European Heart Journal (2013) **34**, 3161–3167
doi:10.1093/eurheartj/eht400

CARDIOPULSE

National Society Cardiovascular Journals and the New European Society of Cardiology Search Engine

A new comprehensive online search engine has been developed to facilitate searches at the European Society of Cardiology

The National Society Cardiovascular Journals (NSCJs) of the European Society of Cardiology (ESC) are high-quality bio-medical journals devoted to publishing original and educational material on cardiovascular diseases. National Society Cardiovascular Journals belong to the corresponding ESC national societies and many of them have achieved major international recognition and scientific impact. Some NSCJs offer full-text English content and are freely available in electronic editions. However, NSCJs are largely heterogeneous and some of them are only published in local languages with a limited visibility. A journal's prestige is based on credibility, distribution, and scientific impact. The Editors' Network of the ESC provides a unique platform for developing editorial initiatives aimed at improving the scientific quality and facilitating the distribution of NSCJs. Herein, we discuss the implications of the Internet, electronic editions, and open access strategies (OA) for the NSCJs. In addition, we will describe a new initiative based on a novel electronic tool located on the ESC website to further increase the visibility of NSCJs.

The Internet and electronic editions

Sharing the results of late breaking research through peer-reviewed journals remains the mainstay of the scientific process. Journals should ensure maximal accessibility and diffusion of their articles. Currently, most publications have already moved into a new 'online era', where the emphasis is placed on the Internet and electronic editions. In this scenario, electronic editions and accessibility on the Internet certainly play a critical role. Nowadays, once a paper is electronically published, the information can propagate rapidly in the community and have extremely high downloads. In addition, uniform resource locators (URLs) are being increasingly used in scientific publications. Citation of URLs offers the possibility to calculate an objective 'electronic' Impact Factor.

The Internet offers a new window into science providing new insights on access and use of research. Currently, web-usage data can be analysed to outline a 'map of knowledge'. When readers click from one page to another while looking through online scientific journals, they generate a chain of connections. By aggregating all these complex relationships using network-visualization algorithms, maps can be generated based on the 'distances' between journals.

Electronic editions offer a flexible layout and structure for articles, new formats, and the possibility of including additional documentation as media enhancements (videos, etc.). Additional data can be now presented as supplementary material without additional cost. Guidelines have been developed for the preparation of 'raw data' for electronic publication. Electronic management systems also facilitate both the processes of peer review and publishing. Statistics on electronic papers (downloads and citation metrics) are offered for the interest of readers and researchers.

Finally, in this Globalized electronic world English represents the *lingua franca* of science. Therefore, in the digital era efforts should be made to prevent tower-of-Babel phenomena. However, this may create unique challenges for non-English-speaking investigators and countries.

Open Access

The two main characteristics of Open Access (OA) publications are: (i) all published contents are freely accessible through the Internet; (ii) readers are given copyright permission as long as authors and publishers receive adequate attribution. This model requires major changes from the traditional subscription-based model. Open access shifts the financing of publication from readers to authors by means of article-processing fees. In the early 1990s, pioneer OA journals were founded by investigators based on voluntary work and hosted in individual or university servers. Thereafter, many established journals made their articles OA when they implemented their digital editions. This was especially the case for journals of medical societies and in non-English-speaking countries in an attempt to increase their readership and impact. In the last decade, many formal OA journals have flourished. Open access has two major pathways: 'gold' OA (via direct publishing) and 'green' OA (traditional publication in subscription-based journals with parallel open posting of the final manuscript on the web). Gold OA is delivered by journals, whereas green OA is delivered by repositories. The health of this model can be demonstrated by data showing the steady growth of papers published in OA journals and also in the number of OA journals.

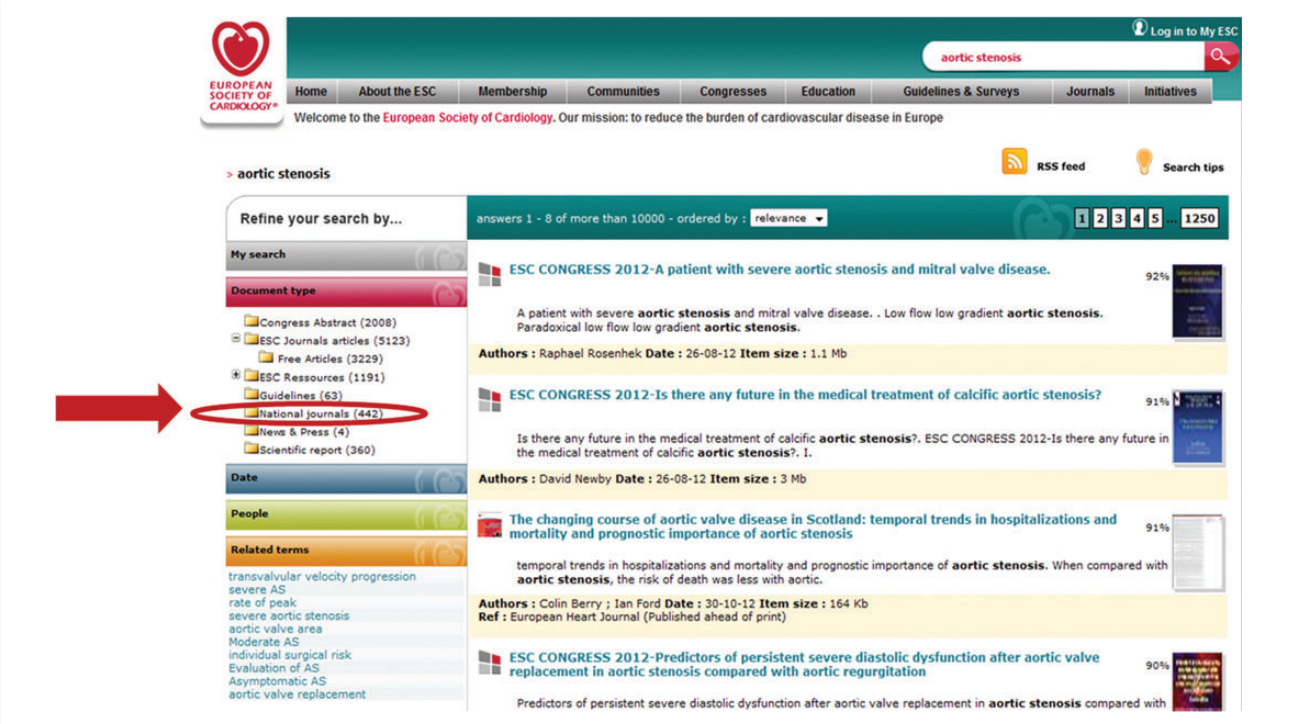

Figure 1 Search Results page with relevant information of documents found. On the left, there is a toolbar with a filtering system to refine the search.

Science benefits from OA as it accelerates dissemination of research findings. Open access initiatives increase diffusion of content, citations and eventually may increase the Impact Factor of the corresponding journals. Interestingly, research funding bodies are becoming increasingly favourable to OA. Many consider it unethical to use research grants from government and not allow the scientific community to have free access to the results of the study. Most countries are currently taking further actions. Researchers are compelled to make their work publicly available in repositories (green road) within 12 months of publication. Other funding bodies directly suggest the use of a gold road. A new OA policy was recently announced by the European Union that recommended OA policies for all member states.

The search engine on the European Society of Cardiology website

In the last decade, the amount of documents and educational material available on ESC websites has increased exponentially. Therefore, the ESC decided to provide a better search experience for visitors. The ESC search engine uses 'semantic analysis' to provide the best results. The search engine project has four goals: (i) to provide a single entry point to multiple data sources (slides, scientific reports, guidelines, abstracts, clinical cases, news, and articles from ESC journals); (ii) to treat requests expressed in natural language; (iii) to facilitate content location and access; (iv) to find content by topic or person. In 2008, the ESC Board decided to support the development of a semantic search engine able to explore the ESC Central website and the websites of the six ESC Associations. This engine is also looking into the ESC journals' family where it is possible to obtain results from >30 000 papers. This tool has had major success, already being the second most visited page of the ESC website.

Now, it is extremely easy to obtain information by just typing in the keywords on the top right-hand side search box on the home page screen **http://www.escardio.org**. The search result is a list of documents addressing that specific topic (*Figure 1*).

This results page contains a lot of information and functions. Within the document preview, you can see how the document looks (*Figure 1* righ-side icon) and its relevance score. Its origin can be easily identified from a small institutional logo and a padlock symbol shows when a document is behind a log-in. The search can be further refined by using filters located in the toolbar on the left. For instance, during a Congress, the user can filter for what is' new since the previous day or only the results where a person is cited. Finally, if the same term is searched on a regular basis, an RSS feed can be subscribed to, to provide regular updates on what is' new in the field.

This project is already mature and the ESC Board supported the launch of a new phase involving the NSCJs. The ESC Editors' Network (*Figure 2*) decided to contact those NSCJs that are already published in an electronic format and in English. This new tool is already implemented and now the user gets two results: one from the ESC documents, and a second from the NSCJs. In a preliminary 'pilot' phase five NSCJs were added to the search results. Today, all NSCJs are welcome to join this project. This initiative aims to improve the visibility of the NSCJs by increasing their readership and their level of reference in other international journals. There is no doubt that this tool will

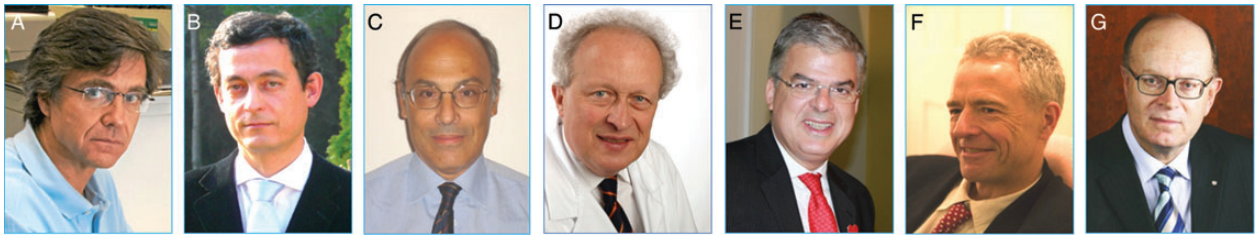

Figure 2 Nucleus members of the Editors' Network and Search Engine. (*A*) Fernando Alfonso MD, PhD, FESC (Chairman Editors' Network); (*B*) Lino Gonçalves MD, PhD, FESC (Chairman Search Engine; ESC Web page; (*C*) Giuseppe Ambrosio MD, PhD, FESC; (*D*) Hugo Ector MD, PhD, FESC (Editor-in-Chief, Acta Cardiologica); (*E*) Fausto J. Pinto MD, PhD, FESC (Editor-in-Chief, Revista Portuguesa de Cardiología, President Elect ESC); (*F*) Adam Timmis MD, PhD, FESC (Editor-in-Chief, Heart); (*G*) Panos Vardas MD, PhD, FESC (Editor-in-Chief, Hellenic Journal of Cardiology, President ESC); on behalf of the Editors Network ESC Task Force.

strengthen even further the bonds between the ESC Central and the National Cardiac Societies, and that European cardiovascular science will become more visible and readily accessible from any place in the world.

This is an abridged version of a joint simultaneous publication initiative involving all interested National Society Cardiovascular Journals of the European Society of Cardiology.

Fernando Alfonso[1,2], Giuseppe Ambrosio[1], Hugo Ector[1], Lino Gonçalves[3], Fausto Pinto[1], Adam Timmis[1] and Panos Vardas[1], on behalf of the Editors' Network European Society of Cardiology Task Force*

[1]Nucleus Members Editors' Network of the European, Society of Cardiology

[2]ESC Editors' Network Task Force Chair

[3]ESC Search Engine Task Force Chair

**Corresponding author. Email: falf@hotmail.com*

Colin Baigent, new International Associate Editor for *European Heart Journal*

Prof. Colin Baigent BM BCh FRCP, from the Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU) at the University of Oxford, has joined the European Heart Journal as an International Associate Editor. His main interest is in cardiovascular epidemiology, and most particularly the design, conduct, and application of large-scale randomized trials in cardiovascular disease. He has coordinated some of the world's largest collaborative meta-analyses of randomized trials, typically with individual participant data, resulting in landmark papers that have helped determine the effects of aspirin (and other antiplatelet drugs), fibrinolytic therapy, and statins in different types of patients. Most recently, his group's work on the cardiovascular hazards of non-steroidal anti-inflammatory drugs led to changes in the European Medicines Agency's guidance on the use of high-dose diclofenac in patients at high risk of cardiac disease.

His group has also contributed to a better understanding of cardiovascular disease in patients with renal impairment through the Study of Heart and Renal Protection (SHARP). This investigator-led randomized trial is the largest ever in patients with moderate-to-severe chronic kidney disease (CKD), recruiting 9438 patients in nearly 400 hospitals in 18 countries. The results showed that lowering cholesterol with the combination of simvastatin 20 mg and ezetimibe 10 mg daily reduced the risk of cardiovascular disease in patients with CKD, chiefly by reducing atherosclerotic events, but did not reduce the rate of loss of glomerular filtration rate among the 6000 patients who were not receiving maintenance dialysis treatment at baseline. This benefit was achieved without any increased risk of adverse effects.

The results confirmed that raised LDL cholesterol is a cause of atherosclerosis in patients with CKD, even though most do not have hypercholesterolaemia, and has led to their classification as 'high risk' in most treatment guidelines and, as a consequence, much wider use of LDL-lowering therapy among them.

Colin Baigent is interested to act as an Associate Editor for one to two papers per week dealing with epidemiology, kidney disease, and trials analysis.

European Society of Cardiology Quiz at European Society of Cardiology Congress 2013 Amsterdam

Defending champions Zurich led all the way to be overtaken at the last minute by Moscow on Sunday 1 September 2013

The European Society of Cardiology (ESC) Quiz was introduced by Pepe Zamorano as a new feature within the programme of the ESC Annual Congress 2012 in Munich. Three medical centres competed, the cardiology departments of Padua, Vienna, and Zurich. Zurich emerged victorious and was invited to participate against Moscow and Rome in Amsterdam, 2013.

The Quiz is a learning and educational experience based on the ESC Guidelines. It was designed with help from Juan Luis Gutierrez (Ludwig Maximilian University, Munich) and the enormous help of the ESC staff. Keith Fox as Congress chair placed it in the Focus lounge, showing its importance.

It is a competition between teams from three European Hospitals. They all receive clinical cardiology questions with patient histories, videos, and ECG as well as lab results from around Europe. The answers are based on the current ESC Guidelines with two 'Judges' giving the verdicts. There is a 'Joker' available for help: the audience can be asked for answers and thereby participate.

In addition there is a poisoned question that each team can use at any time.

All answers require an explanation and in case of disagreement with the Judge's verdict (answers), an appeal can be made to the Supreme Court, composed of ESC leaders in their field of cardiology. In 2013 they were:

Alec Vahanian left, Patrizio Lancelloti centre, Carlo Di Mario right

To show that there is life beyond cardiology, there is also a cultural question in the game. Each team asks a question involving their own country to the opponents. This year Moscow chose a question on music composers, Rome about the Coliseum, and Zurich about cheeses.

Teams consist of one Field Marshal, a senior professor, one renowned key opinion leader, two senior cardiologists as Captains and two junior consultants as Cadets.

The defending champions representing Zurich University Hospital, Zurich, Switzerland:

- Dr Oliver Gämperli
- Dr Matthias Greutmann
- Prof. Thomas F Lüscher
- Prof. Franck Ruschitzka
- Dr Jan Steffel
- Prof. Felix C. Tanner

Champions ESC Cardiology Quiz 2012

The other teams

(1) Representing the Bakulev Scientific Centre for Cardiac Surgery, Moscow, Russia:
   - Miss Victoria Buziashvili
   - Prof. Victoria Ioshina
   - Dr Dzhamshed Kamardinov
   - Dr Maxim Mamalyga
   - Prof. Simon Matskeplishvili

(2) Representing San Giovanni-Addolorata Hospital, Rome, Italy:
   - Dr Luca Di Vito
   - Dr Laura Gatto
   - Dr Fabrizio Imola
   - Dr Francesco Prati

All teams performed well, showing knowledge and expertise. It is not easy to produce a quick answer in front of colleagues on the stage, with the nervousness that exists. All teams used the 'Joker' for assistance, some of them several times. Zurich were ahead up to the last question when the Russian Team led by Simon Matskeplishvili scored with a correct answer. It was an interesting and lively event until the end of the game, with Zurich losing their title by a minimal difference.

The Quiz is science and fun combined. It is a learning experience by patient presentation, based on the ESC Guidelines, and a novel way to educate.

The organizers look forward to seeing the Russian champions defending their title in Barcelona 2014.

Andros Tofield

People's corner new appointment: Francesco Cosentino

Prof. Francesco Cosentino MD FRCP FESC Rome and Zurich receives nomination for chair of Cardiovascular Medicine at the Karolinska Institute, Stockholm

Prof. Francesco Cosentino, born in Rome, Italy, studied medicine there at the University 'La Sapienza,' continuing with his postgraduate training in Internal Medicine and Cardiovascular Diseases. He later moved to the Mayo Clinic, USA, where from 1991 to 1994 he worked with Prof. Zvonimir Katusic in cardiovascular research in the regulation of vascular tone.

In 1995, he moved to the cardiovascular research unit at Inselspital in Bern, Switzerland and returned to his hometown in 1996. Simultaneously, he completed his PhD in Biomedical Sciences, Vascular Pharmacology at the Mayo Graduate School.

He became assistant professor and later associate professor of Cardiology at Sant'Andrea Hospital, University 'La Sapienza' in Rome. Ever since, he has spent part of his time in cardiovascular research at the University Hospital Zurich, leading an international team focusing on the effects of glucose on endothelium and vascular function. In 2007 he had a sabbatical in the cardiac cath lab, and then in 2010 became Titular Professor in Zurich.

His recent work has focused on the molecular mechanisms of diabetic vascular disease and, in particular, the effects of high glucose on endothelial function. In landmark studies, he provided novel insights regarding the role of PKC-β intracellular signalling in hyperglycaemia-

related vascular dysfunction and inflammation. The results are relevant to understanding the intracellular signalling associated with pathological hyperadhesiveness of the arterial endothelium.

He has demonstrated that high glucose activates the mitochondrial adaptor protein $p66^{Shc}$, which causes endothelial dysfunction. Activation of this adaptor protein persists after glucose normalization and may explain the lack of efficacy of many therapeutic interventions to reverse diabetic vascular disease. He recently described an intricate molecular mechanism involving the mitochondrial $p66^{Shc}$, which may explain why, in recent trials, vascular complications of diabetes do not improve with intensive control of risk factors.

Prof. Cosentino strongly believes that the removal of epigenetic tags may be the most promising option to dampen oxidative stress and vascular inflammation, thus preventing cardiovascular complications in diabetes.

He has published in *the Proceedings of the National Academy of Science,* the *Journal of Clinical Investigation*, *Circulation* and *Circulation Research,* and the *European Heart Journal*.

Francesco Cosentino is a member of *European Society of Cardiology (ESC)* guideline writing committee on 'Diabetes, Prediabetes and Cardiovascular Diseases' and an *ESC* Board Councillor.

Since 2009 he has been an Associate Editor of *European Heart Journal*.

Clinical trials: how to get closer to the right answer with less effort

Some clinical trialists are finding it harder than ever to deliver meaningful results, but regulatory bodies are beginning to get back to essentials, while sloppy—and especially fraudulent—investigators will find life more difficult, reports Barry Shurlock PhD, in conversation with Dr Martin Landray PhD, FRCP

Even in the age of evidence-based medicine, a physician faced by a patient almost always has to make a decision based on insufficient information. An engineer faced by a crumbling bridge may be in a similar situation, but at least there is a model on which precise analysis can be based. Physicists are even more fortunate, and can expect experiments to get very close to 'absolute truth'. But physicians must be content with having to deal with extremely complex and inadequate models (not for nothing is the word 'cartoon' often used!) for which the concept of 'absolute truth' is meaningless. Moreover, the physician is often more interested in what to do in a given situation, rather than refining 'the model'.

These matters have interested the editors of *European Heart Journal (EHJ)* recently, resulting in the setting up of an Ethics Review Broad to tackle allegations of fraud and an article on the 'grey zone of truth' with which cardiologists and others often have to deal. Both issues impinge on the conduct of clinical trials, which is currently evolving rapidly. One of those with a special interest in the process is Dr Martin Landray PhD, FRCP, Reader in Epidemiology and Honorary Consultant Physician at the Clinical Trial Service Unit (CTSU) of the University of Oxford, Oxford, UK. As well as holding a cardiology clinic and running major trials, he is a member of the steering committee of the Clinical Trials Transformation Initiative (CTTI). Set up in the USA by Duke University and the FDA, this is a public–private initiative to 'identify practices that will increase the quality and efficiency of clinical trials' and involves >60 organizations. It seeks to move forward from practices that it regards as 'paper-based, slow, and costly'.

Dr Martin Landray

One of the consequences of the efforts of Dr Landray and his colleagues is the recent 7 August 2013 publication of new FDA guidelines for monitoring clinical trials,[1] which are intended to simplify and streamline a requirement that may represent as much as one-third of the cost of a trial—say, $200 million for a large cardiovascular study. He said: 'It represents a complete shift of thinking. The previous guidelines were issued in 1988, before email and the internet, and many of the requirements were simply not fit-for-purpose in today's era of computerised direct data entry systems and electronic medical records. Such moves are broadly in line with the way studies are currently being conducted at the

CTSU, which evolved from the ground-breaking International Study of Infarct Survival trials of Richard Peto, Peter Sleight, and Rory Collins. The CTSU's large, streamlined studies continue to provide important information for patient care. For example, the lack of efficacy and presence of significant safety issues (including bleeding and infection) reported recently in the Heart Protection Study-2 Treatment of HDL to Reduce the Incidence of Vascular Events study, led to the withdrawal of niacin/laropiprant and prompted the European Medicines Agency to initiate a review of all high-dose niacin products (which have been used for many decades)'.[2]

Many researchers believe that the increasingly complex requirements of regulatory bodies with regard to adjudication, monitoring, and source data verification have prospered on a poor understanding of the capacity of the randomized trial to detect differences between treatment and placebo arms, even though the data collected by individual investigators may contain substantial errors. Dr Landray said: 'There is a need to simplify many trial procedures. The randomised trial delivers the answer to the question you ask, but getting the design right is critical. It is important to identify aspects where errors would change the conclusions and where they would not. For example, a slightly imprecise definition [of a clinical endpoint] would introduce a little bit of 'noise' in the data and make it a bit harder to detect differences, but would not bias the conclusions towards one treatment arm or another. In any case the effect could be immaterial providing the study is suitably large. There is a huge potential to reduce the costs and complexities of randomised clinical trials. In the Heart Protection Study, for example, we found that the highly clinically and statistically beneficial effects of simvastatin would have been seen even if there had been no adjudication of events (let alone a minor change in the particular definition of some of one of the endpoints, such as myocardial infarction).

'Many other aspects of trial design can be simplified, resulting in massive reductions in cost and substantial benefits in terms of investigator effort and enthusiasm, and the number of studies that can be carried out. In studies such as THRIVE (Heart Protection Study-2 Treatment of HDL to Reduce the Incidence of Vascular Events) and SHARP (Study of Heart and Renal Protection), large-scale pre-identification of potential trial participants, the use of focussed and intuitive case report forms; and risk-based approaches to quality assurance, clinical oversight and study monitoring, combined to improve both efficiency and study quality. For example, central statistical approaches can be used to monitor study data in real-time, identify outliers and address potential issues, whether they relate to the performance of individuals (usually sloppiness rather than malicious fabrication), equipment or specific processes and processes. These "quality-by-design" methods allow the costs of large cardiovascular outcome trials to be reduced by 80–90% of the standard industry model.

'While the work of the CTTI has resulted in some significant improvements in the regulatory environment, there is still a long way to go.

In 2011, a report from the Academy of Medical Sciences[3] called for appropriate, proportionate, and coordinated research governance. There have been moves in this direction not only by the FDA but also by the European Medicines Agency who now recognize the importance of risk-based approaches to ensuring quality in the conduct of clinical trials.[4] The European Commission now recognizes that the EU 2001 Clinical Trials Directive has hindered rather than facilitated high-quality clinical research, and a new EU Regulation has now been drafted.[5] However, a major setback is the continued reference to ICH-GCP (International Conference on Harmonisation. Good Clinical Practice). Some might say that GCP is neither good, clinical nor practical. What is now needed is a new regulatory framework that instead of placing undue emphasis on details that are easy to check (e.g. study documentation) emphasizes those that really matter (e.g. processes for randomization, meaningful assessment of drug safety, and ascertainment of clinical endpoints)'.

References

1. **http://www.fda.gov/downloads/Drugs/.../Guidances/UCM269919.pdf**
2. **http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Nicotinic_acid/human_referral_prac_000020.jsp&mid=WC0b01ac05805c516f**
3. The Academy of Medical Sciences: A new pathway for the regulation and governance of health research. January 2011. ISBN No: 978-1-903401-31-6.
4. European Medicines Agency. Reflection paper on risk based quality management in clinical trials: EMA/INS/GCP/394194/2011. 4 August 2011 **http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/08/WC500110059.pdf**.
5. *Proposal for a Regulation of the European Parliament and of the Council on Clinical Trials on Medicinal Products for Human Use, and Repealing Directive 2001/20/EC.* Brussels: European Commission; 2012 **http://ec.europa.eu/health/files/clinicaltrials/2012_07/proposal/2012_07_proposal_en.pdf**.

CardioPulse contact: Andros Tofield, Managing Editor. Email: docandros@bluewin.ch