EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

SYMPOSIUM
PROTECT

Monitoring benefits and risks of medicines:
PROTECT results and recommendations, 18-20 February 2015, EMA, London

Dates

Training courses:
18 February 2015
14:00-18:00

PROTECT Symposium:
19 February 2015,
09:00-18:00

20 February 2015,
08:30-15:00.

Place

European Medicines Agency, 30 Churchill Place, Canary Wharf, London E14 5EU

The Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium (PROTECT) is a 5-year public-private partnership of 34 partners initiated in 2009 to enhance the monitoring of the safety of medicinal products and contribute to better evaluate and communicate their benefit-risk profile throughout their lifecycle. To this end, PROTECT planned to develop and test methodological standards and innovative tools.

The objective of the Final PROTECT Symposium is to present the main results and recommendations of PROTECT and discuss their implications from a methodological perspective and for the evaluation of the benefits and risks of medicines. Four parallel pre-symposium training courses will provide in-depth training on specific aspects of the research work performed in PROTECT.

The main topics will include methods to collect data directly from consumers, signal detection, methods to improve consistency between pharmacoepidemiological studies and benefit-risk integration and representation.

FOLLOW THE BROADCAST

ON THE 19TH AND 20TH FEBRUARY 2015

More information at:

www.ema.europa.eu

www.imi-protect.eu

Visit our website

Further information about the PROTECT project is available on our website:

http://www.imi-protect.eu/

Aknowledgments

The PROTECT project has received support from the Innovative Medicines Initiative Joint Undertaking (www.imi.europa.eu) under Grant Agreement n° 115004, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution. The views expressed are those of the authors only.

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PROTECT

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Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium

Pre-symposium training

18 February 2015, 14:00-18:00

Parallel sessions

1. Benefit-risk assessment: concepts and methods *Leaders: Deborah Ashby, Steve Hobbiger, Sharhul Mt-Isa*

This session will review and discuss structured methodologies for the assessment and visualisation of the benefit-risk of medicines and explain how they can support benefit-risk decision-making. Methods and examples for patients and public involvement will be described. PROTECT resources for further learning will be presented.

2. Application of MCDA to real-life decision-making *Leaders: Mireille Goetghebeur, Billy Amzal*

This training will familiarise the audience with structured benefit-risk assessment of medicines using a hands-on exercise based on multicriteria decision analysis (MCDA) and evidence synthesis to handle data heterogeneity similar to that encountered in a product's lifecycle. Based on a real-life example, participants will perform a structured elicitation of weights and performance scores for benefit and risk criteria and discuss the challenges and opportunities of this approach in real life settings.

3. Statistical signal detection *Leaders: Niklas Norén, Jim Slattery*

This training will explain the role of statistical signal detection (SD) in pharmacovigilance and the concept, methods and pitfalls of disproportionality analysis. It will address the need and methods for empirical evaluation of measures, propose factors to be considered for the choice of methods and provide a view of SD processes applied to different information sources. Specific topics in SD will be covered.

4. Methods to control for confounding *Leaders: Olaf Klungel, Rolf Groenwold, Nicolle Gatto*

Starting from an overview of methods to control for confounding and of their importance in epidemiology, this training will address more specifically propensity scores and the use of balance measures; time-dependent confounding and the use of marginal structural models; and the use of instrumental variables. These methods will be illustrated with case studies performed in PROTECT.

Format

Pre-symposium training courses will explain methods developed and tested in PROTECT, starting from basics and progressing towards more advanced knowledge. The audience will be engaged in interactive discussions to ensure good understanding of the concepts and methods.

Each session of the symposium will open with a presentation of the knowledge gaps which PROTECT intended to address, provide the main results of case studies and discuss the implications of the findings for the benefit-risk monitoring of medicines.

Throughout the symposium, posters developed by PROTECT and presented in various conferences will be displayed, giving opportunities for direct discussions during breaks. Websites and databases developed by PROTECT will be made available on laptops to allow one-to-one explanation of their use.

Faculty

For each topic, objectives, results and recommendations will be presented by researchers of the involved work package(s). Non-PROTECT international speakers will be invited for some topics.

Parallel Training Sessions 18 February 2015, 14:00-18:00

I. BENEFIT-RISK ASSESSMENT: CONCEPTS AND METHODS

LEADERS: DEBORAH ASHBY, STEVE HOBBIGER, SHARHUL MT-ISA

1.	Introduction to benefit-risk assessment of medicinal product *Deborah Ashby*	14:00-14:15
2.	Taxonomy of benefit-risk assessment methodologies *Shahrul Mt-Isa*	14:15-14:30
3.	Visualising benefits and risks: concepts and ideas *Christine Hallgreen*	14:30-14:45
4.	*From qualitative to fully quantitative benefit-risk decision-making* *Larry Phillips, Richard Nixon, Ed Waddingham*	14:45-15:30
5.	Open source software for benefit-risk modelling and clinical data analysis: ADDIS and Effects Table *Douwe Postmus*	15:30-16:00
6.	PROTECT resources for further learning *Gerry Downey, Subhakanta Das*	16:00-16:30
	Coffee break	16:30-17:00
7.	Patients and public involvement in benefit-risk assessment and decision-making: methods and applications *Ed Waddingham, Richard Nixon*	17:00 17:30
8.	Patients understanding of benefit-risk balance *Andrea Beyer*	17:30-17:55
9.	Closing remarks and take-home messages *Deborah Ashby*	17:55-18:00

Parallel Training Sessions 18 February 2015, 14:00-18:00

II. APPLICATION OF MCDA TO REAL-LIFE DECISION-MAKING

LEADERS: MIREILLE GOETGHEBEUR, BILLY AMZAL

1.	Overview of multicriteria and statistical methods applied to regulatory decisions *Mireille Goetghebeur, Billy Amzal*	14:00-14:45
2.	Hands on exercise – Preference and weights elicitation from the participants will be performed using the Efalizumab case study	14:45-16:00
	Coffee break	16:00-16:30
3.	Presentation of preliminary results	16:30-17:00
4.	Discussion : Challenges and opportunities	17:00–18:00

Parallel Training Sessions 18 February 2015, 14:00-18:00

III. STATISTICAL SIGNAL DETECTION

LEADERS: NIKLAS NORÉN, JIM SLATTERY

1.	Statistical signal detection in practice – brief perspectives from Novartis, EMA, and WHO	14:00-14:30
2.	Introduction to disproportionality analysis *Andreas Brückner*	14:30-15:15
3.	*Pitfalls of disproportionality analysis* *Niklas Norén*	15:15-16:00
	Coffee break	16:00-16:30
4.	Introduction to empirical evaluation *Jim Slattery, Gianmario Candore*	16:30–17:30
5.	Closing remarks/Questions	17:30-18:00

Parallel Training Sessions 18 February 2015, 14:00-18:00

IV. METHODS TO CONTROL FOR CONFOUNDING

LEADERS: OLAF KLUNGEL, ROLF GROENWOLD, NICOLLE GATTO

1.	Introduction *Olaf Klungel*	14:00-14:15
2.	Introduction/overview of methods to control for confounding *Nicolle Gatto*	14:15-15:15
3.	Control for unmeasured confounding *Rolf Groenwold*	15:15-16:15
	Coffee break	16:15-16:45
4.	Control for time-dependent confounding *Sanni Ali*	16:45-17:45
5.	Closing remarks/Questions	17:45-18:00

Day 1, 19 February 2015, 09:00-18:00

	Registration		08:00-09:00
1.	**Opening of the Symposium** **- Welcome** **- Introduction**	Guido Rasi June Raine	09:00-09:20
2.	**The place of PROTECT in regulatory science**	Fergus Sweeney	09:20-09:30
3.	**PROTECT: shaping objectives into a work programme**	Liz Swain	09:30-09:40
4.	**Signal detection** *Session co-chairs: Suzie Seabroke, Georgy Genov*		**09:40-13:00**
4.1.	Introduction to PROTECT research and recommendations for statistical signal detection	Antoni Wisniewski	09:40-10:00
4.2.	Use of ontologies in signal detection The PROTECT structured SPC-ADR database Grouping of ADR terms	Jim Slattery	10:00-10:30
4.3.	Statistical signal detection for spontaneous reports Which method to use? Subgroups and stratification Unmasking, interactions, and duplicate detection	Suzie Seabroke	10:30-11:00
	Coffee break		11:00-11:30
4.4.	Signal detection from clinical trials	Andreas Brückner	11:30-11:50
4.5.	Signal detection in electronic medical records	Niklas Norén	11:50-12:20
4.6.	**Panel discussion: key recommendations and future priorities**	Niklas Norén Jim Slattery Stephen Evans Gerald Dal Pan	12:20-13:00
	Lunch break		**13:00-14:00**

Day 1, 19 February 2015, 09:00-18:00

5.	**Improving consistency between pharmacoepidemiological studies** *Session co-chairs:* *Jean-Michel Dogne, Corinne de Vries*		**14:00-18:00**
5.1.	Objectives and methods	Robert Reynolds	14:00-14:15
5.2.	Outcomes of studies for six adverse event-drug pairs and five databases: what did we learn?	Olaf Klungel	14:15-14:45
5.3.	Replication of studies based on a common protocol	Stephanie Tcherny Lamiae Grimaldi	14:45-15:10
5.4.	Comparison of methods to control for confounding: review of findings and lessons	Rolf Groenwold	15:10-15:35
5.5.	Measuring the public health impact of adverse drug reactions	Luisa Ibañez	15:35-16:00
	Coffee break		16:00-16:30
5.6.	Canadian initiative: CNODES	Samy Suissa	16:30-17:00
5.7.	US initiatives: OMOP and Mini-sentinel	Tobias Gerhard	17:00-17:30
5.5.	**Panel discussion: PROTECT recommendations in a global perspective**	Samy Suissa Tobias Gerhard Olaf Klungel Robert Reynolds	**17:30-18:00**

Day 2, 20 February 2015, 08:30-15:00

	Welcome – Introduction to participants of Day 2	June Raine Fergus Sweeney	08:30-
6.	**Pilot study of Direct-to-Patient pharmacovigilance** *Session co-chairs: Noël Wathion, June Raine*		**08:30-10:00**
6.1.	Background and objectives of the PROTECT Pregnancy study Tools for direct-to-patient data collection and recruitment strategy Study results and comparison with electronic healthcare records Participation in the Pregnancy study: a qualitative study	Nancy Dreyer Stella Blackburn	08:35- 09:40-
6.2.	**Panel discussion: Lessons learned and recommendations for future direct-to-patient pharmacovigilance studies**	Isabelle Moulon Alison Lightbourne Nancy Dreyer David Haerry	09:40-10:20
7.	**Benefit-risk integration and representation** *Session co-chairs: Peter Bachman, Fergus Sweeney*		**10:20-13:00**
7.1.	Recommendations of the PROTECT Benefit-Risk Group: A roadmap in pursuit of robustness, transparency and harmonisation.	Deborah Ashby	10:20-10:40
	Coffee break		**10:40-11:10**
7.2.	Benefit-risk assessment: a real-life experience	Billy Amzal	11:10-11:30
7.3.	In sickness and in health, and for the greater good: Involving patients and the public in benefit-risk decision-making	Susan Talbot	11:30-11:50
7.4.	Patients' understanding of benefits and risks	Andrea Beyer	11:50-12:20
7.5.	Panel discussion: the past, the present and the future	Deborah Ashby Hans-Georg Eichler Hans Hillege	12:20-13:00
	Lunch Break		**13:00-14:00**

Day 2, 20 February 2015, 08:30-15:00

8.	**Review of experience and lessons learnt** *Session co-chairs: Peter Arlett, Liz Swain*		**14:00-15:00**
8.1.	Contribution from PROTECT to regulatory practice: from science to process improvement	Xavier Kurz	14:00-14:20
8.2.	The Innovative Medicines Initiative: lessons learnt from public-private partnerships and future directions	Hugh Laverty	14:20-14:40
8.3.	Discussion: what is next?	Peter Arlett Liz Swain Hugh Laverty Xavier Kurz June Raine	14:40-15:00
	Wrap-up and closure of symposium	June Raine Fergus Sweeney	15:00