Minutes of the Pharmacovigilance SIG

Hosted by Bristol Myers Squibb, Lawrenceville, NJ, USA

October 21st-22nd 2003

Attendees

John Wise, Tavistock Europe Ltd
Uwe Trinks, Sentrx Inc
*Chris Jones, CERN
Franck Hémont, Ipsen
*Ron Behling, BMS
*John Paugh, Wyeth
Mike O'Connor, Wyeth
Howard Bilofsky
*Rajesh Ghost, Novartis
Craig Funt, BMS

* Attended first day of SIG only.

Minutes

John Wise opened the meeting with a presentation on "Why Pharmacovigilance?". The presentation is attached to these minutes.

The presentation prompted discussion of how one could define Pharmacovigilance. FDA and Risk Management Papers are though to contain definitions. John's presentation outlined the continued change/evolution in regulations, and standards that govern Pharmacovigilance and present the industry with a substantial challenge.

The activities of ICH [1], which includes the Industry associations of Europe, Japan and USA (EFPIA, JPMA, and PhRMA, the regulatory agencies of the EMEA, MHLW and FDA plus observers from WHO, EFTA (represented by Switzerland) and Canada), were touched on. Of considerable concern was the emergence of multiple variations to the E2B standard for submission of Pharmacovigilance ICSRs to different national competent agencies, especially in the EMEA region, presented all companies with a challenge.

The delegates were invited to pair-up, they interviewed each other and then introduced each other to the meeting. Delegates submitted their meeting objectives and anticipated outcomes, which could be summarized as follows:

- Objectives: Obtain a broader understanding of:
    - Pharmacovigilance
    - IT applied to Pharmacovigilance
- Outcomes:
    - Benchmarking
    - Identify business benefits
- 'Roadmap' for Pharmacovigilance & its IT

[1] International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human

- Identify major challenges

- Influence regulators and provide recommendations for the exchange of safety data

- Write a Pharmacovigilance 'White Paper'A complete list of Objectives and Outcomes are appended to the minutes.

Representatives of Novartis, Ipsen, BMS and Wyeth presented the SIG with an overview of the systems that are deployed to support Pharmacovigilance in their companies. An industry comparison of systems was made available to the SIG, and the comparative and anonomized spreadsheet is embedded in this document.

Following lunch, Uwe Trinks, as the subject matter expert presented his *personal view* (not necessarily that of his employers) of Pharmacovigilance challenges and Risk Management. Uwe's presentation covered three key areas:

1. The challenge of signal detection and the need for improved algorithms

2. The extensive and changing regulations

3. Risk Management or "tolerable uncertainty" as advocated by Peter Honig Global Head Risk Management, Merck&Co., former Head of Safety, FDA

His slides are also made available with the minutes.

Following discussion, the group worked together to develop current and future views of the Pharmacovigilance landscape. These views are summarized below:

	Current	Future (3-5 year)	Transition
Process	• Paper driven • Unclear ownership especially for Risk Management • PhV Processes are high quality but… -Redundant data entry across organisation - clinical SAEs, call centers and partners -Reconciliation overhead • E2B + paper reporting process • EMEA legal demands unrealistic • Spontaneous data is undervalued	• Electronic • Phase II, then submission but with on-going Pharmacovigilance • Pre-approval pure safety trials in clinical • One unique source for where the AEs are stored • E2B reporting process • Electronic patient records, the value of patient safety data will increase	• Emergence of recognized Signal Detection algorithms • Evolution of data exchange standards • Adoption of consistent risk management practices
Regulations	• Increasing global diversity of regulations -Multiplicity of regulations -Uncertainty about regulations -Which GFIs are worth commenting on (FDA have withdrawn 60 this year) • Case reporting focus • EMEA regulations weakly imposed upon nation states • Reactive to regulations	• Proactive partnership with regulators • Risk / benefit management focus • Labeling environment changes • Pharmacogenomics	"The Tome" PDUFA III Co-ordinated input from the industry

THE PRISM FORUM

	Current	Future (3-5 year)	Transition
Technology	• Bespoke & O-T-S • Diverse standards e.g. - XML vs SGML - E2B extensions for various countries • Dysfunctional FoI database • Competing dictionaries	• Bespoke & O-T-S • Point-of-Discovery data input componentized, web-based user interface – hyperlinked • Standard electronic patient records and exchange of information • Wireless & handheld (e.g. Sales Reps – NO PATIENTS) • Functional, accurate real-time FoI Database • Sematics and Ontologies – especially for data mining • Greater availability to global epidemiological data base • Trusted Third Party Repository!	More standards required e.g. - HIPPA, - Expanded E2B, - CDISC, HL7m, NCDISC (FMIT) Better dictionaries across product lifecycle
People	• High medical skill, low computer skills • Cost of labour and geographic location • People burden on data collection • Physicians need LAN connection • Safety Physicians are in high demand • Misconception of PhV accountability	• High computer skills • Where they sit won't matter • People burden on data analysis • Physicians want to work from home • Safety Physicians still in high demand • Expectations are for better, faster, cheaper	Major training, development and education THE PRISM FORUM

Once a current and future view of Pharmacovigilance had been formed, the first day of the SIG meeting closed.

Day 2

The SIG reconvened at BMS and spent the morning until 11:30am finalizing the presentation for The PRISM Forum. The group also revisited the original list of outcomes and objectives to evaluate how much ground had been covered. It was felt that a substantial although not complete coverage of the issues had been achieved.

At 11:30am, the SIG joined the main PRISM Forum Meeting and Craig Funt of BMS gave an excellent and animated presentation of the SIG outcomes. Following discussion, it was agreed that John Wise, and Uwe Trinks should be encouraged to write a white paper/briefing document on the future of Pharmacovigilance with a view to getting the article published in an appropriate journal.

Supporting information:

Three PDF files:

1. OpeningRemarks.pdf (opening slides from John Wise)
2. Uwetrinks-PhVWS.pdf (Uwe Trinks slides Subject Matter Expert)
3. Workshoppresenttation.pdf (the outcome presentation made to the PRISM Forum)

Appendix 1 Objective and Outcomes

Objectives

GENERAL UNDERSTANDING:

- ☑ Understand what PhV is? Both current operational and advanced-leading edge.

INCREASED UNDERSTANDING OF THE PHV DISCIPLINE

- Identify any pharmacogenetic developments that could influence/impact safety
- Understand how anti-terrorism surveillance overlaps with PhV
- ☑ What plans for companies to capture and manage all submittable and non-submittable updates
- ☑ Understand the range of compliance options
- ☑ Understand current plans for signal detection
- ☑ EMEA regulations
- ☑ Learn more about the risk management approach

INCREASED UNDERSTANDING OF THE APPLICATION OF IT TO PHV

- ☑ What is the role of IT in PhV
- ☑ Understand more about IT support for PhV
- ☑ Understand the role for innovative IT
- ☑ What does PhV want from a CIO
- How can the regulatory trends be integrated into informatics projects portfolio

BENCH MARKING

- ☑ Gauge state of readiness for upcoming initiatives (E2B)
- ☑ Near term plans and priorities and what will be the key challenge over the next two years
- State of discussion between PhV and Global development
- ☑ Common industry Challenges
- ☑ Review regulatory issues and responses
- ☑ Benchmark the PhV organization
- ☑ How are the MedDRA version upgrades handled at other companies
- ☑ What are current signal detection plans
- ☑ Save time by learning best practice from other companies
- ☑ Understand members plans/direction for PV

- ☑ Understand members plans/direction for risk management
- ☑ How PhV It is organized at other companies
- ☑ Where are other companies in the E2B implementation
- ☑ Understand how other companies follow the regs
- Plans for all trial consolidation (data) related to safety
- ☑ Know more about (IT) initiatives in PhV in other companies
- ☑ Current state of participating companies

BUSINESS BENEFITS

- ☑ To understand future opportunities for PhV analysis to add value to the business
- ☑ Highlight the importance of PhV for company in general and marketing in particular
- ☑ Rapid response capability, reduced costs and finding multiple uses for safety data

BUSINESS ISSUE

- Understand why so little interest in this topic as evidenced by the low attendance

OUTCOMES

- List of requirements/needs for safety IT
- Shared action for a collaborative GRID-based initiative

- Defining a roadmap for risk management solutions and their impact
- List of major challenges for safety IT
- A plan to influence the regulatory authorities to improve safety data exchange and availability (recommendations to FDA – integrate AERS/SRS, etc)
- A white paper overview of the state of the art in PhV
- A successful workshop leading to enhanced understanding of PhV within the PRSIM Forum

Appendix 2 Comparative Spreadsheet of Industry Systems

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	**COMPANY**	***A***	***B***	***C***	***D***	***E***	***F***	***G***	***H***	***I***	***J***	***K***	***L***	***M***	
2															
3	**GENERAL**														
4	# Spontaneous cases annually	<10K	10-50K	50-100K	10-50K	<10K	10-50K	<10K	<10K	50-100K	50-100K	10-50K	50-100K	10-50K	
5	# Clinical study cases annually	<10K	10-50K	10-50K	<10K	<10K	<10K	<10K	<10K	10-50K	10-50K	10-50K	<10K	10-50K	
6	# total cases 2002	5,000	32,000	73,500	26,000	9,000	21,000	NA	4300	82,000	NA	45,000	100,000	33,000+	
7	# total cases 2001	5,000	32,500	64,500	25,000	8,000	16,000	NA	3430	70,000	NA	45,000	115,000	24,000+	
8	Overlap functions	Epidem	NA	NA	Techcomplaints	NA	Medinfo; Techcomplaints; Epidem	Medinfo; Techcomplaints; Epidem	Medinfo; Techcomplaints	Techcomplaints; Epidem	Medinfo; Techcomplaints; Epidem	Techcomplaints	NA	Medinfo; Techcomplaints; Epidem	
9	Outsource functions	Data entry	None	None	None	NA	None	None	None	None	Some data entry	None	Some case processing	Spontaneous for 1 drug	
10	**COMPANY**	***A***	***B***	***C***	***D***	***E***	***F***	***G***	***H***	***I***	***J***	***K***	***L***	***M***	
11	**SOFTWARE**														
12	**Name/type/#sites/ #users**														
13	AE collection	Argus/ client server/ 2-5/ 11-50	NA	Custom	Clintrace/ client server/ 21-40/ 101-200	Argus/ Remote/ <10/ 11-50	Custom/ 21-40/ 50-100	Clintrace/ client server/ 10/ <50	Argus/ client server/ <10/ 11-50	Custom/ client server/ 21-40/ 50-100	Custom/ web/ 11-20/ 101-200	Custom/ web/ 21-40/ >200	Custom/ web/ 21-40/ 51-100	Custom/ client server/ 11-20/ <100	
14	AE processing	Argus/ client server/ 2-5/ 11-50	Clintrace/ client server/ 6-10/ >200	Argus/ client server/ 6-10/ >200	Clintrace/ client server/ 2-5/ 51-100	Argus/ Remote/ 6-10/ 101-200	Aris-G/ Client server/ 21-40/ 51-100	Clintrace/ client server/ 2-5/ <50	Argus/ client server/ 1/ 11-50	Argus/ client server/ 6-10/ 51-100	Custom/ web/ 11-20/ 101-200	Custom/ web/ 2-5/ 51-100	Custom/ remote/ 6-10 / 101-200	Custom/ client server/ 2-5/ 101-200	
15	Signal detection	No	Qscan/ client server	NA	Client server/ 11-50	NA	NA	Client server	Argus, Brio/ client server/ 11-50	Client server	Custom/ web/ 11-50	Adhoc/ web/ 51-100	Lincoln Technol mining website	NA	
16	Ad-hoc queries/reports	Custom/ client server/ 2-5/ <10	Custom/ client sesrver/ 6-10	Custom/ client server/ 2-5/ 51-100	Custom/ client server/ 2-5/ 11-50	Custom/ remote/ 2-5/ <10	Custom/ 21-40/ 50-100	Custom/ client server/ 1/ <10	Custom/ client server/ 1/ 11-50	Argus/ client server/ 2-5/ 11-50	Custom/ web/ 2-5/ <10	Custom/ web/ 2-5/ 51-100	Custom/ remote/ 6-10/ 51-100	Custom/ client server/ 11-40/ >200	
17	E-sub to FDA	NA	NA	NA	NA	NA	NA	NA	NA	Argus	Custom	Custom	Galt Ass.	NA	
18	E-sub to EMEA	NA	NA	NA	Custom	NA	NA	Galt	NA	Argus	Custom	Custom	Galt Ass.	Galt Ass.	
19	Other IT systems	NA	Clintrace Workflow module	NA	NA	Galt DS Navigator	Auto-encoder TMS	NA	Oracle TMS for MedDRA	NA	NA	Custom web-base workflow and imaging	Custom tracking	NA	
20	**COMPANY**	***A***	***B***	***C***	***D***	***E***	***F***	***G***	***H***	***I***	***J***	***K***	***L***	***M***	
21	**STAFFING**														
22	# global safety employees	<50	>250	101-250	101-250	101-250	101-250	<50	NA	101-250	101-250	101-250	>250	>250	
23	# US safety employees	<50	101-250	<50	51-100	<50	<50	<50	<50	51-100	<50	101-250	101-250	101-250	
24	# data entry	10	100	110	>60	25	20	14	5	110	>100	60	60+	40	494
25	# medical review	2	30	25	7	8	15	5	5	25	<50	50	40+	56	228
26	# querying	5	20	90	3	NA	15	14	10	40	<50	4	30+	40	241
27	# 15 Day submissions	3	10	20	3	6	15	14	8	NA	101-200	3	15+	9	91
28	# periodic reporting	2	10	3	15	6	15	14	8	10	<50	25	15+	20-30	108
29	**COMPANY**	***A***	***B***	***C***	***D***	***E***	***F***	***G***	***H***	***I***	***J***	***K***	***L***	***M***	
30	**PLANNING**														
31	**Plan to make operational in 2003**														
32	FDA 15D E-sub	NA	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	
33	FDA periodic E-sub	NA	Yes	NA	NA	NA	NA	NA	NA	NA	Yes	Yes	Yes	NA	
34	EMEA E-sub	Yes	Yes	NA	Yes	NA	NA	Yes	NA	Yes	Yes	Yes	Yes	Yes	
35	EU national E-sub	Yes	Yes	NA	NA	NA	NA	Yes	NA	Yes	NA	Yes	Yes	NA	
36	Japan E-sub	NA	NA	NA	NA	NA	Yes	NA	NA	NA	NA	Yes	Yes	NA	