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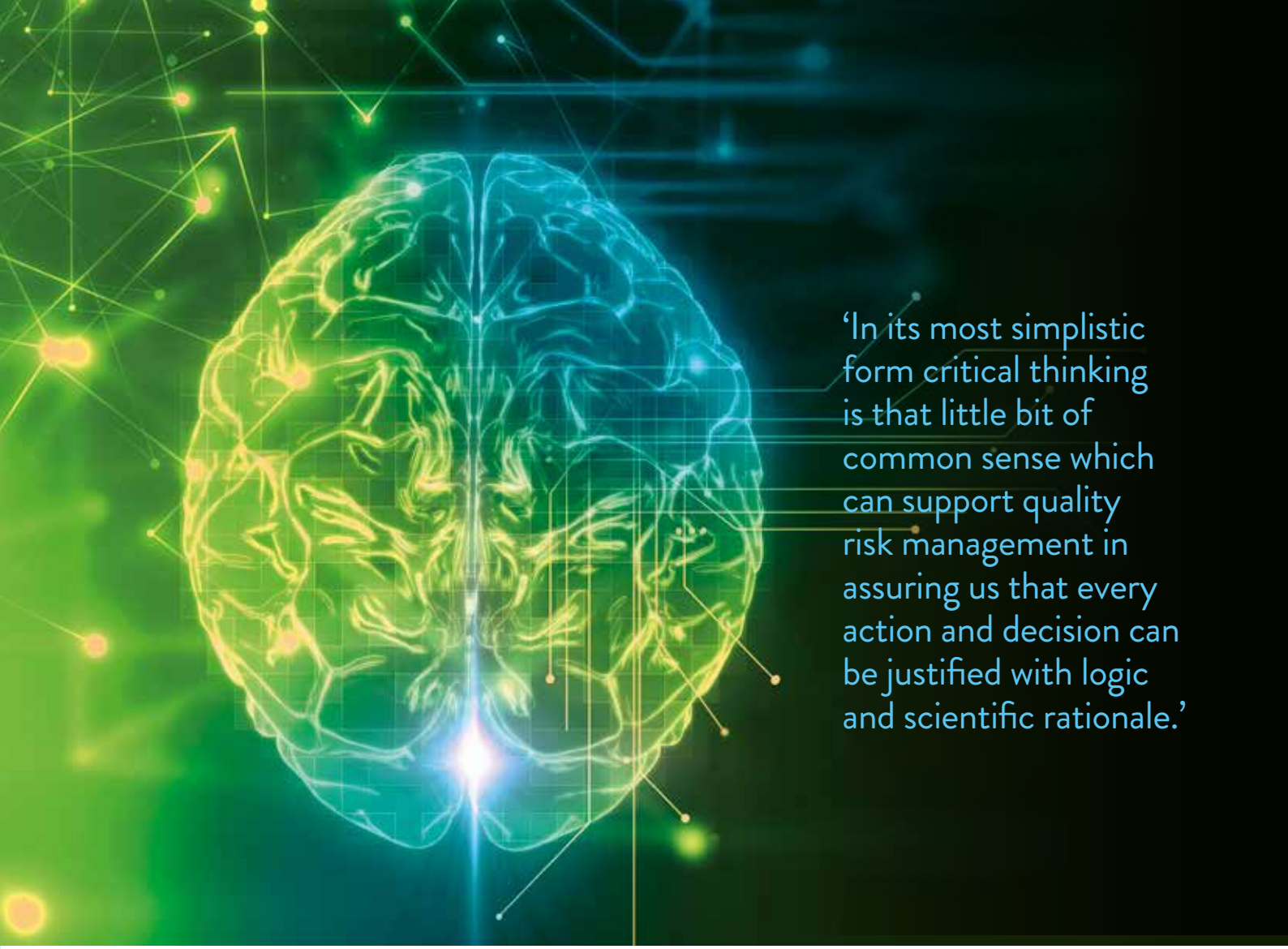
REVALIDATING THE MIND: MAKING THE CONSCIOUS SHIFT TO ADOPTING RISK-BASED COMPUTERISED SYSTEMS VALIDATION

Confidence of in-house system validation has grown over the past decade or so, as the regulations and guidance have remained relatively constant during this time. Procedures and technologies have developed to support such practices. Unfortunately, time and time again the same feedback is observed – CSV takes too long and relies too much on quantity of documentation.



‘In its most simplistic form critical thinking is that little bit of common sense which can support quality risk management in assuring us that every action and decision can be justified with logic and scientific rationale.’

It has been a clear objective within the industry to improve ways of working for CSV to reduce this so-called ‘thump factor’ stereotype; however, without the support from regulations and guidance educating with examples, the confidence in making this shift has not been as strong. 2022 saw improvements to such multiple guidance documents and most recently a concept paper for the revision of Annex 11, which will likely see the much-needed confidence boost across the industry that CSV so desperately needs.

With the publication of ISPE’s updated guidance in July 2022, the Second Edition of ‘GAMP 5: A Risk-Based Approach to Compliant GxP Computerised Systems’, the key words on everyone’s lips have been ‘Critical Thinking’. In fact, the guidance itself mentions the term Critical Thinking on 130 separate occasions throughout the 400-page document, including a new principal appendix dedicated to the topic.

It is important to note that critical thinking has always been an intended feature of CSV. At the very heart of GMP Annex 11: 2011 it states that ‘risk management should be applied throughout the life cycle of the computerised system’ and heavily focuses on the applications of ICH Q9. However, with vague requirements from the regulators on what this risk-based approach can and should look like, the situation often leads to the very opposite – the burdensome ‘do everything’ approach. The first edition of GAMP 5 even fails to define and mention what this should look like.

With that being said, how do we begin to move towards critical thinking-embedded approaches when we have been using the same acceptable procedures for so long?

WHAT IS CRITICAL THINKING?

GAMP 5 defines critical thinking as a concept ‘to ensure quality and compliance of computerised systems within the context of the business processes they support’. Critical thinking moves us away from validating a feature because it’s available to the user in the system, and instead challenges whether a feature is necessary to meet the business process before determining whether it requires validation. In its most simplistic form, critical thinking is that little bit of common sense which can support quality risk management in assuring us that every action and decision can be justified with logic and scientific rationale.

If applied correctly, critical thinking can allow us to consider all areas of validation and ensure the most appropriate risk-based approach is taken.

- **Are there business processes which would verify or capture defects outside of the system?**
- **Is the feature critical to the business processes and intended use?**
- **What would the risk to the patient be if this feature had a defect?**
- **Verification versus testing** – determining the most appropriate rigour of test approach
- **Surveillance versus prevention** – robustness of procedure controls to ensure focus is targeted towards ensuring critical activity is auditable rather than focussing on preventing unauthorised activity.

Employing critical thinking will allow businesses to focus resources in areas where it is needed – and save resource away from areas it is not needed.

It is therefore crucial that all stakeholders involved in supporting CSV understand the business processes relating to each computerised system.

This moves us away from the silo approach some of us may be used to and ensures a more collaborative and agile approach is taken. Agile being another new key appendix to the second edition of GAMP 5. For many, critical thinking is a term perhaps often used but with poor understanding or commitment to the cause. It should therefore be first defined and accepted by the business, before the benefits can be applied to validation in practice. This early adoption must not be a barrier for the business and we must ensure we are able to manage any resistance from existing behaviours and procedures.

Managing resistance to change in an established process is nothing new to a quality professional. For CSV specifically, the regulations are not known for being definitive, nor do they need to be. However, this can quite often develop a culture of doing too much to ensure that the coverage is at least sufficient. The approach can, at times, be damaging to the business resource and, to inspectorates, can demonstrate a poor understanding of what is truly required. When CSV should be an assurance activity, having a poor understanding of the requirements does very little to foster this assurance.

PARADIGM SHIFT

The CSV paradigm shift – introduced in the FDA's 2022 draft Computer Software Assurance document – suggests the largest proportion of resource should be spent on critical thinking versus documentation. The largest amount of benefit to a validation project will be to ensure the project goals are fully understood and the risks identified so that the focus can be tailored towards the high-risk areas; whilst reducing resource towards the lower risk areas.

Some validation professionals approach a project with the same intention, which typically starts with a validation plan and handing over a templated user requirements specification to the users. At this point, the motion of the project is already underway and becomes more challenging to remove and edit once approved. Instead, the recommended approach is to review the system and business process with the subject matter experts (SMEs), the users, GxP management and the quality unit first to fully understand the intended use and risks – see Step 3 for an example of putting this engagement into practice.

Once system risks and the intended use specific to the business process have been understood, it is far easier to construct a validation plan which is reflective and proposes a commensurate amount of resource into the project. Historically, system validations can take anywhere from a few months, to the best part of a year, often held up by documents taking too long to approve and testing protocols in excess. Applying this critical thinking reduces both and in doing so, delivers a validated system to the business in a much shorter time frame. Time is most definitely money here!

It is this critical thinking which will ensure the quality of validation is maintained whilst the quantity of documentation can be reduced.

FIVE STEP APPROACH

Repositioning the mindset to adopt procedures centred on critical thinking is not an overnight activity and nor should it be tackled alone in a single direction. The need to demonstrate with objective evidence that critical thinking can be, and almost always is, a successful means to invest into a validation project, is key to aligning colleagues. As with all culture shifts, it is necessary to segment the challenge and proceed at a pace which is suitable to the business. The phrase 'how do you eat an elephant? One bite at a time!' seems pertinent to mention here.

STEP 1 – GAP ANALYSIS

The first exercise should be to understand the current position and benchmark against the updated guidance. A gap analysis should be conducted to assess where the differences between current ways of working and future ways of working may lay. It is important to ensure this assessment is not over complicated and can clearly identify measurable changes which are achievable by the business. It is also beneficial to interpret the updated guidance into the words most suitable to the business to reduce the risk of misinterpretation and ambiguity. Once reviewed, actions should be attributable to each key point to ensure an action plan can be clearly agreed upon.

A presentable gap analysis can be an ideal tool to demonstrate to inspectorates a solid understanding and appreciation of the updated ways of working – and a clear willingness to strive for change. This gap analysis can also be a good foundation to recalibrate existing staff and realign well established procedures. See Table 1.

STEP 2 – MATURITY MODEL

The Critical Thinking Appendix in GAMP 5, second edition, presents a maturity model table to help businesses monitor their progression as they make a shift to a critical thinking-centric culture. A maturity model can be a helpful tool when monitoring the success of a transition over a medium to long timescale. Following benchmarking captured under a gap analysis, the business should then identify where on the maturity model scale it lies and have a clear indication of what is required to advance through the milestones. It is important for a business to understand that critical thinking maturity should be viewed as a whole and not specific to an individual or small team. The purpose of a maturity model is to establish an understanding of the businesses' capabilities.

TABLE 2. MATURITY MODEL

MATURITY LEVEL	CRITERIA
1	No application
2	Awareness but highly variable and not defined
3	Described in procedures but inconsistently applied
4	Fully incorporated and routinely applied
5	Core value and subject to continuous improvement

Table adapted from ISPE, GAMP 5 2nd edition M12 – page 181.

SMEs within the business and quality professionals should identify a solution for reviewing the current business position on the maturity scale and then identify a solution for how the business may progress. A frequency of review should be established to ensure the business' maturity level is routinely assessed. The most benefit from this will come from establishing communication between a variety of roles and experiences to ensure the full perspective and understanding of the business is respected.

TABLE 1. PRESENTING GAP ANALYSIS

Document Ref.	Guidance/Regulatory Text	Interpretation	Action Required

The model presented in the GAMP 5 chapter is rather subjective, but in being so, allows the applicability to varying businesses. The purpose of this exercise should be to support the business in developing and advancing to improved ways of working and therefore should not be a burdensome exercise to fit into a model which may not be quite right for the business, echoing the actual purpose of applying a risk-based approach.

With experience, the maturity level of the business will naturally progress with the hopes of adopting into core values of the culture. Being able to identify when those leaps into the next maturity level band were observed is a useful tool in bringing others on board and convincing of success.

STEP 3 – EMBED ENGAGEMENT

Stakeholder engagement should be maintained throughout a validation project to guarantee success. It is not uncommon for system validation to be conducted in silo ways of working, with distinct handover to modular departments during the project life cycle. Without sufficient engagement and communication, a project will not succeed.

One of the earliest activities should be a stakeholder engagement to include SMEs, management, CSV, quality and optionally project management and IT teams to fully understand the scope and purpose of the project and to allow any questions or concerns to be raised upfront. This engagement should then continue throughout the project at intervals to ensure alignment. System validation should not be a standalone exercise for the CSV engineers to complete on their own, it should be driven by the users and the SMEs within the business and supported by the quality department.

It is recommended regular project meetings are held with key stakeholders to maintain momentum and a balanced perspective towards critical thinking. The outcome of such project meetings should be documented to support the rationale captured in the validation plan and report.

STEP 4 – PILOT CHANGE

Once identified, there should be no delay in trialling improved ways of working. Although success may be clear to some individuals involved, the business should demonstrate evidence of success before any changes to procedures are to be established. Success should be compared against the current established procedures and consider not just resource savings but also quality attributes. Process improvement on this scale can be managed under change control, where pilots are initiated and tracked.

Exploring pilot changes is a useful tool in all areas of process improvement. The applicability to validation, however, cannot be understated. Each validation project must ensure intended use and risk to the business have been considered and for the project to be crafted around that design. As such each system validation should be commensurate to that risk, whilst following a standard higher-level procedure and master plan. This creates a perfect example to trial pilot change and improved ways of working, having both the validation plan and report as vessels to capture decision making, risk assessment and rationale.

It is important to remember the regulators require the approach for each validation to be defined; however, the control over this approach is in the hands of the business to ensure validation is not a burdensome exercise.

It is recommended that a pilot be trialled on a candidate system which has the flexibility to monitor and document the successes of the change without being biased from business time pressures. It is also recommended to capitalise on stakeholder engagement as an opportunity to educate and promote positive validation culture.

- Alternative approaches to testing, such as unscripted and ad-hoc testing
- Change to documentation required
- Trialling collaborative communication
- Further embedding of risk assessment
- Risk-based approach to auditing.

Once evidence of success or failures has been documented, a review should be conducted to evaluate whether the proposed change is a valuable addition to the documented procedures. Evidence of this evaluation must be available for inspection and will provide a solid rationale for driving the improvement.

The opportunities of trialling change through a pilot format cannot be understated and demonstrates a clear willingness and flexibility of the facility to meet updated guidance.

STEP 5 – EFFECTIVENESS REVIEW

As with any well controlled change, an effectiveness review should be conducted to confirm whether the change was successful or not. Culture shift is not likely to be fully adopted unless there is evidence to support newer ways of working. Having such examples should provide a foundation to driving a critical thinking culture forward.

Gap Analysis – the key observations from the gap analysis should be shared with stakeholders and presented with the identified actions as solutions.

This is also a great opportunity to educate those unfamiliar with the updated guidance. It is much harder to disagree with written text, whether guidance or not.

Maturity Model – the current business position should be presented along with pragmatic actions to progress up the levels. A business is more likely to be on board if they can see a clear progression path rather than a blind stab in the dark. Show them how this can be achieved.

Embedding Engagement – Feedback and success stories should be highlighted and shared to strengthen the benefit engagement can have on a project. If a milestone was met 50% quicker than on a previous project, then indicate this and show how this has benefited the business.

Pilot Changes – where a different way of working has been successful under a trial, make sure the key stakeholders are aware. Review this against current ways of working to highlight the positives this may bring, not only short term but longer term also.

THE FUTURE IS CRITICAL

As businesses become busier, with higher revenue turnover and tighter deadlines, it's increasingly important to ensure efforts are as efficient and as lean as possible. System validation is here to stay, so it's necessary to look to improved ways of working to maintain high quality compliance whilst reducing the burden on already busy resources. Through correct application of critical thinking, this can be achieved. Software and systems developed today are night-and-day compared with those developed almost 15 years ago at the time the first edition of GAMP 5 was published, improving built-in controls for patient safety, product quality and data integrity. As such the validation approach of today should also have developed so that it is not reflective of an approach from 15 years ago.

A business which centralises their validation procedures and culture around critical thinking, rather than being driven by documentation and checklists, will reap the benefits of reduced resource, enhanced quality and improved confidence, ultimately delivering robust operational systems to the business much sooner.

PROFILE

John is a Senior Validation Officer working for a global CRO. He has experience in both GMP auditing and CSV QA where he is championing the adoption of risk-based approaches to Computerised System Validation. John holds an MSci in Biological Sciences and he is trained in Lean Six Sigma principles.