THE REPRODUCIBILITY "CRISIS"
*WHAT IS A*STAR DOING?*

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1. **Compulsory Online Couse on Ethics and Integrity (All Relevant Staff)**
2. **Improving Reproducibility in Biomedical Research**
   - A Short Handbook of Approaches

*"It is key to hold A*STAR to the highest standards for data reproducibility and replicability, depending on the purpose of the research (e.g. industry collaborations, blue-sky research etc)."*
Prof. Lim Chuan Poh, Chairman, A*STAR

GOOD PRACTICE IN BIOMEDICAL LABORATORIES

1. Compliance with Applicable Laws and Policies.

Researchers must comply with all applicable Singapore laws and regulations, as well as A*STAR's policies, guidelines, principles, and standard operating procedures (collectively "applicable laws and policies").

FOLLOW ALL JOURNAL CHECKLISTS!

"Researchers" include employees, students, consultants, and visitors who engage in research with A*STAR's support, either financially or through the use of A*STAR facilities, personnel, equipment, or IP (including trade secrets and confidential information) owned by or licensed to A*STAR.

GOOD PRACTICE IN BIOMEDICAL LABORATORIES

2. Track your reagents.

Many reproducibility problems arise from lack of standardization or poor description of reagents used in the research.

Hence, you should fully document the source, history, production date, retest date (if any), storage protocol, expiry date and previous usage (e.g. aliquots taken, sampling procedures) of all laboratory reagents.

GOOD PRACTICE IN BIOMEDICAL LABORATORIES

3. Be wary of antibodies.

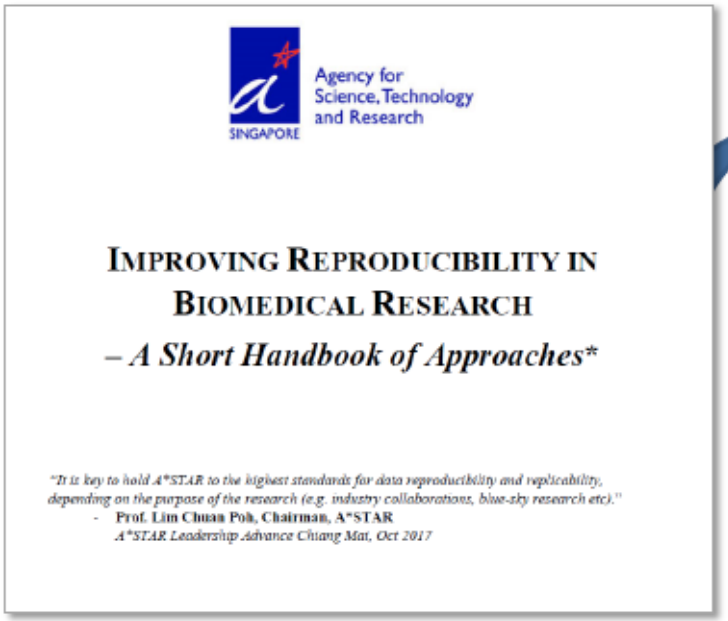
Antibodies have caused particular problems in biomedical research, with potentially large variations in different sources of antibodies allegedly targeting the same antigen, and even batch to batch variations from the same supplier. ***For example, a recent publication in Scientific Reports tested nine commercially available antibodies for specificity and sensitivity and found that only one met all validation criteria.***

It is prudent to check the authenticity of antibody-based results that underlie any perceived novel findings with antigenic blocking and, if possible, complementary approaches such as gene silencing. Indeed, this is a good approach generally: some have called it *triangulation*, verifying the results by separate lines of evidence.

Active Discussions with Suppliers and Internal Validation

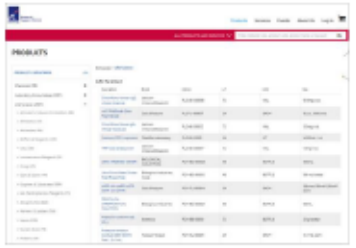
GOOD PRACTICE IN BIOMEDICAL LABORATORIES

Quality management (products) – *to enable Reproducibility*



Translating to daily ops – purchase via RSC portal

Lab consumables



55 SKUs — Antibodies

2,579 SKUs — Lab Reagents

*Supplied by **38 vendors***

Agency for Science, Technology and Research
SINGAPORE

GOOD PRACTICE IN BIOMEDICAL LABORATORIES

Quality management (products) – *RSC Supply Mgmt team*

Action:

- Reach out to Top 20 suppliers by end Oct 2018 (2425 SKUs / 92% Coverage)
- Commitment on :
  - Standard documentation to be updated and loaded *in RSC portal* (Storage protocol / TDS / MSDS)
  - Information upon request for :
    - Source of Cell lines and Lab reagents
    - Manufacturing data (ie. Production dates, Expiry dates, lot numbers, etc)

Benefits :

- **Buying with confidence**
- **Traceability**
- **Easy access to information**

GOOD PRACTICE IN BIOMEDICAL LABORATORIES

4. Document all your research results properly and fully.

Your **laboratory notebook**, whether electronic or hard copy, should be a record of the experiments performed, when they were performed, why they were performed, and exactly how they were performed. The record should be sufficiently detailed to allow others to repeat the work, whether next week or in ten years' time.

We strongly encourage the use of electronic notebooks which directly capture data from instruments, such as those in use at the Experimental Therapeutics Centre (ETC). SERC is working on developing/purchasing and modifying such as notebook.

The data can be captured in the A*STAR cloud and are accessible to all authorized staff.

GOOD PRACTICE IN BIOMEDICAL LABORATORIES

5. Retain *all* original data, including sequences, original photographs of gels, images, traces, printouts etc, to support any material that is put in the public domain (e.g. talks, posters, patents, articles) or given to others (e.g. reports to government bodies, industry etc).

Each item should be date and time stamped. Retain for at least ten years (or for such extended period as may be required by applicable law, policy, grant terms and conditions or other contractual requirements). In particular, researchers should not remove notebooks or e-data from the laboratory. If they wish to take a copy outside A*STAR or when they leave A*STAR, they must seek the necessary approvals (consult the PI and RI ED). Under no circumstances should A*STAR's IP, confidential information, or materials be removed from A*STAR's premises without A*STAR's prior consent. Researchers must never take the original material or results of the research. Ideally, at the outset of of the research programme, the research team should decide about access to and use of the following, by the various team members:

- Materials/means generated for conducting the research
- Data used or created in the course of the research
- The results of the research.

The data are captured in the A*STAR cloud and are accessible to all authorized staff.

GOOD PRACTICE IN BIOMEDICAL LABORATORIES

6. Ensure that all instruments are regularly serviced (at least annually) including calibration to check that they are recording accurately, and that service records are kept safely in a log book, ideally electronic.

7. Pay special attention to the documentation of all animal experiments. Record the IACUC approval details, source, age, Specific Pathogen Free (SPF) status, sex, diet (sources and age), light cycle and strength, bedding (source, how often changed etc), cage type, water treatment, any enrichment, experimental manipulations, and other parameters of all animals used. Be aware that the microbiome can influence results. Follow the PREPARE and ARRIVE guidelines as far as possible in your planning of animal research and in your publications reporting animal research. The full details of any drugs administered to animals should be carefully recorded, since drug formulations may confound results and different animal facilities tend to have different drug distributors. Drug can also deteriorate if improperly stored (paragraph 1 above applies). Be aware of recent discussions on the factors influencing the reproducibility of preclinical animal research.

GOOD PRACTICE IN BIOMEDICAL LABORATORIES

8. Data Analysis

Data mining – Database(s) and data-mining software used should have authenticated sources and references in the published literature. Any new algorithms developed or used should be described in detail.

Source codes of work accepted for publication – Unless for patent application or other official reasons for maintaining secrecy/propriety, all source codes generated for and used in computational simulations and AI research should be published in full and/or deposited in appropriate resource databases as stipulated by the conference/journal.

Appropriate statistical methods should be applied to the analysis and interpretation of data. In all quantitative analyses, there should be full description and documentation of sample size determination, sample randomization, sample blinding, number of experimental replications and any exclusion of data sets/points.

Researchers not well-versed with the use and application of quantitative or statistical methods should consult colleagues with relevant expertise. A basic guide on statistical parameters frequently used for analysis can be found in “Statistical parameters” in the Manuscript reporting summary.