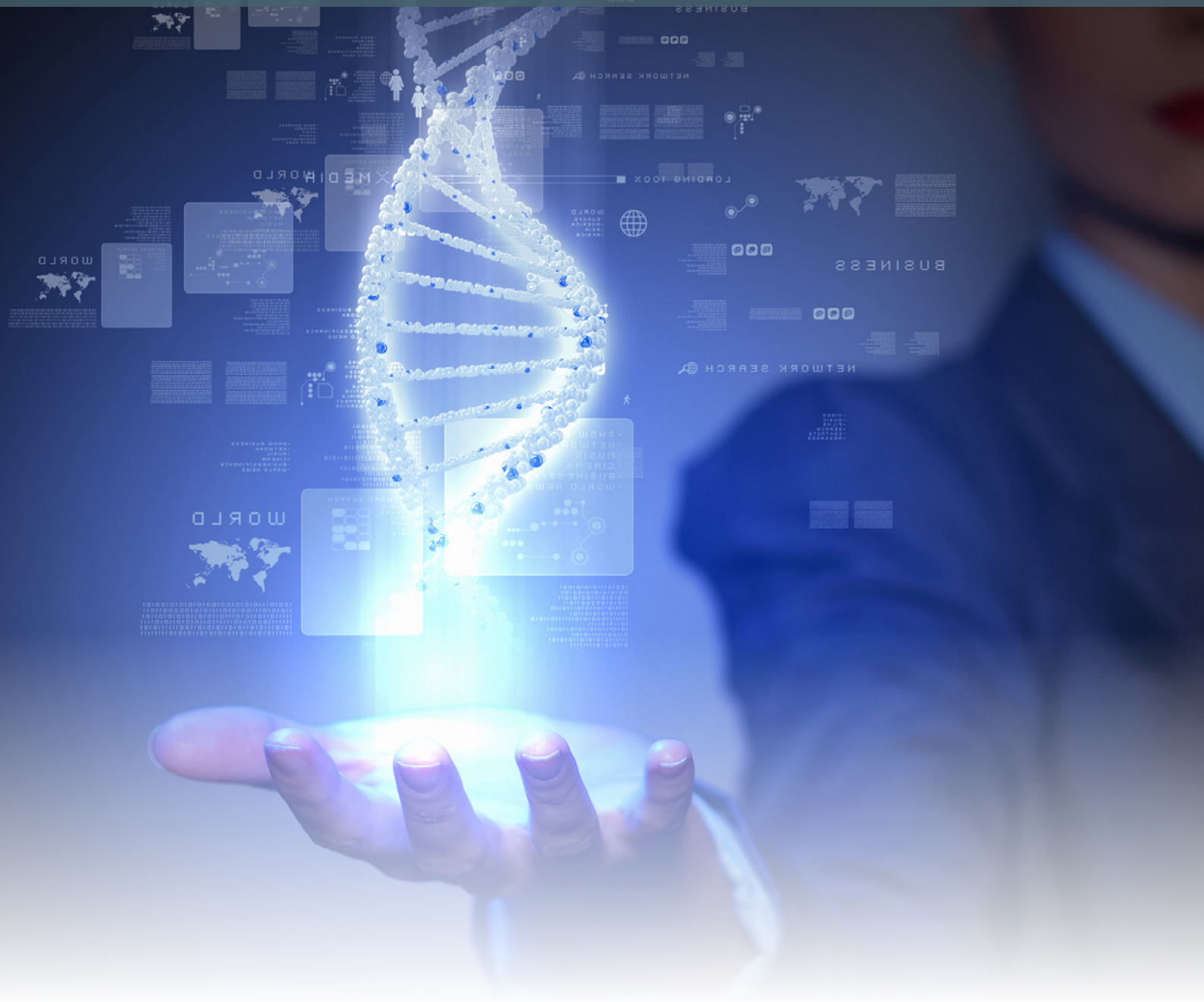
VitalTransformation

The impact of health technology made simple

A ROADMAP FOR SHARING CLINICAL TRIAL DATA

27 August 2013, Vlerick Business School, Manhattan Centre, Brussels



Vlerick Business School

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European Federation of Pharmaceutical Industries and Associations

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AGENDA

13:00 **Networking Lunch**

14:00 **A Presentation of the EFPIA and PhRMA Clinical Trial Data Sharing Proposal**

Richard Bergström, Director General, EFPIA

14:10 **Best practices in the use of clinical trial data**

- *Hans-Georg Eichler, Senior Medical Officer, European Medicines Agency*
- *Ben Goldacre, Wellcome Research Fellow in Epidemiology, London School of Hygiene and Tropical Medicine*
- *Richard Bergström, Director General, EFPIA*
- *Susanna Palkonen, Vice President, European Patients' Forum*
- *Moderated by Alastair Kent, Genetic Alliance*

15:10 **Building a data sharing health infrastructure**

- *Gisèle Roesems, Deputy Head of Unit - Health and Well-being, DG Connect*
- *Beat Widler, Managing Partner, Widler & Schiemann AG*
- *John Crawford, Healthcare Industry Leader Europe, IBM*
- *Nicola Perrin, Head of Policy, Wellcome Trust*
- *Moderated by Duane Schulthess, Vital Transformation*

16:10 **Coffee Break**

16:30 **Balancing public health and commercial confidentiality**

- *Ruxandra Draghia-Akli, Director of the Health Directorate, DG Research of the European Commission*
- *Johanna Gibson, Director, Queen Mary Intellectual Property Research Institute*
- *Neal Parker, Section Head Legal - Biologics Strategic Development, Abbvie*
- *Jacqueline Bowman-Busato, Director General, EPPOSI*
- *Moderated by Alastair Kent, Genetic Alliance*

17:30 **Networking Cocktail**

This event is made possible with the support of:

Vlerick Business School

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SPEAKERS

Richard Bergström

Director General, EFPIA

Richard Bergstrom is a pharmacist by training. He received his MScPharm degree from the University of Uppsala, Sweden in 1988. Until 1992 he worked at the Medical Products Agency as Assistant Head of Registration. He moved to Switzerland where he worked for nine years in regulatory affairs at Roche and Novartis. Before returning to Sweden in 2002, he was Director, EU Regulatory Strategy at Roche Basel. For nine years he was Director-General of LIF, the Swedish Association of the Pharmaceutical Industry. During this time he was member of the Board of EFPIA and the Council of IFPMA, the international association based in Geneva. In Sweden he had several government appointments, incl. as vice chairman of the Board of the Karolinska Institute. He also served on the Board of IMM, the Swedish Institute against Corruption. Since 2006 he is an advisor to the WHO on Good Governance in Medicine.Since April 2011 he is Director General of EFPIA, the European association for the research-based industry.

Jacqueline Bowman-Busato

Director General, EPPOSI

Jacqueline Bowman-Busato is Executive Director of Epposi, the only European think tank which brings together patients' organisations, health professionals & academia as well as various health care industry actors, to collaboratively reach consensus on key healthcare policies impacting European citizens on an equally weighted basis. A lawyer, strategic communicator & MBA by education, and a public affairs and process innovation game changer by profession, Ms Bowman has spent her career spanning almost 20 years in Brussels building trust amongst stakeholders, galvanising policy innovations and building capacity at regional, European and global levels. Ms Bowman-Busato has previously headed the Expert Secretariat for the EPWG on Sexual & Reproductive Health and Rights for Woman in Developing Countries, advised International institutions and governments on health systems strengthening through technology and driven advocacy campaigns on resource mobilisation for communicable diseases which have had significant impact on citizens' access to treatment.

John Crawford

Healthcare Industry Leader Europe, IBM

John has joint responsibility for the development of IBM's Healthcare Business in Europe. He is a member of several European healthcare IT industry associations, including COCIR, EHTEL and the Continua (Europe), and he sits on the Health & Social Care Council of Intellect, the UK high technology trade association. He is a founder member of the Cumberland Initiative, a collaboration of industry, academia and NHS organizations aiming to improve clinical process performance through simulation and modeling. In the EU, he is a member of the Industry Team of epSOS, an EU-funded project to enable cross-border digital health services, and he is the lead IBM representative for the European Innovation Partnership on Active and Healthy Aging (Integrated Care Action Group). He also supported the development and launch of InnovaHealth, an EU project to create an open innovation ecosystem for healthcare, where he co-authored the chapter on eHealth in the November 2012 report.

Ruxandra Draghia-Akli

Director of the Health Directorate, DG Research of the European Commission

Ruxandra Draghia-Akli (MD, PhD) is Director of the Health Directorate at the Research and Innovation DG of the European Commission. Dr Draghia-Akli served as Vice-President of Research at VGX Pharmaceuticals (now Inovio) and VGX Animal Health. Her research activities focused on molecular biology, gene therapy and vaccination. She is a global leader in the field of nucleic acid delivery for therapeutic and vaccination applications. She is an inventor on more than a hundred patents and patent applications.
Dr Draghia published numerous scientific papers and served as ad-hoc reviewer for granting agencies, meetings for gene therapy and endocrinology societies, and scientific journals in Europe and the USA. Dr Draghia received an MD from Carol Davilla Medical School and a PhD in human genetics from the Romanian Academy of Medical Sciences. She also completed a doctoral fellowship at the University of Rene Descartes in Paris and a post-doctoral training at Baylor College of Medicine (BCM), Houston, Texas, USA, and served as faculty at BCM. In 2012, she became an honorary member of the Romanian Academy of Medical Sciences.

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SPEAKERS

Hans-Georg Eichler

Senior Medical Officer, European Medicines Agency

Hans-Georg Eichler, M.D., M.Sc., is the Senior Medical Officer at the European Medicines Agency in London, United Kingdom, where he is responsible for coordinating activities between the Agency's scientific committees and giving advice on scientific and public health issues. Prior to joining the European Medicines Agency, Dr. Eichler was at the Medical University of Vienna in Austria for 15 years. He was vice-rector for Research and International Relations since 2003, and professor and chair of the Department of Clinical Pharmacology since 1992. His other previous positions include president of the Vienna School of Clinical Research and co-chair of the Committee on Reimbursement of Drugs of the Austrian Social Security Association. His industry experience includes time spent at Ciba-Geigy Research Labs, U.K., and Outcomes Research at Merck & Co., in New Jersey. In 2011, Dr. Eichler was the Robert E. Wilhelm fellow at the Massachusetts Institute of Technology's Center for International Studies, participating in a joint research project under the MIT's NEWDIGS initiative.

Johanna Gibson

Director, Queen Mary Intellectual Property Research Institute

Professor Johanna Gibson is Herchel Smith Professor of Intellectual Property Law and Director of the Queen Mary Intellectual Property Research Institute (QMIPRI), Queen Mary University of London, where she researches and teaches in intellectual property law and policy. Gibson consults regularly to industry, the profession, and UK and European government institutions, and has published widely in numerous articles and books including, The Logic of Innovation (2014), Intellectual Property, Medicine and Health (2009), Creating Selves: Intellectual Property and the Narration of Culture (2006), Community Resources: Intellectual Property, International Trade and the Protection of Traditional Knowledge (2005), as well as editing the collection, Patenting Lives: Life Patents, Culture and Development (2008). Before moving to academia, Gibson was in commercial practice in intellectual property, media and competition law at the Melbourne, Australia office of a top-tier international law firm.

Ben Goldacre

Wellcome Research Fellow in Epidemiology, London School of Hygiene and Tropical Medicine

Ben is an award-winning writer, broadcaster, and medical doctor who specialises in unpicking scientific claims made by scaremongering journalists, government reports, pharmaceutical corporations, PR companies and quacks. He was trained in Medicine at Oxford and London, and currently works as an academic in epidemiology. Ben wrote the weekly Bad Science column in the Guardian from 2003-2011.

Bad Science the book (4th Estate) has sold over half a million copies worldwide, reached #1 in the paperback non-fiction charts, and is being published in 25 languages. In his new book, Bad Pharma (4th Estate, September 2012) Ben puts the $600bn global pharmaceutical industry under the microscope. What he reveals is a fascinating, terrifying mess.

Alastair Kent

Genetic Alliance

Alastair Kent OBE is the Director of Genetic Alliance UK – the national charity of over 150 patient organisations, supporting all those affected by genetic conditions. Genetic Alliance UK's mission is to promote the development of the scientific understanding of genetics and the part that genetic factors play in health and disease, and to see the speedy transfer of this new knowledge into improved services and support for patients. Alastair is also the Chair of Rare Disease UK (RDUK) the national alliance for people with rare diseases and all who support them. RDUK has over 1,200 members including over 220 patient organisations, health professionals, researchers, the pharmaceutical industry and individual patients and families. Alastair has worked in the field of genetic and rare disease healthcare for over 20 years. Alastair represents the interests of patients on numerous platforms; he is the president of the European Genetic Alliances Network (EGAN), Immediate Past Chair of the European Platform for Patient Organisations, Science and Industry (EPPOSI) and the EU Committee of Experts on Rare Diseases amongst others.

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SPEAKERS

Susanna Palkonen

Vice President, European Patients' Forum

Susanna Palkonen is Vice President of the European Patients' Forum EPF, which is a voluntary function and works as the Executive Officer of European Federation of Allergy and Airways Diseases Patients' Associations (EFA). EPF is the umbrella association for 55 European level disease specific patient groups and national platforms of patient associations. EPF vision is high quality patient centered care across the EU. Susanna has been involved in the patient movement for over 15 years. She is a patient representative at eTRICKS European Translational Information and Knowledge Management Services Consortium Ethics Management and Advisory Board, member of the EU Consultative Forum on Environment and Health of the European Commission Directorate General (DG) Environment and DG Health and Consumers (SANCO) Indoor Air Quality Expert Group and represents EPF in the European Medicines Agency (EMA) Patient and Consumer Working Party.

Neal Parker

Section Head Legal - Biologics Strategic Development, Abbvie

Neal Parker is a U.S. lawyer specializing in drug and biologic regulatory issues. He began his career more than 20 years ago representing international and domestic clients in matters subject to U.S. Food and Drug Administration (FDA) regulation. In 1994, he left private practice to join the FDA, where he served as a senior lawyer in the agency's Office of the Chief Counsel providing advice to the FDA Commissioner and Center for Drug Evaluation and Research (CDER) Director on novel and emerging issues of FDA law such as biologics, dietary supplements and combination products. At FDA, Neal handled FDA enforcement matters, rulemaking and guidance issues, and also litigated on behalf of the FDA numerous defensive, seizure, and injunctive enforcement actions involving unapproved drugs, generic drugs, dietary supplements, adulterated and otherwise violative medical devices, and biologic products. In 2001, Neal left FDA and joined Abbott laboratories, where he worked on world-wide biopharmaceutical and medical device legal regulatory issues.

Nicola Perrin

Head of Policy, Wellcome Trust

Nicola Perrin is Head of Policy in the Strategic Planning and Policy Unit at the Wellcome Trust, responsible for leading policy development and advocacy work at the Trust. Particular areas of focus include research base funding, data sharing and the use of patient information in research, and research in the NHS. She is currently leading the Trust's thinking in relation to emerging discussions about greater access to clinical trial data.

Prior to joining the Trust, Nicola worked at the Nuffield Council on Bioethics as Communications and External Affairs Manager, and before that, she was an exhibition manager at the Science Museum. She has degrees from the University of Oxford, the University of Cambridge, and Imperial College, London.

Gisèle Roesems

Deputy Head of Unit - Health and Well-being, DG Connect

Gisele Roesems-Kerremans is Deputy Head of Unit of the "(ICT for) Health and Wellbeing" unit within DG CONNECT, the Communications Networks, Content and Technology DG.

A civil engineer in computer sciences (University of Leuven (B)) she started her career as a system engineer in the telecommunication sector and later in the automotive industry.

She joined the European Commission in 1994 as a scientific officer in the domain of Software technologies in the ICT research programme and moved on to the areas Micro/Nanosystems and Nanoelectronics.

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SPEAKERS

Duane Schulthess

Managing Director, Vital Transformation

Duane Schulthess is the Managing Director of Vital Transformation, a consultancy focused on quantifying and communicating the impact of new technologies in the health-care sector. He is a member of the Advisory Board of Health Policy and Technology, and will serve as their Guest Editor in the fall of 2013. His previous positions include Commercial Director of Science|Business and EMEA Head of Corporate Development for The Wall Street Journal.

Duane studied the French horn on a Fellowship at London's Royal Academy of Music and also has an MBA with distinction from the Vlerick Business School where he has been a member of the international steering committee. He has a Bachelor's degree in fine arts from the University of the Pacific where he graduated Magna Cum Laude and Phi Beta Kappa, also qualifying for a duel degree in Economics.

Beat Widler

Managing Partner, Widler & Schiemann AG

Dr. Widler, a Ph.D. graduate from the Swiss Federal Institute of Technology in Zurich. From 1986 till 2011 Dr. Widler worked for Hoffmann-La Roche first as an International Drug Regulatory Affairs officer, then as a Senior Research Scientist. In 1993 he joined the International Clinical Quality Assurance department. From 1997 to 2011 he was the Global Head of the Department for Quality, Ethics and Systems' in Roche Pharma.
He now operates as an independent CQA and Quality Risk Management Expert and is Managing Partner at Widler & Schiemann AG in Zug Switzerland. Dr. Widler is an active member in a variety of international GCP working parties and heregularly lectures at DIA, EFGCP, WHO, ECPM (University Basel) seminars. He was the project leader for the development of the Association of the British Pharmaceutical Industry (ABPI) Clinical Trial Disclosure Toolkit, released this month.

ABOUT US

VitalTransformation

The impact of health technology made simple

What is the impact of new technology on the delivery of health care?

The team at Vital Transformation understands the implications of new medical procedures and technologies. We measure their impact on current clinical practices in close collaboration with health care professionals, researchers, and regulators. The research findings of Vital Transformation have been presented at conferences sponsored by The Royal College of Physicians, The European Commission, The British Embassy – Belgium, London Genetics, The European Science Foundation, The European Microelectronics Summit, and others. Our clients include many of the world's leading health care organisations.

Principles for Responsible Clinical Trial Data Sharing

Our Commitment to Patients and Researchers

Biopharmaceutical companies are committed to enhancing public health through responsible sharing of clinical trial data in a manner that is consistent with the following Principles:

- **Safeguarding the privacy of patients**
- **Respecting the integrity of national regulatory systems**
- **Maintaining incentives for investment in biomedical research**

Companies routinely publish their clinical research, collaborate with academic researchers, and share clinical trial information on public web sites at the time of patient recruitment, after new drug approval, and when investigational research programs have been discontinued.

Biopharmaceutical companies will apply these Principles for Responsible Clinical Trial Data Sharing as a common baseline on a voluntary basis, and we encourage all medical researchers, including those in academia and in the government, to promote medical and scientific advancement by adopting and implementing the following commitments:

1. Enhancing Data Sharing with Researchers

Biopharmaceutical companies commit to sharing upon request from qualified scientific and medical researchers patient-level clinical trial data, study-level clinical trial data, and protocols from clinical trials in patients for medicines and indications approved in the United States (US) and the European Union (EU) as necessary for conducting legitimate research. Companies will implement a system to receive and review research proposals and provide applicable data and protocols to help facilitate such scientific and medical research.

Each company will establish a scientific review board that will include scientists and/or healthcare professionals who are not employees of the company. Members of the scientific review boards will participate in the review of data requests to determine whether they meet the criteria described below regarding the qualifications of the requestor and the legitimacy of the research purpose, unless a company makes an initial determination on its own to share applicable clinical trial data. Companies will publicly post their data request review process and the identity of the external scientists and healthcare professionals who participate in the scientific review board, including any existing relationships with external board members.

Companies will provide access to patient-level data and other clinical trial information consistent with the principle of safeguarding patient privacy; patients' informed consent provided in relation to their participation in the clinical trial will be respected. Any patient-level data that is shared will be anonymized to protect personally identifiable information. Companies will not be required to provide access to patient-level data, if there is a reasonable likelihood that individual patients could be re-identified. In addition, clinical data, in some cases, have been collected subject to contractual or consent provisions that prohibit transfer to third parties. Such restrictions

may preclude granting access under these Principles. Where co-development agreements or other legal restrictions prevent companies from sharing particular data, companies will work with qualified requestors to provide summary information where possible.

Data requestors will be required to submit a research proposal to document the legitimacy of the research question and the qualifications of the requestor. Research proposals should include, and will be evaluated against the following: a description of the data being requested, including the hypothesis to be tested; the rationale for the proposed research; the analysis plan; a publication and posting plan; qualifications and experience of the proposed research team; a description of any potential conflicts of interest, including potential competitive use of the data; and the source of any research funding.

Researchers who are provided access to company data will be encouraged and expected to publish the results of their analysis. Researchers must agree not to transfer the shared data or information to parties not identified in the research proposal, use the data for purposes not contained in the research proposal, or seek to re-identify research participants.

2. Enhancing Public Access to Clinical Study Information

In order to help patients and healthcare professionals understand the results of clinical trials and the evidence used to approve a new medicine, following approval of a new medicine or new indication for an approved medicine in the US and EU, biopharmaceutical companies will make publicly available, at a minimum, the synopses of clinical study reports (CSRs) for clinical trials in patients submitted to the Food and Drug Administration (FDA), European Medicines Agency (EMA), or national competent authorities of EU Member States. Companies will make this information available consistent with the need to protect patient privacy, publication rights, and confidential commercial information through appropriate redaction. In addition, companies will evaluate requests for full CSRs, including patient-level and study-level data, and share them under the terms of commitment 1 above. Companies will make available CSR synopses filed with regulators on or after January 1, 2014; such CSR synopses will be made available within a reasonable period of time after approval of the product and indication.

3. Sharing Results with Patients Who Participate in Clinical Trials

In order to help inform and educate patients about the clinical trials in which they participate, biopharmaceutical companies will work with regulators to adopt mechanisms for providing a factual summary of clinical trial results and make the summaries available to research participants.

4. Certifying Procedures for Sharing Clinical Trial Information

Companies following these Principles for Responsible Clinical Trial Data Sharing will certify on a publicly available web site that they have established policies and procedures to implement these data sharing commitments.

5. Reaffirming Commitments to Publish Clinical Trial Results

All company-sponsored clinical trials should be considered for publication in the scientific literature irrespective of whether the results of the sponsors' clinical trials are positive or negative. At a minimum, results from all phase 3 clinical trials and any clinical trial results of significant medical importance should be submitted for publication. This commitment also pertains to investigational medicines whose development programs have been discontinued.

Implementation of these commitments will begin on January 1, 2014.

Questions & Answers

Q What type of information are biopharmaceutical companies prepared to share with qualified medical and scientific researchers under commitment 1?

A The biopharmaceutical industry is committing to sharing with qualified medical and scientific researchers patient-level data, study level data, and clinical study designs and protocols.

Patient-level data refer to information on individual patients collected during a clinical study, including: demographic data, lab results, baseline characteristics, drug concentration, biomarker and pharmacogenetic data, and adverse events experienced. Such information has been gathered and recorded on case report forms (CRFs), or captured electronically and inputted into electronic databases, where it can be readily organized into patient-level listings and datasets. This information is created through what the Institute of Medicine (IOM) has described as a process by which data in a clinical study originate with CRFs, either handwritten or electronic, then go through several stages of auditing, queries, and refinement by original investigators and study staff to resolve ambiguities, and then ultimately yield "individual participant data."[1]

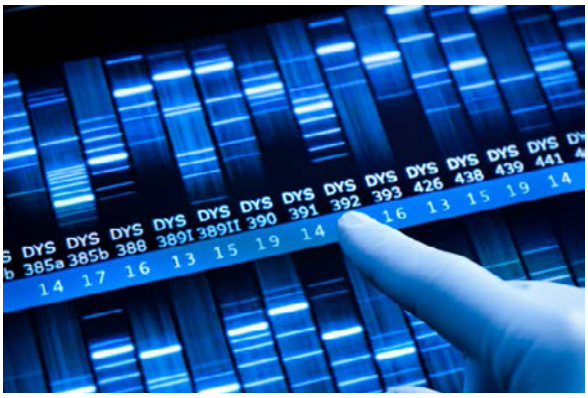
Study-level data consist of patient-level data that have been amalgamated, compiled and tabulated, manipulated, stratified, or otherwise organized into study-level data sets, to be used in interpreting the outcome of a clinical study. Study-level data present clinical trial data in an objective manner, without subjective analysis or interpretation, usually in tabular, graphic, or statistical form showing, for example, averaged, stratified, or patterned presentations of study data gathered. Examples would include a table that presents cross-patient data on baseline patient characteristics (demographic and disease-related), patient disposition (i.e., numbers/percentages of patients who completed or discontinued the trial), endpoints (primary, secondary, and other), study drug exposure, adverse events, vital signs, and laboratory and other safety measures provided for the overall study population, and by subgroups.

Clinical study design information and protocols direct investigators how to run a particular study. Protocols give instructions to the investigators on, for example, what drug to give and when, what study measurements to take and when and how to record them, and how to treat and record adverse events.

Q What is the rationale for providing the synopsis of CSRs in commitment 2?

A Given the volume of data contained in regulatory submissions – often running to millions of pages – companies commit to publishing a synopsis after marketing approval in the US, EU, or member states. The synopsis will provide patients and their physicians with enhanced information about the results of clinical trials and the evidence used to approve a new medicine. The synopsis is a part of the CSR and is reviewed by the FDA and EMA as part of their approval. In order to accelerate research and advance scientific understanding, companies will also evaluate requests for full CSRs, including patient-level and study-level data, and share them under the terms of commitment 1.

In addition to providing the synopsis, some companies may choose voluntarily to provide to the public additional parts of CSRs redacted to protect patient privacy and confidential commercial information.



Q Why may it be necessary to limit the availability of patient-level data for clinical trials conducted involving patients whose data are likely to be re-identified?

A Protecting the privacy of patients who participate in clinical trials is a critical obligation of biopharmaceutical companies that sponsor and conduct medical research. It may be possible even for "anonymized" patient-level data to be re-identified using modern data mining techniques.[2] For this reason, companies generally withhold patient-level information from disclosure when there is a reasonable possibility that patient privacy could be jeopardized. The risk of "re-identification" is significantly higher when the number of patients is small, such as is typically the case for trials involving patients with rare diseases, which may include as few as 25 or fewer patients.

Q Under commitment 1, are companies committing to share patient-level data and other proprietary information with competitors?

A No. Discovering and developing new medicines is a long, complex, and costly process. For every 5,000 to 10,000 experimental compounds considered, typically only one will gain FDA approval, after 10 to 15 years of research and development costing an average of $1.2 billion, based on a 2007 study. The few successes must make up for the many failures. In fact, only two out of every 10 medicines will recoup the money spent on their development.

Biopharmaceutical companies are dedicated to fostering a sustainable research ecosystem that protects the ability of companies to make extremely costly investments to discover and develop new medicines. One of the risks to innovation is disclosure to competitors of companies' trade secrets and proprietary information that could allow others to "free ride" off of the substantial investments of innovators. Such an environment will not foster the ability of companies to make decades-long investments in new medical technology. Therefore, in a sustainable research ecosystem, companies must be certain that their proprietary information will remain secure from disclosure to competitors. That is why commitment 1 calls for a company to share patient-level data and other confidential commercial information — which could be used to help gain approval of a competing medicine — only for legitimate scientific and medical research. Commitment 1 reflects these concerns by allowing companies to consider requests for release of clinical information in light of potential conflicts of interest, including any potential competitive use of the data.

Under commitment 1, companies will evaluate, among other things, whether the research proposed has a legitimate scientific or medical purpose, including whether there is any potential conflict of interest between the data requestor and the company or competitive use of the data. In the latter case, it may be assumed that the data requestor may intend to use the company's patient-level data or other information to help gain approval of a potentially competing medicine. While companies may enter into agreements to co-develop medical products, these data sharing Principles are not intended to allow free-riding or degradation of incentives for companies to invest in biomedical research. Accordingly, it would be appropriate under commitment 1 for companies to refuse to share proprietary information with their competitors.

Q How will companies determine who can receive patient level data or other proprietary information?

A Each company will implement a system for reviewing research proposals and the credentials of requesting researchers to determine that the proposed research is bona fide. Companies may choose to implement these systems individually or with centralized scientific review boards. Among the considerations for protecting patient privacy are the research participants' informed consent and other legal permissions, such as privacy authorizations (e.g., HIPAA in the United States) and/or data use agreements. With respect to these commitments to patients, any patient-level data that can be shared will, therefore, be "anonymized" in accordance with applicable legal requirements to protect personally identifiable information. Companies will not provide access to patient-level data when there is a reasonable likelihood that individual patients could be re-identified. In addition, where co-development

agreements or other legal restrictions prevent companies from sharing particular data, companies will work with qualified requestors to provide summary information if feasible.

Q Will there be any other restrictions on use of data provided under commitment 1?

A Each company will determine the best method for safeguarding the privacy of patients and ensuring that access to patient-level data does not jeopardize incentives for future investment in biomedical research. Commitment 1 requires that data requestors must agree not to transfer shared data to parties not identified in the research proposal, use the data for purposes not contained in the research proposal, or seek to re-identify research participants. Companies may also require that the data are only used for non-commercial purposes. Additional conditions may include granting access to the data only on a company's information system and/or requiring that data requestors notify the company of any safety finding that may be reportable to regulatory authorities or of other significant results.

Q Other than patient privacy information, what type of information could be withheld from CSR information provided to the public under commitment 2?

A In order to maintain incentives for future investment in biomedical research, individual companies may choose at their discretion to withhold from public access to CSRs various business and analytical methods; manufacturing and pre-clinical information or other confidential commercial information; any information not directly related to the conduct of the study or that could jeopardize intellectual property rights; or information that the company has no legal right to share (e.g., due to an existing co-development agreement).

Information withheld from public access to CSRs may nevertheless be available to qualified researchers under the terms of commitment 1.

Q If a company chooses, may it share more clinical trial information than is described in these commitments?

A Yes. Companies will make their own determinations regarding how to implement these commitments and whether to exceed these common commitments to responsible data sharing. For example, companies may choose to provide voluntarily to members of the public the main body of CSRs redacted to protect patient privacy or confidential commercial information.

[1] Institute of Medicine, Sharing Clinical Research Data: A Workshop Summary 10 (2013).

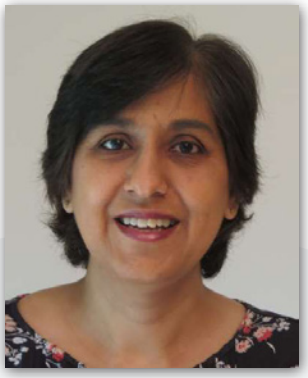
[2] See Melissa Gymrek et al., Identifying Personal Genomes by Surname Inference, 339 SCIENCE 6117 321-324 (2013).

JULY 18, 2013

ABPI toolkit will help members manage clinical trials disclosure process

Research by the ABPI indicates current statistics on the state of play in transparency are not accurate. A toolkit will guide members in complying with disclosure requirements and generate more reliable information on compliance

By Nuala Moran



Bina Rawal, Director of Research, Medical and Innovation at ABPI

The debate of the past year – and the initiatives of some individual pharmas – illustrates that while the industry in increasingly committed to transparency there is no prescribed route for companies making moves to open up clinical trials data stores.

In the UK, the Association of the British Pharmaceutical Industry (ABPI) made a pledge to increase transparency in February this year, by putting in place measures to monitor compliance to the clinical trial transparency provisions contained in its Code of Practice. At the same time the ABPI said it would provide a clinical trial disclosure toolkit to assist members with compliance.

The toolkit, launched in August, is intended to guide companies through the different steps of the disclosure process. "Expectations about transparency are definitely changing, and that's a good thing. Our members vary enormously from small biotechs to large international pharmaceutical companies and we wanted to set out a single generic approach to managing the process of clinical trial disclosure," says Bina Rawal, Director of Research, Medical and Innovation at ABPI, who has spearheaded preparation of the toolkit. "It's ready to take off the shelf and modify and embed within the clinical research process."

Transparency is not something that can be retrofitted, but needs to be threaded through clinical development. This should ensure disclosure is handled in an appropriate and balanced way, and create an audit trail that can be used to demonstrate compliance.

Rawal believes this will help address one of the main sources of dispute between campaigners and the industry, which is that there is no reliable information on the current state of play in clinical trials transparency. "It's become an accepted figure in the public debate that half of all trials go missing; based on my experience of working in the industry that just doesn't resonate with me," Rawal said.

After joining the ABPI in October last year, Rawal commissioned research to test this statistic. The work involved checking to see how many of the trials that fed into the files of the 53 new drugs approved by the European Medicines Agency in the three years from the beginning of 2009 to the end of 2011 had been published.

The research is currently awaiting publication in a peer review journal, so Rawal does not want to give figures at this point, but said, "It's clear the situation is not as bad as it is painted, and is a lot better than in the past." Some of the early studies of the drug approved from 2009 – 2011 were done more than ten years previously, and it is these that are more likely to be missing from the record, rather than later stage trials.

Rawal also pointed to the complications of ascertaining what trials have been published and where. "This is a difficult area to get a handle on the evidence, there's no single registry system, or single type of trial, data could be published in a wide range of places," she said.

One significant and widespread issue that has emerged from the research is that products frequently change ownership during development and current rights owners do not have access to data from earlier trials. Rawal said this underlines the need to embed transparency measures so that when a drug changes hands, the data goes with it. "You have to involve the legal function and ensure clauses are written into deals ensuring access to data," she said.

In the case of the ABPI research all the trials listed in the EPARs (European public assessment reports) of the 53 drugs were tracked down to see if the data was in the public domain. For studies that were not disclosed, the researchers then referred back to the companies concerned to find out why not. "For any that were not disclosed we have a statement from the medical director explaining why," said Rawal.

Overall, says Rawal, "There's a very different picture from that painted in the public debate."

Global consortium is needed to manage access to patient-level data

Providing controlled access to identified patient-level information is an essential element of realising the full potential of clinical data stores. A global agreement is required to put in place formal mechanisms and ensure appropriate access, says Nicola Perrin, Head of Policy at the Wellcome Trust.

By Nuala Moran

All researchers funded by Wellcome are required to maximise access to their data and clinical trials – including ones where the results are negative – are no exception. Specifically, this means all studies must be registered, and the summary results reported, on public registries such as clinicaltrials.gov.

The debate around clinical trials transparency has provided a spur for the Trust to step up its monitoring process to check the researchers it funds are complying with these requirements, says Nicola Perrin, Head of Policy. Overall, she believes it is now generally acknowledged both by academics and industry that there is a duty to register and report trials.

This represents important progress in terms of transparency, but it still leaves much of the potential of clinical trials data under-exploited. There is now a need to put in place formal mechanisms for allowing access to patient-level data. "At present there are some ad hoc approaches. If we could get it right, this would reduce duplication, answer new research questions and stimulate innovation," Perrin said.

Whilst the Wellcome Trust wants to encourage access to identified patient data, patient confidentiality remains the overriding concern. "This type of data should not be openly published; there should not be a free-for-all," said Perrin. Some form of review process is needed, both to check the bona fides of researchers applying for access, and the scientific value of their proposed research. There are models here, such as the procedures for accessing a named individual's samples and data from biobanks, which could form the basis of such a system.

The initial opening up of pharma industry clinical trial data stores, for example by GlaxoSmithKline and Roche, is happening at the level of individual companies, with each setting up its own panels to review research requests. A coordinated approach is required. "What won't work is if everyone has their own system," Perrin said.

Such coordination would allow research to be carried out linking separate industry sponsored clinical studies, and enable access to the relevant data sets via a single portal.

Nicola Perrin, Head of Policy at the Wellcome Trust

Over the past 12 months, the argument over clinical trials data transparency has moved in a positive direction. There is now agreement not only about listing and reporting trials on registries, but also on the value to be extracted from balanced and controlled access to patient-level data. "There is agreement transparency is right. The question is how do we do it, how do you get best practice?" Perrin said.

The Wellcome Trust is now involved in moves to promote the formation of a consortium to steer a system into place. This would apply to future trials. "There needs to be appropriate consent by patients, so the idea is to have something in place so we can get it right from now onwards," said Perrin. "The consortium has to be global, it has to involve academics and industry, and has to cover the whole spectrum of clinical research."

It's time for rapprochement between academic campaigners and pharma companies over clinical trials data transparency

The current polarised debate is not helpful to anyone, least of all patients, says Alastair Kent of Genetic Alliance UK

By Nuala Moran

Alastair Kent, Director of Genetic Alliance UK

"There's absolutely no point in having a polarised debate where people are standing on soap boxes and shouting at each other," says Alastair Kent, Director of Genetic Alliance UK, a body representing more than 160 rare diseases patients' groups, commenting on the current impasse in Europe over opening up access to clinical trials data.

"You are going to end up in a situation where patients lose rather than gain because the pace of development slows and undue attention is given to any problems with a drug, rather than the benefits."

The way forward is to recognise that both patient confidentiality and commercial confidentiality must be factored in to any equitable and practicable clinical trials data transparency system, but that one cannot trump the other, that neither is absolute, and – in particular – that the industry cannot use patient confidentiality as a "magic shield" to avoid answering awkward questions, Kent says.

"Fundamentally, I, and I think most patients' groups are in favour of transparency. But that does not mean putting everything in the public domain for anyone who wants to look at it."

The approach taken in rare diseases provides a model for how to move forward, and will be increasingly useful as the advance of personalised medicine leads clinical trials of drugs for treating common, complex, chronic diseases to be stratified into small subsets of patients.

Patients with rare diseases want the maximum value possible to be extracted from any samples and data they contribute to clinical studies. They are also keen to be on rare disease registries set up to promote research, increase understanding of the natural history of a rare disease, and for identifying patients who could participate in a clinical study.

"When setting up a registry, all sorts of things need to be taken into account and incorporated into the original consent document. By participating in a registry you know data and samples will be available for research purposes, and you also get the benefits of visibility," said Kent.

As Kent noted, those allowed access to registries could be public sector academics, but given rising commercial interest in rare diseases, they could equally be pharma companies, highlighting the fact that a proportionate data transparency regime should not exclude competitors from getting access to data.

Methods for providing access without compromising an individual's privacy already work in practice. Kent pointed to researchers who get grants from the UK Economic and Social Research Council being required to place their raw data in secure archives. Similarly, resources such as the UK Biobank and the 1000 Genomes Project, which relate to named individuals, will be open for public and private researchers who demonstrate appropriate credentials.

"There are models for allowing data transparency, while protecting individual and commercial interests. It's fair enough to share non-identified, pooled data in the public domain, alongside secure data archives that are accessed by approved researchers," said Kent.

Overall, "You can't allow one side or the other of this argument to win," Kent believes. "If the rules are too draconian you will prevent discoveries from happening. If things are too laissez-faire, with no respect for commercial confidentiality there's less incentive to invest and a risk the regulatory system gets undermined," he said.

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VitalTransformation

A ROADMAP FOR SHARING CLINICAL TRIAL DATA

27 August 2013, Vlerick Business School
Manhattan Centre, Brussels

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