



Irish Heart Foundation

**National Cardiovascular and Stroke Research
Network**

Friday June 18th 2010

Croke Park Conference Centre, Dublin

Inaugural Conference Report

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Introduction

Irish Heart Foundation

Collaborative Cardiovascular and Stroke Research Network

Friday June 18 2010

The Irish Heart Foundation has held an inaugural conference at the Croke Park conference centre in Dublin to propose setting up the first Collaborative Cardiovascular and Stroke Research Network in Ireland.

The first meeting was attended by more than 100 people, drawn from a range of backgrounds including hospitals, industry, State agencies, health research organizations, the Department of Health and Children and from the academic sector.

The IHF has expressed its willingness to facilitate the development of a robust research network to provide for collaboration among key stakeholders. As part of the planning process, the Foundation sought views and feedback to the proposal from key groups involved in, or interested, in health research into cardiovascular disease and stroke to establish their needs and to consider how to take the first step.

A set of objectives and a core document were prepared reflecting the views expressed in initial discussions. The details were presented to the inaugural meeting as a source of guidance to five focus groups held on the day. In addition, a commitment to link and communicate with key stakeholders was expressed by the Irish Heart Foundation to the meeting and series of goals for the new Network were put to the meeting.

The initiative was widely welcomed by the speakers representing the State agencies – the Department of Health & Children, the HRB, the IMB, the IDA, and Enterprise Ireland. The meeting was also addressed by Ms Siobhan O’Daly from the Irish Heart Foundation who presented the Network objectives, strategy and structure. The CEO of the successful All Ireland Cancer Oncology Research Group (ICORG), Dr Brian Moulton, also addressed the inaugural meeting. He offered encouragement and a perspective from their 14 years’ experience on the benefits and issues involved in setting up a network.

Fragmentation of resources surfaced repeatedly as a problem for cardiovascular and stroke research, the opportunities for research and the potential gain for Ireland and benefits for patients emerged from the presentations of speaker after speaker.

The need to provide critical mass so that Ireland might become a hub for clinical research; the clear need for communication between all agencies and stakeholders was underlined time and time again.

Calls for harmonization of the current regulatory process were voiced through many of the presentations and discussions during the conference. Change is anticipated in a proposal for a single ethics committee application form. However such changes will await the Health Information Bill expected in September this year, the meeting was told.

June 18 2010, Croke Park Conference Centre, Dublin:

Dr Angie Brown, Medical Director, Irish Heart Foundation, welcomed the participants and thanked them all for attending what was the first national Cardiovascular and Stroke Research Network meeting.

She briefly explained why the Irish Heart Foundation set up the collaborative network. “As everyone would agree, research is fundamental to underpin our good clinical practice, develop new treatments and technologies, highlight deficiencies and provide a rationale for planning future healthcare,” she said.

‘It is becoming increasingly difficult to attract funding and clinical trials in the current economic climate, but at the Irish Heart Foundation we feel the Research Network will be able to provide a platform to overcome many of these difficulties and, hopefully, improve communication’.

The aim is to foster an exchange of ideas and collaboration, to optimise opportunities using the infrastructure already in place, as well as the very high caliber clinical research and strong industry already present in this country. It is intended to enhance the profile of Ireland as an attractive location for doing research

She requested feedback and input so they can determine how they can best support the needs of everyone who is going to be involved. She voiced her thanks to Siobhan O’Daly who had put so much hard work into the Network for the Foundation over recent months.

**Mr. Jim Breslin, Chairman, Health Research Group and Assistant Secretary,
Department of Health & Children**

“The Health Research Group supporting research on a national level”

A new Ethics Committee framework is to be outlined in the Health Information Bill expected to be published in the Autumn this year by the Minister for Health & Children and will provide for multi-site ethical approval for non clinical trials, according to Mr. Jim Breslin, Assistant Secretary at the Department and chairman of the Health Research Group.

The Bill will also establish the Health Information and Quality Authority (HIQA) as the supervisory and support authority for ethics committees; and it will have a role in approving such committees, he told the IHF inaugural conference of the collaborative cardiovascular and stroke research network.

We would see this as a lever for streamlining what is an acknowledged difficulty - trying to get studies approved in multiple sites, he said. In parallel, regulations under the EU directive on clinical trials will be revised to appoint HIQA as the supervisory authority for recognized research ethics committees overseeing clinical trials.

These developments will mean that multi site approval will be available for both clinical trial and non-clinical trial research studies and HIQA will supervise a streamlined research ethics committee review process encompassing both areas.

Mr. Breslin is chairman of the Health Research Group, which includes the main statutory bodies involved in health research in Ireland: relevant Government Departments (e.g. Education & Skills, Enterprise & Innovation and Agriculture & Food), Health Research Board, Science Foundation Ireland, the IDA, Enterprise Ireland and the Higher Education Authority (HEA). In his address to the inaugural meeting, he outlined the measures set out in the “Action Plan for Health Research 2009 – 2013” and the progress to date.

An estimated €200 million of public money goes into health research funding through a range of groups such as HRB, SFI and the HEA. One of the features openly acknowledged in the Action Plan is the fragmentation within the Irish health research

system which starts at funding level. While we have excellent internationally renowned researchers and activity, we don't have the cohesion we need in the research system, he said. This is a significant weakness in participating in the internationally competitive health research arena.

A vibrant health research system is a key part of a high performing health system. Concerns over affordability in the health services and a role for research in trying to move us towards improved quality and, address issues of cost, grew over the months while the Action Plan was being prepared. The commitment in the Action Plan for more internationally linked clinical trials networks recognises the improved patient outcomes possible through research-intensive health service delivery.

The Action Plan also recognizes that health research is a major competitive advantage and that we are trying to move up towards a higher value, more knowledge based economy. There is a focus on commercialisation and industry partnerships in the Action Plan. Ireland has put a high store on competing in biopharma and medical devices and we need a strong health research system to move beyond the manufacturing of existing products to development of the next generation technologies.

Aiming for concrete actions which build on the vision set out in previous health research strategies the Action Plan has set out clear timelines for delivery of each priority action. "We will be judged on delivery rather than the quality of our plans; that is as it should be", he said.

Bio banking has been identified as a critical and competitive piece of infrastructure and a team has been put in place under the Health Research Group to look at the approach to bio banking for the country. A standards based approach is being adopted to take an approach to bio banking which commands support from different stakeholders and funders. The agreed plan is due by the end of the year.

They want to see more clinicians and healthcare providers delivering high quality patient-focused research. They are also looking to more population health and health services research being undertaken.

Increasingly, he added, the HSE is trying to develop its own R & D capability to ensure it identifies the standard of care it wants to have delivered in particular areas. There is recognition of the benefits of research to patients. The importance of using health research to develop care pathways, based on international evidence, and building in a research component is highlighted in the Plan.

And he said there must be mechanisms in place to fully evaluate public investment in health research. They have published the Action Plan so that the wider community can hold Government and, more specifically, those identified as responsible for delivering the Action Plan accountable but also to generate support and to tap into the enthusiasm and passion for research and innovation amongst stakeholders.

The aim is to build a streamlined and predictable regulatory environment and to develop a health research system which, through research excellence and co ordination and accountability across diverse groups is cohesive and responsive to the needs of patients, the health service and the wider economy.

Finally, he welcomed the Irish Heart Foundation initiative in organising the inaugural conference on the proposed collaborative cardiovascular and stroke research. He hoped it would serve as preliminary to the successful establishment of a network of collaborative activity.

Dr Anne Cody, Head of Clinical and Applied Biomedical Research, Health Research Board.

“Enhancing Research through Network Development”

The Health Research Board is supportive of initiatives that will lessen the fragmentation of clinical research. Dr Anne Cody, Head of Clinical and Applied Biomedical Research at the HRB, told the inaugural conference of the National Cardiovascular & Stroke Research Network.

The importance of networks is increasingly recognised by all parties and, she added, many researchers and clinicians are realising that they cannot do the research they want to do on their own. However, the term ‘network’ is used to describe very different approaches, and the cardiovascular and stroke research network needs to define what type of network would be the most useful to its members. The financial resources available do not pre-determine the model.

While there is an underlying assumption that networks support multi site studies, Dr Cody outlined two basically different approaches adopted by existing research networks: either they are groups of clinicians, who exchange information, set priorities in their specialist areas, and (depending on resources) carry out clinical studies. Examples for this model include the Dublin Ageing Research Network (DARN), which facilitates research through advocacy, promoting best practice and sharing research outcomes; the Dublin Centre for Clinical Research (DCCR), which has some resources to carry out studies based on research priorities agreed by groups of clinicians, but where these clinicians will also jointly apply for further competitive funding; and the All Island Clinical Oncology Research Group (ICORG) - a large clinical trials group with significant resources to carry out trials across 11 hospitals and a central office in Dublin with about 100 staff.

The second model is based on supporting clinicians through expertise in various aspects of clinical research design, regulation and execution. Examples of this model include the Irish Clinical Research Infrastructure Network (ICRIN), which drove the development of the common application form for research ethics committees - a very useful and practical step facilitating research across all specialties. Other networks carry out clinical studies on behalf of clinicians. She pointed to the National Institute for Health Research Clinical Research Network Coordinating Centre in the UK

(NIHR CRN CC) which offers supports around data management, pharmacovigilance or study monitoring. The European Clinical Research Infrastructures Network (ECRIN) is looking to provide similar services on a European basis in the near future, and coordinates information on clinical research in different country.

Dr Cody highlighted a range of measures such as better research governance in hospitals, strategic priorities, a research career framework, bio banking, a patient identifier, as well as the coherence of available expertise, as some of the issues which could help our national research efforts. She stressed the importance of lowering the barriers for clinicians to engage in research and making it easier to do good research. New legislation around more efficient ethics approval is expected in the autumn, she added.

The HRB has published its own strategic business plan 2010 - 2014 in conjunction with the Health Research Group Action Plan. Dr Cody told the meeting the HRB funding strategy has two goals

1. To drive the development of an excellent clinical and applied biomedical research within a coherent health research system
2. To build capacity for high quality population health sciences and health services research

A network might include one or both aspects.

Dr Cody outlined that the HRB will establish more clinical networks in targeted areas by introducing seed funding. At present the HRB funds various infrastructure initiatives supporting clinical research, such as ICORG, ICRIN, Clinical Research Facilities (CRFs) in Dublin, Galway and Cork, and the HRB Centre for Support and Training in Analysis and Research (CSTAR). They also fund through projects and programmes.

Dr Cody also told the Croke Park meeting a number of elements necessary for a functioning clinical research system are in place right now, including infrastructures funded by the HRB and others; a competent authority and research ethics committees.

There has been a lot of talk about a one-stop-shop which could facilitate academic and clinical researchers through provision of regulatory expertise, IT, statistics, data managers, training and other knowledge and capacity. The HRB aims to put the support for clinical research on a more coordinated and firmer footing. Dr

Cody queried what form such support would have and exactly what remit would it have?

There is quite a breadth of expertise in carrying out research here, but a lot is scattered and the level of expertise varies in the different pockets. The next challenge for the HRB will be to figure out the best way of connecting the various pieces already in place, to build on existing expertise in the most effective and cost efficient way.

Ms Siobhan O’Daly, Research Development Manager, Irish Heart Foundation.

“The Research Network: objectives, Strategy and Structure”

The days of individual investigators looking for research grants and being supported are diminishing, Ms Siobhan O’Daly, Irish Heart Foundation, told the inaugural Collaborative Cardiovascular and Stroke Research Network conference.

Funding is increasingly competitive, especially in these times of fiscal constraint. More and more funding agencies are moving towards supporting research activities engaged in collaborative networks, she told the conference.

Underlining the trend, she referred to the current Framework 7 (FP7) call out to fund clinical trials in the area of cardiovascular and stroke. Proposals are invited for investigator driven clinical trials for cardiovascular disease and stroke management and for biomarkers in the prevention and management of cardiovascular disease and stroke, one of the mandatory stipulations is that applicants are operating as part of a European consortium

Ms O’Daly set out the eight objectives proposed for the Research Network. Based on initial discussions and feedback, she advised participants that a core document had been prepared reflecting the views expressed in initial discussions. She highlighted that the network development is a dynamic process; stakeholder feedback from the conference would provide the leverage to develop a truly workable Network strategy. In her address, she urged all stakeholders to identify what their needs are in relation to the proposed Research Network.

One of the main objectives for the new network, outlined by the Irish Heart Foundation document, is to establish Ireland as a globally competitive country for conducting high level research. In its most simplistic terms, at this initial stage, the Network is described as a group structure defined by formal agreements between clinicians, scientists, industry and key stakeholders, committed to collaborating towards the same objectives, goals and quality standards in the area of cardiovascular and stroke research.

The aim is to facilitate collaboration; to dismantle the walls between clinical, academia and industry to stimulate creativity and innovation and to strengthen research outputs. Through the organizational structure of the Network, it is proposed that members would be enabled to meet and collaborate on an ongoing basis;

stimulating dialogue and debate, identify research priorities ultimately leading to engagement in clinical research activity.

In the areas of basic and translational research, they want to remove the barriers to multidisciplinary collaboration, optimizing partnership between basic and clinical scientists in institutions, developing an innovative framework facilitating increased translation to health and economic benefit.

As many are aware, she said Ireland is not considered to be an optimal place to conduct industry led clinical research. The pharmaceutical industry has described Ireland as a non core country to conduct clinical trials citing the barriers to participation as; high costs, fragmentation and lack of predictability. Ireland is a leading country in the manufacture and export of medical medical devices, however, due to key barriers our engagement in clinical investigations very poor. The strong industrial presence presents opportunities. The centralized Network would act as a central point of contact to engage with industry. It would lend coherence to a complex environment and through meaningful engagement with key stakeholders, work to overcome the obstacles ultimately developing a research enabled environment. The Network would facilitate industry with access for early engagement at protocol development and study start up which would enhance investigator attainment of target recruitment.

The network would enable multicentre, investigator driven clinical research initiatives, whereby links with the research infrastructure supports could be maximized. She acknowledged the barriers to progress include the lack of a national disease registry in Cardiovascular disease and Stroke and the complex EC application process. The Department of Health and Children and HIQA are looking at changes in relation to the ethics committee submission process – through the Health Information Bill - for investigator driven, non EU directive covered, clinical research activity. It is envisaged that the proposed delivery of a single ethics application form will enhance the application process. Nevertheless, the present system requires separate applications to each of the relevant ethics committees. “We hope we might be able to support and direct you in this area,” said Siobhan O’Daly. The cost of health care delivery is the perennial topic of concern, she stated that the introduction of health technology assessment to assess clinical and cost-effectiveness of medicines, devices, diagnostics, and services across the health system, to ensure optimisation of resources

and to maximise patient outcomes will become an essential and significant feature of future research initiatives.

The setting up of the network is proposed to ensure equity of access for patients to clinical research initiatives throughout Ireland. Collaboration with patient groups and a forum to educate and inform the patient population, and the general public, of the benefits of clinical research and participation would be provided through the Network.

The development of research alliances both nationally and internationally, given the potential access to funding, is another objective proposed for the Network. She stressed the importance of developing alliances within Ireland with primary health care providers to ensure research needs, in pre hospital and post hospital settings, are met. There is a need to interact with other research networks where there is potential overlap of research objectives.

The commitment from the Irish Heart Foundation, according to Siobhan O'Daly is to link, communicate and inform. They aim to optimize communication between stakeholders, streamline administrative and management aspects of research collaboration through the provision of project management support for multicentre project delivery. The development of a web site is proposed, the circulation of a quarterly newsletter covering updates, news and information on research activity, as well as periodic bulletins highlighting funding calls are also proposed to provide a platform to communicate and inform the Network and its stakeholders.

The Network will organize meetings, develop international network alliances, provide funding updates and develop stakeholder communications. What they ask from stakeholders is feedback, engaging with research sub committees, support for the web site in terms of biography of researchers, updates on publications, research activity and special interest areas.

She concluded by saying they hope “to develop our governance and administration of the Network in a way that it meets your needs, that is open, accessible, responsive, transparent, professional and accountable to its members”.

**Dr Brian Moulton. CEO All Ireland Cooperative Oncology Research Group
(ICORG)**

“The benefits of the collaborative network”

The all Ireland Cooperative Research Group (ICORG) has succeeded for a number of reasons described by chief executive, Dr Brian Moulton – they are proactive, unified, data quality has been key and they have been able to provide a critical mass for clinical research

Addressing the collaborative cardiovascular and stroke research network, he gave examples of the issues they faced and benefits they gained since ICORG was set up in 1996, initially to get early access to Irish patients for latest cancer treatments. He offered encouragement stating, “The road you’re setting off on is very achievable”.

He advised there are a number of different elements needed even in a fledgling stage. Dr Moulton stressed the importance of infrastructure and pharmacovigilance. In house protocols are a key part and are very resource intensive; the network should provide quality and a training facility if possible.

Currently there are 44 ICORG trials and they started off clinical research focusing on breast cancer as they did not have enough resources to cover all the areas of research and, he added, it would have been a mistake to do so. They needed to create a reputation in one area, and similarly, he advised the cardiovascular and stroke research network may have to make difficult decision to concentrate on a small number of research areas initially.

They have seen the benefits of collaboration in cancer research; in 2009, 12 out of 14 locations on the island accrued 25 or more patients. For translational studies, eight out of 14 locations accrued 50 or more patients, which he said was quite impressive for a country of our size. Many of the clinical research accruals would have had a significant translational component; they have started a portfolio of translational trials and Dr Moulton feels this is an area gaining momentum and is less time consuming and less intensive from the point of view of resources and the central coordination role.

They reckon almost everyone interested in clinical research in cancer is involved with ICORG. Dr Moulton emphasized the importance of everybody on the island working together providing a critical mass and that is what makes the network attractive for clinical research.

While they have achieved critical mass, he said, most importantly the investigators within ICORG are very committed, the group culture is proactive, deadline driven, they provide high quality data and they are unified. In the end, actual accrual and commitment get the network noticed and the momentum going. As a result of their efforts, ICORG is regarded as a tier one country in terms of oncology research by many companies.

They started with four research nurses one central office co ordinator and with help of the national cancer charity grew to 30 people. The HRB got involved, as part of Good Friday agreement, and provided a planning grant, then moved on to a programme grant which was renewed last year.

In 2010, funding at research sites is around 85 per cent from the HRB. Funding at the central office is 50 per cent from the HRB, a contribution from the national cancer charity, plus funding from collaborative groups and the pharmaceutical industry.

The ICORG executive is a core of 23 members. There is a Principal investigator from every institution which is HRB funded - or hopes to be in the future.

Last year they had eight ICORG investigators present in-house industry studies at a leading oncology meeting. In time, he said the cardiovascular and stroke research network could achieve this.

In October 1996, 32 people came along to the inaugural meeting for ICORG. What happened was a number of US trained oncologists, used to working with a new cancer agent in the US, were frustrated on their return to Ireland to be told Ireland was down the list from a regulatory perspective. When it was suggested if they were involved in Phase III research there would be many opportunities to use the agent, they set up ICORG. In 2000, it became an all island organization and recently membership passed 404 people.

At the moment they have a trial, TAILORX, seeking to identify patients who may avoid chemotherapy on the basis of the genetic profile of their tumor. “We’re absolutely leading the way within ECOG (US Eastern Co-operative Oncology Group)...our 15 centers have enrolled close to 15 per cent of all of their accrual,” he said, “proof you can make an impact”.

Mr. Dave Shanahan Global Head of Life Sciences IDA

“Ireland’s Clinical Research Opportunity”,

Cardiovascular disease represents over half of healthcare spending annually and is a major contributor to healthcare cost escalation within international healthcare systems, according to Mr. Dave Shanahan, Global Head of Life Sciences at the IDA.

He outlined Ireland's potential to generate new jobs via better co-operation and collaboration in the clinical research sector.

There is a multiplicity of state-funded and state-supported bodies influencing healthcare development; all having separate interests and agenda including, the area of research.

He expressed concern that lack of collaboration and a shared set of simple goals and objectives have hindered and continue to hinder Ireland's ability to leverage its world leading invested life science base.

He said Ireland though small has unique potential via its academic and industrial base to marshal the large amount of resources already available and urged people to put aside institutional and organisational loyalty and communicate with one another to find the best collaborative platforms to develop Irish clinical and applied research.

Enhanced collaboration, communication and connection would better enable us to use existing funding in the system through HRB, /HSE operations, the Programme for Research in Third-Level Institutions (PRTL) and Framework 7 (FP7) and EU funds.

We should be harnessing these supports for relevant research designed to improve health delivery and outcomes thus providing Ireland inc. with value propositions we can sell to the world.

He told the inaugural conference for the proposed cardiovascular and stroke research network that the IDA sees tremendous opportunities to develop Ireland's healthcare



sector as an engine for economic renewal. Improved academic and industrial collaboration requires people to embrace new ways of working and a commitment to develop the environment in Irish healthcare where experimentation, prototyping, cross functional team working with Ireland's life science business sectors in Pharmaceuticals, Medical Devices and Information and Communications Technology becomes part of business as usual.

This needs to be a shared national commitment not just an IDA aspiration.

Dr Niall MacAleenan, Clinical Assessment Manager, Irish Medicines Board

“Current Legislation and Enhancing our Participation in Clinical Investigations”

The Irish Medicines Board (IMB) is the regulatory authority for medical devices in Ireland. The IMB earlier this year, following agreement with the Department of Health & Children, adopted a parallel review approach to applications received to conduct clinical investigations of medical devices in Ireland. This means that applications to conduct device research can be made to the IMB and the relevant ethics committee at the same time. Final opinion from the ethics committee is required prior to the completion of the IMB review. It is hoped that this will be of benefit in attracting device research to Ireland, Clinical Assessment Manager at the IMB, Dr Niall MacAleenan told the IHF inaugural Research Network conference.

Ireland is exceedingly well placed to become an international centre for medical device clinical investigations, however only a small amount of such research is currently being undertaken in Ireland. Dr. MacAleenan is hopeful that through initiatives like the IHF Research Network and collaboration between stakeholders that Ireland can attract more research. In his address, he talked exclusively about how the medical device system works, making a very clear distinction between clinical research relating to medical devices and medicinal products. “Clinical investigations” is the legislative term to describe medical device research - controlled under specific directives for medical devices, while the Clinical Trials Directive relates to pharmaceuticals and medicinal products.

Dr MacAleenan focused on the IMB approach - as the body with responsibility for the review and approval of applications to conduct clinical investigations for devices in Ireland. He stated that he is keen to facilitate research as much as is possible within the regulatory framework. He discussed potential ways the IMB can help collaborate with networks – such as the proposed research network - to facilitate the conducting of clinical research for devices in Ireland. He noted that currently there is limited communication between stakeholders, and stressed the benefits of collaboration which can help clarify clinical investigation applications, regulatory requirements and help demonstrate how the regulatory pathway is navigated. Collaboration between the IMB and the

clinical and technical expert community while allowing the IMB access to key expertise on specific device issues also helps ensure that the regulatory guidance associated with the device legislation is appropriate and actionable

He underlined the importance of making Ireland a hub for research of all types.

Bringing medical devices to market is quite different to the process for a medicinal product. The time to market for medical devices is generally much shorter and less costly than for medicinal products. Development of devices tends to be based on previous generations of devices rather than new devices so clinical data for existing devices is of relevance. There is also a focus placed on the ongoing performance and safety of the device when it is in clinical use, this post-market surveillance is considered on an ongoing basis to update and add to the technical and clinical dataset used to bring the device to market.

Medical devices are not authorised at a national level in Europe. Rather, when a device manufacturer has completed their pre-clinical and clinical testing for that device they present this technical document to a notified body (NB) for medical devices. The notified body assesses this data and if satisfactory allows the manufacturer to place a CE mark on their device. The CE mark allows for free trade across Europe without a specific national authorisation. The National Standards Authority of Ireland (NSAI) is the notified body in Ireland. Any appropriately qualified NB can assess a medical device and allow CE marking and thereby free access to the European market. The IMB and its European regulatory partners qualify NBs to assess specific device technologies and monitor their assessments and activities on an ongoing basis.

Conscious of a limited awareness of the current regulatory system for devices, the IMB has met with many ethics committees and is happy to meet with other stakeholders such as research networks or clinical conferences to clarify the regulatory system for devices.

Currently, only between five and 10 device investigations for pre-market devices (i.e. prior to CE marking) are conducted in Ireland per year. While this is similar to many other European Countries, when considered on a per capita basis, Ireland should be able to attract more research. Dr MacAleenan suggested that there are multiple reasons for this small amount of research including difficulty in recruiting adequate numbers of patients, identify relevant populations, identifying

clinical centres and perceived difficulties in achieving ethics and regulatory approval.

They are happy to help people through the regulatory process at any time in the development process for a device and are happy to correspond with sponsors, clinical investigators and manufacturers throughout the review process.

However he highlighted that the approach taken by regulatory agencies to medical device clinical investigations differs in the different European Member States. Some Member States require only an administrative notification and an ethics committee opinion to allow device investigations to process. Ireland, and now the majority of other European agencies conduct a clinical, technical and regulatory review of investigation applications to ensure that investigational devices do not pose a safety risk to patients and that the proposed investigations are scientifically robust. While the notification approach may allow manufacturers to start clinical investigations more quickly, the review approach taken by the IMB maximises the protection to Irish patients. At the same time it is critical to balance this with the need to further clinical development and allow Irish patients to access innovative therapies.

He strongly urges anyone proposing clinical investigation to go in and talk to the IMB, prior to submission of an investigation application. For a non-CE marked device, once the application is made, the clock starts for a 60 day review period. Applications should include the clinical investigation plan, the investigator's brochure, the informed consent and patient information documentation in addition to the technical data and pre-clinical testing and the risk management assessment that was conducted on the investigational device.

Clinical investigations of non-CE marked devices form part of the clinical dataset for a device which make up the clinical evaluation document. Specific clinical investigations are required for class III, active implantable medical devices (AIMD) and long term implantable devices – unless not conducting an investigation can be adequately justified e.g. substantial existing literature; clinical literature/ equivalence – must be of an equivalent device, and data must adequately address all relevant ER and indications for use. There is also an obligation on device manufacturers to conduct post market surveillance and to plan post-market clinical investigations to gather clinical data on ongoing clinical performance.

Applications to conduct device clinical investigations to the IMB are distributed to an internal review team. Frequently they go to external experts - a clinician with expertise in using that device or similar devices- and they commonly go to a technical expert who has experience with the particular materials, or designs, proposed for the device. Following satisfactory review, they make a recommendation to the management committee of the IMB. Sometimes, they do have to raise an objection on the basis that the risk outweighs the benefit or on the basis of that insufficient pre-clinical data has been presented, but they do work with sponsors to try to resolve any such issues.

Academic research devised by clinicians or academics when devices are used within professional and ethical boundaries generally does not require notification to IMB. When there is no direct commercial intent, according to Dr MacAleenan, but he said this was a borderline area.

“Ultimately, what we want to see is effective regulation and communication between all stakeholders to ensure safe and effective device trials are undertaken in Ireland,” he told the IHF conference.

Rosemary Durcan, Senior Commercialization Specialist, Enterprise Ireland.

“Building life science networks together”

Enterprise Ireland is open for business, according to Commercialization Specialist Rosemary Durcan, and there are a lot of new and innovative start ups in cardiovascular technologies and products where companies really want to work with the clinical community, and she told the inaugural conference “we are very glad to do anything we can”.

Enterprise Ireland has spent a lot of time building networks with academics and clinicians; their remit is to build indigenous industry and the life sciences sector is extremely important with 250 companies working here at present. A lot of their work is with pre start up companies and the strongest products result from a collaboration of academic business people and clinicians. This works because, when everyone has a say, it can be tailored to make a real difference in the market place. Trying to develop new products and get to the market on your own is risky, she cautioned. And now more and more people are beginning to use Irish based clinicians and they find, if they work with groups that take in professional advice, they can create large exports, brands and jobs. This network would be excellent to build on that, she added.

Concept is one thing; developing the product, putting clinical trials in place and carrying out clinical evaluations is not something industry can do on their own. She stressed that all stakeholders need to work together.

They have helped applied research and she told the meeting they have two funds available. One is the “Commercialization Fund” a 100 per cent funding for academic studies. Clinicians, or the clinical community, developing a product with a five to six year timeline can apply for grant aid of between €100,000-€300,000.

A second fund is the “Innovation partnership fund” at €100,000 plus. This funds a research body for work done for a company.

They have published a Life sciences directory of the very diverse companies working here. There are several types of diagnostic companies, finished medical device companies and a sub supply sector which supplies components into multinationals.

She stressed the collaborative research network would prove very useful in their work with the many sub supply companies that are looking to “up value” their products. However, as there is no supporting infrastructure they are doing this on a one to one basis. What they need is help from clinicians and the academic community in order to get the concepts right, to determine what the patient wants.

Exports from the indigenous sector are directly to the US, the UK and Europe. Nonetheless, Enterprise Ireland would like to see some of those products here, even to have a first reference site in our hospitals - and to export after that.

Exports are lower than multinationals at €608 million in 2009 but this innovative sector employs from two to several hundred. For the last four years exports have grown by 18 per cent. New product development is keeping employment stable in this sector at 5,300.

Enterprise Ireland operates a global life science team to provide commercialization, building business teams, to help identifying finance, growing and scaling up and market advisers updates as the product gets closer to launch.

The agency is developing international links with the Cleveland Clinic on the possibilities of clinical trials and has held initial discussions with the Mayo Clinic. Enterprise Ireland also works closely with private hospitals in Ireland to get them to export their services.

Rosemary Durcan also outlined one case study to the meeting involving an innovative medical device - called “EndoVe”- to treat gastrointestinal cancers which is being developed at UCC/Cork Cancer Research Centre.

Starting in 2005, they helped build a team of business people and clinicians around the product. They have worked closely with UCC to ensure the Intellectual Property is ring fenced and have been aligning private investors. They hope this technology will launch from UCC in December; it has IMB approval for a proof-of-concept trial and the first patient was treated recently. They hope is that it will go to market place in about 2 years’ time.

Medical devices

Constraints to clinical investigative activity and the way forward

- Summary of a large focus group discussion presented to the meeting by Fionnuala Gibbons, Irish Clinical Research Infrastructure Network (ICRIN) Clinical Trial Liaison Officer

Key points

- A centralized access point is needed to advise on where to go to get information and to provide details on the regulatory and ethics processes for multinationals coming to Ireland, or for SMEs, to facilitate the flow of clinical trials being undertaken in Ireland.
- The predictability of the time needed by ethics committees considering medical devices is an issue. The current approach needs to be changed. The timelines are known for an Investigational Medicinal Products (IMP), but an application for medical devices might come back in six weeks or in six months; this framework needs to be changed.
- A standardized system for contracts is needed. As an example, CIST have developed standardized templates on - “*How to do Clinical trials*” and these have been put in place for private hospitals. Currently, CIST has two very good clinical trials up and running where they are meeting the target numbers.
- *Time-to-Market* is a challenge for companies and, if they can get their product to market in a quicker timeframe by going through Germany, then they are going to bypass Ireland. This needs to change.
- There are a lot of opportunities to do clinical investigations and physicians want to meet with companies an earlier stage and more frequently, and;
- The mindset must change. Examples of positive experiences need to be highlighted to change the perception that clinical trials and medical devices cannot be carried out in Ireland. The focus group believed they can and that message needs to be communicated. There are opportunities here. But again we have to change the mindset and move this forward.

Enhancing partnerships between the health system, academia and industry

Defining needs and developing collaborative pathways

- Summary of a focus group discussion presented to the meeting by Ms Siobhan O'Daly, Research Development Manager, Irish Heart Foundation

Key points

A need for research nurses was identified; they are the main engine in facilitating and enabling research activity in hospitals

Options

- A potential for funding research nurses to be supported by the pharmaceutical sector or the HSE could be enabled through a strategic business plan which would detail strengths of innovation, and the strength of the research and potential outcome
- Development of a business plan to be provided by the Irish Heart Foundation - to support this initiative of going to the pharmaceutical industry and HSE.
- As a collaborative system this could encourage hospitals not currently engaged in research

Clinical Research Infrastructure.

The HRB has supported the development of significant infrastructure to support research, the group felt that there was not enough awareness of the facilities on available and believed that the IHF Network would be a supportive mechanism to

- Advertising of the role and services provided.

Objections were expressed to charges by CSTAR for statistical and methodological support; it was proposed that the IHF Network could perhaps provide a bursary to support PhD initiatives in obtaining CSTAR support.

IHF Network Support to Researchers

- a bursary by the IHF for researchers starting up costs in the initial stages should be considered, and an expert group could be provided to review studies and give support and advice to PhD students planning to carry out research
- it was clearly acknowledged that we have a pool of high caliber people engaging in research among cardiovascular and stroke consultants

Regulation

A number of issues were raised for pharmaceutical clinical trials with regards to the Irish Medicines Board (IMB) and the ethics committees

- The regulator has become involved in reviewing the Patient Information Leaflet while the group believed, according to the legislation, is the responsibility of the ethics committees.
- This has created issues for pharmaceutical companies in achieving timelines, as they are going to and from the regulator.
- No systematic review of applications exists when they go into the IMB. A departmental review with regulators creates delays with staggered issuing of queries
- this results in delays for study start up times
- it is hoped that meaningful dialogue on these issues can be achieved through Network to look at this matter further and provide solutions

Enhancing clinical research capacity

Optimizing relationships with research infrastructure to augment our research capabilities

Overcoming the issues that impede the flow of research

- *Summary of a focus group discussion presented to the meeting by Siobhan Gaynor, Senior Associate, Irish Clinical Research Infrastructure Network (ICRIN)*

Key points

- The key benefits of the proposed network were considered and highlighted including: the collective expertise of all different players, the need for the Network to capitalize on collective expertise from a clinical, nursing, SME and national perspective, at all the different hospitals
- A Network would offer one voice with cardiovascular and stroke healthcare professionals working as a group
- One representative voice would have a stronger influence on funding and, informed by strong research, could have an impact on healthcare strategy, health priorities and delivery of services, particularly in the stroke area.
- One group would have access to the same information - in the focus group they discovered multiple examples of both private and public systems, including data and registry collection systems, that were unknown to all the members of the group. Gaining access to what is out there, as well as inputting into the research, was described as an important benefit

What should a Network provide?

- Data

- in the short term a network should provide epidemiological data to inform groups on collaborative research possibilities and provide a voice from 'Ireland Cardiovascular Inc' to the world
- research should inform how the whole platform of current developments could be utilized, in particular the use of telemedicine and connected health and looking at acute stroke care; arising from the recently published *Changing Cardiovascular Health: National Cardiovascular Health policy 2010-2019*

- In the long term: the development of disease registries and medical device registries.
- healthcare delivery needs to be informed by data from the Irish setting and not just through international research
- primary care needs to be involved from the outset
- it should be ensured that non teaching hospitals outside the Dublin area have the same voice and the same level of involvement
- the Institutes of Technology should be involved as academic partners particularly in relation to medical device innovations – not just the universities

- Issues identified:

- lack of incentive for the Network to develop innovations due to the lack of a national policy and problems around intellectual property (IP)
- a general lack of recognition for the value of research
- this network should move forward the issue of research strategies for hospitals
- As there are no research strategies in hospitals and research is not seen as a core activity - it is cut in times of fiscal restraint. Typically research nurses posts are cut
- there is a need for protected time for research
- the need for collaboration was stressed as the fragmentation of clinical research capacities is a major issue, and;
- ‘How do we mandate that national priorities should be placed above institutional priorities?’ Something to be considered as a nation

Network constitution and structure

To develop structures for the network. What enhances collaboration for the stakeholder?

- Summary of a focus group discussion presented to the meeting by Dr Brian Moulton, CEO, All Ireland Cooperative Oncology Research Group (ICORG)

Key points

- A broad and inclusive Executive for the Network– which may become smaller in time - was one of the principles agreed.
- the decision process for new trials should be carried out through a sub group structure and the exact composition of the sub groups to be agreed at a later stage, but;
- The principle was agreed that sub group structure would include all those deemed to be interested in this area, and should play to their strengths and recognize all abilities.
- Building up *Central Office* type expertise may be the best way forward for the Network.
 - Project management supports
- The challenge presented by essential paperwork was widely acknowledged.
- The group advised the Network should build on recent successes and were very positive about the opportunities that would become available for the proposed Network once set up and running.

Translational studies

- *Summary of a focus group discussion presented to the meeting by Dr Robert O' Connor, Senior Programme Leader, Translational Cancer Pharmacology, DCU*

Key points

The group tried to identify some of the current issues and make suggestions focused on potential solutions

Network -

- The critical importance of the Research Network was identified. It was suggested all the contact details, and brief interests, of the participants at the inaugural conference should be circulated by the Irish Heart Foundation
- The proposed development of a website and web portal was felt to be a very useful as a method of directing people and of providing up to date details of available expertise; this would facilitate people to identify what they need.
- Regular meetings were recommended for the Network, including a large annual meeting, in addition to sub specialty meetings.
- A brief business plan with short term, medium and long term goals was recommended -

short term: identify some 'quick wins' - some outputs that can be carried out

medium term: identify funding and networks

longer term: bring in some patient metrics

Education -

- identify people who can provide mentorships
- of particular importance is the identification of leading researchers as well as selling their expertise in Ireland to funders, state agencies, and philanthropists
- make use of educational resources in the university and IT sector
- the development of courses was suggested but also the setting up mentorships within industry to take advantage of expertise through placements

Regulation -

- streamlining was considered necessary to overcome a number of regulatory hurdles in the area of translational research
- an effective structure is needed to open access to the professionalism available within the regulatory and ethical agencies, and to provide opportunities for the agencies to come together.
- protection of intellectual property (IP) is needed if industry is going to commit to further developments

Databases -

- where possible, schemes to allow sharing of information between different hospitals need to be identified; many are maintaining databases with no standardisation of information

Funding -

- come together to identify funding and it is important industry is involved at an early stage
- send out questionnaires to identify resources
- make better use of available funding, such as Framework 7 or EU funding
- state agencies might consider re focusing some of the funding and looking at practical outputs
- approaching industry collectively would be more successful, rather than as individuals
- it was strongly suggested IHF would put in some seed funding

Links –

- link into other international heart foundations, learning from they have what they have done, mistakes they have made and working on joint projects
- link with industry providing meetings on translational research activity
- make more use of state agencies providing a ‘one stop shop’ including the IDA or Enterprise Ireland

Conclusion:

Mr Michael O’Shea, Chief Executive, IHF.

Thanked those who attended, the guest speakers, the co-ordinators and those who chaired the focus groups for their energy and commitment.

He echoed thanks by Dr Brown to Siobhan O’Daly for her hard work on the Research Network initiative.

He also expressed his thanks to Tracy Egan, conference organizer and Ann O’Leary who is assisting on conference organization.

Online Directory

Quick links: agencies and reports mentioned at the inaugural conference proposing the establishment of a Collaborative Cardiovascular and Stroke Research Network. June 18th 2010 - Croke Park, Dublin

“Action Plan for Health Research 2009 – 2013”: Department of Health & Children.
http://www.dohc.ie/publications/pdf/action_plan_health_research.pdf

“Building Ireland’s Smart Economy” 2008. A framework for sustainable economic renewal 2009-2014.
http://www.taoiseach.gov.ie/attached_files/BuildingIrelandsSmartEconomy.pdf

“Changing Cardiovascular Health: National Cardiovascular Health Policy 2010 – 2019”: Department of Health & Children May 2010.
http://www.dohc.ie/publications/changing_cardiovascular_health.html

CIST: RCSI has established the Centre for Innovation in Surgical Technology (RCSI-CIST). For further information Derek Young at derekyoung@rcsi.ie
<http://www.rcsi.ie/index.jsp?nID=1544&pID=122>

CSTAR: The HRB Centre for Support and Training in Analysis and Research.
<http://www.cstar.ie/>

DARN: Dublin Ageing Research Network, a physician and psychiatry based research collaboration comprising geriatricians and old age psychiatrists based in Dublin’s medical schools. <http://www.medicine.tcd.ie/medical-gerontology/overview/darn.php>

DCCR: Dublin Centre for Clinical Research provides the infrastructure – the physical space, facilities and the expertise – needed to support patient focused clinical research studies across Dublin. <http://www.molecularmedicineireland.ie/page/g/s/45>

ECRIN: European Clinical Research Infrastructures Network for the support of trans-European clinical research projects. Currently includes 12 networks of clinical research centres (CRC) and clinical trial units (CTU), acting in any medical field in nine EU countries. <http://www.molecularmedicineireland.ie/page/g/t/25>

Enterprise Ireland: Commercialization Fund: €100,000 – €300,000. Innovation Partnership Programme: €100,000 to €200,000.
Contact: rosemary.durcan@enterprise-ireland.com

FP7 is the short name for the Seventh Framework Programme for Research and Technological Development. The EU's main instrument for funding research in Europe 2007-2013. The FP7 national support office: <http://www.fp7ireland.com/>



“Health Research Board Strategic Business Plan 2010 – 2014 (The Future of Irish Health Research)” 2009 .<http://www.hrb.ie>

ICORG: All Ireland Clinical Oncology Research Group, all island since 2000.
<http://www.icorg.ie/>

ICRIN: Irish Clinical Research Infrastructure Network - created under a Memorandum of Understanding between University College Dublin (UCD), The University of Dublin, Trinity College, Dublin (TCD), Royal College of Surgeons in Ireland (RCSI), University College Cork (UCC), The National University of Ireland, Galway (NUIG) and Dublin Molecular Medicine Centre (DMMC). Ireland’s representative within the European Clinical Research Infrastructures Network (ECRIN). ICRIN is supported by the Health Research Board (HRB) and the Health Services Executive (HSE).
<http://www.molecularmedicineireland.ie/page/g/s/44>

IMB: Irish Medicines Board: <http://www.imb.ie/>

IHF: Irish Heart Foundation.<http://www.irishheart.ie>

“Life sciences Directory” from Enterprise Ireland
http://www.biotechnologyireland.com/SITE/UPLOAD/DOCUMENT/Life_Sciences_Directory.pdf

MMI: Molecular Medicine Ireland set up by the NUIG, UCC, UCD, TCD and their associated academic hospitals. Research partnership to accelerate the translation of biomedical research into improved diagnostics and therapies for patients.
<http://www.molecularmedicineireland.ie/home>

NIHR CRN CC: National Institute for Health Research Clinical Research Network Coordinating Centre in the UK. <http://www.ukcrn.org.uk>

NSAI: National Standards Authority of Ireland, Notified body/CE mark. Certification recognized worldwide through a network of Mutual Recognition Agreements with other major certification bodies. <http://www.nsai.ie/>

PRTL: Programme for Research in Third-Level Institutions
<http://www.heai.ie/en/prtli>

“Towards Better Health – Achieving a Step Change in Health Research in Ireland” November 23 2006. Advisory Science Council - provides policy advice to the Irish Government on medium and long term science, technology and innovation (STI)
<http://www.sciencecouncil.ie/publication/ascSearch.jsp?yr=2006>