EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HCPWP PCWP

WITH SPECIAL THANKS TO EMA COLLEAGUES
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EMA,
AMSTERDAM
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A bit of history

PhV originated in an attempt to better understand the safety of medicines to better protect individuals

driven by disasters and events and the wish to prevent

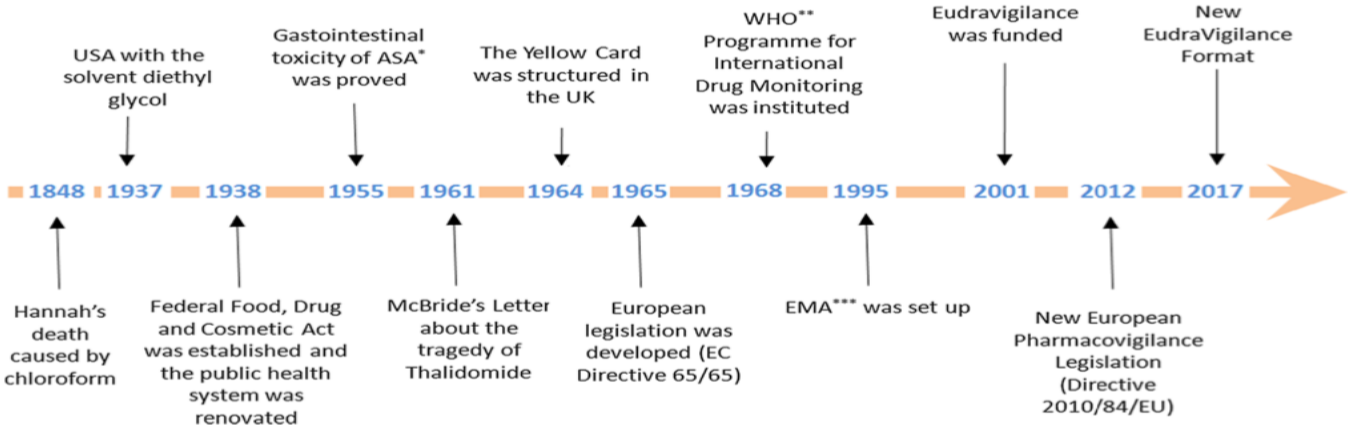
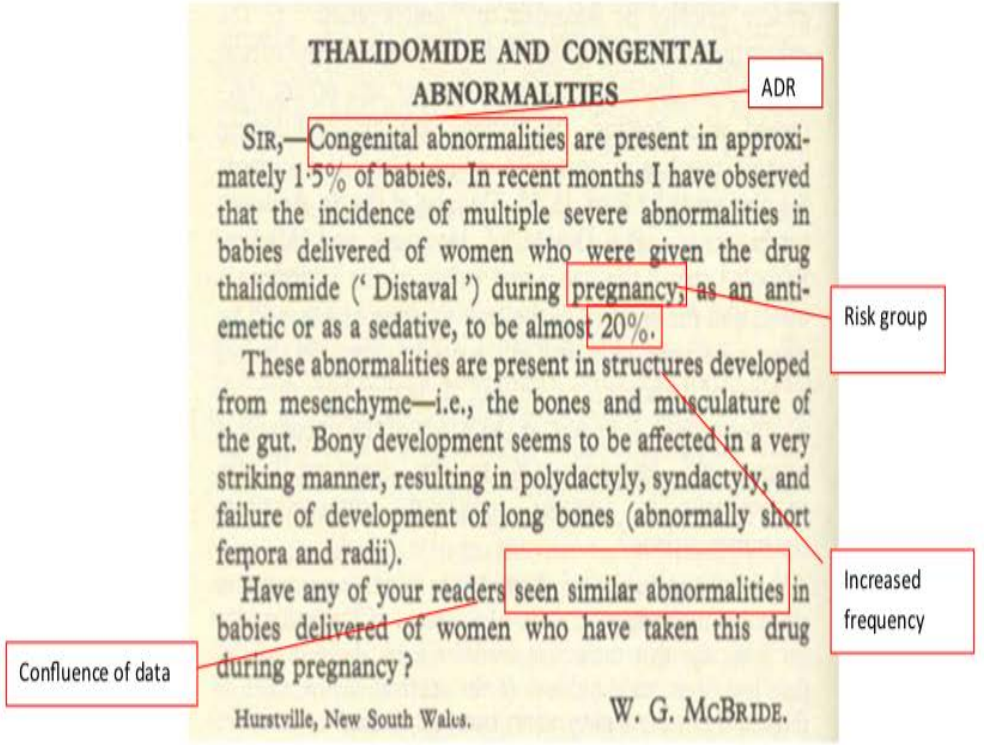


Fig. 1 Timeline of the historical evolution of Pharmacovigilance. *ASA: acetylsalicylic acid; **WHO: World Health Orgnaisation; ***EMA: European Medicines Agency

Analysis of a case report

Fig. 2 McBride's letter and important elements for generating spontaneous reporting



THALIDOMIDE AND CONGENITAL ABNORMALITIES

SIR,—Congenital abnormalities are present in approximately 1·5% of babies. In recent months I have observed that the incidence of multiple severe abnormalities in babies delivered of women who were given the drug thalidomide ('Distaval') during pregnancy, as an antiemetic or as a sedative, to be almost 20%.

These abnormalities are present in structures developed from mesenchyme—i.e., the bones and musculature of the gut. Bony development seems to be affected in a very striking manner, resulting in polydactyly, syndactyly, and failure of development of long bones (abnormally short femora and radii).

Have any of your readers seen similar abnormalities in babies delivered of women who have taken this drug during pregnancy?

Hurstville, New South Wales. W. G. McBRIDE.

Paradigm shift

From elementary quality requirements to safety and efficacy

From quality control of finished product to control of quality of manufacturing (inspection)

From "population" treatment to more "personalized" treatment

From structured to rapidly changing

From closed door to transparancy

FROM YES/NO TO LIFECYCLE

FROM SILO TO INCLUSIVE

Pharmacovigilance Risk Assessment Committee Mandate

All aspects of the risk management of the use of medicinal products including the detection, assessment, minimisation and communication relating to the risk of adverse reactions, having due regard to the therapeutic effect of the medicinal product, the design and evaluation of post-authorisation safety studies and pharmacovigilance audit

Pharmacovigilance Risk Assessment Committee

Membership of PRAC

Appointed by each Member State:

1 member + alternate

28 + EEA countries non voting members

Appointed by European Commission:

6 members - relevant expertise

1 member / 1 alternate representing patient organisations

1 member / 1 alternate representing healthcare professionals

How does PRAC involve patients and HCPs

Representation in PRAC plenary

- involvement in all discussions

Consulting on DHPCs

Public hearings

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Impact research

Pharmacovigilance impact research aims to

i) determine the effects of regulatory interventions on knowledge, behaviour and patient health outcomes and examine how these effects are distributed at population level, and

ii) provide evidence-based recommendations to inform regulatory decision-making

9.7.3 Outcomes of regulatory action

The strengths and weaknesses of the European PhV System regarding the outcomes of regulatory action can be summarised as follows:

Strengths of the PhV System	Weaknesses of the PhV System
•	• The outcomes of regulatory action are only assessed in exceptional cases. • There is very little information about what prescribers do with label information and label changes. Moreover, when information is there, the results are not very encouraging. • The missing information on outcomes is partially attributed to far too few inspections of MAHs with a pharmacovigilance focus.

Generally, the outcomes of regulatory action cannot easily be evaluated, because even the agencies do normally not have such information. Actions are not evaluated pro-actively, and even if changes in the morbidity and mortality caused by ADRs were detected they could not causally be related to single regulatory acts.

Original Contribution

December 20, 2000

Contraindicated Use of Cisapride

Impact of Food and Drug Administration Regulatory Action

Walter Smalley, MD, MPH; Deborah Shatin, PhD; Diane K. Wysowski, PhD; et al

» Author Affiliations

JAMA. 2000;284(23):3036-3039. doi:10.1001/jama.284.23.3036

in the 12 months following this regulatory action, hundreds of thousands of patients in whom cisapride use was contraindicated were likely to have received this drug. The exposure of these patients to inappropriate cisapride use, despite the prominent publication of case reports, label changes, and Dear Health Care Professional letters, highlights the need to develop more effective methods for modifying practice to reflect new information about a drug's risks and benefits.[13-15]

JAMA | Original Investigation

Assessment of the FDA Risk Evaluation and Mitigation Strategy for Transmucosal Immediate-Release Fentanyl Products

Jeffrey Eric Rollman, MPH, NRP; James Heyward, MPH; Lily Olson, BA; Peter Lurie, MD, MPH; Joshua Sharfstein, MD; G. Caleb Alexander, MD, MS

IMPORTANCE Transmucosal immediate-release fentanyls (TIRFs), indicated solely for breakthrough cancer pain in opioid-tolerant patients, are subject to a US Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategy (REMS) to prevent them from being prescribed inappropriately.

OBJECTIVES To evaluate knowledge assessments of pharmacists, prescribers, and patients regarding appropriate TIRF use; to describe sponsor assessments, based on claims data, of whether the REMS program was meeting its goals; and to characterize how the FDA responded to REMS assessments.

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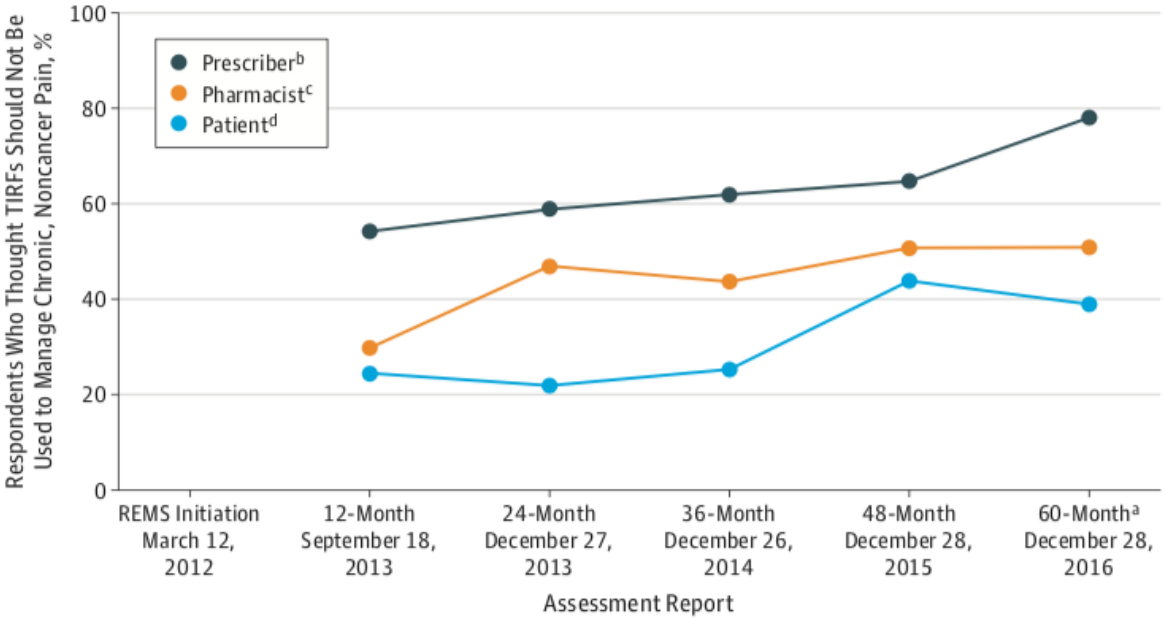
Supplemental content

CME Quiz at jamanetwork.com/learning

Figure 3. Pharmacists, Prescribers, and Patients Who Believe Transmucosal Immediate-Release Fentanyls (TIRFs) Should Not Be Used to Manage Chronic, Noncancer Pain and Associated US Food and Drug Administration (FDA) Actions



FDA Review

August 21, 2014	August 3, 2015	November 10, 2016	December 4, 2017
FDA requested additional survey question to understand why the prescribers who prescribe TIRFs for chronic, noncancer pain do so	FDA reiterated request for additional survey question	FDA requested meeting to discuss low awareness of the need to prescribe TIRFs to appropriate patients	FDA reached conclusion that REMS is not meeting its goal of prescribing TIRFs to appropriate patients

Conclusions

In this review of FDA documents pertaining to the TIRF REMS, surveys of pharmacists, prescribers, and patients reflected generally high levels of knowledge regarding proper TIRF prescribing, yet some survey items as well as claims-based analyses indicated substantial rates of inappropriate TIRF use. Despite these findings, the FDA did not require substantive changes to the program.

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY (2013)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3481

ORIGINAL REPORT

Concomitant use of isotretinoin and contraceptives before and after iPledge in the United States†

Simone P. Pinheiro[1]*, Elizabeth M. Kang[1], Clara Y. Kim[2], Laura A. Governale[1], Esther H. Zhou[1] and Tarek A. Hammad[1]

A study conducted in The Netherlands,[11] where a less stringent risk management program has been in place, suggested higher, albeit still insufficient, concomitant contraception use with isotretinoin prescriptions. In the Dutch study, the proportion of women with total monthly overlap of isotretinoin and contraceptives ranged 38%–41% for systemic contraceptives and was approximately 12% for local contra-

Valproate case study

- Active substance used in epilepsy, bipolar disorder and migraine
- Life-saving treatment for epileptic women
- Teratogenicity with frequent and severe congenital malformations and adverse neurological impact long-term for the child
- Last risk minimisation measures taken in the EU in 2014 showed lack of effectiveness
- New EU referral procedure initiated in 2017 and concluded in January 2018 with a comprehensive pregnancy prevention programme including counseling
- Involvement of patient and healthcare professional organisations through all available mechanisms in 2017, i.e.
  - ❖ Written consultation –implementation of risk minimisation measures (RMM)
  - ❖ Public hearing NEW
  - ❖ Dedicated meetings (3)

Content analysis

- Patients' and healthcare professionals' agreement on need for access to valproate
- Patients' and healthcare professionals' majority agreement on informed choice of the female patient
- Identification of lack of coordination, resources and processes in healthcare for implementation of RMM
- Many RMM proposals with plausible expectations but little evidence on appropriateness/effectiveness = research gap
- Little convergence on practicalities of implementation, in particular delivery of RMM to HPs and patients and its integration with existing healthcare structures, processes and resources and related responsibilities
- Identification of training needs for HP communication skills

Conclusions for regulators

- **Engage** as input from patients and healthcare professionals is important and useful for regulatory decision-making on RMM

- **Discuss implementation- and solution-focussed questions** for filling areas of relevance to regulatory decision-making for RMM that feasible in healthcare, maybe facilitated by the AAA-CIT tool – to be piloted

- **Support implementation of RMM** as expected by the public

Changing landscape

Future perspective “ P4” medicine

- Prevention
- Prediction
- Personalised
- Participation

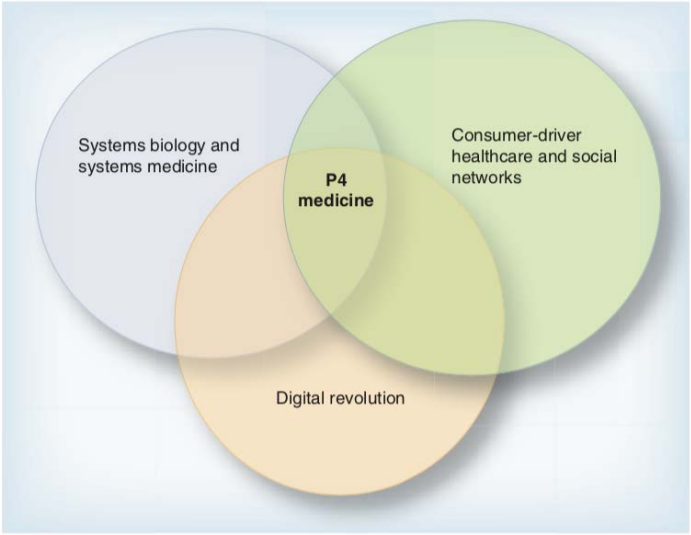


Figure 1. Three converging megatrends driving the transformation of healthcare. P4 healthcare is emerging at the intersection of these megatrends. P4: Predictive, preventive, personalized and participatory.

Improved engagement of patients and healthcare professionals

New forms of participation by patients and healthcare professionals are key to delivering the vision for transformation of healthcare in the digitally networked era.

One of our society's greatest assets is the increasing determination of healthcare consumers to better manage their own health using the internet to gather information and their ability to self-organize using social networking tools

Networked and activated consumers have increasing demands