GxPs for Drug Discovery?

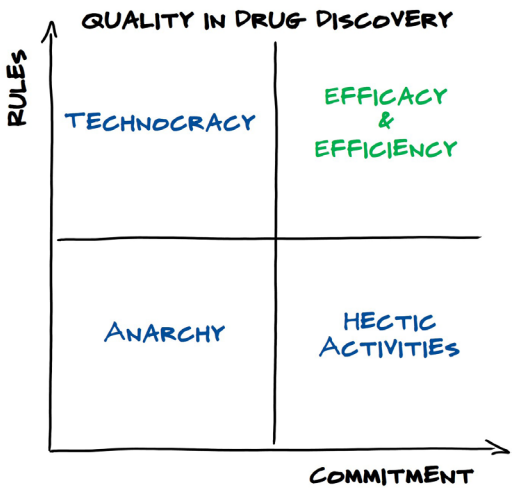
GLP and GMP are inevitably linked to the pharmaceutical industry. Well, not to the complete industry. The exception is the discovery part of the business, balking at the very idea of GLP in research and painting dark pictures of pointless regulations smothering creativity.

Quality Systems - Guilty of Killing Creativity?

True, the GxPs do not apply. Nevertheless, the significance of quality is hardly debatable which raises an important question: If the GxPs do not define the quality requirements of drug discovery, WHO DOES?

Quality Definitions

The exclusion approach – "GxPs do not apply to drug discovery" – is of course some kind of definition but obviously a bit limited in terms of what should be done. Even worse, it is easily interpreted as "rules do not apply at all". This is a dangerous attitude, since no rules and no commitment quickly lead to quality anarchy.



Quality Definition Dillema

Relevance of quality accepted, commitment to quality available but applicable rules are missing – this is another frequently observed situation in drug discovery. One common outcome of this situation are hectic activities – enthusiastic but uncoordinated, over- or under-shooting quality targets and quite frequently wasting resources in the process.

Overwhelming quality regulations in place but no commitment from the discovery team, the other observable extreme, leads to technocracy. Rules are defined and forced on discovery teams by faceless "governance units", resulting in a predictable lack of acceptance and poor performance.

The sweet spot of drug discovery quality is obviously defined by adequate quality rules (but nothing beyond adequate!) in combination with real commitment on the side of the discovery team. Characteristics for this situation are efficacy (quality targets are reached ...) and efficiency (... with a minimum of effort and investment). Hitting this sweet spot requires some initial effort and reflection, some use of common tools like risk management and the application of a simple concept: quality is fitness for purpose.

Quality Definition Strategies and their Consequences

Fitness for Purpose

The fitness for purpose concept focuses discovery teams on the (quality) demands of discovery projects. Activities or experiments within a project usually aim at achieving at least one project relevant purpose. Clearly, not every type of result is "fit for purpo-

se". Apart from having the desired value, the result needs to have a certain quality as well, normally described in terms like "correct" or "reliable".

Bio assays for instance usually aim at the selection of development candidates. In order to avoid costly errors, assay results need to comply with certain quality attributes like adequate reproducibility. However, recent publications suggest significant room for improvement in this field (see The Economics of Reproducibility in Preclinical Research, Leonard P. Freedman et al, June 9, 2015, PLOS Biology).

In order to improve reproducibility, careful experimental design based upon scientific understanding is one prerequisite, smart use of basic quality processes is another. Changes of experimental conditions during project life time for instance clearly put reproducibility of results at risk. However, some changes will probably be unavoidable. Therefore, a defined quality process that tracks, evaluates and controls those changes (change management) is an obvious necessity. The same is true for documentation standards, error free data analysis, training of lab staff, storage and handling of reagents and so on.

Quality is Fitness for Purpose

The fitness for purpose concept leads quality considerations along a directed cascade of thought – project, experiment, purpose, quality attributes, quality process – starting at the scientifically relevant end of the business. Best qualified to follow this cascade of thought and to come up with meaningful quality processes are obviously the major contributors – the discovery team members themselves. This way, the resulting quality processes will be project and purpose oriented, scientifically relevant and they will make sense to the discovery team which leads to acceptance and compliance.

Seemingly pointless and frustrating quality governance (remember for instance the EU quality standards for cucumbers) is replaced with meaningful and accepted rules with a good chance to be applied with a high degree of commitment and with few if any mistakes.

Free of Purpose

Scientific Flexibility needs Reliable Quality

"Science has gained most from all the unplanned results." is a much used argument against (over)regulation of discovery processes. Variability in experimental outcome compared to the original plan quite frequently adds more value to a project than the desired result would have done. While this is true, it does not argue the case against quality requirements for those unplanned results. Any result with dubious quality translates best case into "do it again", worst case it leads to plain wrong decisions.

Is it GxP?

Of course it is. The EU GMP guidelines for example are all about quality concepts and quite a lot of those are useful and applicable in drug discovery as well – change management for instance or handling of reference standards.

Of course it is not. Improving drug discovery quality by copying existing concepts in a smart way, absorbing their valuable aspects and avoiding at the same time all the negative ones is not GMP, it is just common sense.

Does it Hurt?

Well, this depends mainly on the purpose of the quality activities. As soon as the quality system becomes an end in itself, chances are high that the trouble solved is less than the trouble created.

As long as quality activities remain focused on the Fitness for Purpose concept, advantages will outweigh disadvantages. Done smartly the process should even be resource neutral. Invested resources and gained resources (less double work, less error correction, …) should at least be equal.

Results seen in the industry indicate that keeping focused on Fitness for Purpose is a challenge, probably because drug discovery scientists frequently have to face hardened QA professionals in a tug of war over quality regulations.

Some initial effort by the drug discovery scientists could tip those scales in their interest. Defining their own quality goals and needs would be a good starting point and at least some understanding of the “enemy” (the GxPs) would help as well.

Scientists should Drive their Own Quality Initiatives