Why and How a Research Lab Should Embrace Research Quality

Discussing the need for quality in medical research with each group of research colleagues I shared this with, each were aware of a worker whose use of a local technique was flawed. On discovery of the problem, several months' work sometimes had to be discarded. My latest colleague offered support with a comment I didn't expect – "try years".

Introduction

The development of therapeutic products balances benefits and adverse consequences so research quality is required for the development of the new therapeutic. Astute use of research quality earlier can add to the value of intellectual property (IP), especially when the IP is subject to quality assurance due diligence (QADD). This is recognised in RQA publications supporting non-regulated research[1].

Problems with the reliability and integrity of research have large, complex and lasting negative effects. Requirements for research quality are enforced in regulated research but there is no common agreement of when a quality system or quality assurance should begin. Outside regulated research, an approach that includes quality is traditionally considered unnecessary or even counter-productive. The aim of this article is to explore the reasons for a lab to apply research quality to improve their science, its reliability and productivity and to consider how to begin to apply research quality.

Logical Reasons for Research Quality

The complexity of research is greater than ever as we expand our understanding of life and the universe, even in a confined area of medical research. Further layers of growing complexity continue to develop in compliance areas of the research environment – animal and human research ethics, research grant governance, health and safety, protection of the environment and waste disposal, to name some. Clearly a system for each is impractical when a single lab system can provide workers with guidance approved by the lab's and the organisation's research leader(s) to both produce reliable research data and satisfy the requirements of multiple regulators simultaneously.Productivity may be the most significant benefit of research quality. The reduction in wasted research should be reflected by less research that needs to be repeated, corrected or retracted.

Compelling Evidence of Problems with Research Reliability

If logical reasons aren't enough, there are sufficient compelling reports of problems in research to suggest the real magnitude of problems needs attention. Here are some of those reports.

Irreproducibility is a pervasive, systemic problem that has multiple direct and systems-level causes. These causes range from individual laboratory decisions, such as lack of an appropriate control for a particular experiment; to variability in journal publication requirements; to lack of consistent research quality systems. Fundamentally, irreproducibility stems from undefined variance in reagents, practices and assays between laboratories. Global Biological Standards Institute (GBSI)[2].

GBSI's comprehensive report, *The Case for Standards in Life Science Research*[2], found widespread problems.

Begley[3] provides evidence for the commercial damage from lack of reproducibility: *"scientific findings were confirmed in only 6 (11%) cases"* of 53 papers deemed 'landmark studies'.

'Loss of confidence can affect research funding, delay discoveries and provide ammunition to attacks on proven science.'

Possibly more telling is that this didn't seem to have sparked outrage. Is it possible the price of IP is discounted by an order of magnitude to allow for irreproducibility? Research quality would be a useful tool to demand and defend QADD audit and ask the full price for IP.

Withdrawal of about 80 of Boldt's publications has not stopped the damage from their previous influence on emergency department choice and use of blood volume fluids. The damage was quoted by Ian Roberts, a lead Cochrane review author, as "probably killing between 200 and 300 people every year in the UK"[4]. It is ironic that academic research influential in the use of approved therapeutics isn't subject to any of the regulation needed for market authority.

"Royalty deal lower than hoped" is a headline (*Australian Life Scientist*, 14th February 2012) no one wants. Powerful reasons exist, though, for under-reporting of this problem. But how do the owners and sellers of IP really know if shareholder value is maximised? Financial due diligence is well known but QADD may significantly write down the value of IP. QADD can be defined as: the process of analysis (usually by an investigative audit) prior to an acquisition of a technology, product or business or before entering into a partnership with a third party (the licensing sponsor) in order to determine the status of compliance with the applicable GxPs, the validity of processes, data and the inter-compatibility of regulatory and quality systems[1].

Retractions, from various sources, also show problems continue. British media reporting, ca. 2002, of the mix-

up of cattle and sheep brains in bovine spongiform encephalopathy research was short of a retraction that may have had a greater effect on confidence in research data.

Flaws in contemporary science harm society on multiple levels, within research and more generally. They damage the productivity of the work, wasting precious research funds, and demotivate scientists, some of whom move to more fulfilling endeavours. Loss of confidence can affect research funding, delay discoveries and provide ammunition to attacks on proven science. At worst, poor-quality research can result in harm.

Doing the Right Thing

The need for research quality exists because, one way or another, the investment in science isn't reaching its potential and we shouldn't simply react to the problems. Research quality should be adopted for the right reasons:

- The public deserves the best use of and greatest productivity from taxpayer funding of research. Industry research should be a good use of shareholder funds
- High-quality research data generates greater prosperity, needed for a country to lift healthcare and for industry to stay in business
- Patients benefit sooner if research doesn't need to be repeated in a 'GLP' facility
- IP is better protected if the research quality is demonstrably high.

Doing the right thing should be reason enough.

Embrace a System

Published systems are available from regulators, standards entities and professional associations. Some examples include:

- **ISO 9001**. The global system, can be applied to any activity
- **ISO 17025**. A system for testing and calibration laboratories
- **OECD GLP**. The management system for non-clinical safety testing
- **RQA R&D**. System for non-regulated R&D
- **RQA GCLP**. System for analysing samples as part of a clinical trial
- **RQA QSW**. Quality Systems Workbook is a tool for mapping the scope of a facility's quality management system needs.

The value of these systems is that they provide a taxonomy that has broad understanding. This can have benefits for the training of new staff and for hosting future audits. For the lab worker, the taxonomy provides signposts to important information.

Getting the System to Work

Like any change process, the first essential is recognising the need and gaining the commitment from the team. Making the system beneficial is critical. Each team member should find what they need in the system. It works even better if everyone can see their contributions in the system.

We need to be respectful of the sceptics and mindful their views are important and often correct. Remember The Private Cooper Hat (Quasar 129): I use the term 'morale man' to describe a soldier whose personality means that everyone around him will feed off his morale, high or low.

A sceptic whose concerns are addressed may become a champion of the new system.

With this in mind, start the discussion – RQA's Quality Systems Workbook provides an excellent template for doing this.

Many questions should flow from an early discussion. What is the scope of activities and what must we achieve? Are there risks in need of management? Are there improvements we can make? Are benchmarks available and applicable? Choose a framework to provide the taxonomy or skeleton for our system. Add flesh to the skeleton as needed.

Be pragmatic – where available, use pre-existing material. Research plans or protocols approved by research ethics committees provide ready-made peer-reviewed research plans. Righteously ignore factors we believe can be ignored and record this, not to blame but to learn and justify.

Where an expected benchmark exists, measure our success to prove it or point to the need for changes. A research institute that offers cell line testing generates either proof of good practice or defines the improvement needed.

Working to a SOP or lab method can save time in recording and permits the experimenter to be more observant of the experiment. Lab methods also assist with knowledge management, especially when key staff leave. Checklists can help beyond reducing errors. For example: equipment may require user specific adjustment – expensive loupes that need to be shared can have a method that includes each user's inter-pupillary distance, making for rapid adjustment each time.

There is much more than this but it is beyond this article. Fortunately it is within quality assurance skills. A final thought – it doesn't have to be called a quality system. Some organisations don't mention 'Quality', but they apply it rigorously.

Conclusion

A quality system, however named, is a powerful tool for lab productivity and research reliability. With new staff correctly inducted, the old habit of showing people what to do and then 'letting them loose' should disappear. The frequency and magnitude of flawed research should diminish.

References

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