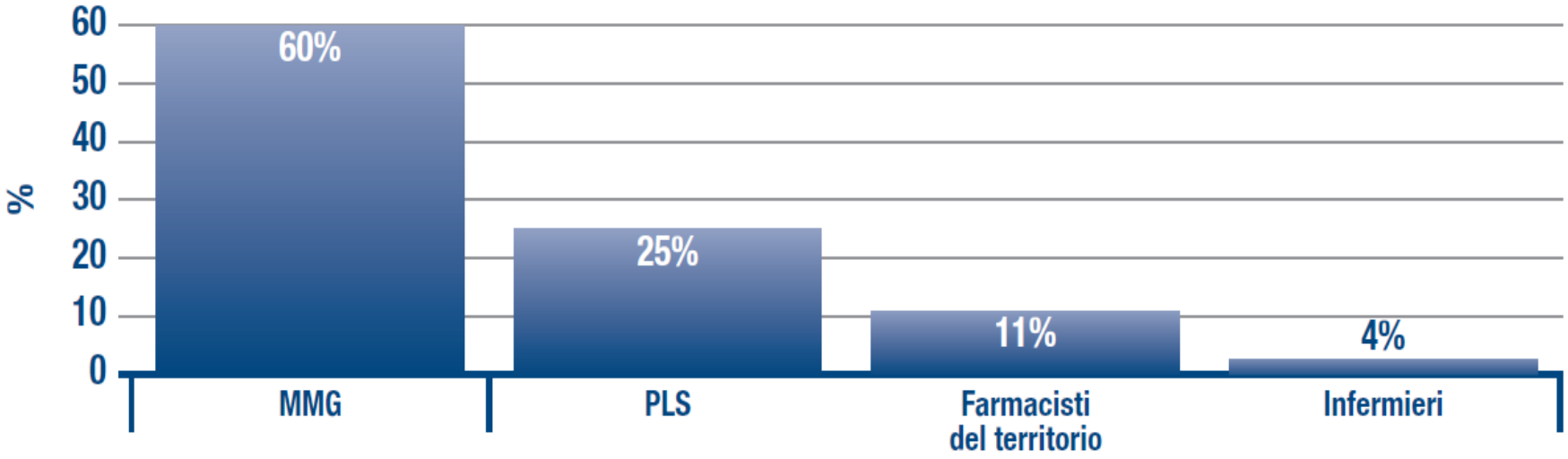


*Istituto Superiore di Sanità - ISS (n=2), Società scientifiche (n=2); Associazioni no profit (n=1); Associazioni di categoria (n=1).

Distribution (%) of 139 projects per number of centres on territory diffusion



Distribution (%) of HCPs in the Regional projects (n=36)



Regional projects for specialistic area

Progetti regionali per area specialistica (n=139)

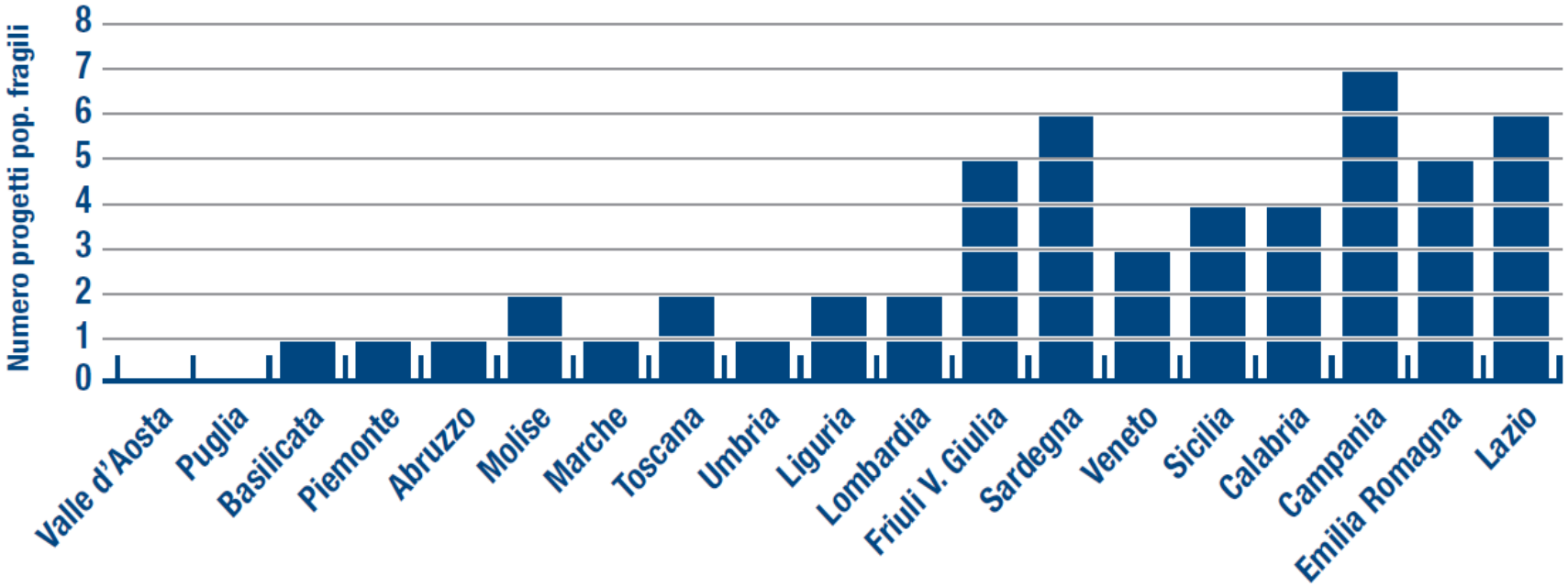
	Numero	%
Area specialistica definita	**66**	**47,5**
Oncologia	20	18,0
Disturbi cardiovascolari/ Endocrinologia	15	10,8,
Uso antibiotici (incluso profilassi in chirurgia)	9	6,5
Immunologia/Reumatologia	7	5,0
Neurologia/Psichiatria	6	4,3
Nefrologia	2	1,4
Terapia del dolore	2	1,4
Malattie infettive	2	1,4
Malattie rare	2	1,4
Malattie respiratorie	1	0,7
Non definito/tutte le aree	**73**	**52,5**
Totale progetti	139	100,0

Regional projects for type of “fragile” population

Progetti per tipologia di popolazione fragile coinvolta (n=53)

	Numero	%
Progetti su anziani	**23**	**16,5**
progetti dedicati	15	10,8
progetti non dedicati	8	5,8
Progetti pediatrici	**18**	**12,9**
progetti dedicati	12	8,6
progetti non dedicati	6	4,3
Progetti su pazienti istituzionalizzati	**7**	**5,0**
Progetti su donne (gravidanza/età fertile)	**5**	**3,6**
Totale popolazioni fragili	53	38,1

Project distribution of the “fragile” population per Region (n=53)



Scheduled term of the Regional projects (n=139)

Day 0 is the attivation of the project, i.e. the transfer of funds from Regions to Regional centres.

Eight multi-regional projects financed with 10% of 2008-2009 budget

Regione	Pop. residente ≥ 3 mln.	Titolo Progetto Multiregionale 1	2	3	4	5	6	7	8	Totale adesioni per regione
Piemonte	Si	•	•	—	—	—	—	—	—	2
Valle d'Aosta	No	—	—	—	—	—	—	—	—	—
Lombardia	Si	—	C	C	C	—	—	—	—	—
Veneto	Si	•	—	—	—	—	C	C	C	1
Friuli V. Giulia	No	—	—	—	—	—	—	—	•	1
Liguria	No	C	—	—	—	—	•	•	—	2
Emilia Romagna	Si	—	•	—	—	•	•	—	—	3
Toscana	Si	•	•	•	•	•	•	—	—	6
Umbria	No	•	—	—	—	—	—	—	—	1
Marche	No	—	•	—	—	—	—	—	—	1
Lazio	Si	•	•	—	—	—	—	—	•	3
Abruzzo	No	—	•	—	—	—	—	—	—	1
Molise	No	—	—	—	—	—	•	—	—	1
Campania	Si	—	•	•	•	—	—	—	•	4
Puglia	Si	—	—	•	•	—	—	—	•	3
Basilicata	No	—	—	—	—	—	—	—	•	1
Calabria	No	—	—	—	—	—	•	•	•	3
Sicilia	Si	—	—	—	—	C	•	—	—	1
Sardegna	No	—	—	—	—	—	—	•	—	1
Totale Regioni partecipanti ai progetti (incluse le Regioni capofila)		6	8	4	4	3	7	4	7	35

LEGENDA

1: Sorveglianza della sicurezza di farmaci e vaccini e valutazione dell'efficacia della vaccinazione antinfluenzale in pediatria;
2: MEREAFAPS: Monitoraggio Epidemiologico di Reazioni ed Eventi Avversi da Farmaci in Pronto Soccorso;
3: MEAP: Monitoraggio degli eventi avversi in pediatria;
4: FARVICAV: Farmaco e tossico vigilanza degli eventi avversi ("errori terapeutici"ET) ed delle reazioni avverse (ADR) che si verificano sul territorio nazionale desunti dalla casistica dei Centri Antiveleni;
5: Vigilanza sulle reazioni avverse derivanti dall'uso di fitoterapici e integratori alimentari durante la gravidanza;
6: Sorveglianza sulle reazioni avverse da vaccino;
7: Sorveglianza delle reazioni avverse da prodotti biologici e biosimilari;
8: Il farmacista nella segnalazione delle reazioni avverse da farmaci da parte del cittadino.

Multi-regional projects funds 2008/09 – 1/8

(total budget: 7,4 milioni di euro)

FARVICAV_ET: Drug and e toxic vigilance of AEs ("Therapeutic Errors", TE) and ARs which occurs on the national territory as reported by the poison control centers (CAV) (active surveillance).

- Activation of a data stream on ET, maintanance of the database; data analysis and annual reports;
- Follow up cases by CAV;
- Structures: CAV and National Health Institute.

Multi-regional projects funds 2008/09 – 2/8

MEAP-Monitoraggio degli eventi avversi in pediatria (pediatric AE monitoring) (active surveillance):

- Role of monitors to promote sensibilization in pediatric specialist;
- Setting: pediatry.

Multi-regional projects funds 2008/09 – 3/8

Surveillance of biologic and biosimilar ADRs (prospectic cohort study):

- Objectives: estimated prevalence of serious ADR: comparison biosimilars/originator safety profiles;
- Setting: oncologic patients, emodialitic patients (erythropoietin).

Multi-regional projects funds 2008/09 – 4/8

MEREAFaPS- Monitoraggio Epidemiologico di Reazioni ed Eventi Avversi da Farmaci in Pronto Soccorso – Epidemoliogic Monitoring of AEs and ADRs in Emergency Depts. (active surveillance):

- Objectives: sensibilization of the HCPs through the presence of monitors; Analysis of emergency Dept. Admissions to detect the iatrogenic patology;
- Setting: Emergency Depts.

Multi-regional projects funds 2008/09 – 5/8

Vigilance on ADRs caused by the use of phytotherapics and food supplements (FS) during pregnancy (cohort study):

- Objectives: prevalence of ADR due to FS, phytotherapics and MPs in pregnancy; use in pregnancy and brestfeeding; analysis of the outcome of the deliveries;
- Setting: pregnants;
- Structures: ginecological regional centers, National Health Institute.

Multi-regional projects funds 2008/09 – 6/8

Monitoring of the safety of MPs and vaccines and evaluation of the efficacy of influenza vaccination in children (active surveillance ADRs in Emergency Depts. with case-control analysis):

- Objectives: risk of hospitalization associated with taking drugs and vaccines; efficacy of vaccines in preventing hospitalization from influenza;
- Setting: pediatric patients admitted to Emergency Depts.

Multi-regional projects funds 2008/09 – 7/8

Surveillance of adverse reactions on the vaccines (intervention training; active surveillance):

- Objectives: promote integration between PhV and prevention services; test the model “Green Channel” in other situations
- Setting: Pediatrics

Multi-regional projects funds 2008/09 – 8/8

The role of pharmacist in the reporting of adverse drug reactions by citizens (active surveillance):

- Objective: raise awareness in pharmacists in the collection of ADR reports from citizens
- Setting: pharmacies open to the public, the citizens.

Main results of the first years of the implementation of the Law - 1/2

Not only increases in spontaneous reports

- Greater completeness and reliability of the data
- Strengthening of Regional centers and signal mngm

(10 new RPhVC)

- Training to physicians and pharmacists
- More attention to safety issues and appropriate use of medications

Main results of the first years of the implementation of the Law – 2/2

- Increased interaction between Regions;
- Better skills and launch ad hoc studies;
- Use of regional funds tied to the execution of activities or projects;
- Public use of the allocation of funds.

Weakness of the program

- Regional heterogeneity in the management of funds (both during the procedure and during activity on the territory);
- delays in the transfer of funds from Regions to the territory;
- To implement guidelines to establish the necessary State-Regions Agreement;
- insufficient connection AIFA - Regions;
- inadequate coordination between the regions
- sometimes many ADR reports are “solicited” by the projects of PhV active.

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PLOS | ONE

Informing Women on Menopause and Hormone Therapy: *Know the Menopause* a Multidisciplinary Project Involving Local Healthcare System

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Abstract

Background: Hormone therapy (HT) in the menopause is still a tricky question among healthcare providers, women and mass media. *Informing women about hormone replacement therapy* was a Consensus Conference (CC) organized in 2008: the project *Know the Menopause* has been launched to shift out the results to women and healthcare providers and to assess the impact of the cc's statement.

Methods: **And Findings**: The project, aimed at women aged 45-60 years, was developed in four Italian Regions: Lombardy, Tuscany, Lazio, Sicily, each with one Local Health Unit (LHU) as "intervention" and one as "control". Activities performed were: survey on the press; training courses for health professionals; educational materials for target populations; survey aimed at women, general practitioners (GPs), and gynaecologists; data analysis on HT drugs' prescription. Local activities were: training courses; public meetings; dissemination on mass media. About 3,700 health professionals were contacted and 1,800 participated in the project. About 146,500 printed leaflets on menopause were distributed to facilitate the dialogue among women and health care professionals. Training courses and educational cascade-process activities: participation ranged 25- 72% of GPs, 17-71% of gynaecologists, 14-78% of pharmacists, 34-85% of midwives. Survey: 1,281 women interviewed. More than 90% believed menopause was a normal phase in life. More than half did not receive information about menopause and therapies. HT prescription analysis: prevalence fell from 6% to 4% in five years. No differences in time trends before-after the intervention. Major limitations are: organizational difficulties met by LHU, too short time for some local activities.

Conclusions: A huge amount of information was spread through health professionals and women. The issue of menopause was also used to discuss women's wellbeing. This project offered an opportunity to launch a multidisciplinary, multimodal approach to menopause looking not only at pharmacological aspects, but also at quality of life and information.

Citation: Donati S, Satolli R, Colombo C, Senatore S, Cotichini R, et al. (2013) Informing Women on Menopause and Hormone Therapy: *Know the Menopause* a Multidisciplinary Project Involving Local Healthcare System. PLoS ONE 8(12): e85121. doi:10.1371/journal.pone.0085121

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Competing interests: Co-author Roberto Satolli is a partner of Agenzia Editoria Scientifica Zadig, Milano. There are no patents, products in development or marketed products to declare. This does not alter the authors' adherence to all the PLOS ONE policies on sharing data and materials.

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Project Viger

PERSPECTIVE

LESS IS MORE

Allopurinol Overuse in Asymptomatic Hyperuricemia

A Teachable Moment

Carla Carnovale, PharmD; Mauro Venegoni, MD; Emilio Clementi, MD, PhD *JAMA Intern Med.* 2014;

Table. Adverse Reactions to Allopurinol Treatment in Patients With Asymptomatic Hyperuricemia

Sex/ Patient Age, y	Indication/ Allopurinol Dose	Adverse Drug Reaction	Reason Why Treatment With Allopurinol Was Unnecessary[1-3]: Uric Acid Level, mg/dL	Dechallenge/ Rechallenge
Female/78	Asymptomatic hyperuricemia/300 mg	Stevens-Johnson syndrome	9.7	Positive dechallenge
Male/65	Asymptomatic hyperuricemia/300 mg	Severe skin reaction	11.6	Positive dechallenge
Female/84	Asymptomatic hyperuricemia/300 mg	Severe skin reaction	8.9	Positive dechallenge and rechallenge
Male/73	Asymptomatic hyperuricemia/300 mg	Severe skin reaction, facial edema	8.8	Positive dechallenge
Female/81	Asymptomatic hyperuricemia/150 mg	Severe skin reaction	6.6	Died
Male/89	Asymptomatic hyperuricemia/300 mg	Severe skin reaction	5.8	Positive dechallenge
Male/71	Asymptomatic hyperuricemia/150 mg	Skin reaction, orthopnea, dizziness	6.7	Positive dechallenge

SI conversion factor: To convert uric acid to micromoles per liter, multiply by 59.485.

Quantification efficacy/risks fragile population study

Influenza Vaccine Effectiveness Against Severe Cases in Children: Results from Two Influenza Seasons

R. Da Cas[1], G. Traversa[1], C. Santuccio[2], F. Trotta[2], F. Menniti-Ippolito[1], and the Italian Multicentre Study Group of Drug and Vaccine Safety in Children

(1) National Institute of Health, Rome, Italy, (2) Italian Medicines Agency, Rome, Italy

- Objective: To estimate efficacy of influenza vaccines in children admitted to Emergency Dept.
- Methods: 11 centers, children in the emergency room with a diagnosis of ILI, following confirmation of the virus in lab, then questionnaire to verify exposure to the vaccine. Analysis with case-control model (case: ILI +; control ili-)
- Results: OR of developing influenza = 0.70 (95% CI 0.2-1.7)

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Agenzia Italiana del Farmaco
AIFA

DIEP Lazio
Dipartimento di Epidemiologia del Servizio Sanitario Regionale Regione Lazio

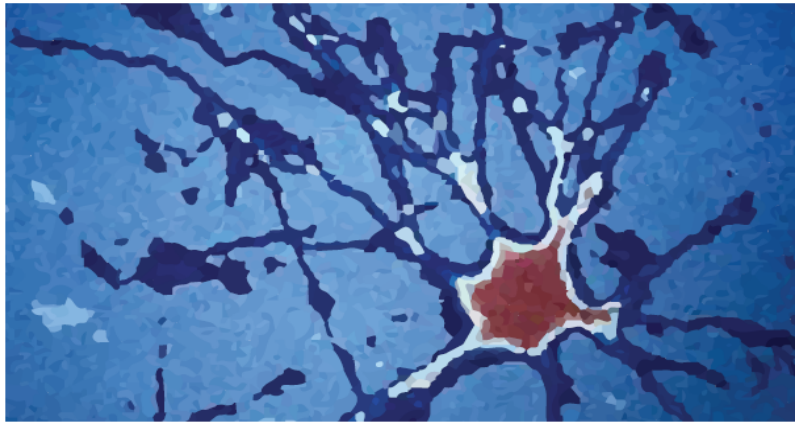
SISTEMA SANITARIO REGIONALE
ASL ROMA E

REGIONE LAZIO

Epidemiologia della Sclerosi Multipla nel Lazio

Uso integrato dei dati clinici e dei dati dei Sistemi Informativi Sanitari

Progetto di Farmacovigilanza Regione Lazio - Bando 2011



Roma, 11 Giugno 2015 ore 14.30

Complesso Monumentale S. Spirito in Sassia
Sala Teatro - Borgo S. Spirito, 3 Roma

Project MEREAFAPPS

ClinicoEconomics and Outcomes Research

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ORIGINAL RESEARCH

Seriousness, preventability, and burden impact of reported adverse drug reactions in Lombardy emergency departments: a retrospective 2-year characterization

This article was published in the following Dove Press journal:
ClinicoEconomics and Outcomes Research
3 December 2014
Number of times this article has been viewed

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Objective: The purpose of this study was to determine the prevalence of adverse drug reactions (ADRs) reported in emergency departments (EDs) and carry out a thorough characterization of these to assess preventability, seriousness that required hospitalization, subsequent 30-day mortality, and economic burden.

Methods: This was a retrospective cohort study of data from an active pharmacovigilance project at 32 EDs in the Lombardy region collected between January 1, 2010 and December 31, 2011. Demographic, clinical, and pharmacological data on patients admitted to EDs were collected by trained and qualified monitors, and deterministic record linkage was performed to estimate hospitalizations. Pharmacoeconomic analyses were based on Diagnosis-Related Group reimbursement.

Results: 8,862 ADRs collected with an overall prevalence rate of 3.5 per 1,000 visits. Of all ADRs, 42% were probably/definitely preventable and 46.4% were serious, 15% required hospitalization, and 1.5% resulted in death. The System Organ Classes most frequently associated with ADRs were: skin and subcutaneous tissue, gastrointestinal, respiratory thoracic and mediastinal, and nervous system disorders. The most common Anatomical Therapeutic Chemical classes involved in admissions were J (anti-infectives and immunomodulating agents), B (blood and blood-forming organs), and N (nervous system). Older age, yellow and red triage, higher number of concomitantly taken drugs, and previous attendance in ED for the same ADR were significantly associated with an increased risk of hospitalization. The total cost associated with ADR management was €5,184,270, with a mean cost per patient of €585. Fifty-eight percent of the economic burden was defined as probably/definitely preventable.

Conclusion: ADRs are a serious health/economic issue in EDs. This assessment provides a thorough estimation of their seriousness, preventability, and burden impact in a large population from a representative European region.

Anti HPV registry

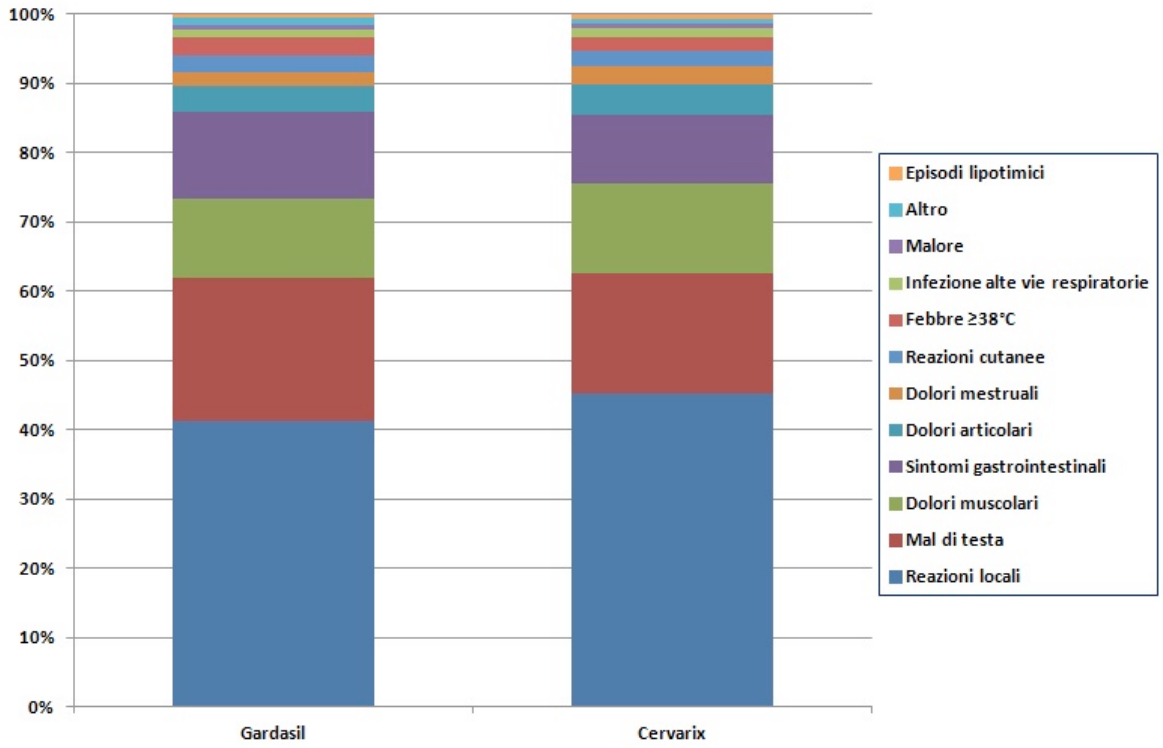
agreement 18 Oct. 2007

- Multi-regional coordinated by NHI
- Active surveillance (9-26 ys) who have received the anti-HPV vaccine (Gardasil quadrivalent HPV 16&18-6&11 and Cervarix bivalent HPV 16&18) in 35 LHU o Vaccine District iin 9 Regions.

  – Methods: AEs occurred in the 15 days after vaccination are collected in a special diary. Web platform launched in Apr 2010. Data collected retrospectively and prospectively. ADR reporting in the National PhV Web.

  – Results: from Aug. 2008 to Sept 2011enrolled 12.066 female (9084 used Cervarix, 2982 Gardasil), for a total of 29.494 administered doses. Thel 53% of the girls has concluded the cicly (74% Gardasil and 4% Cervarix).

Event distribution at first dose per vaccine



61% of girls reported at least one event after the first dose. The> of the events was of mild or moderate clinical relevance.
The typology is similar for the two vaccines.
Higher prevalence of local symptoms: headaches, muscle pain, gastrointestinal symptoms and joint pain. 96 girls have reported serious events.

Active PhV program to use funds 2010-11

Presidenza del Consiglio dei Ministri

CONFERENZA PERMANENTE PER I RAPPORTI
TRA LO STATO, LE REGIONI E LE PROVINCE AUTONOME
DI TRENTO E BOLZANO

Accordo, ai sensi dell'articolo 4 del decreto legislativo 28 agosto 1997, n. 281, tra il Governo, le Regioni e le Province autonome di Trento e di Bolzano sulla proposta del Ministro della salute concernente la definizione degli indirizzi per la realizzazione di un programma di farmacovigilanza attiva, attraverso la stipula di convenzioni tra l'AIFA e le singole regioni per l'utilizzazione delle risorse di cui all'articolo 36, comma 14, della legge 27 dicembre 1997, n. 449, per gli anni 2010-2011.

Rep. Atti n. 138/CSR del 26 settembre 2013

LA CONFERENZA PERMANENTE PER I RAPPORTI TRA LO STATO, LE REGIONI E LE PROVINCE AUTONOME DI TRENTO E BOLZANO

State-Regions agreement 26 Sept 2013

Art. 4

(Modality to distribure regional funds in PhV)

50.000 euro/year: continuity regional activity;

- 40%: establishing/maintenance dei Regional PhV centers, i.e. the strenghtening of the PhV activity on the territory through defined structures;
- 30%: multi-regional projects;
- 30%: regional projects;

- 5% of the funds remains in AIFA for coordination and safety emergencies.

Aims of the program for Active PhV for the use od funds 2010-11

- ADR study (ADR caused by vaccins, phytoterapics, food supplement)
- Evaluation of the use of drugs (promote the appropriate use)
- Information and training (promote the appropriate use and evaluation of efficacy of the training)
- Foster the activities of the Regional PhV Center and other Regional structures
- Foster Multi-Regional projects
- Increase the quality of the Regional projects

17 Multi-Regional projects will be

Progetti Multi regionali – Fondi 2010-2011	Piemonte	VdA	Lombardia	Veneto	FVG	Liguria	ER	Toscana	Umbria	Marche	Lazio	Abruzzo	Molise	Campania	Puglia	Basilicata	Calabria	Sicilia	Sardegna
Programma di sorveglianza sulla sicurezza farmaci biologici nella pratica clinica quotidiana												C			X		X		X
Studio multiregionale di Farmacovigilanza attiva per valutazione di sicurezza ed appropriatezza prescrittiva ed aderenza alla Terapia di Farmaci biologici impiegati in Centri Regionali di						X						X				X	C	X	
Nuovi farmaci antivirali per Epatite cronica HCV RNA positiva in Friuli Venezia Giulia/Liguria: appropriatezza prescrittiva, impatto economico e clinico delle nuove terapie, farmacovigilanza eventi					X	C													
Valutazione comparativa di efficacia e sicurezza dei Nuovi Anticoagulanti Orali per la prevenzione dell'ictus in pazienti con fibrillazione atriale – sviluppo ed implementazione pilota di un'attività' di			X					X			C								
Sorveglianza della sicurezza di farmaci e vaccini nella popolazione pediatrica	X			X		C		X	X		X			X				X	
MEREAFAPS: monitoraggio della reazioni avverse e degli eventi avversi a farmaci in Pronto Soccorso	X		C				X	X						X					
FarViCAV- Regionale: Progetto di FarmacoVigilanza attiva basato sui dati rilevati dai CAV			C					X						X					
Monitoraggio degli Eventi Avversi nelle Popolazioni a rischio (MEAP)			C				X	X						X					
Stima del rischio di gravi eventi avversi dermatologici attribuibili a farmaco	X		C				X												

…with the PhV funds

Progetti Multi regionali – Fondi 2010-2011	Piemonte	VdA	Lombardia	Veneto	FVG	Liguria	ER	Toscana	Umbria	Marche	Lazio	Abruzzo	Molise	Campania	Puglia	Basilicata	Calabria	Sicilia	Sardegna
Studio REDS (Respiratory Drugs Survey). Sorveglianza attiva dei farmaci respiratori ed in particolare degli steroidi inalatori (CSI) in età pediatrica.							X		X				C						
Valutazione dell'utilizzo di farmaci biologici nel paziente oncologico								X		X	X	X						X	C
Monitoraggio a breve e lungo termine del profilo beneficio-rischio dell'uso intravitreale dei farmaci anti-VEGF tramite network di dati clinici ed			X													X	X	C	
Valutazione e riconoscimento delle reazioni avverse in pazienti affetti da Sclerosi Multipla trattati farmacologicamente						X								X				C	X
un portale web curato, data mining e analisi semantica di contenuti generati dagli utenti dei social media (Active pharmacovigilance surveillance trough a curated web portal, data mining and			X		X			C		X				X					
atriale e rischio di sanguinamenti: analisi periodica delle schede di dimissione ospedaliera e dei dati di consumo dei farmaci – lo studio TYRION. (Anticoagulant TherapY in patient with atrial								C		X	X			X					
Sorveglianza sulle reazioni avverse da vaccino				C			X			X								X	
Rete Regionale di Farmacie attive in Farmacovigilanza (Progetto VIGIRETE)				C	X	X				X	X			X	X	X			

Future goals

1) Promoting the merit:

-Relevant and innovative of the basic idea

-Appropriateness of the study design

-Adequacy of the organization

2) To promote a transparent, efficient and rigorous mechanism

3) To promote the lifelong quality of the projects:

Guidelines, feedback and support activities, infrastructure, critical mass

4) Stability, Continuity, Periodicity of funding

5) Avoid repetitive tasks, share projects ('networking')

6) Analysis of the data collected (go beyond the descriptive analysis)

7) Documenting activity (publication of all the results)

Agenzia Italiana del Farmaco
AIFA

http://www.agenziafarmaco.gov.it/it/content/fondi-regionali-di-farmacovigilanza-0

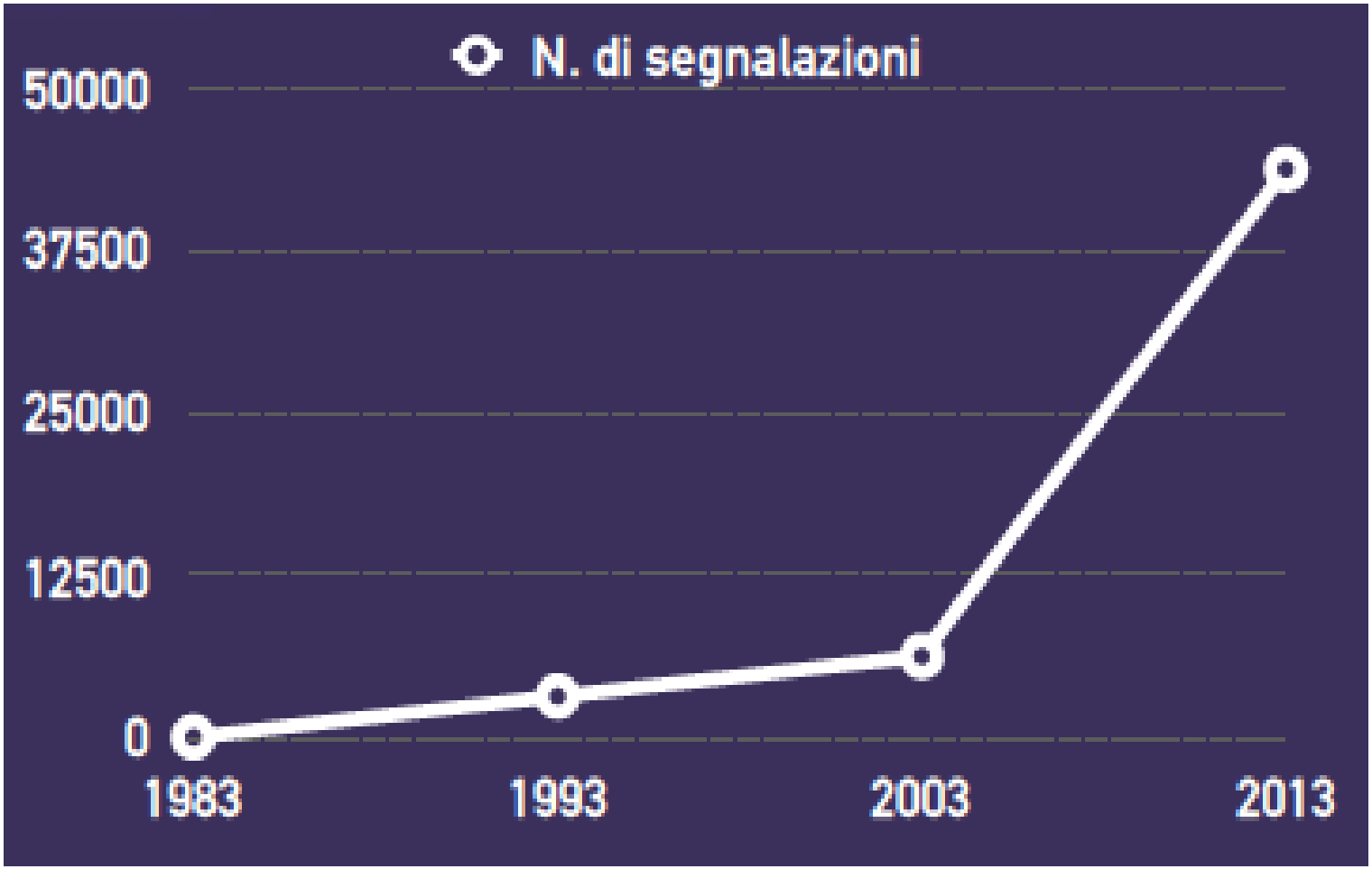
Overview

1. The National Pharmacovigilance System

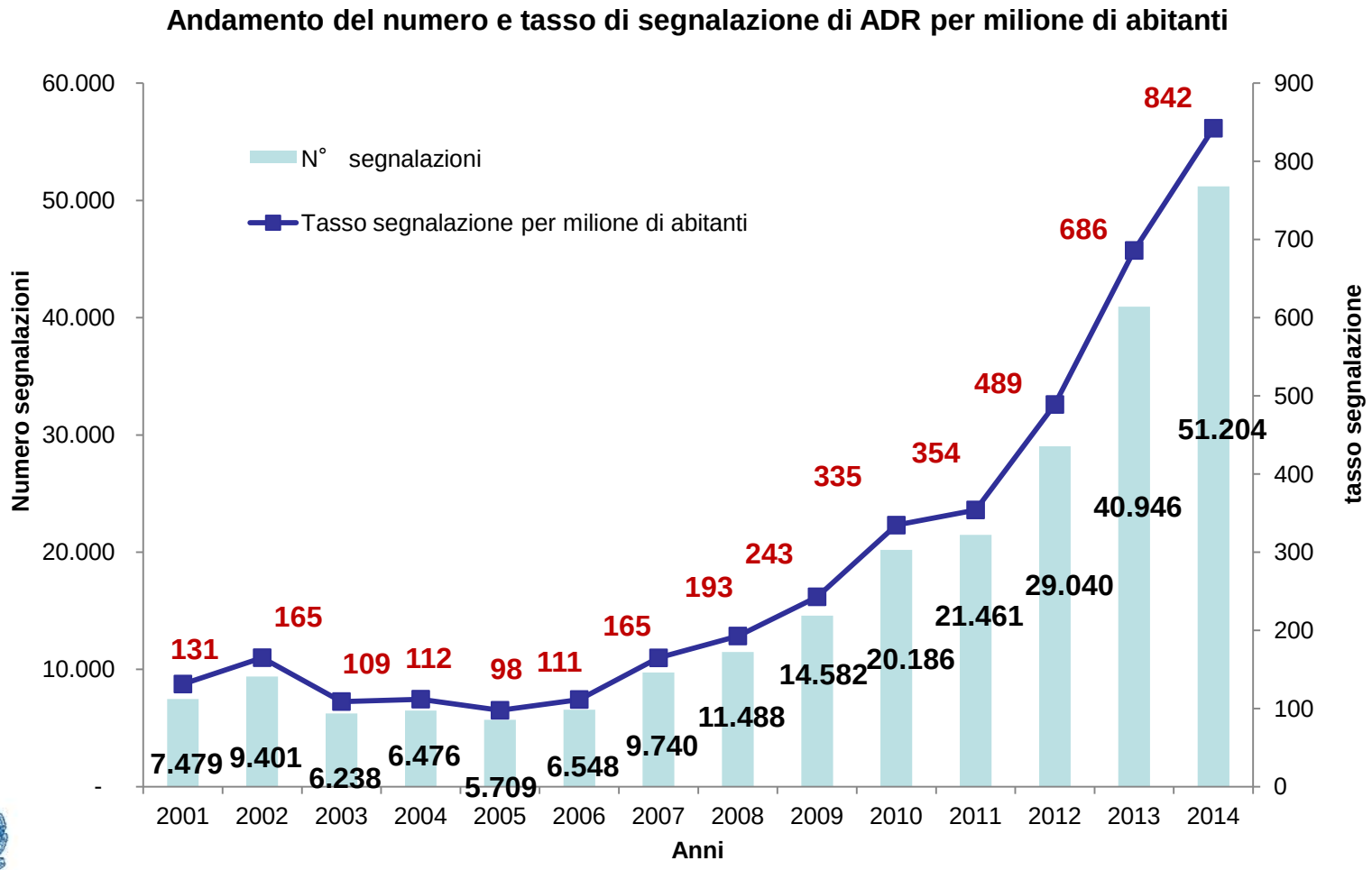
2. Regional pharmacovigilance funds

3. Italian ADR reporting figures

Spontaneous Reporting



Number and rate of ADRs per year 2001-2014



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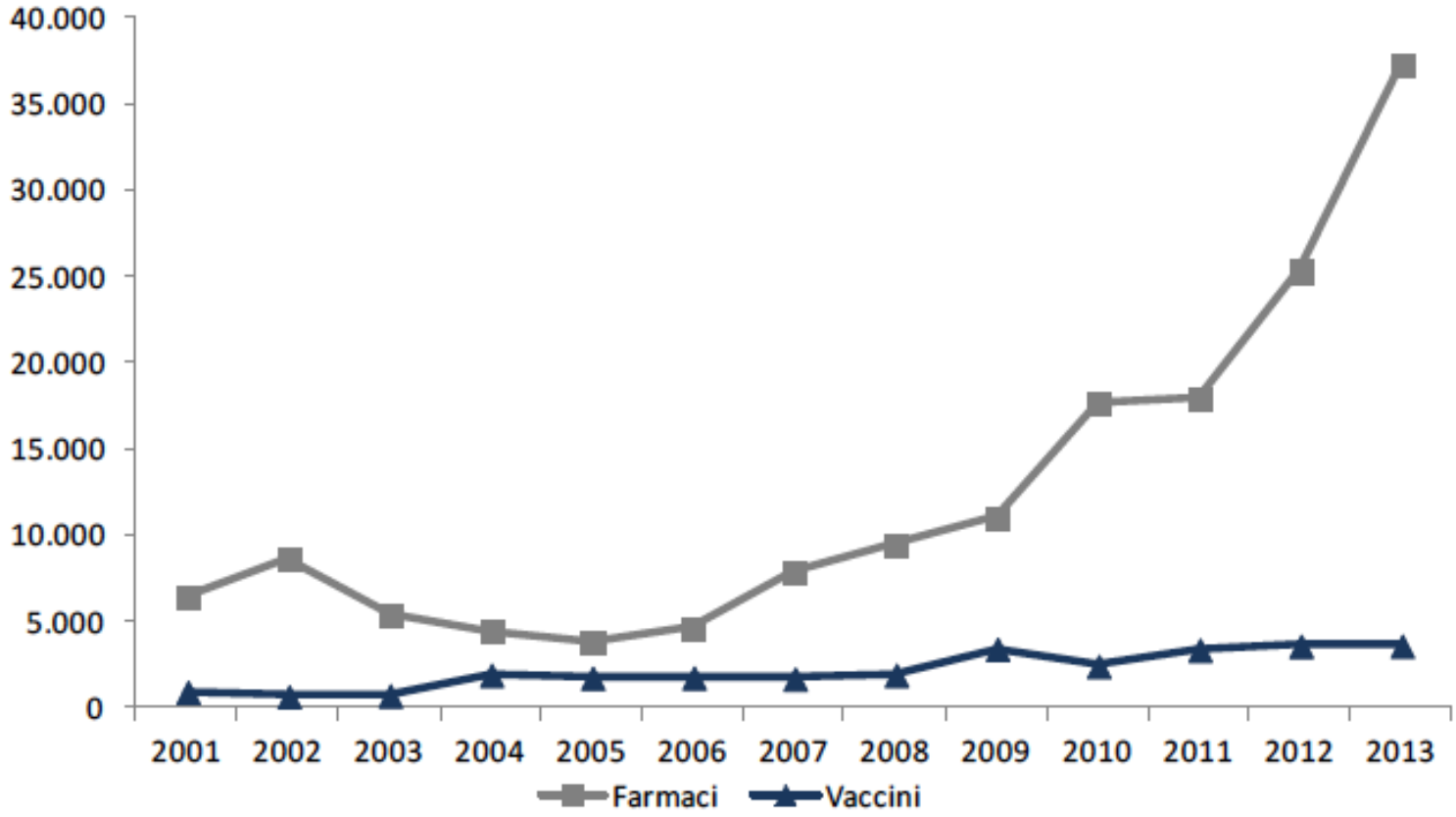
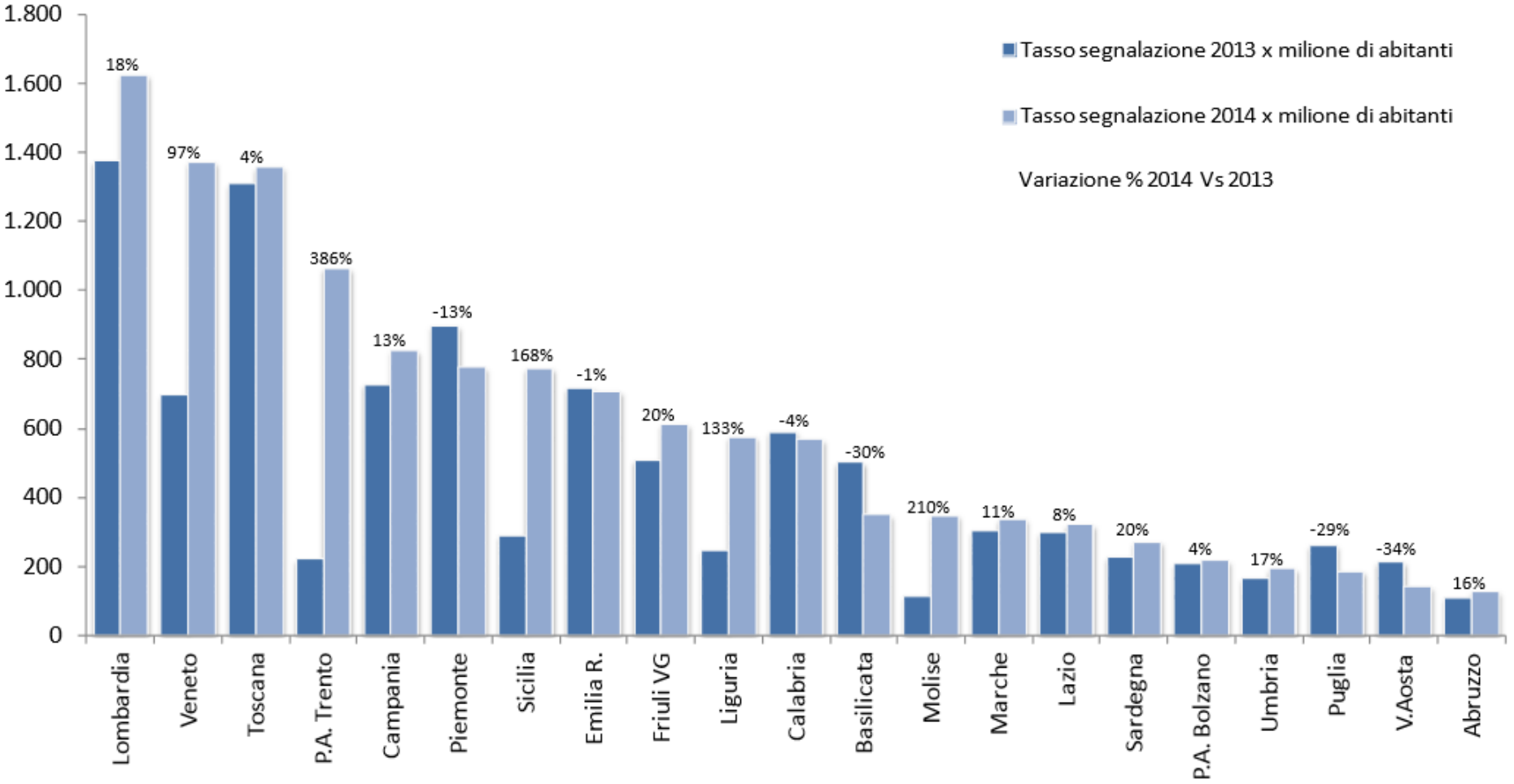
Reports vaccines vs other medicinals 2001-2013



Distribution per source

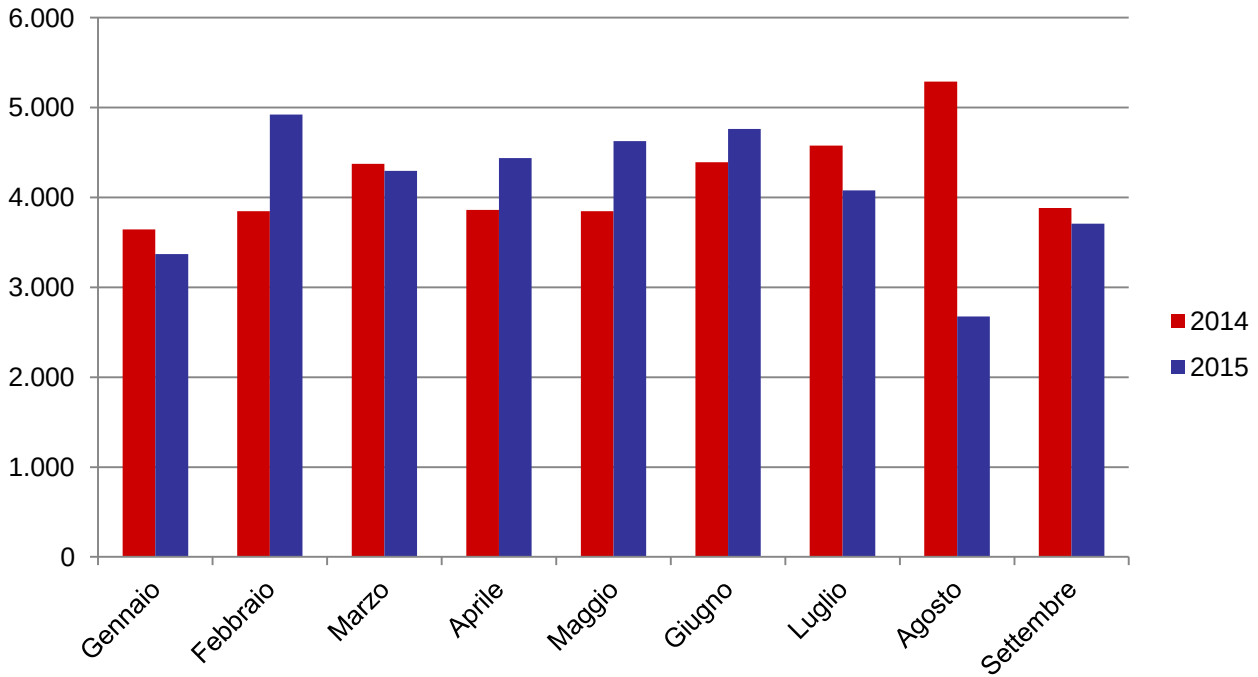
Ruolo segnalatore	2014	2015*	2014	2015*
medico ospedaliero	23.802	17.257	43%	43%
specialista	7.126	7.768	13%	20%
farmacista	9.225	4.681	17%	12%
non specificato	605	3.572	1%	9%
letteratura	4.085	2.826	7%	7%
medico di medicina generale	3.412	1.787	6%	5%
infermiere	1.650	986	3%	2%
azienda farmaceutica	2.184	449	4%	1%
centro anti-veleno	302	188	1%	0%
altro	2.139	146	4%	0%
paziente	351	27	1%	0%
pediatra	357	18	1%	0%
forze armate	10	2	0%	0%
dentista	11	1	0%	0%
Totale	55.259	39.708	100%	100%

Regional distribution reporting rate per million inhabitants

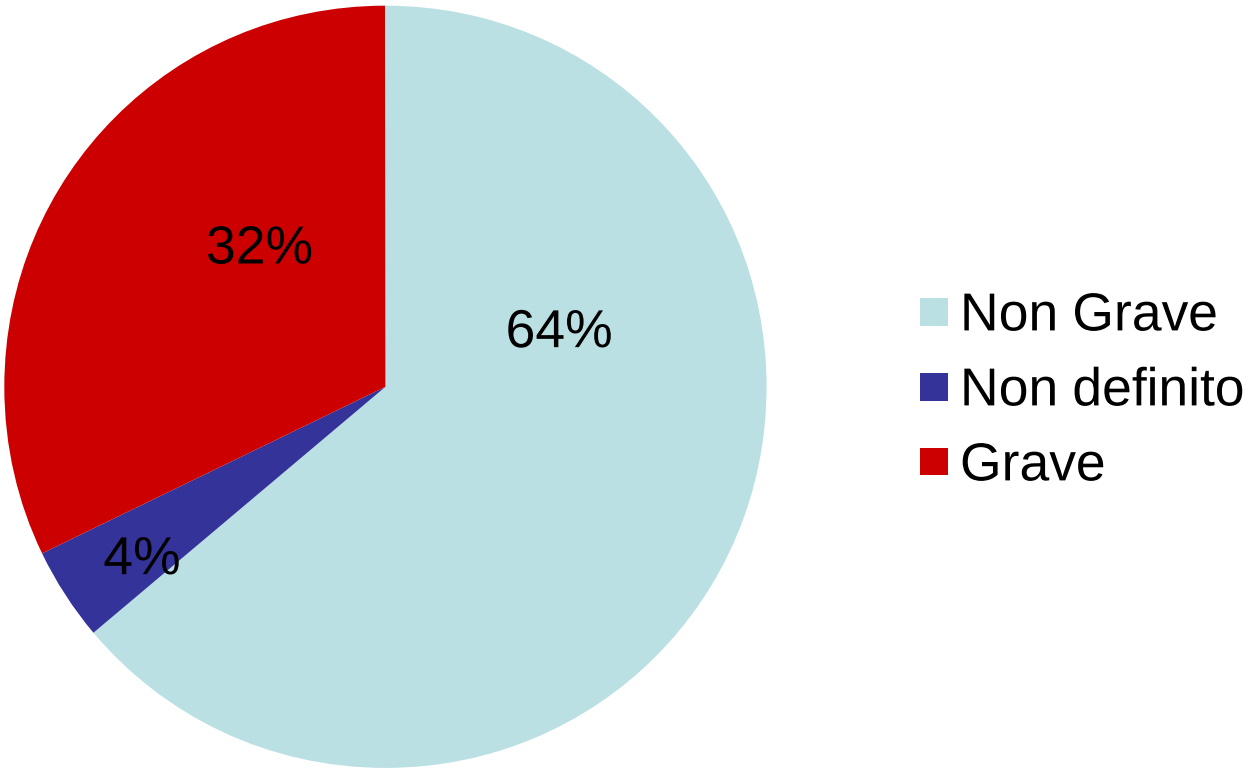


2015 (9 months) vs 2014

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Total
2014	3.645	3.846	4.373	3.863	3.846	4.392	4.576	5.291	3.884	37.716
2015	3.369	4.923	4.297	4.438	4.627	4.761	4.080	2.677	3.710	36.882
Variaz %	-8%	28%	-2%	15%	20%	8%	-11%	-49%	-4%	-2%



Seriousness 2015* (no literature)



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