Il punto di vista dell' AIFA

Entela Xoxi

Genova, 13 febbraio 2015

I Registri come strumento per valutazioni di effectiveness
Corso di formazione sul campo a cura della sezione regionale SIFO Liguria

AIFA
Agenzia Italiana del Farmaco

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Interests in pharmaceutical industry	NO	Currently	Last 2 years	More than 2 years but less than 5 years ago	More than 5 years ago (optional)
Direct interests:					
Employment with a company	x				
Consultancy for a company	x				
Strategic advisory role for a company	x				
Financial interests	x				
Ownership of a patent	x				
Indirect interests:					
Principal investigator	x				
Investigator	x				
Individual's Institution/Organisation receives a grant or other funding	x				

*Entela Xoxi, in accordance with the Conflict of Interest Regulations approved by AIFA Board of Directors (26.01.2012) and published on the Official Journal of 20.03.2012 according to 0044 EMA/513078/2010 on the handling of the conflicts of interest for scientific committee members and experts

N.B. I am not receiving any compensation

The outlines of this talk

① Regulatory access pathways

② HTA & MEAs

③ Italian context

④ AIFA Registries

⑤ Conclusions

① Regulatory access pathways

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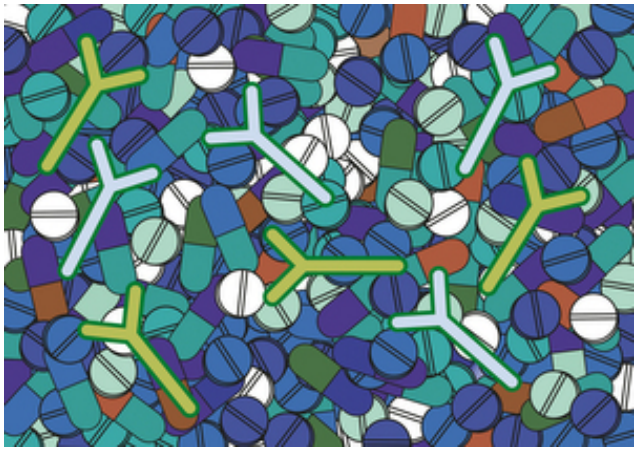
⑤ Conclusions



Existing, new and emerging regulatory access pathways

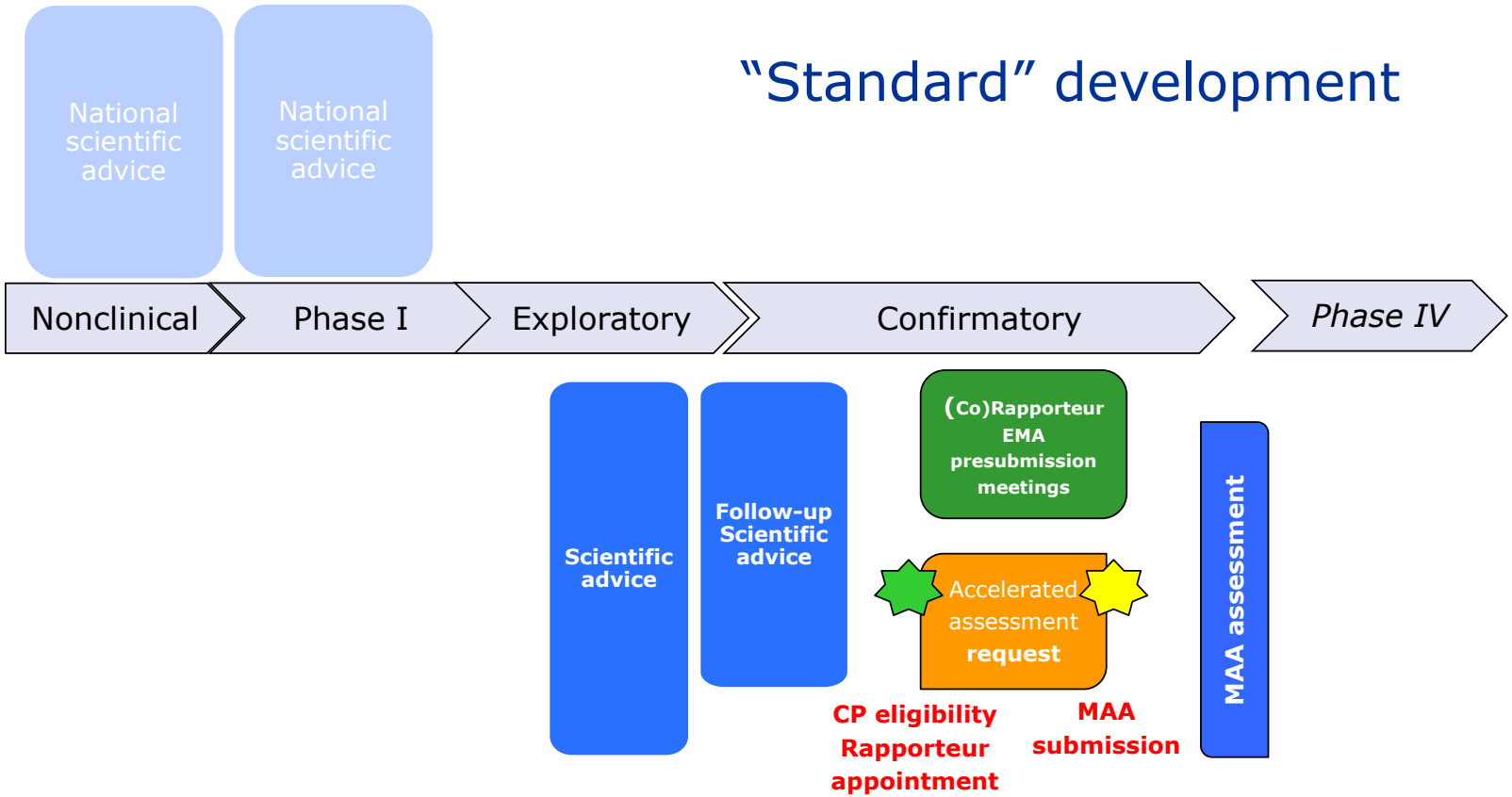
Emerging access pathway at the EMA

The EMA recognized that existing regulatory pathways, while useful, might not be sufficient to satisfactorily address the "access versus degree of evidence" challenge. The EMA Road map to 2015[8] identified the following as an important issue to be addressed by the agency: ". . . whether a more "staggered" approval (or progressive licensing) concept should be envisaged for situations not covered by conditional marketing authorizations. . . . The Agency would like to launch a debate with all stakeholders on the appropriateness of introducing such a concept, including a consideration of appropriate incentives to support new medicines development."

Accelerated Access to Innovative Medicines for Patients in Need

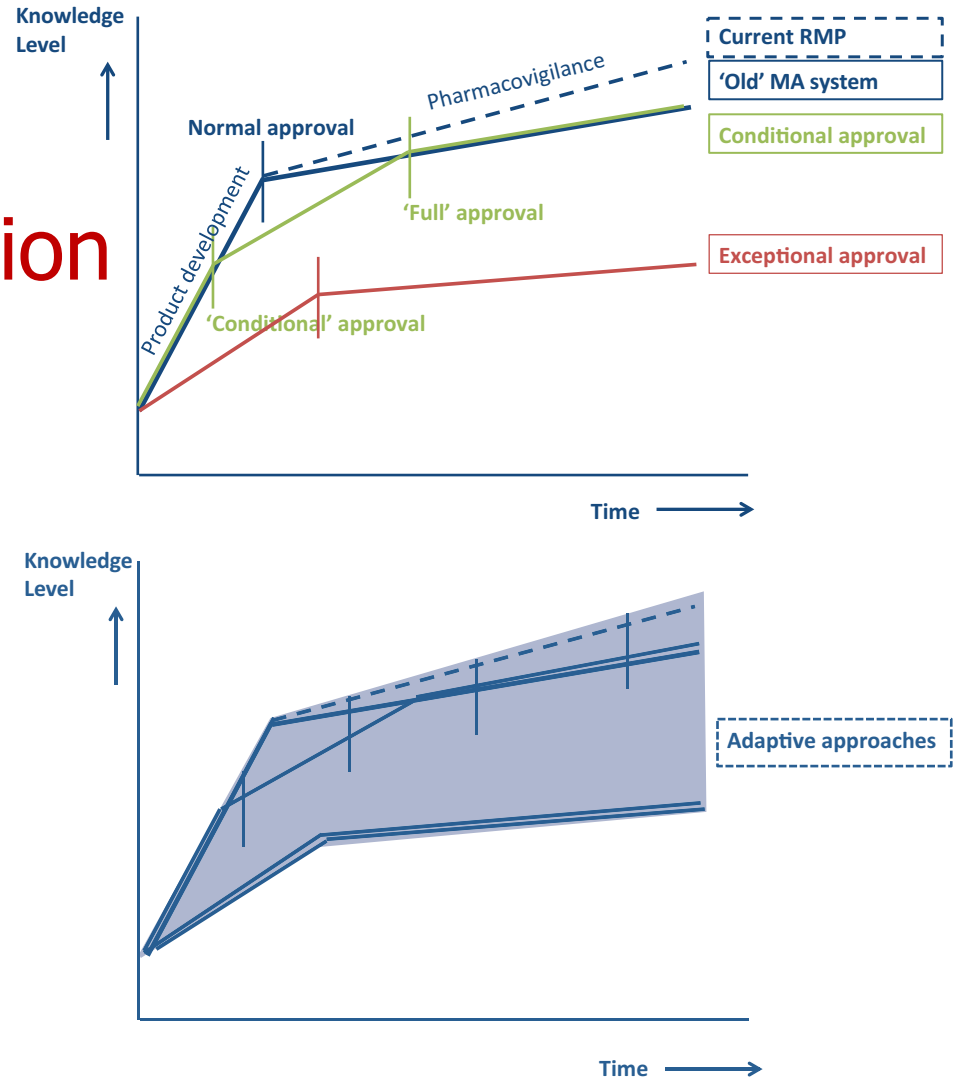
LG Baird[1], R Banken[2], H-G Eichler[3], FB Kristensen[4], DK Lee[5], JCW Lim[6], R Lim[5], C Longson[7], E Pezalla[8], T Salmonson[9], D Samaha[2], S Tunis[10], J Woodcock[11] and G Hirsch[1]

"Standard" development

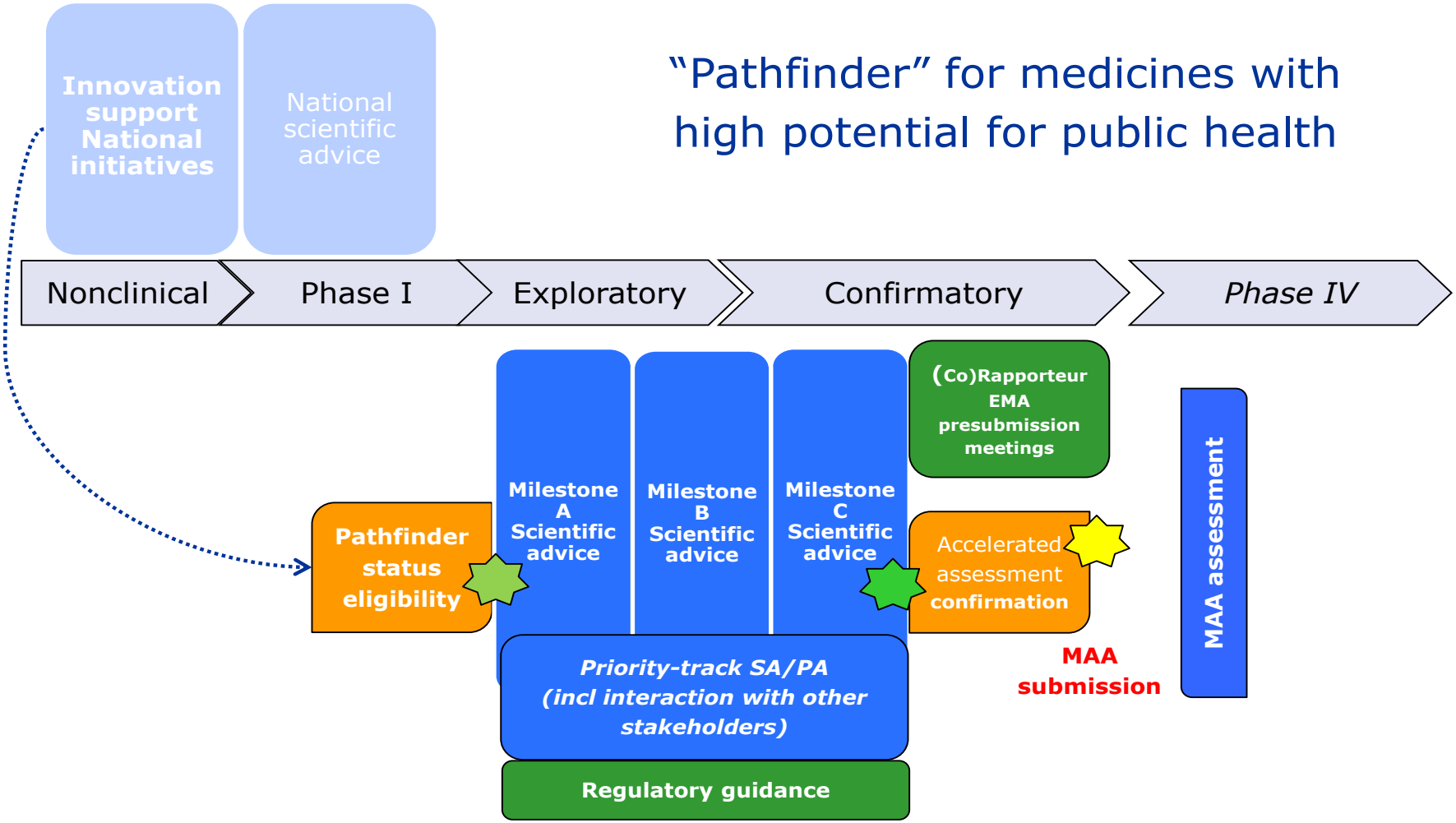


Regulatory & HTA drug life cycle approach

Marketing Authorization and the discussion about 'adaptive' approaches

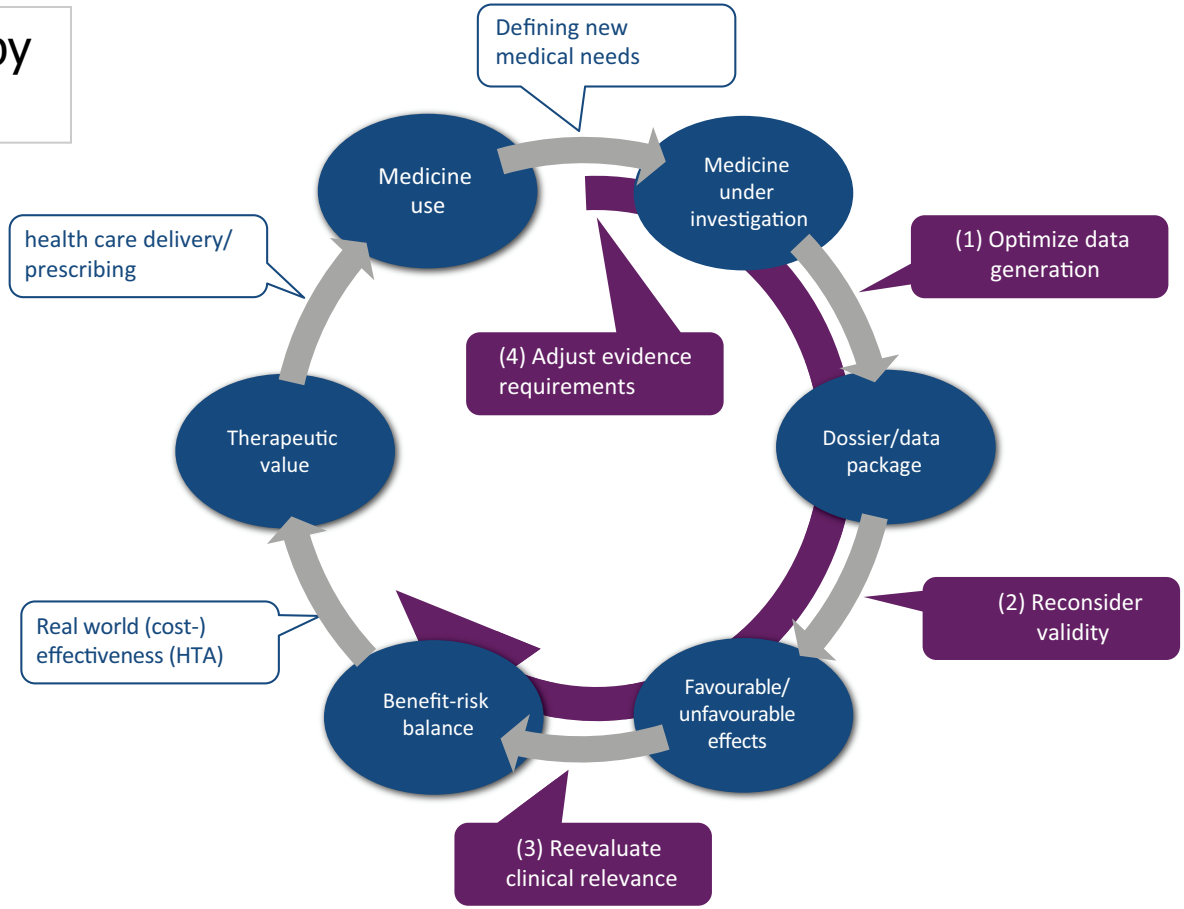


"Pathfinder" for medicines with high potential for public health



Evidence generation, step by step

Discussion paper by the Escher Project



This model is based on the model developed by Ashcroft, which consists of the following steps: from the 'world' (medicine use/drug under investigation) to data (dossier); from data to information (effects); from information to knowledge (benefit-risk balance); and from knowledge to wisdom (therapeutic value). Ackoff, R. L., "From Data to Wisdom", Journal of Applied Systems Analysis, Volume 16, 1989 p 3-9.

How to systematize benefit-risk decision making?

Towards appropriate levels of evidence - A regulatory science perspective on adaptive approaches to marketing authorization. Discussion paper by the Escher Project

Strategy based on simple principles

How to achieve better outcomes and control the cost curves?

What is the cut-off to be considered between therapeutic utility of a new medicine and its costs?

- An innovative drug should be reimbursed only if effective.
- The welfare systems cannot take anymore responsibility for the failures in front of such high costs
- Identification of responders in order to ensure an effective therapy against the poor prediction of clinical response at the time of recruitment

① Regulatory access pathways

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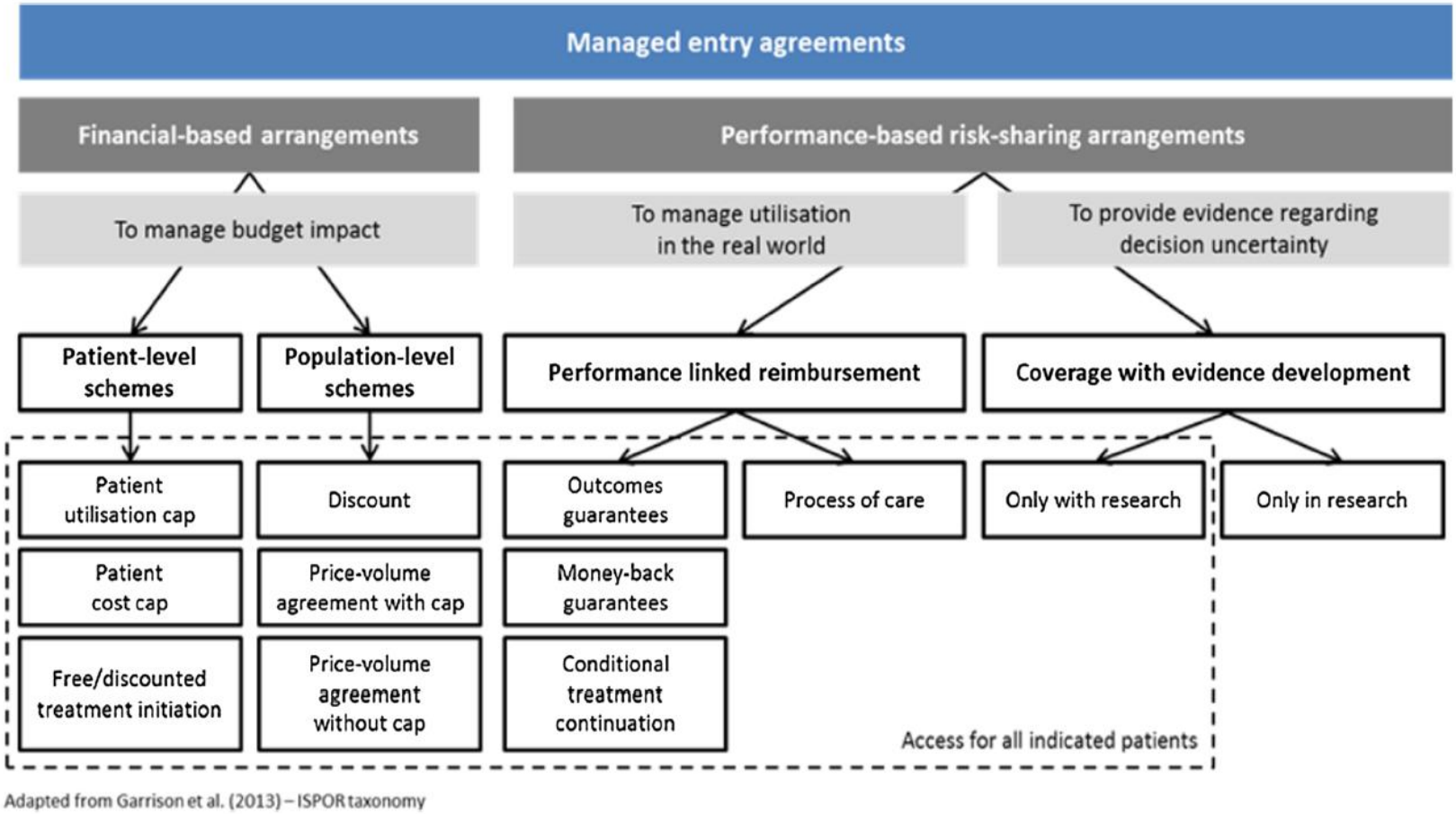

Figure 1 A taxonomy of managed entry agreements (MEAs).

Healthcare payers are adopting a range of innovative reimbursement approaches called MEAs

Definition: Managed Entry Agreements (MEAs)

A MEA is an arrangement between a manufacturer and payer/provider that enables access to (coverage/ reimbursement of) a HT subject to specified conditions.

These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize effective their use, or limit their budget impact

Klemp, *et al.*, 2011

Performance - based risk-sharing arrangements

PBRSAs are payment schemes – they involve a plan by which the performance of the product is tracked in a defined patient population over a specified period of time and the level of reimbursement is based on the health and costs outcomes achieved.

ISPOR performance based Risk sharing arrangements TF Report

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The Italian Managing

1- Refusal

2- Reimbursement (without conditions)

3- Managing budget impact

Non Outcome based MEAs

- Cost sharing
- Capping
- Volume Agreements
- Budget cap

4- Managing uncertainty relating to clinical benefit & cost-effectiveness

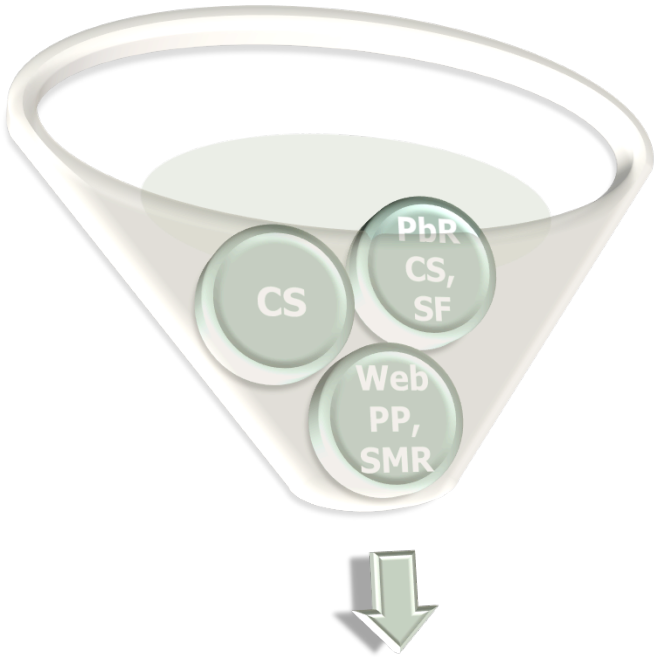
Outcome based MEAs

- Payment by result
- Risk sharing
- Success fee

5- Managing utilization to optimize

Performance based

- Appropriateness verification (SMR)
- Prescription plans
- AIFA Notes



Unique web platform of AIFA Registries

Data collected through Registries is owned by AIFA

Maintenance costs are charged by industry

① Regulatory access pathways

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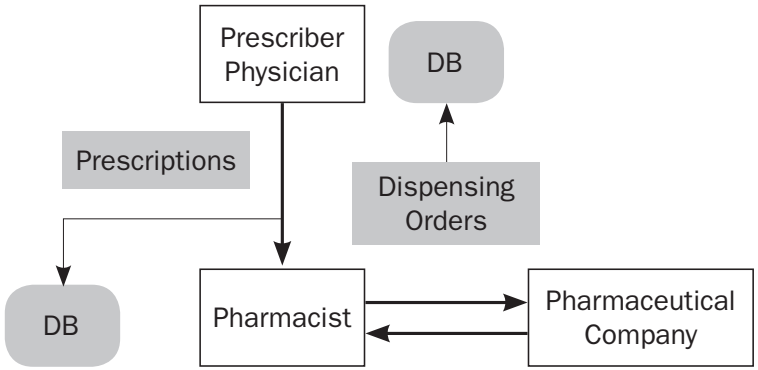
What the AIFA Registries are?



Are telematic & dynamic tools

at national level

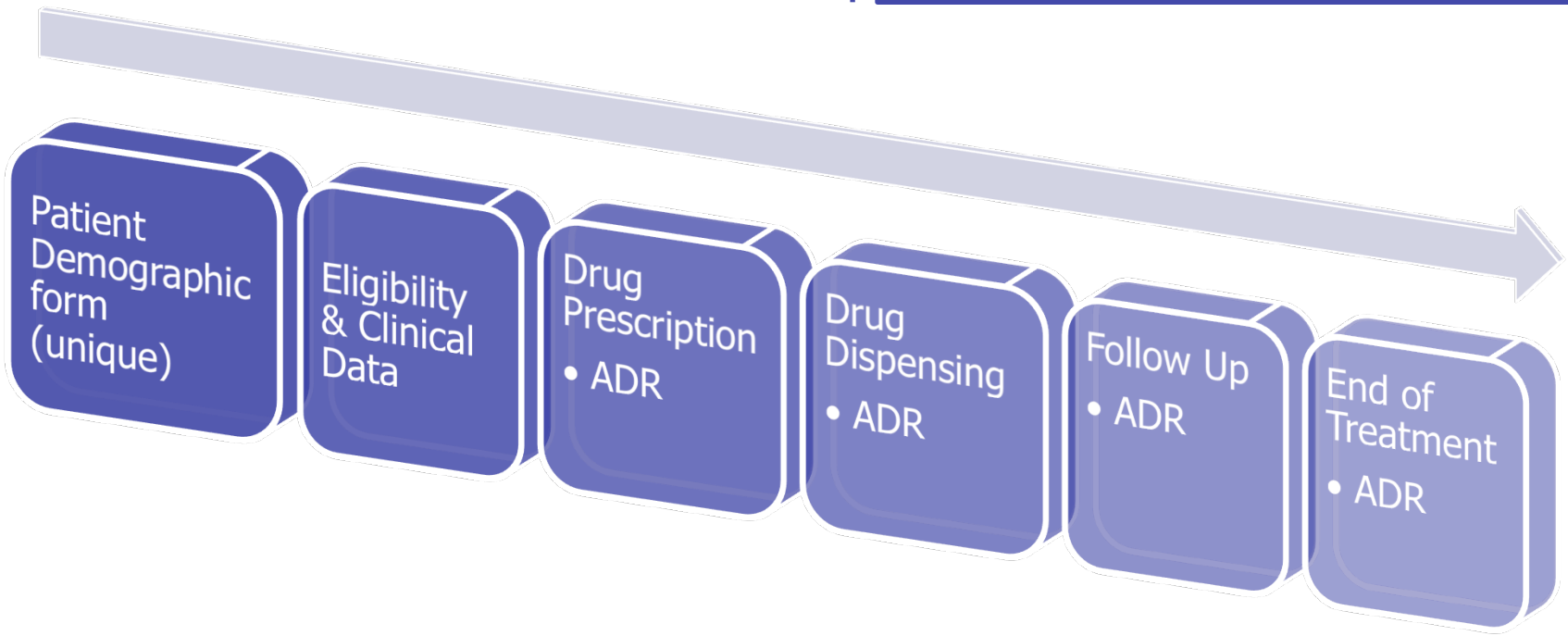
placed in the early phases after MA of new drugs, in some cases for the 'authorized' off label use

with a clear purpose and typically short defined lifespan

designed to

measure real world safety and effectiveness and apply the MEAs' procedures

Criteria E&O: all mandatory
Fup controls: temporally range



2013: (R)evolution

New platform

Towards the '*Disease centered approach*'

Accreditation system

Region

Identification of hospital & local prescriber centers

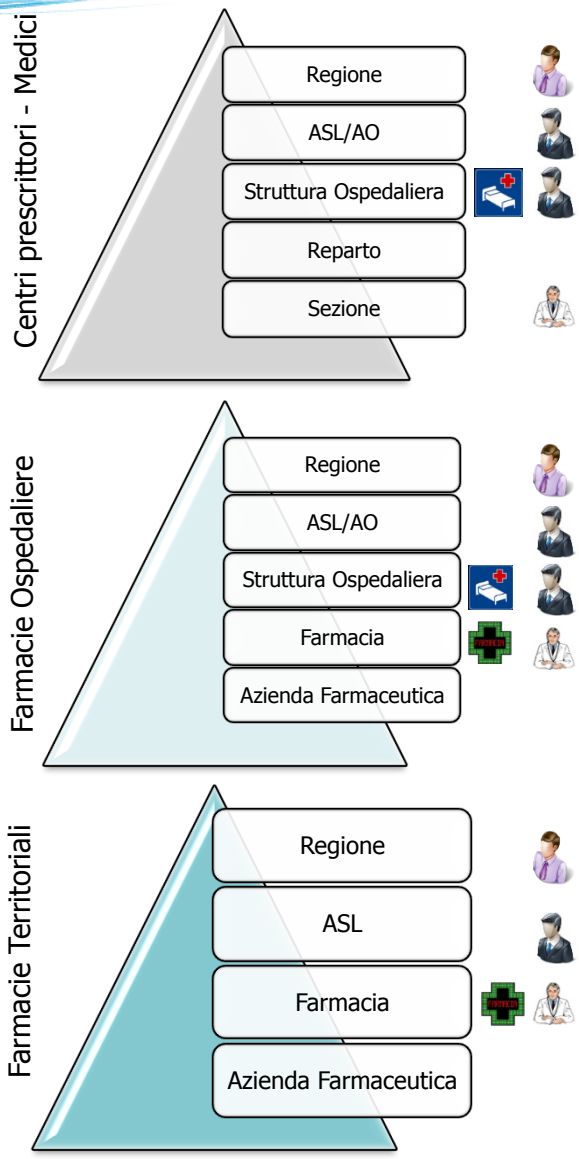
Health Managers

Users accreditation (physicians & pharmacist)

Accreditation

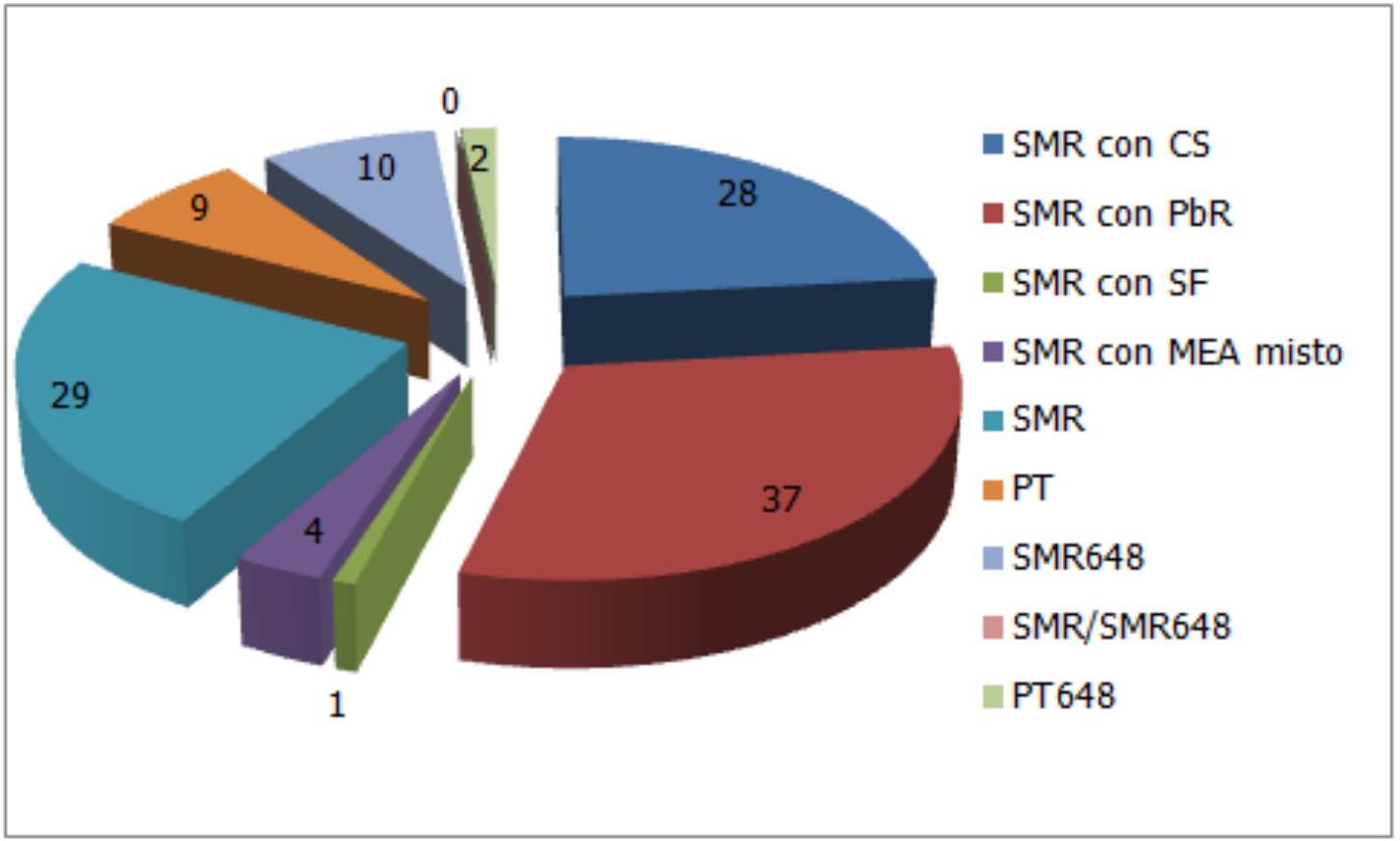
Region	Prescriber center (local or hospital) AND Reparto
Health Manager	Physicians & Pharmacists

Users



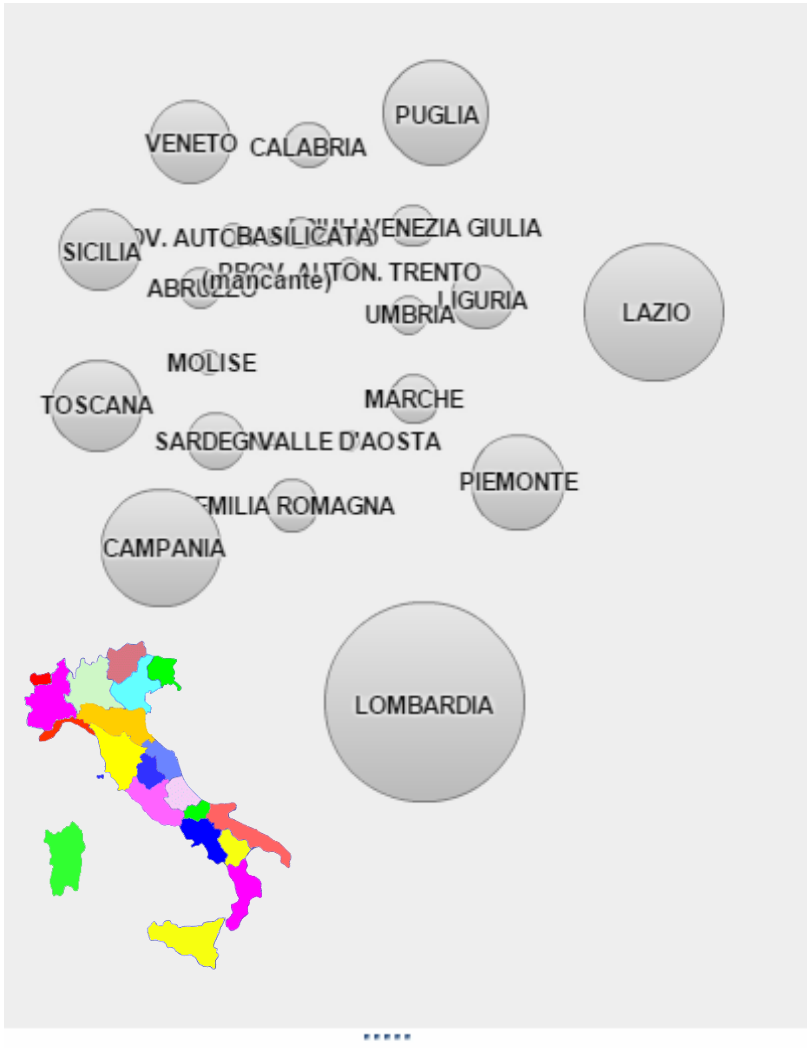
Profilo utenza	Funzionalità
Utente Regione	Abilitazione Utente | Abilitazione Registri
Direttore Sanitario ASL/AO	Abilitazione Utenze
Direttore Sanitario	Abilitazione Utenze
Utente Medico	Registrazione Pazienti eleggibili| RF | Follow Up | FT | Trasferimento Pazienti
Utente Regione	Abilitazione Utente | Abilitazione Registri
Direttore Sanitario ASL/ AO	Abilitazione Utenze
Direttore Sanitario	Abilitazione Utenze
Utente Farmacista Osp.	DF | Gestione Pratiche Rimborso
Utente AZF	Gestione Pratiche Rimborso
Utente Regione	Abilitazione Utente | Abilitazione Registri
Direttore Sanitario ASL/ AO	Abilitazione Utenze
Utente Farmacista Territoriale	DF | Gestione Pratiche Rimborso
Utente AZF	Gestione Pratiche Rimborso

Totale Registri web



Network diagram

Regional distribution

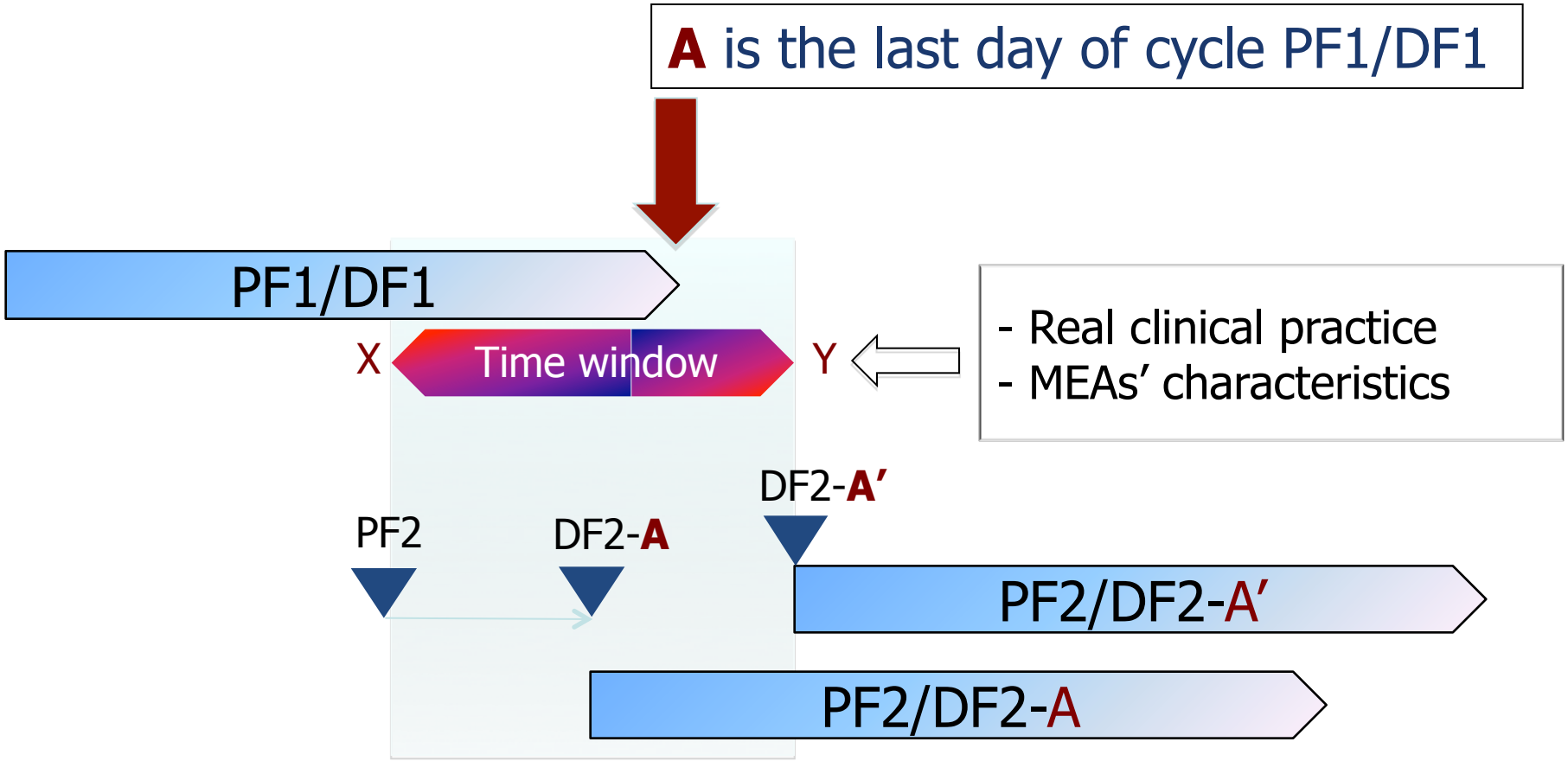


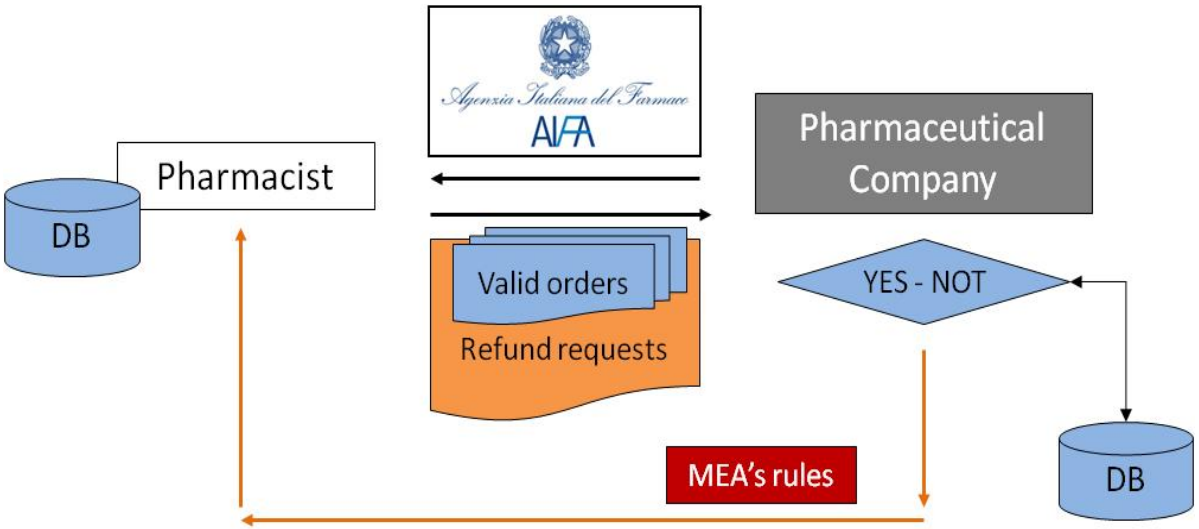
Drug Product Registries – Work in progress

① Historical - Task
- Monitoring appropriate use (i.e. as reimbursed by NHS)
- Application of Managed Entry Agreements (PbR, CS, etc.)
- Exception: Monitoring implementation of Pregnancy Prevention Program for thalidomide and lenalidomide

② Ongoing (R)evolution - Additional tasks
- Assess effectiveness
- Monitoring safety
- Education

Controls


A is the last day of cycle PF1/DF1
PF1/DF1
X
Time window
Y
- Real clinical practice
- MEAs' characteristics
DF2-A'
PF2
DF2-A
PF2/DF2-A'
PF2/DF2-A



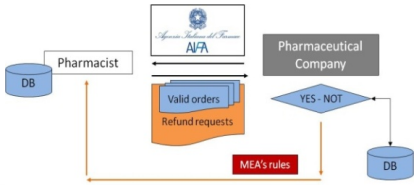
① Payment by results (PbR)

② Risk sharing (RS)

③ Cost Sharing (CS)

④ Capping (Capp)

ePayment by Result



Start of the new treatment in all eligibles

Evaluation after xx days/cycles

Non Responders

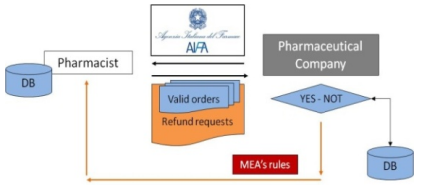
Treatment is stopped: eEoTF

Fixed discount rate applied to patient's cost treatment*

Pay back by MAH to public pharmacy (PbR & RS)

* Predefined n. of initial packages (RS)
100% refund of initial cycles (PbR)

eCost sharing

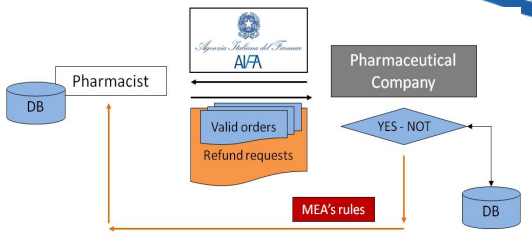


Start of the new treatment in all eligibles

Discount applied to the initial cycles of therapy for all **eligibles**

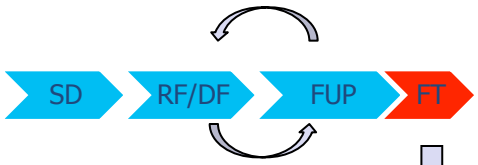
Pay back by MAH to public pharmacy

MEAs Algorythm



PbR RS SF	Maximum n° of Prescription & Dispensing forms	Maximum time elapsed between the last Dispensing form and the End of treatment form (days or weeks)	Maximum duration of monitoring (days or weeks)
The End of treatment must confirm the treatment failure: mandatory			
CS	Maximum n° of Prescription & Dispensing forms	-	Maximum time (days or weeks)

Payback flow



Dynamic evaluation

Treatment refundable

Reimbursement Request (RR)

Evaluation of RR by Pharma company

Treatments for the same register for a specific pharmacy

Treatment not refundable

- **Data Analysis**
- **Other conditions.,**

Evaluation of PP by public Pharmacy

Proposal for payback (PP)

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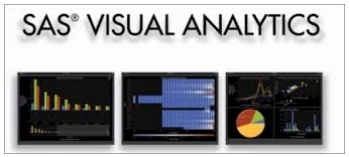
Reporting



File Guida

Disconnetti

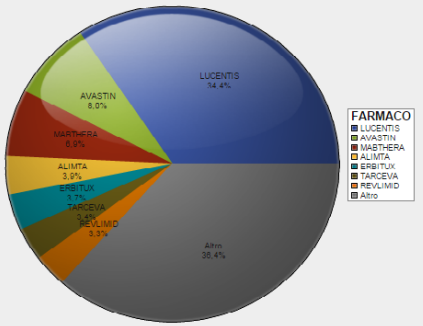
RIEPILOGO | DATI DI SINTESI | TRATTAMENTI CHIUSI/DECESSI | ANALISI TREND | MOBILITA' SANITARIA

RIEPILOGO

FARMACO	PATOLOGIA	RAGIONE SOCIALE	DATA DETERMINA	DATA CHIUSURA REGISTRO VECCHIA PIATTAFORMA	DATA INIZIO MONITORAGGIO
ADCETRIS	LINFOMA HODGKIN CD30+ RECIDIVANTE O REFRATTARIO	TAKEDA ITALIA FARMACEUTICI S.P.A.	01 novembre 2012	15 febbraio 2013	15 febbraio 2013
ADCETRIS	LINFOMA ANAPLASTICO A GRANDI CELLULE SISTEMICO RECIDIVANTE O REFRATTARIO	TAKEDA ITALIA FARMACEUTICI S.P.A.	01 novembre 2012	15 febbraio 2013	15 febbraio 2013
AFINITOR	CARCINOMA MAMMARIO	NOVARTIS EUROPHARM LTD	21 luglio 2013	.	22 luglio 2013
AFINITOR	TUMORE NEUROENDOCRINO PANCREATICO	NOVARTIS EUROPHARM LTD	21 dicembre 2012	15 febbraio 2013	15 febbraio 2013
AFINITOR	CARCINOMA RENALE	NOVARTIS EUROPHARM LTD	25 giugno 2010	01 gennaio 2013	01 gennaio 2013
ALIMTA	CARCINOMA POLMONARE NON A PICCOLE CELLULE	ELI LILLY NEDERLAND BV	04 maggio 2009	01 maggio 2013	01 maggio 2013
ALIMTA	CARCINOMA POLMONARE NON A PICCOLE CELLULE	ELI LILLY NEDERLAND BV	04 maggio 2009	.	09 luglio 2014
ALIMTA	CARCINOMA POLMONARE NON A PICCOLE CELLULE	ELI LILLY NEDERLAND BV	09 luglio 2014	.	09 luglio 2014
ARZERRA	LEUCEMIA LINFATICA CRONICA	GLAXO GROUP LIMITED	14 giugno 2011	01 maggio 2013	01 maggio 2013
ATRIANCE	LINFOMA LINFOBLASTICO A CELLULE T	GLAXO GROUP LIMITED	05 giugno 2008	01 gennaio 2013	01 gennaio 2013
ATRIANCE	LEUCEMIA LINFOBLASTICA ACUTA A CELLULE T	GLAXO GROUP LIMITED	05 giugno 2008	01 gennaio 2013	01 gennaio 2013
AVASTIN	CARCINOMA POLMONARE NON A PICCOLE CELLULE	ROCHE REGISTRATION LIMITED	09 luglio 2008	01 luglio 2013	01 luglio 2013
AVASTIN	CARCINOMA DEL COLON-RETTO	ROCHE REGISTRATION LIMITED	11 ottobre 2005	01 luglio 2013	01 luglio 2013
AVASTIN	CARCINOMA MAMMARIO	ROCHE REGISTRATION LIMITED	09 luglio 2008	01 luglio 2013	01 luglio 2013
AVASTIN	CARCINOMA DEL COLON-RETTO	ROCHE REGISTRATION LIMITED	11 ottobre 2005	.	08 luglio 2014

Dati aggiornati al	Trattamenti avviati	Registri attivi
13 novembre..	184.825	115

N° TRATTAMENTI AVVIATI



(R)evolution just started (since january 2013)

① Monitoring appropriate use and application of MEAs still the main tasks

② 'New' AND 'Old' approach still co-exist

③ Challenges faced: innovate while ensuring continuity

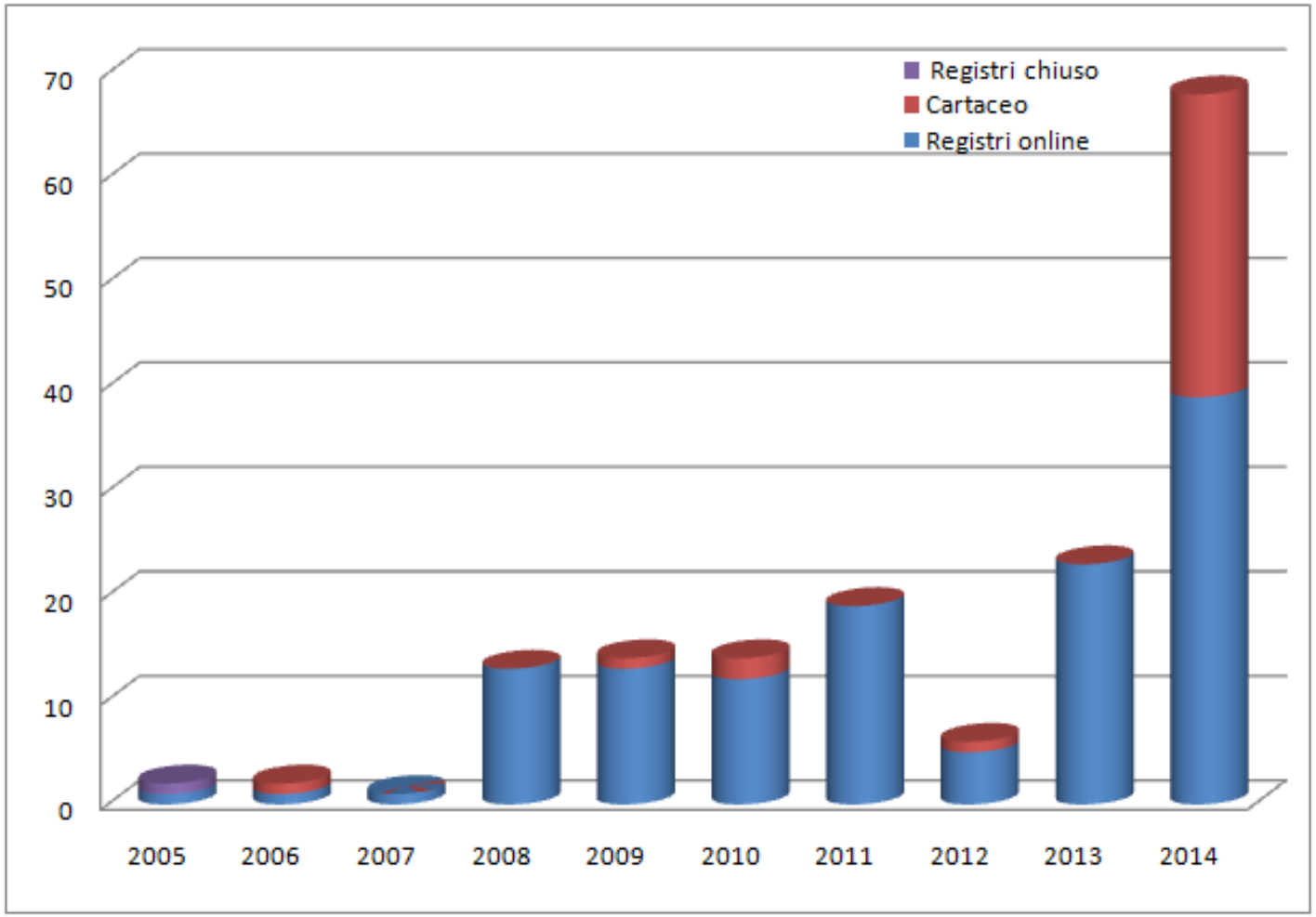
④ Cultural shift, from a pure administrative to an evidence-generating tool, needs time

Figures

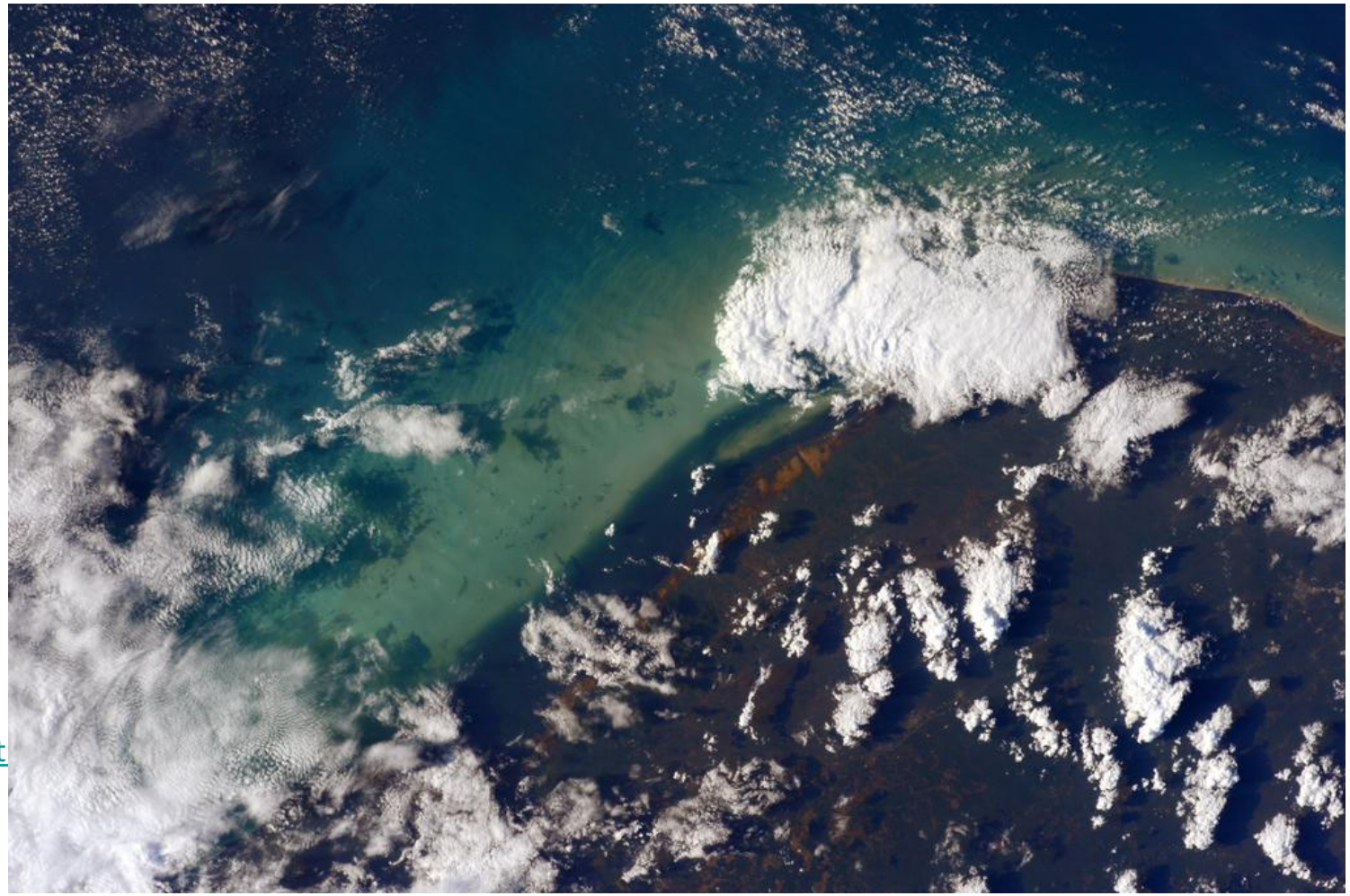
Pharma companies	32
Medicines	75
Therapeutic indications	~58
Web Registries & Prescription plans	120
Registries & Prescription plans (total, paper included)	156

Update 06/02/2015

Trend Registri




Network
MEAs
Drug
Product
Registry
Data collecting
Pharmacovigilance



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