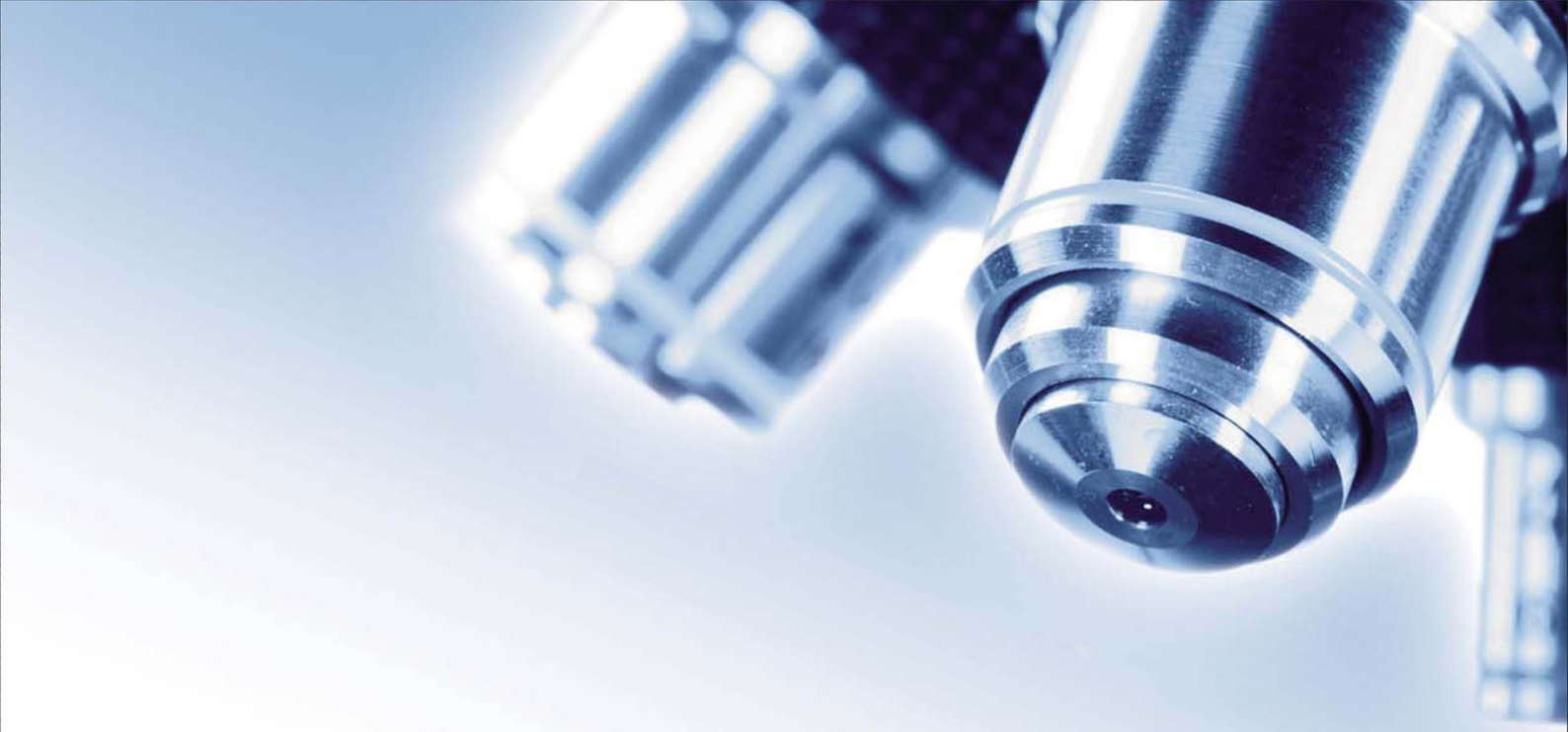

CLINICAL TRIALS OF DRUGS IN ITALY

14th National Report 2015

Agenzia Italiana del Farmaco
AIFA

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CLINICAL TRIALS OF DRUGS IN ITALY

14th National Report
Year 2015

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Italian Medicines Agency

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Data sources

Research and Clinical Trial Unit

EudraCT (European Clinical Trials Database)

Farmindustria (Pharmaceutical Companies Association)

OsMed (Medicines Utilization Monitoring Centre)

14th National Report

data from 1st January to 31st December 2014

available on the Portal of the Italian Medicines Agency

http://www.agenziafarmaco.gov.it/it/content/pubblicazioni

AIFA

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Introduction

As in previous years, the final section of the National Report on clinical trials concerns the legislation updating. Only one provision has been introduced in 2014, the year this report refers to. Nevertheless, the importance of this measure at a national and international level, not only in Europe, is likely to be reflected on the entire report and the entire Italian research system with an impact that will be perhaps even greater than the one subsequent to the Pharmacovigilance legislation introduced in 2012, at that time defined as a *tsunami*.

2014 was indeed the year of the publication and entry into force of Regulation 536/2014, which gave clear indications - in its final version - on how the clinical research will have to be reorganized in Europe and, consequently, in Italy, during the next few years. The clinical trials' evaluation at the national level will be replaced by a co-ordinated management at the European level: this will require the application of shared standards and procedures and the consequent need to rethink criteria and mechanisms currently in force in the planning and evaluation of pharmacological clinical trials. Stakeholders are already considering how to adapt their strategies and organizations to meet the requirements of the new Regulation, and also the Member States are actively working to program the necessary reorganizations nationwide. The data of the past year are therefore essential food for thought in the planning of the change to be put in place over the next two years.

The new web-based National Monitoring Centre was released in 2014: as a unique tool for managing clinical trials on drugs, in an exclusively electronic way, it places Italy in a situation similar to the one designed by the Regulation with a few years in advance. Now that we are almost sure that the Regulation will be implemented on December 2017, the setting in of the online platform from October 2014, and for the next few years, has been and will therefore be useful to make the OsSC fully operational and adequate to support the interface with the European portal at the national level. In 2014 however the OsSC has not been fully utilized, given the small number of studies uploaded, also due to the incomplete ethics committees' reorganization process. The 2014 report thus reflects a mixed management of the trials, still largely on paper, and in a transition phase with a gradual increase in the number of ethics committees validated in the OsSC itself.

Looking at the numbers, if the figures concerning 2013 had shown a general balance of Italy in the field of clinical trials compared to the rest of Europe, the 2014 data show even a slight upward trend, with a general recovery on the total clinical trials' number if compared to the rest of Europe, although the oscillations are small and need confirmation in future years in order to draw more definitive conclusions. A significant fact to interpret these numbers, and do not arouse much enthusiasm, is the resumption of no profit trials, which had recorded a fall in 2013 compared to 2012. The figure for 2013 seems to reflect the need for more time, for the no profit sector, to fully adapt to the new regulatory requirements and to implement the regulatory changes come into effect in 2012, resulting in the reorganization of the ethics committees system. The increase in the total number of trials may therefore reflect, at least in

part, this recovery of no profit trials, while the profit trials are substantially unchanged. This is also an important signal to think about as concerns the implementation of Regulation 536/2014, which does not provide for special rules for no profit trials. So, in this important area Sponsors and PI will have to be ready to apply the necessary adjustments with more flexibility and timing. In fact, the difficulties encountered in the implementation of the new national rules, which have resulted in a very long time, and well beyond the deadlines laid down for the ethics committees reorganization, raise fears on the fact that similar reaction times will be necessary to adapt the system to the new rules introduced by Regulation 536/2014, even more stringent and that will impact on an even greater degree on the current national organization.

The reorganization will also rely on improvements in the clinical trials management, as a timely approval will have to be followed by an equally rapid activation of clinical trials; this is however a result that can only be assessed by measuring in the coming years the incidence of the international multi-center trials, very sensitive to the efficiency of the system they necessarily interact with.

The OsSC's progressive activation led us this year to introduce changes in the report, that will be developed and completed, to give factual information on clinical trials.

It should first be clarified that data on trials submitted do not match that of the trials evaluated, being the process of evaluation and authorization an on-going process over different years. The 723 clinical trials submitted in 2014 were not all completed within the same year and a part of them has been assessed in 2015.

The data statistical analysis, however, concentrated on the total of the trials ended in 2014, part of which had probably been submitted at the end of 2013, since trials evaluated are those who actually have begun in the year under review.

The total number of them, if compared to 2013, records a slight increase, statistically not significant: if we cannot talk of a real raise, we are at least allowed to confirm the endurance of the entire system. We are still far from the average values of the years 2010 to 2012, although the increasing percentage out of the European total is interesting, which is the highest in the last five years.

Looking at the data in detail, there is a congruent and progressive shifting in the percentage of the type of drugs involved, which is a sign of the significant changes planned for the coming years in the drug development: the percentage of biological/biotechnological drugs and drugs combining chemical and biological active ingredients remains essentially stable, while ATIMP trials have almost doubled. Innovative new drugs and breakthrough therapies are appearing, raising high expectations also in patients, more and more updated on developments in drug research. It is therefore important to continue to support the research system in Italy, which allows broader and early access to innovative therapies, especially in the context of widespread access to information that, in the absence of alternatives with a sufficient degree of effectiveness and safety, risks to lead only to an increase in requests for access to treatments through accelerated paths for diseases currently incurable. These shortcuts are

dangerous as indiscriminately directed to access to drugs that have not yet proven efficacy and safety, forgetting the essential role of research to prove indeed efficacy and safety, and undermining the conduct of a proper audit process; moreover, if exaggerated and caused by deficiencies in the system of pharmacological research in Italy, they would lead to a progressive exclusion of our country from clinical trials and to a reduced possibility of controlled access to new drugs in clinical trials. In 2014, too, most trials were conducted on patients, a fact that strongly supports the role of clinical trials as an important hope of treatment for Italians patients.

In fact, the upward trend of phase I and II clinical trials continues if considered together, and the figure for phase III trials remains constant, while for phase IV trials slightly decreases. The sum of phase I and II trials, however, exceeds the total figure of phase III trials (46.8% and 43.6% respectively for authorized trials): this figure could further confirm the trend of moving towards clinical trials on developing drugs, potentially innovative. This finding is also reflected by the high number of not controlled trials (35.8%), distinctive feature of exploratory phase I and II studies.

As anticipated, there was an increase in no profit trials (5% more than in 2013). Mono-centre trials also rose, even if 4% of them are international.

About a third of the studies is on biological/biotechnological active ingredients and ATIMP trials double from 1 to 2%.

In the field of rare diseases, trials relating to the stages of drug development are significantly more numerous than those of phase IV, as expected, while it is interesting to see how profit studies are in total 75% of the trials on rare diseases: this gives hope in the possible increase in registration applications for targeted drugs to treat such diseases.

Examining trials by therapeutic category, it is very interesting to see how the percentages for therapeutic class are significantly different compared to expenditure data for the same therapeutic classes. Expenses for antineoplastic and immunomodulating agents are now at 28.9%, while almost half of the trials submitted (47%) concern this class; percentages related to blood and blood-forming organs studies are double compared to data on the percentage of pharmaceutical expenditure. The cardiovascular system has a percentage expenditure 6 times higher than the percentage of clinical trials in this category; percentage expenditure for alimentary tract and anti-infective drugs is double if compared to the one of the relevant clinical trials. And after the oncology and hemato-oncology trials category, the first therapeutic class for the total amount of studies is that on the nervous system and not that on the cardiovascular system, unlike the ranking on expenditure.

These data prove therefore that pharmacological research is always oriented towards areas where effective treatments still need to be found. In conclusion, all data confirm the need to continue working to strengthen the positive signals, avoiding the risk of freezing factors that negatively impact on clinical trials and that always involve the risk of triggering a vicious circle, issuing in a contraction of investments and developments in the sector that has been most active in the Italian economy panorama. For this reason it is important to start from the

encouraging data of this report and plan a renovation and a reorganization of the ethics committees and experimental sites, adapted to the new demands and complexity required. Italy is in fact the third European country for pharmaceutical expenditure, and it would be logical to expect that investments in research could reach similar proportions and honor the scientific and health prominent personalities of our country during the next few years. AIFA is already engaged in the forefront and will continue to implement all the measures within its competence to ensure maximum support to clinical research, according to the mission it has pursued since its establishment.

Overview

Table 1

Global pharmaceutical markets – 2014

Countries	Ex factory values (million EUR)	%
USA	284,933	*42.0*
Japan	59,356	*8.7*
EU Big countries	**119,468**	***17.6***
Germany	33,873	*5.0*
France	29,504	*4.3*
Italy	**21,459**	***3.2***
United Kingdom	18,835	*2.8*
Spain	15,798	*2.3*
BRIC countries	**88,407**	***13.0***
China	53,441	*7.9*
Brazil	17,980	*2.6*
India	9,255	*1.4*
Russia	7,732	*1.1*
Canada	15,702	*2.3*
Australia	9,125	*1.3*
Venezuela	6,903	*1.0*
South Korea	6,082	*0.9*
Mexico	5,624	*0.8*
Turkey	5,597	*0.8*
Polonia	5,239	*0.8*
Belgium	4,501	*0.7*
Switzerland	4,196	*0.6*
Argentina	3,950	*0.6*
Sweden	3,434	*0.5*
Austria	3,365	*0.5*
Portugal	2,851	*0.4*
Taiwan	2,649	*0.4*
Romania	2,613	*0.4*
Other countries	45,170	*6.7*
World Total	**679,165**	***100.0***

Source: elaboration of Farmindustria data ("Indicatori Farmaceutici", July 2015)

Table 2

Public pharmaceutical expenses per therapeutic classification – 2014

Therapeutic classification – ATC 1st level		Class A NHS (million EUR)	Public health structures purchases (million EUR)	Total public pharmaceutical expenses (million EUR)	%
L	Antineoplastic and immunomodulating agents	252	3,647	3,899	*19.5*
C	Cardiovascular system	3,423	208	3,631	*18.2*
A	Alimentary tract and metabolism	1,988	602	2,590	*13.0*
J	General anti-infectives for systemic use	887	1,573	2,460	*12.3*
B	Blood and blood forming organs	548	1,322	1,870	*9.4*
N	Nervous system	1,396	473	1,869	*9.4*
R	Respiratory system	1,044	60	1,104	*5.5*
V	Various	66	514	580	*2.9*
G	Genito urinary system and sex hormones	421	112	533	*2.7*
M	Musculo-skeletal system	452	54	506	*2.5*
H	Systemic hormonal preparations, excluding sex hormones and insulins	191	297	488	*2.4*
S	Sensory organs	223	110	333	*1.7*
D	Dermatologicals	60	22	82	*0.4*
P	Antiparasitic products, insecticides and repellents	13	1	14	*0.1*
	Total	**10,964**	**8,995**	**19,959**	***100.0***

Source: elaboration of OsMed data
("National Report on Medicines use in Italy" Year 2014. Rome, Italian Medicines Agency, 2015)

Clinical trials

Table 3

Clinical trials submitted in 2014 per outcome and phase

CT submitted: 723

Outcome	Phase I		Phase II		Phase III		Phase IV		Bioeq / Bioav		Total	
	CT	%	CT	%	CT	%	CT	%	CT	%	CT	%
Authorisation	48	*9.7*	187	*37.9*	215	*43.5*	43	*8.7*	1	*0.2*	**494**	***100.0***
Refusal	1	*1.8*	24	*42.9*	23	*41.1*	8	*14.3*	0	*0.0*	**56**	***100.0***
Withdrawal	2	*22.2*	5	*55.6*	1	*11.1*	1	*11.1*	0	*0.0*	**9**	***100.0***
Expiration	0	*0.0*	0	*0.0*	0	*0.0*	4	*100.0*	0	*0.0*	**4**	***100.0***
Interruption	0	*0.0*	3	*100.0*	0	*0.0*	0	*0.0*	0	*0.0*	**3**	***100.0***
In progress	12	*7.6*	51	*32.5*	70	*44.6*	23	*14.6*	1	*0.6*	**157**	***100.0***
Total	**63**	***8.7***	**270**	***37.3***	**309**	***42.7***	**79**	***10.9***	**2**	***0.3***	**723**	***100.0***

Table 4

Clinical trials ended in 2014 per outcome

Reviewed CT: 682

Outcome	2014	
	CT	%
Authorisation	592	*86.8*
Refusal	73	*10.7*
Withdrawal	11	*1.6*
Expiration	6	*0.9*
Total	**682**	***100.0***

Chart A

Clinical trials ended in 2014 per outcome
Reviewed CT: 682

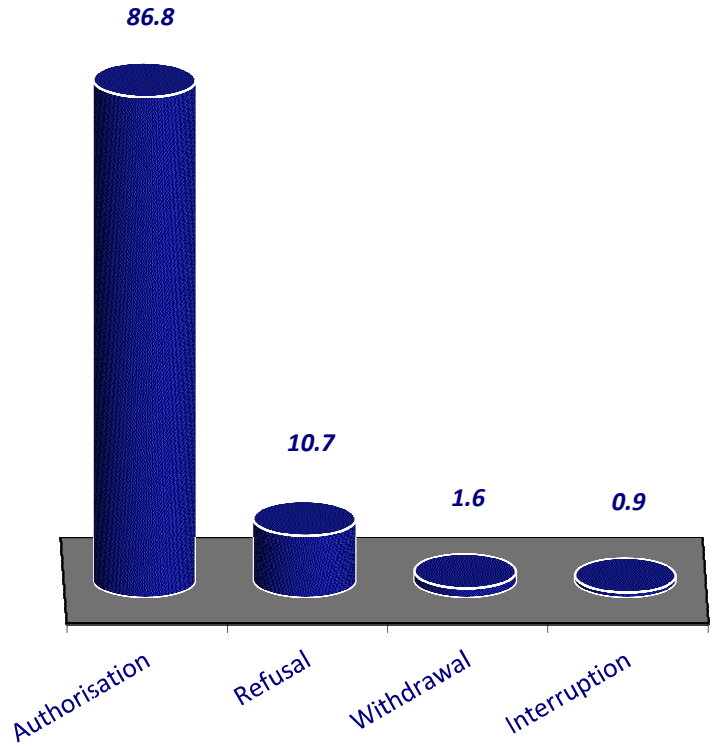

Table 5

Clinical trials ended in 2014 per outcome and phase
Reviewed CT: 682

Outcome	Phase I		Phase II		Phase III		Phase IV		Bioeq / Bioav		Total	
	CT	%	CT	%	CT	%	CT	%	CT	%	CT	%
Authorisation	60	*10.1*	217	*36.7*	258	*43.6*	56	*9.5*	1	*0.2*	**592**	***100.0***
Refusal	2	*2.7*	30	*41.1*	31	*42.5*	9	*12.3*	1	*1.4*	**73**	***100.0***
Withdrawal	2	*18.2*	7	*63.6*	1	*9.1*	1	*9.1*	0	*0.0*	**11**	***100.0***
Expiration	1	*16.7*	0	*0.0*	0	*0.0*	5	*83.3*	0	*0.0*	**6**	***100.0***
Total	**65**	***9.5***	**254**	***37.2***	**290**	***42.5***	**71**	***10.4***	**2**	***0.3***	**682**	***100.0***

Table 6

Clinical trials with favourable opinion issued by the Competent Authority

(favourable single opinion issued by the coordinating centre's EC between 1st January 2000 and 31st December 2012, entered in the OsSC, and authorization issued by AIFA since 2013)

Year	CT
2000	557
2001	605
2002	560
2003	568
2004	624
2005	664
2006	778
2007	796
2008	880
2009	761
2010	670
2011	676
2012	697
2013	583
2014	592
Total	**10,011**

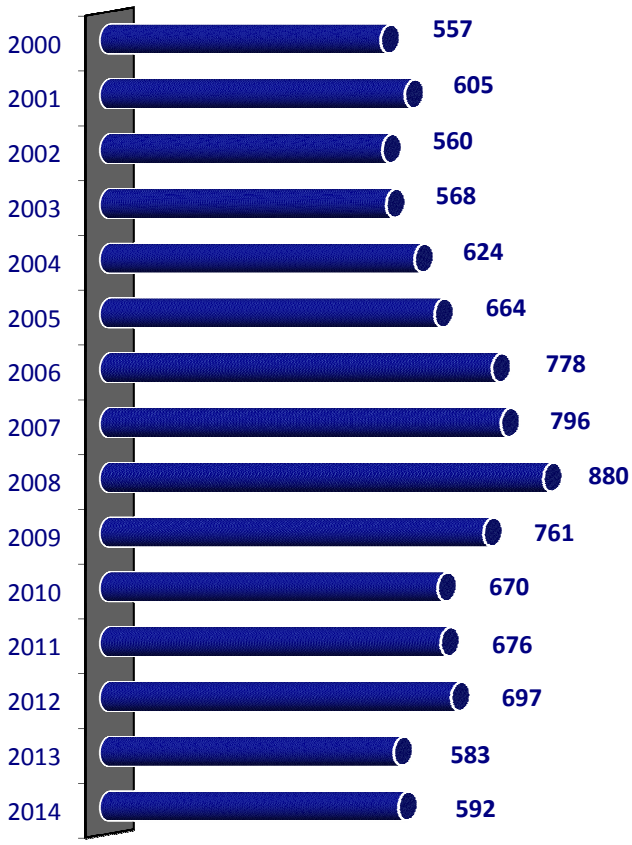

Table 7

Clinical trials per year: comparison EU – Italy

(last five years)

Year	CT in EU *	CT in Italy **	*% Italy / EU*
2010	4,153	670	*16.1*
2011	4,127	676	*16.4*
2012	3,943	697	*17.7*
2013	3,383	583	*17.2*
2014	3,249	592	*18.2*

* number of trials registered in EudraCT

** number of trials authorised by the Competent Authority

The number of clinical trials in the EU was derived from statistics published on the EudraCT site ("EudraCT supporting documentation" – "EudraCT statistics", *https://eudract.ema.europa.eu/document.html*). The number of clinical trials performed in Italy derives from Table 6.

Table 8

Clinical trials per year and phase
Total CT: 3,218 (last five years)

Year	Phase I		Phase II		Phase III		Phase IV		Bioeq / Bioav		Total	
	CT	%	CT	%	CT	%	CT	%	CT	%	CT	%
2010	53	*7.9*	250	*37.3*	283	*42.2*	79	*11.8*	5	*0.7*	**670**	***100.0***
2011	46	*6.8*	261	*38.6*	284	*42.0*	82	*12.1*	3	*0.4*	**676**	***100.0***
2012	41	*5.9*	258	*37.0*	308	*44.2*	87	*12.5*	3	*0.4*	**697**	***100.0***
2013	68	*11.7*	192	*32.9*	267	*45.8*	55	*9.4*	1	*0.2*	**583**	***100.0***
2014	60	*10.1*	217	*36.7*	258	*43.6*	56	*9.5*	1	*0.2*	**592**	***100.0***
Total	**268**	***8.3***	**1,178**	***36.6***	**1,400**	***43.5***	**359**	***11.2***	**13**	***0.4***	**3,218**	***100.0***

Chart B

Clinical trials per year and phase
Total CT: 3,218 (last five years)

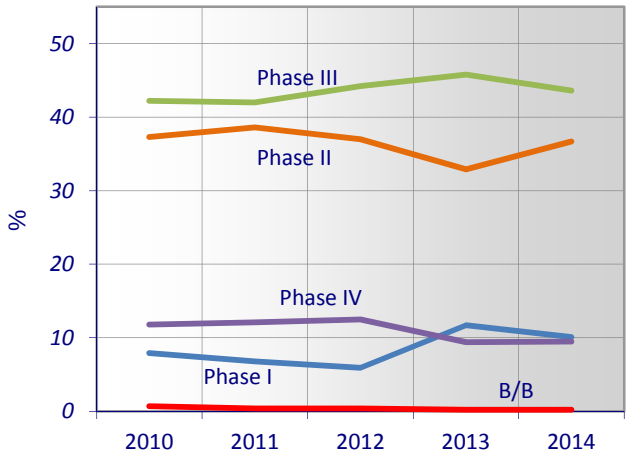

Chart C

Clinical trials per year and typology: mono-centre / multi-centre
Total CT: 3,218 (last five years)

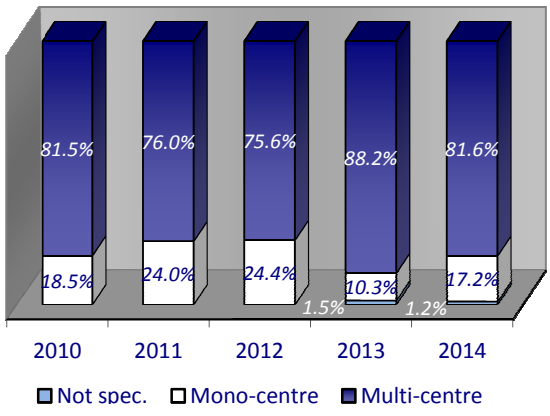

Chart D

Mono-centre and multi-centre clinical trials, national and international
CT authorised in 2014: 592

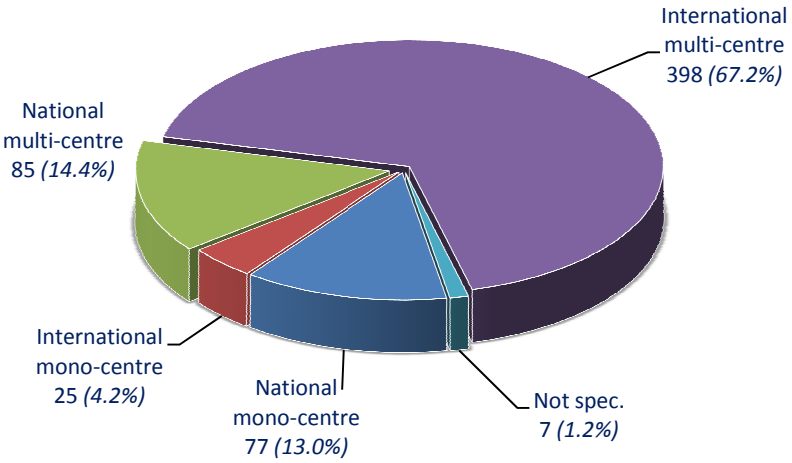

Chart D bis

Mono-centre and multi-centre clinical trials, national and international
CT NOT authorised in 2014: 90
(refusal, withdrawal, expiration)

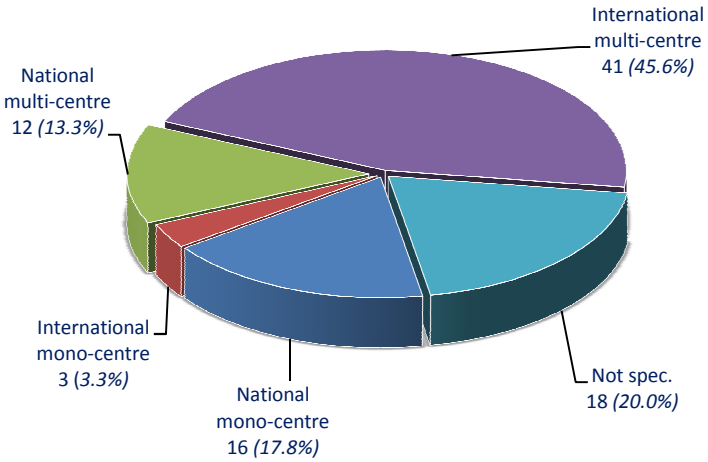

Chart E

Mono-centre and multi-centre national clinical trials
National CT authorised in 2014: 162

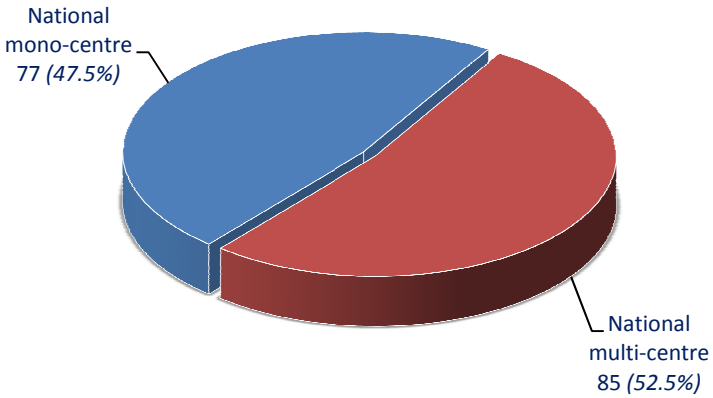

Chart E bis

Mono-centre and multi-centre national clinical trials
National CT NOT authorised in 2014: 28
(refusal, withdrawal, expiration)

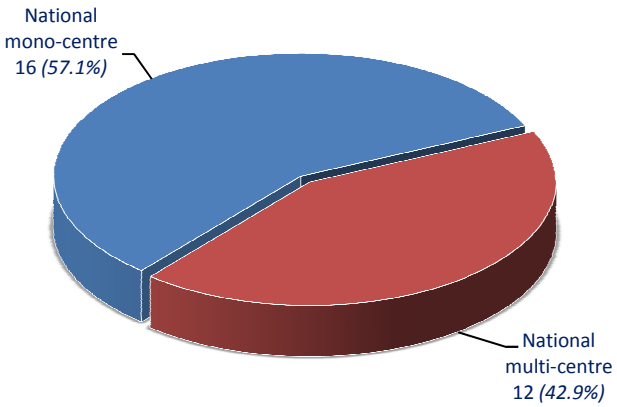

Table 9

Clinical trials per study population typology
CT authorised in 2014: 592

Typology	2014	
	CT	%
Patients	570	*96.3*
Healthy volunteers	9	*1.5*
Patients & healthy volunteers	6	*1.0*
Not specified	7	*1.2*
Total	**592**	***100.0***

Table 10

Clinical trials per study population typology and phase
CT authorised in 2014: 592

Typology	Phase I		Phase II		Phase III		Phase IV		Bioeq / Bioav		Total	
	CT	%	CT	%	CT	%	CT	%	CT	%	CT	%
Patients	54	*9.5*	215	*37.7*	250	*43.9*	51	*8.9*	0	*0.0*	**570**	***100.0***
Healthy volunteers	2	*22.2*	2	*22.2*	4	*44.4*	0	*0.0*	1	*11.1*	**9**	***100.0***
Patients & healthy volunteers	0	*0.0*	0	*0.0*	2	*33.3*	4	*66.7*	0	*0.0*	**6**	***100.0***
Not specified	4	*57.1*	0	*0.0*	2	*28.6*	1	*14.3*	0	*0.0*	**7**	***100.0***
Total	**60**	***10.1***	**217**	***36.7***	**258**	***43.6***	**56**	***9.5***	**1**	***0.2***	**592**	***100.0***

Table 11

Clinical trials per study population gender
CT authorised in 2014: 592

Gender	2014	
	CT	%
Females & males	513	*86.7*
Females	46	*7.8*
Males	28	*4.7*
Not specified	5	*0.8*
Total	**592**	***100.0***

Table 12

Clinical trials per study population gender and phase
CT authorised in 2014: 592

Gender	Phase I		Phase II		Phase III		Phase IV		Bioeq / Bioav		Total	
	CT	%	CT	%	CT	%	CT	%	CT	%	CT	%
Females & males	48	*9.4*	187	*36.5*	229	*44.6*	48	*9.4*	1	*0.2*	**513**	***100.0***
Females	6	*13.0*	18	*39.1*	18	*39.1*	4	*8.7*	0	*0.0*	**46**	***100.0***
Males	2	*7.1*	12	*42.9*	10	*35.7*	4	*14.3*	0	*0.0*	**28**	***100.0***
Not specified	4	*80.0*	0	*0.0*	1	*20.0*	0	*0.0*	0	*0.0*	**5**	***100.0***
Total	**60**	***10.1***	**217**	***36.7***	**258**	***43.6***	**56**	***9.5***	**1**	***0.2***	**592**	***100.0***

Table 13

Clinical trials per forecast age group
CT authorised in 2014: 592

Age group	2014	
	CT	%
Adults (18-64 years of age)	521	*88.0*
OAPs (>= 65 years of age)	457	*77.2*
Minors (< 18 years of age)	82	*13.9*

Enrolled subjects could fall into more than one age group; therefore the same trial may be counted more than once.

Table 14

Clinical trials per therapeutic area
CT authorised in 2014: 592

Therapeutic area	2014	
	CT	%
Neoplasms	230	*38.9*
Nervous system diseases	41	*6.9*
Cardiovascular diseases	38	*6.4*
Hemic and lymphatic diseases	36	*6.1*
Respiratory tract diseases	23	*3.9*
Immune system diseases	21	*3.5*
Virus diseases	21	*3.5*
Musculo-skeletal diseases	19	*3.2*
Nutritional and metabolic diseases	17	*2.9*
Neonatal diseases and abnormalities	14	*2.4*
Skin and connective tissue diseases	14	*2.4*
Bacterial infections and mycoses	13	*2.2*
Digestive system diseases	13	*2.2*
Endocrine system diseases	10	*1.7*
Anesthesia and analgesia	8	*1.4*
Mental disorders	8	*1.4*
Immune system phenomena	8	*1.4*
Eye diseases	6	*1.0*
Metabolic phenomena	5	*0.8*
Female urogenital diseases and pregnancy complications	5	*0.8*
Pathological conditions, signs and symptoms	5	*0.8*
Genetic phenomena	3	*0.5*
Surgical procedures, operative	3	*0.5*
Musculoskeletal and neural physiological phenomena	3	*0.5*
Digestive system and oral physiological phenomena	2	*0.3*
Male urogenital diseases	2	*0.3*
Circulatory and respiratory physiological phenomena	2	*0.3*
Ocular physiological phenomena	2	*0.3*
Not specified	11	*1.9*
Others	9	*1.5*
Total	**592**	***100.0***

Table 15

Clinical trials per drug typology
CT authorised in 2014: 592

Typology	2014	
	CT	%
Chemical active ingredient	394	*66.6*
Biological/biotechnological active ingredient	167	*28.2*
ATIMP	12	*2.0*
Chemical and biological/biotechnological active ingredient	10	*1.7*
Not specified	9	*1.5*
Total	**592**	***100.0***

Table 15 bis

Clinical trials per drug typology
CT NOT authorised in 2014: 90
(refusal, withdrawal, expiration)

Typology	2014	
	CT	%
Chemical active ingredient	56	*62.2*
Biological/biotechnological active ingredient	15	*16.7*
ATIMP	0	*0.0*
Chemical and biological/biotechnological active ingredient	1	*1.1*
Not specified	18	*20.0*
Total	**90**	***100.0***

Table 16

Clinical trials on rare diseases per phase
CT authorised in 2014: 592 of which 139 (23.5%) on rare diseases

Phase	2014		
	CT	*% on CT in rare diseases*	*% on authorised CT*
Phase III	62	*44.6*	*24.0*
Phase II	54	*38.8*	*24.9*
Phase I	20	*14.4*	*33.3*
Phase IV	3	*2.2*	*5.4*
Bioeq / Bioav	0	*0.0*	*0.0*
Total	**139**	***100.0***	

Table 17

Clinical trials on rare diseases per profit / no profit Sponsor, national and international
CT authorised in 2014: 592 of which 139 (23.5%) on rare diseases

Sponsor typology	National		International		Total	
	CT	*%*	CT	*%*	CT	*%*
Profit	5	*20.0*	99	*86.8*	**104**	***74.8***
No profit	20	*80.0*	15	*13.2*	**35**	***25.2***
Total	**25**	***18.0***	**114**	***82.0***	**139**	***100.0***

Table 18

Clinical trials per therapeutic classification and phase

CT authorised in 2014: 592 of which 272 (45.9%) with ATC of at least one test drug specified

Therapeutic classification ATC 1st level		2014 CT	%	Phase I		Phase II		Phase III		Phase IV		Bioeq / Bioav	
				CT	%	CT	%	CT	%	CT	%	CT	%
L	Antineoplastic and immunomodulating agents	**136**	***46.9***	17	*12.5*	61	*44.9*	46	*33.8*	12	*8.8*	0	*0.0*
B	Blood and blood forming organs	**18**	***6.2***	0	*0.0*	4	*22.2*	10	*55.6*	4	*22.2*	0	*0.0*
N	Nervous system	**21**	***7.2***	0	*0.0*	4	*19.0*	9	*42.9*	7	*33.3*	1	*4.8*
A	Alimentary tract and metabolism	**18**	***6.2***	0	*0.0*	5	*27.8*	11	*61.1*	2	*11.1*	0	*0.0*
J	General anti-infectives for systemic use	**33**	***11.4***	0	*0.0*	8	*24.2*	19	*57.6*	6	*18.2*	0	*0.0*
H	Systemic hormonal preparations, excluding sex hormones and insulins	**14**	***4.8***	2	*14.3*	9	*64.3*	3	*21.4*	0	*0.0*	0	*0.0*
V	Various	**9**	***3.1***	0	*0.0*	2	*22.2*	5	*55.6*	2	*22.2*	0	*0.0*
M	Musculo-skeletal system	**5**	***1.7***	1	*20.0*	2	*40.0*	2	*40.0*	0	*0.0*	0	*0.0*
R	Respiratory system	**5**	***1.7***	0	*0.0*	1	*20.0*	3	*60.0*	1	*20.0*	0	*0.0*
C	Cardiovascular system	**10**	***3.4***	0	*0.0*	3	*30.0*	5	*50.0*	2	*20.0*	0	*0.0*
D	Dermatologicals	**3**	***1.0***	0	*0.0*	0	*0.0*	1	*33.3*	2	*66.7*	0	*0.0*
G	Genito urinary system and sex hormones	**9**	***3.1***	0	*0.0*	1	*11.1*	5	*55.6*	3	*33.3*	0	*0.0*
S	Sensory organs	**8**	***2.8***	0	*0.0*	4	*50.0*	2	*25.0*	2	*25.0*	0	*0.0*
P	Antiparasitic products, insecticides and repellents	**1**	***0.3***	0	*0.0*	1	*100.0*	0	*0.0*	0	*0.0*	0	*0.0*
	Total	**290**	***100.0***	**20**	***6.9***	**105**	***36.2***	**121**	***41.7***	**43**	***14.8***	**1**	***0.3***

The same clinical trial can involve more than one test drug and therefore shall be counted in more than one ATC classification.

Table 19

Clinical trials per year and profit / no profit Sponsor
Total CT: 3,218 (last five years)

Year	Profit		No profit		Total	
	CT	%	CT	%	CT	%
2010	431	*64.3*	239	*35.7*	**670**	***100.0***
2011	441	*65.2*	235	*34.8*	**676**	***100.0***
2012	472	*67.7*	225	*32.3*	**697**	***100.0***
2013	444	*76.2*	139	*23.8*	**583**	***100.0***
2014	424	*71.6*	168	*28.4*	**592**	***100.0***
Total	**2,212**	***68.7***	**1,006**	***31.3***	**3,218**	***100.0***

Chart F

Clinical trials per year and profit / no profit Sponsor
Total CT: 3,218 (last five years)

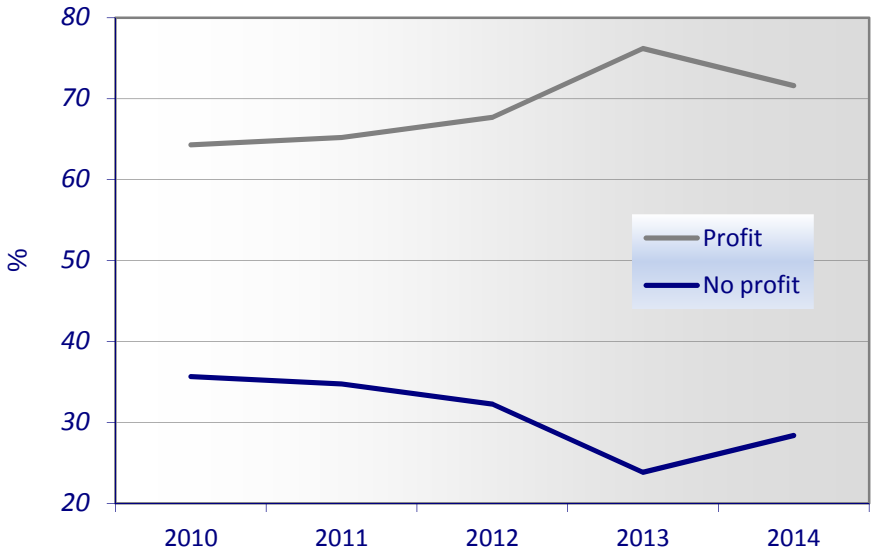

Table 20

Clinical trials per design
CT authorised in 2014: 592

Design	2014	
	CT	%
Controlled	375	*63.3*
Not controlled	212	*35.8*
Not specified	5	*0.8*
Total	**592**	***100.0***

Table 21

Clinical trials per design – details
CT authorised in 2014: 592

Design – details	2014	
	CT	%
Randomised	376	*63.5*
Not randomised	202	*34.1*
Not specified	14	*2.4*
Open	296	*49.8*
Double blind	212	*35.6*
Single blind	14	*2.4*
Not specified	70	*12.2*
Parallel groups	263	*44.4*
Cross over	23	*3.9*
Not specified	306	*51.7*

The information concerning the clinical trial design is not univocal; therefore the same trial may be associated to more than one design.

Table 22

Clinical trials per objective
CT authorised in 2014: 592

Objective	2014	
	CT	%
Safety	531	*89.7*
Efficacy	528	*89.2*
Therapy	322	*54.4*
Pharmacokinetics	285	*48.1*
Pharmacodynamics	155	*26.2*
Pharmacogenetics	89	*15.0*
Pharmacogenomics	80	*13.5*
Dose-response studies	74	*12.5*
Prophylaxis	41	*6.9*
Pharmaco-economics	32	*5.4*
Diagnosis	9	*1.5*
Bioequivalence	1	*0.2*
Not specified	4	*0.7*

The same study could have more than one objective and therefore be counted more than once.

Table 23

Clinical trials with a Scientific Advice per outcome and phase
CT authorised in 2014: 592 of which 168 (28.4%) with a Scientific Advice

Outcome	Phase I		Phase II		Phase III		Phase IV		Bioeq / Bioav		Total	
	CT	%	CT	%	CT	%	CT	%	CT	%	CT	%
Authorisation	9	*5.8*	30	*19.4*	116	*74.8*	0	*0.0*	0	*0.0*	**155**	***100.0***
Refusal	0	*0.0*	2	*15.4*	11	*84.6*	0	*0.0*	0	*0.0*	**13**	***100.0***
Total	**9**	***5.4***	**32**	***19.0***	**127**	***75.6***	**0**	***0.0***	**0**	***0.0***	168	***100.0***

APPENDIX

Legislation & Training

Updates

List of relative legislation regarding clinical trials of drugs published in 2014

Regulation (EU) No 536/2014 of 16 April 2014 *O.J. of the European Union n. L 158 of May 27, 2014*	Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC

Conferences, Workshops and Training Courses on clinical trials on drugs organised by AIFA

2014

"Training course on the new National Monitoring Centre on clinical trials of drugs – OsSC"
AIFA, Rome

February 18-19	OsSC's contact persons of Applicants (Sponsors and CROs)
February 25-26	OsSC's contact persons of Applicants (Sponsors and CROs)
March 5	Competent Authority (AIFA)
March 11-12	OsSC's contact persons of Applicants (Sponsors and CROs)
March 17-18	OsSC's contact persons of Applicants (Sponsors and CROs)
March 25-26	OsSC's contact persons of Applicants (Sponsors and CROs)
April 8-9	OsSC's contact persons of Ethics Committees
April 14-16	OsSC's contact persons of no profit Sponsors and Ethics Committees
October 21	Competent Authority (AIFA and ISS)
November 19-20	OsSC's contact persons - various
November 24-25	OsSC's contact persons - various