

Research Integrity Challenges

A Singapore Perspective

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Biomedical
Research Council

Singapore as a Global Player in Biomedical R&D

- Singapore aspires to be the biomedical R&D hub for Asia and has been growing its R&D capabilities over the past 10 years
- Establishment of Biopolis and Fusionopolis, research intensive institutes of higher learning, academic medical centres, infrastructure for translational and clinical research



Building Research Capabilities - Biopolis

Phase 1 (2000-2005)

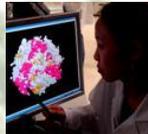
Phase 2 (2006-2010)



Institute of Molecular & Cell Biology



Genome Institute of Singapore



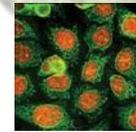
Bioinformatics Institute



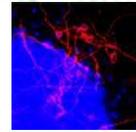
Institute of Bioengineering & Nanotechnology



Bioprocessing Technology Institute*



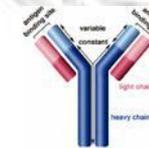
Singapore Bioimaging Consortium



Singapore Stem Cell Consortium



Singapore Institute for Clinical Sciences



Singapore Immunology Network



Experimental Therapeutics Centre



Institute of Medical Biology^

Before 2000

2000

2001

2003

2005

2006

2007

*Set-up as BTU in 1990. Became BTC in 1995, established as BTI in 2003

^ The Centre for Molecular Medicine (CMM) was established in 2004, and was repositioned to Institute of Medical Biology in 2007

Public Healthcare Landscape

Supporting the Translational & Clinical Research (TCR) initiative

2 Public Healthcare Clusters

		
Hospitals	 Singapore General Hospital  Changi General Hospital  KK Women's and Children's Hospital	 Tan Tock Seng HOSPITAL  Alexandra Hospital  National University Hospital  INSTITUTE of MENTAL HEALTH <small>WOODBIDGE HOSPITAL</small>
National Centres/ Specialty Institutes	 Singapore National Eye Centre  National Cancer Centre Singapore  National Neuroscience Institute  National Heart Centre  National Dental Centre	 National Healthcare Group EYE INSTITUTE <small>Adding years of heal</small>  THE CANCER INSTITUTE <small>NATIONAL HEALTHCARE GROUP</small>  THE HEART INSTITUTE <small>NATIONAL HEALTHCARE GROUP</small>  JOHNS HOPKINS SINGAPORE <small>INTERNATIONAL MEDICAL CENTRE</small>  National Skin Centre <small>Dedicated To Excellence In Dermatology</small>
Polyclinics	 Polyclinics SingHealth	 National Healthcare Group POLYCLINICS

2 Academic Medical Centres: Kent Ridge & Outram campuses

Integrating & strengthening education, research, & clinical care

NUHS
National University Health System



@ Kent Ridge

- National University Hospital
- Yong Loo Lin School of Medicine
- Faculty of Dentistry

Hospital & Medical School @ Outram



DUKE NUS
GRADUATE MEDICAL SCHOOL SINGAPORE

 Singapore General Hospital

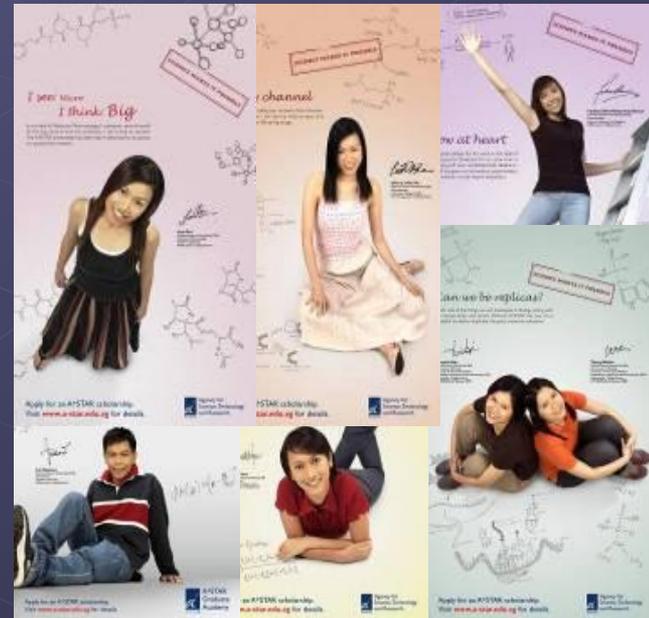
Building Research Capabilities – Human Capital

- Singapore actively recruits foreign talent in addition to nurturing local budding scientists
- Cosmopolitan research environment with scientists of different backgrounds and training
- High quality science by responsible scientists with a good understanding of bioethics and research integrity

Foreign Talent Recruitment



Local Talents





***RESEARCH INTEGRITY - A
HOLISTIC APPROACH IN
SINGAPORE***

Measures In Place

- Strong anti-corruption policies and enforcements (2009 – Transparency International ranked Singapore as 3rd least corrupt country in the world)
- Strong IP protection policies (2008 – ranked 2nd in the world for IP protection by IMD World Competitiveness Report)
- Various other Acts/Regulations: such as
 - Medicines Act (1975)
 - Medicines (Clinical Trials) Regulations (1978)
 - Private Hospitals & Medical Clinics Act (1980)
 - Human Organ Transplant Act (1987)



Guidelines & Policies

- As a global player in the research and to ensure the standards of ethics and research integrity are on par to those in advanced economies, Singapore has established internationally-recognised guidelines & policies
- All staff involved in biomedical research are expected to take steps to acquaint themselves with available guidelines as to “best practices” in research ethics and research integrity



Guidelines & Policies

Notable Examples:

- (a) Singapore Guideline for Good Clinical Practice (1998), adapted from ICH for GCP;
- (b) IACUC & NAACLAR for use and care of animals;
- (c) IRBs set up in research intensive healthcare institutions;
- (d) Health Sciences Authority (FDA equivalent) for approval of clinical trials; and
- (e) Bioethics Advisory Committee, appointed by Cabinet, examines legal, ethical and social issues associated with life sciences research.





***ENSURING RESEARCH
INTEGRITY IN A*STAR***

A*STAR Biomedical Research Funding

Intramural

Research Institutes/Consortia:

- Genomics
- Immunology
- Bioprocessing
- Bioinformatics
- Bioimaging
- Bioengineering and Nanotechnology
- Molecular and Cell Biology
- Medical Biology
- Stem Cell Research
- Neuroscience
- Clinical Sciences

Extramural

Via Grant Calls to:

- Universities
- Academic Medical Centres and Hospitals
- National Disease Centres
- Other academic institutions

Upholding Research Integrity in the Intramural Community

- Compromise in research integrity takes many forms, ranging from questionable research practices, such as failure to report conflict of interest to more serious infringements such as republication of published data, to outright research misconduct, e.g. falsification of data
- To address these concerns, A*STAR has implemented several policies



Upholding Research Integrity in the Intramural Community

Measures to address research integrity issues:

- Code of best research practices – available to all staff in their orientation handbook and in the intranet of A*STAR
- Declaration of conflict of interest – members of the A*STAR family are required to declare and disclose any conflict of interest whenever necessary, in addition to an annual declaration. These written declarations are kept as official records.



Upholding Research Integrity in the Intramural Community

Measures to address research integrity issues:

- Research Integrity Guidelines (including a Whistleblowing Policy) – A*STAR has practical and transparent procedures to investigate and resolve allegations of research misconduct
- Regular reminders – A*STAR leadership are encouraged to take preventive measures by regularly reminding their research staff:
 - to avoid situations where conflict of interest may arise
 - adhere to guidelines (such as guidelines on authorship qualifications and peer review processes).
 - adhere to guidelines on research record-keeping.



Upholding Research Integrity in the Extramural Community

- As a funder of research in the wider scientific community in Singapore, we are also concerned with integrity in A*STAR-sponsored research
- To ensure A*STAR grants are not being utilised for research conducted in an irresponsible way, A*STAR:
 - provides grants only to institutions with reputable records and proper mechanisms to uphold research integrity (IRB, IACUC, proper use of funds, etc.)
 - includes a conditional clause in the grant terms that allow A*STAR to terminate funding should the labs be found to have compromised research integrity.



Upholding Research Integrity When Assessing Extramural Grants

● **Grant review process:**

(a) General grant calls

- > 2 tiers – external independent reviewers & local reviewers
- > all reviewers are required to declare-and-disclose conflict of interest
- > cross-check between grant applicants and reviewers
- > cross-check to prevent duplication of grant applications
- > all grant review procedures are ISO-certified and ISO-audited



Upholding Research Integrity When Assessing Extramural Grants

● **Grant review process**

(b) Collaborative grant calls

- > Examples: A*STAR-UK MRC, A*STAR-NKTH, etc.
- > A*STAR require collaborating funding agencies to disclose grant review protocols/procedures
- > To date, all collaborators adopt grant review procedures that are transparent and rigorous
- > The usual terms on conflicts of interest, duplication of applications, etc. are applicable



***CHALLENGES IN
RESEARCH INTEGRITY
IN INTERNATIONAL
COLLABORATIONS***

Building International Networks

Solutions to global challenges of today can only be realised through the exchange of knowledge and the sharing of ideas.



Transnational and International Collaborations

- The most innovative research flows out of transnational and international research collaborations especially when expertise is complementary
- Singapore scientists collaborate with many others throughout the world where different norms, rules and guidelines apply
- These cross-cultural, cross-national collaborations pose particular challenges towards upholding of research integrity



Research Integrity Challenges in International Collaborations

- Harmonisation of ethical and research integrity standards and practices by adopting international standards, e.g. International Society for Stem Cell Research (ISSCR) guidelines on research on stem cells
- Adherence to such guidelines may be formalised in research collaboration agreements
- For research collaborations involving clinical samples, approval from institutional IRBs in Singapore is required. The Singapore IRB review procedures are based on international guidelines

Research Integrity Challenges in International Collaborations

- Another potential challenge to research integrity in international collaborations is authorship/publication of results
- Prior agreement with collaborators on the criteria for authorship and publication. The agreement includes rules on data ownership, data collection and roles in report-writing
- Conduct best practices in data handling and protection to ensure confidentiality of data, especially data pertaining to clinical samples



***CHALLENGES IN
RESEARCH INTEGRITY
IN INDUSTRIAL
COLLABORATIONS***

Research Integrity Challenges in Industrial Collaborations

- Singapore recognises the importance of translating basic research into practical applications to provide health & wealth to the nation
- In A*STAR, scientists are encouraged to participate in industrial collaborations to enhance translational research
- For industry-related research, specific research integrity issues can arise if they are not addressed or anticipated

Research Integrity Challenges in Industrial Collaborations

Common Issues with Industrial-Related Research:

- (a) Reporting practices – delay in publishing due to IP protection; withholding negative results; publication in dubious journals
- (b) “Gift authorships” and “ghost authorships”
- (c) “Expert opinions” from paid scientific advisors
- (d) Clinical trials in developing countries with less stringent regulatory standards



Research Integrity Challenges in Industrial Collaborations

Measures to minimise problems in industrial collaborations:

- Establish clear open channels of communications before any collaboration, to build an atmosphere of trust that facilitate discussion of even sensitive issues such as integrity standards;
- Co-funding financially or in-kind by public agencies/ govts, could allow insistence on strict adherence to publication/authorship guidelines (ICMJE); monitor participation of researchers; enforce prompt & accurate disclosure of (positive as well as negative) research data



Research Integrity Challenges in Industrial Collaborations

Measures to minimise problems in research integrity:

- Disclose-and-declare (interests/relationships between authors and industrial partners) – allows screening of research participants before conduct of collaboration as well as documentation in publications.
- Participation in multicentre trials – to ensure that ethical standards are adhered to.



A 3D grid of spheres on a blue background. The spheres are arranged in a perspective view, receding into the distance. The background is a solid, dark blue color.

BUILDING AN ETHOS

Research Integrity Ethos – Education & Training

- Many young bright scientists and PhD students are also recruited from abroad
- In addition to providing these budding scientists with knowledge and analytical skills, it is equally important to inculcate a sense of responsible research in them
- A*STAR believes a self-regulating society is more conducive to responsible research than a top-down approach

Research Integrity Ethos – Education & Training

- Components of A*STAR education programme towards responsible research:
 - (a) Clear definitions and guidelines (publicised in A*STAR intranet)
 - Integrity in Research
 - Code of Best Practices
 - Good Clinical Practices
 - Whistle-Blowing Policy & Procedures
 - Conflicts of Interest

Research Integrity Ethos – Education & Training

- Components of A*STAR education programme towards responsible research:
 - (b) Regular workshops using case studies
 - Provide real-life examples for discussion on research integrity
 - Attendance by all ranks in the A*STAR family
 - Encourage bottom-top discussions and interpretations
 - Encourage discussion on prevailing policies (i.e. open and transparent system)
 - Allow fine-tuning via feedback from participants



Thank you!



Biomedical
Research Council