Future opportunities for Pharmacovigilance

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Eleventh Stakeholder forum on the Pharmacovigilance legislation

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Disclaimer

- The views and opinions expressed in the following presentation are those of the individual presenter and should not be attributed to the EMA, one of its committees or working parties or the HPRA.

Future Drivers for Pharmacovigilance

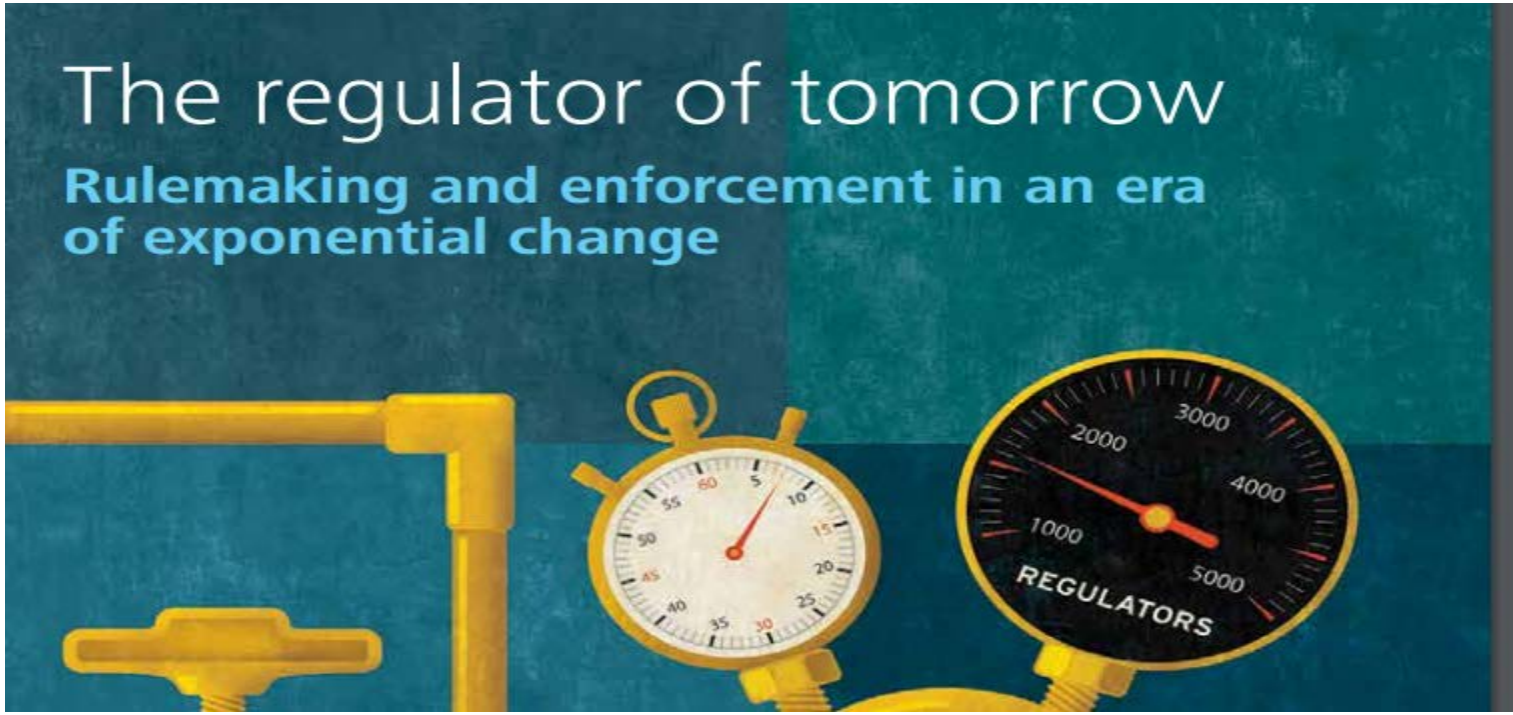
1. Engagement and enhancing the involvement of consumers and patients
2. Outreach: Harnessing technology, smart phones, social media and 'big data'.
3. New ways to generate evidence including real world evidence
4. Increasing EU capacity for vaccine benefit-risk studies
5. Enhancing monitoring for special populations: pregnancy, the elderly.
6. Development and deployment of scientific methods to facilitate safeguards for innovation, new evaluation and monitoring approaches.
7. Measuring the effectiveness of risk minimisation
8. Optimising our methods and tools to minimise risk including methods to communicate with patients and Healthcare Professionals.
9. Adapting and navigating change.
10. Increasing efficiency and optimal use of resources

A GovLab report in the Deloitte *Future of Government* series

A Regulator of the Future

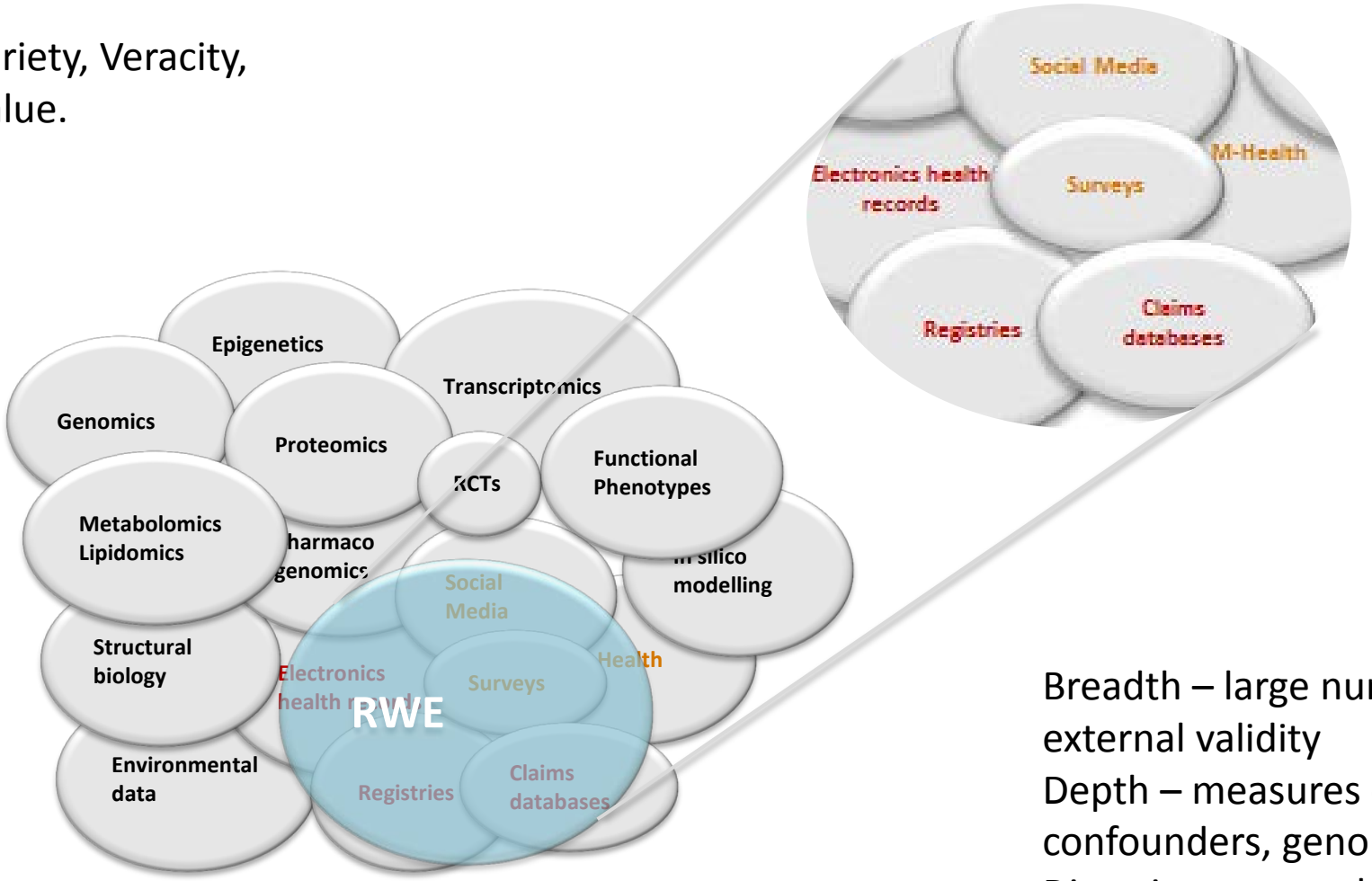
“Rethinking outreach”

“I know no safe depository of the ultimate powers of the society but the people themselves; and if we think them not enlightened enough to exercise their control with a wholesome discretion, the remedy is not to take it from them, but to inform their discretion by education. This is the true corrective of abuses of constitutional power.” — Thomas Jefferson



Real World Data - Which Data?

Volume, Variety, Veracity,
Velocity, Value.



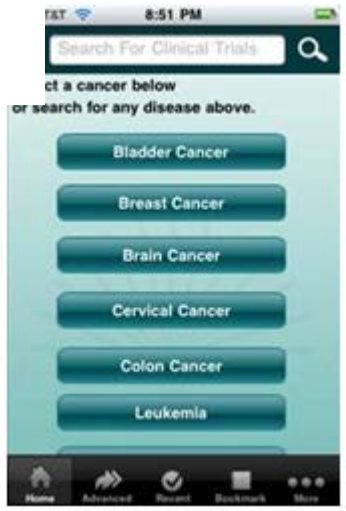
Breadth – large numbers – external validity
Depth – measures of likely confounders, genomics
Diversity – cross-check findings, control for residual bias

Wearables and wellbeing devices

Remote glucose monitoring

GSK, MedTrust Online Launch Clinical trials iphone app

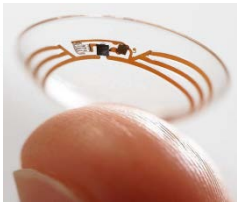
Medscape launch iphone interaction checker



Infection Spread

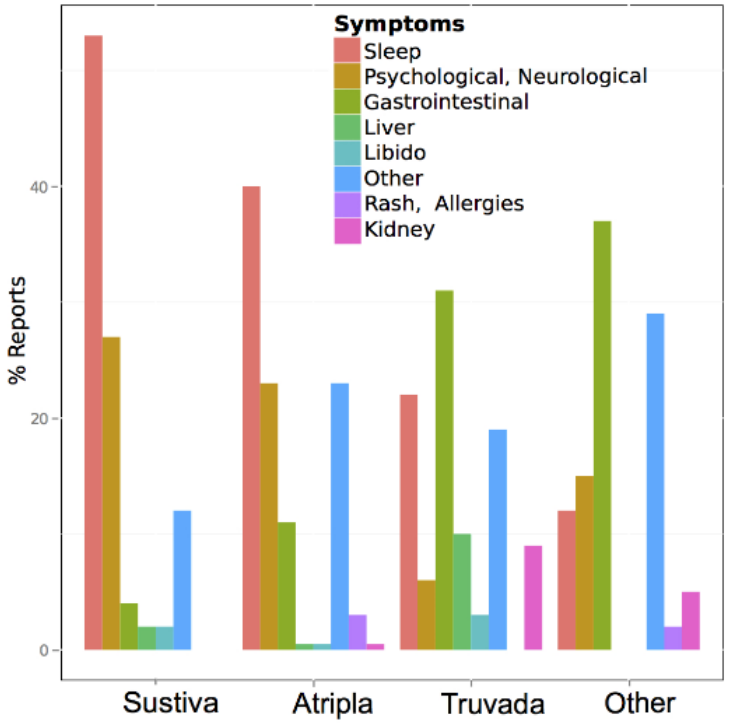
Google Baseline Study: small, huge

- Intense digital health data collection from 175 subjects
- Using a variety of sensors
  - May include experimental contact lens for diabetes data



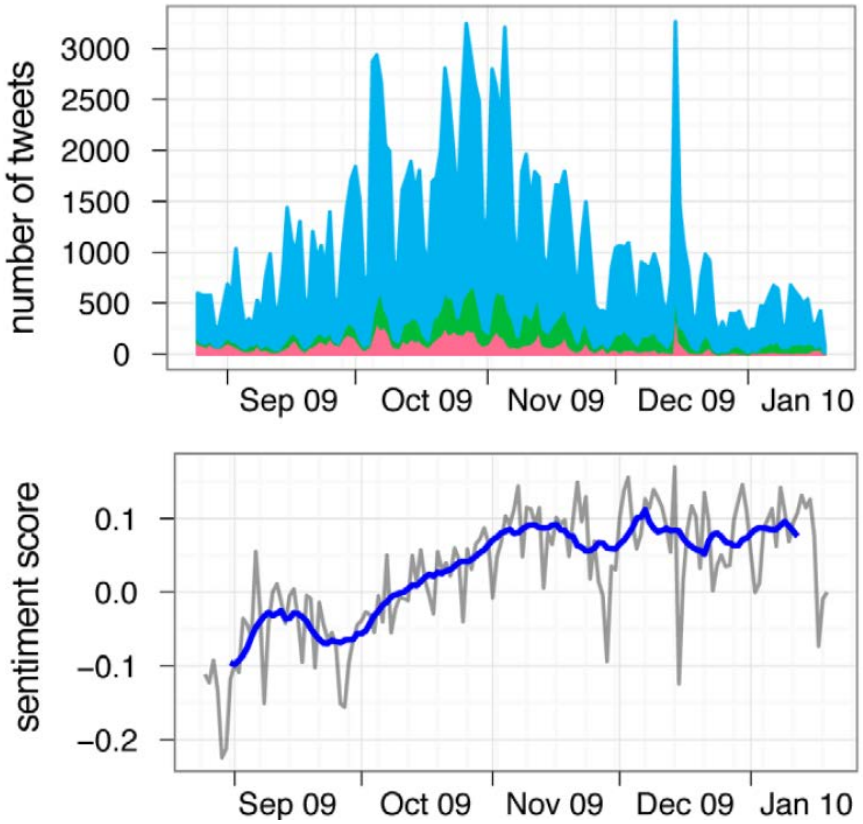
Social Media tweets tracking insomnia

Adverse Drug Reporting of HIV Drug Treatment with Twitter



Adrover et al, 2015

Vaccine Sentiments with Online Social Media



Salathe´ and Khandelwal, 2011

OPEN ACCESS Freely available online PLoS COMPUTATIONAL BIOLOGY

Assessing Vaccination Sentiments with Online Social Media: Implications for Infectious Disease Dynamics and Control

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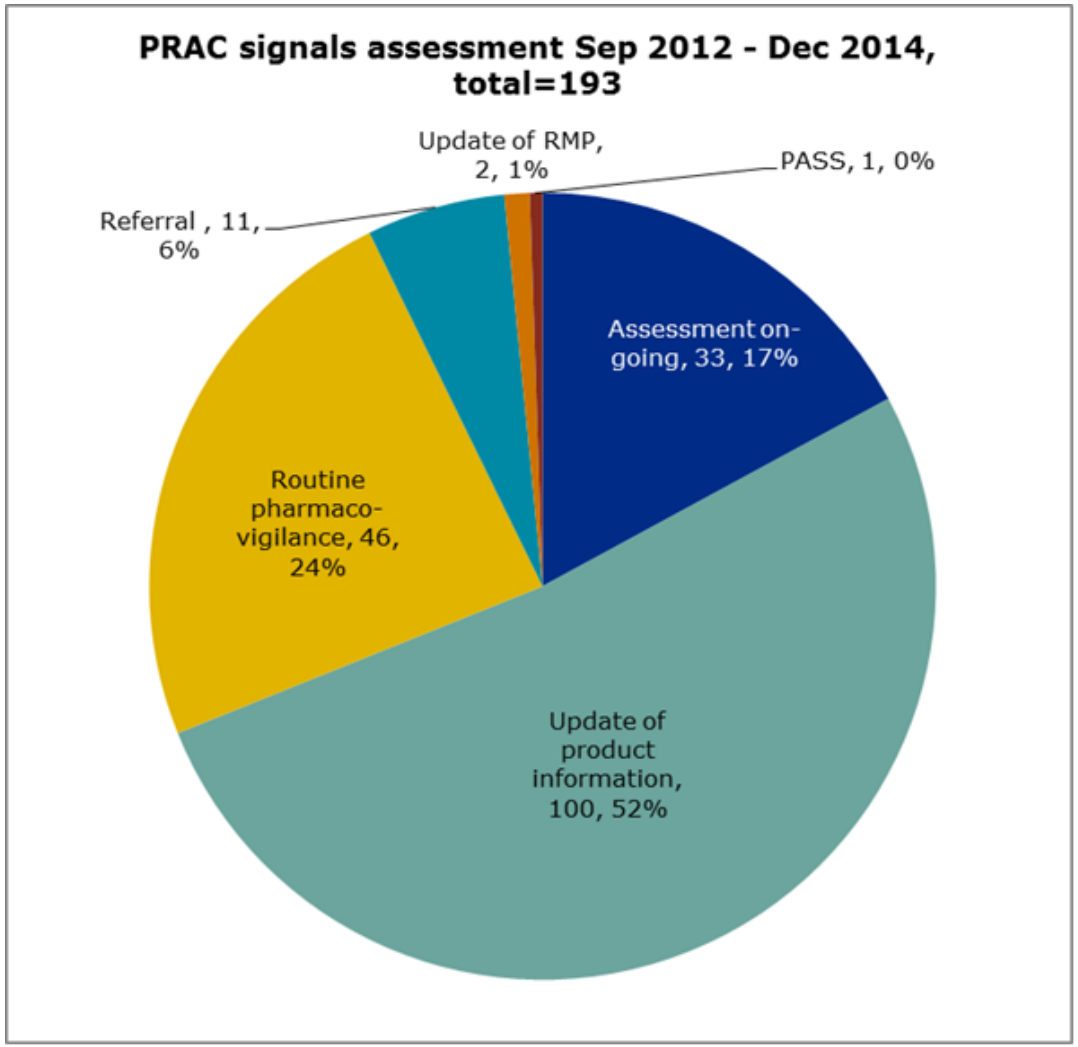
Abstract

There is great interest in the dynamics of health behaviors in social networks and how they affect collective public health outcomes, but measuring population health behaviors over time and space requires substantial resources. Here, we use publicly available data from 101,853 users of online social media collected over a time period of almost six months to measure the spatio-temporal sentiment towards a new vaccine. We validated our approach by identifying a strong correlation between sentiments expressed online and CDC-estimated vaccination rates by region. Analysis of the network of opinionated users showed that information flows more often between users who share the same sentiments - and less often between users who do not share the same sentiments - than expected by chance alone. We also found that most communities are dominated by either positive or negative sentiments towards the novel vaccine. Simulations of infectious disease transmission show that if clusters of negative vaccine sentiments lead to clusters of unprotected individuals, the likelihood of disease outbreaks is greatly increased. Online social media provide unprecedented access to data allowing for inexpensive and efficient tools to identify target areas for intervention efforts and to evaluate their effectiveness.

Signal detection outcomes

PRAC recommendations on safety signals are published.



Beyond outreach? Or hypothesis-generating? The aspiration…..?

5/8/2014 Pharma's Great Hope: Big Data

McKinsey: Digital Advantage

We provide insights into marketing and sales.

CMO NETWORK 6/25/2012 @ 2:34PM | 5,565 views

Pharma's Great Hope: Big Data

McKinsey & Company, Contributor

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The proliferation of information technology at the point of care and the improvement of payor data sets have sparked an explosion in the availability of real-world data (RWD) in healthcare. Pharmaceutical customers and regulators are eager to mine this data for any insights that can drive down cost and protect patient safety. Eventually, analyzing RWD could become a cornerstone of value-based pricing methods that could redefine the basis of competition and access.

Big health data: the need to earn public trust

Ipsos Mori -2014 & 2016

- GP, Health System Providers and academic institutions more trusted
- ‘Data-trust-deficit’
- While there is a core group of people who do not want this health data shared *at all*, many people find that sharing health data with commercial organisations is acceptable if there is a **clear public benefit** for this sharing”

=> DATA + SCIENCE **+ TRUST**

Digital Epidemiology

Map generated by more than 250 million public tweets (collected from Twitter.com) with high-resolution location information, broadcast between March 2011 and January 2012.

Exploiting M Health Data in Regulatory Decision Making

Challenges

- Quality - EC seeking to provide common quality criteria and assessment methodologies
- Reliability
- Consistency and standardisation
- Ease of use
- Interoperability- Number of recommendations and guidelines available
- Privacy concerns
- Adherence

Opportunities

- Impact research
- Resource utilisation
- Clinical trials
- Disease progression
- Disease monitoring
- Quality of life recording
- Adverse event reporting
- Infection spread and monitoring of vaccine effectiveness

Can observational evidence be relied on?

Stephan Evans

Stephan Evans,
MSc, C Stat, FRCP, FISPE
Hon. FRCP LSHTM

"No single method performs uniformly better, and none is really excellent at distinguishing real from false effects...

"We are not there yet, with the solution to problems of drug safety, but we are moving in the right direction."

Evans. Drug Saf. 2013 Oct;36 Suppl 1:S3-4.

Do we have a gold standard for evidence generation?

- **Or maybe there is just a spectrum of methodologies on a continuum of internal and external validity.**
- Among these, the RCT has the highest level of internal validity.
- But as for any test, PPV<100%; unknown confounders cannot be excluded; many RCTs not perfectly planned, executed or analysed; results often heterogeneous, sometimes contradictory & external validity often low.
- Randomised or not, any evidence requires post-licensing verification by way of a life-span approach to evidence generation and to ensure robust information on benefits

Data sufficiency and trade-offs

Four key characteristics of successful RWD analyses:

- **Meaningful** evidence: Relevant and context-informed evidence based on fit-for-purpose data sufficient for interpretation and making decisions.
- **Valid** evidence: Evidence that meets scientific and technical quality standards to allow causal interpretations.
- **Expedited** evidence: Incremental evidence generation that is synchronized with decision making.
- **Transparent** evidence: Evidence that is reproducible, replicable and trusted by decision makers

Schneeweiss et al. Clin Pharmacol Ther 100 (6), 633-646. 2016 Oct 19.

What is sufficient?

Basic data requirements:

- Exposure
- Outcome of Interest
- Confounders

Appropriate method

To answer the question of interest

To a satisfactory level of precision

Session 3, EMA Big Data Workshop 2016

Making the most of data sources

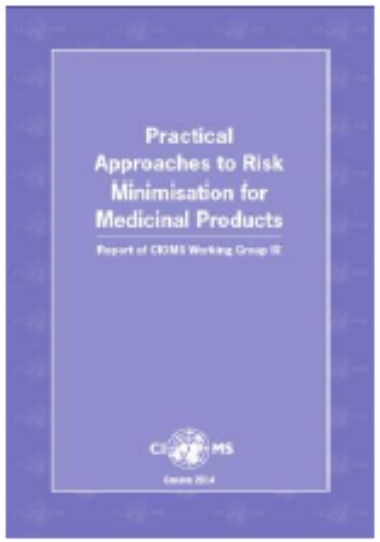
- Different data sources for different questions
- Data linkages
- Enriching existing datasets / or better use of existing data?
- Common protocols?
- Increased collaboration?
- What is sufficient? Decision relevant?

Opportunities and challenges

- Evidence based on a diversity of data sources and methodologies complementing not replacing RCTs
- Variance as the focus of scientific interest (rather than noise)
- Shift from population focus to patient focus
- Shift from single agent treatment to personalised combinations
- Generation of decision relevant data through the product lifecycle – uncertainty won't be eliminated but how can it be progressively reduced?
- New evidence may reassure/raise concerns- importance of transparency and communication.

Incorporating new methodologies & building on the best practices

PROTECT



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Cross-Functional Regulatory Challenges

New Medicines

- Innovative products and regulatory challenges (Innovation Taskforce trends)
- ATMPs (gene therapy, stem cell and tissue therapy)
- Vaccines
- Biologicals and biosimilars

Methodological challenges

- Globalisation
- New evaluation methods
- New ways to generate evidence
- New marketing authorisation and monitoring procedures

Wider regulatory focus

Adapt and evolve

Skilled to respond to increased levels of complexity

Eager to engage

Innovation and Preparedness

“Change is inevitable, and conscious involvement in directing change is empowering, and very different from drifting with change.

Being the arrow, not the target means being active, not passive, in this time of challenge and change.”

President Michael D. Higgins August 23rd 2017

Acknowledgments

- PRAC and EMA colleagues