



Research Ethics Policy in USM

*Professor Dr Nor Hayati Othman
Director, Centre for Research Initiatives
(Clinical & Health Sciences)*

USM



All Acts begins with (mis)Actions

.....

UK - Human tissue law

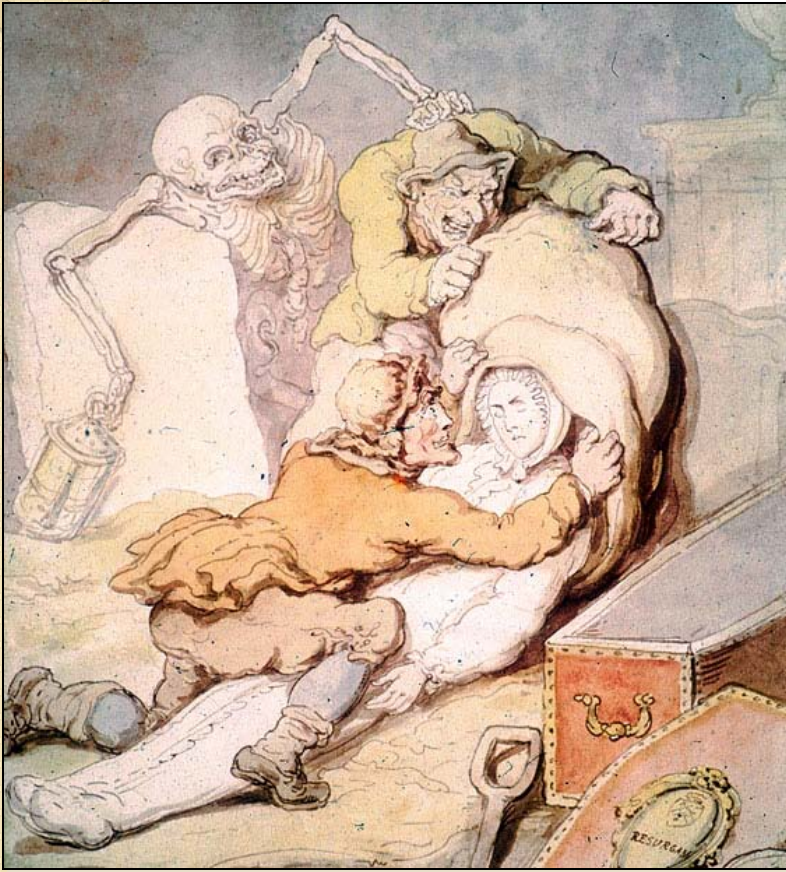


The Reward of Cruelty (William Hogarth)

- Murder Act 1752
 - Corpses of executed murderers could be used for dissection

Source: JCE Underwood -*Human tissue: the matter of life and death*

UK - Human tissue law



The Resurrectionists (Thomas Rowlandson)

- Murder Act 1752
- Anatomy Act 1832
 - Lawful to use unclaimed corpses
 - Consented donation
 - Licensed anatomists

Source: JCE Underwood -*Human tissue: the matter of life and death*

UK - Human tissue law



Limb transplantation by
Saints Cosmas and Damian

- Murder Act 1752
- Anatomy Act 1832
- Human Tissue Act 1961
 - Lawful to use tissue after death for treatment, education or research if no relative objects

Source: JCE Underwood -*Human tissue:
the matter of life and death*

UK - Human tissue law



- Murder Act 1752
- Anatomy Act 1832
- Human Tissue Act 1961
- Human Tissue Act 2004
 - The living and the dead
 - The “golden thread” of consent
 - Regulation by licensing

Source: JCE Underwood -Human tissue:
the matter of life and death

UK - Human tissue law



- Murder Act 1752
- Anatomy Act 1832
- Human Tissue Act 1961
- Human Tissue Act 2004
- Coroners (Amendment) Rules 2005
 - Coroner must inform relatives about retention
 - Relatives choose to donate or discard

Source: JCE Underwood -*Human tissue: the matter of life and death*

Supreme scientist of South Korea

TIME

Person of the Year

Year In Pictures

Best & Worst

CNN's Year In Review

Search

PEOPLE WHO MATTERED 2004

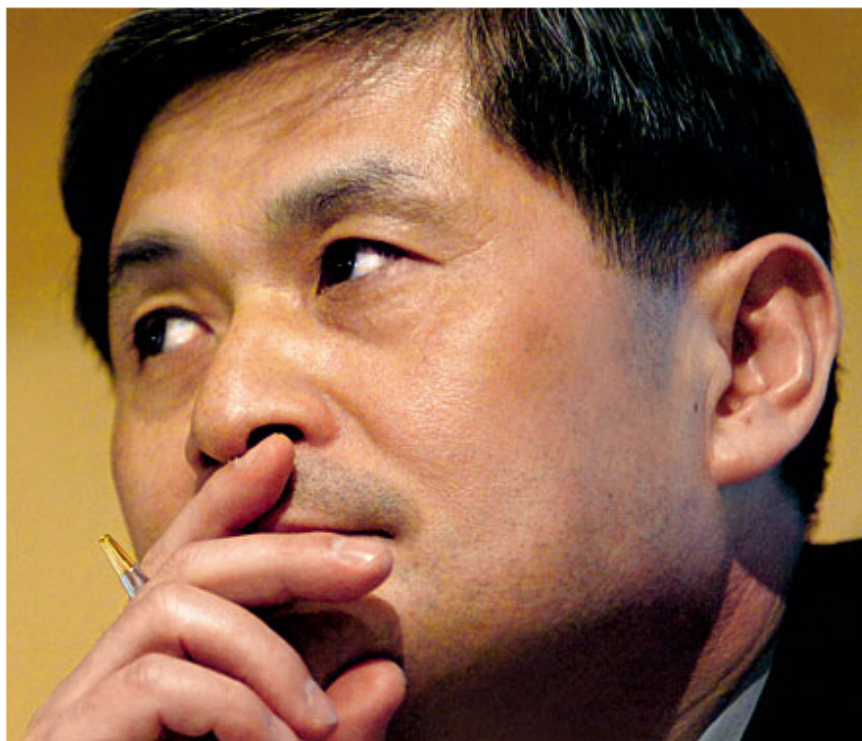
TIME

THIS YEAR'S CHOICE

PEOPLE WHO MATTERED

IN MEMORIAM

PAST CHOICES



PHOTOGRAPH BY RON WURZER / GETTY IMAGES

Dr. Hwang Woo Suk

A veterinarian by training, Hwang began to research cloning for a practical purpose: he wanted to create a better cow. But his work didn't stop in the barnyard. Hwang and his team at Seoul National University became the first to clone human embryos capable of yielding viable stem cells that might one day cure countless diseases. While such research raises troubling ethical questions, Hwang has already proved that human cloning is no longer science fiction, but a fact of life.

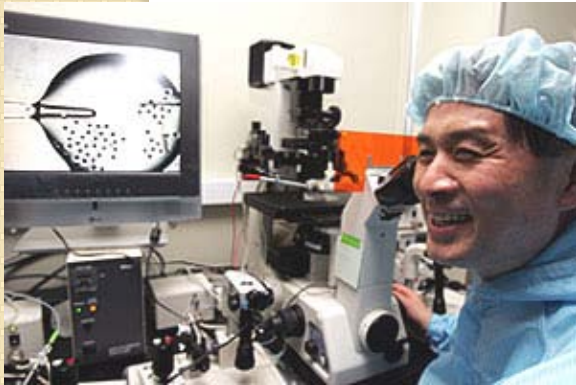
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Hwang "has already proved that human cloning is no longer science fiction, but a fact of life."



1. February 1999 -cloned dairy cow, *Yeongrong-i*
[failed to provide scientifically verifiable data]
2. April 1999, cloned a Korean cow, *Jin-i*
[did not provide scientifically verifiable data]
3. claimed to have created a BSE-resistant cow, which
hasn't been verified yet
4. August 3, 2005, Hwang and his team of researchers
became the first team to successfully clone a dog,
an Afghan Hound, named Snuppy.





Snuppy with creator



Glory days.....



The beginning of the end.....

1. In February 2004, Hwang successfully created an embryonic stem cell with the somatic cell nuclear transfer method, [242 eggs to create a single cell line] -- published their paper in the March 12 issue of *Science*.
2. May 2005 claimed created 11 human embryonic stem cells using 185 eggs. His work, published in the June 17 issue of *Science*

The controversies

- Close scrutiny revealed that several of the photos of purportedly different cells were in fact photos of the same cell
- “...*certain elements of the report may be fabricated*”.
...
- Roh Sung-il, who collaborated on that paper, stated to media outlets that nine of those eleven lines had been faked
- *Nature* raised possibility that the eggs were provided by lab co-workers [RO under coercion]

W. S. Hwang et al. *Science* 303, 1669–1674; 2004

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Originally published in *Science Express* on 12 February 2004
Science 12 March 2004:
Vol. 303, no. 5664, pp. 1669 - 1674
DOI: 10.1126/science.1094515

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REPORTS
This article has been retracted

Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst

Woo Suk Hwang,^{1,2*} Young June Ryu,¹ Jong Hyuk Park,³ Eul Soon Park,¹ Eu Gene Lee,¹ Ja Min Koo,⁴ Hyun Yong Jeon,¹ Byeong Chun Lee,¹ Sung Keun Kang,¹ Sun Jong Kim,³ Curie Ahn,⁵ Jung Hye Hwang,⁶ Ky Young Park,⁷ Jose B. Cibelli,⁸ Shin Yong Moon^{5*}

Somatic cell nuclear transfer (SCNT) technology has recently been used to generate animals with a common genetic composition. In this study, we report the derivation of a pluripotent embryonic stem (ES) cell line (SCNT-hES-1) from a cloned human blastocyst. The SCNT-hES-1 cells displayed typical ES cell morphology and cell surface markers and were capable of differentiating into embryoid bodies in vitro and of forming teratomas in vivo containing cell derivatives from all three embryonic germ layers in severe combined immunodeficient mice. After continuous proliferation for more than 70 passages, SCNT-hES-1 cells maintained normal karyotypes and were genetically identical to the somatic nuclear donor cells. Although we cannot completely exclude the possibility that the cells had a parthenogenetic origin, imprinting analyses support a SCNT origin of the derived human ES cells.

¹ College of Veterinary Medicine, Seoul National University, Seoul 151-742, Korea.
² School of Agricultural Biotechnology, Seoul National University, Seoul 151-742, Korea.

W. S. Hwang et al. *Science* **308**, 1777–1783; 2005

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Originally published in *Science Express* on 19 May 2005
Science 17 June 2005:
Vol. 308, no. 5729, pp. 1777 - 1783
DOI: 10.1126/science.1112286

REPORTS
This article has been retracted

Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts
Woo Suk Hwang,^{1,2*} Sung Il Roh,³ Byeong Chun Lee,¹ Sung Keun Kang,¹ Dae Kee Kwon,¹ Sue Kim,¹ Sun Jong Kim,³ Sun Woo Park,¹ Hee Sun Kwon,¹ Chang Kyu Lee,² Jung Bok Lee,³ Jin Mee Kim,³ Curie Ahn,⁴ Sun Ha Paek,⁴ Sang Sik Chang,⁵ Jung Jin Koo,⁵ Hyun Soo Yoon,⁶ Jung Hye Hwang,⁶ ~~Youn Young Hwang,~~⁶ Ye Soo Park,⁶ Sun Kyung Oh,⁴ Hee Sun Kim,⁴ Jong Hyuk Park,⁷ Shin Yong Moon,⁴ **Gerald Schatten**^{8*}

Patient-specific, immune-matched human embryonic stem cells (hESCs) are anticipated to be of great biomedical importance for studies of disease and development and to advance clinical deliberations regarding stem cell transplantation. Eleven hESC lines were established by somatic cell nuclear transfer (SCNT) of skin cells from patients with disease or injury into donated oocytes. These lines, nuclear transfer (NT)-hESCs, grown on human feeders from the same NT donor or from genetically unrelated individuals, were established at high rates, regardless of NT donor sex or age. NT-hESCs were pluripotent, chromosomally normal, and matched the NT patient's DNA. The major histocompatibility complex identity of each NT-hESC when compared to the patient's own showed immunological compatibility, which is important for eventual transplantation. With the generation of these NT-hESCs, evaluations of genetic and epigenetic stability can be made. Additional work remains to be done regarding the development of reliable directed differentiation and the elimination of remaining animal components. Before clinical

1. **Gerald P. Schatten** is a stem cell researcher at the University of Pittsburgh
2. Broke off his 20 month collaboration with Hwang Woo-suk, commented that *"my decision is grounded solely on concerns regarding oocyte (egg) donations in Dr. Hwang's research reported in 2004."*
3. He requested editors of *Science* to remove his name from a joint paper he wrote with Hwang (and 23 other co-authors) in June 2005
4. He had previously run afoul of controversy twice before in the 1990s when it was found out that he had used eggs obtained illegally by University of California researchers and at the University of Wisconsin.



1. The University of Pittsburgh withdrew \$16 million NIH grants awarded to Hwang's co-author, Gerald Schatten, on the basis of the research that is now known to be fraudulent
2. Allegations against Schatten
 1. Involved in laboratory-related misconduct
 2. Illegally procured eggs by fertility doctors at the University of California-Irvine.
 3. Investigated for three "miscommunications" that included a "misstatement"

Before that there was Dolly.....

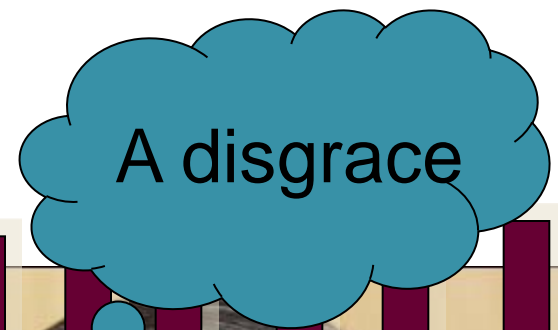
1997, **Ian Wilmut** - created the first cloned mammal; a lamb named Dolly, at Roslin Institute laboratory in Edinburgh. He was awarded the Paul Ehrlich Prize Ludwig Darmstaedter Prize

2005- he admitted in court that he did not exactly clone the first sheep.

He explained that he had a "non-trivial" supervisory role, but that "66 per cent" of the credit belonged to his official co-author, **Keith Campbell**, who left Roslin soon after the event, reportedly unhappy at the assignment of credit.



1. A disciplinary committee at Seoul National University fired him and cut his pension in half.
2. The Korean Society for Molecular and Cellular Biology expelled him,
3. Health Ministry removed his license to conduct embryonic stem cell research (which means that no one is allowed to do human cloning research in South Korea at present).
4. Hwang admitted wrong-doing and apologized. ***"I did not follow the procedures that a scientist should follow and I was driven by greed,"***
5. Ministry of Science and Technology, stripped him of the title "Supreme Scientist," which was worth up to \$3 million a year for five years.



▲ 황우석 박사(오대일 기자/노컷뉴스)

Lessons from Hwang's story -Ethics violations

- In 2009, Hwang was convicted of embezzling research funds
- Illegally buying human eggs for his research.
- Dubious manner in which the team persuaded women to donate their eggs (oocytes) for research.
- Many of the women who provided eggs had not given valid, informed consent
- Nearly 75% of them reported that they were given cash or enticed by various financial incentives (Baylis 2009).



**The world suspended cloning
research temporarily**

Key points in ethical research

- Researchers must have Integrity
- Research protocol must be scientifically sound
- Reason to do research must be justified
- If patients are used :
 - fully informed consent must be obtained
 - Confidentiality maintained
 - Anonymity preserved
- When publishing findings – adhere to ethical guidelines

Research ethics policy in USM

- All studies involving humans [including obtaining human data from registry] must get ethical approval
- Studies by USM researchers must get approval from USM REC [JEPeM]
- [Jawatan Kuasa Etika Penyelidikan Manusia USM]
- Members of JEPeM are appointed by VC
- The Committee adopts research ethics guidelines outlined by the Helsinki Declaration based on Nuremberg Code agreed by the World Medical Association and CIOMS (Council for International Organizations of Medical Sciences).

WORLD MEDICAL ASSOCIATION: DECLARATION OF HELSINKI

[Adopted 1964, last amended 2000]

Some important paragraphs:

- Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.
- In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
- Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights.
- The subjects must be volunteers and informed participants in the research project.
- The right of research subjects to safeguard their integrity must always be respected.

Role of the Ethics review board

- Uphold the principles of research ethics
 - Ensure compliance to regulations and policies
 - Constructive review – ethical and scientific
 - *Membantu bukan Membantut*
 - Education of research community
 - Monitoring of data
 - Continuing review ...SAE
- ➔ Facilitate SAFE and ETHICAL research

REC - membership

- According to CIOMS
 - Chairman [neutral, non administrator]
 - Scientists [at least 2]
 - Non-scientist [at least 1]
 - Lady member [at least 1]
 - Lay member [at least 1]
 - Minimum quorum: 5 [chairman, 2 scientists, 1 lay, 1 lady]

JEPeM members - 17 [till 2013]

- Chairman & Co-chairman - Professors
- Members –
 - Clinicians
 - bio-statistician,
 - social scientists
 - Director of Hospital USM [HUSM] or representative
 - Director of Hospital Kota Bharu or representative
 - Lay persons [ex public servants, non science based; lawyer, ustaz]
 - Lady members
 - secretary [Research officer]

History of REC in USM

- 1987 as JKP
- 1994 – renamed JKPE; clinical trials started
- 2002- the only JKPE in USM as the whole campus decided to use ours
- Meet every month [full review; 2X for expedited review]
- 2004 – Registered under Office for Human Research Protections (OHRP) USA till April 2015; **FWA00007718**
- 2007 – moved under CRP and renamed JEPeM

Terms of Reference of JEPeM

To vet and regulate proposals on;

1. Research involving human subjects [patients or normal people]
2. Research involving human samples
3. Research involving data derived from humans
4. Research using products [biological or non-biological] which will be tested on humans

2 types of review :

- expedited review
- deliberated review

Schools applying for ethical approval from JEPeM

- Medical
- Dental
- Health
- Pharmacy
- Arts-based Schools
 - PPSeni: Gamelan on cerebral palsy patients
- IPPT
- Engineering
- Chemistry

Some real eg.....

- **Pusat Pengajian Ilmu Kemanusiaan**
 - Breast, Cervical and Colorectal Cancers: A Geographical Analysis of Case Distribution and Their Relationship with Service Facilities.
- **Pusat Penyelidikan Arkeologi Global**
 - Phylogeography Study of the Aboriginal People in Malaysia.
- **Pusat Pengajian Ilmu Kemanusiaan**
 - A Comparative Analysis of the Experiences of International Students in Malaysia and Australia on University Learning Environment and Support Services: Implications for Sustainable Higher Education.
- **Pusat Pengajian Sains Kemasyarakatan**
 - Sexual Identity and Sexual Behaviour: Case Studies of Gay Men in Penang.
- **Pusat Pengajian Seni**
 - Gamelan Music Therapy: Gross Motor Function in Children with Cerebral Palsy: A Pilot Study.

How JEPeM records the decisions

JEPeM maintains a record of all research protocols received and reviewed, including:

- ▶ Name of responsible institution or organization where the research is carried out;
- ▶ Project identification number(s);
- ▶ Principal researcher(s);
- ▶ Title of project;
- ▶ Ethical approval or non-approval with date;
- ▶ Approval or non-approval of any changes to the protocol;
- ▶ The terms and conditions, if any, of approval of any protocol;

Our. Ref. : USMKK/PPP/JEPeM [263.3.(13)]
 Date : 28th March 2013

Dr. Foo Leng Huat
 School of Health Sciences
 Universiti Sains Malaysia
 16150 Kubang Kerian, Kelantan.

Universiti Sains Malaysia
 Kampus Kesihatan,
 16150 Kubang Kerian,
 Kelantan, Malaysia.
 T: 609 - 767 3000 samb. 2352 / 2362
 F: 609 - 767 2351
 E: jepem.usm@gmail.com
 www.research.usm.my

The Human Research Ethics Committee, Universiti Sains Malaysia (FWA Reg. No: 00007718; IRB Reg. No: 00004494) has approved in principle the study mentioned below:

Title	Influence of Dietary and Lifestyle Practices on Metabolic Syndrome Risk in Middle-Aged Chinese Men and Women of Urban Communities in Kelantan.		
Protocol No	-	Principle Investigator	Dr. Foo Leng Huat
Date of approval Protocol received Reviewed by Committee Received Amended Protocol	28 th March 2013 28 th January 2013 19 th March 2013 21 st March 2013	Co-Investigator(s)	Assoc. Prof. Dr. Azidah Abdul Kadir
Research Center	Kota Bharu, Kelantan.	Date of study start	April 2013 – March 2015
Financial Support	Short Term Grant, USM.	Number of Samples	380 subjects

The following item (✓) have been received and reviewed:-

- (✓) **Ethical Approval Application Form**
- (✓) **Study Protocol**
- (✓) **Participant Information Sheet and Consent Form**
- (✓) **Questionnaires**

Investigator(s) are required to:

- follow instructions, guidelines and requirements of the Human Research Ethics Committee, Universiti Sains Malaysia (JEPeM)
- report any protocol deviations/violations to Human Research Ethics Committee (JEPeM)
- comply with International Conference on Harmonization – Guidelines for Good Clinical Practice (ICH-GCP)
- note that Human Research Ethics Committee (JEPeM) may audit the approved study.


PROFESSOR DR. MOHD SHUKRI OTHMAN
 Chairman
 Human Research Ethics Committee


Date of meeting: 19 March 2013
 Venue : Meeting Room, Centre for Research Initiatives,
 Clinical and Health Sciences, USM Kampus Kesihatan.
 Time : 9.00 a.m – 1.15 p.m
 Meeting No : 263

Universiti Sains Malaysia
 Kampus Kesihatan,
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 Kelantan, Malaysia.
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 F: 609 - 767 2351
 E: jepem.usm@gmail.com
 www.research.usm.my

Members of the Sub Committee of the Human Research Ethics Committee, Universiti Sains Malaysia who reviewed the protocol/documents are as follows:

Member (Title and Name)	Occupation (Designation)	Male/ Female (M/F)	Tick (✓) if present when above items, were reviewed
Chairperson : Professor Dr. Mohd Shukri Othman	Chairman of Human Research Ethics Committee	M	✓ (Chairperson)
Chairperson : Professor Dr. Hans Amin Van Rostenberghe	Chairman of Human Research Ethics Committee	M	✓ (Chairperson)
Secretary II : Mr. Mohd Bazlan Hafidz Mukrim	Research Officer	M	✓
Members :			
1. Associate Professor Dr. Nor Azwany Yaacob	Lecturer, School of Medical Sciences	F	✓
2. Dr. Noraida Ramli	Lecturer, School of Medical Sciences	F	✓
3. Dr. Aniza Abd. Aziz	Lecturer, School of Medical Sciences	F	✓
4. Dr. Wan Nudri Wan Daud	Deputy Director, Pusat Islam Universiti Sains Malaysia	M	✓
5. Tuan Hj. Elias Zakaria	Lecturer, School of Humanities	M	✓
6. Mrs. Zawiah Abu Bakar	Community Representative	F	✓

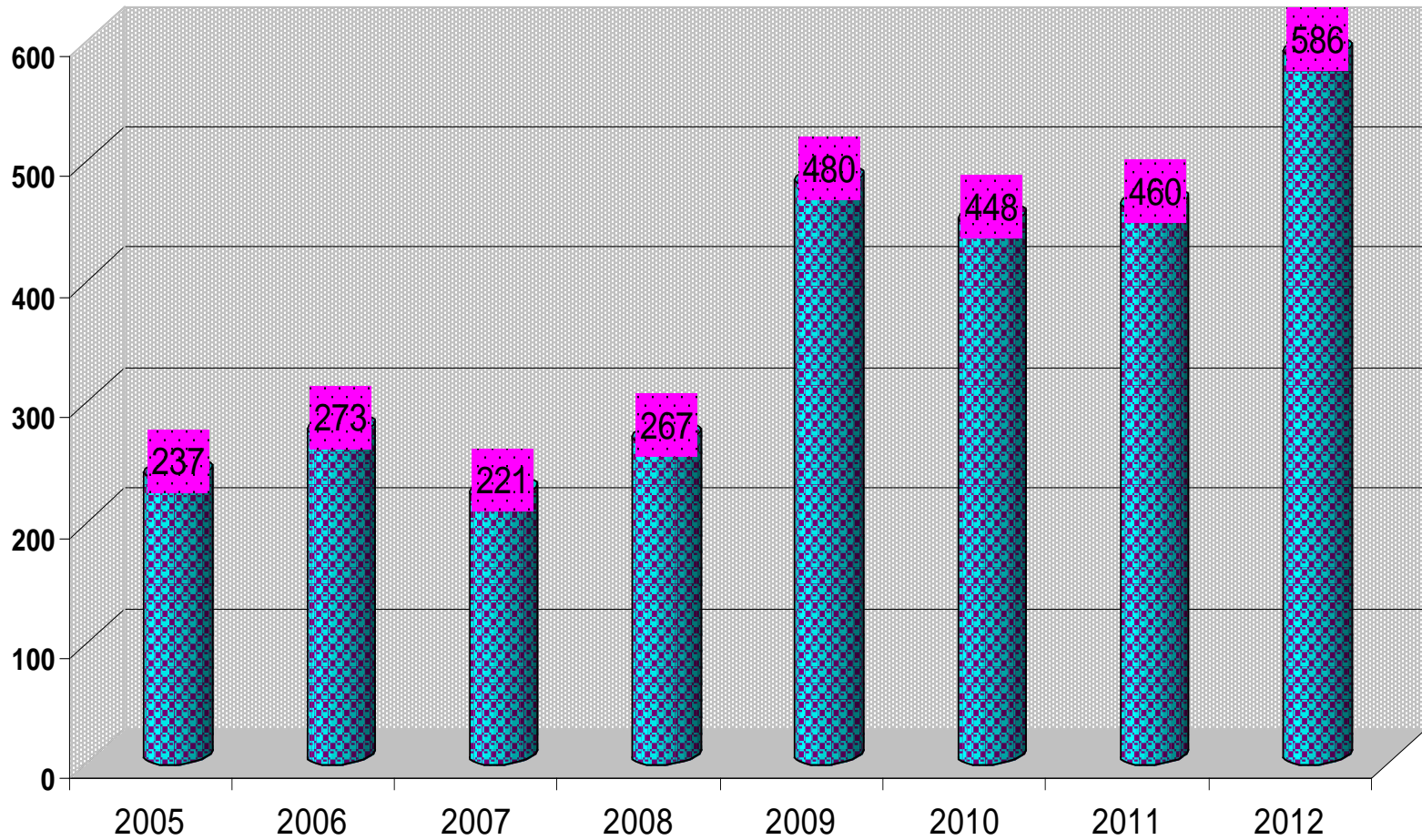
The Human Research Ethics Committee of Universiti Sains Malaysia is in compliance with International Conference on Harmonization–Guidelines for Good Clinical Practice (ICH-GCP) guidelines and Declaration of Helsinki.


PROFESSOR DR. MOHD SHUKRI OTHMAN
 Chairman
 Human Research Ethics Committee



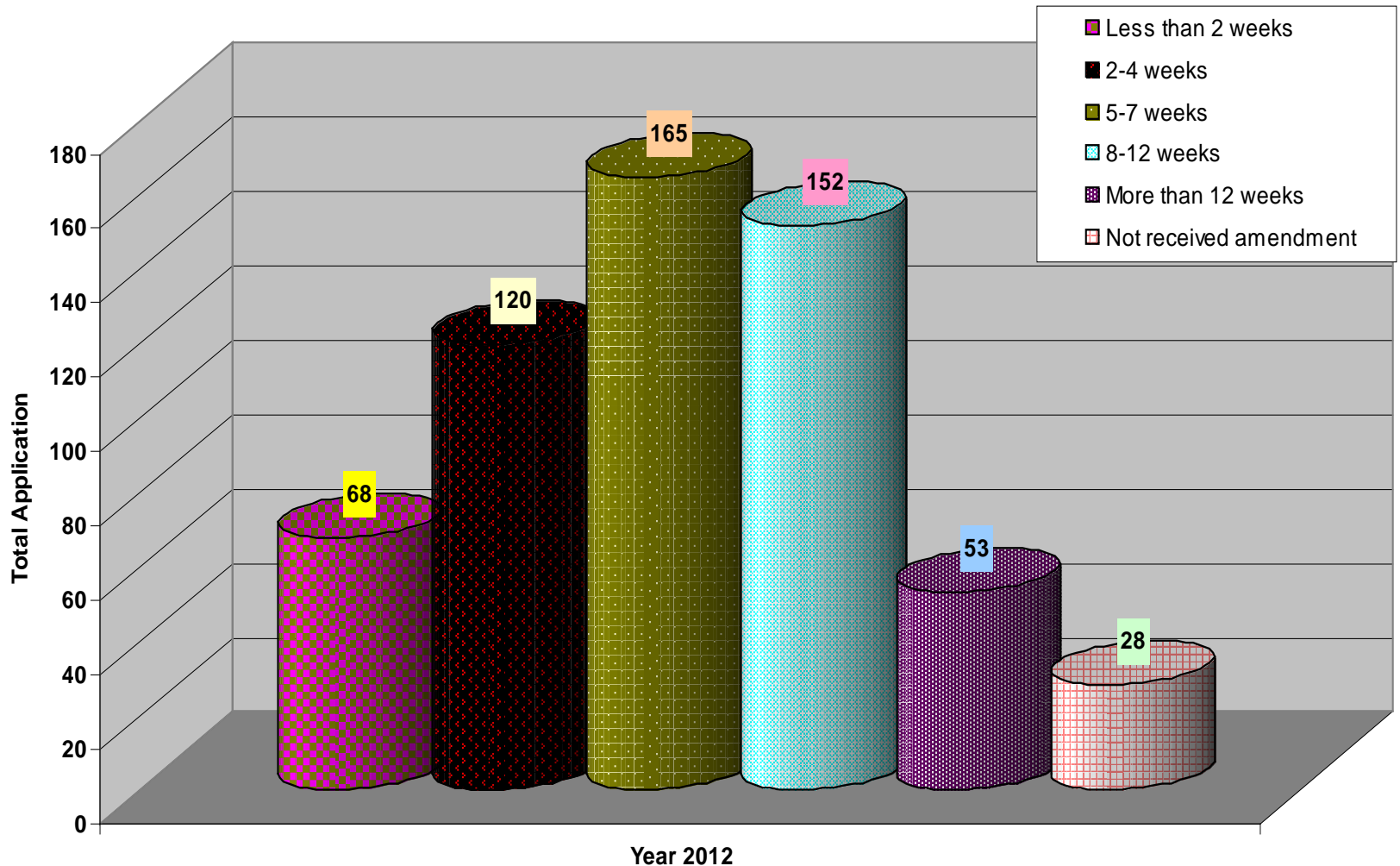
Some statistics.....

Jumlah Permohonan Kelulusan Etika Penyelidikan (Manusia) dari Tahun 2005 sehingga Tahun 2012



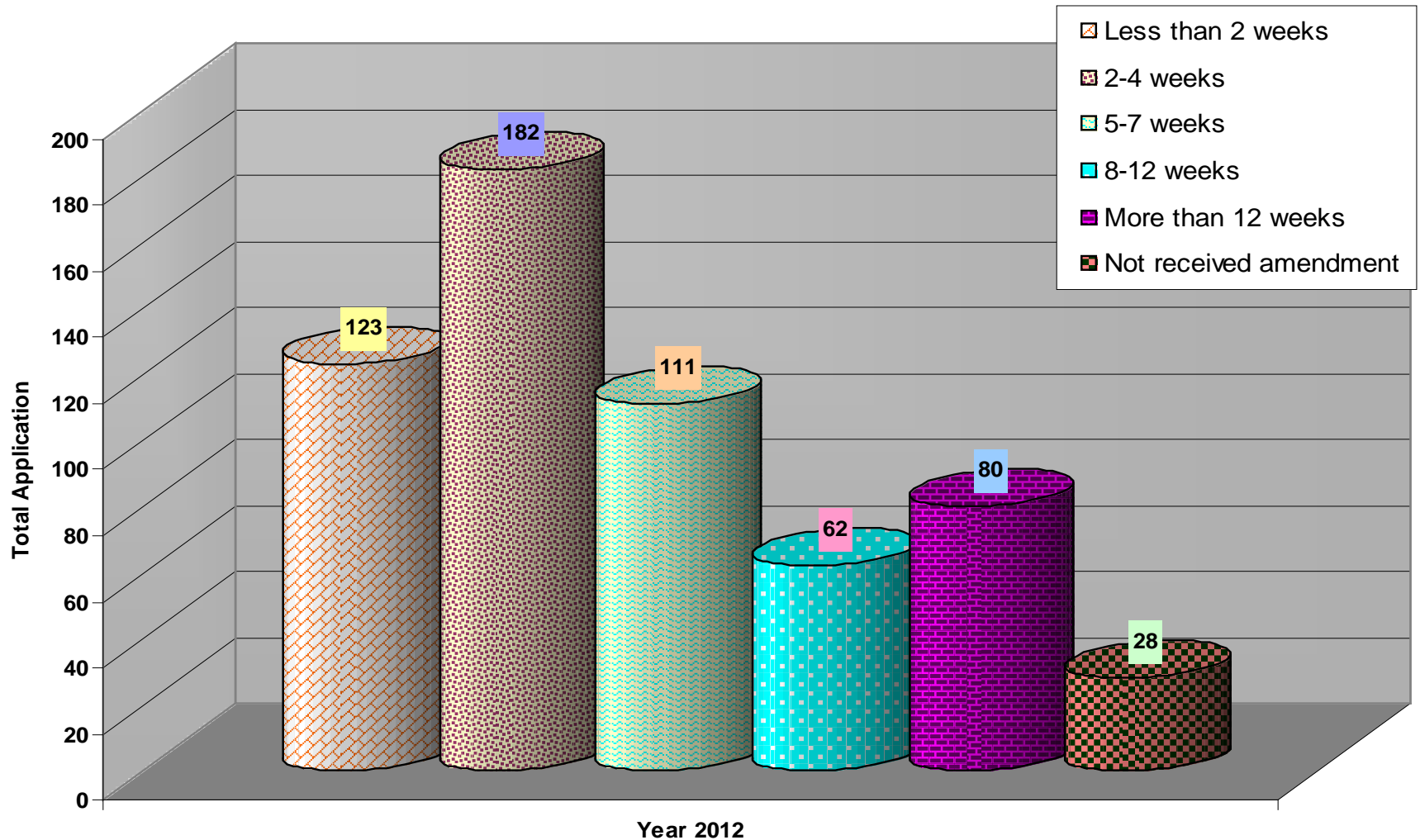
Timeliness 2012 – Tempoh permohonan- tempoh mesyuarat

Timeline of Ethical Approval Applications
- From Date of Submission to CRI-CHS -> Date of JEPeM Meeting -



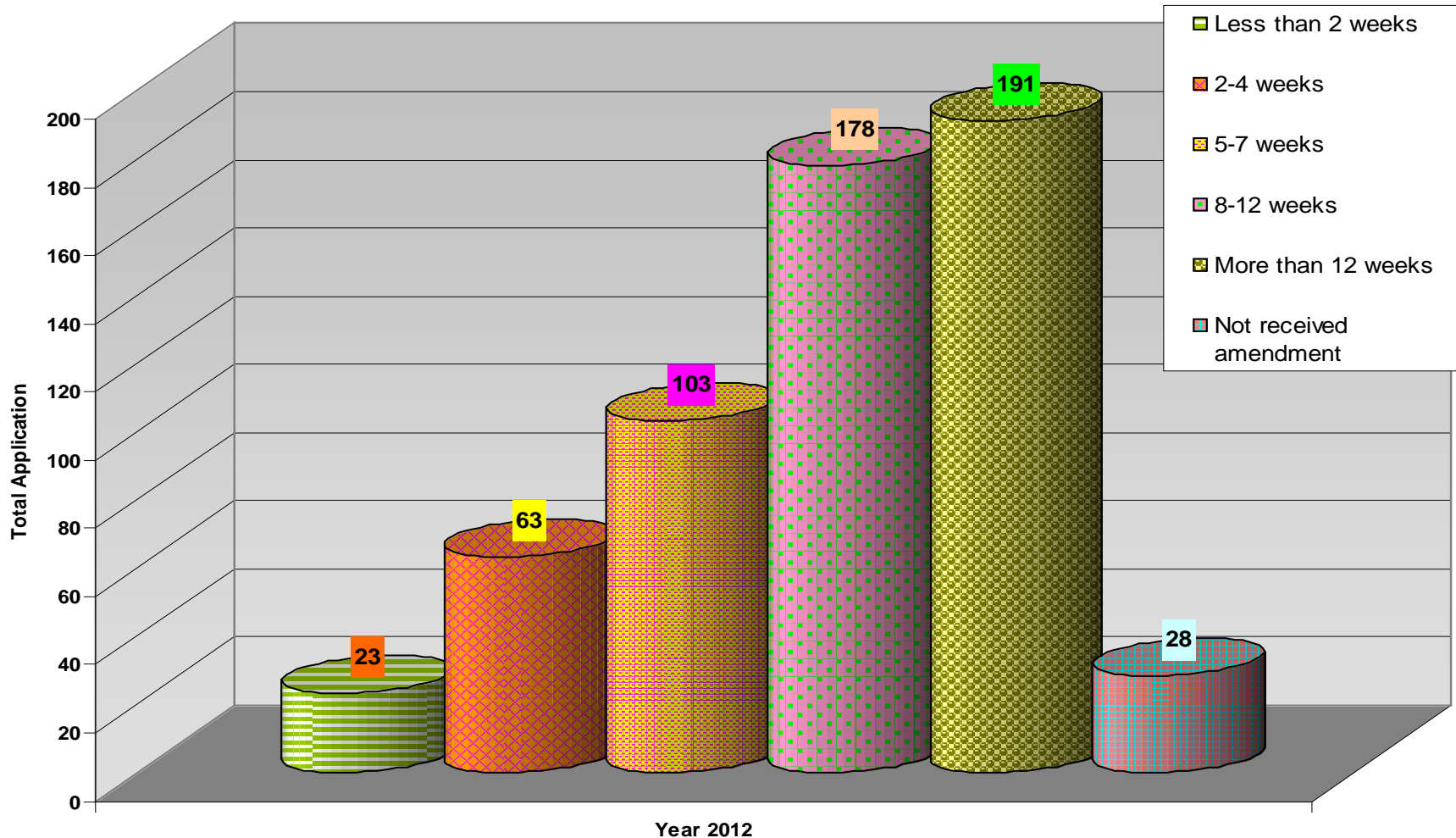
Timeliness 2012 – Tempoh mesyuarat - tempoh kelulusan

Timeline of Ethical Approval Applications
- From Date of JEPeM Meeting -> Issuing of Ethical Approval Letter -

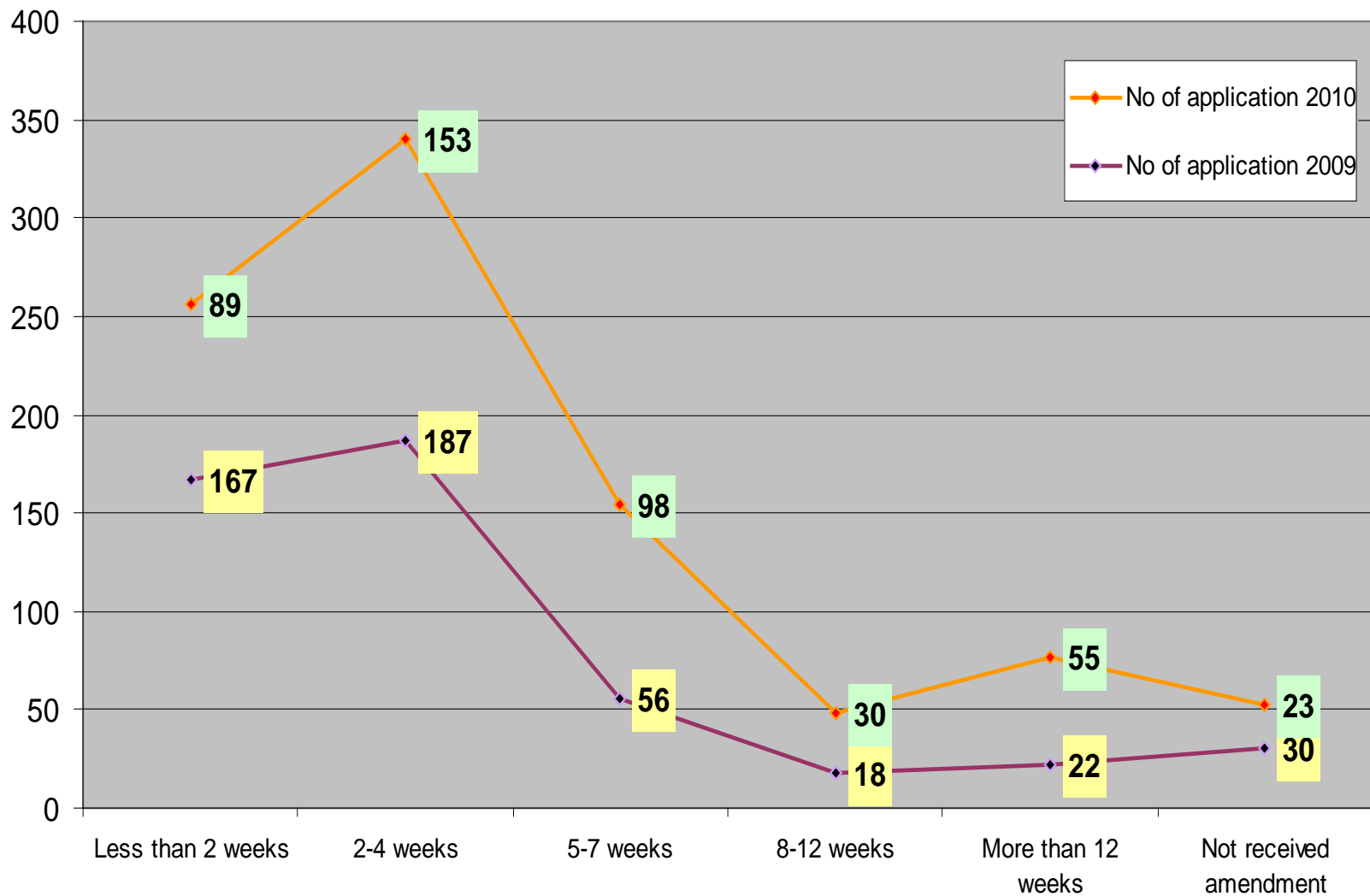


Timeliness 2012 – Tempoh permohonan - tempoh kelulusan

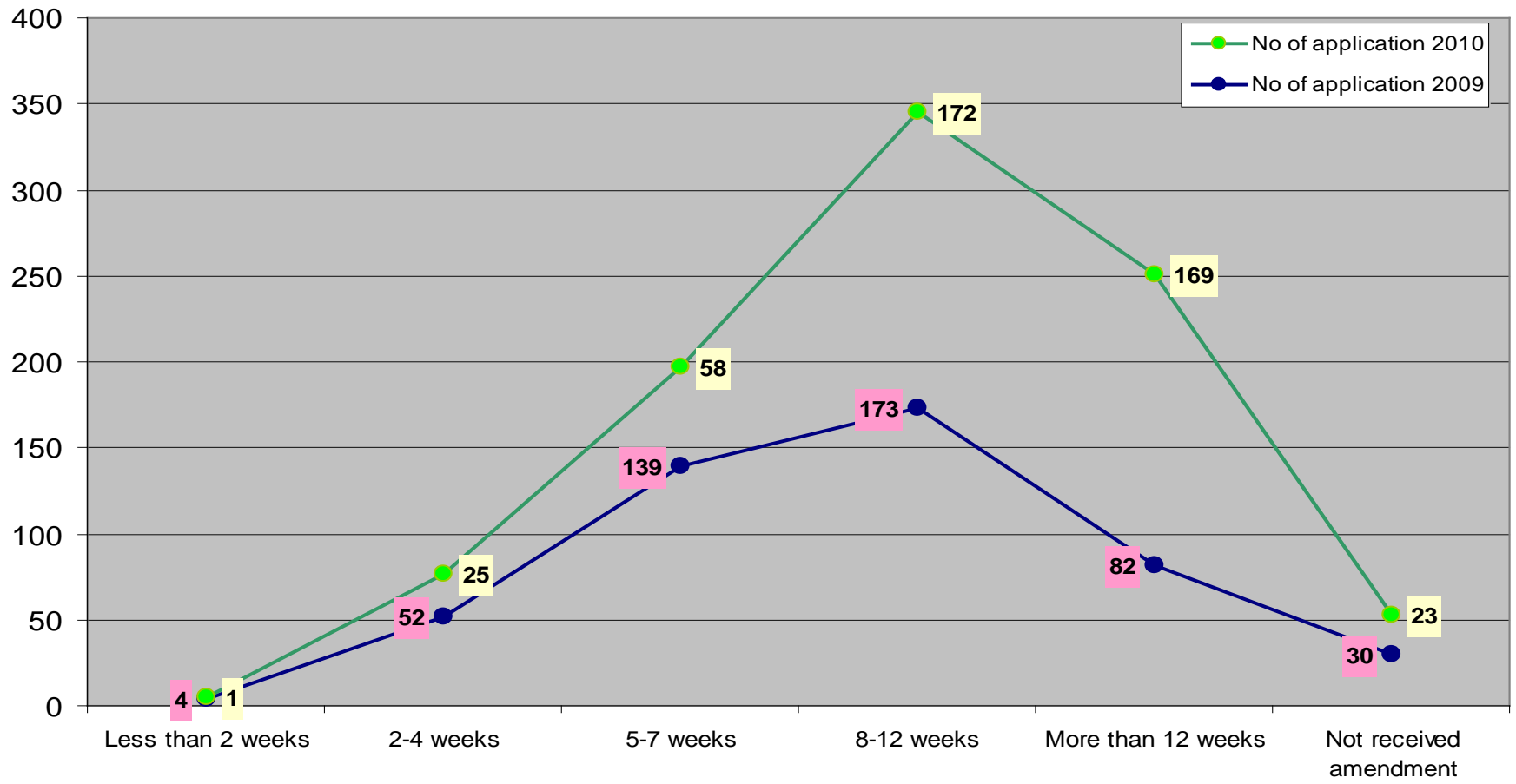
Timelines of Ethical Approval Applications
- From Date of Submission to CRI-CHS -> Issuing of Ethical Approval Letter -



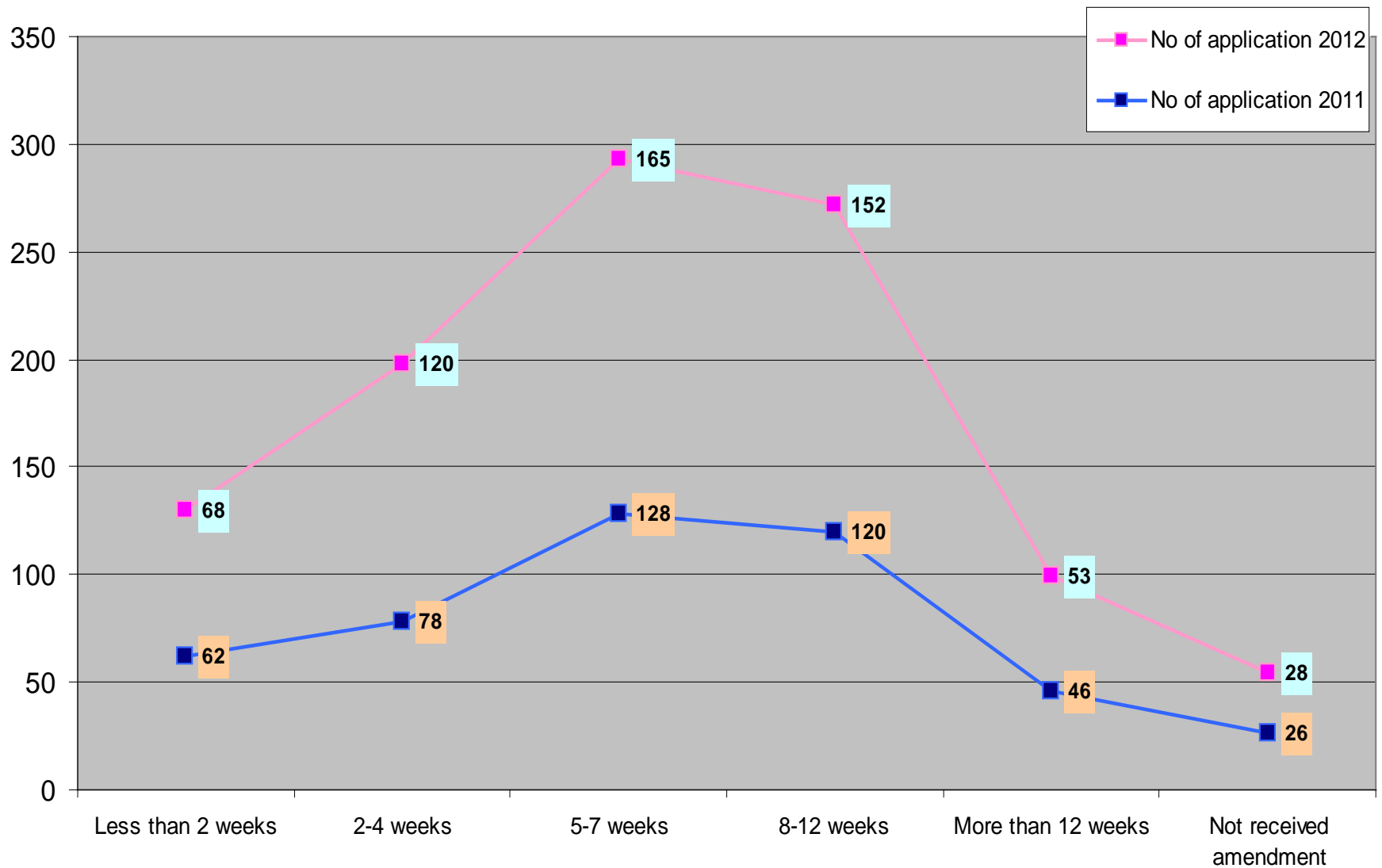
Tempoh mesyuarat JEPeM - tempoh kelulusan (2009 vs 2010)



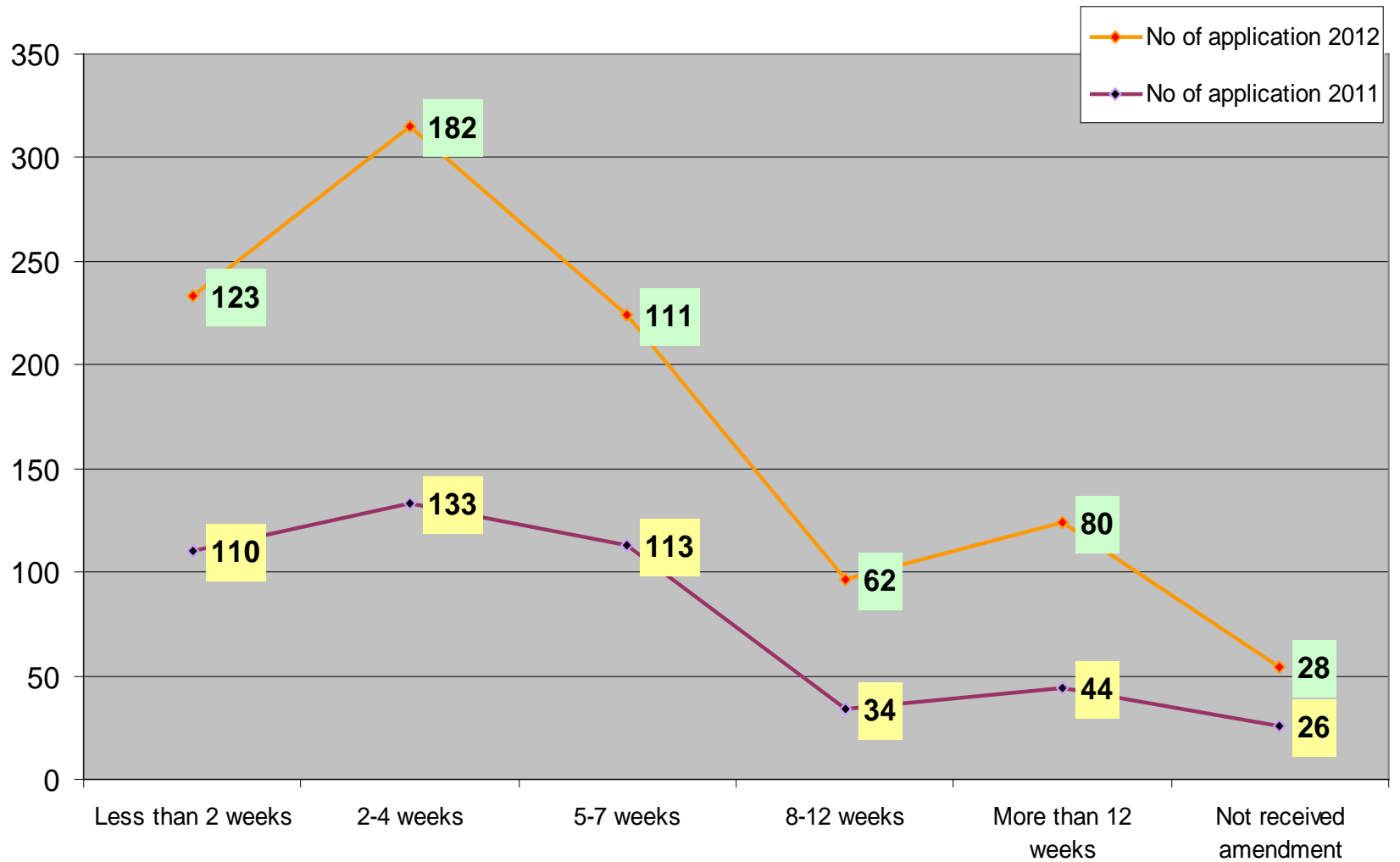
Tempoh permohonan - tempoh kelulusan (2009 vs 2010)



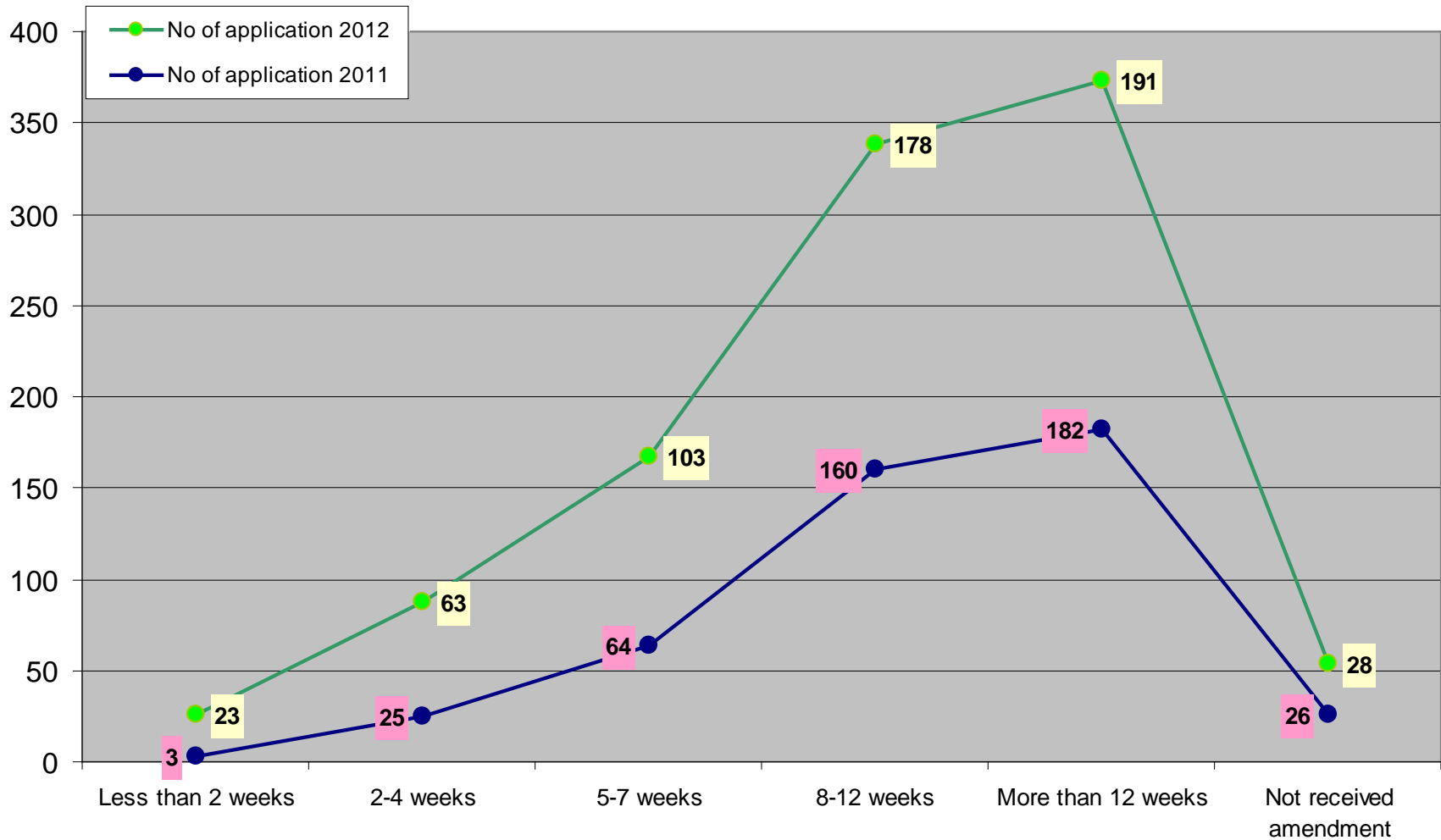
Tempoh permohonan - tempoh mesyuarat JEPeM (2011 vs 2012)



Tempoh mesyuarat JEPeM - tempoh kelulusan (2011 vs 2012)



Tempoh permohonan - tempoh kelulusan (2011 vs 2012)



FAQs

- I am doing a survey, why do I need an ethical approval
- I am only doing small research – no grant is needed thus why do I need to get ethical approval?
- Why should I get ethical approval? – I am only looking at patients folders
- Why do I need ethical approval? – I am only doing observational study
- Where should I get ethical approval? – my study takes place in Taiping
- My co-researcher has already obtained ethical approval from Sabah – I am now doing in Penang
- It is really a harmless study – why do I need to get ethical approval?

Summary

- All proposals involving human requires ethical approval
- Most journals require authors to upload ethical approval certificate
- Arts-based researchers are having increasing awareness on the need to get ethical approval before conducting a study
- Research Ethics committee in USM is JEPeM, secretariat is in Kelantan campus [email: jepem.usm@gmail.com or jepem.kk@gmail.com]