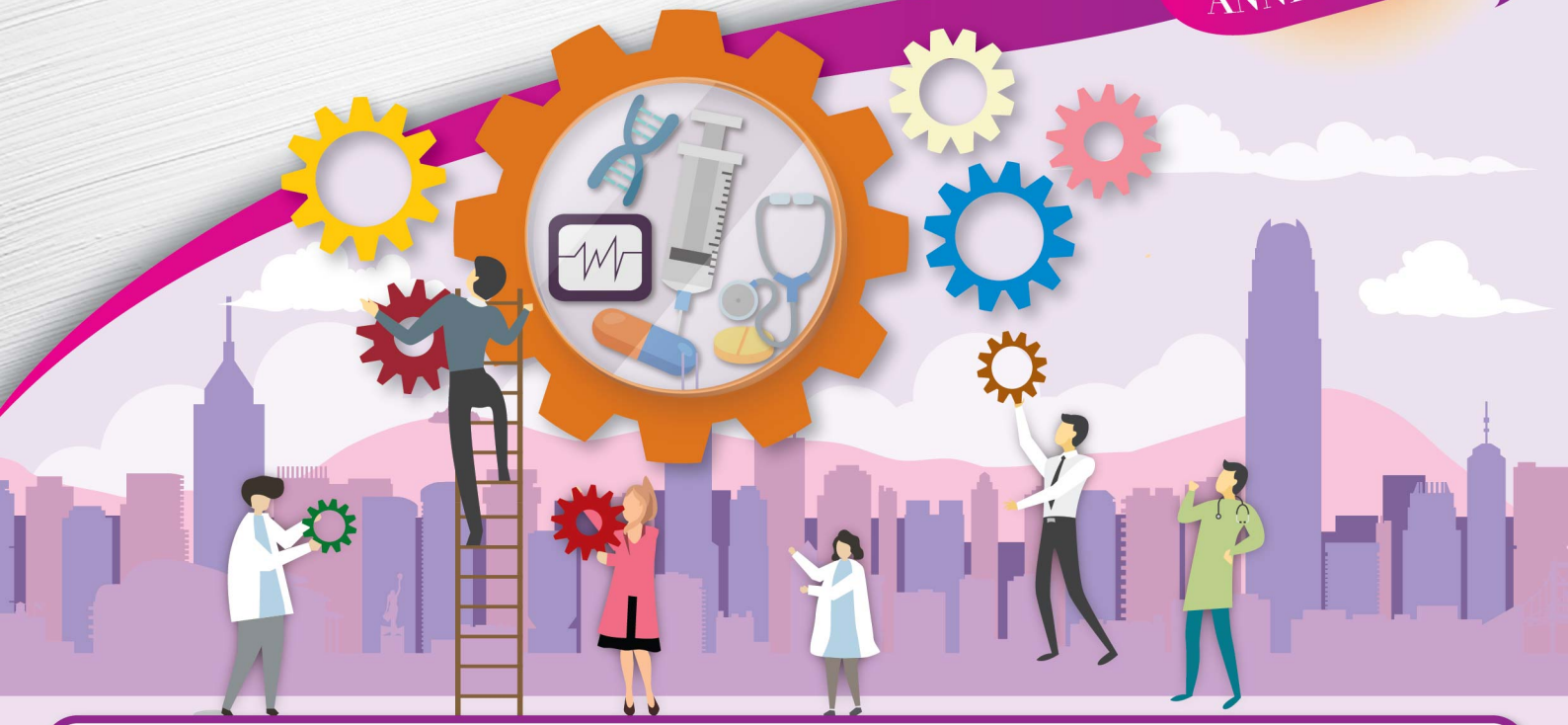
香港中文大學－新界東醫院聯網臨床研究統籌處通訊
Joint CUHK-NTEC CRMO Newsletter

Issue 11 Dec 2018

追求卓越達五載
夥伴同行迎未來

Aspiring for Excellence Through Partnerships
A Journey of 5 Years and Beyond

5th ANNIVERSARY



時間飛逝，醫院管理局（HA）新界東聯網（NTEC）與香港中文大學（CUHK）醫學院於2013年携手成立香港中文大學—新界東醫院聯網臨床研究統籌處（CRMO）已有5年。

完善的管理是我們追求高質素臨床研究和保障受試者健康的重要基石。過去5年，CRMO推出了一系列質素改善計劃，促進卓越的臨床研究管理。計劃包括 ： 統一適用於所有臨床研究單位（CRU）覆蓋全面的標準操作規程（SOPs）、建立專屬各CRU的內聯網帳戶、舉辦專業工作坊/研討會，並成立由中大—新界東醫院聯網臨床研究倫理聯席委員會（CREC）、藥劑部（臨床研究）(CRP)、中大一期臨床研究中心及HA組成的質素及安全監督小組委員會，討論與臨床研究有關質素和安全的問題。在各方鼎力支持下，每一項臨床研究管理的重要環節已全面執行，成績令人滿意。

Times flies! It has been 5 years since the Hospital Authority (HA) New Territories East Cluster (NTEC) and Faculty of Medicine of the Chinese University of Hong Kong (CUHK) joined hands to establish the CUHK-NTEC Clinical Research Management Office (CRMO) in 2013.

Good governance is the cornerstone in our pursuit of conduct of high quality clinical trials and human safety protection. During the last five years, the CRMO has introduced a series of quality improvement programmes to promote excellence in clinical trial management. These include harmonization of a comprehensive set of standard operation procedures (SOPs) applicable to all Clinical Research Units (CRU), establishing an intranet account for each CRU, organization of professional training workshops/seminars and setting up a Clinical Research Quality Assurance And Safety Monitoring Subcommitee including members from the Clinical Research Ethics Committee (CREC), Clinical Research Pharmacy (CRP), Phase 1 Clinical Trial Centre (P1CTC) and HA to discuss issues related to quality and safety of clinical trials. With the unfailing support from all parties concerned, we are pleased to report that each of these elements of the clinical trial management system is now fully executed.

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香港中文大學－新界東醫院聯網 臨床研究統籌處總監 陳重娥教授 (左)
Professor Li Chi-kong (Chairman of Joint CUHK-NTEC CRMC) (Right)
Professor Juliana Chan (Director of Joint CUHK-NTEC CRMO) (Left)

自2013年，有超過900項由CRU領導的干預性臨床研究已記錄在我們的數據庫。為了提升我們的研究質素，我們利用電子系統協助各CRU來追踪和監察其臨床研究的進展。我們亦成立了一支臨床研究視察團隊，進行實地視察並提供意見，幫助我們的研究人員為院外組織的視察做好準備。我們許多CRU已多次通過國際製藥公司總部的稽查及/ 或各監管機構（包括美國食品藥品監督管理局 US FDA和日本厚生労働省 MHLW）的視察。於2016年，我們16個CRU通過嚴謹的視察，成功獲得國家食品藥品監督管理總局（CFDA）認證。是次成果有賴各CRU、CRMO、CREC及CRP一齊同心協力。除了提供管理及支授予各CRU外，我們樂意成為CRU、藥廠、合同研究組織（CRO）及世界知名研究機構之間溝通的橋樑，開拓更多聚焦亞洲人士特殊需求的合作機會，將醫藥用品及設備等相關的研發帶入香港。

Since 2013, more than 900 interventional studies led by CRUs have been recorded in our database. To enhance the quality of our trials, we have been using an electronic system to help CRUs keep track and monitor progress of their clinical trials. We have set up an inspection team to conduct on-site inspection to provide feedback and help our investigators prepare for inspection by external parties. Many of our CRUs have been audited by headquarters of international pharmaceutical companies and/or inspected by regulatory authorities including the US Food and Drug Administration (FDA) and Japan Ministry of Health, Labour and Welfare (MHLW). In 2016, 16 CRUs underwent rigorous inspection and successfully received CFDA accreditation through joint efforts of CRUs, CRMO, CREC and CRP. Apart from providing governance and supporting CRUs, the CRMO serves as a conduit between our CRUs and pharmaceutical companies, contract research organizations (CROs) and world-leading research institutes where we explore opportunities of bringing pivotal trials including investigational medical products and devices to Hong Kong for research and development, focusing on special needs in Asian populations

我們眾多的研究者在其專業範疇具領導地位，在多中心研究（包括由研究者發起的臨床研究）（IST）擔任首席研究者或區域協調員。為了加強我們從事IST的能力，CRMO自2018年開始提供臨床研究監查服務，為申辦者提供一站式的解決方案。研究批核的獲取、病人/ 受試者的招募及完成研究等項所需時間，是決定能否引入臨床研究的競爭關鍵。為此，CRMO一直與中大研究及知識轉移服務處（ORKTS）緊密合作，加快審批跟申辦者和學術機構合作的臨床研究協議。隨著任命專職同事監督這些法律文件，CRMO將與研究者密切合作，在分判多中心IST給其他研究組織時，確定合約條款及各方的角色與責任。

Many of our investigators are world-leaders in their areas of expertise who are lead investigators or regional coordinators of multi-centre trials including investigator-sponsored trials (ISTs). To increase our capacity in conducting these ISTs, since 2018, the CRMO has introduced clinical trial monitoring services to provide a one-stop solution for our sponsors. Time to study approval, patient/subject recruitment and trial completion are key factors in our competitiveness to bring in clinical trials. To this end, CRMO has been working closely with the CUHK Office of Research and Knowledge Transfer Service (ORKTS) to expedite the vetting and approval of clinical trial agreements with sponsors and academic institutions. With the appointment of dedicated staff to oversee these legal documents, the CRMO will work closely with investigators to define the contract terms, roles and responsibilities during the sub-contracting of these multi-centered ISTs to other study sites.

行政長官在最新的政府施政報告中，已承諾加大投資力度，將香港打造成為醫療創新和生物技術發展的中心。隨著大灣區發展，CRMO將繼往開來，將累積了30年臨床研究的策劃、從事、管理、監管經驗，發展成知識轉移中心。在未來5年及往後日子，CRMO會透過夥伴合作將我們的科研推向新的高峰。

In her latest Government Policy Address, the Chief Executive has committed substantial investments to develop Hong Kong into a hub of medical innovation and biotechnological development. With the development of the Greater Bay Area, the CRMO will continue to leverage on the three decades of CUHK experience in the planning, conduct, management and governance of clinical trials to develop into a knowledge transfer hub, and take our scientific research to new heights through partnerships in the next five years and beyond.

CRMO 5載成就
5 YEARS of ACHIEVEMENTS of CRMO

專業培訓（例如GCP，SOP，復甦法培訓等）
（已有~1600人次參加培訓）

Professional trainings, e.g., GCP, SOP resuscitation
(~1600 research personnel are trained)

專業的臨床及管理團隊
（~800位人員參與臨床研究）

Professional Clinical & Management Team
(~800 research personnel)

14項 綜合服務
例如：處理批刻申請，審閱臨床研究協議，
安排臨床研究保險，院外存檔服務，
質量保證和監查服務

14 centralized services
(E.g., Handle application of approvals, CTA vetting, arrangement of insurance, archival service, QA and monitoring service)

完善的在線數據庫管理和監控平台
（監控 >900項干預性的研究）

Well-established online database management and monitoring platforms
(>900 interventional studies are being monitored)

16個
獲 CFDA 資格認定的
臨床研究專科部門

16 CFDA accredited units

由專門的臨床研究視察團隊定期進行
實地視察

Regular on-site inspection by the dedicated clinical research inspection team

25份
全面SOP適用於
中大/ 新界東聯網醫院

25 Comprehensive SOPs for all disciplines in CUHK/ NTEC hospitals

環球合作
(與多個國際製藥公司和CRO結成合作夥伴)

Worldwide Collaboration
(Alliance with international pharmaceutical companies and CROs)

香港中文大學外科學系泌尿外科組
Urology Unit of the Department of Surgery of CUHK

Research Unit Highlight 卓越研究團隊掠影

泌尿外科組成立於1984年，一直積極開展臨床和轉譯研究。縱然面對香港學術研究人才缺乏的挑戰，仍無減泌尿外科組對改善病人的熱忱。通過與不同學科緊密的合作，他們的研究成果不僅造福香港及其他亞洲國家的患者，還有助制定更合適的醫療政策，保障人們健康。

Established since 1984, Urology unit of the Department of Surgery is an active research team in conducting both clinical and translational research. Facing the challenge of scarce manpower in academic research in Hong Kong, the urology unit is still enthusiastic in improving the patient's needs. Through the close multi-disciplinary collaborations, the researches of the unit not only benefit the patients in Hong Kong and Asian countries, but they also contribute to better policy making in protecting the health of mankind.

改善前列腺癌預測結果，惠及本地及亞洲地區患者
Improvement of prediction of prostate cancer for local and Asian patients

前列腺癌是全球常見癌症中的第二位，其病發率在亞太區不斷升高。測試前列腺特異抗原 (PSA) 血清中的含量，是診斷罹患前列腺癌的重要工具。 然而，PSA會因不同情況而增加，例如前列腺增生和前列腺炎。因此，病人往往要進行較準確但具侵入性的活檢TRUSPB，以便準確診斷是否罹患癌症。結果顯示，血清中含有4-10 ng/ml PSA的病人只有15%是患有前列腺癌，而85%病人卻進行了不必要的活檢TRUSPB。

Prostate cancer is the second most common cancer in the world, and its incidence in the Asia-Pacific region is increasing. The use of serum level of prostate-specific antigen (PSA) is an important tool for diagnosing prostate cancer. However, PSA level is easily elevated by many other conditions such as benign prostatic hyperplasia and prostatitis. Hence, patients are subjected to perform specific but invasive transrectal ultrasound-guided prostatic biopsy (TRUSPB) for more accurate diagnosis. The results showed that only 15% of patients with PSA level of 4-10 ng/ml were diagnosed with prostate cancer, while 85% of patients underwent unnecessary TRUSPB.

為了改善檢測前列腺癌的準確率及減少進行具入侵性但不必要的活檢，檢驗PSA 異構體及其衍生物並計算出前列腺健康指標(*phi*)是較準確的非入侵性評估。根據泌尿外科組血清庫的研究數據，現行本地人的病發率與根據高加索人數據開發的*phi*的病發率相差甚遠。就以*phi*值介乎24-35為例，有18.1%高加索人會患有前列腺癌，本地中國人則只有7.6%（表一）。因此，他們提倡在決定應否為病人(其PSA值4-10ng/ml)進行具入侵性的活檢TRUSPB前，須先檢測其*phi*值，而*phi*的參考範圍應選用適合本地中國人的範圍。他們的研究結果現已於各公立醫院應用，大大改善診斷本地中國人罹患前列腺癌的準確性。

To improve the accuracy of diagnosis and reduce the unnecessary invasive biopsy, checking the PSA isoform and its derivatives and calculating the Beckman Coulter Prostate Health Index (*phi*) is a more accurate and non-invasive assessment of prostate cancer. According the data of the serum bank of the Urology unit, they found that the incident rate of prostate cancer in local people is largely different from the *phi* which is developed based on the Caucasian's database. For example, the incident rates of prostate cancer in local Chinese and Caucasian whose *phi* value 25 - 34.9 are 7.6% and 18.1%, respectively (Table 1). Based on their result, they suggested to check patient's *phi* level (if the serum PSA level is 4-10 ng/ml) before selecting patient for a TRUSPB. Also, the local reference range of *phi* should be adopted. Their findings improve the accuracy of diagnosis of prostate cancer for the local Chinese, they have been accepted and applied in all public hospitals.

urce: A57210 Beckman Coulter Access HybriTech Free PSA Instructions for Use 2011.

obability of prostate cancer by phi in patient with total PSA between 2 to 10 ng/mL

Prostate Health index (phi)	0-24.9	25.0-34.9	35.0-54.9	55.0+
Prostate Cancer Probability (% Pca)	11.0%	18.1%	32.7%	52.1%

urce: Catalona WJ, Partin A, Sanda MG et al.

obability of prostate cancer by phi in Chinese with total PSA between 4 to 10 ng/mL

Prostate Health index (phi)	0-24.9	25.0-34.9	35.0-54.9	55.0+
Prostate Cancer	3.6%	7.6%	22.9%	38.1%
High-grade Prostate Cancer	0.5%	0.9%	6.9%	19.0%

urce: PHK CHIU, CF NG et al.

表一 (Table 1)

此外，他們更與新加玻、台灣及上海三地合作，根據四地的數據設計了合適亞洲區的*phi*的參考範圍。他們的研究成果已獲泌尿科最具影響力的期刊European Urology接納。他們的研究結果若能應用於亞洲區，實在是病人的福音。

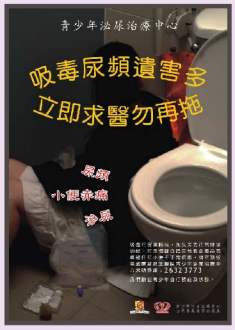
In addition, Urology unit collaborated with other research teams in Singapore, Taiwan and Shanghai and designed the reference range of *phi* for Asian based on the database from 4 areas. Their results have been accepted by the highest impact journal in urology, European Urology. It will be a great news to Asian patients if their results can be accepted and applied in the Asian countries.

設立一站式診所治療氯胺酮引致的尿路病
One-stop clinic for ketamine-associated uropathy

泌尿外科組對社會中一群受氯胺酮(俗稱K仔)影响的隱青十分關心。濫用氯胺酮導致下泌尿道症候群(LUTS)(當中包括尿頻、失禁、膀胱疼痛等)是時至今日眾所周知「索K」的後遺症。然而，醫學界對其禍害及治療氯胺酮導致的排尿功能障礙，在2007年前是毫無頭緒。

Urology unit concerns the young ketamine abusers who suffer from lower urinary tract symptoms (LUTS). Today, it is well-known that Ketamine abuse induces LUTS including urinary frequency, urge incontinence and bladder pain. However, there is no clue about its scourge and no standardized treatment protocol before ketamine-associated urinary tract dysfunction came to light in 2007.

在社工請求協助下，泌尿外科組聯同小兒外科及小兒泌尿外科組向政府的禁毒基金申請資助，在醫管局的支持下設立了青少年泌尿治療中心(YUTC)，為吸食氯胺酮而患有排尿功能障礙的30歲以下年青病人提供服務。YUTC為患者提供一站式的早期泌尿外科檢查及治療。服務的對象是不受居住地區限制，有需要的青年可直接致電YUTC熱線預約而無須醫生轉介信。透過經驗集中於單一個中心，YUTC研究出務實可行及具成本效益的各個醫療方案，以合適不同LUTS病患階段。



除了提供醫療服務外，泌尿外科組還出任保安局禁毒處常務委員會委員，負責向政府提出有關戒毒治療和康復設施發展的意見，協助政府制定禁毒政策。經過多年的教育及宣傳，大眾對氯胺酮的禍害有更多認識，濫用氯胺酮的過案也因而減少了。泌尿外科組不但關心本地青年，他們更希望其治療經驗能受惠中國及世界各地的患者。他們將其研究成果翻譯成中文並刊載於中國的研究期刊，好讓中國內地的醫療人員也能參考到他們的數據，為國內的患者帶來適切的治療。他們還建議國際衛生組織 WHO 將氯胺酮納入受管制藥物，以減低大眾接觸到氯胺酮的機會。

泌尿外科組負責人吳志輝教授寄語:「臨床研究不但有助深入認識疾病及改善現行的治療方案外，本地患者更有機會獲得新一代還未在港註冊上市的藥物。另外，實質的研究數據更能為政府制定醫療政策提供基礎。我們希望更多本地泌尿科的醫療人員投身臨床研究，令醫療及社會各個層面能從臨床研究中受惠。」

Under the urge request from the social workers, urology unit collaborated with Division of paediatric surgery and urology to establish the Youth Urological Treatment Centre (YUTC) funded by the Beat Drugs Fund of the Hong Kong Government and the support from Hospital Authority (HA). YUTC provides one-stop services include early urological assessment and treatment to young abusers under the age of 30 who suffer from Ketamine-associated urinary tract dysfunction. Patients from whole territory are welcomed to join the services. They can make appointment via YUTC hotline by themselves or their social workers without medical referral. YUTC formulated a set of practical and cost-effective management protocols to suit different stage of the LUTS by concentrating the experience in a single centre.

In addition to providing clinical services, the urology unit also joins the membership of the action committee of the Narcotics Division of Security Bureau to provide advice on treatment and rehabilitation and assist the government to develop anti-narcotics policy. After years of education and publicity, the incidents of ketamine abuse decline as the public has more understanding about the scourge of ketamine. The urology unit not only cares local ketamine abuser, but they also hope that their findings and experience can benefit the patients around the world. They translated their data into Chinese and published in the Chinese journals so that the healthcare professionals in China can provide appropriate treatments in reference to their data. They also approached WHO to classify Ketamine as a controlled drug to minimize the availability of Ketamine by the public.

Prof. Chi Fai NG, the research unit head of urology unit, said “Clinical study deepens our understanding of the disease and improves current treatment protocol, it also brings hope to the patients to have new generation of drugs that have not yet been marketed in Hong Kong. Moreover, the research data can provide foundation for the government to formulate the medical policies. We hope that more local urological healthcare professionals participate in clinical research, hence benefits healthcare and different aspects of the society. ”.

通告 Announcement

臨床研究議書的新安排

於2018年8月1日起，CRMO負責所有臨床試驗相關協議書（新的協議及修正案）的檢閱及審核，以進一步加快臨床試驗審閱程序。

所有與中文大學簽訂的臨床試驗相關協議書（新的協議及修正案），需電郵到CRMO郵箱 crmo.cta@cuhk.edu.hk；電子郵件主題必須包含三項資料：臨床試驗方案號碼、首席研究者姓名和申辦者名稱。CRMO將處理和審閱該協議書。

如有任何查詢，歡迎致電 3505 1032 與我們聯絡。

New Arrangement of Clinical Trial Related Agreement

In order to further enhance the clinical trial related agreements review process, with effective on 1 Aug 2018, all clinical trial related agreements (initial and amendment) will be reviewed and vetted by CRMO.

All CUHK clinical trial related agreement (initial and amendment) should be routed to CRMO at crmo.cta@cuhk.edu.hk. The email subject must contain all three information including Protocol no./PI name/ Sponsor. CRMO will handle and review the agreement.

For any queries, please contact CRMO at 3505 1032.

登記臨床研究於公共領域事宜 (二)
Clinical Trial Registration in Public Domain (Part 2)

我們在上一期回答了幾條有關在公共領域登記臨床研究的問題，包括
1)在公共領域註冊的目的
2)於公共領域登記臨床研究是何時為強制性的要求?
3)如我的研究沒有登記在公共領域上會有的後果

在本期中讓我們回答其他的查詢

We answered few questions about the clinical trial registration in public domain in the last issue including
1)The purpose of registration in public domain.
2)When did the registration become mandatory?
3)The possible consequence of the study if it has not yet registered.

In this issue, let's answer other enquiries.

4.什麼是國際醫療雜誌編輯委員會(ICMJE) 接納的註冊處?
What are the International Committee of Medical Journal Editors (ICMJE) acceptable registries?

- www.anzctr.org.au (澳洲/新西蘭)(Australia/New Zealand)
- www.clinicaltrials.gov (美國)(USA)
- www.ISRCTN.org (英國)(UK)
- www.umin.ac.jp/ctr/index/htm (日本)(Japan)
- www.trialregister.nl (荷蘭)(Netherlands)
- https://eudract.ema.europa.eu/ (歐盟)(EU)
- 其他獲WHO接納的“主要登記冊”，包括中國臨床試驗註冊中心 (ChiCTR)
  Other“Primary Registries” accepted by WHO, including Chinese Clinical Trial Registry (ChiCTR)
  http://www.who.int/ictrp/network/primary/en/

5.哪些註冊處適合於香港進行的臨床研究?
What are the recommended registries for clinical trials in Hong Kong?

- 中國臨床試驗註冊中心 (ChiCTR)
  Chinese Clinical Trial Registry (ChiCTR)
  - 可透過香港中文大學臨床研究及生物統計中心進行登記 https://www2.ccrb.cuhk.edu.hk/web/?page_id=746
    Can be registered via Centre for Clinical Research and Biostatistics, CUHK
  - 只能註冊前瞻性的研究 (需在第一次招募患者前登記)
    Can only register prospective studies (before first patient recruited)
- www.clinicaltrials.gov
  - 可由個別研究員或代表進行登記
    Can be registered by individual investigator or delegates

6.如我未為已開始的研究進行登記，我該怎麼辦?
What can I do if I have not registered my study before it starts?

- 若獲clinicaltrials.gov特別許可，你仍可為已展開的研究在clinicaltrials.gov進行登記
  It is still possible to register your study after it starts via clinicaltrials.gov. Special permission might be needed from clinicaltrials.gov for such studies.

- 請注意，ICMJE要求所有臨床研究在招募第一名患者前作出登記。若你的登記屬追溯性質，你或需要獲得期刊編輯的特別批准。
  Please note that ICMJE requires all clinical studies to be registered before the recruitment of the first patient. Special permission might be needed from the journal editor if your study was registered retrospectively.

報告嚴重不良事件時間表
SAE Reporting Timeline

根據臨床研究倫理聯席委員會的標準操作規程（CREC-SOP），所有嚴重不良事件（SAE）應在得悉24小時內向CREC報告。SAE包括以下任何不良事件:

According to CREC-SOP, all serious adverse events (SAEs) should be reported to CREC within 24hr of awareness. SAE includes any adverse events which:

1）導致死亡;
2）有生命危險;
3）需要住院治療或延長住院治療;
4）導致持續或嚴重殘疾/無行為能力; 或者
5）導致先天性異常/出生缺陷。

1) results in death;
2) is life-threatening;
3) requires inpatient hospitalization or prolonged hospitalization;
4) results in persistent or significant disability/incapacity; or,
5) results in a congenital anomaly/birth defect.

請注意，報告SAE的24小時時限是從「知悉」SAE開始計算，而非SAE的實際發生時間。例如，如果今天有一名研究受試者告知你，她曾於上月入院接受治療，那麼她該次入院很明顯會被視為SAE，而你將在知悉後24小時內向CREC報告。由於你今天剛收到有關入院治療的通知，你現在要在24小時內向CREC報告。

Please note that the reporting timeline of 24hr starts upon the “awareness” of the SAE, not the actual onset time of the SAE. For example, if a study patient told you today that she was admitted to the hospital last month, then her hospitalization would obviously be regarded as a SAE and you will have 24hr to report the case to the CREC. Since you have just been notified today about the hospitalization, you would now have 24hr to report to the CREC.

有些研究申辦者會要求研究團隊使用他們特定的SAE報告表格而非CREC提供的報告表格。若是如此，請同時向CREC遞交研究申辦者的SAE報告表格及CREC的*SAE Comment Element Form.*

Some sponsors may ask the study site to use their study specific SAE reporting forms instead of the one provided by CREC. If so, please submit to CREC both the sponsor’s SAE reporting form and the CREC *SAE Common Element Form* at the same time.

聯絡方法
Contact us

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