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DIRECTOR GENERAL OF HEALTH MALAYSIA
Kementerian Kesihatan Malaysia
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Tarikh : 2 APRIL 2015

SENARAI SEPERTI EDARAN

Y.Bhg. Datuk / Dato' / Datin / Tuan / Puan,

SURAT PEKELILING KETUA PENGARAH KESIHATAN MALAYSIA BILANGAN 4/2015 : TATACARA PROSEDUR PERMOHONAN BERKAITAN PENYELIDIKAN SEL STEM DAN CELL-BASED THERAPIES

TUJUAN

1. Tujuan Pekeliling ini dikeluarkan adalah untuk menerangkan mengenai tatacara prosedur yang perlu dipatuhi dalam membuat sebarang permohonan penyelidikan berkaitan sel stem, khasnya kajian yang melibatkan subjek manusia.
2. Surat Pekeliling ini juga berkaitan dengan Pekeliling KPK Bil. 7/2011 yang telah dikeluarkan pada 14 November 2011.
3. Di atas sebab terdapatnya keperluan semasa yang perlu dipatuhi, maka pekeling terdahulu telah dikaji semula dengan mengambil kira input-input teknikal berkenaan tatacara permohonan berkaitan penyelidikan sel stem dan *cell-based therapies*.

LATARBELAKANG

4. Setiap permohonan bagi menjalankan penyelidikan berkaitan sel stem haruslah mematuhi **Checklist For Research On Stem Cell And Cell-Based Therapies (Lampiran 1)** yang telah disediakan oleh Jawatankuasa Kebangsaan Etika Penyelidikan dan Terapi Sel Stem (NSCERT).

5. Penyelidikan sel stem yang ingin dijalankan itu juga haruslah mematuhi etika yang ditetapkan dalam buku *Guidelines For Stem Cell Research and Therapy*, MOH/P/PAK/177.08(GU) yang telah diterbitkan oleh pihak Kementerian Kesihatan Malaysia pada Julai 2009.

6. Objektif penerbitan *Guidelines For Stem Cell Research and Therapy*, MOH/P/PAK/177.08(GU) adalah sebagai rujukan dan panduan kepada mana-mana pihak samada dari Kementerian Kesihatan Malaysia, mahupun universiti dan juga swasta dalam menjalankan penyelidikan sel stem di negara ini. Setiap penyelidik perlu mematuhi garis panduan yang telah diwujudkan itu.

PROSEDUR PERMOHONAN BERKAITAN PENYELIDIKAN SEL STEM DAN *CELL-BASED THERAPIES*

7. Tatacara berikut haruslah dipatuhi semasa membuat permohonan berkaitan penyelidikan sel stem dan *cell-based therapies* :-

- (i) Semua permohonan (*protokol*) daripada pihak KKM dan swasta perlu dikemukakan kepada JEPP (*MREC*) dengan mengikuti prosedur yang telah ditetapkan iaitu berdaftar melalui *National Medical Research Register* (NMRR).

- (ii) Manakala permohonan (*protokol*) daripada pihak universiti, perlu dikemukakan kepada *Institutional Review Board* (IRB) dan *Institutional Ethical Committee* (IEB) dari universiti masing-masing.
- (iii) JEPP (*MREC*) / IRB / IEB akan menyemak setiap protokol samada menepati *checklist* NSCERT. Sekiranya protokol tersebut tidak lengkap dan tidak menepati *checklist* NSCERT, maka JEPP (*MREC*) / IRB / IEB akan mengembalikannya semula kepada penyelidik terbabit.
- (iv) Protokol yang lengkap akan dikemukakan kepada Jawatankuasa Kebangsaan Etika Penyelidikan Dan Terapi Sel Stem (NSCERT) untuk rekomendasi.
- (iii) NSCERT akan bermesyuarat dan membuat rekomendasi berdasarkan bukti-bukti saintifik yang dikemukakan. Rekomendasi NSCERT akan dikemukakan kepada JEPP (*MREC*) / IRB / IEB.
- (iv) JEPP (*MREC*) / IRB / IEB akan memberi keputusan akhir (*final decision*) berkaitan dengan permohonan penyelidikan tersebut, dan seterusnya memaklumkan kepada pihak penyelidik keputusan yang telah dibuat itu.

8. Carta alir permohonan penyelidikan sel stem ini adalah seperti di **Lampiran 2**.

TARIKH KUATKUASA

9. Pelaksanaan Pekeliling ini adalah berkuatkuasa dari tarikh surat Pekeliling ini dikeluarkan.

10. Dengan ini, **Pekeliling KPK Bil. 7/2011 yang dikeluarkan pada 14 November 2011 adalah terbatal.**

PERTANYAAN

11. Sebarang pertanyaan mengenai pelaksanaan Pekeliling ini boleh dikemukakan kepada :-

URUSETIA JAWATANKUASA KEBANGSAAN ETIKA PENYELIDIKAN DAN TERAPI SEL STEM (NSCERT)

Bahagian Perkembangan Perubatan

Kementerian Kesihatan Malaysia

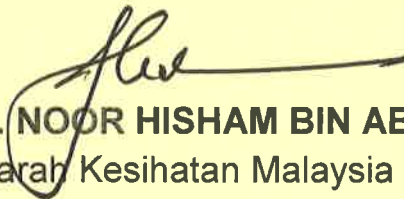
Aras 5, Blok E1, Parcel E, Kompleks Kerajaan Persekutuan
62590 Putrajaya

Tel : 03-88831153 atau 03-88831161 , Fax : 03-88831155

Sekian dan terima kasih.

“BERKHIDMAT UNTUK NEGARA”

Yang Ukhlas,



DATUK DR. NOOR HISHAM BIN ABDULLAH

Ketua Pengarah Kesihatan Malaysia

- s.k
- Ketua Setiausaha Kementerian Kesihatan Malaysia
 - Timbalan Ketua Pengarah Kesihatan Malaysia (Perubatan)
 - Timbalan Ketua Pengarah Kesihatan Malaysia (Kesihatan Awam)
 - Timbalan Ketua Pengarah Kesihatan Malaysia (Penyelidikan dan Sokongan Teknikal)
 - Pengarah Amalan Perubatan, Bahagian Amalan Perubatan KKM
 - Pengarah Biro Pengawalan Farmaseutikal Kebangsaan, KKM
 - Semua Ketua Perkhidmatan Kepakaran / Subkepakaran

SENARAI EDARAN

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Perlis

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Kedah

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Pulau Pinang

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Perak

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Selangor

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Sembilan

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Melaka

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Johor

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Pahang

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Terengganu

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Kelantan

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Sabah

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Sarawak

Pengarah Kesihatan Negeri
Jabatan Kesihatan Negeri Wilayah Persekutuan Kuala Lumpur / Putrajaya /
Labuan

Semua Pengarah Hospital KKM

Semua Pengarah Hospital Universiti

Pengarah Institut Penyelidikan Perubatan

Pengarah Pusat Penyelidikan Klinikal

Pengerusi

Jawatankuasa Etika dan Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

Pengerusi

Joint Ethics Committee of School of Pharmaceutical Sciences
Universiti Sains Malaysia

Pengerusi

Ethics Committee
Kuliyah of Medicine
International Islamic University Malaysia
Kuantan, Pahang

Pengerusi

Jawatankuasa Penyelidikan & Etika Penyelidikan Perubatan
Pusat Perubatan UKM

Pengerusi

Joint Penang Independent Ethics Committee
Gleneagles Medical Centre, Penang.

Pengerusi

International Medical University Joint Committee of the Research and Ethics
Committee
International Medical University

Pengerusi

Jawatankuasa Etika Penyelidikan Institut Jantung Negara
Institut Jantung Negara

Pengerusi

Jawatankuasa Etika Penyelidikan Universiti Teknologi MARA
Institut Pengurusan Penyelidikan
Universiti Teknologi MARA
Shah Alam Selangor

Pengerusi
Jawatankuasa Etika Untuk Penyelidikan Yang Melibatkan Manusia
Universiti Putra Malaysia

Pengerusi
Jawatankuasa Etika Perubatan
Pusat Perubatan Universiti Malaya

Pengerusi
Jawatankuasa Etika Penyelidikan (Manusia)
Universiti Sains Malaysia
Pejabat Pelantar Penyelidikan Sains Klinikal
Kubang Kerian, Kelantan

Pengerusi
Independent Ethics Committee Sime Darby Healthcare
Sime Darby Medical Centre Subang Jaya

Pengerusi
Sunway Medical Centre Independent Research Ethics Committee
Sunway Medical Centre Berhad

Lampiran 1

CHECKLIST FOR RESEARCH ON STEM CELL AND CELL-BASED THERAPIES

Phase/Process	Key requirements	Researcher (Please tick ✓)	Secretariat MREC (Please tick ✓)
1. Pre-clinical studies (investigators must show their own data and not from other laboratories)	<ul style="list-style-type: none"> Approval letter from animal ethics committee is recommended 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Accreditation of animal research facility in institution requiring GLP compliance 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Evidence that the pre-clinical studies was subjected to rigorous and independent peer review and regulatory oversight 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Safety data in small animals 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Safety data in large animals 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Comprehensive toxicology data in small animals (including contamination, acute infusional toxicity, deleterious immune responses, unexpected behavior of the cellular product, and tumorigenesis) 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Comprehensive toxicology data in large animals (including risks of contamination, acute infusional toxicity, deleterious immune responses, unexpected behavior of the cellular product, and tumorigenesis) 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Proof of principle of the desired effect (that the cells have repaired the damage/disease) – unequivocal efficacy data 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Show biological distribution data 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Show evidence of physiologic integration and long-lived tissue reconstitution 	<input type="checkbox"/>	<input type="checkbox"/>
<ul style="list-style-type: none"> Show that differentiation (either <i>in vitro</i> before transplantation or <i>in vivo</i> after transplantation) occur only along the desired lineages 	<input type="checkbox"/>	<input type="checkbox"/>	
	<ul style="list-style-type: none"> Design based on clinical expectations 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Mechanistic studies to show biology (done by the group) 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> GLP compliant 	<input type="checkbox"/>	<input type="checkbox"/>

Lampiran 1

CHECKLIST FOR RESEARCH ON STEM CELL AND CELL-BASED THERAPIES

Phase/Process	Key requirements	Researcher (Please tick ✓)	Secretariat MREC (Please tick ✓)
	<ul style="list-style-type: none"> Evidence that the pre-clinical data has been submitted to the NPCB 	<input type="checkbox"/>	<input type="checkbox"/>
2. Phase I trials	<ul style="list-style-type: none"> Comprehensive pre-clinical studies have been done and data showed safety and efficacy in animals (performed by the group) is recommended 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Procedures on how the cells be tracked in terms of homing to the target area, viability and longevity of the cells 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Procedures on how the safety be monitored 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Procedures to assess risks of tumorigenicity by an independent body must be implemented 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Procedures to assess short, medium and long term side effects 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> GCP compliance 	<input type="checkbox"/>	<input type="checkbox"/>
3. Phase II trials	<ul style="list-style-type: none"> Data from Phase I trials (performed by the group themselves and if the trial is not performed by the group, explain why the data should be used for this trial) 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Procedures on how the cells be tracked in terms of homing to the target area and viability of the cells 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Optimisation of dose, route, regimen, patient population, endpoints, and controlled 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Procedures on how the safety be monitored 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Independent data safety monitoring board 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Plan to assess short, medium and long term side effects 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> GCP compliance 	<input type="checkbox"/>	<input type="checkbox"/>

CHECKLIST FOR RESEARCH ON STEM CELL AND CELL-BASED THERAPIES

4. Phase III trials	• Data from Phase II trials (performed by the group themselves)	<input type="checkbox"/>	<input type="checkbox"/>
	• Design to show safety and efficacy	<input type="checkbox"/>	<input type="checkbox"/>
	• Independent data safety monitoring board	<input type="checkbox"/>	<input type="checkbox"/>
	• GCP compliance	<input type="checkbox"/>	<input type="checkbox"/>
	• Conduct 'randomised' control	<input type="checkbox"/>	<input type="checkbox"/>
5. Cell processing and manufacturing	• Evidence by a letter of conformance for GMP compliance and issued by relevant authority	<input type="checkbox"/>	<input type="checkbox"/>
	• Show evidence of relevant processes: Standard operating procedures, quality standards, environmental control, equipment qualification, analytical methods, audits, staff training, etc.	<input type="checkbox"/>	<input type="checkbox"/>
	• Cell processing and manufacture of any product must be conducted under scrupulous, expert, and independent review	<input type="checkbox"/>	<input type="checkbox"/>
	• Demonstrate that the product is safe, pure and potent	<input type="checkbox"/>	<input type="checkbox"/>
6. Product registration	• Show that the product has been registered with the National Pharmaceutical Control Bureau before use in human trials	<input type="checkbox"/>	<input type="checkbox"/>
	• License for clinical trial has been obtained	<input type="checkbox"/>	<input type="checkbox"/>
7. Cell characterization (pre-requisite to clinical trials)	• History of the cells in the stem cell or cell-based product	<input type="checkbox"/>	<input type="checkbox"/>
	• Biological characterisation of cell type	<input type="checkbox"/>	<input type="checkbox"/>
	• Demonstration of purity	<input type="checkbox"/>	<input type="checkbox"/>
	• Demonstration of potency (e.g. cells produce insulin in a physiological manner)	<input type="checkbox"/>	<input type="checkbox"/>
	• Manufacturing standards and independent certification, where relevant	<input type="checkbox"/>	<input type="checkbox"/>
	• Evidence that cells are free from contamination	<input type="checkbox"/>	<input type="checkbox"/>

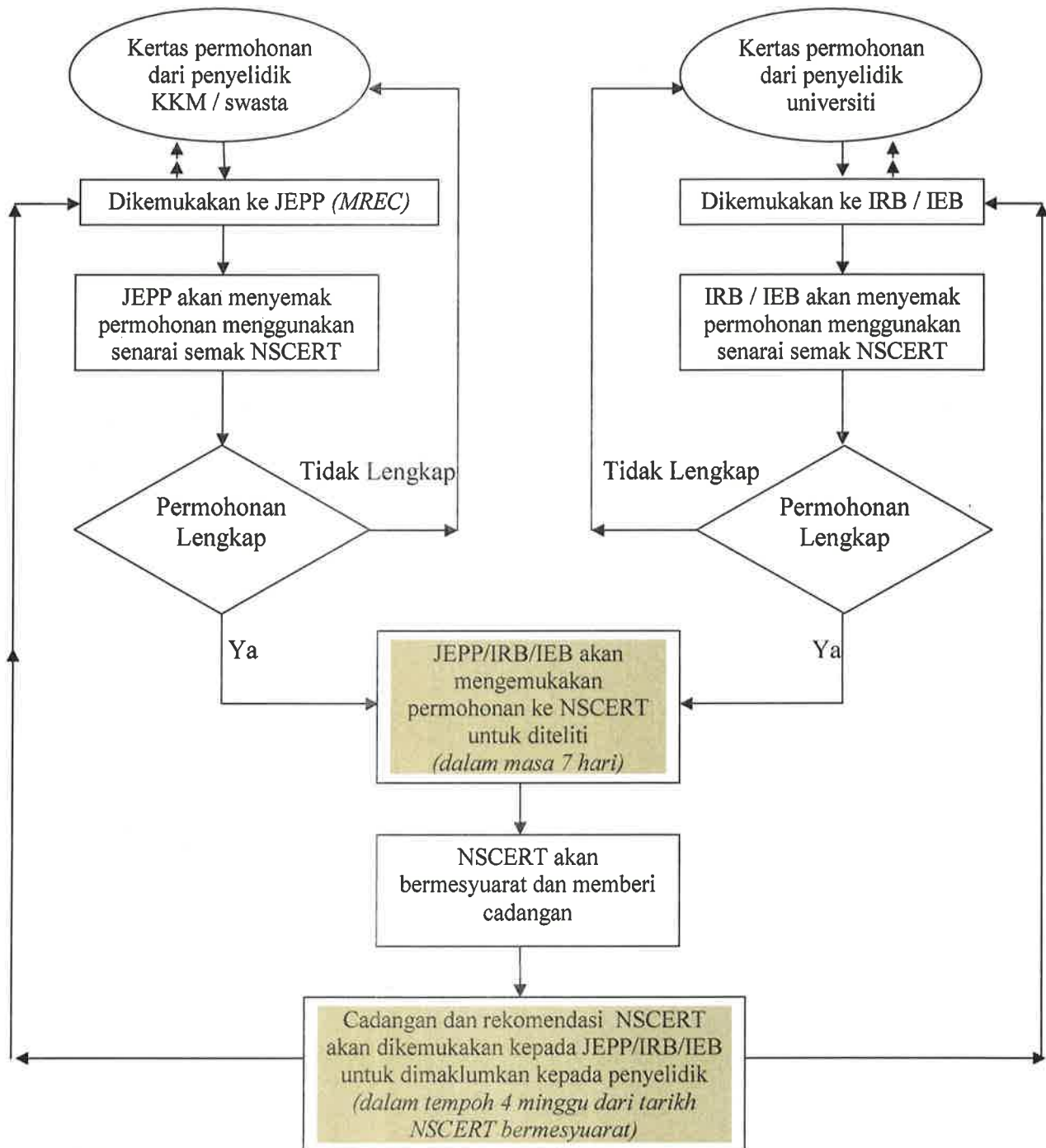
Lampiran 1

CHECKLIST FOR RESEARCH ON STEM CELL AND CELL-BASED THERAPIES

	<ul style="list-style-type: none"> Evidence of viability and longevity of cells after transplantation (to determine the likely duration of the therapeutic effect) 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Evidence that cells will home into the area of damage or repair 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Evidence of genomic stability during culture 	<input type="checkbox"/>	<input type="checkbox"/>
8. Investigators and researchers	<ul style="list-style-type: none"> Is the Principal Investigator trained in cell transplantation? (Show evidence of credentialing) 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Are other investigators trained in cell transplantation? (Show evidence of credentialing) 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Qualifications of scientists and researchers 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Registration with National Medical Research Register, Ministry of Health (MOH) 	<input type="checkbox"/>	<input type="checkbox"/>
9. Centres performing therapy (Information for patients)	<ul style="list-style-type: none"> Registration with PHCFS Act, Ministry of Health 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Informing subjects about the human embryonic cell source, if applicable 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> The unique risks; and disclose honestly that the treatment have not been tried before 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Utmost clarity on the potential benefit 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Disclosing financial and non-financial conflicts of interest 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Provide monitoring patients long term 	<input type="checkbox"/>	<input type="checkbox"/>
	<ul style="list-style-type: none"> Providing a clear, timely, and effective plan for adverse event reporting 	<input type="checkbox"/>	<input type="checkbox"/>

Lampiran 2

PROSEDUR PERMOHONAN BERKAITAN PENYELIDIKAN SEL STEM DAN CELL-BASED THERAPIES



Nota :

NSCERT – Jawatankuasa Kebangsaan Etika Penyelidikan dan Terapi Sel Stem

JEPP (MREC) – Jawatankuasa Etika Penyelidikan Perubatan KKM

IRB / IEB – Institutional Review Board / Institutional Ethical Board