initial analyses on their premises, as well as booking specialist visits and examinations.
In implementation of the aforementioned law, Legislative Decree of 3 October 2008, n. 153, and the subsequent implementing Decrees have formalised the new role of the community pharmacy, outline the type of services distributed and the activities that the pharmacist can carry out.
The Health Ministry is supporting this transformation phase and has drawn up the "Guidelines on the instruments to contribute to reducing the errors in pharmacological therapy and in the delivery of care services through the community pharmacies" with the involvement of FOFI, FNOMCEO, IPASVI, SIFO and the Regions. The Manual provides a framework of reference for the new role that the community pharmacies are taking on and represents the rolling out in Italy of the Pharmaceutical care applied in the territory.
Pharmacies, alongside traditional services, are reinforcing their role in health supervision, offering new services of great value in terms of health and social services, in synergy with the other health service operators.
The new role of the pharmacists includes, alongside the counselling activity, the responsibility for understanding the psycho-health-social situation of the person and the management and monitoring of the new professions that are not organised in professional associations and boards. The pharmacy may prove to be a guardian of vital importance in the case of emergencies and first aid, especially in rural and mountain areas, in the small islands or in situations of significant influxes of populations. Technological innovation and remote pharmacy services will be useful, especially in needy areas and for chronic illness, and can contribute to the optimisation of the resources and the monitoring of the health of patients.
The remuneration criteria, on the part of the SSN, for the new services and functions are defined by national collective agreements.

4. The hospital networks

4.1. Reorganisation of the hospital networks

The reorganisation of the hospital network and the redefinition of the nodes of the Accident and Emergency (A&E) network have encouraged the development of an organisational model with a specific clinical path, for patients undergoing heart-related (ACS), neurovascular (stroke) or trauma-related emergencies. The outcome of these pathologies depends very much on the time and way in which healthcare is provided. A timely, appropriate response must include a suitable integration between the territorial emergency system and the hospital structures, with the different clinical specialities, structured according to the Hub & Spoke model. At present, all Regions have identified a network for each of these time-dependent pathologies, even if their development on national territory is not yet standardised.
The analysis of data collected from the discharge reports for these pathologies, has enabled confirmation to be obtained of the differences seen between different Regions in terms of network activation.

Keywords Accident and emergency network, acute coronary syndrome (ACS), Hospital Discharge Register (SDO), Hub & Spoke, stroke, time-dependent pathologies, hospital facilities, trauma

4.2. Emergency network

The aim of the emergency network is to guarantee suitable timely healthcare intervention through a capillary organisation that is able to stabilise the patient and take them safely to the most appropriate place.
At present, the healthcare emergency network is undergoing a major restructuring process both in Regions subject to the Recovery Plan and elsewhere, as a result of the generalised revision of the healthcare networks aimed at reducing the imbalances between hospital and territory and meeting the new demands of the population.
In this context, the main restructuring interventions launched by the Regions relate to the rationalisation of the network nodes, aiming at a configuration in accordance with the Hub & Spoke model, the activation of the First Points of Intervention (FPI), the revision of the basins of users of the Operating Centres, the integration of the Emergency System

Table. Regional distribution of public hospital facilities and equivalent by class of beds and average size of the facilities (Year 2013)

Region	N. Public institutions and equivalent by classes of beds			Total public institutions and equivalent	Average size (beds)
	≤ 120	121-400	> 400		
Piedmont	7	16	14	37	396
Valle d'Aosta	0	0	1	1	457
Lombardy	47	58	20	125	245
Aut. Prov. of Bolzano	3	3	1	7	262
Aut. Prov. of Trento	5	2	1	8	210
Veneto	6	13	19	38	455
Friuli Venezia Giulia	2	8	3	13	346
Liguria	1	2	8	11	532
Emilia Romagna	3	11	14	28	526
Tuscany	17	15	9	41	275
Umbria	1	7	2	10	292
Marche	2	11	3	16	320
Lazio	17	30	13	60	284
Abruzzo	7	8	3	18	208
Molise	0	5	0	5	254
Campania	17	21	11	49	259
Puglia	8	23	7	38	286
Basilicata	3	5	1	9	211
Calabria	11	9	3	23	175
Sicily	36	23	8	67	186
Sardinia	12	12	4	28	182
Italy	**205**	**282**	**145**	**632**	**285**

Note: All types of beds (day-hospital, day-surgery, standard hospitalisation and private standard hospitalisation) were considered, survey, through the HSP.12 form, of the active hospital departments at the start of the year.
Source: Health Ministry – General management of the digital information and healthcare statisics system – Office of Statistical Management.

with the Continued Care service and the suitability in general of the services.
The degree of implementation of the actions relating to the revision of the network nodes is diversified and, in most cases, the situation is still evolving.
Nationally, the first data on the EMergency URgency (EMUR) information flow prepared for 2012, is available.

Keywords Accident and emergency network, continued care, EMergency URgency information flow (EMUR),-first aid, First Points of Intervention (FPIs), Hub & Spoke, 999 operating centres (999 OCs), paediatric emergencies

4.3. Oncological hospital networks

Patients diagnosed with neoplasia must be globally accepted and be assigned a treatment process based on managerial factors that can guarantee an integration of resources. Continued, integrated treatment must be assured, based on an organisation of services hinged on networked models, with a view to promoting the highest possible quality standards and reducing the disparity of the range of oncological treatments available regionally. The Ministry of Health, together with the Autonomous Regions/ Provinces and AgeNaS, is involved in developing indications for the implementation

of oncology networks laid out according to the dimensions of quality (organisational-managerial, technical-professional and perceived). The development of oncology networks, already started in many Regions, is also related to a reflection in the sizing of the hospital network, for which reference must be made to general regulatory guidelines, scientific evidence and territorial specificity. The matter of the patient being central is also important, in order to verify the effective equivalence of the structured routes and needs declared and the coherence of service integration models and continued care experience. Monitoring and evaluation is underway of continued care, from the patient's viewpoint, which will enable the: increase of knowledge of the subjective component of quality; exploring of critical and successful aspects; embracing of the patient's request for care, according to organisational methods that are increasingly aware of the clinical, treatment and existential complexity of the oncological pathology. Special attention should be paid to breast cancer, which is the most frequent tumour found in women and accounts for 29% of all new tumour diagnoses. The European Parliament has asked all Member States to ensure that by end 2016, multi-disciplinary breast units have been established throughout national territory: the Ministry of Health has activated a working party to provide a guide guaranteeing uniformity of structures.

Keywords AgeNaS, Breast Unit, continued care, Ministry of Health, oncology, oncological routes, oncology networks

4.4. Transplant network

Today's organisation of the transplant network and its function is the result of a progressive development of the system, which has been assured through the need to provide an effective, efficient answer to the demand for transplant, also in view of the need for system sustainability.

Following the changes made to the institutional structures and the effects deriving from European integration and the consequent need for the reorganisation of the national transplant network, an adaptation, including in operative terms, of the National Transplant Centre (NTC) has now also become essential; this should seek to ensure not only the "technical-organisational" coordination and national control of the network, but also the operative coordination of the allocation of organs, in line with the provisions of Directive 2010/53/EU on the quality and safety of organs for transplant and the Implementing Directive 2012/25/EU of 9 October 2012 on the information procedures for the exchange of human organs intended for transplant between Member States, both being implemented through the decree of the Ministry of Health envisaged by Italian Law n. 228 of 24 December 2012 (Art. 1, paragraph 340), the issue procedure of which is currently being completed.

To this end, the Operative National Transplant Centre (CNTO) has been established, with the main aim of allocating organs. It makes for the operative connection of the NTC with all structures of the national transplant network.

The NTC and the National Transplant Network continue to innovate and seek to be, on the national health scene, a valid planning and management model of a complex clinical-assistance system.

As concerns organ donation and transplant, the data processed by the NTC confirm that the Italian system remains basically stable. Some positive indicators also show the dynamic nature of the Italian transplant system and its capacity to evolve, meeting the patients' needs for care.

4.5. Transfusion network

Transfusions are governed by a complex corpus of national and European legislation. The sector framework law (Law n. 219 of 21 October 2005) has defined the key principles and strategic objectives, introducing the establishment of the national (Permanent technical consultation for the transfusion system and National Blood Centre (NBC) and regional coordination organisations (Regional coordination structures, SRC), the definition of Essential Levels of Care (LEA) and transfusions and indications for the revision of the authorisation requirements and sector ac-

creditation. Moreover, the same law sets the strategic objectives of the system as regional and national self-sufficiency of blood and its products, high quality and safety levels of products and services supplied by the transfusion services and, last but not least, the suitability of clinical use and management of blood resources.
The State-Regions Agreement of 16 December 2010 aimed at ensuring compliance of transfusion activities with national and European standards, including the production of plasma intended for the manufacture of blood-derived medicinal products, is currently being implemented; this is being achieved through the authorisation and regional accreditation of transfusion services and collection units, which also includes an on-site inspection of all transfusion structures operating throughout national territory, scheduled for completion by 31 December 2014 (terms established by Art. 2, paragraph 1-*sexies* of Italian Law n. 10 of 26 February 2011, the "Thousand Extensions" Law). The team of inspectors called to make the inspection shall, according to the State-Regions Agreement of 16 December 2010, including an assessor, previously qualified through training courses run by the NBC and included on the specific national list, established by Ministerial Decree of 26 May 2011 and managed by the NBC.
The national transfusion system is in charge of disbursing products and strategic provisions for the support of numerous care routes in medicine, surgery, urgency and emergency and highly-specialised areas. In 2012, the data collected through the web platform of the Transfusion Service Information System (SISTRA) indicates a total of 1,739,712 donors, with a slight increase on last year, thereby confirming the positive trend seen in the last five years.
In 2012, a total of 3,193,149 donations were made, basically stable on 2011. Total blood donations account for 84% of total donations, whilst aphaeresis donations come to 16%. The total indicator of donations nationally, in 2012, is 53.8‰, significantly above the average recorded in other Member States of the European Council, equal to approximately 43‰. In Italy, however, great variability is seen between Regions. The national average donation indicator per donor is 1.8 per year. In 2012, 3,178,526 blood components (red blood cells, plasma and adult therapeutic platelet doses) were transfused, making for 8,708 units per day. There were a total of 650,516 transfusion patients, down 1.62% partly due to the increased suitability of transfusion therapy. SISTRA also aims to detect any side effects associated with transfusion and donation, as well as information on the monitoring of infectious diseases that can be transmitted through transfusion in blood donors. Since 2009, the cover of infectious diseases has reached 100%, enabling a complete picture to be outlined of considerable epidemiological value, which, moreover, is a key requisite for achieving complete quality compliance of the plasma intended for industrial production with respect to European Community standards.

Keywords Accreditation, authorisation, blood, donations, donors, epidemiological surveillance, National Blood Centre (NBC), plasma, regional coordination structures, SISTRA, transfusion activities, transfusions

5. Integration between essential care levels

5.1. Prevention in primary care

The strategies used to suitably cope with chronic diseases require a different role in primary care, based on initiative medicine and an entirely specific attention with regards to social determinants of health. It has been shown, in fact, that the burden of non-communicable diseases can be considerably reduced with suitable prevention, control and care.
The reorganisation of primary care, with the full operational territorial functional aggregations and the Complex Primary Care Units will enable due importance to also be given to aspects of prevention/counselling/information to the healthy population, as well as fulfilment of the activities necessary for a better management of the health of all types of patients.
Moreover, the 2010-2012 NPP extended to 31 December 2013 also highlights the fact that, in going about primary, secondary and tertiary prevention, GPs and PCPs play a key role.

One example of initiative medicine in Italy is that of cardio- and cerebrovascular pathologies. In this case, the comprehensive prevention strategy includes the promotion of health and correct lifestyles amongst the population and the early identification of subjects at risk. The assessment of cardiovascular risk amongst the general adult population is carried out by the GPs through the application of the cardiovascular risk sheet validated by the ISS.
For the effective prevention and management of chronic pathologies, the "pigeon-holing" of interventions between professionals on different care levels must be overcome and a global, integrated approach promoted involving the various sectors (GPs, PCPs, specialists, prevention departments, districts and hospitals), ensuring the integration of the different care structures (primary care, hospitals, A&E, etc.).
One example of integrated treatment in Italy is that for diabetes mellitus. For some years now in Italy, the aim has been to secure continued care through the use of care models that, with a very general term, are defined as Integrated Management. These are organised, integrated, proactive, population-oriented systems that put the informed, educated patient right at the centre, playing an active role in managing the pathology from which he suffers.
Integrated Management, therefore, through the establishment of shared care choices, currently provides the prototype organisational model focused on improving care and preventing complications.

Keywords General practitioner, initiative medicine, integrated management, prevention, primary care paediatrician, primary care

5.2. Palliative care and pain therapy

The route implementing the Law on "Provisions to guarantee access to palliative cure and pain therapy" approved by parliament on 15 March 2010, in 2013 made some essential progress.
Approval during the Conference of the State and Regions held on 25 July 2012 of the understanding implementing Art. 5, paragraph 3, defining the minimum requirements and organisational methods necessary for the accreditation of the terminal patient care structures and palliative care and pain therapy units for adults and children, enables the development of a care network that is able to offer standardised services throughout national territory and ensure that citizens are guaranteed suitable quality care.
During the works on finalising the text of the understanding and at the specific request of the Region, the provisions of art. 5, paragraph 4 on tariffs have been eliminated, deferring the examination at a subsequent specific technical table, in order to sanction a new understanding to be stipulated in accordance with Art. 8, paragraph 6 of Italian Law n. 131 of 2003, during the Conference between the State, Autonomous Regions and Provinces of Trento and Bolzano; this will take place on the basis of a technical document prepared by a specific table of experts including representatives of the Ministry of Health and experts from the National Commission, the Ministry of the Economy and Finance and the Regions.
Legislative interventions implementing decisions on training have proved to be particularly important. Following the favourable opinion of *Consiglio superiore di sanità* (hereinafter also referred to as the "Council") given on 07 February 2013, the Permanent Conference for Relations between the State, Autonomous Regions and Provinces ordered the identification of the discipline "Palliative Care" in the area of diagnostic medicine and services for the professional category of doctors, amongst disciplines in which managerial roles can be assigned of multi-purpose structures in hospitals. This means recognition of the palliative care physician also for competition terms, with complete recognition of the "specificity of the knowledge and ability of palliative care doctors".

Keywords Care network, "no longer alone in pain", paediatric patient, pain therapy, palliative care, "palliative care" discipline, tariff system, training

5.3. Vegetative states

In recent years, people in Vegetative States (VS) or States of Minimal Consciousness (SMC) reaching clinical stability (results stage)

are being considered differently, and are now considered as people with "Very severe disabilities"; it is therefore essential to provide for integrated care solutions, both at their homes and at dedicated non-hospital structures. In these terms, the State-Regions Agreement of 05 May 2011, with the document entitled "Guidelines for assisting people in Vegetative State or State of Minimal Consciousness", has stressed the need to define standardised diagnostic-therapeutic-care choices based on the suitability and centrality of people in VS and SMC and their families. Moreover, the State-Regions Agreement of 22 November 2012 on the Priority Objectives of National Relevance has also confirmed the project guideline "Promotion of healthcare organisational models for patients in chronic vegetative state and minimal consciousness", as well as introducing a restriction of 20 million Euros for projects ensuring the management of people in VS and SMC during the results stage.

An analysis of the discharge reports for 2012 for patients with code 780.03 ("Persistent vegetative state" ICD-9-CM), it was seen that the total number of discharges in 2012 came to 1,554, mainly male (885) with fewer female patient discharges (669). The age group most represented is between 45 and 64 years old with a higher prevalence of males (310) to females (167). This is followed by the over-75s, with a total of 389 people, with a prevalence of women (235). The most common discharge was "ordinary at home", with 527 patients (33.9%), followed by "ordinary discharge to Residential Care Home (RCH)" with 277 patients (17.8%).

Keywords State of Minimal Consciousness, Very severe disabilities, Vegetative State

5.4. Management of post-acute conditions and intermediate structures

The increased number of fragile patients and patients with chronic disease and the management of post-acute conditions are matters that the NHS is dealing with by adopting new care and organisational strategies aimed at improving the suitability and quality of care through the use of so-called "intermediate structures"; these structures aim to guarantee management of patients during post-acute conditions and to prepare them for their return home.

In these terms, the hospital is required to provide ever-more specialised and technologically advanced assistance during acute stages, whilst the territory is to reinforce its role as guarantor of continued care; it shall do so through offering a range of services that, on the one hand, cover the care needs of people in the post-acute stage of the disease and, on the other hand, intercept the needs for care with solutions other than hospitals, acting as a filter to prevent inappropriate hospitalisation.

By virtue of this, a great many Regions are fitting-out primary care residential structures referred to as "community hospitals", namely places of temporary residence, often managed by nurses and under the clinical responsibility of the GP or PCP, with a limited number of beds (15-20) intended for the care of acute pathological states for which hospitalisation is not appropriate, but which certainly require continued medical and nursing care.

In the same way, various Regions are preparing territorial intermediate structures mainly aimed at guaranteeing protected patient discharge if physical conditions need consolidating, the functional recovery route is to be pursued or accompaniment provided through the initial stage after discharge, in view of their individual and social fragility.

The presence of territorial primary care units and intermediate structures is today fairly widespread; this results in a need to rationalise the whole post-acute network in order to offer patients an appropriate, high quality flexible response that can guarantee the definition of a care plan as quickly as possible, and management by the territorial services.

5.5. Mental health

Recent international strategies of the WHO and EU have shown a commitment to invest in mental health, drawing attention to: the fact that work must be multi-disciplinary and multi-sector; the organisation of a network of mental health services open to all; a range of care options based on scientifically-validated choices that are appropriate, high

quality and effective; the promotion of interventions aimed at encouraging the possibility of living a normal life in society as far as possible, including through patient empowerment and support of the needs of family members and carers; the training of healthcare, social-health and primary care workers; and focused research.
National data on the range of services available and the characteristics of care for people suffering from mental disorders highlights the many reasons why strengthening mental health services, in terms of the number and skills of staff, should be considered a priority. The data obtained from the computer systems of some Regions show greater percentages of severe mental disturbances amongst the main cases and emotional disorders common amongst patients at their first contact with the services. This trend is standard in countries where a mature community mental health system has been developed, where the prevalence is influenced by patients with severe mental disorders, making lengthy use of services, whilst the incidence essentially depends on common emotional disorders with shorter episodes of care.
The strengthening of the national Mental Health Computer System (SISM) is therefore essential, within which a specific working party (Ministry of Health, Regions and ISS) has developed a set of indicators that will enable the information to be used in order to monitor the action developed and national, regional and local planning.

Keywords Computer systems, network of mental health services, policies and strategies, quality of care of mental disorders

6. Drugs

6.1. The generic drug registration process

The equivalence of a generic drug and its reference drug is established by industry legislation – in Italy, it is Italian Legislative Decree n. 219/2006 that incorporates Directive 2001/83/EC Community Code for medicinal products for human use – which guarantees equivalent quality, safety and efficacy of the two products. It therefore follows that the authorised generic drug can be declared as "equivalent" to its point of reference.
The bioequivalence of the two drugs is the therapeutic equivalence of the two formulas, which are essentially similar, containing the same active substance. The difference in price between the generic drug and its corresponding original version is due to the fact that the owner of the original medicinal product has had to prove the safety and efficacy of the drug at the time the first application was submitted for Marketing Authorisation (MA), whilst for the generic drug, the file is easier and less expensive to prepare, as the safety and efficacy, once a pre-established period of time has passed, is shown by data, now known, on the reference drug.

Keywords Bioequivalence, generic drug

6.2. Innovative drugs

The definition of pharmacological innovation is open to new scenarios involving the development of individualised/customised therapies aimed at certain sub-groups of patients and, therefore, connected with the identification of specific biomarkers. The evaluation of the innovative nature of a solution is a multicriterion decision-making analysis method where the most significant problem is how to measure innovation, namely the quality of the clinical trials, the robustness of the endpoints, the choice of comparative treatments and the evaluation of the dimension of the therapeutic effect. This is the direction taken by the new evaluation route promoted by the Italian Medicines Agency (AIFA). For a regulatory agency, it is a particularly important evaluation insofar as the risk-benefit ratio shown by a drug must go hand-in-hand with a correct valuation of the therapeutic benefit in actual clinical practice and a fair price of the NHS and, therefore, an advantage that can be measured for individual patients, thereby ensuring the sustainability of the NHS. A legislative reference to innovation can be found in Italian Decree-Law n. 158 of 13 September 2012, under Art. 10. The legislation aims to reduce inter-regional disparity. The Decree has also entrusted AIFA with the task of identifying "drugs of exceptional therapeutic

and social relevance", which, together with orphan drugs and hospital pharmacies are to undergo a quicker procedure for classification by the NHS and price definition.
The EMA is responsible for the centralised approval of new drugs, a compulsory procedure for oncology, diabetic and biological drugs and for other conditions including neurodegenerative and rare diseases. In 2012-2013, the European Commission approved 139 new drugs. For 5 drugs, conditional approval was granted, and for 4 drugs, approval was in exceptional circumstances, including the 2012 approval of the first gene therapy drug.

Keywords Benefit-risk ratio, biomarker, drugs of exceptional therapeutic and social relevance, evaluation of the therapeutic benefit, innovative nature, pharmacological innovation, sustainability

6.3. Drug traceability

Through the data and instruments available on the various different governance levels (State, Regions and Health Trusts), Italy is one of the few countries that manages to carry out a systematic monitoring of medicinal products, as a guarantee of the availability of legal drugs in the intermediate (distributors) and final (pharmacies, hospitals, etc.) distribution chain, as well as ensure an effective control of consumptions and expenses incurred by the public structures of the NHS.
The main source of information is the Central Drug Traceability Database, which, as part of the New Health Information System (NSIS) enables the collection and management of data on medicinal products on national territory, including any outgoings from the distribution chain (thefts, losses, disposals) and the corresponding economic value if deliveries are made to the public structures of the NHS. Additionally, through the integration with the information flow for direct and third party distribution of medicinal products distributed through the health structures and with the information flow for the consumption of medicinal products used in hospitals and outpatient surgeries, the Central Drug Traceability Database enables the drug to be monitored through to the hospital ward or dispensing to patient if direct or third party distribution, as well as having information on the related average unit purchase cost.
The comprehensive economic data on the supplies of the NHS present in the Central Drug Traceability Database equate to more than 8.5 billion Euros in 2013; of this, more than 5.2 billion relate to the direct distribution channel and more than 2.8 relate to the hospital and outpatient channel.
The Central Database data, together with that of the OsMed flow, go towards governing both territorial (authorised and class A of direct and third party distribution) and hospital (hospital, outpatient and direct and third party distribution apart from class A) pharmaceutical spending. Amongst other aspects, they enable the application of measures for defining, monitoring and controlling the hospital budget system and corresponding measures for recovering any exceeding of these.

Table. Monitoring of medicines distributed in Italy. Number of packets delivered to final recipients (Years 2010-2013)

Recipients	N. packets delivered to final recipients			
	2010	2011	2012	2013
Pharmacies	1,660,412,057	1,680,493,175	1,640,572,109	1,646,437,796
Health facilities	376,416,893	426,472,499	526,585,332	446,577,560
Commercial businesses (parapharmacy)	22,566,605	24,274,965	26,521,327	26,913,619
Abroad	27,106,617	27,192,169	26,156,539	24,413,585
Other recipients	33,479,805	34,788,189	40,850,151	38,501,549
Total	**2,419,666,178**	**2,522,428,419**	**2,669,818,890**	**2,527,231,920**

Source: Health Ministry – Traceability of the medicine – Production and distribution, situation at 28 March 2014.

Keywords Ceiling limit to pharmaceutical spending, consumptions, counterfeiting, database, drugs, expenses, health technologies, medicines, New Health Information System (NSIS), pharmaceutical budgets, safety

6.4. Drug registers

The AIFA drug registers are innovative technological-scientific and regulatory instruments that aim to verify the prescriptive suitability in actual clinical practice and application of the MEAs (Multilateral Environmental Agreements – also referred to as risk sharing agreements – conditional reimbursement, like PbR, RS, SF or CS).

By means of these registers, the Agency seeks to efficiently combine, as part of its HTA route, the evaluation of the risk-benefit of a medicinal, with that of cost-efficacy. In accordance with art. 15, paragraph 6, letter c and paragraph 10 of Italian Decree-Law n. 96 of 6 July 2012, converted into law, with amendments, by Italian Law n. 135 of 7 August 2012, the AIFA registers have officially become a part of the NHS Information system.

Most of the medicinal products included in the AIFA registers come from a centralised authorisation procedure (often speeded up, conditional or in exceptional conditions), of above all biological drugs, sometimes orphan drugs, which are expensive for the NHS. In this context, the possibility of designing registers able to record changes to specific indicators able to predict response to treatment (biomarkers), thereby effectively limiting the target sub-population that would obtain maximum benefit from the medicinal product, optimises the processes by which it is reimbursed.

The drug registers (SMR and TP) have been included, since 1 January 2013, in the implementation stage of the new information system designed by the Agency to allow for the total integration of all AIFA systems, through the development of a KMS (Knowledge Management System). Their new transversal, modular, flexible architecture, enables more significant analyses to be performed and guarantees better quality data records and, at the same time, a greater commitment by users.

In accordance with the Regions, the new registers have established the pyramid network of regional reference persons and health directors. This is an important step that will enable a qualitative-based planning over the next few years, of the qualified prescribing centres, with the aim of ensuring the more effective verification of the prescriptive suitability and control of pharmaceutical spending.

Keywords Cost Sharing (CS), Health Technology Assessment (HTA), Knowledge Management System (KMS), Managed Entry Agreements (MEA), National Health Service (NHS), Payment by result (PbR), Risk Sharing (RS), Standard Monitoring Registry (SMR), Success Fee (SF), Therapeutic Plan (TP)

6.5. Pharmaceutical assistance

One of the challenges for the sustainability of the health systems is to guarantee access to new therapies, ensuring a balance of the demand for the recognition of the innovative nature of the products and pressure towards the availability of all new therapies. In addition to epidemiological factors, there are also other levels of analyses, to clarify the current needs connected with the sustainability of welfare systems and the continuous increase in the cost of new therapies. These include the ratio of progress made in scientific knowledge and the poor capacity to influence the pathology action mechanisms, the ratio of individual expectations from the treatment and the reality and the ratio of regulatory science and valuation in economic terms of the innovation. The meaning of market access and the concept of "time-to-market" have changed drastically. The MA must go hand-in-hand with the decision on whether or not, and to what extent, the product may be reimbursed. As the conditions under which the drug is to be used in actual clinical practice are influenced by pathological factors, as well as physiological and environmental factors, it is important to continue monitoring drug safety. The evolutions that the new legislation on pharmacovigilance (European Directive 2010/84) has proposed enable an evolved approach in the authorisation process, moving away from a "static" authorisation concept and towards one of progressive authorisation. This approach requires an interaction

between regulatory agencies and care systems. Managed Entry Agreements between a treatment system/payer and manufacturers, to enable reimbursement at certain conditions, are used by AIFA to guarantee the sustainability of costs and bring the clinical outcome into direct relationship with the use of real life. The choice of pharmaceutical policy adopted by Italy and promoted by AIFA has thus far guaranteed access to new medicinal products.

Keywords Clinical outcome, innovative nature, legislation on pharmacovigilance, Managed Entry Agreement, market access, progressive authorisation, sustainability

6.6. The new drug prescription methods in the national health system

The methods for the prescription of drugs by the National Health Service have recently been altered, both in terms of the making prescriptions digital, with the introduction of the electronic prescription and its validity throughout national territory, and in terms of the adoption of measures to limit costs for pharmaceutical assistance and the rationalisation of the use of medicines.

As concerns this latter aspect, in fact, it has been established that the doctor is responsible for informing the patient, when prescribing, of any availability of medicinal products with the same active substances and pharmaceutical form, method of administration, method of release and unitary dosages.

In the same way, the obligation of the pharmacist, unless otherwise requested by the client, to supply the equivalent medicinal product at the lowest cost, has also been confirmed.

Finally, as concerns the way in which the prescription is prepared, the new rules oblige the doctor to specify the name of the drug's active substance on the prescription – but only for the first treatment of a chronic disease or a new episode of a non-chronic disease – with a view to encouraging the use of generic alternatives.

Most recently, a new regulation has been issued aimed at making drugs considered as "innovative" by AIFA immediately accessible to citizens.

Keywords Electronic prescriptions, generic drugsinnovative drugs, prescription of active substance, sustainability of medicinal products

6.7. Drugs for rare diseases and for specific, severe pathologies

"Orphan" drugs are drugs used for the diagnosis, prevention and treatment of rare diseases. In the EU, orphan drugs are regulated by Regulation (EC) n. 141/2000 and 847/2000. In Italy, access is granted to an orphan drug thanks to various legislative tools. The centralised authorisation procedure is the main rule of access. Alternatively, Law n. 648/96 enables the disbursement by the NHS for pathological conditions for which there is no valid therapeutic alternative. Art. 43 of Law n. 326/2003 established a national fund for the use of orphan drugs to treat rare diseases and medicinal products representing hope in care, whilst awaiting marketing, for specific, severe pathologies. The term "compassionate use of drugs" is used, in accordance with art. 83, paragraph 2 of Regulation (EC) n. 726/2004, to mean "making a medicinal product (...) available for compassionate reasons to a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorised medicinal product. The medicinal product concerned must either be the subject of an application for a marketing authorisation (...) or must be undergoing clinical trials". "Therapeutic use of a medicinal product undergoing clinical trials" (Ministerial Decree of 8 May 2003) is the legislative tool laying down the procedures for accessing experimental pharmacological treatments. Art. 3, paragraph 2 of Italian Law n. 94/1998 (formerly the "Di Bella" Law) allows a doctor to prescribe medicinal products available on the market for use outside the conditions under which they were registered. Their specific nature means that orphan drugs have been excluded from recovery procedures as may be applied by government legislation on hospital pharmaceutical spending.

Keywords Compassionate use, Law n. 648/1996, Law n. 94/1998 art. 3, paragraph 2

(formerly the "Di Bella" Law), Law n. 326/2003 art. 48, "orphan" drugs, rare diseases, therapeutic use of drugs undergoing clinical trials

7. Prevention in public veterinary health and food safety

7.1. Italian food safety authority

The food crisis that struck European countries early in the century, following various emergencies, have led the entire EU to begin a major reconsideration of the food safety policy, and has brought about an overhaul of all legislative regulations, introducing the concept of the separation of management functions from those of assessing food risk. The "hygiene package" is based on this essential principle, representing a set of rules that pursue the aim of guaranteeing a high level of protection of human health. Regulation (EC) n. 178/2002 is the cornerstone of this set of rules.

Another innovative element has been the involvement and consultation of consumers in the decision-making process, based on scientific evidence evaluated by independent institutions.

It is on this basis that Regulation n. 178/2002 established the European Food Safety Authority (EFSA).

With the objectives laid down by the new regulation, EFSA, the European institutions and the Member States have all committed, over the years, to adopting appropriate, effective measures – based on a risk analysis (in all its components: assessment, management and communication) – that aim to protect health through a risk assessment process based on independence, objectivity and transparency and on information and scientific data available.

The EFSA guarantees the necessary scientific and technical assistance to the European institutions competent to manage the risk in the food chain and is the point of scientific reference, whose independence in the assessment, information and communication of the risk go towards securing consumer trust.

The European Authority has been specifically called to act in close collaboration with the national bodies with similar functions to its own.

In Italy, the need to make the envisaged collaboration a concrete reality was achieved in 2006 with the establishment of the National Secretariat for risk assessment in the food chain, included under the Department of Public Veterinary Health, Nutrition and Food Safety, under the scope of which the tasks of risk assessment, management and communication were organised.

Within this same Department, the National Food Safety Committee (CNSA) has been established, providing technical-scientific consulting for all administrations dealing with risk management, and which represents the national body of reference interfacing with the EFSA.

By Italian Presidential Decree n. 108 of 11 March 2011 setting out the regulations for organising the Ministry of Health, the attribution of these competences was confirmed with the Department of Public Veterinary Health, Nutrition and Food Safety and the collegial bodies to protect health, which includes, in addition to the Directorate General for Animal Health and Veterinary Drugs, the Directorate General for Health, Food Safety and Nutrition, in charge of risk management, and the newly-established Directorate General of the Collegial Bodies for the Protection of Health, under the scope of which the CNSA operates, with specific duties to assess risk in the food chain.

The CNSA collaborates with the EFSA and is in charge of issuing scientific opinions on food safety, where requested by the central Italian administrations and the Autonomous Regions and Provinces of Trento and Bolzano.

This Committee is appointed by Decree of the Ministry of Health and consists of experts of proven scientific experience and great professionalism in the matters relating to risk assessment in the food chain.

In 2012 and 2013, the National Food Safety Committee, re-established by Ministerial Decree of 18 March 2011, issued opinions on the following matters:

- "Energy drinks and alcoholic drinks";
- "Food allergies and consumer safety";
- "Risk connected with the finding of thorium in foods of animal origin";
- "Opinion on the proposed modernisation of the inspection of pork";

- "Human consumption of sheep and goat meats from breeding grounds of BSE (Bovine spongiform encephalopathy)";
- "Problems relating to Glucose-6-phosphate dehydrogenase deficiency (fauvism)";
- "Review of the criteria for monitoring BSE in properly butchered animals";
- "Problems of Aflatoxin M1 in cheese - Applicability of the coefficients for the transformation in milk equivalent (Annex 2 to Ministerial Decree of 31 July 2003 of the Ministry for Agricultural and Forestry Policies)".

To complete the structure of the functions on risk assessment in the food chain, the Advisory Committee of consumer and producer associations on food safety, has been established.
This Committee is assigned the task of encouraging the exchange of information by consumer and producer associations, in order to facilitate the consumer's capacity to choose, making for an aware consumption and correct diet and helping aid the communication initiatives organised by the competent bodies.

Keywords Committee of consumers and producers on matters of food safety, consumers, European food safety authority, National food safety committee, risk analysis, risk assessment, risk management

7.2. Experimental zooprophylactic institutes
An integral part of the SSN, with responsibility for the safety of food intended for human consumption, the health of the national livestock heritage, the wellbeing of the animals and animal research in the sectors under their responsibility, the Experimental Zooprophylactic Institutes (EZI), Health Organisations governed by public law, through their distribution on national territory, are a network of laboratories that constitute a fundamental operational instrument that ensures the country has the technical-scientific services necessary in order to ensure the safety of foodstuffs and animal productions.
It can be stated that the EZI network, in the service of the State and the Regions, is a necessary link in the chain between the protection of the consumers and the development of an agro-food and livestock production the remains at the cutting edge. This consideration is important for Italy, which bases an important part of the economic success of its agro-food businesses on the capacity to transfer raw materials into high-value products, for the markets of third-party countries that require the highest guarantees of food safety. The capacity to ensure high safety levels along the production chain, therefore, becomes not only a determinant factor for the safety of the consumers, but also for economic development.
Given the experience and the scientific value gained over the years by the EZIs, international organisations such as the Office Internationale des Epizooties (OIE), the World Health Organisation (WHO) and the Food and Agriculture Organisation (FAO) have recognised a number of Zooprophylactic Institutes as Centres of Collaboration and laboratories of reference.
The national regulations also envisage the establishment, at the EZIs, of National Centres of Reference considered as operational instruments of high and proven expertise that carry out specialist activities in the sector of animal health, food hygiene and livestock hygiene.
The veterinary health organisation has recently been provided with 3 new centres of reference established by Decree of the Health Ministry:

- National Centre of Reference for biological investigations on anabolic animals at the Experimental Zooprophylactic Institute of Piedmont, Liguria and Valle d'Aosta;
- National Centre of Reference for emerging risks in food safety at the Experimental Zooprophylactic Institute of Lombardy and Emilia Romagna;
- National Centre of Reference for urban hygiene and non-epidemic emergencies at the Experimental Zooprophylactic Institute of Abruzzo and Molise.

7.3. Phytosanitary products and food safety
Phytosanitary products, also referred to as pesticides, anti-parasite treatments and phytodrugs, aim to protect crops, before and after harvest, from diseases and parasites re-

sponsible for severely reducing the yield of agricultural and fruit and vegetable crops.
In order to protect consumer health, provisions have been issued both on a European and national level, including Regulation (EC) n. 1107/2009 and Regulation (EC) n. 396/2005 and Italian Legislative Decree n. 150/2012, implementing Directive 2009/128/EC, establishing a framework for EU action to ensure the sustainable use of pesticides. Under this scope, the systematic recording of acute intoxication caused by phytosanitary products has also been envisaged.
In order to verify the implementation of these laws and regulations, controls are run on the release to the market and use of phytosanitary products and residual levels of these in foods, by the Autonomous Regions and Provinces of Trento and Bolzano and the other authorities. Controls on phytosanitary products for 2011 organised by the regional authorities, increased with respect to 2010, whilst the percentage of irregular samples of residues of phytosanitary products in foods is very limited and falls below the average irregularities recorded in Europe. Irregularities account for just 0.4% of controls performed, which were 6,864. These results are transmitted in a standardised form, in accordance with the guidelines issued by the European Food Safety Authority.
Scientific measures have also been taken to guarantee protection of the weaker categories of the population, such as, for example, developing organisations. In actual fact, toxicological values of neonicotinoid substances have been revised and the authorised ingredients with potentially concerning effects on foetuses and children (endocrine, neurotoxic, immunotoxic interfering drugs, etc.) have been reviewed.

Keywords Anti-parasites, child, endocrine interference drugs, foetus, neonicotinoids, pesticides, phytodrugs, phytosanitary products, residues

7.4. Production technologies and biotechnologies

Production technologies and food safety. Food production technology has developed with the aim of improving quality, preservation, flavour and appearance of food in respect of food safety.

Additives, aromas and enzymes. Guidelines have been approved for the description of new "food categories", in which the same additives may be used. The new Implementing Regulation (EU) n. 1321/2013 has been disseminated, establishing the first list of authorised smoke flavouring primary products in the EU.

Materials intended to come into contact with food. Indications and guidelines have been disseminated aiming at applying the new specific provisions for plastic materials (Regulation EU N 10/2011) and the use of recycled plastic for food. By Decree n. 134/2013, the use of recycled plastic is permitted in Italy for the production of tubs and bottles intended to come into contact with all food types.

Contaminants. Monitoring of acrylamide in various categories of food products has continued; in 2012, 191 samples were analysed. "Extraordinary operating procedures for the prevention and management of the risk of contamination from aflatoxins in the dairy-cheese-making chain and the production of maize intended for human and animal consumption, following extreme weather conditions" have been prepared and implemented.

Biotechnologies/National official control plan for the presence of genetically modified organisms in foods 2012-201. Results for 2012. The data relating to controls performed in the territory reveal what should generally be considered as positive results. For a total of 842 samples, no non-conformities were detected in relation to labelling provisions on authorised GMOs in the territory. At import, in 2012, 67 samples were analysed of which 4 were found to be non-compliant due to the presence of unauthorised GM rice.
In 2012, it was confirmed that the presence of authorised and unauthorised GMOs in food in Italy is clearly limited and on a trace level; basically, on the Italian market, food products comply with the labelling requirements

laid down by current legislation, ensuring correct consumer information.

Keywords Additives, biotechnologies, contaminants, enzymes, flavourings, Genetically Modified Organisms (GMO), materials in contact

7.5. Animal welfare

In 2013, implementation was confirmed of the National Animal Welfare Plan, outlining minimum controls to be carried out in farms, during transport and during butchering. As concerns animal welfare in farming, the sector legislation has been further implemented, particularly as concerns the protection of egg-laying hens, hens farmed for their meat and the welfare of farmed pigs. The memorandum of understanding with the Home Ministry intended to improve controls on national and EC transport and prevent and repress violations of animal welfare, has been implemented. On 7 January 2013, the new European Community Regulation on animal welfare at butchering came into force, for the application of which the Ministry of Health has now issued the first operative indications for the territory. Thirty-nine inspections were carried out at plants using animals, for the issue of the require authorisations and the verification that requirements continued to be met and maintained by structures that had already been authorised; they also sought to verify the correct application of current legislation on animal trials. Law n. 96/2013 has been approved, laying down standards and criteria of delegation for the government, with a view to implementing Directive 2010/63/EU on the protection of animals used for scientific or experimental purposes, with the subsequent drafting by the Ministry of Health of the text of the legislative decree. The Operational Unit for animal protection, the fight against cruelty and the fight against strays, continued to monitor the correct application of current legislation. Forty-one inspections were carried out at kennels, catteries, abused animal shelters and zoos and 27 police interventions requested to protect health. Approximately 200 meetings and round tables were also organised and attended with the territorially competent authorities and animal protection associations. Monitoring continued of the correct application of the OM on events involving horses and intense work was also carried out in terms of animal-assisted interventions.

Keywords Animal protection, animal welfare at butchering, animal welfare during transport, animal welfare in farming, fight against strays, National Animal Welfare Plan, protection of animals used for trials

7.6. Animal feed

In 2012, 30,641 inspections were carried out with Animal Feed Industry Operators (OSM), recording 1,272 structural/managerial non-conformities, accounting for 4.1%. In relation to these, in 7.2% of cases, administrative penalties were applied: 92. For severe cases, eight reports were made to the legal authority. Sampling numbered 11,610 samples taken as compared with the 11,066 scheduled (+544), meaning that plans were fulfilled entirely (104.92%); 71 non-conformities were found: 0.61%. The figure shows that 99.3% of animal feed is compliant. One hundred and seventeen samples were taken on suspicion of emerging risks. The exceptional weather conditions of 2012 resulted in increased contamination by mycotoxins, making extraordinary action necessary, with the collection of 333 samples of maize recording 12 non-conformities. Out of 3,689 batches imported, 309 samples were taken, thereby exceeding the minimal frequency of 5%; this resulted in the detection of 7 non-compliant batches (0.1%) for which due corrective action was taken. The mycotoxin emergency led to the sampling of 40 batches out of a total of 85 transported (47.05%) and the recording of one non-compliant batch of maize.

Animal feed is critical to food safety in a Single Health and Protection approach. In 2013, the EFSA developed innovative criteria for risk assessment on additives and animal feed components for: i) animals, proposing new maximum limits in animal feed (e.g. for iron compounds) and preservatives; ii) consumers, with specific attention paid to the transfer to

foods of metabolites and nutrients (e.g. vitamin A) with potential toxicity and, for probiotics, the presence of toxins or antibiotic-resistance factors); iii) workers (sensitising products or those with potential inhalation toxicity); iv) the environment, evaluating the possibility of reducing the supplementation - and therefore presence in waste - of copper and zinc. The recommendations were generally adopted by the European legislator. As concerns the undesired substances, the opinions of the EFSA on the update of criteria for the inspection of meat, are extremely important in categorising risks making best use of available data, including that on contaminants in food for productive livestock.

Keywords EFSA, extraordinary mycotoxin plan, imports, inspections, risk assessment, sampling

7.7. Imports and intra-Community exchanges of animals and animal-origin products

The Italian Frontier Inspection Posts (PIF) and the Veterinary Offices for Compliance with European Union Obligations (UVAC) are peripheral offices of the Ministry of Health, responsible for controls on animals, animal-origin products and animal feed imported from third party countries or introduced from other Member States (intra-Community trade). A total of 52,219 batches were presented for import at the Italian PIF in 2012 (–11.1% compared with the previous year) and 50,312 in 2013 (–3.7% compared with the previous year). The control of these goods was systematic, in order to verify that documents and product identity were correct; veterinary inspection and sampling, on the other hand, were carried out at different frequencies according to the type of product and country of origin, as established by European Community legislation and the PIF monitoring plan. Following 2012 controls, 178 non-compliant batches of animal-origin food were reported and three non-compliant batches of live animals; in 2013, there were 224 non-compliant batches of animal-origin food and three of live animals. These irregularities were mainly document-related and, to a lesser extent, laboratory and other cause-related, such as, for example, poor preservation, organoleptic alterations, parasites, moulds, etc. As concerns the UVAC, in 2012, 1,555,952 batches were pre-notified (+11.9% compared with 2011) and 1,665,159 batches in 2013 (+7% on 2012). Following controls ordered at destination by the UVAC, 97 non-conformities were noted in 2012 and 130 in 2013. A considerable portion of these unfavourable outcomes were caused by the presence of *Listeria monocytogenes*, *Escherichia coli*, mercury and carbon monoxide in fishing products and salmonella in meat.

Keywords Imports, intra-Community trade, PIF, Veterinary Offices for Compliance with European Union Obligations (UVAC)

7.8. Import of non-animal origin products, plant-origin product hygiene and fungi

Import of non-animal origin products. The Offices of Maritime, Aerial and Frontier Health (USMAF) carry out official controls on the imports from third party countries of non-animal origin foods and materials intended to come into contact with foods (MOCA).

During the first half of 2014, it is expected that this will be operative in all peripheral structures of the Customs Point, aiming to simplify imports, mainly by telematic means. Controls are carried out by the physician at the port/airport and/or by technical staff, always with the medical supervision of the port/airport.

More specifically, in 2013, 127,187 batches were controlled, of which 68% food, and 5,067 samples were taken with 361 rejections.

Hygiene of plant-origin products and fungi. "General food hygiene" is the sector of food safety that lays down rules and requirements applicable horizontally to all food productions, whether or animal origin or plant origin, and which constitutes the basis on which specific rules then apply, enabling suitable food safety and quality to be assured: safe food.

In 2013, a particular epidemic was seen, deriving from the presence of the hepatitis A vi-

rus in various lots of frozen fruits of the forest coming from Poland. A specific working party was established, involving not only the DGISAN, but also the ISS and IZSLER.
The examination and validation of correct practice manuals continued, as prepared by food industry operators, in accordance with Regulation (EC) n. 852/2004, and which proved to be a useful tool by which to implement, on the level of the individual businesses, the standards of hygiene in the production and marketing of food, enabling the competent authorities to verify their application, considering the unique nature of each business applying the manual. To date, 29 manuals have been validated.
As concerns controls on fungi, the sector legislation is currently being updated by the technical commission appointed by the Ministry. The USMAF monitor health and hygiene on batches of fresh, dried and preserved wild and farmed mushrooms coming from third party countries, as long as they are acknowledged as being edible by the competent authority of the country of origin or legally marketed in Italy, using the territorially competent mycological inspectorate that carries out sample checks on the batches marketed.

Keywords Controls at import, correct practice manuals, fungi

7.9. Health and safety of animal-origin foods

The official controls aim to verify compliance with the food safety criteria established by European or national legislation. For 2012, official controls relating to all stages of production, processing and distribution were found, as a whole, to be fit for the achievement of the objectives pursuant to Regulation (EC) n. 178/2002, art. 17 and Regulation (EC) n. 882/2004 and the provisions on animal welfare and health.
Throughout national territory, a total of 222,772 accesses were gained to facilities of animal-origin food, for which requirements are laid down in accordance with Annex III to Regulation (EC) n. 853/2004. In 2012, throughout national territory, as for 2011, the highest number of non-conformities were recorded with regards to structural conditions and equipment (6,744). The lowest number, as in 2011, was seen for the management of by-products and specifically at-risk materials (1,352). An evaluation of the data reveals that the level of attention paid by the official control for 2012 is greater with regards to the following sectors: butchering of red meats (n. accesses 76,967), meat-based products (41,690 accesses) and dairy-cheese-making (35,149 accesses). A comparison drawn with the two previous years for audits of individual operators in the food sector (FSOs) shows, for 2012, an increased level of audit for all facility types.
The search for residual chemical substances in the farming of productive livestock and during the first processing of animal-origin products (National Residues Plan) saw 40,614 random specific samples taken, of which 15,202 to search for category A substances (unauthorised, anabolising effect substances) and 25,412 to search for category B substances (pharmacologically active substances and environmental contaminants).

7.10. Food safety of dietary supplements, novel food and food with vitamin and mineral supplements

In 2012-2013, the Ministry continued its controls aimed at ascertaining the compliance with specific legislation of dietary supplement products pursuant to Italian Decree-Law n. 169/2004 and foods with vitamin and mineral supplements, pursuant to Regulation 1925/2006.
These years also saw an update of the Guidelines to vitamin and mineral supplements that can be used in dietary supplements, in accordance with the latest scientific knowledge, to guarantee the maximum level of protection for consumers. The intervention of the Ministry is very important, as to date, there is no European definition of standardised supplements, despite the constant, active commitment and work of the dedicated European Community groups.
Moreover, Ministerial Decree of 9 July 2012 has been adopted on the use of plants and derivatives able to be used in supplements, to achieve a standardisation also on the use of plants and parts thereof.
In 2013, the objective was achieved of having a monthly update of the Register of dietary