Joint CUHK-NTEC CRMO Newsletter

Issue 3: Jun 2015

Director's Message

We are always pride of our investigators and research personnel in NTE cluster hospitals as you are active in pursuing improved healthcare and evidence-based medicine through clinical research. Currently we have more than 500 colleagues in NTE cluster involving in clinical research. Eighty studies are commenced in 2014, and by the end of 2014, there are more than 200 ongoing studies and more than 100 to-be-started studies in our institutions. Among these studies, around 60% are company-sponsored studies and 40% are investigator-sponsored trials. The strong research management and governance in our cluster, including CRMO and CRP, both reporting to Clinical Research Management Committee (CRMC), strengthens our capacity of clinical research.

From left to right: Ms. Iris Chan, Dr. So Hing Yu, Prof. Juliana Chan, Prof. Anthony Chan, Dr. Li Chi Kong, Prof. Paul Lai, Prof. Benny Zee, Dr. Benjamin Lee

We are glad that the Joint-CUHK-NTEC Clinical Research Pharmacy (CRP) are officially in operation. A flyer regarding the CRP service is enclosed and please contact CRP before starting clinical trials that involve study medication.
(http://www.crmc.med.cuhk.edu.hk)

Events

Basic Life Support Workshop

Thanks to Prof. David Chung and Ms. Charlotte Lam of the Kai Chong Tong Clinical Skills Learning Centre, three Basic Life Support (BLS) workshops for clinical research staffs were successfully completed. Thirty-five research staffs from ten different research units were taught on cardiopulmonary resuscitation, the proper use of automatic external defibrillators and the management of choking incidents. With overwhelming demands, additional workshops will be scheduled for the second half of 2015. You may contact CRMO (crmo@cuhk.edu.hk / 2632 4276) for early-bird reservation.

ICH-GCP Workshop

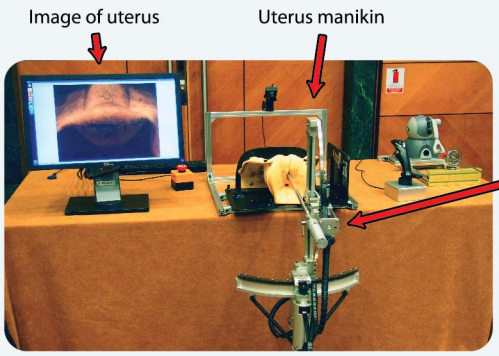
A one day GCP workshop was held on 7th March 2015 for our colleagues. The training was recognized globally by various international pharmaceutical companies.
Additionally, a half-day Chinese workshop on GCP (co-organized with the Institute of Integrated Medicine) was held on 18th April 2015 for our colleagues who conduct clinical trials with Traditional Chinese Medicine. Instructed by seasoned professionals, both workshops received raved reviews with constructive exchanges.

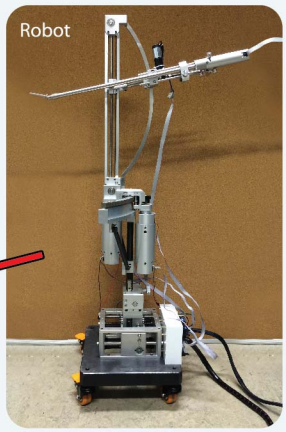
Feature Article

Department of Obstetrics and Gynaecology (O&G) of Prince of Wales Hospital (PWH)/ the Chinese University of Hong Kong (CUHK) has been excelled in clinical researches for decades for improving clinical practices and unmet patient's need. In this issue, we have invited colleagues of O&G department to share their achievements in clinical research with our NTE cluster colleagues.

A robot assistant for uterus positioning during hysterectomy

In traditional laparoscopic hysterectomy, a uterus manipulator is held by an assistant to facilitate the surgical procedures. The assistant may easily get fatigue by holding the tool for more than an hour throughout the surgery, and this may affect the surgery performance and patient safety. Thus, a robot assistant which can be controlled directly by primary surgeon to position the uterus stably can be an ideal solution. This can also lessen the manpower tension on labor-intensive procedure as well.





In collaboration with the Department of Mechanical and Automation Engineering, Department of Surgery of CUHK and City University of Hong Kong, the research team has developed a prototype of robot assistant which has four degrees of freedom (DOF) to position the uterus.

The robotic assistant comprises of a 3-DOF robotic positioning arm, a 1-DOF motorized uterus manipulator and a supporting stand. The positioning arm allows the manipulator to move in a partial spherical manner, while the motorized uterus manipulator allows to perform anteversion and retroversion (*Robotics Biomim.* 2014; 1:9). The latest model allows the robot assistant to have higher degree of mobility stand on the ground without mounting on the operating table. This project has been supported by the grant of Research Grant Council (RGC) Collaborative Research Fund (CRF) on nearly 10 million dollars.

In vitro Fertilization (IVF) and Perimplantation Genetic Diagnosis (PGD)

The Assisted Reproductive Technology Unit (IVFHK) PWH/CUHK has provided private and public personalized IVF services for more than 30 years and has been granted treatment license by the Council on Human Reproductive Technology to offer infertility treatment. IVFHK not only brings hopes to infertile couples, but also provides solid foundation for the researches in assisted reproductive technology. The multidisciplinary team of the IVFHK involves doctors, embryologists, geneticists and scientists.

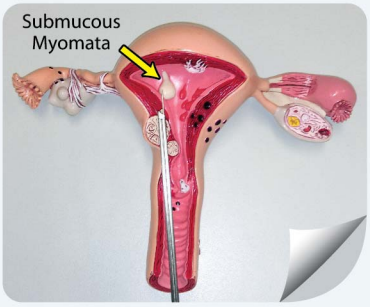
The Assisted Reproductive Technology Unit (IVFHK)

Blastomere biopsy

IVFHK is one of the frontiers in Hong Kong using preimplantation genetic testing including preimplantation genetic diagnosis (PGD) and preimplantation genetic sequencing (PGS) in conjunction with *in vitro* fertilization (IVF). It aims at improving successful birth rate and minimizing the risk of inheriting a genetic abnormality such as Down syndrome and Thalassaemia (*Best Pract Res Clin Obstet Gynaecol.* 2012; 26(1): 37-51.). New platforms, e.g., microarray, whole genome analysis using next-generation sequencing (NGS) are being equipped to increase the effectiveness and accuracy of the PGS. Lately, O&G Department has detected a balanced chromosomal rearrangement (BCA) which plays an important role in infertility by advancing the application of high throughput whole-genome low-coverage analysis (*Hum Mutat.* 2014; 35(5):625-636.). With PGD and PGS, they are conducting clinical researches to unfold the disposition of recurrent miscarriage through genetic approach.

A New Technique in Hysteroscopic Myomectomy

Hysteroscopic myomectomy is considered as the optimal surgical approach for submucous myomata. Nonetheless, resection of submucous myomata is frequently challenged by bleeding, fluid intravasation, and perforation which prompt complications to the surgical procedures and can lead to life-threatening condition. Recently, Dr. Alyssa Wong and her team carried out a randomized control trial using transcervical intralesional vasopressin injection on 40 patients. It significantly reduced the volume of inflow fluid, fluid intravasation, intraoperative blood loss and improved visual clarity (*J Laparoendose Adv Surg Tech A.* 2013; 23(3):258-62; *Obstet Gynecol.* 2014; 124(5):897-903). It is unquestionable that this new technique reduces the complication and life-threatening situation in hysteroscopic myomectomy.

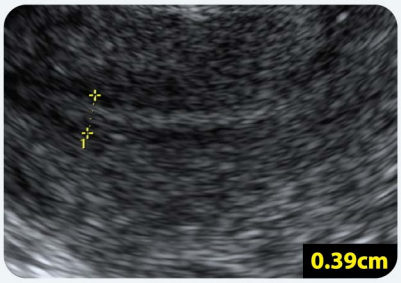


Model of transcervical intralesional vasopressin injection

Feature Article

Reappraisal of Endometrial Thickness for Endometrical Cancer Detection

In addition to the surgery technique, Dr. Wong and her team also reappraised the guideline of transvaginal ultrasound (TVS) endometrial thickness measurement for endometrial cancer diagnosis. It is believed that TVS is the first-line investigation for endometrial cancer. At present, various cut-off values of endometrial thickness are recommended but are limited by the sample size and methodology of the available meta-analyses.



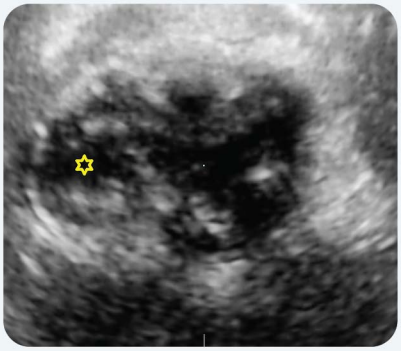
Endometrial thickness measurement by transvaginal ultrasound (TVS)

Thanks to the integral database of more than 4000 patients developed by O&G department, Dr. Wong concluded that transvaginal ultrasound using 3-mm cut-off has high sensitivity for detecting endometrial cancer and can identify women with postmenopausal bleeding (PMB) who are highly unlikely to have endometrial cancer. Her finding supports a cut-off of 3mm should be used instead of 4 or 5mm (*BJOG.* 2015 Mar Epub ahead of print).

Dr. Wong is grateful that continuous support from her teammates and pragmatic trainings offered by the department are the keys for her successful studies.

Evolution of Pelvic Floor before, during and after Pregnancy

Researches on pelvic floor are mainly conducted in Caucasian women, however these data may not be generalized locally because of the racial difference. Dr. Symphorosa Chan, Dr. Rachel Cheung and their team have conducted a number of clinical and imaging studies on pelvic floor of local Chinese women.


Right levator ani muscle injury in a woman at 8 weeks after delivery (asterisk)

There are progressive anatomical changes of the pelvic floor during pregnancy which are reflected by pelvic floor biometry such as increase in hiatal area and descent of the bladder neck (*BJOG.* 2014; 121: 121-129) and about 21% of women had levator ani muscle (LAM) injury after vaginal delivery (*Ultrasound Obstet Gynecol.* 2012; 39:1027-1033). Most of these changes can partially recover after delivery, except hiatal distension is more persistent as a result of LAM injury after vaginal delivery (*Ultrasound Obstet Gynecol.* 2014; 43: 466-474). This may prompt to the onset of pelvic floor disorder. Meanwhile a short follow-up till one year after delivery has not yet found significant adverse effect of LAM injury on pelvic floor disorders and health-related quality of life of the women. (*Int Urogynecol J.* 2014; 25(10): 1381-1388). They hope their findings can fill the knowledge gaps about the evolution of pelvic floor and improve the current practices. They are conducting a 3 years follow-up study on these women. Last but not least, they would like to express their gratitude to women participating in the study.

Announcements

SOP online training

Online training of all CRMO SOPs have been launched on CRMO website! Training record of the SOPs, including those by online training, as well as those previously conducted in SOP Train-the-Trainer workshop in 2014 and those conducted by individual research unit, are available on the website. Please do not hesitate to contact us if you would like to arrange live-demonstration of the online training.

CRMO website (Chinese version)

To facilitate the use of CRMO website by different stakeholders, Chinese version (including traditional and simplified Chinese) of CRMO website is introduced! You may choose the language on the first page of the website.

Partnership with 2 international CROs

CRMO has formed site alliance with 2 Contract Research Organizations (CRO), namely Parexel and Quintiles, in order to enhance the mutual cooperation and exchanges on clinical research.

Tips of the Day

Case Scenario 1: Dr. Simon is carrying out a clinical study of which fasting blood glucose test is part of the study procedures. He would like to recruit his patient, Jane, in the study, and hence he asked her to fast before the consultation visit next Monday. Jane followed the instruction of Dr. Simon of not taking breakfast, and she signed the informed consent before blood test for the clinical study. Is the procedure appropriate?

Study procedure should be commenced only after the informed consent form is signed by the subject and PI (or delegates). In this case, even though the blood test is conducted after informed consent form is signed, Jane is instructed to fast BEFORE the informed consent form is signed. Dr. Simon should obtain the signed informed consent before giving instruction of fasting to Jane. For details, you may go through CRMO-SOP-011 about reviewing and obtaining informed consent. ✓✓

Q1: During the reporting of adverse event (AE) in a clinical trial, we need to assess the causal relationship between AE and the investigational medicinal product. Who should make the assessment of the casual relationship?

It is a professional medical assessment to evaluate and determine the causal relationship between adverse event (AE) and the investigational medicinal product, therefore it should be done by site investigator, i.e. physician, only. ✓✓

Q2: What is the storage requirement for clinical research document?

Clinical research documents serve to demonstrate the compliance of investigators, hence the document must be filed and managed timely and properly. The documents should be stored in locked cabinets where the temperature and relative humidity are well-maintained to avoid fluctuation from season to season. Regular pest control should also be arranged. You can go through CRMO-SOP-006 for details. ✓✓

Upcoming Events

CREC and CRMO Workshop on Clinical Trial Approval

We are planning an interactive workshop on the CREC approval process and "Application for Conducting Clinical Trial/ Research Involving Patients in NTEC" on 26th Jun 2015 for our colleagues who would like to learn more about these topics. Research personnel including investigators, research nurses, research assistants as well as administrative staff who are involved in these processes are welcomed to join. Details will be announced in upcoming email from CRMO.

ICH-GCP on-line Examination

Another round of online GCP certification examination will be arranged in June for our colleagues to test their GCP knowledge. Some questions will be modified and new questions will be added to widen the question types. The format of the exam will remain the same with 50 multiple choice questions and a passing score of 80%.

Clinical Research Financial Management Workshop

After reviewing the comments from our previous seminars and workshops, a seminar on clinical study financial management will be held on 14th July 2015 to share our experience in study cost estimation and negotiation techniques. More information will be sent via email from CRMO.

Contact us

Joint CUHK-NTEC Clinical Research Management Office (CRMO)

Address: 8/F, Lui Che Woo Clinical Sciences Building, Prince of Wales Hospital, 30-32 Ngan Shing Street, Shatin, Hong Kong
Website: http://www.crmc.med.cuhk.edu.hk E-mail: crmo@cuhk.edu.hk Tel: (852) 2632 4276

香港中文大學－新界東醫院聯網臨床研究統籌處通訊

第三期：2015年6月

處長的話

新界東醫院聯網內的研究者和研究工作人員，一直致力進行各種臨床研究，提升醫療保健和循證醫學，我們為你們的努力感到自豪。目前有超過500位聯網內的同事參與臨床研究；在2014年開展了80項研究項目，而直至2014年底，聯網內有超過200項進行中的研究項目，及100項將會展開的研究項目。在這眾多的項目中，約六成為由藥廠申辦的臨床研究、及四成為研究者申辦的臨床研究。臨床研究管理委員會 (CRMC) 轄下的的臨床研究統籌處 (CRMO) 及藥劑部 (臨床研究) (CRP)，負責執行臨床研究管理和督導，強化了臨床研究的能力。

由左至右的排列為: 陳虹小姐，蘇慶餘醫生，陳重娥教授，陳德章教授，李志光醫生，賴寶山教授，徐仲錤教授及李成章博士

香港中文大學－新界東醫院聯網藥劑部 (臨床研究) (CRP) 已正式投入服務，現附上CRP服務範疇的單張；如有與藥物相關的臨床研究，請於研究開始前先與CRP聯絡商討安排 (http://www.crmc.med.cuhk.edu.hk)。

活動剪影

成人初級心肺復甦法 (BLS) 工作坊

多謝繼昌堂臨床技術學習中心的張志偉顧問醫生及林少慧女士的悉心指導，為臨床研究同事開辦的三次BLS工作坊已圓滿結束。來自10個研究單位的35位同事，學習了心肺復甦法、哽塞處理及正確使用心臟除顫器。由於反應熱烈，我們將會在2015的下半年度加開工作坊。歡迎與CRMO (crmo@cuhk.edu.hk / 2632 4276) 聯絡，預早留位。

藥物臨床試驗質量管理規範 (ICH-GCP) 工作坊

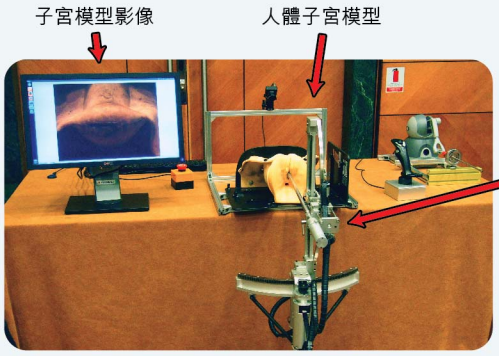
為同事而設的一天GCP工作坊已於2015年3月7日舉行；是次訓練獲全球不同藥廠研究申辦者所認可。

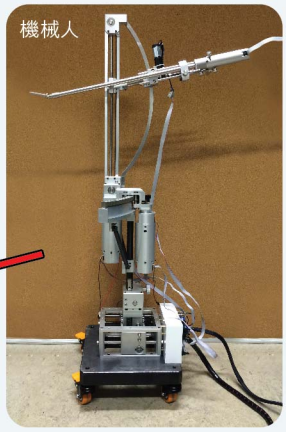
另外，在2015年4月18日，我們與中西醫結合醫學研究所協辦，為從事臨床研究的中醫師舉辦一個半天的中文GCP工作坊。兩次工作坊均由臨床研究經驗豐富的專業人士教授，甚獲好評。

卓越團隊掠影

威爾斯親王醫院香港中文大學婦產科學系在過去的三十年，一直為改善臨床實踐和滿足病人的需要而努力。今期我們邀請了婦產科部門的同事，和大家分享他們在臨床研究的成績。

子宮定位機械人





子宮定位機器人雛型應用於人體子宮模型的示範

在傳統腹腔鏡的子宮切除術中，手術過程中需由一名醫生拿著舉宮器協助子宮定位。長時間拿著舉宮器容易導致疲累，有機會影響手術表現和病人的安全。如果由負責進行摘除手術的醫生直接操控機械人助手，為子宮穩定地定位之餘，亦減少耗費人力，機械人助手確是理想的解決方法。有見及此，婦產科學系與中文大學的外科學系和機械及自動化工程學系及香港城市大學合作，共同研發出有4維自由度的機械人雛型，它是由一隻3維自由度的定位機械臂、一支1維自由度的舉宮器和支架所組成。定位機械臂可作局部球形移動，而舉宮器能執行前、後傾的動作 (*Robotics Biomim.* 2014;1:9)。最新的機械人模型具有更高的活動性，能自行站立而不需要安裝在手術枱上。這項研究由大學教育資助委員會協作基金撥款約一千萬元資助研發。

人工受孕 (IVF) 與胚胎植入前遺傳學診斷 (PGD)

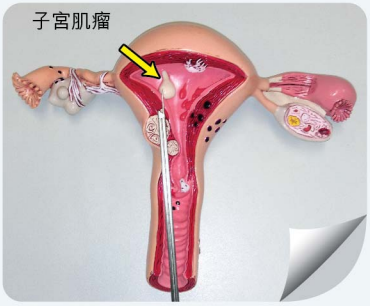
威爾斯親王醫院香港中文大學輔助生育技術中心 (IVFHK)

卵裂期胚葉切片

威爾斯親王醫院香港中文大學輔助生育技術中心 (IVFHK) 提供私家症和公家症的試管嬰兒服務超過30年；並獲人類生殖科技管理局准予治療不育的牌照。IVFHK不單為不育夫婦帶來希望，同時亦為輔助生育技術的研究提供穩健的基礎。IVFHK專業團隊包括醫生、胚胎學家、遺傳學家和科學家等多範疇專家共同合作。

IVFHK使用尖端技術進行植入前胚胎基因測試，包括植入前遺傳學診斷 (PGD) 和基因序列測定 (PGS)，與試管嬰兒的技術結合，有助提升出生成功率和將遺傳異常基因 (例如唐氏綜合症和地中海貧血) 的機會減至最少 (*Best Pract Res Clin Obstet Gynaecol.* 2012; 26(1): 37-51)。而新的設施如微陣列、全基因組測序和新世代定序技術 (NGS) 等，均有助提升PGS的有效性和準確性。染色體平衡性重編 (BCA) 在不育範疇擔當重要角式；最近婦產科學系透過優化現行分析技術把BCA探測出來 (*Hum Mutat.* 2014; 35(5):625-636)。另外，團隊運用PGD和 PGS正進行臨床研究，從遺傳學角度揭開習慣性流產的傾向。

新宮腔鏡子宮肌瘤切除技術

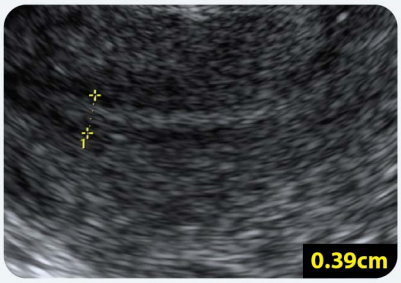


經子宮頸向肌瘤直接注射加壓素的模型

雖然宮腔鏡子宮肌瘤切除術是切除子宮黏膜下層肌瘤最理想的處理方法，但切除肌瘤時會出現出血、液體血管內滲和穿孔等手術併發症，可危害病人生命。黃思慧醫生和其團隊，邀請了40位病人，進行了一項經子宮頸向肌瘤直接注射加壓素的隨機對照臨牀試驗。研究結果顯示，無論在流入液體的容量、液體血管內滲和手術期間的失血量有明顯的減少。此外，子宮內的能見度亦因滲出子宮的血流減少而提高 (*J Laparoendose Adv Surg Tech A.* 2013; 23(3):258-62; *Obstet Gynecol.* 2014;124(5):897-903)。毫無疑問，新技術有助減低宮腔鏡子宮肌瘤切除術的併發症和生命的風險。

卓越團隊掠影

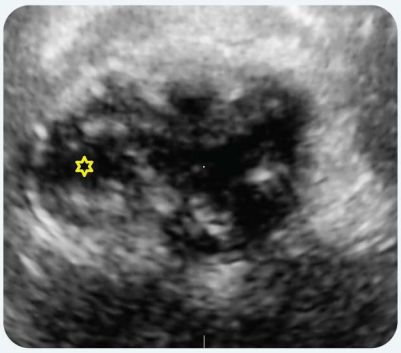
宮內膜厚度對宮內膜癌檢測指引的重新評估



經陰道超聲波 (TVS) 量度宮內膜厚度

此外，黃醫生和其團隊就經陰道超聲波 (TVS) 量度宮內膜厚度與宮內膜癌的診斷指引作出重新評估。TVS一向被認為是宮內膜癌的第一線檢查，目前量度宮內膜厚度的篩截值是來自有限的樣本數量或是薈萃分析 (meta-analyses)。黃醫生感謝婦產科學系建立了完整的資料庫，經分析超過4000位病人資料後，她認為TVS以3mm的宮內膜厚度為篩截值，對檢定宮內膜癌有高敏感度；亦能辨別婦女停經後出血與宮內膜癌的可能性。她的研究可支持以3mm取代4或5mm為篩截值 (*BJOG.* 2015 Mar 暫未有印刷版)。黃醫生感激團隊的支援和部門提供實效的培訓，這都是取得有成效研究的關鍵。

盆底在懷孕期和分娩後的演變


孕婦於分娩時受傷的右肛提肌(✡)，
於8個星期後覆診時的情況

大多數的盆底研究報告是來自對白種婦女的研究，因著種族的差異，這些資料未必能概括論述本地婦女的情況。為此，陳丞智醫生和張優嘉醫生及其團隊為本地的中國籍婦女進行臨床和影像的盆底研究。

盆底生物統計顯示盆底的解剖結構在懷孕開始時逐漸改變，例如裂孔區域增加和膀胱頸下降 (*BJOG.* 2014; 121: 121-129)，21%經陰道分娩的婦女的肛提肌 (LAM) 有受損情況 (*Ultrasound Obstet Gynecol.* 2014; 43: 466-474)。盆底大部份的改變在分娩後都能局部復原；但陰道分娩後肛提肌受損引致的裂孔擴張會持續 (*Ultrasound Obstet Gynecol.* 2014; 43: 466-474)，這可能是盆底毛病開始的訊號。跟進這些婦女至分娩後一年，發現肛提肌受損對盆底毛病和與健康相關的生活質素，並沒有顯著的不良影響 (*Int Urogynecol J.* 2014; 25(10): 1381-1388)。他們希望是次的發現能改善現行的臨床實踐之餘, 亦能為盆底演變的認識上填補空缺。目前，他們繼續為這些婦女進行為期3年的跟進。最後，他們向參予研究的婦女表達衷心的感激。

通告

標準操作程序 (SOP) 線上培訓

所有CRMO的SOP已可以在CRMO網址內進行線上培訓。SOPs的培訓記錄，包括所有的線上培訓、2014年所參與的「SOP培訓師訓練工作坊」和各研究單位內的自行培訓等，都可記錄在網址內。歡迎聯絡我們安排使用線上培訓的現場示範。

CRMO雙語網址 (中文及英文版)

為了方便不同人士使用CRMO網頁，CRMO網頁已提升為雙語網頁，你可在CRMO網址首頁選擇英文或中文 (包括繁體及簡體字) 版本。

與兩間國際合同研究組織 (CRO) 結成伙伴關係

CRMO與Parexel和Quintiles兩間CRO成為伙伴，加強雙方在臨床研究的交流和合作。

每日提要

個案事例 (1) ：Dr. Simon 正進行一項臨床研究，空腹血糖檢驗是其中一項研究程序。Jane 是其中一位預備邀請進入研究的對象。 Dr. Simon 要求 Jane 在下周一早上覆診前禁食，她遵照指示於當天沒有進食早餐，並在抽血前簽署了知情同意書。這些程序的先後次序是否正確？

所有研究程序展開前，受試者及首席研究者(或代表)必須先在知情同意書共同簽署。
在這案例中，雖然Jane簽了知情同意書後才抽血，但因是先被指示禁食，然後才簽同意書，所以程序上是不合適的。 Dr. Simon 應該先取得已簽署的知情同意書才給予禁食的指示。
有關審核和獲得知情同意書的詳情，可參閱CRMO-SOP-011。 ✓✓

探討問題 (1) ：在臨床研究的不良事件 (AE) 呈報中，不良事件 (AE) 和研究藥品 (IMP) 之間的相互關係應由誰來評估？

由於評定AE與IMP兩者的相互關係是一項專業的醫療評估，所以應由研究者 (即是醫生) 負責。 ✓✓

探討問題 (2) ：儲存臨床研究文件的環境有什麼特別的要求？

臨床研究文件適時及適當的存檔及管理，能反映研究者是否合規地進行研究。這些文件應該儲存在上鎖的公文櫃內，而室內的溫度及濕度必須恒常妥善控制，避免受季節轉變影響；及定期作蟲害控制的安排。有關詳情請參閱CRMO-SOP-006。✓✓

重點活動推介

CREC和CRMO審批臨床研究程序工作坊

為增加同事對CREC (臨床研究倫理聯席委員會) 及CRMO審批臨床研究程序的認識，我們將於2015年6月26日舉行一場工作坊，由CREC和CRMO同事作解說。歡迎任何研究工作人員包括研究者、研究護士、研究助理及有關的行政同事參加。詳情CRMO將於日後透過電郵公佈。

國際協調會議－藥物臨床試驗質量管理規範 (ICH-GCP) 線上考試

為幫助同事測試自己對GCP的認識，新一輪的線上GCP證書考試將於六月舉行。考試的形式如前，有50條的多項選擇題及合格分數為80分，今次會修改以往的試題及加入新試題以豐富試題的類型。

臨床研究財務管理研討會

整合了各方面的意見之後，我們將會在2015年7月14日舉辦一場臨床研究財務管理研討會，分享臨床研究中成本計算和協商技巧的經驗。詳情CRMO將於日後透過電郵公佈。

聯絡方法

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