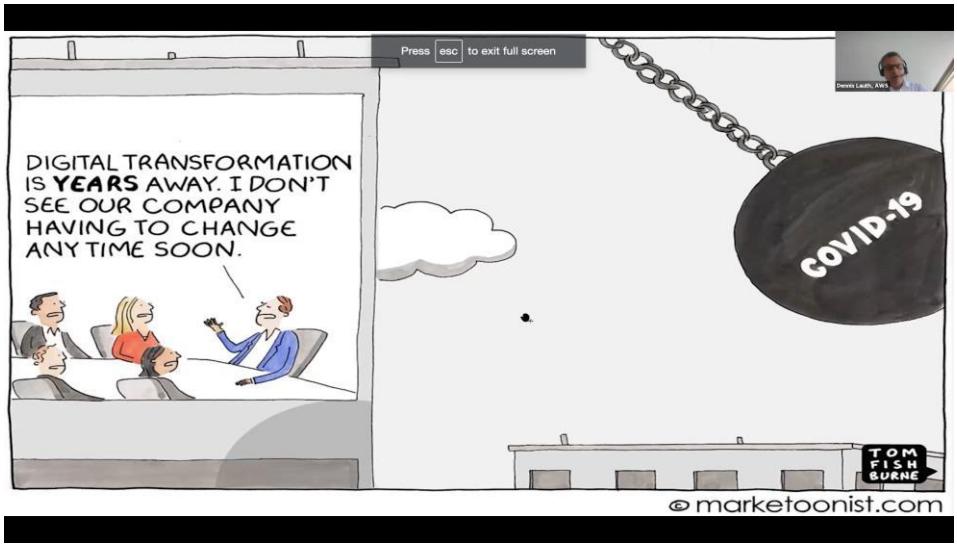
PCMG live 2020 – The people, the event, the discussions, the conclusions

Has Covid-19 accelerated innovative transformations in the conduct of clinical trials and the migration to a "new normal?"

June 2020 - four months into the introduction of social restrictions due to Covid-19 throughout the world. The pandemic has impacted everybody's lives and their working practices and the conduct of clinical trials everywhere, whether managed and delivered by pharma or by CROs. PCMG was forced to cancel their flagship annual conference, which was to have taken place early June in Krakow, Poland.

This three-day online, interactive event was created and delivered by PCMG for their members and for the European outsourcing community to capture learnings from these unprecedented times. The event was designed to explore how the pandemic has transformed the way in which we work, both as outsourcing professionals in Sponsor companies and as employees within CROs and the rest of the service sector. To explore how this transformation has manifest, what has changed, whether or not it is for the better and to look to the future and ask what changes will endure, once the pandemic is over. There have been many bad things happen as a result of Covid-19; this event asked what good would come out of it in the arena of clinical trial outsourcing.



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Day 1

Richard Scaife (PCMG Chairman) opened the meeting and welcomed all delegates. He emphasised the unique nature of the PCMG annual conference as an opportunity for networking and collaboration. PCMG live has been developed in very quick time and under the extreme circumstances of the Covid restrictions, to be informative, inspiring and interactive in the best traditions of the PCMG Annual Conference.



L to R: Co-chairs Richard Scaife (PCMG); Mark Bee (European Head of Sales, Clinical Development at Covance) and presenter Dennis Lauth (Amazon Web Services)

Dennis Lauth of Amazon Web Services gave the keynote address on Day 1: "Transforming clinical trials by leveraging the power of the cloud". An online poll of the 146 delegates demonstrated that almost exactly half the audience had used cloud-based digital technology in the conduct of clinical trials, whilst almost a half had not. Dennis described the enormous costs of clinical trials (estimated at $1.5b per product) and an efficiency gap which means that 80% of trials are delayed, 48% miss their recruitment target, there is a 30% patient withdrawal rate and 40% of trials have protocol amendments prior to the first subject visit, delaying trials by 4 months on average (data from Tufts Centre for the Study of Drug Development). Each day delay was estimated to cost $8m in lost revenues for a new drug (data from Deloitte). Perhaps even more impactful for the audience were the stark challenges in engaging patients using existing clinical trial (CT) processes, which means the industry is truly ripe for transformation. Covid 19 has presented profound challenges overnight for the successful completion of clinical trials and the need for innovation has been highlighted. Sixty percent of the audience felt Covid 19 would stimulate an inflexion point to a new normal in the conduct of clinical trials, whilst 30% were not sure what the new normal would be.

Dennis talked about a convergence of three aspects, which would underpin the emergence of the new normal:

- Secure, agile, cloud-based infrastructure
- Development of medical grade, validated, wearable detection and transmission devices
- Modern trial management systems using a telehealth platform

Dennis describe the Amazon web-based service offerings which have been designed to support hybrid- and virtual- clinical trial conduct through the implementation of cloud-based solutions. The potential for these technologies in helping to deliver efficient and compliant clinical trials has been highlighted by the Covid crisis and the need for ongoing trials to be managed remotely, without the need for face to face meetings at site. Dennis outlined the need to plan and design clinical trials from the start to be hybrid- or virtual- and supported with appropriate platforms that were validated and qualified. He also emphasised the opportunities for greater patient-centricity and championed the principle of democratisation, stating that "democratisation of clinical trials is pivotal to patient-centric, decentralised clinical trials". The five imperatives for thriving in the new normal will be:

- Patient- and customer-centricity
- Security and compliance
- Capability build/change management
- Digital innovation
- Breadth and depth of cloud-based services

Dennis then provided a very detailed description of where cloud-based technologies could improve the efficiency of CT design, site selection, patient recruitment and retention and the conduct of virtual trials. He backed this up with real data from the use of Amazon Web Services in various ways to address these challenges. Editor note: I am sure there are other providers of similar technology-based services.

Regarding the hurdles to transformational outsourcing, 63% of delegates responded that one of the top three barriers to establishing a new normal was conservatism by the pharmaceutical industry. This was substantially ahead of other potential hurdles. Conservatism is not so surprising in such a highly regulated industry, but even so, we are a world away from the "don't do what you are told" innovation mantra of Dave Kelleher (see Day 3 summary).

There were many questions, on topics which reflected the confusion some people have about migrating to virtual trials, their conduct, the confidentiality issues around GDPR, the cost of such services, and the regulatory acceptance of these changes.

In the breakout discussion rooms there was much talk about how quickly these changes might be implemented and who would be the key drivers of the changes – Sponsors or CRO/service providers. It was commented that CROs are generally more agile at identifying new technologies and platforms which could improve the efficiency of their clinical trials AND, crucially, they were better at incorporating such technologies into a seamless offering. Pharma were seen to be slow and cumbersome by comparison. One outsourcing professional said he expected CROs to constantly devise ways to "do more with less" and the cloud based, virtual approach seemed an obvious opportunity. His CRO partners were empowered to introduce change where they thought it could benefit themselves and the client. The group

considered the contractual models which might evolve as a result of hybrid or virtual trials in the future. It was felt that CROs would want to migrate from activity-based contracts to outcomes-based contracts, akin to the earned value models championed by Roger Joby and others.

This was seen to be an opportunity for differentiation for the CRO/service provider community. There are a large number of new entrants entering the arena, particularly technology companies offering IT-based solutions, and who might one day end up as part of a seamless CRO service offering or indeed designed into the conduct of trials by pharma.

A representative from a medium sized, regional CRO commented that at the moment their clients were all still interested in the conventional ways of conducting clinical trials and that Covid had not changed this. His assertion was that many sponsors would continue to require their outsourced trials to be conducted with face to face monitoring and interaction directly with the site staff, rather than a hybrid or virtual approach.

Rikke Winther in action with an expert summary of Day 1

A recording of PCMG live day 1 can be viewed at https://vimeo.com/439224983
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David Davies

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Day 2

Co-hosts Jean Edwards and Roy Ovel opened the day with their personal highlights of Day 1 – in particular the excellent interactions for the delegates and the focus on patient-centricity as part of the new normal.


Jean Edwards (PCMG livetime achievement award winner, 2018) and Roy Ovel (Chief Commercial Officer, Ergomed PLC); joint co-chairs of PCMG live day 2

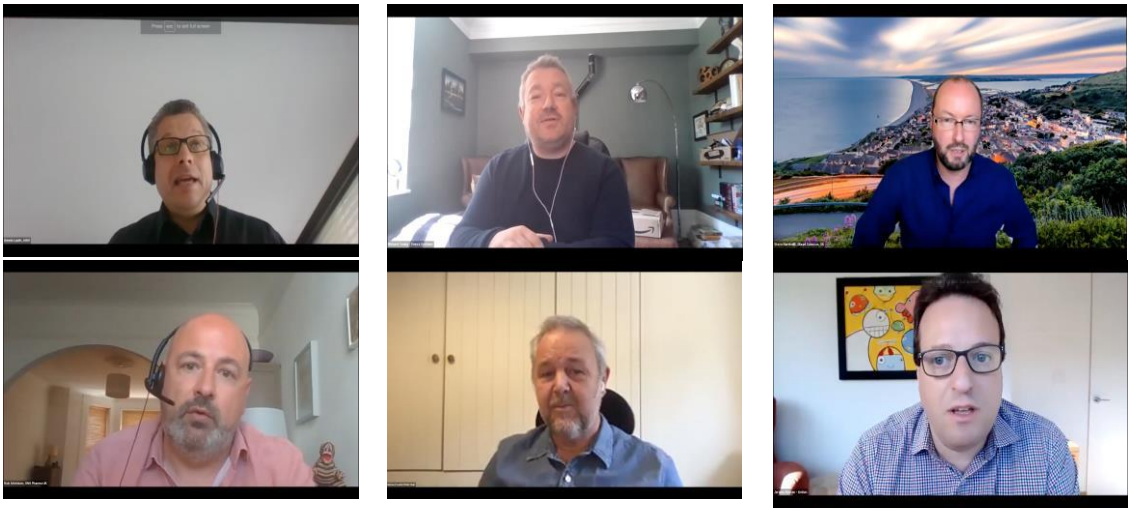
The main event of Day 2 was a panel of experts discussing the forces for change brought about by Covid and how the conduct of clinical trials and the business of outsourcing had been impacted. The panel was also challenged to forecast what changes would persist in the future, once the social restrictions had been lifted and the threat of infection had been extinguished.

The panel comprised:

- Steve Martindill (VP Clinical Operations, Gilead, VP of clinical operations for EU & JAPAC at Gilead Sciences where he leads teams supporting Gilead's development trials and post-marketing studies outside of US)
- Jeremy Rassen (Co-founder, president, and chief science officer at Aetion, a health care technology company that delivers real-world evidence for life sciences companies, payers, and regulatory agencies)
- Dennis Lauth (Business Development Lead Life Sciences/Healthcare, Global Accounts EMEA Amazon Web Services)
- Richard Young (Vice President, Strategy, Vault CDMS, where Richard is responsible for defining strategy and direction for Vault CDMS, especially with respect to clinical data management

There was a consensus that digital technology could help make trials more efficient and effective as part of the ongoing evolution of the industry. Covid has forced the introduction of technical innovations to drive forward the development of Covid treatments and vaccines at record speed, assisted by revolutionary transformations in the speed and conduct of regulatory processes. However, it was acknowledged that the pharmaceutical industry is very conservative, for the following reasons:

- Very highly regulated
- R&D generally is highly risk averse
- Big pharma tends to be a collection of operational silos with conflicting priorities and there remains a huge challenge to align these silos to achieve harmonised, coordinated, synchronised processes.



Panelists (clockwise from top left): Dennis Lauth, Richard Young, Steve Martindill, Jeremy Rassen and co-chairs Richard Scaife and Rob Aitchison

Dennis Lauth was convinced of the need to learn from Covid, for companies to upgrade their digital technologies throughout the organisation and to achieve sustained changes for the future. He felt that platforms to achieve high quality remote monitoring had advanced during COVID and would be sustained. He added that the industry has an opportunity to define a new normal in designing trials around patient needs and desires, eliminating flaws and using technology to improve the patient experience of taking part in clinical trials.

Richard Young was sceptical that COVID has accelerated innovation. His simple and devastating point was that innovation meant simplification and he hadn't seen much evidence of things getting more simple; in fact his observation was that a lot of technology pieces were being thrown at clinical trial challenges in a haphazard way, so that true innovation is not being achieved.

Steve Martindill painted a vivid picture of some of the real challenges faced by a pharma sponsor company at the forefront of Covid research (Gilead developed the anti-viral Remdesivir to fight Covid) during the crisis. He commented that sponsors like Gilead had been bombarded by companies offering technology that addressed a part of the CT process, but which was not necessarily the priority issue (leading to the comment "sounds good, but is it needed?"). And he emphasised his own observation that individual countries present

very particular contexts for CT conduct and innovation, with different regulatory sentiments, different social restrictions and different impacts on access to medical care, to name but three elements). He felt that global solutions were not as effective as local, focussed strategies. He also made the crucial point that patients generally were happy to embrace new technology but what keeps them in a trial is speaking with the site staff and being encouraged to continue. Finally, he stated that the Gilead team had recruited technical experts to better evaluate the technology offerings which were being offered to them. Do they address a key need and do they present a real benefit that they don't already have? He felt that we would need more information to evaluate the impact of technology and the strides in innovation.

Dennis Lauth reminded the audience that for some cancer patients the clinical trial might represent their last hope and that such a patient needed to be progressed through studies with sensitivity and care that could only be given by direct human contact. He felt the human element was essential but that new technology could be an enabler to improve the patient experience.

Jeremy Rassen made a different set of points, based around the use of Real World Evidence (RWE) to accelerate stages in development and the regulatory review. He stated that we don't necessarily need to invent new things, but apply knowledge we already have in new ways to drive innovations. Covid has forced us to use RWE to enable solutions, for example the use of historical disease progression data as a comparator instead of a placebo arm. Aetion had used RWE ("research and knowledge known for years") to evaluate vaccine candidates for their potential efficacy against the Covid virus. They collaborate on the RCT duplicate program (funded by FDA) to look at 30 pivotal trials considered recently to see if the same conclusions could have been derived from the use of RWE. This important work is ongoing and the outcomes will be fascinating and could highlight the value of RWE in expediting clinical development programs. Covid has demonstrated how quickly the industry can collaborate to evaluate old molecules for their activity against Covid on the basis of existing data. Jeremy was convinced that RWE enabled companies to move quickly and nimbly in the pre-approval phase and that RWE represented a real opportunity to further evaluate efficacy and safety in diverse patient populations.

RWE collected during Covid is demonstrating immediate changes which are manifest in very short time periods (ie days, not weeks or months). There have been big shifts in a very short time and we will have the chance in the longer term to see whether or not these changes are sustained. As an example, he quoted the uptake of telemedicine (consultations with medical staff via telephone). This has increased by 200-fold during Covid in the US and is being sustained in spite of relaxations in social restrictions. It remains to be seen whether or not the American public continue to use telemedicine in preference to attending clinics and meeting site staff in person.

Steve Martindill reminded the audience of frustrating, persistent out-dated practices such as the rejection of electronic signatures on site contracts at Turkish investigator sites. He again reminded the audience that countries are all different in their implementation of new technologies. The US culture was more accepting of new technologies that could enable

hybrid and virtual studies, compared to Europe. FDA is frustrated with pharma for their failure to adopt new technologies, whilst pharma keep asking for more guidance.

Dennis Lauth added further realities and urged caution in rapid adoption of new technologies before the fundamentals are in place and the service is fully validated for compliance (eg with GDPR legislation) and security (ie protection from cybercrime). He felt that maintaining trust during multi-agency innovations was vital. Richard Young reminded us all to think what is best for patients and then do the right things to encourage patient recruitment and compliance and enrich the patient experience throughout the trial. He also raised the interesting fact that technology companies present a different value proposition to CROs and therefore want significant up-front payments included in the milestones, whilst CRO upfront payments are generally modest and proportionate to their activities.

Steven Martindill emphasised the challenges in evaluating new technology. He described a formal digital strategy at Gilead to define the road map for all the silos in how the company expected to implement new technologies in the future. Gilead conduct proper pilot studies to evaluate new technologies against the existing systems and processes and will only adopt if the outcomes demonstrate real benefits. However, the pilot studies take time to complete and to analyse.

In response to a difficult question from the Chairs, Richard Young reflected that new technologies were a differentiator between CROs and that the functional service provider outsourcing model would facilitate adoption of new technologies better than Full service outsourcing, presumably as the contribution of the new technologies would be easier to see.

The panel were asked about the use of open source technologies and whether these could improve the effectiveness and efficiency of clinical trials. Dennis Lauth felt open source technology could only be used where the same fundamental problems had been resolved by the technology in a parallel industry. And where all the stakeholders were aligned on the adoption of the new technology. He agreed that pilots were important and that they needed to be scalable. Jeremy Rassen added that the assumptions and extrapolations with open source solutions had to be valid in the context in which you intended to use it.

In conclusion, the panel were asked about their levels of optimism for the future post Covid. Steven commented that the industry was facing their biggest challenge ever and was responding “magnificently” with extensive collaborations demonstrating the power of cooperation. However, industry ROIs are at an all-time low and things “had to change”. Dennis was “super-optimistic” and felt the industry would establish a new normal, with clarity around challenges and technology innovations used as fully integrated enablers to accelerate speed to market in areas of high unmet need. Richard was also very optimistic at the prospect of a “new dawn” in partnering with connected users and anticipating and then meeting their demands. He felt partnership was the absolute key to implementing and adopting new technologies and working practices.

The panel ended this panel discussion with expressions of universal optimism for the future, driven primarily by the extent to which the industry had cooperated to respond to the

COVID challenges. However, there was a feeling that whilst COVID had accelerated innovation, the pharma industry would likely slip back into old working practices due to various reasons, but chiefly inertia and risk aversion within pharma. At times during the discussions the scepticism was palpable. Definitely a topic worthy of review once the Covid crisis is eventually over.

The session was expertly chaired by Richard Scaife (PCMG Chairman) and Rob Atkinson (PCMG Steering Committee)

A recording of PCMG live Day 2 can be viewed at https://vimeo.com/439228523
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David Davies

PCMG live 2020 – The people, the event, the discussions, the conclusions

Day 3 – The human element in innovation


Day Chair Conor Byrne (European Head of Business Development, DOCS) and main speaker Dave Kelleher (Co-founder and CEO, 4G Clinical)

Conor Byrne began the third day of events with his own reflections on the event so far, that technology is only an enabler and the keys to innovation is to simplify and ask the right questions. He is convinced that we have the right people in the industry to effect innovation, but that we need to listen and collaborate more with regulators and CROs. Conor himself was looking forward very much to renewing working relationships in person with colleagues once the restrictions are over, echoing many people's sentiments, for sure.

David Kelleher is a former Army Ranger who was diagnosed with Multiple Sclerosis in his early 20's. He is active in finding a cure, having served as Board Chair of the Oregon Chapter of the National MS Society and also in multiple national roles. A consultant to the pharmaceutical industry, he decided that he could achieve most impact as head of his own company implementing change and innovation through technology, and hence 4G Clinical was born.

David espoused the excellent approach of PCMG to lead discussions on best practice and to achieve real collaborations and cooperation across the industry and across operation silos for the best interests of patients and other stakeholders. He also felt PCMG members were able to demand excellent standards from internal and external stakeholders with a sincere focus on achieving a common purpose.

How do we ensure that the purpose is at the centre of innovation? 4G Clinical exists to make a meaningful difference to patients' lives. David and his business partner, Ed Tourtellotte, had both suffered through disease and are committed to improving other people's lives through technology, but were also both aware that technology alone would not achieve innovation. Driving speed and efficiency in the conduct of clinical trials, 4G Clinical develops innovative randomisation and trial supply management (RTSM) via cloud-based technology for global pharma. David stated that the human element is now more important than ever, as highlighted by the current Covid crisis. As a specific example, direct to patient initiatives were not a reality until April this year, with 4G Clinical launching a DTP initiative to overcome Covid restrictions. An inspiring response to a public crisis and a result of huge collaboration and cooperation. Also, everyone is aligned around a common purpose and the desire to bring real benefits to patients.
Many things happening now that will be retained. How can we maintain the pragmatism and prevent reversion to the old ways? Do not be constrained by process and policy. Three takeaways:

- Focus on the purpose, evangelise the purpose, align on the purpose
- Get close and stay close to the science and the patient to ask the right questions and get the right answers. Entire 4G Clinical company meets twice a year and bring sponsors and patients in to talk about the science and the potential for patients. Appreciated hugely by the staff. Clarify what you are working on, why and what positive effects they are going to achieve for patients
- "Don't do what you are told" mantra. Very innovative for the conservative and highly regulated clinical trial industry, but it is the conservatism and need for compliance that sometimes unnecessarily stifles innovation

The Covid crisis has forced real innovation. As procurement leaders, we have a charter to demand these three key factors from our internal and external customers, to ensure that humans drive innovation, with technology as an enabler (doing exactly what it is told to do).

Rob Aitchison commented that procurement and outsourcing managers don't always have the traction to achieve change in their respective industries. David commented that the key opportunity is for outsourcers to identify innovations from the external community that can be brought in house to internal customers. The array of new technologies can be very confusing for outsourcing managers who cannot know all the details of new technologies. David felt the opportunity was to truly deeply understand the problem to be resolved. Then bring the best together and force them to collaborate to address the key problem.

What does 4G Clinical do specifically to work with patients and incorporate their thinking into innovation. Difficult within trials because of lack of direct access via clinical trial sites. Companies like 4G Clinical are often held at arms' length; closest is patient representatives speaking to 4G Clinical, but otherwise they go through sites.

Real acceleration in clinical trials – where will it happen? Therapeutic study set up in 6 days. Simplification, regulatory burden reduced, flexible technologies, focus on the purpose.

How scalable are innovations in different sized sponsor companies? Smaller companies generally move faster but bigger companies have more resources and can move "superfast"

if they want to. It needs the right mind-set and prioritisation from the top of the organisation. In David's experience, innovations tend to be more readily and aggressively pursued by, for example, oncology companies on the West coast than by European and Japanese larger pharma.

There followed a protracted and excellent discussion session with delegates split up into pre-designed breakout groups to discuss the three principles ("adapt, implement, improve"). The groups were balanced, where possible, for service providers, sponsors and independents and were excellently moderated by members of the PCMG committee. The conclusions were shared during the final session, which was moderated by Tanja Hoffman (Industry Consultant).

The final two events of PCMG live were eagerly anticipated by all delegates. The 2020 PCMG lifetime achievement award was presented to Pauline van Heiningen by PCMG Vice Chair Gill Slater – click here to see the separate report of this award. Secondly, Richard Scaife, PCMG Chairman was delighted to announce that the 2021 PCMG Annual Conference will take place during 2-4 June at the Hotel Melia Calvia on the island of Mallorca – click here for more details and to register your place. Delegates were encouraged to pre-book their places on the PCMG website and for sponsors to express their interest in the remaining sponsorship opportunities before they are all gone.

Finally, Richard proposed a vote of thanks to Sandra Johnson and the rest of the PCMG organising team who had done such a fine job in adapting and evolving the annual conference content into this innovative and highly successful online format for PCMG live in double quick time. The Committee were ably assisted by Candi and her team at KSAM and thanks were also offered to Samme Allen, who had chaired the event and ensured our own innovative technology was behaving as planned.

PCMG live steering committee chair Sandra Johnson leading from the front

PCMG vice-chair Gill Slater presents the Lifetime Achievement award to Pauline van Heiningen

Pauline van Heiningen – popular winner of the PCMG Lifetime Achievement award

A video recording of PCMG live day 3 can be viewed at https://vimeo.com/439211113 (password **PCMG2020)**

David Davies