Manufacture of medicinal products in Italy: challenges for the Italian Medicines Agency

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Italian Medicines Agency (AIFA)

CPhI worldwide - «Pharmaceutical CDMO»

Barcelona, Spain - 4 October 2016

Public Declaration of transparency/interests*

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

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

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

N.B. I am not receiving any compensation

Agenzia Italiana del Farmaco

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Italian Medicines Agency (AIFA)

- The Italian Medicines Agency (AIFA) was established in 2003 and it is the only national authority responsible for human drugs regulation in Italy
- AIFA is a public administration operating autonomously, transparently and according to cost-effectiveness criteria

Italian Medicines Agency - Network

- AIFA cooperates with Regional Authorities, National Institute of Health (ISS), Research Institutes, Patients' Associations, Health Professionals, Scientific Associations, Pharmaceutical Industry and with all Regulatory Authorities Worldwide

AIFA's Core Mission

- To promote and protect public health through the safe and appropriate use of pharmaceuticals
- To ensure unity of the national pharmaceutical system in agreement with Regional Authorities
- To assist innovation, efficiency and simplification of marketing authorizations, in order to grant rapid access to innovative drugs and to drugs used for rare diseases

AIFA's broader Mission

- Provide drug expenditure governance in the framework of economic and financial viability and competitiveness of the national and multinational pharmaceutical industry
- Encourage investments in R&D in Italy
- Interact with the community of patients' associations, the scientific medical world, pharmaceutical companies and distributors
- Promote pharmaceutical culture and knowledge

AIFA' s governing principles

Belonging

Responsibility

Transparency

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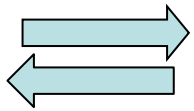
Transparency: Duty, Value and Commitment

- Trasparency, Participation and Accountability are part of the Open Government, regulated by Law
- In 2012, 2013 and 2014 AIFA was officially recognized first among Italian Public Administration with regard to compliance to legal provisions on transparency

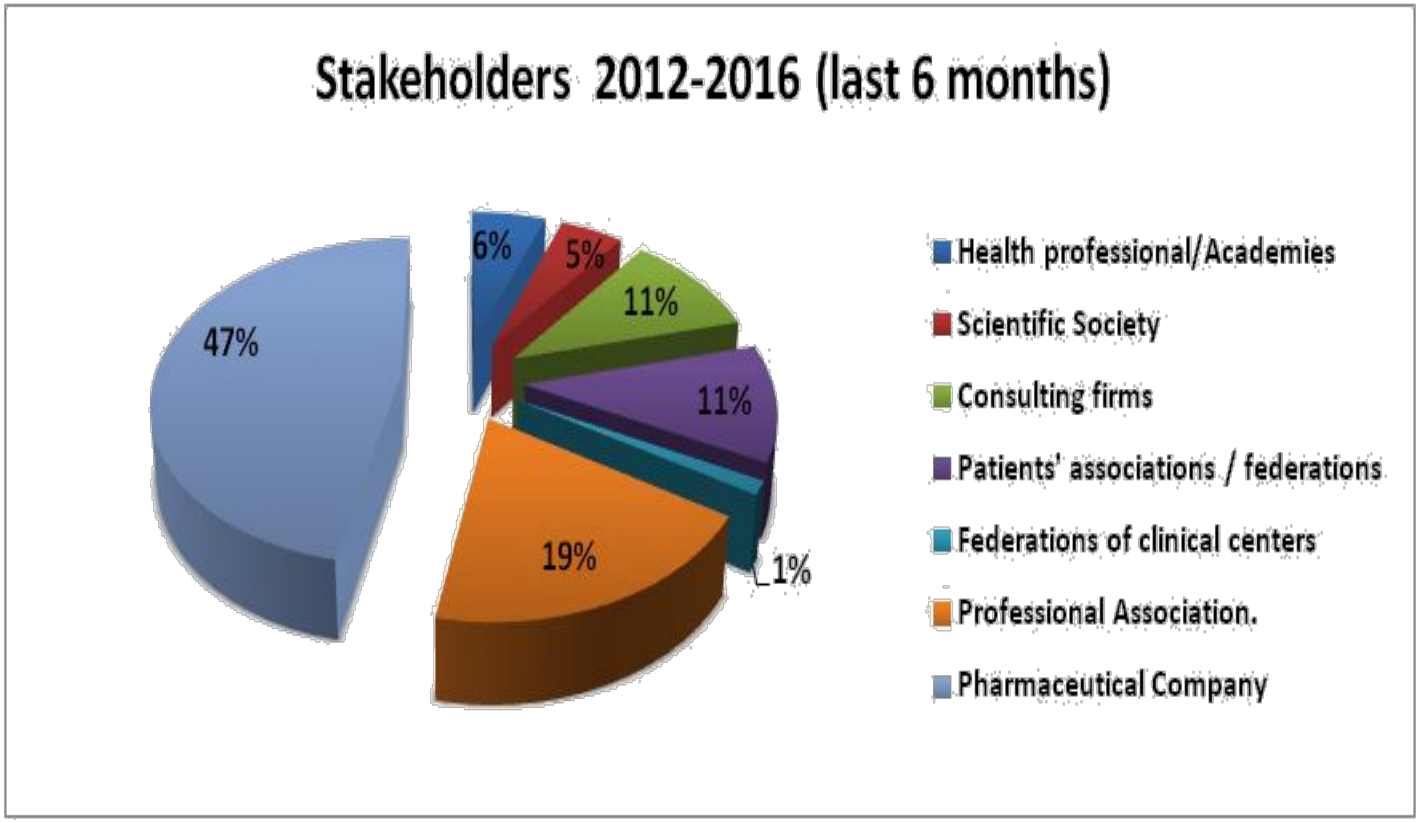
Transparency  Communication

We opened the doors

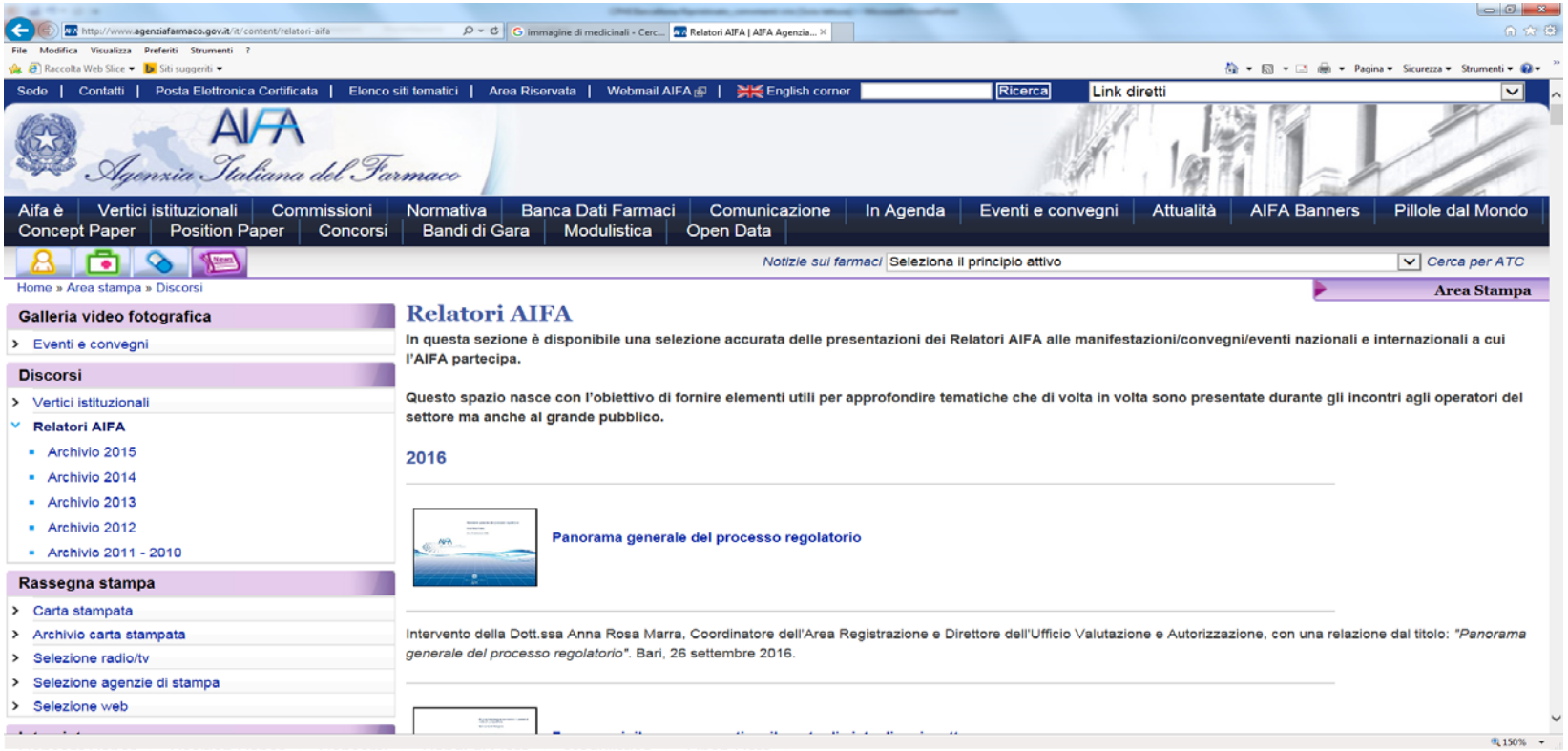
Meetings with our stakeholders with the aim to establish a direct dialogue, to optimize regulatory decision paths and to know the impact in real life

- Meetings called “OPENAIFA” managed by the Director General
- 4 years and ½ - 225 meetings - 44 dedicated days (about 112 hours)
- Since 2012 (until June 2016) AIFA met representatives of:
  - 11 scientific societies
  - 24 consulting firms
  - 26 associations/federatior
  - 3 Federations of Centres
  - 44 associations / federations
  - 107 pharmaceutical companies
  - 13 health professionals and academia

Open AIFA


Stakeholders 2012-2016 (last 6 months)
6%
5%
11%
11%
1%
19%
47%
Health professional/Academies
Scientific Society
Consulting firms
Patients' associations / federations
Federations of clinical centers
Professional Association.
Pharmaceutical Company

Participation to national/international conferences to exchange knowledge



National Scientific Advice (SAN)

- Purpose
  - Provide early scientific and regulatory support to projects under development

- Types of SAN
  - National Registration
  - GMP
  - HTA

Scientific Advice on GMP (1)

- Peculiarity of AIFA: it is the only EU Agency to provide SAN on GMP
- Due to the high presence of manufacturers in Italy and the expertise of the Agency on manufacturing operations
- Opportunity to get a early advice on new manufacturing site/new production lines/new technologies prior to investment
- Applicable both to finished products and API manufacturers
- No legally binding

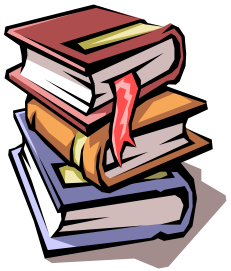
Scientific Advice on GMP (2)

- Submission before/during the development/implementation of a project to get advice regarding specific applications and interpretation of GMP topics.

- Closure (final report signed and sent to the applicant) within 90 days from signing the contract with the Agency

Consultancy Process

Briefing Document



Team of experts

Resources

Internal/external experts

Draft answer

Meeting

Minutes meeting

SA Final report

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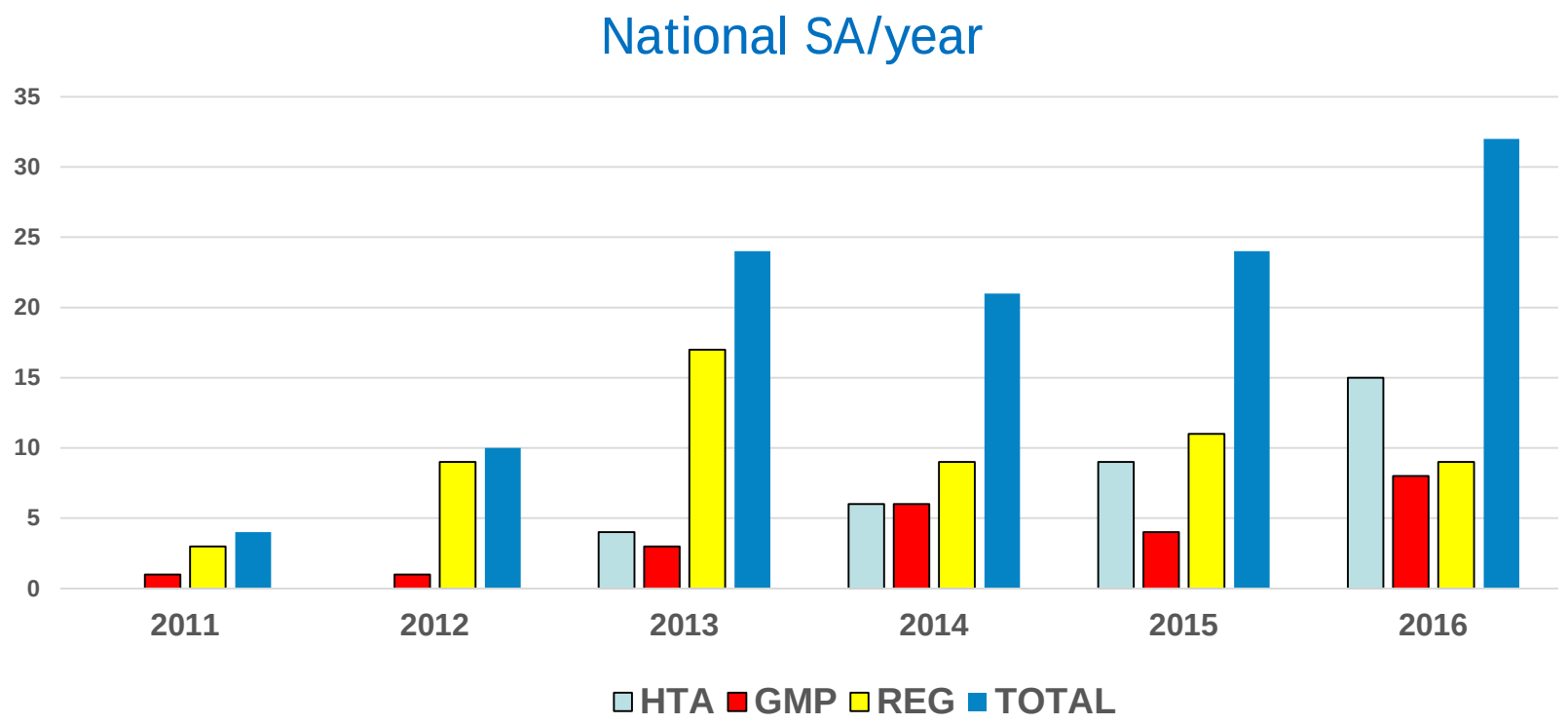
SAN Trends 2011-2016 (1)

NATIONAL SCIENTIFIC ADVICE /YEAR						
	2011	2012	2013	2014	2015	2016 (*)
HTA	0	0	4	6	9	15
GMP	1	1	3	6	4	8
REG	3	9	17	9	11	9
TOTAL	4	10	24	21	24	32

REG: referring to Regulatory SA pre-submission

(*) overall: closed and ongoing

SAN Trends 2011-2016 (2)



Manufacturing sites: some figures

- Currently authorized 567 manufacturing sites:

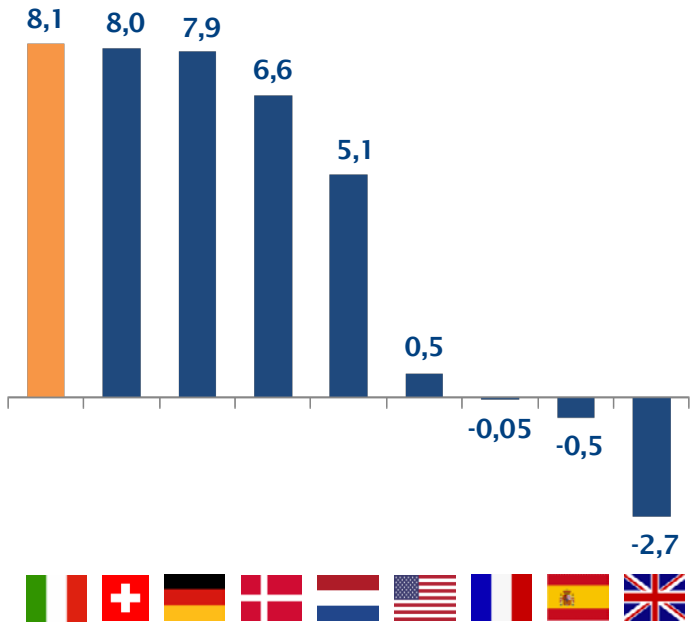
- 266: manufacture/importation of medicinal products
- 146: manufacture/importation of APIs (the figure does not include importers of APIs for captive use)
- 155: primary and secondary manufacture of medicinal gases

Market destination

- About 75% of the medicinal products manufactured in IT are exported
- More than 80 % of the active substances manufactured in IT are exported

Italian production achievement

Export of medicinal products and vaccines: 2010-2014
(billions of US dollars)



Between 2010 and 2014 the export of medicinal products and vaccines manufactured in Italy increased by 50%

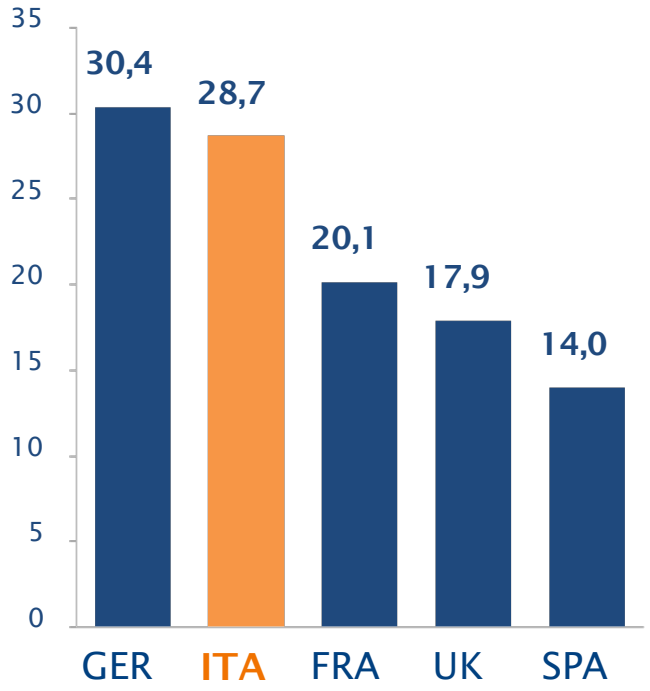
Need to be competitive in the international market

Italy can be considered as a pharmaceutical hub in Europe

Source: Farmindustria, Fondazione Edison, Data in International Trade Center

Italian production achievement

Pharmacetical production (billions of euros, 2014)



Italy is the second major manufacturer in EU in terms of absolute value

Italy is the first manufacturer in EU for pro capita production

Source: revision of Istat data, Eurostat; kindly provided by Farmindustria

CDMO

- Contract Development and Manufacturing Organizations, which perform outsourced production, increased continously in the last years
- Between 2010 and 2015 there was an increase of 24%

Currently Italy is the major country in EU for CDMO production (1,5 billion €), representing the 29% of the European CDMO full production (5,1 billions €)

Source of data: Prometeia (Consultancy & Economic Research), Report of February 2016; kindly provided by Farmindustria

CDMO: excellence of the Italian production

	1.5 bil. €
	1.2 bil.€
	1.0 bil. €

Source of data: Prometeia (Consultancy & Economic Research), Report of February 2016; kindly provided by Farmindustria

Forecasts

- A positive trend is foreseen for the next 5 years
- Investments are essential and maintanance of high standards in production will be crucial
- Services provided will have a growing impact

⇨

Efficiency of regulatory procedures will be of paramount importance, alongside with maintenance of a high level of control, in order to guarantee quality

The challenge for AIFA

Keep quality high - Moving forward

Inspections & Certifications Department Challenges (1)

- Manufacturing Authorizations Office:

Follow-up of inspections, Manufacturing License (MIA), API authorization and registration (API REG), withdrawal/ suspension of manufacturing license, issuance of GMP certificates, issuance of CPP and CPO certificates, QP appointment

Inspections & Certifications Department Challenges (2)

- GMP Inspectorate Office (medicinal products)

Inspections of medicinals products manufacturers

- API Inspection Unit (active substances)

Inspections of API manufactures and importers

Some Figures on inspections

- > 1.000 inspections performed in the last three years

- 577 : medicinal products manufacturers
- 229 : active substance manufacturers
- 108 : non EU countries (medicinal products and active substances, EMA, EDQM and AIFA inspections)
- 152 : medicinal gas manufacturers

Manufacture Authorization Office: Improving communication

- Since December 2014:

- Establishment of a dedicated email infouao@aifa.gov.it

- 36 Clarification notices/guidances published on the website http://www.agenziafarmaco.gov.it/it/content/ispezioni

- 55 Meetings with Companies and Associations

Improving efficiency

- Full revision of templates to be used to submit requests (extension of the authorizations, major and minor changes, registration of API importation etc.) http://www.agenziafarmaco.gov.it/it/content/modulistica-autorizzazioni-officine

- Template for early notification of revamping/new production lines

- Full revision of the Inspections & Certification Dept. Quality system

Improving simplification

- New procedures for internal processing of the regulatory burden, with the aim to simplify and speed up the issuance of manufacturing authorizations

- Revision of the «Rules for classification of major and minor changes» of manufacturing facilities, by using historical data and experience to establish a classification mostly based on risk evaluation

GMP Inspectorate: participation to the network

- Participation to the EMA GMDP - IWG
- Participation to the EMA GMP Compliance Group
- Participation to the EMA PAT team
- Participation to the EMA WG on ATMPs
- Participation on EMA WG on shortages due to manufacturing issues

GMP Inspectorate: PIC/Sparticipation (1)

- Participation to the PIC/S Committee of Officials:
  - Deputy Chairmanship of the PIC/S SubCommittee on Hamonization
  - De Facto Membership of the SubCommittee on Expert Circles
  - Chairmanship of the Coordinating Committee of PIC/S Expert Circle on Human Blood, Tissues, Cells and ATMPs
  - Participation to the PIC/S WG on Aide memoire of ATMPs

GMP Inspectorate: PIC/S participation (2)

- Participation to the PIC/S WG Working Group on Controlling Cross-Contamination in Shared Facilities (CCCISF)
- Participation to the PIC/S WG on Data Integrity
- Participation to the assessment of PIC/S appplicants

- 21th PIC/S Expert Circle on Human Blood, Tissues, Cells and ATMPs, hosted by AIFA – October 2015

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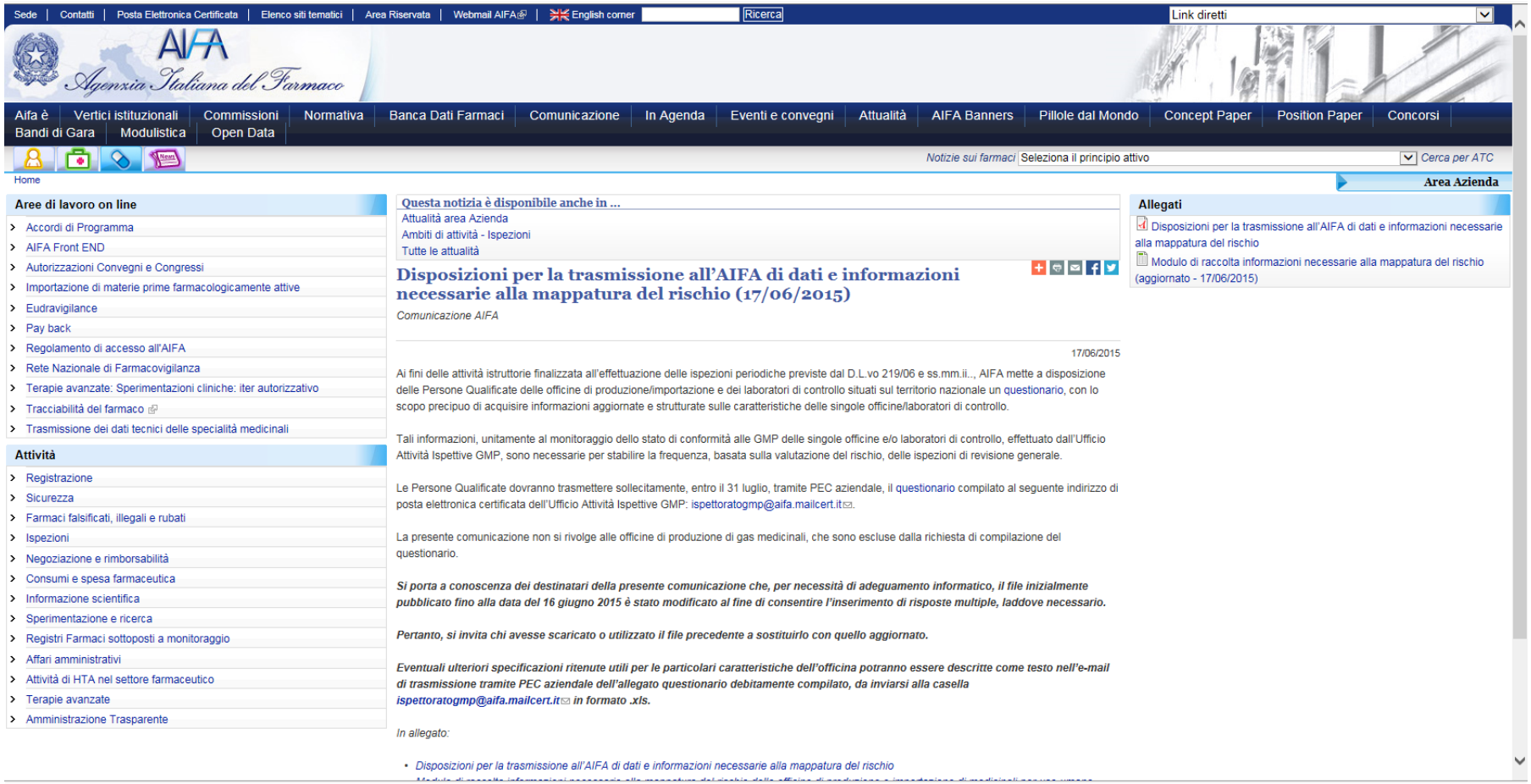
PIC/S
21st PIC/S Expert Circle Meeting
On Human Blood, Tissues, Cells & ATMPs
Rome, Italy - 26th/30th October 2015

Periodic Inspection: risk based approach for medicinal product manufacturers

- Model for a risk assessment for inspection planning of periodic inspections

- Intrinsic Risk and GMP Compliance Risk are taken into account to establish the risk rating of a site and adapt the inspection frequency accordingly

Intrinsic risk of the site



Sede | Contatti | Posta Elettronica Certificata | Elenco siti tematici | Area Riservata | Webmail AIFA | English corner | Ricerca | Link diretti

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- Importazione di materie prime farmacologicamente attive
- Eudravigilance
- Pay back
- Regolamento di accesso all'AIFA
- Rete Nazionale di Farmacovigilanza
- Terapie avanzate: Sperimentazioni cliniche: iter autorizzativo
- Tracciabilità del farmaco
- Trasmissione dei dati tecnici delle specialità medicinali

Attività

- Registrazione
- Sicurezza
- Farmaci falsificati, illegali e rubati
- Ispezioni
- Negoziazione e rimborsabilità
- Consumi e spesa farmaceutica
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Questa notizia è disponibile anche in ...

Attualità area Azienda
Ambiti di attività - Ispezioni
Tutte le attualità

Disposizioni per la trasmissione all'AIFA di dati e informazioni necessarie alla mappatura del rischio (17/06/2015)

Comunicazione AIFA

17/06/2015

Ai fini delle attività istruttorie finalizzata all'effettuazione delle ispezioni periodiche previste dal D.L.vo 219/06 e ss.mm.ii.., AIFA mette a disposizione delle Persone Qualificate delle officine di produzione/importazione e dei laboratori di controllo situati sul territorio nazionale un questionario, con lo scopo precipuo di acquisire informazioni aggiornate e strutturate sulle caratteristiche delle singole officine/laboratori di controllo.

Tali informazioni, unitamente al monitoraggio dello stato di conformità alle GMP delle singole officine e/o laboratori di controllo, effettuato dall'Ufficio Attività Ispettive GMP, sono necessarie per stabilire la frequenza, basata sulla valutazione del rischio, delle ispezioni di revisione generale.

Le Persone Qualificate dovranno trasmettere sollecitamente, entro il 31 luglio, tramite PEC aziendale, il questionario compilato al seguente indirizzo di posta elettronica certificata dell'Ufficio Attività Ispettive GMP: ispettoratogmp@aifa.mailcert.it.

La presente comunicazione non si rivolge alle officine di produzione di gas medicinali, che sono escluse dalla richiesta di compilazione del questionario.

Si porta a conoscenza dei destinatari della presente comunicazione che, per necessità di adeguamento informatico, il file inizialmente pubblicato fino alla data del 16 giugno 2015 è stato modificato al fine di consentire l'inserimento di risposte multiple, laddove necessario.

Pertanto, si invita chi avesse scaricato o utilizzato il file precedente a sostituirlo con quello aggiornato.

Eventuali ulteriori specificazioni ritenute utili per le particolari caratteristiche dell'officina potranno essere descritte come testo nell'e-mail di trasmissione tramite PEC aziendale dell'allegato questionario debitamente compilato, da inviarsi alla casella ispettoratogmp@aifa.mailcert.it in formato .xls.

In allegato:

- *Disposizioni per la trasmissione all'AIFA di dati e informazioni necessarie alla mappatura del rischio*

Allegati

Disposizioni per la trasmissione all'AIFA di dati e informazioni necessarie alla mappatura del rischio
Modulo di raccolta informazioni necessarie alla mappatura del rischio (aggiornato - 17/06/2015)

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Risk based approach: outcome

- Starting from 2016 a new risk based approach for periodic inspections planning, aiming at:

  - ✓ A dynamic system of planning
  - ✓ Optimization of available resources
  - ✓ Promoting virtuous behaviour of manufacturers

API Inspection Unit: participation to the network

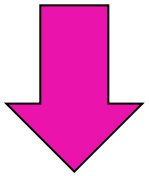
- Participation to the API International Program
- Participation to the GMDP- IWG
- Participation to the FMD task force with in the HMA, for the impact of the directive on the API importation
- Participation to the EDQM Inspection Program
- Participation to the PIC/S expert circle on API Coordinating Committee
- 6th PIC/S expert circle on API, hosted by AIFA - May 2014
- Participation to the CEP *Ad Hoc Commitee*
- ICH working group on ICH Q7 Q&A

API Periodic Inspection: risk based approach for national manufacturers

Joint Audit Program

Inspections and Certifications Dept. was audited in November 2015 from a team appointed by the European Commision to assess the compliance of the system to the Compilation of Community Procedures and legal framework

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/joint_audit_programme.jsp&mid=WC0b01ac058006e06f



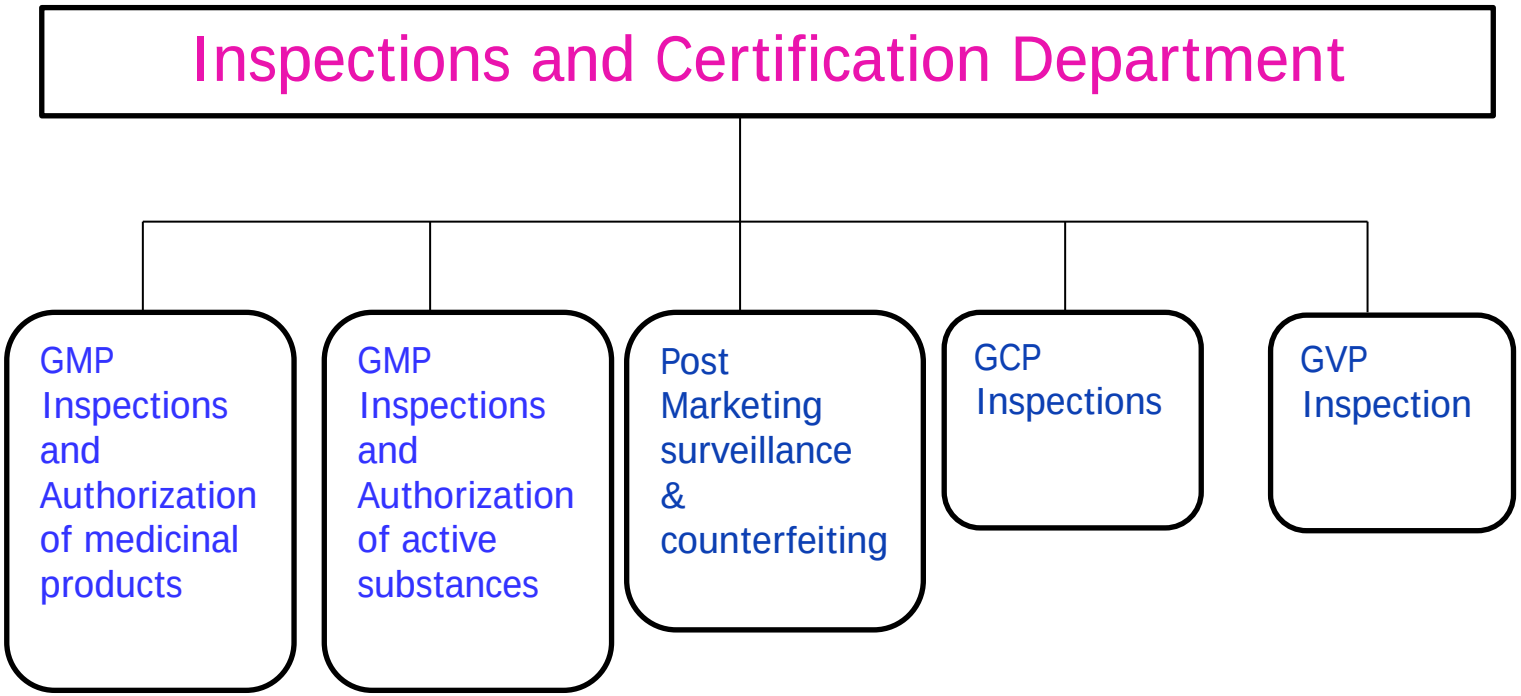
Outcome very positive: no deviations were found

New challenges and further improvements

- AIFA is under reorganization according to the new Regulation published on the Official Journal the 17th June 2016

- A new Department of Inspection and Certification is in place starting the 1st October, aiming at increasing the efficiency of the system

New Organizational Chart



Final Remarks

- The growth of the system will depend on several drivers, but the two main players will be:

➢ High quality standards and technologies adopted by the manufacturers

➢ Regulatory Governance based on:

  - Strict regulatory control
  - Effectiveness and Efficiency of the manufacturing authorizations process

Acknowledgements:

M.Delbò: Head of GMP Inspectorate
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E.Cogliandro: SAN coordinator

THANK YOU FOR YOUR ATTENTION!

CONTATTI

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