IRISH MEDICINES BOARD

news MEDICAL DEVICES LETTER

AUGUST 2011 Vol. 1 No. 32

IRISH MEDICINES BOARD, KEVIN O'MALLEY HOUSE, EARLSFORT CENTRE, EARLSFORT TERRACE, DUBLIN 2 TEL: 01 676 4971 FAX: 01 634 4033 EMAIL: MEDICALDEVICES@IMB.IE

# Letter from the Editor

*Welcome to the second edition of the medical devices newsletter for 2011.*

2011 continues to be another busy year for medical devices at the Irish Medicines Board (IMB) and in this edition of the newsletter, we feature articles on the recently published IMB safety notices relating to medicine feeders and the safe use of blood glucose monitoring systems. An update is also provided on recent changes to the EUDAMED medical device registration data requirements.

We are also pleased to feature an article from The Bone and Tissue Engineering Research Group of the Royal College of Surgeons in Ireland (RCSI), which provides an overview of tissue engineering and the research being undertaken by this multidisciplinary group in this emerging field.

Updates on the range of European meetings attended by the IMB are also provided.

As always, readers are encouraged to provide feedback, particularly in relation to articles that may be of interest, by contacting us at medicaldevices@imb.ie

## CONTENTS

# EUDAMED Medical Device Registration Data Requirements

*The Irish Medicines Board (IMB) has operated and maintained a medical device registration database since 2001 which captures data relating to Irish based medical device manufacturers and authorised representatives of Class I and custom-made medical devices, system or procedure packs and all classes of* in vitro *diagnostic medical devices (IVDs).*

Commission Decision 2010/227/EC, adopted on 19th April 2010, concerning the European Databank on Medical Devices (EUDAMED), came into effect on the 1st May 2011, which obliges Member States to capture, and upload, additional information to that which was previously required. It should be noted that only data generated from the 1st May 2011 will be affected by these changes; manufacturers may, however, amend any data existing prior to May 1st by submitting an amendment to the IMB.

In the case of general medical devices, registration with the IMB is required under Article 14 (1, 2) of Council Directive 93/42/EEC. There are no changes to the organisation details; they remain as per the current registration system i.e. name, role, contact details, etc. The changes brought about by Commission Decision 2010/227/EC relate to the device details which must be supplied to the Competent Authority. All medical device registrations as of 1st May 2011 must be accompanied by either the Global Medical Device Nomenclature (GMDN) or another internationally recognised nomenclature. Additionally, device registrations must also refer to either the generic name or the name/make of the device. The generic name refers to the generic name of the device as assigned by the manufacturer, whereas the name/make refers to the brand name (trademark) under which the medical device is marketed. With regard to system or procedure packs, the IMB will also be requesting that the classification of the device be supplied in the cases where the packs are CE marked as a device in their own right (i.e. in cases where the component devices have not already been individually CE marked). Data relating to custom-made medical devices are neither captured by, nor uploaded to, the EUDAMED system and as such, are not covered in this article.

As per Article 10 (1), (3) and (4) of 98/79/EC, IVDs must also be registered with the IMB where the manufacturer

or authorised representative is based within Ireland. As with general medical device registrations, IVD registrations made from 1st May 2011 must also be accompanied by either the GMDN or another internationally recognised nomenclature. In the case of Annex II List A, Annex II List B and self-test IVDs, both those which have been CE marked or are undergoing performance evaluation, either the name/make or model information must be provided, where the model refers to the reference of the device model as assigned by the manufacturer. In the case of general category IVDs, either the generic name or the name/make of the device must be provided. The most notable change following the implementation of EUDAMED is that the transitional provision in Article 10(6) of Directive 98/79/EC, which obliges IVD manufacturers to give notification to every Member State concerned by the placing on the market of devices, now ceases to apply. As such, in cases where a non-Irish based IVD manufacturer or authorised representative wishes to place an IVD device on the Irish market, the IMB does not require notification prior to doing so, provided that all relevant registration information has been uploaded to EUDAMED. However, if the manufacturer or authorised representative is aware that such information is not already present or in the process of being uploaded to the EUDAMED system, the IMB would be grateful if it could be provided on a voluntary basis.

All data contained on the EUDAMED system is accessible to both the national Competent Authorities and to the European Commission. This information is not publically available. As part of the IMB registration system redesign, a validation project concerning all registered details currently on the system has recently commenced. All registrants will be contacted shortly via post/email and asked to confirm their registered details. Details concerning the process of confirmation will be contained in that communication.

# Overview of Tissue Engineering

Prof. Fergal O'Brien, Dr. Tanya Levingstone, Dr. Ciara Murphy, Dr. Orlaith Brennan

*Everyday thousands of surgical procedures are performed to replace or repair tissue that has been damaged through disease or trauma.*

Current clinical approaches focus on the transplantation of tissue from one site to another in the same patient (autograft) or from one individual to another (allograft). Both techniques have associated disadvantages. Autografts are expensive to harvest and cause pain and donor site morbidity due to inflammation and hematoma formation. Allografts have limited availability and additional constraints relating to the risk of rejection and transfer of disease from donor to patient. The demand for new therapies has led to the emergence of the field of Tissue Engineering (TE), a term used interchangeably with regenerative medicine, which is an interdisciplinary area comprising different specialties such as medicine, materials science, cell biology, genomics and chemical engineering. TE offers a paradigm shift in medicine: rather than simply replace damaged tissues, it aims to regenerate the tissue through the use of biological substitutes that restore, maintain or improve tissue function.[1] Researchers have been developing tissue engineered constructs for the regeneration of practically every tissue and organ in the body.[2]

TE technologies are based on a biological triad which involve the successful interaction between three components: (1) the cells that create the tissue (2) the scaffold that holds the cells together to create the tissue's physical form and, (3) the biological signalling molecules, such as growth factors, that direct the cells to express the desired tissue phenotype. In selection of the cellular component of the triad it is essential to select cells that can facilitate matrix deposition and integration of the scaffold with host tissue *in vivo*. The choice of cells includes primary cells, cultured from explants of tissue, cells from an immortalised cell line, or stem cells. Stem cells, under appropriate conditions, can differentiate into different cell types such as osteoblasts, chondrocytes and adipocytes. Stem cells have shown significant potential as they have a higher proliferative capacity than cells from adult tissue (primary cultures) which gives them an advantage over these cell types. The current clinical standard involves autologous cells from patient's bone marrow, which are either directly implanted or cultured *in vitro* prior to implantation. However, the risk of complications following the bone marrow harvesting procedure has led to the search for alternative sources of stem cells that can demonstrate the potential for therapeutic use. Sources that have shown potential include peripheral blood, adipose tissue, umbilical cord blood and amniotic fluid-derived stem cells.

Cells derive a vast wealth of information from their environment. The microstructure, composition and mechanical cues provided by the scaffold influence cell behaviour. It is essential that the scaffold is biocompatible, biodegradable and has mechanical properties consistent with the anatomical site into which it is being implanted. Scaffold stiffness has also been shown to direct the differentiation lineage of stem cells.[3] Scaffold architecture is also of critical importance, with porosity, pore interconnectivity and pore size all influencing cellular infiltration, nutrient diffusion and ultimately the survival of cells.[4,5]

In addition to biomechanical signals, cellular behaviour is strongly influenced by biological and biochemical signals from the extracellular matrix. Scaffolds can therefore be used as delivery systems for growth factors, adhesion peptides and cytokines.[6] Another area of importance is the host immune response to implanted tissue engineered constructs. The incorporation of drugs, such as inflammatory inhibitors, into scaffolds in order to control the host response is another major area of research within the field and provides the opportunity for targeting drug delivery directly to diseased tissue to provided localised treatment.[7] Scaffolds have also shown potential for use as delivery systems for therapeutic genes.[8] The gene therapy approach utilises DNA encoding for therapeutic genes to potentially provide a more stable and effective approach to allow sustained and controlled release of therapeutic factors.

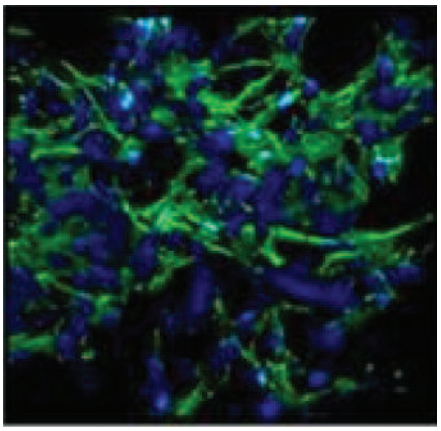

*Figure 1: Microvessels in a collagen-GAG scaffold*

Promoting vascularisation of scaffolds and tissue engineered constructs following implantation is a major challenge in the field of TE. Lack of vascularity leads to the problem of core degradation which is one of the primary causes of graft failure post-implantation. One approach currently under investigation by a small number of groups, including the group based at RCSI, is the development of a pre-vascularised construct that can support blood flow and thus improve oxygen and nutrient delivery throughout the tissue engineered construct (fig.1). Additionally, a range of bioreactor systems are being utilised in the culture of constructs pre-implantation to improve cell distribution, and to provide biophysical stimulation to increase levels of differentiation and matrix deposition within the scaffolds. Alternatively, developing scaffolds with embedded pro-angiogenic signals (such as growth factors or genes) might also provide a solution.

In the Royal College of Surgeons in Ireland, regenerative medicine is one of the key research pillars i.e. an area of strategic research importance within the College. The Bone and Tissue Engineering Research Group is headed by Prof. Fergal O'Brien and carries out

continued on following page

## Overview of Tissue Engineering

*continued from previous page*

research in areas including tissue engineering of bone, cartilage and cardiovascular tissues. Research is ongoing in the areas of biomaterial development, stem cell biology, drug delivery, gene therapy, mechanobiology and bioreactor development, translating to *in vivo* models. The group is truly multidisciplinary with physicists, material and life scientists, engineers and veterinary surgeons all working together. Of major importance are our links with the medical community and we typically have a number of surgical trainees carrying out research in our group at any time. At present there are over 40 researchers encompassing principal investigators, postdoctoral researchers, graduate and undergraduate students working in the group. The group maintains very much a translational focus and two recently patented technologies, *HydroxyColl*,[9] a bone repair technology, and *ChondroColl*,[10] a cartilage repair technology, are being commercialised through a spin-out campus company, which is focused on clinical translation of technologies developed in our lab. The group has numerous national and international collaborations, most significantly with the Centre for Bioengineering in Trinity College Dublin.


1. Langer, R., Acc Chem Res (2000) 33, 94.
2. Atala, A., Rejuvenatation Res (2004) 7, 15.
3. Engler, A.J., et al., Cell (2006) 126, 677.
4. Murphy, C.M., et al., Biomaterials (2010) 31, 461.
5. O'Brien, FJ., et al., Technol Health Care (2007) 15, 3.
6. Place, E.S., et al., Nat Mater (2009) 8, 457.
7. Huang, D., et al., J. Biomater Sci Polym Ed (2010) Jun 21.
8. Endo, M., et al., Tissue Eng (2006) 12, 489.
9. O'Brien, F.J., et al., W02008096334, (2008).
10. Gleeson, J.P, et al., WO 2010/084481, (2010).


# Medicine Feeders

*Medicine feeders, including spoons, droppers, syringes, cups and pacifiers/soothers, which are intended for use for administration of medicines, are classified as medical devices.*

Such devices can be categorised as:

(1) Medicine feeders with volumetric markings or specifications and
(2) Medicine feeders without volumetric markings or specifications.

Medicine feeders without volumetric markings or specifications are not intended to provide a measuring function or to accurately measure medicine doses.

For companies wishing to place medicine feeders on the Irish market, they must be in compliance with Medical Devices Directive 93/42/EEC and S.I. No. 252 of 1994, as amended. As such, these devices and their labelling are required to bear a CE mark. There are two categories of medicine feeders:

1. *Medicine feeders provided with volumetric markings/specifications*

   Medicine feeders with volumetric markings or specifications are classified as class I medical devices with a measuring function. Notified body assessment is required for the aspects of manufacture concerned with the conformity of the metrological requirements as outlined in the Medical Devices Directive 93/42/EEC and S.I. No. 252 of 1994, as amended. These devices are required to bear a four digit notified body number under the CE mark on the device and its packaging.

2. *Medicine feeders provided without volumetric markings/specifications*

   Medicine feeders without volumetric markings or specifications are classified as class I medical devices. These devices are not intended to provide a measuring function or to accurately measure medicine doses. These devices are also required to bear a CE mark on both the device and its packaging. However, according to Medical Devices Directive 93/42/EEC and S.I. No. 252 of 1994, as amended, there is no requirement for a notified body to review any aspect of these devices and as such, they will not bear a four digit notified body number.

The IMB has become aware of a number of non-compliant medicine feeders (including spoons, droppers, syringes, cups and pacifiers/soothers) that have been provided to pharmacy outlets, retail outlets and hospitals in Ireland. The non-conformances noted have varied from inadequacies in the labelling, to products that have not been assessed by a notified body. A number of customer communications regarding these non-conforming devices have already been issued by individual manufacturers/suppliers. Copies of these customer communications accompany the IMB Safety Notice SN2011(16) on medicine feeders on the IMB website www.imb.ie.

The IMB is advising **pharmacists, hospital personnel and retailers** to ensure their staff is made aware of IMB Safety Notice SN2011(16) on medicine feeders, to be aware of the differences between the above products and consider the intended purpose/accuracy of these products prior to use. In instances where a device is not supplied to the consumer with its original packaging/labelling, ensure that the use, accuracy, cleaning, etc. of the device is clearly outlined to the customer.

The IMB is advising **consumers** to ensure that they have confirmed with the pharmacist how a medicine should be administered before using it, particularly an oral liquid. It is important that consumers understand the dosage required and how best to measure the dose. Consumers with any concerns or questions should consult with their pharmacist or general practitioner.

Should you notice any further non compliant products on the Irish market, please contact the medical device vigilance and compliance team by email at vigilance@imb.ie or by telephone +353-1-6764971.

# Safe Use of Blood Glucose Monitoring Systems

*A new safety notice, SN2011(06), has been published on the IMB website, www.imb.ie, to highlight the risk of transmission of blood borne agents associated with the use of blood glucose monitoring systems.*

Blood glucose monitoring systems generally consist of a blood glucose meter, test strips, lancing device and control solution. These devices may be intended by the manufacturer to be used by a single patient for self-monitoring or by healthcare professionals for the monitoring of multiple patients.

Where a blood glucose meter is used for the monitoring of multiple patients, it is crucial to ensure that the device used is intended by the manufacturer to be used by healthcare professionals in a multi-patient setting and that recommended precautions for the prevention of transmission of blood borne pathogens are adhered to. When using devices intended to be used with multiple patients, it is essential to follow the manufacturer's guidance in relation to the proper cleaning of the device, as outlined in the user manual.

Similarly, where a blood glucose meter is used by a single patient for self-testing, users should follow the manufacturer's instructions regarding the proper cleaning of the device which can be found in the user manual supplied with the meter.

Blood glucose test strips are single use only devices that should only be used once and then disposed of following the manufacturer's instructions for use supplied with the test strips.

Lancing devices are single patient use only devices that may be intended


by the manufacturer to be used once by an individual patient or more than once by a single patient. Lancing devices should not be used on more than one patient. The use of these devices on multiple patients could potentially result in the transmission of blood borne pathogens to patients who use the same lancing device, even when the lancet is changed between patients.

When using a lancing device for self-testing, users should not re-use the same lancet or share their lancing device with others. Users should refer to the user manual for guidance on the safe use of lancing devices and the safe disposal of lancets.

The IMB is advising **hospital / healthcare professionals** to ensure that this notice is communicated to the appropriate personnel within your organisation. Ensure that procedures are put in place so that (i) single use devices such as lancets and blood glucose test strips are only used once and (ii) single patient use devices such as lancing devices are only used on a single patient. Examine the guidance provided by the manufacturer in the user manual before use. Follow the manufacturer's instructions in relation to the proper cleaning of the device as outlined in the user manual. Ensure that facilities are in place to ensure the safe disposal of these devices in accordance with the manufacturer's directions.

The IMB is advising **members of the public** to talk to a healthcare professional, such as a GP, before buying a medical device. Members of the public should ensure that the devices that they are planning to buy bear the CE mark. Follow the manufacturer's guidance with regard to cleaning both the blood glucose meter and lancing device. Follow the manufacturer's guidance with regard to the safe disposal of lancets and blood glucose test strips. Complete the warranty form (if provided) so that the manufacturer can make contact if they need to (e.g. if they need to recall the product). If members of the public are concerned about a result given by a medical device, seek medical advice. Lancing devices should not be shared with anyone else due to the risk of transmitting infection.

In addition, the safety notice provides a useful list of reference documents, including relevant standards, codes of practice and guidance.

# Regulatory Update

## COMPLIANCE AND ENFORCEMENT WORKING GROUP (COEN)

A meeting of the COEN Working Group was held in Brussels on 25th May 2011. Discussion took place among Member States on enhancing cooperation between market surveillance authorities and customs authorities. The role of economic operators in the context of Regulation 768/2008 was also discussed. Progress was made on the market surveillance frequently asked questions (FAQ) guide to ensure consistent application of the medical device legislation across Member States. Updates were provided by a number of Member States on specific market surveillance projects and various issues of mutual interest. The next meeting of the COEN group is scheduled for October 2011.

## UNIQUE DEVICE IDENTIFICATION (UDI) WORKING GROUP

The UDI Working Group met in June. The goal of the group is to further discuss the development of a European UDI System to improve patient safety by enhancing the identification of devices, especially in the case of adverse events, and to facilitate traceability of devices in the event of a field safety corrective action. The work which has been done at the Global Harmonisation Task Force (GHTF) level in the UDI Working Group was considered as a foundation for the European initiative.

At the June meeting, the UDI Work-

*continued on following page*

ing Group reviewed recent changes proposed by the GHTF to the draft guidance document 'GHTF Draft Proposal for Guidance on Unique Device Identification (UDI) System for Medical Devices'. The revised guidance document was reviewed and Member States discussed similar systems that have already been implemented in Member States.

## NOTIFIED BODY OPERATIONS GROUP (NBOG)

The Notified Body Operations Group met in June both for its normal meeting and also to conduct a workshop on the peer review system for authorities responsible for designation and monitoring medical devices. The peer review system allows opportunity for European colleagues to accompany national authorities while they are auditing a notified body and aims to ensure that the same criteria and standards are being applied to notified bodies across Europe. The workshop in June allowed an opportunity to discuss how the peer review system may be further developed and improved and also to discuss some of the main challenges that had been encountered by authorities and peer reviewers while participating in this system to date. The IMB have participated in peer review system on five occasions to date, being reviewed twice and acting as a peer reviewer on three occasions.

## CENTRAL MANAGEMENT COMMITTEE

The Central Management Committee for medical devices held its third meeting in Brussels in June. Work items underway include: development of specific criteria for notified body designation; to define the contents of notified body certificates; to define the contents of a manufacturer's declarations of conformity; to improve the readability of instructions for use; to agree on periods of grace for manufacturers correcting non-conforming product (e.g. after an up-classification) and the coordination of consultations on documents relevant to the medical devices sector. New work items were also discussed and agreed including a proposal to revise the designation process for notified bodies. Further details of these work items and a meeting note will be published on www.cmc-md.eu.

## CLINICAL INVESTIGATION & EVALUATION (CIE) WORKING GROUP

The Clinical Investigation & Evaluation Working Group met in Brussels. The group finalised its review of comments on the draft MEDDEV guidance on post-market clinical follow up. In addition, the draft GHTF guidance document on serious adverse event reporting during clinical investigations was also reviewed. Of key interest were presentations made to the group on the number of pre-market clinical investigations currently being conducted in Europe, a presentation from a European clinical society on implant registers and a paper on pre-market evaluation of medical devices recently published by the Belgian Health Technology Assessment agency.

## HEADS OF MEDICINES AGENCY (HMA) – COMPETENT AUTHORITIES FOR MEDICAL DEVICES (CAMD) WORKSHOP

A workshop was hosted by the Hungarian Presidency on 27th April 2011 to increase mutual understanding and explore potential collaborations between the network of the Heads of Medicines Agency (HMA) and the Competent Authorities for Medical Devices (CAMD) network. In approximately 20 Member States, single agencies are responsible for both medicine and medical device regulation and so these 20 agencies are already represented by their Chief Executives on the HMA. An overview of the different regulatory systems and related structures was provided, the Commission updated on the recast and key discussions were held on resourcing and funding of device authorities and exploring alternative fee models. Specific work items included discussion on resourcing, assessment of drug-device combination products, companion diagnostics and clinical research of both medicines and devices. The workshop was successful and a further work programme and ongoing cooperation is envisaged.

## MEDICAL DEVICE EXPERT GROUP (MDEG)

The MDEG met in Brussels in June. Discussions included an update on key medical device issues. Updates were provided on the progress of new/revised legislative measures on e-labelling of medical devices, devices incorporating animal tissues and legislative revisions relating to the inclusion of provisions for screening assays for new variant CJD in the IVD Directive. In addition, discussions took place on the progress made to resolve issues relating to the formal objections on harmonised standards and also on the next steps for the recast of the medical devices directives. A presentation was made by the notified body association on their proposed Code of Conduct for notified bodies. In addition, significant discussions took place on the future role for the GHTF and on the development of Unique Device Identifiers (UDI) for medical devices.

## RECAST WORKING GROUP

The recast working group was established by the CAMD in February to provide detailed input to the Commission and specific suggestions as to how the legal texts might be structured/changed for the purposes of the recast. The meetings afford a key opportunity for Member States to discuss together and with the Commission the various elements of the medical devices regulatory system which may be subject to revision. The meetings to date have allowed for detailed technical, clinical and regulatory aspects of the proposed recast to be considered. Topics highlighted by the group may be considered by the Commission for inclusion in the impact assessment report and in the legislative proposals which are expected to be published in 2012.

IRISH MEDICINES BOARD

*Bulletin of the Medical Devices Department is designed by Ashfield Press Publishing Services for*

IRISH MEDICINES BOARD, KEVIN O'MALLEY HOUSE, EARLSFORT CENTRE, EARLSFORT TERRACE, DUBLIN 2
tel: +353 1 6764971 fax: +353 1 6344033 email: medicaldevices@imb.ie: http://www.imb.ie