Summer 2009 • ISSUE 70

acdm
association for clinical data management

DataMatters

RISK MANAGEMENT SPECIAL ISSUE

Introduction to Risk and Risk Management

Clinical Risk Management

Quality Risk Management at F. Hoffman – La Roche

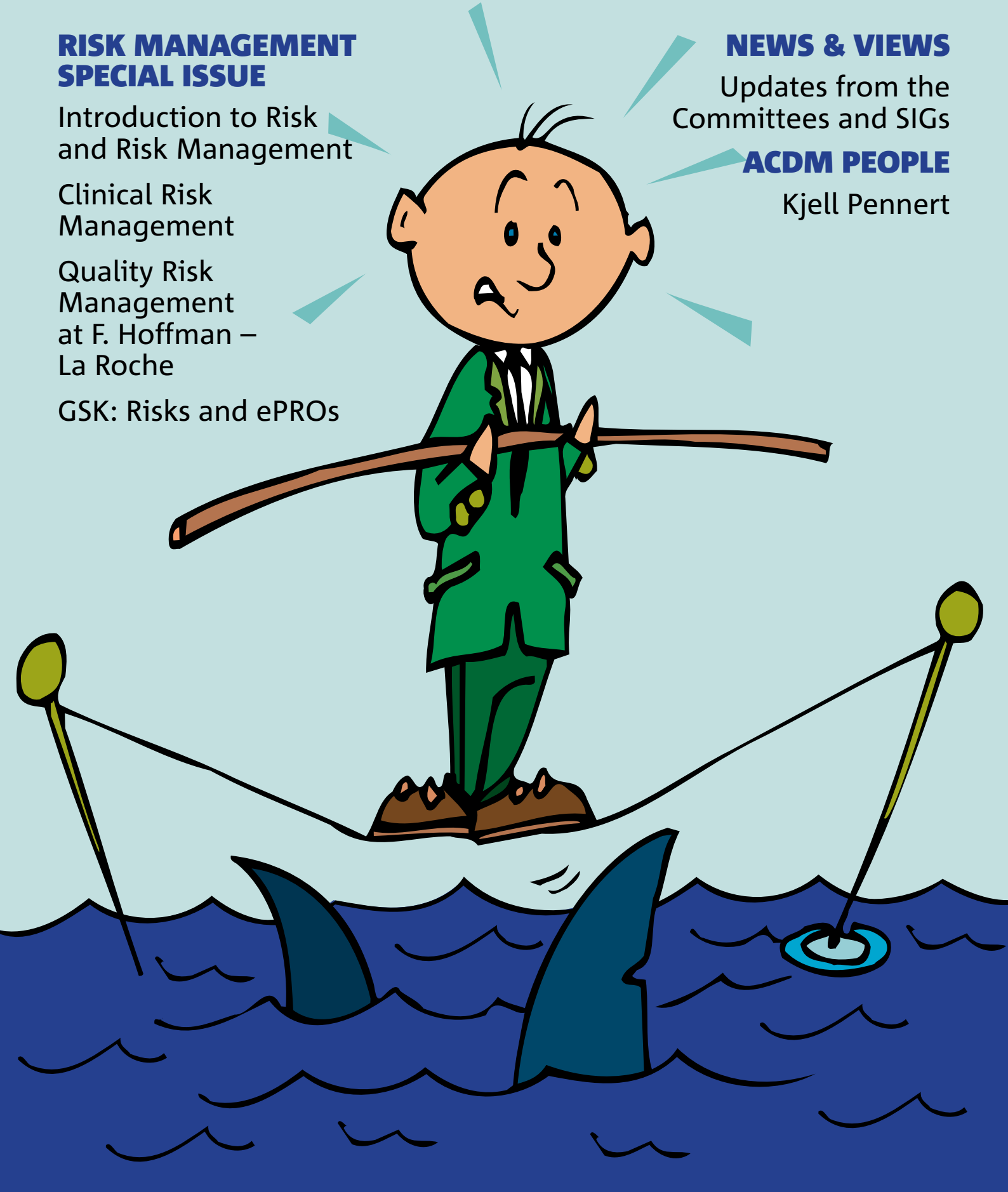
GSK: Risks and ePROs

NEWS & VIEWS

Updates from the Committees and SIGs

ACDM PEOPLE

Kjell Pennert



acdm
association for clinical data management

Newsletter Committee
Email to the Editor: editor@acdm.org.uk

Jon Milton (Chairperson/Editor)
Pfizer Global Research and Development
Tel: 01304 645788
Fax: 01304 652218
Email: jon.milton@pfizer.com

Nazma Ahmed
GlaxoSmithKline R&D
Tel: 020 8587 5204
Email: nazma.5.ahmed@gsk.com

Gill Lawrence
Kendle
Tel: 01344 751537
Fax: 01344 751549
Email: lawrence.gill@kendle.com

Jean Cornhill
PAREXEL International Limited
Tel: 01895 614539
Fax: 01895 614081
Email: jean.cornhill@parexel.com

Chinnie Nwandu
Roche Products Ltd
Tel: 01707 362896
Fax: 01707 373083
Email: chinnie.nwandu@roche.com

Usha Parekh
Roche Products Ltd
Tel: 01707 366927
Fax: 01707 384118
Email: usha.parekh@roche.com

Guidelines for Contributors

Articles range from 700 words to over 2,000. Photographs, diagrams and illustrations help to break up large areas of text. News items can range from 80 – 400 words to include photographs if relevant. Profiles can range from 300-600 words, and photographs will enhance these pages.

Photographs – We need good quality digital images taken at the highest resolution possible. With digital photography the more mega pixels the camera has, the better.

Illustrations – Charts and diagrams drawn in Excel or Word will normally need to be redrawn for the printing process. If images are embedded in Word documents they need to be supplied as separate jpegs as well.

Preferably, articles should be sent via Email or CD. Plain ASCII text is best, but many WP formats can be imported. Contact the Editor for help if you are unsure.

All articles should be sent to the Editor in good time for the copy deadline. Articles may need to be edited to fit the constraints of publishing, with full text available on request. All articles are subject to editorial approval.

The opinions expressed within this newsletter are those of the individuals concerned and not necessarily those of their employers or of ACDM. All advertisements included with it are done so independently and the Editor reserves the right to refuse any, which, in his opinion, do not conform with ethical advertising standards.

Designed and Produced by Character Design
Tel. 01981 541154 • info@characterdesign.co.uk

NEWSLETTER DEADLINES AND PUBLICATION DATES

If you would like to submit an article to the Newsletter or include an advertisement, then the following dates will help you plan:

Issue	Copy Deadline	Delivery of mailing
Autumn 2009	14 September	2 November
Winter 2009/10	4 December	1 February

ACDM E-shots

ACDM notices can be included in our twice monthly e-shots sent on the 1st and 15th of each month. ACDM notices should be emailed to the ACDM office 6 working days in advance.

ACDM ADVERTISING

ACDM offers advertising in the quarterly online Newsletter – *Data Matters* – and/or on the ACDM website at *www.acdm.org.uk*

Data Matters features articles on industry news and issues and ensures your advertisement will be viewed by an active audience of more than 1,200 data management professionals.

www.acdm.org.uk provides a classifieds section where your advertisement can be uploaded in a matter of hours. Not only will your advertisement reach all ACDM members but also the wider community of data management and other professionals who access the website.

ACDM ADVERTISING RATES

SPECIAL OFFER – 65% OFF ALL RATES UNTIL 1ST OCTOBER 2009

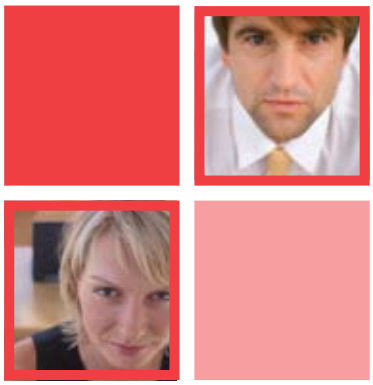
Effective from 1st August 2009

Newsletter	Full Page Colour*	£1000
	Half Page Colour*	£800
	Quarter Page Colour*	£450
Web advertising	One month*	£350
	Renewal per month (no changes)	£250
	Annual advert (up to 6 updates)	£2000

* bulk discounts available – please contact the ACDM office for details
(Tel: +44 (0) 1727 896080, email: admin@acdm.org.uk)

Download the latest advert specification sheet from the adverts section of www.acdm.org.uk

All items, excluding membership and publications, will be subject to VAT



ACDM COLLEGE WEEK

2-6 November 2009

Training Committee

CONTENTS

Strength to Strength

Welcome to the first ever eNewsletter for the ACDM, Data Matters is now available to all members via eshots and the website.

In the last year Data Matters has gone from strength to strength under the expert guidance of editor, Jon Milton, so it was a tough decision for the ACDM Board of Directors in considering adapting the traditional printed, paper format of the Newsletter to become 100% electronic. Key drivers were to continue the ACDM's commitment to becoming a paperless organisation wherever possible but also cost is a significant factor in many areas of running the ACDM and the organisation is as vulnerable to the effects of the "credit crunch" as the rest of us. The Board of Directors constantly monitor the organisation's expenditure and moving to an eNewsletter allows us to manage costs and direct funds to other development areas such as the expansion of the ACDM's portfolio of training courses and webinars.

Risk Management is the theme of the summer edition, a topic recently covered by an excellent Senior Forum Meeting earlier this year. That particular meeting reported on Risk Analysis Planning and several speakers shared their tools and methodologies they employed in their organisations. Look out for these half day meetings, which are held throughout the year – the topics are pertinent to the current, challenges we are all facing in our industry and there is ample opportunity to network and discuss or brainstorm "hot topics" with like-minded professionals.

Data Matters Summer edition also incorporates a thought-provoking article on ePRO: "Why Paper Diaries Should be Banned in Clinical Trials". Dr. Valdo Arnera poses the positive aspects for ePRO over paper in respect to improved compliance, ease of use for many patient populations and critically producing more conclusive outcomes for studies using ePRO data.

Sadly this will be the final Newsletter edited and managed by Jon Milton. Jon and the Newsletter Committee have set a very high standard for content and presentation of Data Matters in the last 12 months but now Jon needs to step down from the role of editor and chairperson. On a positive note this presents an exciting opportunity for any budding Editors residing out amongst you – if you are keen to take the Data Matters torch forward then please contact Jon Milton, email Jon.Milton@pfizer.com or editor@acdm.org.uk.

Along with the promise of long hot summer days to come (yes we're always the optimists!) we hope you will enjoy this edition of Data Matters and also take the opportunity to check out the new portfolio of training courses/webinars which are rolling out over throughout the summer and autumn months. These new courses have all been developed as a result of your feedback – *what you need and want* – so do take a moment to look over the course synopses on the ACDM website and book your place!

Tracy Fells & Fred Daniels, Joint ACDM Chairs

A fresh new menu of training courses now available for summer...

There is now an excellent new range of ACDM training courses for you to sample, ranging from all day sessions to half-days and shorter webinars, which can be accessed wherever you are located. The new menu now covers: CDISC, Regulatory Topics, Personal Development and specialised Therapeutic Area training, to name just a few!

Laboratory Data
Special Interest Group

Shaping the Future for Lab Data Handling

The summer Lab SIG meeting on 1st July was held at the Roche site in Welwyn Garden City.

It was the first meeting for Noel Redden as new Chairperson. Noel has been with Roche since 2002 as a Lab Data Manager (LDM), progressing to Project LDM. In January 2006 Noel took on the role of Team Leader for the UK LDM group and in January 2008 became Global head of Data Specification and Integration (DSI).

The creation of DSI follows a restructure of the LDM group and the transition of lab data management activities to the Data Management (DM) group. The DSI group remains responsible for all activities related to electronic data loading and management of lab reference ranges. Much of 2008 was spent training the DM group on lab data management activities and 2009 has been focused on embedding the process and associated documentation.

The same process change for lab data management is now being implemented for the early phase studies, which are managed by a separate function within Roche.

The SIG meeting is an opportunity to discuss the different approaches for lab data handling and cleaning, e.g. specialist vs. integrated DM, early vs. late phase. It is also a platform that we can use to link to similar groups and extend our links internationally.

With the increased complexity of laboratory assessments we hope to enable knowledge sharing, support and perhaps even drive standards for lab data handling in clinical trials. We would like to hear from ACDM members what they would like to get from the SIG and set up a network for ongoing interaction. Through such a network and the use of the ACDM website and SIG meetings we can shape the future for lab data handling.

Noel Redden, Chairperson, Lab Data SIG

Collaboration and Improvement

Website
Committee

Over the past few months the website committee have been working hard in the background to bring to you some new improvements to the website and the fortnightly Eshots.

Our website providers are in the process of upgrading their system and so we will see some improved functionality over the next few weeks. Members should see this change visible in the fortnightly Eshots, we are hopeful these will soon include your membership number and password to make it easier for you to log onto the website.

Another improvement that is currently being implemented is the addition of news feeds from other organisations. Pharmatimes have agreed we can have a link to their news feed on our home page and we hope to have links to other organisations soon too. The objective of this is to provide people with updates to important industry news in one place so we hope you will find the time to visit www.acdm.org.uk to check this new feature out.

We would also like to remind all you contractors out there to add your contact details, experience and dates available to the contractors database, in the times of credit crunch you need to advertise yourselves as much as possible.

We are also collaborating with the PR committee to think about ways of promoting the ACDM to new members and encouraging companies to advertise with us. As part of this we will soon be introducing company advertising to the homepage which we hope will also be useful for members as you will be able to click through to their website to learn more about their services.

We have had a team member change as well due to work commitments Chris McEleney has unfortunately had to step down from the website committee, thanks for all your help Chris.

Carly (chair), Lewis, Gill and Paul

If anyone else is interested in joining us, the PR committee or another committee please get in touch at admin@acdm.org.uk

Training
Committee

Your Development is our Priority – Make it yours too!

You will be aware from recent communications that over the last couple of years the ACDM has invested significant time and effort in developing new and improved training courses. Our aim is to ensure we provide relevant, up-to-date training for your professional development.

So, how has the ACDM training offering changed over the years? Those old enough (unfortunately, I am amongst that group!) will remember the good ol' days of "Fundamentals", "Intermediate" and "Advanced" CDM courses. These courses were very successful in their time, but the ACDM recognised that the CDM environment was changing rapidly and the training offering needed to keep pace with these advances. And how times have indeed changed!

In 2006, the format of course delivery was totally revamped to provide all courses into a one-week intensive training event, otherwise known as "College Week". This proved hugely successful, with delegates having the opportunity to "mix-and-match" courses according to their personal needs. Courses ranged from the familiar Fundamentals of CDM to those covering EDC, People Management, Computer System Validation, CRO/Pharma relationships, Appreciation of Statistics and many more.

College Week in September 2008 saw a refreshed blend of new and redesigned courses intended to appeal to all levels of data management professionals. New courses included CDISC/CDASH, Managing Offshore Teams, Working with Different Cultures, Impact of Regulations/Guidelines on CDM and Essential Documents and therapeutic area training. As you can see, these new offerings reflected the ever-changing landscape of CDM with increased emphasis on standards and the rapidly evolving use of global resources covering many time-zones and cultures.

This year, we have again revamped the training schedule with the introduction of standalone courses and webinars as well as the tried-and-tested College Week format. Check out the calendar of events to see which courses you should attend to make sure you are at the forefront of your profession. And if you find that you need training in an area that is not currently covered, let us know – your feedback is really important to ensure that we continue to address your needs.

Remember, ongoing professional development is critical to ensure your career stays on track, particularly in the challenging economic climate we face.

Your Development is our Priority – Make it yours too!

For more information, go to www.acdm.org.uk or email training@acdm.org.uk

Training
Committee

Too Busy for Training? Never!

The ACDM Training Committee is constantly exploring new ways to meet your training requirements. This year we are excited to introduce webinars, as an alternative to traditional class-room training.

The webinars will be delivered by experienced and professional trainers using the latest state-of- art technology. There is no need for time consuming downloads of software, you are always only one click away from joining a webinar!

During the training session you will be able to raise your hand, ask questions to the trainer, to other individual participants or to the whole virtual class-room. You will be able to share information in any multi-media format, or just enjoy a cup of coffee while you take in all the new information.

All Webinars are 90 minutes in duration and the best thing is that you only pay per connection, not per participant! In other words, "buy one and get as many as you can squeeze in the meeting room for free"! There are obviously no travel costs involved, so if you and your organisation are looking for cost-effective Data Management training, ACDM Training Webinars are your answer!

The next Webinars take place on Thursday 17 September and on Tuesday 20 October. The topics are "Managing Remotely" and "Therapeutic Area Training – Pain", respectively.

Too busy for training? Never!

For more information, go to www.acdm.org.uk or email training@acdm.org.uk

CR-CSV FORUM *Coming soon!*

Why Paper Diaries Should Be Banned in Clinical Trials

By Dr Valdo Arnera

Every now and then, a shift in technology revolutionises an entire industry. Consider the advent of email and automatic banking machines. Once the mainstream adopts these processes, it is difficult to imagine how we managed without them. Today a similar transformation is taking place in the pharmaceutical world, as more companies worldwide replace paper diaries with electronic patient diaries in clinical research.

Electronic patient reported outcome (ePRO) solutions capture self-reported data directly from patients at home or at investigator sites around the world. Most often patients use PDA devices which transmit these data to a central server. An ePRO system provides sponsors with higher quality data than paper, accurate timestamps and real-time access to vital compliance, enrollment and safety information.

If market adoption continues at its current pace, in ten years paper diaries will no longer exist for studies using PRO as primary or secondary endpoint data. I propose that we accelerate the pace and call for paper diaries to be banned.

If your study depends on what patients tell you, you have no choice but to use electronic diaries. It very well could be the difference between making your study a huge success or a failure.

It is impossible to get high quality data from paper

Paper diaries offer no controls over timeliness or quality. Subjects make entries that are incomplete (skipped items), illegible (poor handwriting), and illogical (inappropriate responses). Further, patients respond days later, complete diaries in batches, invent data, forward-fill, and mark multiple responses in the same question. All these situations present serious data analysis problems.

We are all familiar with "parking lot syndrome," in which patients retrospectively complete days or weeks of diaries just prior to a site visit. Patients also forward fill paper diaries. A study published in the British Medical Journal showed that 45 percent of subjects in a pain study invented data by forward filling at least once.

With paper, the burden is placed on patients to remember diary response times. Paper diaries can be confusing for patients to understand and accurately answer. In many studies, the questionnaires branch into different paths depending on the patient's responses. The burden is on the patient to understand which set of questions to answer based on their reactions or symptoms.

Electronic diaries allow sites to obtain accurate, real time information on patients' reactions during a trial. They are the best way to collect both objective and subjective assessments of patient experiences.

Paper is slow

If a patient is not performing well in a study by failing to complete diaries regularly or more importantly, because of worsening symptoms – it can take weeks or months for sites to notice. Site personnel have to spend time reviewing paper diaries and making manual, error-prone calculations and measurements where needed. These activities detract from time that could be spent caring for patients – one of the reasons site investigators become study coordinators in the first place.

Electronic patient diaries allow responses only during the appropriate times specified by the protocol. They use controls to ensure complete, legible and logical reports; encourage compliance through alarms; reduce respondent burden; and provide real-time site management of patient performance. In short, electronic diaries solve the problems of paper diaries.

Electronic diaries promote a fast, honest response

In a Merck Research Laboratories insomnia study comparing paper and electronic diaries, one patient reported that he enjoyed using the paper diary because he only had to play catch-up about 60 percent of the time. This is the kind of statement that should convince all of us involved in data quality that paper diaries are nightmares.

Studies prove that electronic diaries motivate subjects to complete their diaries. It is much more efficacious to be able to ask patients how they feel at a precise moment and get an immediate, accurate answer.

Electronic diaries empower subjects to be more compliant

An elderly female fibromyalgia patient in the UK once reported that her electronic diary alert sounded during a wedding reception. She simply laughed, excused herself, and took five minutes to complete and send her diary. It did not occur to her that this activity was a burden. It is highly unlikely that she would have carried a paper diary with her to the wedding. History tells us that she would have completed her diary retrospectively, or not at all.

Patients using electronic diaries enjoy a much higher degree of privacy. They can respond more freely than on a piece of paper that will be read by others. In a study on female sexual dysfunction using a cross-over design, patients reported 80 percent more sexual episodes on the electronic diary than they reported on paper.

Electronic diary patients say that they are encouraged to comply because they feel that someone is paying attention to their symptoms whenever they transmit their data. They are aware also that their study coordinators are supposed to review their data, which compels them to complete reports as expected.

Patients in a year-long lower back pain trial showed 90 percent compliance because they could hold the electronic diaries in any position they pleased. One man said he would not have been able to fill in detailed responses with paper because he was too uncomfortable to write. These patients completed electronic diaries six times a day, seven days a week because they could use the device even when lying down. And they felt encouraged because they were actively involved in managing their pain and health.

Electronic diaries enable more reliable, smaller, faster, safer trials

One of the major advantages of ePRO solutions is that they have been shown to reduce data variance as compared to paper. This enables smaller, more conclusive studies.

Biostatisticians could adjust and lower estimates on how many patients are needed to prove efficacy in Phase II studies, based on the expected variance of paper data at hand. This can create a significant savings in money and time. In Phase III studies, such high quality data provide more reliable scientific conclusions. Instant access to upto- the-minute ePRO data allows adaptive trial designs which are almost impossible with paper.

Electronic diaries are the future, today

Paper might do well enough in rare exceptions, such as when time sensitivity is not an issue and a question relates to patient experiences over a week. But when it matters if a subject completes the diary on Monday instead of next Thursday, it is certain that paper data ultimately will fail.

Despite continued increasing adoption in the ePRO industry, some companies still are reluctant to change. Managers may worry that if there is a problem with electronic diaries it will hurt their careers, because no one was ever reprimanded for using paper yet. The real danger lies in spending millions on trials that failed because of outdated, inaccurate paper diaries. If the primary efficacy endpoint is coming from the patient it makes no sense to use paper diaries. Trials are all about data. It is the only thing they produce.

For efficacy and faster, smaller, less expensive trials it is time to put away the paper and pick up what has proven to be extremely effective technology: the electronic diary.

Dr Valdo Arnera

Dr Valdo Arnera has more than 18 years of experience in the pharmaceutical industry. He is skilled in both science and management, and speaks frequently on these topics. Dr Arnera has been an active co-chair of the DIA's Special Interest Area Communities (SIAC) eClinical and Standards committee.

> “If your study depends on what patients tell you, you have no choice but to use electronic diaries. It very well could be the difference between making your study a huge success or a failure.

Older folks like Cellphones, Wii, and PCs, too

by Patrick Hughes

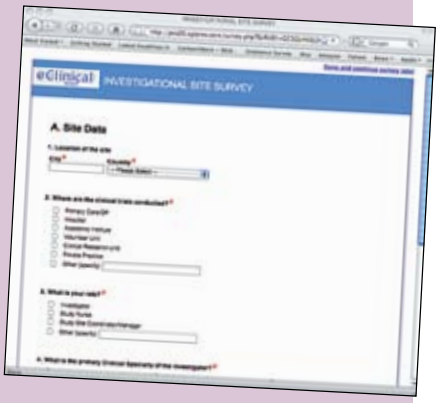
According to Forrester Research, U.S. adults 64 and older who bought technology in a recent three-month period spent an average $365 on consumer electronics products and $429 on computer hardware and peripherals. And Forrester points out that Americans 55 to 64 are more active in online finance, shopping and entertainment than those under 55.Health issues forced Ted Campbell, 79, to give up real bowling in 1965. But Campbell, a resident of the Greenspring retirement community in Springfield, Va., bowls all the time now – on a Nintendo Wii video game system in a bowling league he organized at Greenspring.

Seniors like Campbell are helping dispel an age-old stereotype: that folks getting on in years have little or no interest in the latest technology. Video games, PCs, cellphones and such can help keep minds and bodies sharp. Tech companies are starting to pay closer attention to the mature market, and to folks with physical disabilities.

The Exco InTouch experience reinforces this phenomenon as most of the retention, compliance and ePRO solutions feature patients in the 65 to 85 age range. Many of these seniors already use Cellphone technology to correspond with their children and grandchildren and have found the use of alerts and notifications via their own phone to be of significant benefit to ensuring compliance with their required study contact. Once patients in any age range are involved with an Exco InTouch program they don't opt out of the reminder or eDiary solutions as they provide such a valuable aid in ensuring they comply with all study obligations and, as each message can include site contact details, there is an added safety angle too.

First published by Exco InTouch, Volume 3 Issue 4, April 2009. Reproduced with permission.

eClinical Forum – Global Clinical Investigational Site EDC Survey



The eClinical Forum, in collaboration with the ACDM is conducting an in-depth, global survey of investigational site experience with eClinical trial technologies. This year's survey, the first of this scale in seven years, will show how EDC usage has changed and provide insight into trends that will provide important information as you make decisions regarding use of eClinical technologies.

The survey only takes about 15 mins to complete and in order to facilitate you and /or your company in disseminating the information on how to complete the survey, an information sheet together with example emails to the site and monitors have been created and attached. There is also a PDF file of the survey so that it's content can be viewed in advance.

By sponsoring this initiative all ACDM members will have access to the results, the presentation and the report in advance to it being available in the public domain."

For all the information on the survey visit www.acdm.org.uk/news_24.aspx

CR-CSV FORUM *Coming soon!*

See page 15 for more details

How the Evolution of R&D Might be Good News for Clinical Data Management...

The article you are reading now is an extended version of an internal briefing I prepared as part of my company's newsletter. When I had completed the initial piece, I felt it would sit very well in the ACDM newsletter. In particular, I felt it would help to address a question that was being widely discussed when I sat on the ACDM Board of Directors; what is the future of Clinical Data Management? Of course the Board discussed industry trends such as off-shoring and the growth of EDC, but it was difficult to see if any fundamental changes would impact the profession at that point. That was 5 or 6 years ago; things may be clearer now, and I hope to show how the focus in clinical development programs might be set to move back to the data and biometrics functions.

I have always had a great interest in data and how they are collected and handled; my career has included roles in statistical programming, database design, systems implementation, and EDC. Anyone who works in the biometrics field knows that as technology has advanced, more and more data has become available from increasingly diverse sources. The technical component of the role of a Clinical Data Manager has increased greatly over the last 10 years and is set to continue to do so. For complex studies, the planning required to bring the data together in a reportable state is a big job, but in assessing the risks of the overall study, teams spend much less time examining this area than say, patient recruitment rates. That may be absolutely correct in the current development model; after all in terms of budget overrun the biggest risk might well be slow recruitment, and so much effort is devoted to protecting against it. The biometrics portion of the project is relegated down the agenda, and there may be some talk of "discussing the *back end* services further down the line."

Well here is the good news; that is going to change.

I was very lucky to see Steven Burrill present his view on the life sciences sector earlier this year, and his vision inspired me to do some further research on what is happening in the sector at a macroeconomic level. What are governments looking to achieve? Where is money being spent in healthcare? How will the market collapse of 2008 affect the industry? I did this because Burrill outlined his vision of the R&D environment over a ten-year horizon. His view: the development time for new drugs will drop from a norm of around ten years to a norm of around two years. Most of the audience probably felt such a change was impossible until he went on to outline his thinking. I hope to share some of that thinking with you, supplemented by some of my findings in asking the questions above.

For those of you not familiar with Steven Burrill, he is the CEO of Burrill and Company.[1] His company is heavily involved in the funding of life science companies and corporate activities in the sector such as mergers and acquisitions; they also publish a great deal of research on the life sciences sector. This background lends great credibility to Burrill and his vision for R&D, a vision which describes a significant change in how things will be done.

All change needs a driver, the "burning platform."[2] In the case of the current healthcare model, this driver is an economic imperative. The world cannot afford to treat everyone; the current system does not function now, and yet the number of new drugs approved is slowing down year on year and the population is growing. Even if it was felt that things were ok now, the model is not scalable in its current form. This problem is illustrated very well by the healthcare system in the US, and not surprisingly, reform is very high on President Obama's agenda. Influential stakeholders are also crucial to successful change. Obama is certainly influential and has the energy that comes with a new appointment to drive transformation. He addresses the problem at a very good time. The 2008 economic 'correction' (which is ongoing) has dramatically affected the pharma/biotech companies and changed the way their business is viewed. With diminishing pipelines and increasing R&D costs, pharma had considered partnering with or acquiring biotechs as a way to boost product pipelines, and in fact examples of this are seen on a regular basis, including some high profile acquisitions this year. The problem going forward is that with a tightening credit market, a very high proportion of biotechs will fail over the coming months. This is bound to have some effect on the pipeline and will undoubtedly affect the rate of joint ventures and acquisitions over at least the next 12 months. As pharma companies (and the large biotechs) seek to improve margins, the next option is cost reduction. One way this can be achieved is through merger (another way of boosting individual portfolios, but of course not increasing the overall pipeline) and the current activity in terms of mergers will continue. The problem is that much work has already been done in terms of cost reduction; a lot of efficiency gains have already been taken. Current activities will not get the sector where it needs to be.

So, there is political will in a major market (other nations are facing the same problem – think about the job the National Institute for Health and Clinical Excellence do in the UK) and economic conditions having a real effect on the sector and the model for R&D. These pressures on their own might be enough to force change, but probably not a reduction from 10 years to 2 years for approv-

Continued on page 10

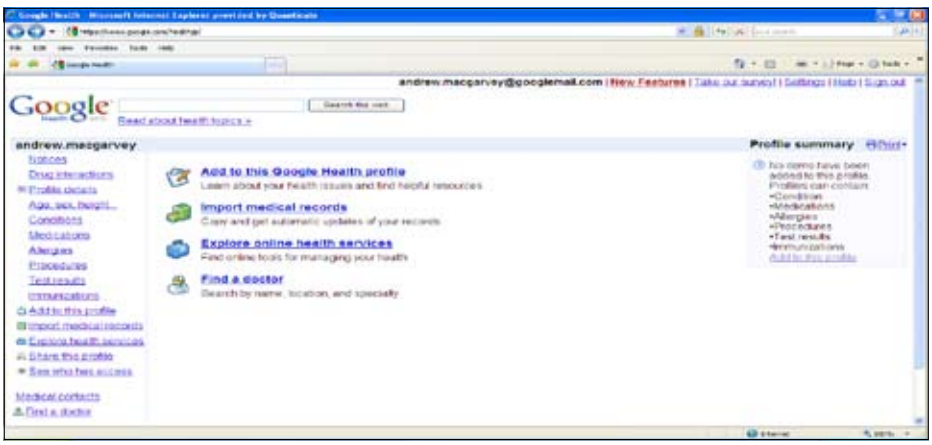
Continued from page 9

als. Burrill thinks he can see a third strand, and I think this might be the most important factor. His belief is that there will be a shift away from "sickness management" to "wellness management", and it is this that will reshape R&D.

What Burrill is saying, is that the paradigm will move from doctors reacting to illness and fixing the problem, to you spending more money on preventing illness and maintaining your health (for all but the obvious acute and chronic illnesses). In this new world, you go to the supermarket to do the weekly shopping and have several diagnostic checks run as you enter the store. While you are shopping, the results will be produced along with any necessary prescriptions. As you complete your shopping, you pick up your medication (for both prevention and cure), and your electronic health record is updated. You may or may not be referred for secondary care. The point is that blood pressure, cholesterol, insulin and others can be tested and managed in this way, and as more sophisticated diagnostics become available, increasingly complex testing and treatment regimes can be deployed. This world is actually not very hard to imagine; we are seeing in-store treatment rooms appearing already and not just in traditional pharmacies and healthcare stores. If you think the leap to seeing this in supermarkets is far-fetched, then take a look at www.walmart.com/clinics to see some of the conditions they can deal with. Walmart is also investing significantly in the electronic health records market working with Dell to provide a 'cost effective' solution. In other words, the shift has started. The industry is taking notice too; J&J were very close to establishing a 'wellness and disease-prevention' business unit, but have now announced it will be folded into their consumer business. Anticipated revenues? $20 billion a year. This whole approach requires patient centric systems and thinking. This means a cultural shift, known to be one of the most difficult transformations to effect. Again, much work has already been done, and the emergence of social networking sites has played a significant role. The age of "privacy" may well be past. Social networking sites have encouraged people from all over the world, from every demographic, to disclose all manner of information (in many cases to anyone that cares to read it). There is some way to go, but the evidence is that a shift from withholding personal information to publicizing it is well under way with the associated 'comfort level' growing all the time. In researching this article, I looked at Google Health for the first time. If you want to see one way to manage wellness (and indeed sickness), visit www.google.com/health.

This online resource allowed me to log details related to my demographics, medical history and so on. I could also import my electronic health records, prescription records, and lab tests from participating sites. If I had had paper records, the site would have linked me to service companies that can convert them to electronic records. I found the terms and conditions very interesting, particularly the clause:

"I hereby authorize Google to share the health information contained in my Google Health profile(s) in its entirety, to only those entities and individuals I designate, for the purpose of providing me with medical care and for the purpose of sharing my information with others that I choose."

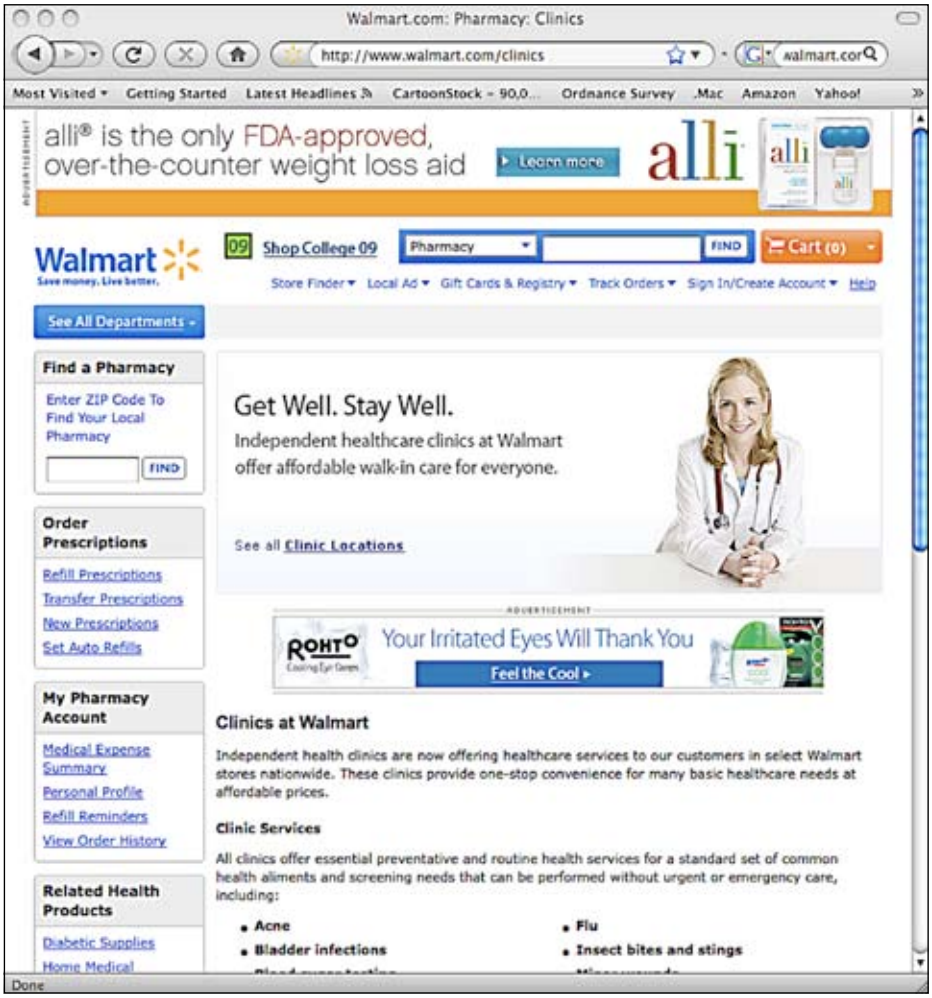


Google will be using my information to provide me with medical care!

So, our corporations are working away to make this new paradigm a reality; there are many other large retailers and internet companies aiming for market share. All of this should be good for us, the patients. A wellness management approach detects conditions early, and hence the level of reversibility is high; the current, reactive model has lower reversibility. It seems like everyone wins. Burrill notes that if you wonder if populations will be willing to pay for more expensive diagnostics and for managing their wellness, you only have to look at what they will pay for nutraceuticals. A recent report in Nutraceuticals World quoted Global Industry Analysts whose projections suggest that sales in the global nutraceutical industry will reach $187 billion by 2010. I think this is a valid indicator. After all, the money spent here is spent to maintain or improve well-being.

So how does this all lead to an increasing focus on data? The answer is in what becomes of 'sickness management' in the new paradigm, once you are all dealing with your own 'wellness management'.

With the onset of an environment of Prediction, Pre-Emption and Personalization the clinical study process is set to fundamentally change. With drugs being targeted to specific populations, the importance of in-silico modelling will increase and become more widely accepted. Programs will then run more quickly, and the FDA and other regulators will approve drugs much earlier once a response in the target population has been proven. It is because of this that Burrill sees the clinical phase reducing in time. Given the economics, it is clear that



this will be very acceptable to healthcare providers, as the cost of development will be dramatically reduced, allowing for cheaper drugs. The win for pharma/biotech (and he sees most of these treatments being from biotech) is one of improved cash flow with revenues coming on stream far earlier than they do now. If patent protection rulings are static, then the negative effect on those revenues by generics or biosimilars is reduced by virtue of prolonged exclusivity. It is fairly easy to see how all of the stakeholders could be satisfied by this model. However, the key to all of this working is the design of the shorter clinical development program; that is where the skill sets of biometricians come to the fore.

In the new model, the importance of intelligent design, conduct, and reporting of studies will be crucial. The regulators will require increasing amounts of data, which in turn will be more complex and come from more sources. How biometricians collect and use these data will be vital to a successful outcome, and expertise in the biometrics arena will become a focal point. Attention will shift from patient recruitment issues to data issues. It is in biometrics (and pharmacovigilance) that the risks will be weighed.

Is it realistic to bring down the time to market of new drugs even allowing for targeted therapies? I wonder if a parallel can be drawn with off-label use of drugs. With sophisticated in-silico modelling providing credible information with respect to how the drug might act, and intelligently designed trials gathering extended volumes of useful data, the regulators may well be comfortable approving drugs into targeted populations. In 2008, a report in Nature Biotechnology estimated that "off-label use of cancer drugs run from 50%-70% of total usage, and perhaps higher."[3] In critical care, there is always additional pressure to get new treatments to the patient. When sickness management is addressed in 10 years, if the technology in diagnostics has advanced sufficiently and more is known about how the drug will effect its population, the pressure to get new treatment to the patient will only increase. With the economic and demographic challenges ahead, the industry may have to rely on the benefit from a new approach. They can focus on accelerating the delivery of targeted therapies to specific populations. The main concern surrounding targeted medicine has been the cost; can a return on investment be made when the market is limited? Under a model where sales begin at the 2- or 3-year point and where pre-clinical work has also been accelerated, it may be possible.

This article has touched on a few different areas, and each area does rely on certain critical success factors. I hope that what it offers is some view of the potential for change in how we approach the development program when viewed against the challenges the industry is facing at the time of writing. The data has always been important; my view is that more attention will be placed on mitigating the risk of bad data in our studies going forward, and this can only be a good thing, not just for the biometrics profession, but for development programs as a whole.

Andrew MacGarvey
President
Quanticate Inc
andrew.macgarvey@quanticate.com

1. www.burrillandco
2. Leading Change – John P Kotter 1996
3. Off-label or off-limits – Mark Ratner, Trisha Gura Nature Biotechnology 26, 867-875 (31 July 2008)

THERE IS NO CHARGE FOR ATTENDANCE AT THIS FORUM

Senior Forum
Committee

Senior Clinical Data Managers Forum

Proving the Case for Process Improvements

Amgen,Uxbridge, West London
Wednesday 7th October, 2009 • 13.00-17.30

How do you convince your company of the need for a change?

Proving the case for process improvement is a critical skill for today's CDM leaders. During this Forum presenters will describe real examples of methodologies which have been used within CDM to demonstrate the rationale, benefits and return on investment of proposed changes in working practice. There will be an opportunity to discuss issues raised during the presentations and exchange ideas on the most effective way to present your case.

Forum Keynote Speaker:
Stephanie Langouet – Global Head of Biometrics, CMed Research

Registration will be from 13.00.
There will be an opportunity to socialise and network after the forum, with everyone welcome to join us for a drink and/or meal at a local pub.

acdm
association for **clinical data management**

Risk Management Special Issue

An Introduction to Risk and Risk Management

Introduction to Risk

I joined the Clinical Research industry with Covance in 1993 and I don't think I ever heard the term 'risk' or 'risk management' until at least 1997 – and then it was only because I was 'volun-told' (a mix between being volunteered and told!) that a project management trainer was needed to deliver and then design and deliver project management training courses to all of its Clinical Project Managers and Project Leads from the Data Management and Statistics functions.

Twelve years later the world has changed the terms 'risk' and 'risk management' are commonplace in the pharmaceutical industry and especially within service providing companies who are contractually bound to deliver a certain level of performance based on an agreed set of assumptions. I'll explain more about this previous sentence as this article progresses, but it is safe to say that although the terms 'risk and 'risk management' are more commonplace than ever, they are still commonly misunderstood.

I have been fortunate enough to have delivered hundreds of project management training courses to thousands of drug development professionals and I can honestly say that the two most important aspects of project management to master are 1) stakeholder management and 2) risk management – and in many important ways these two aspects are intrinsically linked.

Let me ask you a question: what were you doing in the evening of the 31st December 1999? The chances are that you were celebrating the turn of the millennium. Let me ask you another question: what criteria did you use to judge the successfulness of that evening? Again, the chances are high that a) attending, and b) enjoying the event, were high on your list. This brings me to the first principle of risk. The concept of risk has to be applied to the list of criteria that will make your project successful (key success criteria). Sometimes it is assumed that risk is only related to timelines and that is not always the case. Here is another example: imagine that you have a hobby such as needlework and that you decide to knit a beautiful jumper for a baby that has just been born into your family – it is not really important whether the jumper is finished in time for the day of the birth, but it is important that it looks good, feels nice, and fits. The key success criteria for this project are therefore that the jumper looks good, feels nice, and fits – and the idea of timelines are nowhere to be seen.

Continued on page 14

Continued from page 13

So, what are the key success criteria for clinical trials? The answer includes:

- the clinical trial is set up in the correct way that meets applicable laws and guidelines and ensures that data is collected, interpreted, reported and presented in a scientific and rigorous manner
- the quality and quantity of data and the resulting interpretations and reports are sufficient to satisfy regulators that a clinical trial can be approved or a marketing licence awarded
- regulatory approval or a marketing licence is granted in the shortest time possible to reduce the cost of developing the drug and to maximise sales especially during the period of patent protection.

The word 'risk' means 'what can go wrong', and for clinical trial projects this must be based on key success criteria similar to the three statements above. The 'risk management' process is a series of steps that anticipates the risks and reduces the likelihood of them happening and/or their impact if they do happen.

The Risk Management Process

The diagram below illustrates the steps of a simple risk management process.

Step 1

Based on the key success criteria for clinical trials, think about the typical project risks. It is likely that you will have identified factors.

It is likely that you will have thought of some of the following (in no particular and not an exhaustive list):

- poorly designed protocol
- poorly designed CRF
- regulatory rejection
- poor feasibility
- competitor products and trials
- lack of investigator interest
- slow patient recruitment
- lack of resource (clinical monitors, data managers etc)
- poor supplier performance (CROs, vendors etc)
- lack of drug supply including drug import/export issues
- poor data quality.

Step 2

Step 2 is to rate each risk event in terms of likelihood of occurrence and impact if it does happen. One great way to do this is to involve the project team and use a tool which I call a Risk Assessment Grid. All you need to do is to consider each risk in turn and decide how likely it is to happen and what the impact is on the project's key success criteria if it does happen. Below is an example.

Let us consider that you selected the following three risks:

- slow patient recruitment
- poorly designed protocol
- one investigator being ill for a week.

It is possible that you believe the risk of slow patient recruitment to be major because it is high probability and high impact.

It is possible that you believe the risk of a poorly designed protocol to be medium because it is low probability and high impact.

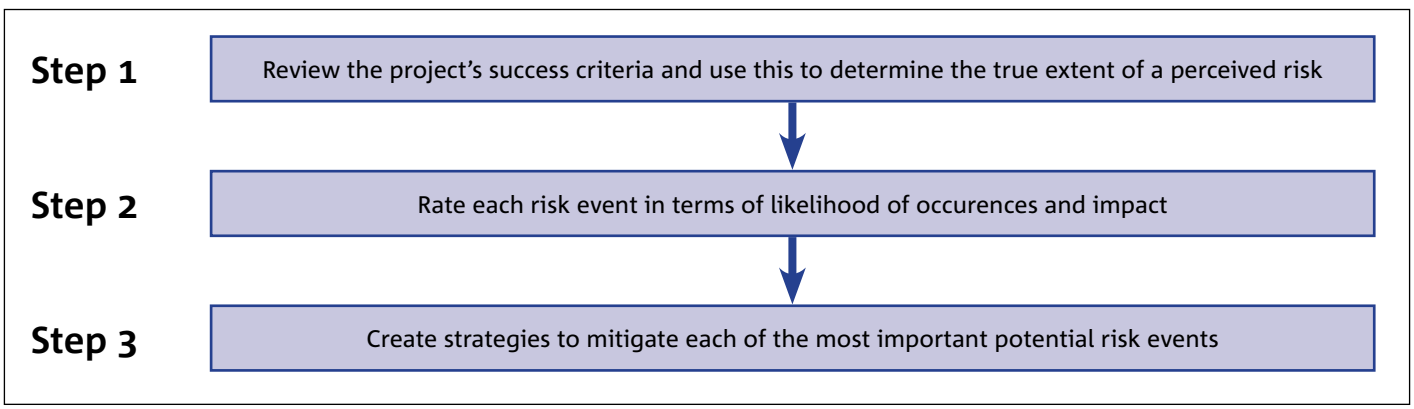
It is possible that you believe the risk of one investigator being ill for a week to be minor because it is medium probability and low impact.

What the Risk Assessment Grid allows you to do is understand the scale of the risks that you face and therefore what to do about them – and what to do about them is step 3.

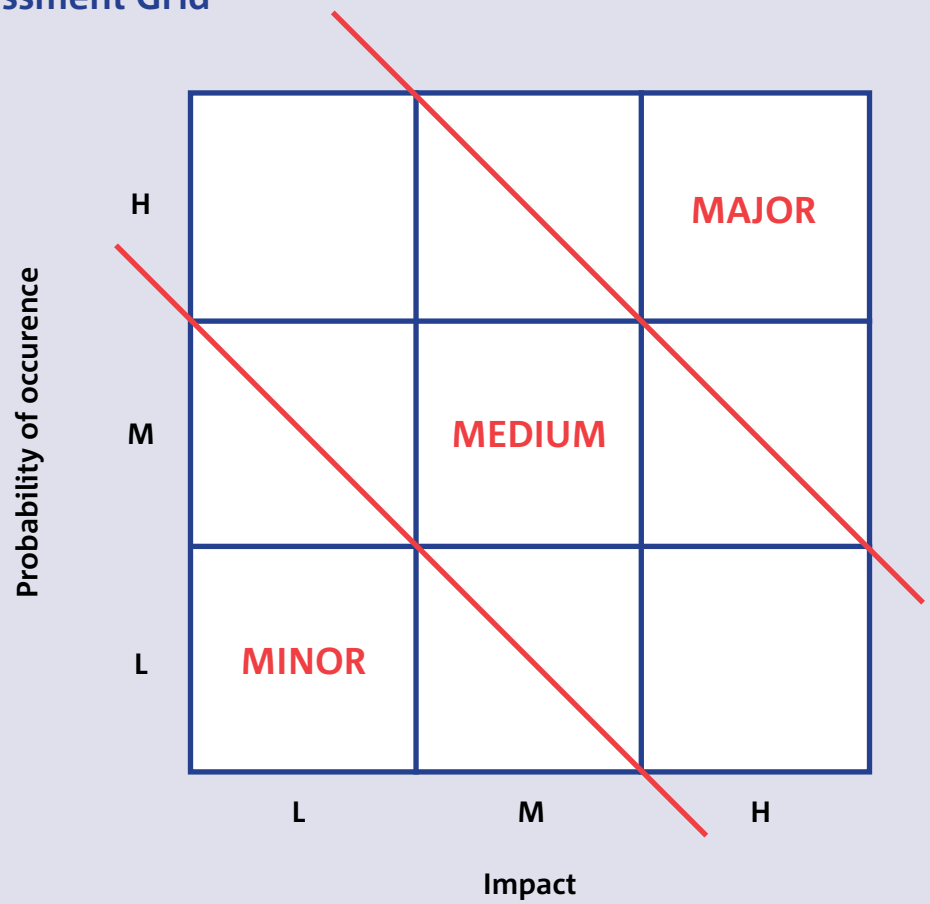
Step 3

Step 3 is to create strategies to mitigate each of the most important potential risk events. In general, the concept is that you will not have the time or resources to eliminate every risk and therefore the key is to manage the risk based on its ability to reduce the overall benefit of the project.

For major risks typically you would try to find strategies to reduce the risk – and this can be thought of as 'risk prevention'. If we think about the risk of slow patient recruitment and how to prevent that risk we may decide to pursue strategies such as performing the study in more countries and involving more sites. We may also want to think about inclusion/exclusion cri-



Risk Assessment Grid



teria, better advertising and improved feasibility.

For medium risks typically you would try to find contingency strategies which essentially means having a 'Plan B' if the risk does occur. It may be expensive to prevent the risk of slow patient recruitment by adding additional countries so an example of a contingency plan is to have identified additional sites which could be activated should patient recruitment fall behind schedule in the original sites.

For minor risks the strategy is usually to accept the risk and react if they do happen. It is not a perfect world with abundant resources which means that Project Managers must concentrate their focus and attention on the largest risks to their projects – and these will be the 'major and minor' ones.

Advanced Risk Management

The intention of this article was to introduce and explain risk and risk management and reveal some tools and principles that can assist the Project Manager to increase the likelihood of the success of their project – and hopefully reduce some of the stress, frustration and pressure.

The academic literature contains much research and revelations on the subject of risk management and interested people can learn more through literature searches, researching professional project management organisations such as the Association of Project Management and the Project Management Institute – and many training courses are offered both internally in organisations and by respected training companies.

In the third paragraph of this article I stated that stakeholder management and risk management are the most important aspects of project management to master, and I also said that they were linked. The reason for this statement is that stakeholders are the keys to project performance whether that be project recovery or project acceleration. By managing and communicating well with clinical trial stakeholders such as regulators, investigators, study site staff, CROs and other vendors, patients, the project team, and senior management, these groups of people will progress the clinical trial by 'taking action'. The identification of risk and risk strategies is not enough to achieve project success – it is the support and action-taking of the people who can make the trial succeed that will achieve the quality standards and timelines required.

The phrase 'its all about the people' may be a cliché – but where project management is concerned it may just turn out to be a true cliché!

Brian Swindley
Director,
ICON Clinical Research

Introduction to Risks Assessment

What is risk?

A risk is defined as ***"An uncertain, future event – which, should it occur, will have an impact on our objectives"***

It does not say will adversely affect anything – 'impacts' may be negative **or** positive! It is quite possible that performing a risks assessment at the beginning of an activity will identify positive opportunities as well as potential pitfalls! The most important thing is that they are uncertain and in the future.

N.B. – it is however quite acceptable to capture, within a risks assessment process, issues that have already actually occurred (i.e. not unknown or in the future) – they still need addressing and managing in order that the activity concerned can progress successfully.

Risk is inherent in everything we do. You took a risk getting out of bed this morning (assuming that you are not reading this article in bed!) – you may have stubbed your toe putting on your slippers or tripped over clothes left on the floor last night. But you still got out of bed, you decided to manage the inherent risks and get on with what needed doing. Risks **cannot** be eliminated from life – personal or working. We cannot afford to be risk averse, but must manage all risks appropriately. **Appropriately** is the vital word in that sentence. I have been known to shout at the television(!!) when watching news reports of local councils or other authorities who have banned processions with people carrying candles, because there is a risk someone may get burned. Upon investigation there may have been no previous examples of significant injury in hundreds of years of the process occurring, so the likelihood of it happening in the future is probably low. The 'appropriate' management of this risk may perhaps be to ensure that everyone is reminded about the dangers of flames before the start and get St. John's Ambulance to be in attendance – NOT cancel the whole event!!

The risks inherent in any activity will result from one or more 'sources of uncertainty', or risk drivers. When getting out of bed the 'source of uncertainty' may be the state of the floor until you open your eyes and look! When crossing a street a 'source of uncertainty' may be the state of the street, but that may relate to a number of different risks:

a. Is the tarmac uneven and potholed so you might trip?
b. Are there large puddles so you may get wet feet?
c. Are there vehicles coming so you may get run over?

One source of uncertainty (or risk driver) but three different risks, each with different levels of severity:

a. twisted ankle
b. wet shoes/socks
c. broken bones or worse

Not all risks have the same significance, so without conscious effort you decide to look to left and right to check for oncoming vehicles, rather than looking at your feet for potholes or puddles. You have assessed risks, prioritised them and taken appropriate mitigating action without even thinking about it!

What are the regulatory impacts of Risks Assessment?

So where does this all fit in with our pharmaceutically regulated working environment? Since 2003 FDA, MHRA, EMEA etc. have all been expecting computerised system validation activities to take 'a risk based approach' – i.e. we need to identify the most significant risks and ensure that validation activities address these.

This term 'risk based approach' also started coming up in other regulated areas. Sarbanes-Oxley in the US and Turnbull in EU are both financial regulations that govern how corporate finances should be handled and they also stipulate 'a risk based approach' as do various regulations within banking, health and safety and many other regulated areas.

It also became apparent that various regulatory authorities and corporate audit departments were taking a 'risk based approach' to inspections/audits. That is if there was an area that was deemed as high risks due to it's past audit history, frequency of process change, innovative use of technology etc. etc. it could expect more frequent audits/inspections. As a consequence most companies may require all staff to take 'a risk based approach' to all they do in their general working life. That means being aware of the risks involved in routine tasks, new projects, clinical trials etc. by ensuring that potential risks are identified up-front and documented appropriately; then responding/mitigating the most significant ones – NOT ALL OF THEM.

What does doing a Risks Assessment involve?

The right people and good communication between them, that's all – it's all about communication!

Who are the 'right' people?

- Representatives of *all* stakeholder communities
- The sponsor of the activity
- Any relevant technical experts (if not present as stakeholders)
- Any relevant process experts (if not present as stakeholders)
- Representatives of any outside companies/agencies if necessary
- An independent facilitator

Where and how does this communication happen? It must happen in real time – not necessarily face to face in the same room – a virtual room will suffice but it MUST be in real time, with every stakeholder group represented effectively. As meetings of large groups – often globally represented – are difficult to schedule, if a primary stakeholder cannot be present they must ensure that they del-

Table 1: The 3 point scale

Likelihood				
	High	4	7	9
	Medium	2	6	8
	Low	1	3	5
		Low	**Medium**	**High**
		Impact		

Table 2: The 5 point scale

Likelihood						
	Very High	9	16	20	23	25
	High	7	13	18	22	24
	Medium	4	11	15	19	21
	Low	2	6	12	14	17
	Very Low	1	3	5	8	10
		Very Low	**Low**	**Medium**	**High**	**Very High**
		Impact				

Table 3: Template – Risk Management Plan

Names(s):			Facilitated by:				
Authored by:			Risk Sponsor:				
Risk Escalation Details:							Action/Response Strategy (what and when)

egate attendance to someone else with adequate experience and knowledge to be able to effectively contribute to the discussion.

These meetings are often standard 'brain-storming' events which take each previously identified area of uncertainty one by one and ensure that everyone gets adequate opportunity to raise risks relevant to their area of expertise. As usual in any well managed brainstorming activity all suggestions are valid and nothing is too 'off the wall' to be captured. All risks captured will be prioritised as appropriate.

How should a risks assessment be documented?

Clear risk statements are vital. A Risk Management Plan may need to be reviewed as part of a project audit or inspection in 10 or more years time so the statements captured need to be clear enough to be able to be understood by people who have no pre-existing knowledge of the area involved.

A 3 part risk statement has proved successful in some companies:

- Because of ...
- There is a risk that ...
- Resulting in ...

e.g. *Because of* the seasonal changes in clocks in the US but not in India

there is a risk that working with contractors in India will be more difficult in the winter (10.5 hour time difference)

resulting in resistance in the US to use of these contractors.

Once the risks have been effectively described it will then be necessary to give each one a unique identifier – 1, 2, 3 will do – only make the identifiers more complicated if it makes your process of referring to them at a later date easier.

It will then be necessary to prioritise the risk by identifying how likely the risks is to occur [N.B. Try to avoid classifying this as 'probability' it causes awful problems if you have statisticians among your stakeholders!] and the potential impact it would have if it did and the likelihood that it would be detected if it did occur.

You could classify these on a 3 point scale – High/Medium/Low (or 1/2/3) ***see Table 1: The 3 point scale.*** or a 5 point scale – Very High/High/Medium/Low/Very Low or (1/2/3/4/5) ***see Table 2: The 5 point scale.***

Then, ONLY for the most significant risks the ones with the highest scores, determine what actions could be taken to minimise the risk (you cannot make a risk go away) i.e. reduce the likelihood of occurrence, limit the potential impact or increase the likelihood of detection. Having agreed an action with all stakeholders then determine who will own the action and a time point for a first review of the potential success of the action.

A possible template for documenting the output of the brain storm session may look like ***Table 3: Template – Risk Management Plan.***

Once agreed by all stakeholders it is advisable for the Sponsor to agree and sign off the plan in it's initial form which can then be archived in an appropriate location. Plans will then be needed for ongoing management; review and update of the plan as mitigating actions are completed. The Risk Management Plan can become the central tracking document for the team to reference, all ongoing activities should be the mitigating actions for significant risks, if any activity is being performed that is not within

Continued on page 18

Continued from page 17

this category it may be a waste of project resources OR it may be that something has changed and resulted in the identification of a new risk which needs adding to the plan AND prioritising so ensure that it's relative significance compared to all the other risks means that it justifies action being taken.

It is advisable to identify a specific person to own and update the Risk Management Plan, ensure that as response updates are due they are presented and new dates agreed and that a significant points of the project/activity the entire contents of the Risk Management Plan are re-visited, re-assessed and re-prioritised if necessary.

When is the right time to do a Risks Assessment?

Any time!!!

At the planning stage of any project/activity e.g:

- System development
- Process Improvement
- Re-engineering
- Clinical trial
- Resource planning
- Office re-location ...etc. etc

As changes occur in any project (whether you did it at the outset or not). A Risks Assessment is always related to a specific activity at a specific point in time – it's the risks related to X activity today. If there was no Risks Assessment at the outset, that doesn't matter it just changes the potential profile of risks now.

It is always advisable to do a Risks Assessment prior to any critical phases of a project – e.g. pre User Acceptance Testing or before decommissioning, even if you have an ongoing Risk Management Plan, the team of stakeholders for a specific activity may have a more detailed focus that the high level stakeholders so may identify some more detailed risks that may need attention.

If anything changes about a project/activity – new Team Leader, organisational change, system upgrade, protocol amendment etc. etc. it would be of benefit to perform a risks assessment, however brief, just to ensure that all stakeholders are up-to-speed and that all implications of the change are understood.

What are the benefits of Risks Assessment?

The greatest benefit to come from any Risks Assessment is the improved understanding and communication among those involved – this is ALWAYS the first comment that any attendees will make. It is also regularly noted that as mitigation strategies are identified one strategy will be found to mitigate multiple different risks i.e. a single root cause has been identified.

Most projects will traditionally be working with limited resources. This structured methodology provides a useful tool for ensuring that limited resources are focussed on the areas of greatest significance, and that resources are not wasted on activities that are not mitigating strategies for the most significant risks. Team members will be involved in less fire-fighting activities and more proactive working.

The involvement of a Risks Management Plan within the project/activity documentation will also ensure that the reasons decisions as to why decisions were taken will be more readily available for future reference. You will always have a document to justify why decisions were taken, the information that was used as the basis for the decision and when the decision was taken.

After Risks Assessment then what?

Ongoing Risk Management will flow from initial Risks Assessment.

As responses/mitigating strategies are established and are proving successful for the most significant risks; the team can re-visit the Risks Management Plan and perhaps identify risks which were of lesser significance initially; but for which resources may now be available for additional mitigating strategies to be identified for the next layer down, if appropriate.

During ongoing review of the Risk Management Plan if a response strategy is identified to be unsuccessful or not successful to an acceptable level, it may be necessary to plan an alternative strategy or potentially escalate the situation to the Sponsor for review and higher level decisions making. The Risks Management Plan will give you all the necessary details you will need to pass onto the Sponsor.

If the project/activity is one of a series of similar ones e.g. one protocol from a drug program; one clinical trial using a technology being used for other trials; one development activity within a larger change program etc., there may be benefit to pass on the contents of the Risks Management Plan to other teams with similar activities as they may also face similar risks and may be able to benefit from documentation of successful mitigation strategies or, even more, of mitigation strategies that were unsuccessful and had to be re-structured!

Summary

Risk is inherent in everything we do and **cannot** be avoided, just minimised and managed. In any arena taking an appropriate risk based approach to anything will deliver significant overall benefits.

Successfully identifying risks needs all the right people to be present and communicating effectively and can happen at ANY stage of any activity. However it is not possible to respond to all risks, it is pragmatic to respond to only the most significant ones, so it is essential to score risks appropriately, with agreement of all stakeholders.

To deliver all it's potential benefits the ongoing management of risks identified for an activity, it needs to be actively owned, as do all the defined responses to the most significant risks. Finally the effectiveness of the management of any activity can be improved if it is based on the ongoing management of the risks and their associated responses.

Jane Tucker

Quality Risk Manager, GSK

There will be no charge for attendance

CR-CSV FORUM

Thursday 22nd October 2009
GSK The Frythe, Welwyn, Hertfordshire

CR CSV

"Electronic data systems in Clinical Trials, are they fit for purpose?"

A viewpoint from an Academic Research Organisation

Karen Molloy from Imperial College will be giving us the ARO perspective on how well eClinical Trial systems meet both end user and regulatory expectations

Attendees may include (but are not limited to) people involved in:

- **Support and management of Clinical Trials**
- **Clinical Monitors**
- **Data Management**
- **IT and support services**
- **Development or customisation of computerised systems.**
- **Statistical programming and analysis**
- **QA**

This meeting will be from 12:30 - 5:00pm and will be followed by a buffet.

For further information or to register to attend please send an e-mail to: liz.a.adams@gsk.com Before 9th October 2009

Please pass details of this meeting on to your colleagues in Pharma and especially those in Niche companies or Academia.

Clinical Risk Management, Moving Away from Blame to Openness!

Risk management is a broad subject covering both clinical and non-clinical aspects. It can be described as the systematic identification, assessment, prioritization and reduction of risk to patients, staff and members of the public. Sometimes it is used as a buzzword for handling disasters or near misses.

The most challenging aspect to the implementation of a successful and effective risk management technique is going to be the required change in culture from "blame" to "openness".

This article proposes some suggested solutions based on developing a culture of openness, reporting and safety consciousness.

Most clinical organizations use Information Technology (IT) systems to process their information for better support of their missions. However, recent advances in technology have blurred the boundaries between information technology and medical technology. What was not too long ago a simple personnel computer used for word processing and emails is now an integral and critical component of many medical devices e.g. reading, recording, displaying, and dispersing real time patient data.

Most importantly recent advances in technical systems are being used to sound alarms to care givers about any change in patient's conditions i.e. adverse event (can be defined as any event or circumstance that could have or did lead to unintended or unexpected harm, loss or damage. Another definition often used by researchers is that adverse events are undesirable deviations in health away from baseline).

From a clinical prospective, management of clinical risks tends to be associated with the cost of clinical negligence. It draws attention to the scale of the problem of potentially avoidable events that result in unintended adverse events.

Hence, reporting systems should be introduced to identify adverse events in clinical trials and healthcare. These systems should include reporting of specified near misses (an occurrence, which but for luck or skilful management would in all probability have become an adverse event), gathering information as to their causes. This is required in order to synthesize, learn and act to prevent similar events occurring.

Patient safety must be placed first, rarely; serious failures occur with devastating consequences and are very distressing. Some adverse events can result in serious consequences with patient's death or are seriously injured. Usual response has been to apportion blame based on the lack of communications between investigators and clinical staff.

Steps towards enhanced communication and openness

- Unified mechanisms for reporting and analyzing when things go wrong.
- A more open culture, in which errors or service failures can be reported and discussed.
- Mechanisms for ensuring that, where lessons are identified, necessary changes are put into practice.
- A much wider appreciation of the value of the electronic system approach in preventing, analyzing and learning from errors.

Clinical risk management

Clinical risk management, with human factor concepts as its foundation, aims to achieve the following principle objectives:

- Identification of organizational, system failures or defense inadequacies. This is so that managers can act to remedy the situation before an accident occurs.
- Pro-active analysis of incident data would help reduce risk, that is analyzing what is likely to go wrong. This may also help identify what the costs are of getting things right versus getting things wrong.
- The prompt collection of all relevant records as soon as possible after an accident.
- Early incident reporting and analysis enables lessons to be drawn. This is through an objective assessment of all the active and latent human failures surrounding a particular event.

The forms used to collect adverse event data might include a list of anticipated adverse events and must include a list of those important adverse events for which the sponsor is required to gather incidence data. Each investigator should ask the same question in the same way and should be trained to query subjects about possible adverse events in a neutral manner so as to minimize bias. For example, "How are you doing?" is a less biasing question than "Has anything gone wrong?" Subjects would be more likely to answer the latter question in a negative manner because they think the investigator is seeking information about problems and wish to please him or her. It's a good idea to make up several mock adverse event examples that might arise and then work with the investigators to complete the data forms.

To do list for investigators

- Keeping comprehensive legible case records and avoiding abbreviations.
- Extending scope of practice only after accreditation to undertake extended roles.
- Introduce competency-based assessments for all staff in specific clinical tasks.
- Introduce professional development profiles for all staff, in addition to professional development plans
- Introduce reflective diaries and use

these in staff discussion forums on clinical management of interesting or complex cases.
- Act on lessons learnt.

What to report

Regardless of format of the adverse event form the following information should be collected:

- Date of report (Date of event's onset or checkbox indicating its absence)
- What happened? (Description or name of event.)
- Where did it happen? (Date and time)
- Why did it happen? (Underlying root causes)
- What action was taken? (Immediate and longer term)
- What impact did the event have? (Seriousness, hospitalization; prolonged hospitalization resulting from a potential disability, danger to life, or intervention; death; fetal distress; fetal death; congenital anomaly; or malignancy).
- Date of resolution.
- Intensity (ranked as mild, moderate, or severe).
- Relationship to investigated device (probably related, possibly related, or not related).
- Anticipated (yes or no).
- Treatment given.

Conclusions

The main challenge for the clinical organization will be to create a system in which the demand for paper work is proportional to its value in reducing risk.

Developing a pro-active safety culture through collaborative working is extremely important. This is where risk management is seen by staff to be worthwhile and not another instrument of control or yet more hurdles to cross. Successful risk Management will also depend on good cooperation and communication between Healthcare practitioners and sponsors.

Looking at ways to keep paper work to an absolute minimum and improve communication will help encourage staff to report incidents and near-misses from which valuable lessons can be learnt and acted upon.

Mrs Aous Mahdi (B.Sc, M.Sc)
Clinical Consultant
aousmahdi@gmail.com
Dubai/UAE

Quality Risk Management (QRM) at F. Hoffmann – La Roche: A Fundamentally New Approach to Quality Management and Compliance

Summary:
Quality functions in the pharmaceutical industry allocate by far most of their precious time and resources to fire fighting and correction of audit or inspection findings. Quality Risk Management (QRM), on the other hand, guides continuous improvement of key business processes by ensuring early and comprehensive detection of deviations from external and internal compliance standards. QRM facilitates and enforces related correction, mitigation, and prevention activities. At Roche QRM was developed and successfully launched on a global scale for the GCP (conduct of clinical studies) and Pharmacovigilance areas. It is now part of daily business routine of more than 1,000 users and has provided measurable process improvements and quality related benefits. QRM makes quality risk assessments consistent, more robust, and quantifiable in a comparable manner across different areas, functions, and geographies. It thereby enables fact based decision making by Senior and Middle Management by having transparency on the entire Roche risk landscape in GCP and Pharmacovigilance. QRM allows early detection of potential issues and thereby provides time for issue prevention. It supports integration of risk information across entities and thereby allows identification of any systemic issues and the underlying common root cause, i.e. QRM helps to focus and increase efficiency of mitigation. It enables all functions involved to direct their activities proactively to high risk areas and optimize resource deployment on quality-related issues. Additionally, QRM offers business owners in functions with tailored but comparable, quantitative risk assessments and standardized, proven risk mitigations, in order to increase efficiency and effectiveness of quality management. Continuous coaching and consulting of all individuals involved and automatic follow-up to mitigation success based on regular risk assessments represents key enablers.

The secret behind QRM's success is to leverage existing information/data, collected through a variety of routine business processes and stored in central databases. Analyzing this wealth of information in an automatic and standardized way helps business owners, task owners, and other stakeholders to assess at "a glance" whether processes in their responsibility do/will yield the intended results and quality.

Looking into the future, QRM will provide functions with reliable recommendations for successful risk/issue mitigation by sharing of best practices. In summary, QRM makes a significant contribution to saving time and costs while improving quality and reducing risks.

> "QRM makes quality risk assessments consistent, more robust, and quantifiable in a comparable manner across different areas, functions, and geographies."

How does QRM work?

Quality Risk Management (QRM) is a fundamental, new, and trendsetting quality management solution and a robust response to increased scrutiny by Health Regulators. The traditional approach was purely reactive – 'Creating an SOP and audit compliance'. Issues were identified during an audit and functions were expected to fix those. Follow up to issue correction was a challenge as it required another audit in many cases.

QRM introduces an entirely new philosophy to quality management by analysing existing data on quality risks, i.e. in order to allow proactive mitigation before an issue becomes a problem. This is based on so called *Key Risk Indicators* (KRIs). In most cases, KRIs do not directly measure occurrence of issues but the indication that they might occur in the future, if not addressed appropriately. An above-average number of protocol violations at a clinical trial center, for instance, is an indicator that the site is not adhering to the protocol as required. This may be because they were not appropriately trained, or they may have recruited more patients than they can handle in a very short time frame and therefore have violated inclusion/exclusion criteria. The KRI information is shared on a continuous basis with functions and empowered teams, in order to define and implement successful mitigation actions.

QRM provides several advantages compared with the traditional Quality Assurance approach:

1. QRM works as a "radar system" and provides early detection of potential quality and compliance issues, therefore it gives the responsible people enough time to identify areas of

weakness or non-compliance and take timely and effective corrective and preventive actions.

2. QRM provides a broader reach through comprehensive, automated risk assessments in all entities involved in clinical studies and drug safety. It provides a quantifiable exposure and through this enables prioritization and focused allocation of resources.
3. QRM allows for deeper insights by differentiating local and global issues and by the possibility of trend and pattern analyses, which lead ultimately to process improvements

All this is possible, because QRM uses the wealth of information Roche already routinely collect in daily business and analyses it in a simple but "smart" way.

One key feature of QRM is to share best practices in successful risk/issue mitigation. Both, risk levels and risk mitigating actions will be documented in a standardized way. Clinical QA is integrating this information and shares it as part of the coaching and consulting process with the functions. Therefore, the 'wheel does not have to be re-invented' each and every time. Rather well-proven risk mitigating actions can be shared across teams and can then also lead to process improvements over time.

In order to develop QRM, we deliberately looked outside Pharma to other risk management-attuned industries: to Aviation, Insurance and other industries that are significantly "ahead of the curve" in risk management. We consequently leveraged lessons learnt from other industries, in order to develop the most powerful quality management solution for pharma industry: QRM.

Volker Roenicke, PhD (Booz & Co.) &
Peter Schiemann, PhD (F. Hoffmann – La Roche Ltd.)

GlaxoSmithKline: Risks and Electronic Patient Reported Outcomes (PRO)

Article based on a presentation given by Roland Caller, GSK, at the ACDM Senior Forum, 25th February 2009 – Royal Statistical Society, London

Over the last few years, GlaxoSmithKline (GSK) has become more risk aware and has engaged in conducting risk assessments for the majority of important or critical projects, including clinical trials. GSK determined risk assessments were a priority specifically where use of electronic patient reported outcome technology supported clinical trials data collection. A process was drafted to include the following activities:

- Risks assessments to be conducted during the set up phase of each project.
- Actively managed actions (mitigations) for identified "priority" risks.
- Risk Management Plans fully documented with a risk owner assigned for each risk and all risks periodically reviewed during the set up phase.

Study teams engaged with the above risk process by duly conducting risk management throughout the trial set up phase. They ensured that all associated risks were captured, documented and all actions (mitigations) effectively managed until the trials went live.

Unfortunately, for many trials issues arose after patient enrolment and from these "unexpected" issues staff found themselves 'fire fighting' the problems and looking for and applying the 'quick fix' resulting in too many change initiatives at the trial level.

This, if left unchecked, could have resulted in a loss of confidence from Investigators and patients with the use of electronic PRO devices. For example, some instances arose where study teams demonstrated a loss of confidence with their device vendors resulting in a breakdown in communications which hindered resolving the problems.

Why then had this occurred? Both the sponsor and vendor were unaware of how "small" technical issues impact sites and study teams. A "simple matter" of a failed device often results in hours of additional site and sponsor staff effort that goes way beyond the call of duty (one Site Coordinator personally delivered devices to patients after clinic hours because site staff could not get devices to work while the patients were in the clinic). Hence there is a need to display more understanding of the repercussions when issues do arise.

For example:

- Problems relating to data transmission through digital phone devices in countries such as the USA which still rely heavily on analogue services and phone lines.
- Supplying wi-fi cradles for data transmission in investigator sites where wi-fi is already over-subscribed on band width hindered data transmission.
- Not supplying the correct electrical plug adapters for Australian sites might be a problem when it comes to recharging the batteries.
- An assumption that wi-fi technology is readily available in hospitals, clinics and the home in the developed world... this is a myth.

As you would expect, some of these above examples will hinder the 'use' of the device if the solution is to transmit an upgrade no connection = no upgrade.

Large *volumes* of small issues require up to half of a study managers'/monitors' time to deal with these on a constant basis. And of course there will be the potential for delays with patient recruitment as well as loss of real time data analysis or missing PRO data itself as a result of missed entries or missed data transmission.

Quite simply many study teams did not understand or identify with the need to continue with the risks assessment process after trials went live.

What did GSK do to mitigate our electronic PRO risk?

A project team was set up and talked to the study teams and monitors who had been involved with trials using an electronic PRO to find out what the "real" issues were. This project team held focused meetings with participants from 14 individual trials, asking them to provide input and details on actual problems encountered. Input from their perspective on what would improve study conduct and compliance was collected, with emphasis particular on the monitors who are closer to the problems at site.

From the information obtained a root cause analysis was performed. The table below details the top 5 most consistent issues occurring in clinical trials where an ePRO was deployed.

ePRO risk process (abridged)

Improved Risks Assessment training and support offered for the entire study team including monitoring staff.

All clinical trials employing a PRO undergo risks assessments at two distinct time points, before the PRO selection (after concept protocol approval) and after PRO selection (if it is agreed to use an electronic PRO for a clinical trial). The GSK model also employs pre-identified risk drivers and for each risk driver a number of

Risk Description	Resulted in	Possible Mitigation
Lack of adequate vendor Resourcing (Project Management)/turnover of vendor resource	Poor turnaround times, lack of effective communication.	Vendor to add dedicated project management resource to this project.
3rd Party Help Desk; delays to issue resolution, site/patient dissatisfaction, lack of knowledge of device and protocol	Results in answers that make situation worse, rudeness.	Continued training of help desk 3rd party by vendor. Extended help desk coverage hours.
Patient demographics not compatible with the complicated eligibility criteria built into electronic diary	Additional just-in-time training for study teams and patients.	Needs to be addressed when drafting clinical protocol. Better communication / sharing of experience with vendor will ensure vendor is better placed in providing qualified guidance for design decisions.
Device inventory management; inaccurate inventory figures	Resulted in delays when additional devices & equipment had to be ordered.	Enhance inventory management model with vendor.
Telecom - change to dial-up numbers not communicated out by vendor; inadequate backup plan for changed dial-up numbers.	Devices had to be reprogrammed to use new dial-up numbers over a 4 month time period resulting in delays. No data received in the meantime, and reprogramming was very disruptive to site/patient.	Future programs should have rollover to backup number upon first failure of primary telecom number.

pre-identified risks with suggested actions or mitigations for the study teams to use as a starting point and guidance. This does not mean though that these are the only risks to be considered and study teams do still need to "think for themselves".

Only one risk is considered requiring contingency planning and that is to revert to paper after go live. It is not advocated or recommended that the study teams consider a split process (paper and electronic) during the design phase, only as a contingency to losing the capability of collecting PRO data electronically.

What is the starting point, what drivers should be considered?

Actually, it really should be no different from considering at the implementation of an electronic data capture (EDC) tool for any clinical trial. Though there will be additional considerations to be discussed and considered when looking at patient populations and new PRO's.

- What risks are important to study conduct (protocol)?
- Do device limitations need to be considered?
- Does the patient population need to be considered?
- Are there any regulatory risks to consider?
- What about the risks for inventory Management?
- What vendor risks may be significant?
- Experience in programming electronic PRO?
- Help Desk outsourced?
- What are the user "compliance" risks with diary entries?
- Does an electronic PRO improve compliance?
- What risks need considering with protocol amendments?
- Risks for using a new rating scale in this trial?
- Concordance studies required?
- Which risks may require detailed contingency planning?

Some thoughts to consider; the majority of vendors for ePRO are the experts with the devices; they (not the sponsor) should also be the experts when it comes to inventory management. Therefore, sponsors need vendors and suppliers to take over micro-managing these examples of risks and issues.

Supplier relationships can be improved if sponsors get out of "baby-sitting" mode and place more responsibility with vendors and suppliers. After all, the primary aim of pharmaceutical sponsors is to provide medicines based on good science, not become programming vendors.

In summary, risk assessments are a key tool for our business if used effectively within clinical trials. They have found there worth within the GSK organisation when applied to electronic data capture tools such as ePRO. By talking to our internal customers, and by being proactive in finding out the problems even when on the surface looked to be working well, we identified further gaps in our own development of the risks process. I believe that the efforts and resource which kept this particular project team busy for two years has resulted in a better streamlined process with support readily available for those new to the ePRO risk assessment process within GSK.

Roland Caller,
Compliance & Audit Ready Lead,
GSK

Whatever can go Wrong will go Wrong, and at the Worst Possible Time, in the Worst Possible Way

Stuart Redding, MICR, CSci & Chair ICR PM SIG

When we drop a piece of toast, why does it always land with the buttered side down? – When it leaves our hands we know that this will happen – it's Murphy's Law!! When we set up a clinical trial, we think it is going to run according to plan ... but inevitably, in the majority of cases, it lands buttered side down! Risk management is often overlooked by Project Managers, who are over optimistic about how the trial is going to progress; the pessimistic Project Manager is the wise Project Manager who has been there and seen the issues before. Risk Management has to be an essential part of trial set up and ongoing trial management, irrespective of the cost and time required.

We all implement risk management strategies as part of everyday life; we make sure our children hold cups with two hands and use the toilet before long journeys, we leave more time than needed when driving to meetings. We assume the worst will happen and take steps beforehand to ensure the problem is either avoided or at least minimised.

Why is risk assessment often overlooked? In many cases project set up is constrained by both time and budget; first patient enrolled becomes the ultimate goal and what happens beyond that it is not considered. When setting up our trials, risk management should be a compulsory step; we wouldn't avoid obtaining regulatory or ethical approval to reduce timelines or budget, but we ignore risk management! Risks within the trial need to be assessed and categorised based on their likelihood to happen and the impact they will have; contingency plans can then be constructed to overcome the most likely and largest impact risks, whilst possibly ignoring those with less impact to contain cost. This process balances the costs against the ultimate deliverables.

Clinical trials are complex and involve many stakeholders with their own agendas, therefore we have to assume that we will never have control, but we should plan to keep the overall project on track as best we can even when it is threatening to get out of control.

It is not a great mystery where trials go off plan ... sites take longer to set up than planned for, often due to regulatory, ethics or contract issues; recruitment is slower than expected due to protocol issues or site issues; patients fail to consent or drop out early; CRF data is not as 'clean' as expected and query resolution is more long winded and time consuming than projected.

> "Risk Management has to be an essential part of trial set up and ongoing trial management, irrespective of the cost and time required."

Risk management therefore has to start at the very beginning of the programme and trial planning stages; each protocol has an aim and should be focussed on that aim. Nice-to-have assessments and visits should be considered carefully to determine whether they really are essential and if not, then they should probably be removed. The simpler a protocol is, the less there is to go wrong later. Visit intensive trials will recruit poorly, as the patient and investigators will struggle with the burden imposed on them. Simple inclusion criteria will open up patient populations and therefore improve recruitment, whilst simple and infrequent visits will keep patients in the trial. Including home visits into the trial can dramatically improve recruitment and retention as the burden on the site and patient is decreased making it ultimately more attractive to the uncontrollable stakeholders i.e. the subjects.

Site selection is critical, if the investigators are not enthusiastic and do not have the resource or patients then there is little point in selecting them and setting them up. The feasibility processes have to review in the detail the patient populations, the resources, competing trials and enthusiasm of the investigator and their staff. All recruitment information has to be taken with a pinch of salt! Where sites are lacking resource or patient populations are unproven, dedicated research staff can be provided to the sites to identify patients up front and to drive forward the recruitment processes.

Set up activities (including regulatory and ethics submissions, set-up of contracts, labs, CRFs) must be implemented early. The key stakeholders must be identified and relationships with them developed to enable dialogue and rapid problem solving. Over selection of sites can ensure that adequate numbers of sites are on board in time to kick start the recruitment and keep ahead of the planned recruitment curve as much as possible. Increasing levels of communication and motivation should be agreed within the team and budgeted beforehand, so that they can be implemented immediately without the need for further delay. The increased use of site set up specialist teams or more experienced team members can alleviate these prob-

Continued on page 28

The Swedish Chef

NAME: Kjell Pennert
ACDM POSITION: Chair Project Management SIG, Member of Training Committee
COMPANY: Richmond Pharmacology Ltd

When I was in my mid-teens I proudly declared to anyone who could be bothered to listen that there were two professional careers I would never, ever seek; in the banking world and in the pharmaceutical industry. After almost thirty years in the latter all I can say is, you say so many stupid things when you are young...

My first job was as a statistician at Sahlgrenska University Hospital in Gothenburg where I worked as a part of a team in a cardiovascular research unit. An important part of my role was to help and assist physicians with their theses, something I thoroughly enjoyed. But it could sometimes be a bit frustrating, as the time when I was contacted by a Cardiologist wannabe who informed me his thesis was almost completed, he had to finalise it within two weeks time and "the only thing left to do is the stats"!

In 1984-85 I joined ICI Pharmaceuticals in Alderley Park and moved to the UK for the first time, to Cheshire. Congleton is not exactly the centre of the Universe but I loved my time there and at ICI. The summer of '85 was hot, the price of a pint of Boddingtons was 68p, England won the Ashes, Norway won the Eurovision Song Contest, and Bob Geldof still did not like Mondays and made us all stay in on a Saturday night giving our money to a good cause instead of spending it all on beer.

Back in Sweden I joined ICI Pharma as a statistician, or rather the statistician as I was the first statistician ICI employed outside of the UK and the US. As there was not enough stats work to keep me fully occupied, I split my time as a CRA, primarily monitoring cardiovascular and oncology phase III studies. I was actually one of the very first monitors to do site source data verification in Sweden, in 1987! ICI Pharmaceuticals became Zeneca in the early 90's and I was now line managing a small team of statisticians and data managers. After 10 years with ICI/Zeneca I felt it was time to move on and left in 1996 to join the first of the CROs I have worked for, Clinical Data Care (CDC).

Kjell
My name is by the way is pronounced as shell in sea-shell, shell-shock, etc. I have heard all the jokes before...

I really do not know what I expected (or cannot remember anyway, which is true for a lot of things these days!), but the step from a safe job in a major worldwide pharmaceutical company to a small, family run CRO was not big, it was a complete shock! But I soon found my feet and headed a constantly growing Biometrics department.

Another thing I said in my younger days was that I would never stay with the same company for more than five years, so when the 21st century saw the light it was time to move on again. (Even though I stayed with Zeneca for 10 years, they changed name from ICI to Zeneca after my first 5 years so I changed company in a way). Having lived in the UK in the 80's and worked for a British company for 10 years, I always felt like home whenever I visited Britain (I suspect I was an Anglo-Saxon in a previous life!). So when I was offered a position as Director EDC Services at Nexigent in Maidenhead, I quickly made up my mind and moved from Sweden again. Nexigent was a very short-lived subsidiary of Covance, and, hence, unfortunately became a parenthesis in my working career.

Time for yet another move, from one capital to another – Edinburgh. By now, my career had slowly drifted more and more away from statistics and I joined PPD as Director of Data Management in 2001. Even though I did not understand much of what people said to me in the first year, I soon fell in love with the city (in spite of deep-fried Mars bars and deep-fried pizzas) and really enjoyed working for a large, global research organisation.

My working career had so far taken me on a journey from academia to large pharma, from small CRO to large CRO. So when I last summer was offered to join Richmond Pharmacology as Director of Data Management, Statistics and Programming it felt like a fresh, new and exciting challenge and I once again moved to London.

As much as I love working, I always strive to

Continued on page 28

Continued from page 27

have a "real life" outside of work and a good balance work/life. One of my interests is cooking, and I started really young helping my mum in the kitchen, almost before I could walk. A scar on my upper lip is a reminder of when I as a four-year old tripped on the kitchen threshold holding a can of tomatoes between my hands. It was not only the tomatoes that were peeled and red that day... As much as I love Britain I am proud of my Swedish heritage which shows in my cooking, Svensk Husmanskost.

However, music is my biggest interest. In my younger days I played the drums in a rock band, these days I settle for listening to my collection of records and going to gigs. I still do festivals but am too old for camping these days, so I cheat staying at a nearby B&B.

Another passion is (watching) sports, and in particular football. I became a life-time member of Everton Football Fan Club when I was thirteen years old. My other favourite teams are Celtic and IFK Gothenburg.

Rugby is not a big sport in Sweden; however I have learnt to appreciate a good game, especially at international level. One sport I have never understood though, and probably never will, is cricket. How can you take a game where you break for lunch and for tea seriously?!

That is pretty much it. Have I ever regretted my pharmaceutical career and that I did not follow my early promise? Well, I would have loved to become a rock and roll star, but I am happy I did not choose a banking career!

I have always had a big interest in project management, in cross-functional team work and training and I am excited to chair the PM SIG and to be a member of the Training Committee.

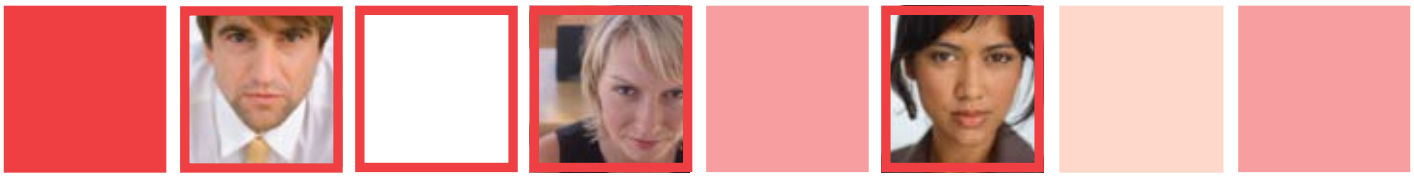
See you around!

Continued from page 26

lems, but not eradicate them.

Technology in trials is becoming ever more prevalent and selection of the correct tools can have both positive and negative effects. For larger, geographically dispersed trials, systems such as EDC and eTMF can be hugely beneficial, counteracting the time delays and risk of document movement. If all else fails and recruitment is delayed, using EDC can decrease the time it takes to get data in the database, as well as ensure that patient recruitment and drop out rates are assessed in real time. Using the incorrect tools can lead to over complication in trial reporting and drive up cost unnecessarily. Assessing resource for later trial activities and allocating appropriately is also essential, but that can only be done with appropriate communication and planning.

Often contingencies measures are agreed and documented at the set up phase, but many can be implemented before the project starts because we know they are going to be required ... why wait for the toast to hit the floor before getting a plate! Cleaning up the mess requires more effort than trying to avoid it from the outset!



ACDM College Week – 2-6 November 2009

Training Committee

Monday	Tuesday	Wednesday	Thursday	Friday
Project Management (2 days)	Project Management	Managing Projects & Alliances for all Clinical Phases of DM (1 day)	TAT - Oncology (half day)	Successful Trials - eClinical Technology (1 day)
Fundamentals of CDM (2 days)	Fundamentals of CDM	Working as part of an Effective Project Team (1 day)	The ABCs of Standards: A CDISC Primer for Data Managers (half day) e-CRF Design (half day)	Regulatory Update (GCP / EU Dir / Fraud & Misconduct / Prep for Regulatory Authority Audits) (1 day)

Book your place online NOW! Don't miss it....

AUGUST

26
ACDM
CDISC Special Interest Group Meeting
Amgen, Uxbridge, West London

SEPTEMBER

9
ACDM
ACDM Preparing for a Regulatory Inspection
CIM, Cookham, Berkshire

17
ACDM
Managing Remotely
ACDM Training Webinar

28-30
eClinical Forum
Autumn Meeting
Windsor, Berkshire

OCTOBER

4-6
SCDM
Annual Conference
Seattle, USA

6-9
ISoP
9th Annual Meeting
Reims, France

7
ACDM
Senior CDM Forum – Proving the Case for Process Improvements
Amgen, Uxbridge, West London

OCTOBER

7-9
TOPRA
6th Annual TOPRA Symposium
Clarion Hotel, Stockholm, Sweden

16
ACDM
Managing Offshore Teams
CIM, Cookham, Berkshire

19-21
DIA
3rd Annual Clinical Forum
Nice Acropolis, Nice, France

20
ACDM
Therapeutic Area Training – Pain
ACDM Training Webinar

22
CR-CSV
CR-CSV Forum – Electronic data systems in Clinical Trials – are they fit for purpose
GSK, The Frythe Welwyn, Herts

27-28
PSI
Data Monitoring Committees
Ascot, Berkshire

28-30
BARQA
BARQA Annual Conference 2009
Grand Hotel, Brighton

NOVEMBER

2-6 **ACDM**
College Week
CIM, Cookham, Berkshire

18
ACDM
Preparing for a Regulatory Inspection
ACDM Training Webinar

DECEMBER

2-4
DIA
10th Conference on European Electronic Document Management
Vienna, Austria

9
ACDM
GCP/EU Directive Update
ACDM Training Webinar

FEBRUARY 2010

24
ACDM
Senior CDM Forum
TBD

MARCH 2010

7-9
ACDM
Annual Conference – Driving Success
Whittlebury Hall, Northamptonshire

MARCH 2010

8-10
DIA
22nd Annual EuroMeeting
Grimaldi Forum Monaco, Monaco

14-16
SCDM
Leadership Forum
San Antonio, Texas, USA

APRIL 2010

28-29
CDISC
CDISC Interchange Europe
Royal Lancaster Hotel, London

JUNE 2010

13-17
DIA
46th DIA Annual Meeting
Washington Convention Center, Washington DC, USA

ACDM events can be booked online at www.acdm.org.uk

For ACDM events contact:

Association for Clinical Data Management
105 St Peter's Street
St Albans, Herts AL1 3EJ
Tel: +44 (0) 1727 896080
Fax: +44 (0) 1727 896026
Email: admin@acdm.org.uk

ACDM membership can be applied for via the internet at www.acdm.org.uk, or call the ACDM Office for an application form.

For ACDM events: **www.acdm.org.uk**
For BARQA events: **www.barqa.com**
For CDISC events see: **www.cdisc.org**
For CR-CSV events: **www.cr-csv.org**
For DIA events: **www.diahome.org**
For eClinical Forum events: **www.eclinicalforum.com**
For ICR events: **www.instituteofclinicalresearch.org**
For ISoP events: **www.isoponline.org**
For MHRA events: **www.mhra.gov.uk**
For PSI events: **www.psiweb.org**
For SCDM events: **www.scdm.org**
For TOPRA events: **www.topra.org**

acdm
association for clinical data management

Association for Clinical Data Management
105 St Peter's Street, St Albans, Herts AL1 3EJ
Tel: +44 (0) 1727 896080 • Fax: +44 (0) 1727 896026
Email: admin@acdm.org.uk • www.acdm.org.uk

ACDM DIRECTORS

Co-Chairperson	**Fred Daniels** Premier Research Limited	**Tel** 01344 752375 **Fax** 01344 752374 **Email** fred.daniels@premier-research.com
Co-Chairperson	**Tracy Fells** CMed Research	**Tel** 01403 755095 **Fax** 01403 755051 **Email** tfells@cmedresearch.com
Treasurer	**David Baker** Chiltern International Ltd	**Tel** 01753 647802 **Fax** 01753 647879 **Email** david.baker@chiltern.com
Secretary	**Paul Fardy** Eisai	**Tel** 0208 600 1400 **Fax** 0208 600 1479 **Email** paul_fardy@eisai.net
	Sue Gales Wyeth	**Tel** 01628 413893 **Fax** 01628 413862 **Email** galess@wyeth.com
	Andrew Green Pfizer	**Tel** 01304 642242 **Fax** 01304 652218 **Email** andrew.o.green@pfizer.com
	Ian Pinto Roche Products Ltd	**Tel** 01707 365904 **Fax** 01707 384513 **Email** ian.pinto@roche.com
	Harshad Sodha Omnicare Clinical Research	**Tel** 01403 823064 **Fax** 01249 444189 **Email** harshad.sodha@omnicarecr.com
	David Walpole GlaxoSmithKline R&D	**Tel:** 01279 644501 **Fax:** 01279 644848 **Email:** David.J.Walpole@gsk.com

COMMITTEES

Conference	**Gail Kniveton** i3 Pharma Resourcing	**Tel** 01895 451 801 **Fax** 01895 451819 **Email** gail.kniveton@i3pr.com
International Collaboration	**Eva Hammarström-Wickens** Orion, UK	**Tel** 0115 948 7116 **Fax** 0115 948 7119 **Email** eva.hammarstrom-wickens@orionpharma.com
Newsletter	**Jon Milton** Pfizer	**Tel** 01304 645788 **Fax** 01304 652218 **Email** jon.milton@pfizer.com
Public Relations	**Ian Pinto** Roche Products Ltd	**Tel** 01707 365904 **Fax** 01707 384513 **Email** ian.pinto@roche.com
Technical Meetings	**Chris Cramer** PharmaNet Ltd	**Tel** 01494 896248 **Fax** 01494 896261 **Email** ccramer@pharmanet.com
Training	**Jacqueline Johnson** Dovetail Training Limited	**Tel** 01628 784906 **Email** jkjohnson@dovetailtraining.com
Senior Forum & Postgraduate Qualifications	**Gill Lawrence** Kendle	**Tel** 01344 751537 **Fax** 01344 751549 **Email** lawrence.gill@kendle.com
Website	**Carly Baker** AstraZeneca	**Tel** 01625 582828 **Fax** 01625 583074 **Email** carly.baker@astrazeneca.com

WORKING PARTIES

Clinical Research Computer System Validation	**Jane Tucker** GSK	**Tel** 020 8966 3658 **Fax** 020 8966 5339 **Email** jane.e.tucker@gsk.com

SPECIAL INTEREST GROUPS

CDISC	**Lauren Shinaberry** PRA International	**Tel** 01792 525 612 **Fax** 01792 525 601 **Email** ShinaberryLauren@PRAIntl.com
Coding & Dictionaries	**Ian Slack** Parexel	**Tel** 01895 614198 **Fax** 01895 614451 **Email** ian.slack@parexel.com
Electronic Data	**Richard Young** CMed Research	**Tel** 01403 755081 **Fax** 01403 755051 **Email** ryoung@cmedresearch.com
Laboratory Data	**Noeleen Redden** Roche Products Ltd	**Tel** 01707 365646 **Fax** 01707 383 158 **Email** noeleen.redden@roche.com
Project Management in Data Management	**Kjell Pennert** Richmond Pharmacology Ltd	**Tel** 020 8664 5200 **Fax** 020 8664 5201 **Email** k.pennert@richmondpharmacology.com