



Innovative Medicines Initiative

WEBAE - Leveraging Emerging Technology for Pharmacovigilance

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Basel, 05 Jul 2013



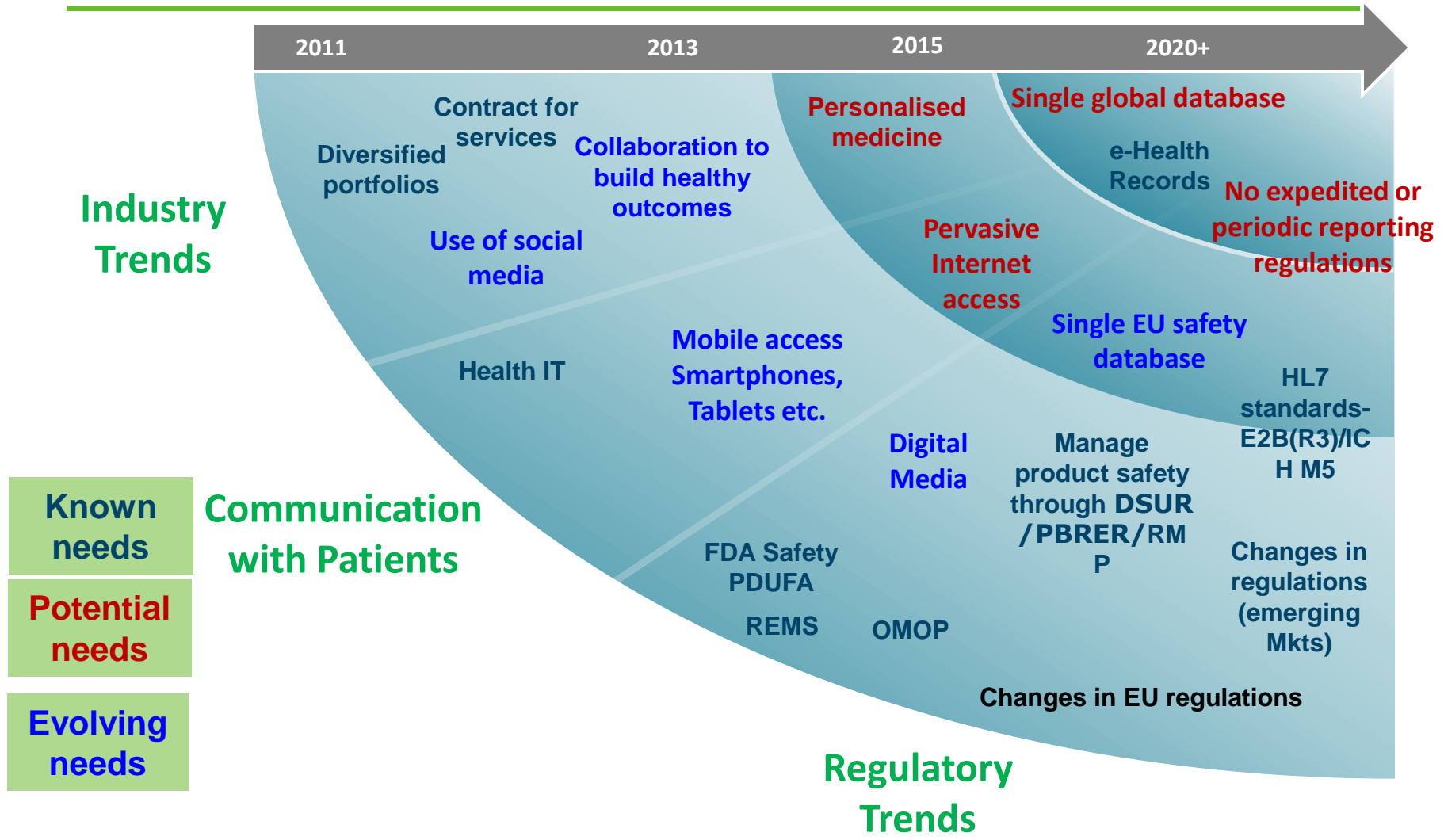
efpia



Pharmacovigilance (PV) legislation

- European PV legislation {Regulation 1235/2010, Directive 2010/81/EU and Implementing Regulation 520/2012} has strengthened safety monitoring of human medicines in the EU & EEA
- Supporting guideline Good PV Practices: Module VI ***Management and reporting of adverse reactions to medicinal products***
 - Enabling of direct reporting to Marketing Authorisation Holders (MAH) and to the Competent Authorities through development and provision of standard web-based forms
 - EMA has a responsibility to develop, in cooperation with the Member states, web-based reporting forms for adverse reaction reporting by patients and healthcare professionals
 - Patients and healthcare professionals can choose to report to the MAH, whereby reporting should ideally be facilitated by modern technologies as well

Factors impacting pharmacovigilance systems



Social Media Landscape



From: Rishi Chopra - Pharmacovigilance & Digital Media
 (<http://de.slideshare.net/rkc78834/pharmacovigilance-digital-media>)

Current advice on the role of digital media in PV (GVP Module VI)



- ***VI.B.1.1.4. Information on suspected ADRs from the internet or digital media***

MAHs should regularly screen internet or digital media under their management or responsibility, for potential reports of suspected adverse reactions. In this aspect, digital media is considered to be company sponsored if it is owned, paid for or controlled by the MAH.

- The frequency of the screening should allow for potential valid ICSRs to be reported to the competent authorities within the appropriate reporting timeframe
- Marketing authorisation holders may also consider utilising their websites to facilitate the collection of suspected ADRs

Current advice on the role of digital media in PV (GVP Module VI)



- ***VI.B.1.1.4. Information on ADRs from digital media (ctd.)***

If a MAH becomes aware of a report of suspected adverse reaction described in any **non-company sponsored digital medium, the report should be assessed to determine whether it qualifies for reporting.**

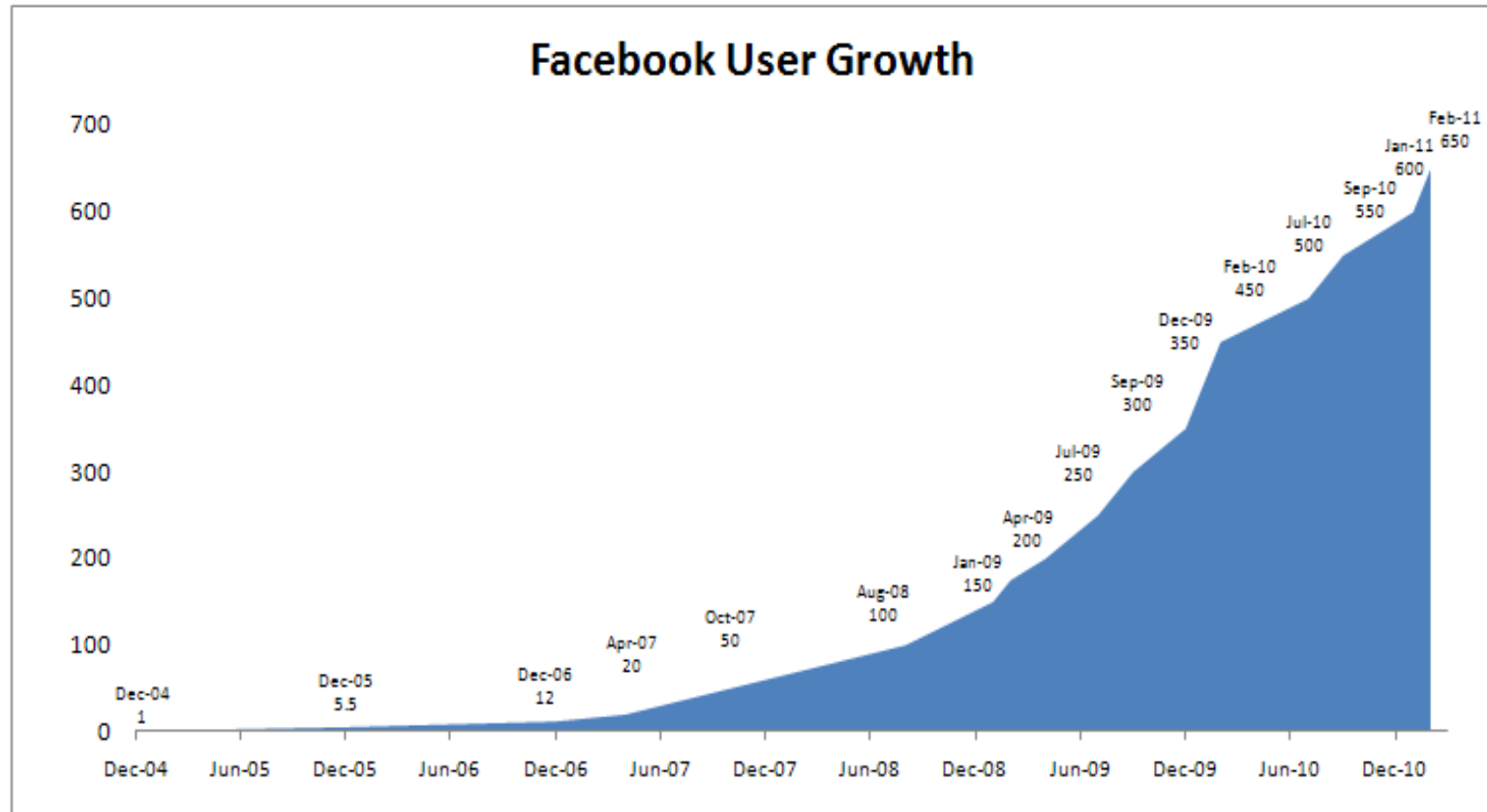
- ***VI.C.2.2.6 Emerging safety issues***

Good practice for the MAH to monitor special internet sites or digital media (e.g. patients' support or special diseases groups)

- Check if they describe **significant safety issues** which may necessitate reporting in accordance with VI.C.2.2.6.
- Frequency of the monitoring depends on the risks associated to the medicinal product

Trends in Consumer Technology

Facebook User Growth



> 200 Facebook groups on rheumatoid arthritis

Trends in Consumer Technology

Social media user metrics



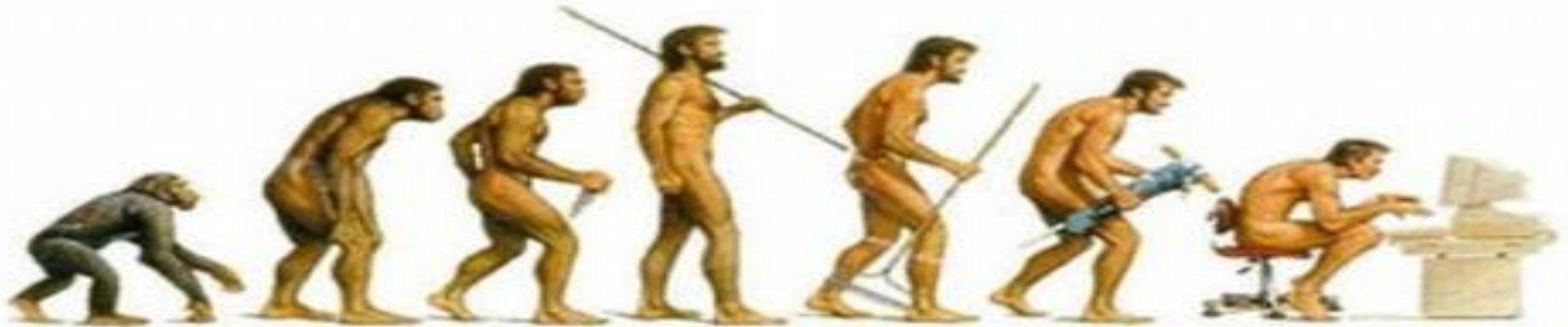
Social Medium	Description	Number of Users	Mobile Friendliness	Website Widgets and Integration	Photo sharing	Video Sharing	Advantages	Disadvantages
Facebook	Largest social network; users share and interact with stories, images and video	845 million	Apps for iPhone, iPad, Android, Blackberry, Windows and more	YES	YES	YES	User-friendly interface, connects with many other online media	Privacy settings confusing, may hinder user interactions with page
Twitter	Microblogging site; users send messages of 140 characters or less	140 million	Apps for iPhone, iPad, Android, Blackberry and Windows	YES	YES	NO	Focused, straightforward features; brevity of posts appeals to busy practices	Frequent updates necessary to maintain follower engagement
YouTube	Video sharing website where users can share and upload new videos	800 million	Apps for Android, Blackberry, iPhone, Nokia, Windows and others	YES	NO	YES	Video offers clear, visual means of communicating procedural content	Difficulty obscuring patient identity may limit procedural videos
Pinterest	Online "pin board"; users collect and curate pictures and videos of interest	21 million	App for iPhone. 3 rd party apps for Android and Windows	YES	YES	YES	Intuitive visual interface	Reorganization of "pins" impossible at present

from: Robin L. Travers: **Social Media in Dermatology: Moving to Web 2.0**, Figure 1. Comparison of 4 social media for dermatologists

<http://dx.doi.org/10.1016/j.sder.2012.06.003>, 2012 Published by Elsevier Inc

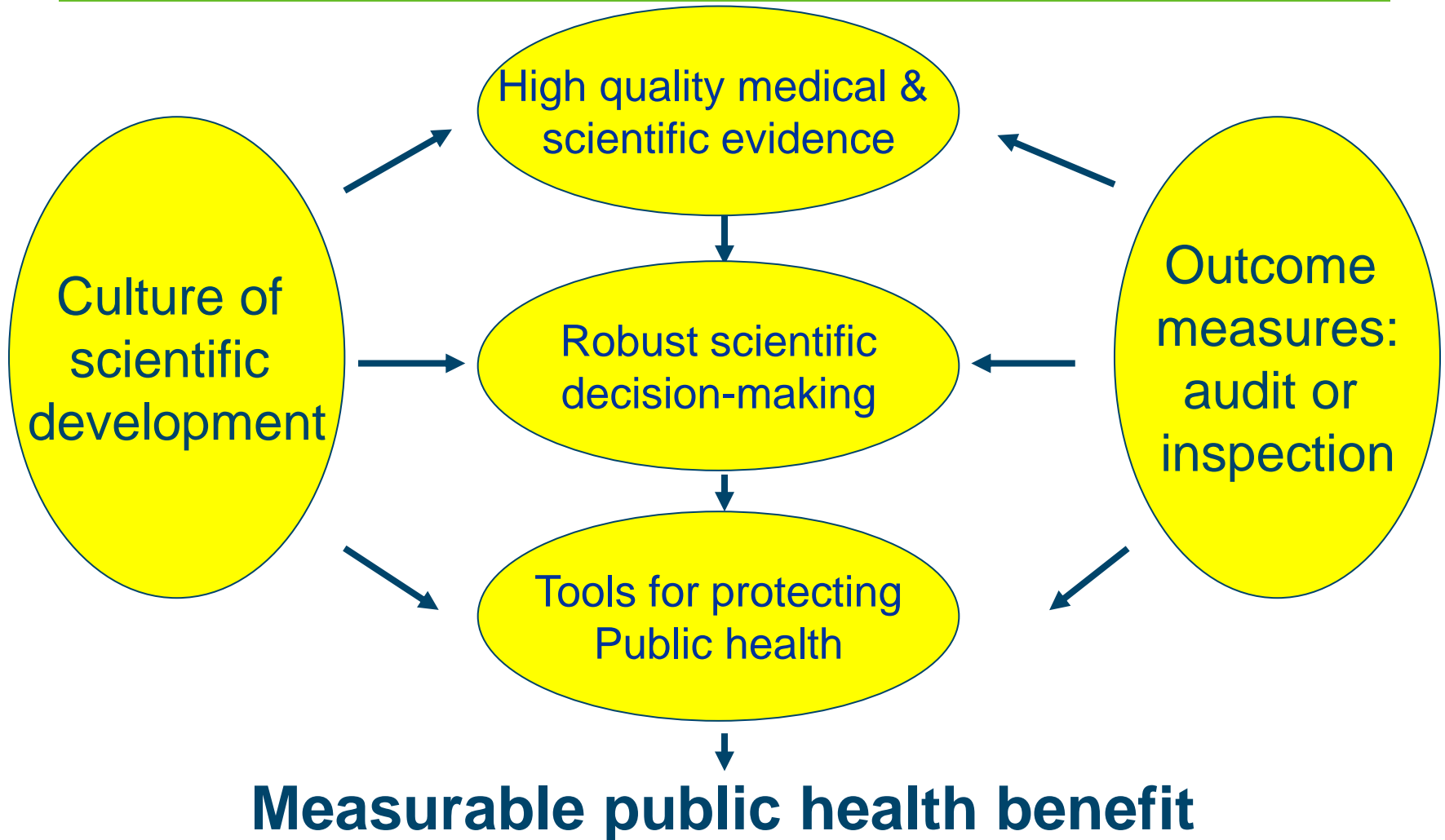
Trends in Consumer Technology

The smartphone market



Model for excellence in PV*

Scientific basis for protection of public health



IMI Call 9 Webinar EFPIA 05 July 2013

* Adapted from Waller and Evans (2003)

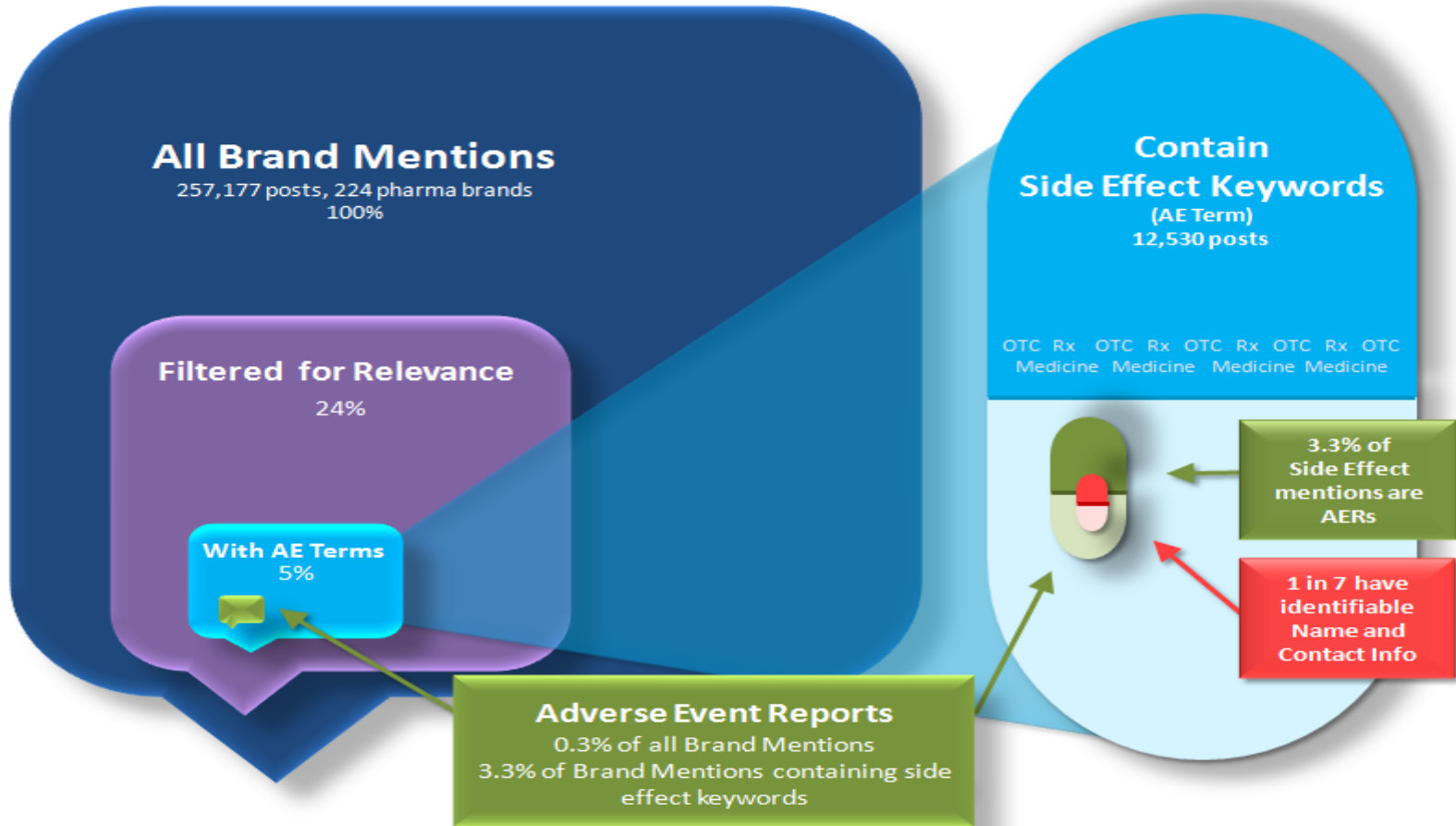


Hypothesis

Data capture, collation, timely data mining and appropriate analysis can provide actionable intelligence in relation to protection of public health. Hence research can provide value to stakeholders including patients, healthcare professionals, regulators and to the pharmaceutical industry.

- Emerging communication technology is changing the way people interact with their healthcare providers and products
 - Large body of health care data is being generated in social media
 - Mobile technology creates an environment where people are constantly connected to the Internet
- The value of such data is not fully established
- Mining and analysis of social media is an emerging science
- Regulatory guidance is behind the emergence of new technology

Adverse Event reporting in social media



Source: White paper on Adverse Event Reporting by Visible^R, Oct. 2011, <http://www.visibletechnologies.com/resources/white-papers/adverse-events/>

Example: Patients Like Me

Analysis of social media discussions



"An analysis of 141 posts in the discussion forum based on the keyword 'Tysabri', comparing the period from January 1, 2008, to July 31, 2008, to the three-week period after the July PML announcement, found that overall opinions toward Tysabri remained positive. Although **patients were discouraging more on the topic of product safety**, announcing the PML cases did not adversely affect the overall positive sentiment. This was confirmed by the number of patients taking Tysabri, which increased almost 12% between June 2008 and September 2008 according to Biogen-Idec (Cambridge, MA, USA), the drug's manufacturer"



The power of social networking in medicine. **Nature Biotechnology 27; 888 – 890: 2009**

Example: Adverse Event Reports on Facebook



- Facebook group established
- 1000+ members during 7-month experiment
- ADR Education
- On-line questionnaire for ADR reporting
- High sensitivity (based on Naranjo score of causal relationship)
- High “yield” (2% vs. 0.01% historical)
- Skewed demographics (young, female) and relevant educational background (medical/pharmacy field)

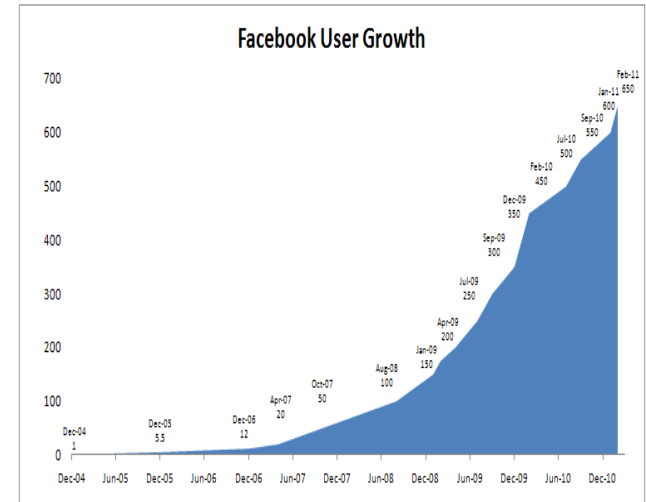


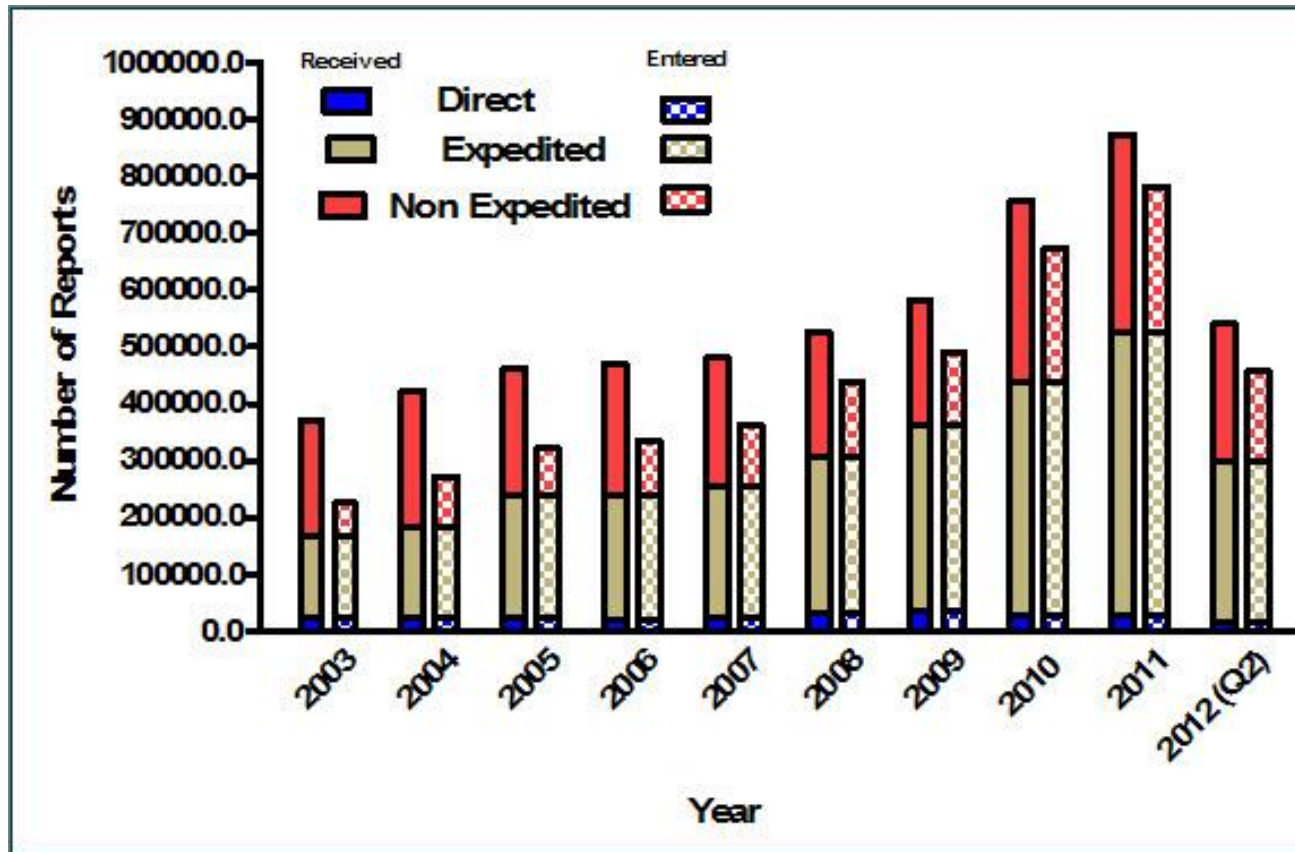
Table 1. Reported adverse drug reactions (ADRs)

Drug and formulation, if known	Adverse reaction	Naranjo score ^a (10)
Aciclovir, oral	Urticaria	5
Oral contraceptive (ethinylestradiol/gestodene)	Increased body temperature (>37.5°C)	6
Aspirin (acetylsalicylic acid) 100 mg, oral	Pruritus	4
Ginkgo biloba leaf extract, oral	Skin rash	4
Fero-Il-fumarate, oral	Gastrointestinal upset, constipation	8
Aspirin 100mg, oral	Bruising	5
Multivitamins, oral	Skin rash, desquamation	3
Ergotamine, oral	Vertigo, weakness	9
Ofloxacin	Dyspnoea	4
Amoxicillin	Skin rash	5
Combination (paracetamol [acetaminophen] + codeine + caffeine + propylphenazone), oral	Vertigo	9
Pentaerythritol tetranitrate, oral	Vomiting, fainting	9
Diclofenac, oral	Paraesthesia, stiff neck	9
Lamotrigine, oral	Skin rash, oral cavity enanthem, enlarged neck lymph glands, tiredness, blurred vision	8
Echinacea	Increased body temperature (>37.5°C)	7
Doxycycline, oral	Nausea	8
Sertraline, oral	Headache, tinnitus, loss of appetite	6
Dextriferron + vitamin B12	Pemphigus medicamentosa	4
Pseudoephedrine + ibuprofen	Palpitations, tachycardia, vertigo	4
Nifedipine, slow release, oral	Facial flush, headache, hypotension	7
Cotrimoxazole, oral	Skin rash, pruritus	6

^a Definite ADR (Naranjo score ≥9), probable ADR (Naranjo score 5–8) and possible ADR (Naranjo score 1–4).

MZ Knezevic et al: Using Facebook to Increase Spontaneous Reporting of Adverse Drug Reactions. Drug Saf 34:351-2 (2011)

FDA: AE reports by Year



Number of reports received by FDA and entered into AERS/FAERS by type of report since the year 2003 {FDA Adverse Event Reporting System (FAERS)}

WEBAE challenges & questions (1/2)



Domain	Challenge	Key Questions
Technology	Reporters carry a variety of mobile devices	Should the focus be a single platform (iOS) or multiple platforms (iOS plus Symbian and Blackberry)?
	Reporters are busy people and already have multiple points of data entry at work or home	Should this be a separate mobile app or be integrated into electronic health records (EHRs)?
Organisation	Spontaneous AEs are reported globally and have to be channelled to multiple stakeholders	Should this be an industry-wide solution that can channel multiple inputs (reporters in multiple countries) to multiple stakeholders (sponsors and regulators)?

WEBAE challenges & questions (2/2)



Domain	Challenge	Key Questions
Data	Regulators require quality data, especially where public health impact is high	How will data from unstructured sources, e.g. social media, be handled? Should this be proactively sought? Should there be a filter? Will the regulators allow this?
	Data models not standard between sources	What data standards needs to be in place to integrate AEs from various sources?
	Definitions of medical terms are not standardised across sources or countries	Are standard ontologies required to allow integration of data from multiple sources?
Process	Burden of processing additional data sources will impact the internal PV organisation	Is there a need to replace or enhance some services, e.g.: <ul style="list-style-type: none">- Data mining, e.g. Social networks?- Analysis, summarising, and reporting?- Follow-up and checking?

Future vision: WEBAE

Web/App-based AE reporting



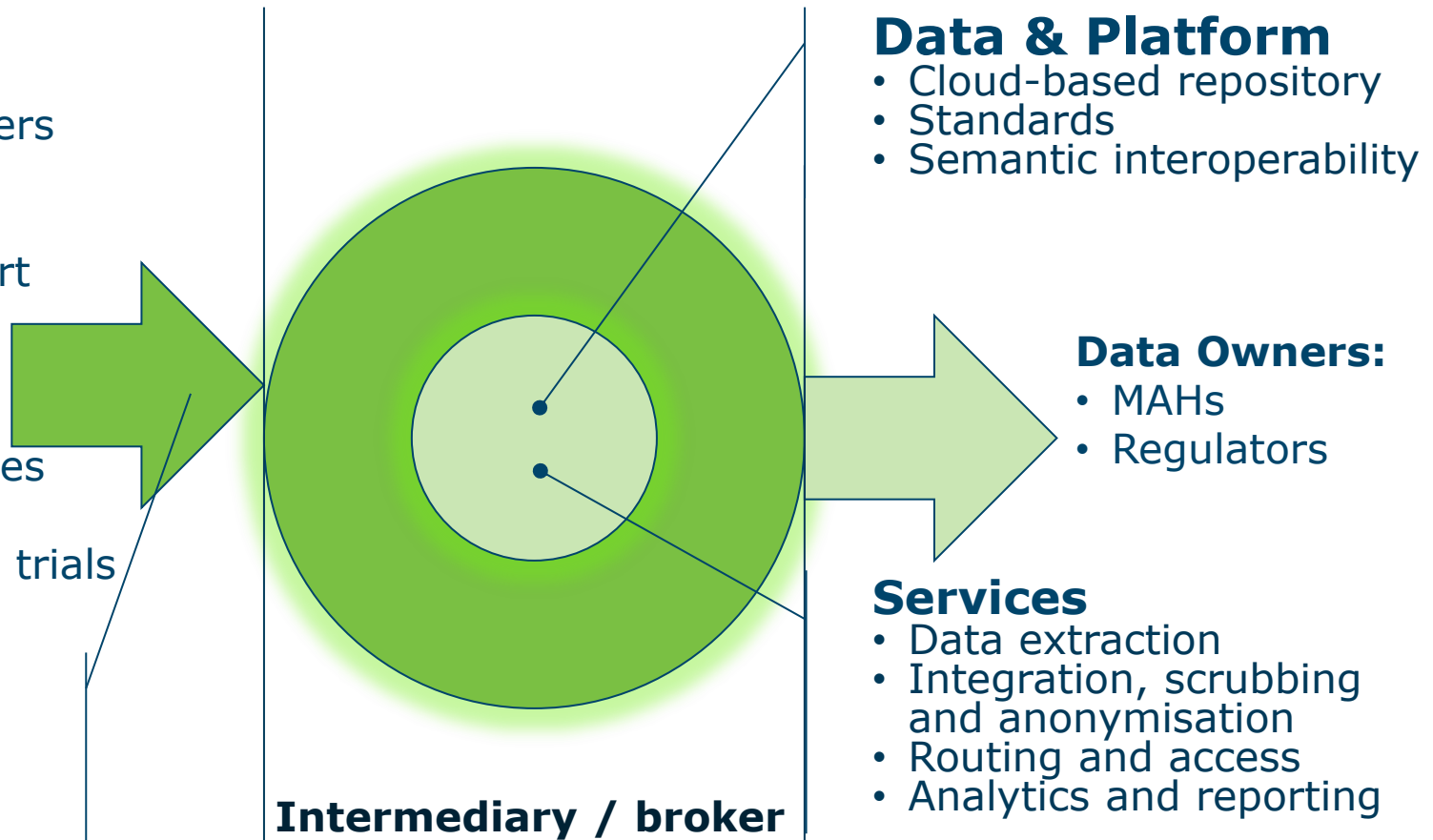
- A universal application will address many of the key questions and challenges.
- Industry moving this way, regulators already there www.yellowcard.mhra.gov.uk

Sources

- HCPs
- Patients / carers
- Sales reps
- Call centres
- Patient support programmes
- Registries
- Social media
- Brand web sites
- PASS
- Observational trials

Capture

- Module embedded in EHR



Further applications of the proposed WEBAE solution(s)



- **R&D Topics of Interest**
 - Emerging unknown side (beneficial) effect of a drug
 - Emerging off-label/alternative use of a drug
 - Recognizing/tracking emerging disease/public health threat
 - Inaccurate and inappropriate statements and claims about drugs and devices
 - Drug abuse and misuse
 - **Commercial Topics of Interest**
 - Product quality complaint
 - Medication errors
 - Reports of counterfeiting
 - Opinion/sentiment trends of a drug, device, or company
 - Lack of effectiveness or comparative efficacy of a drug
-

Theme 1: Policy Advancement



- Provide policy and regulatory guidance for market authorisation holders of how such social media surveillance can be used in practice when taking into account of both the European Medicines Agency guidelines and the European Union Data Protection Directives
- Ability to track the provenance of the data - implications with respect to data privacy

Data privacy - Who am I?



- **Age:** 50-year-old
- **Gender:** Male
- **Suspected ADR:** Respiratory arrest
- **Suspect drugs:** Diprivan, pethidine, alprazolam & sertraline
- **PMH:** Low BMI, vitiligo, and lupus syndrome
- **Outcome:** Fatal
- **Occupation:** Rock star
- **Narrative:** Patient was being treated by his personal physician at his mansion. Administration of propofol led to respiratory arrest and paramedics were called to assist. The resulting court case saw the attending doctor found guilty of involuntary manslaughter.



http://en.wikipedia.org/wiki/Death_of_Michael_Jackson

Who am I? medical data

Personal



- **Age:** 41 years
 - **Gender:** Male
 - **Suspected ADR:**
Possible drug interaction with alcohol
 - **Suspect drugs:**
Fluoxetine, tiapride, and albendazole
 - **PMH:** Alcoholism?
 - **Outcome:** Fatal
- **Occupation:** Deputy Head of Security, Ritz Hotel, Paris
 - **Narrative:** Patient was driving a Mercedes at high speed in the Pont d'Alma tunnel in Paris. He lost control of the car and crashed, killing himself and two passengers.



Theme 2: Technical Advancement of Social Media Analytics



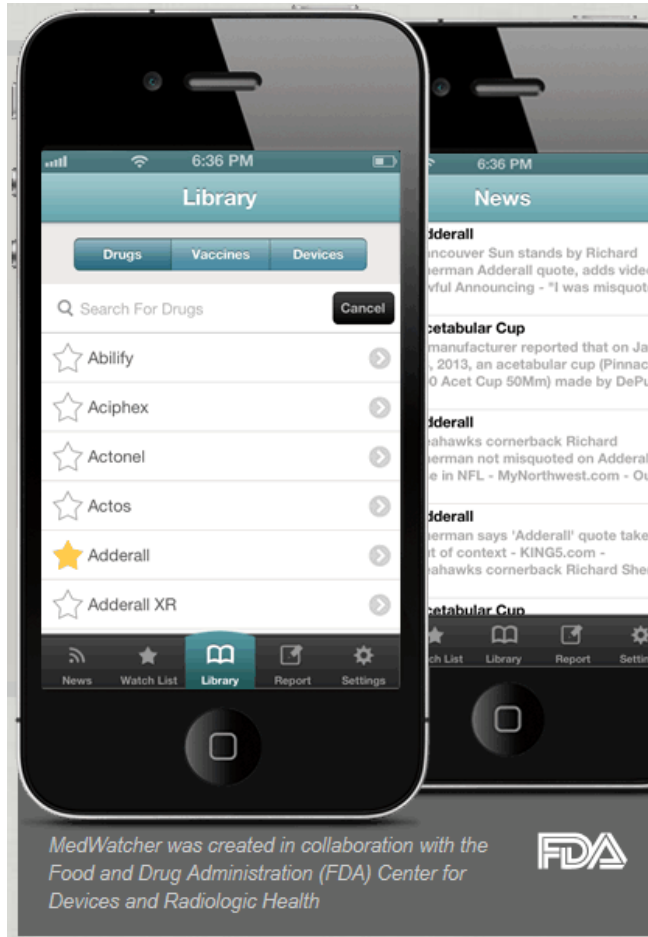
- The technical work packages of this project are required to provide several deliverables that together provide a reference platform for social media surveillance. These deliverables include
 - An open platform for gathering content from different web sources in real time and organizing such content in a format suitable to analysis
 - A series of algorithms that are coupled to the data gathering platform and enable the extraction and identification of ADRs
 - A series of algorithms and tools that are coupled to the data gathering platform and enable the provenance of data to be established across multiple social media source.

Theme 3: Deploy a mobile platform



- Free to use EudraVigilance Patient Reporting app across multiple platforms
- Free to use EudraVigilance Healthcare Professional Reporting app.
 - Both apps (or versions of one app) would be based on the XEVMPD in the context of the implementation of Article 57(2), 2 of the new pharmacovigilance legislation
 - Both apps would allow storage of reports
 - The patient app would enable storage of personal list of meds
 - The HCP app would enable storage of patient specific data with main focus on ADRs
- Geographic interactive display illustrating patterns of ADR reporting in real time.
- Interface to the EudraVigilance system enabling creation of ICSRs directly from electronic health records.
- Potential for two-way communication (data interchange) with reporters, including:
- Online social marketing campaign for publicizing and adopting the apps.

The MedWatcher App

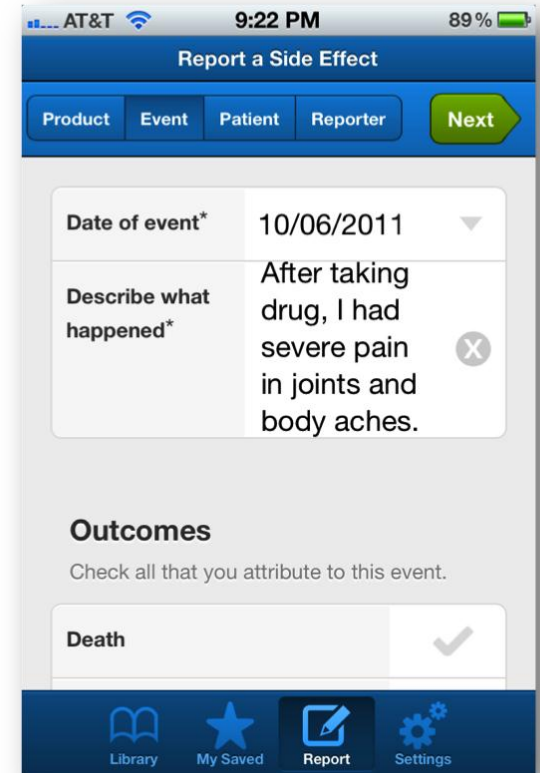
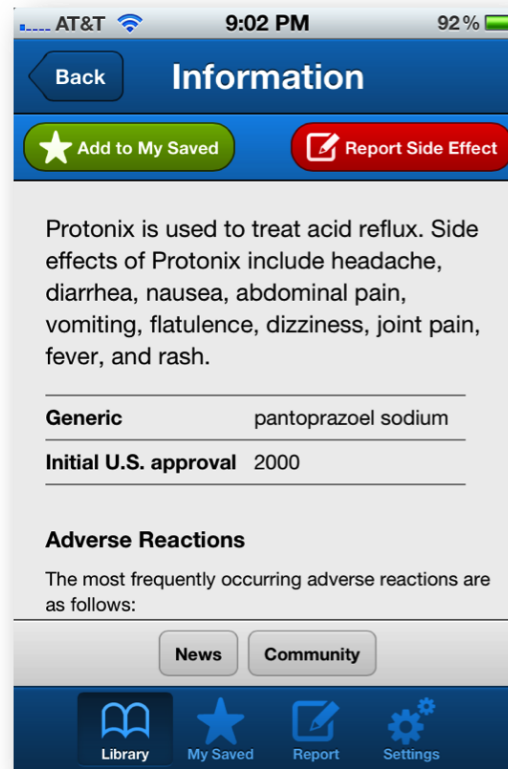
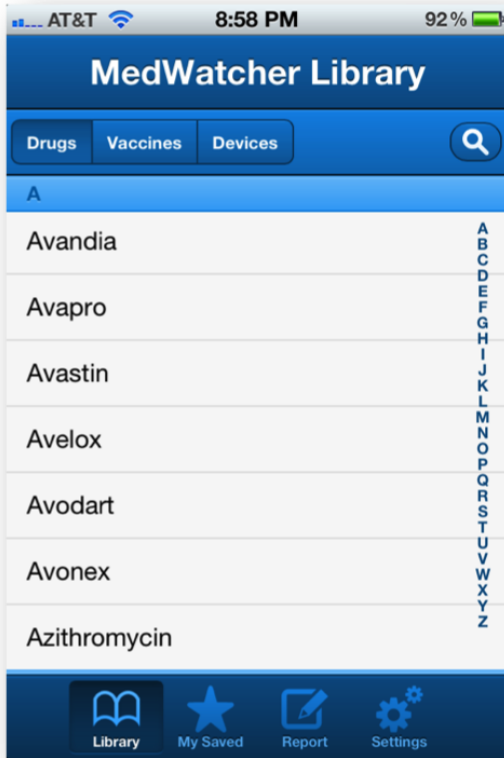


Potential Approach: MedWatcher App

- MedWatcher is a project out of Boston Children's Hospital and Harvard Medical School.
- It was created in collaboration with the FDA Center for Devices and Radiologic Health.
- The system is run by Epidemico, a Boston Children's spin-out company

<http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/FormsandInstructions/ucm348271.htm>

The MedWatcher App - Screens



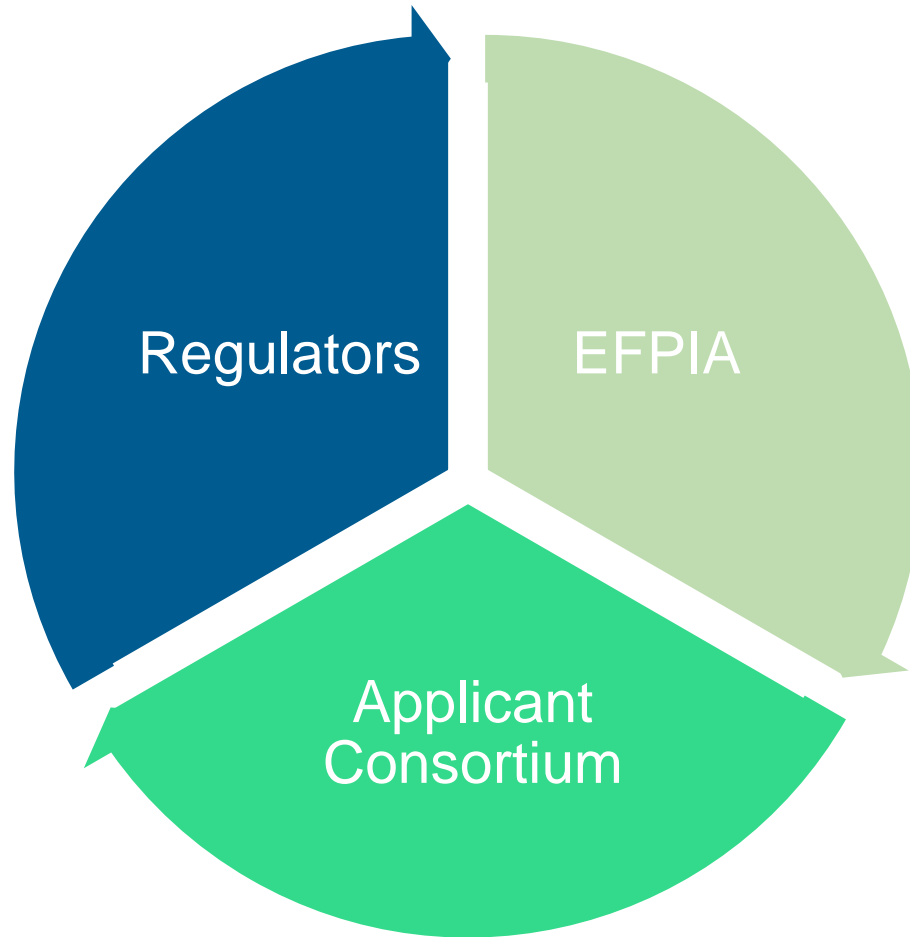
<https://medwatcher.org/>

Involved EFPIA Companies to date



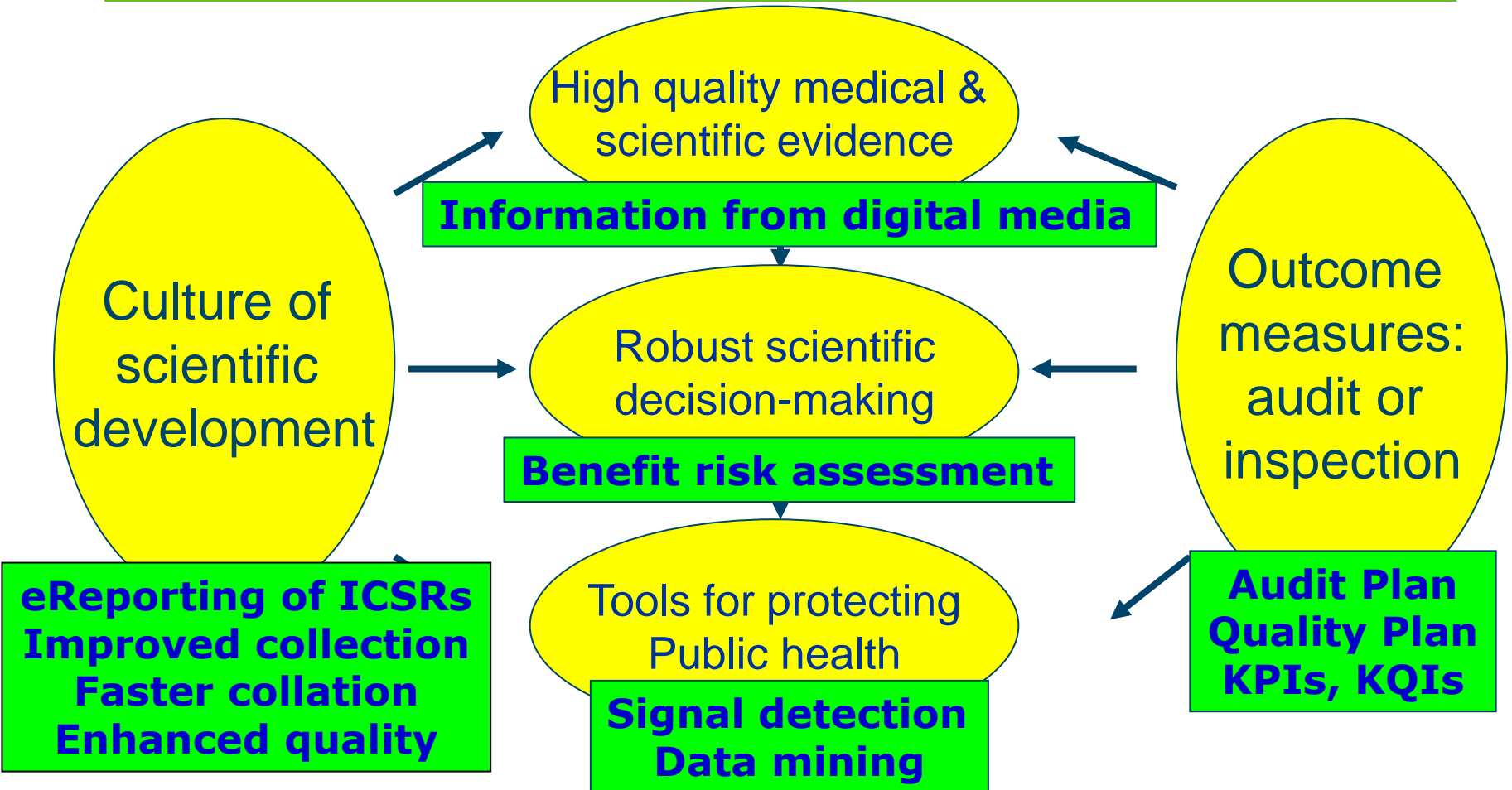
- **WEBAE committed Pharma industry partners:**
 - Novartis, Janssen, UCB, AstraZeneca, Sanofi
 - 3-year project timeframe
 - MAH funding >€2.5m
 - Expertise includes PV policy, PV operations and information technology
- **Under consideration:** Roche, Pfizer
 - Formation of a Pistoia working group to catalyse EFPIA group discussion during the IMI Call

Ideal WEBAE Consortium Structure



Model for excellence in PV*

Scientific basis for protection of public health



Measurable public health benefit

WEBAE Summary & conclusions



- Increasing use of social media and mobile IT devices, fast developing IT technology, combined with current regulations will increase have a dramatic impact on pharmacovigilance practice
 - WEBAE is an opportunity to develop a shared platform to support the collection, management and analysis of AE reports
 - WEBAE will provide a comparative test bed in the developing sciences of information extraction (IE), natural language processing (NLP) as well as data mining (DM)
 - WEBAE will enable a continued AE reporting policy review and adaptation in dialogue with the regulators
-