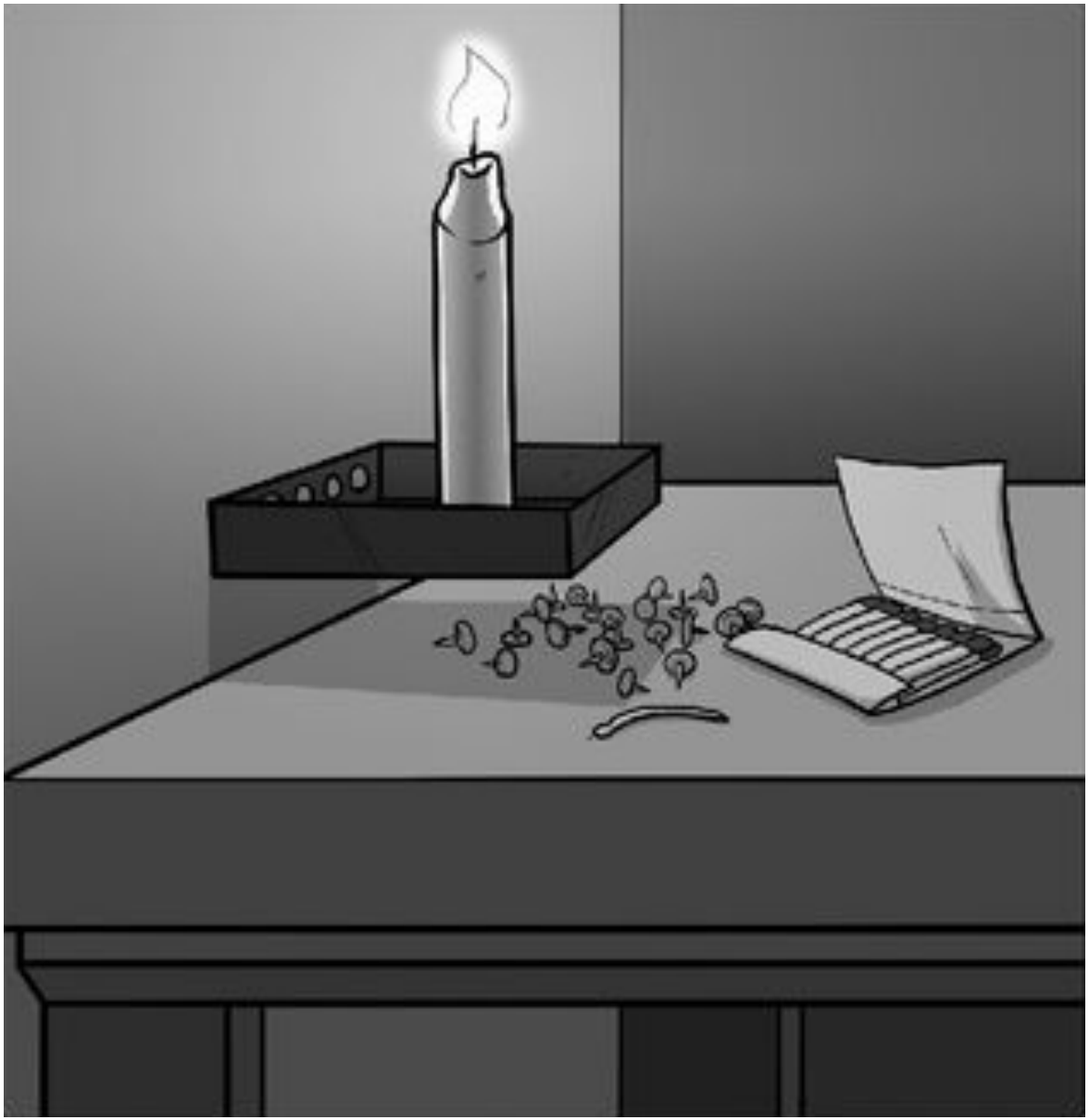
A Sponsor Perspective on Validating Regulated Systems

From Traditional Waterfall Approaches to Agile Continuous Improvement

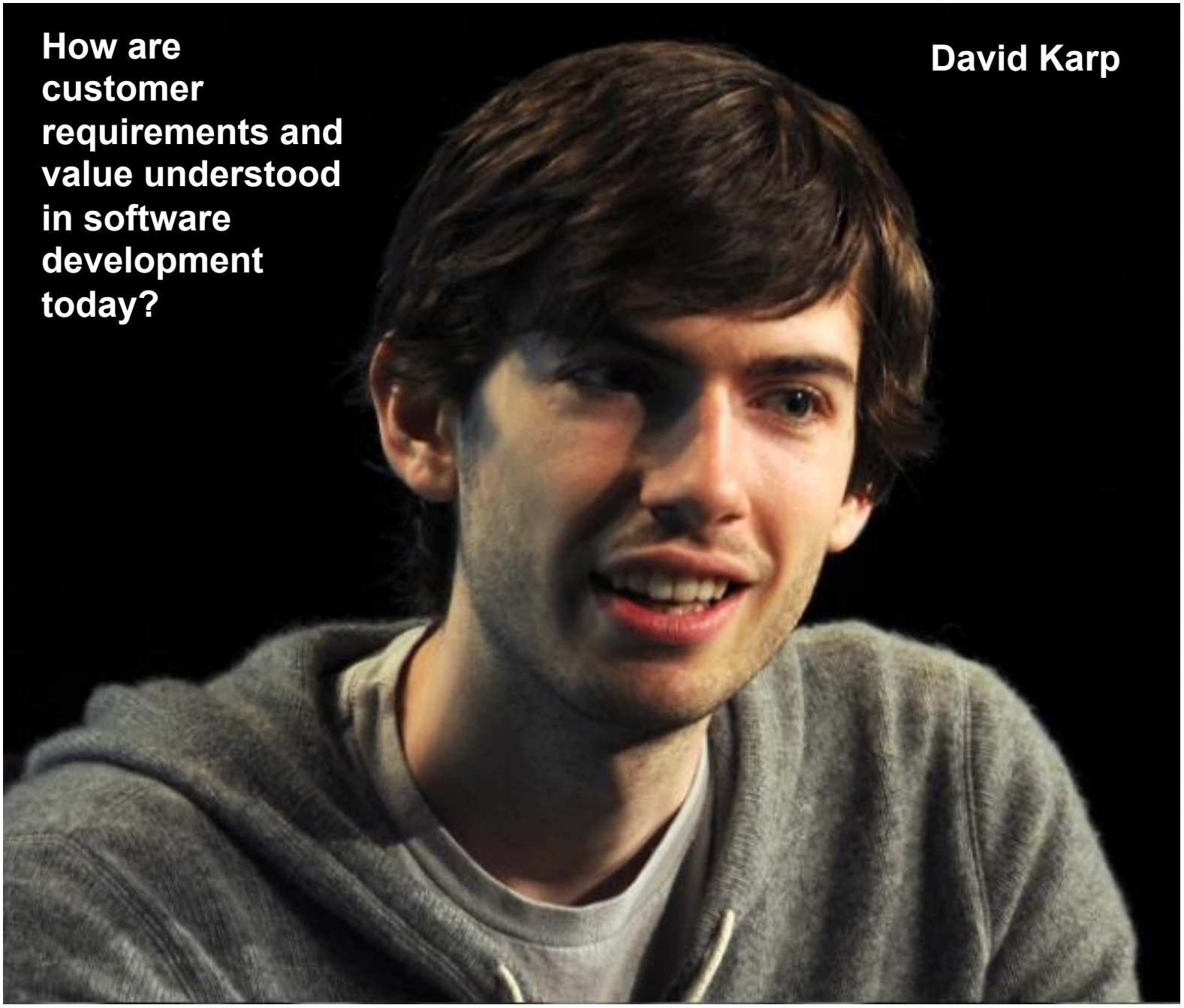
- **PhUSE Wayne PA Single Day Event**
- **Nate Blevins, IS Business Relationship Director, Global Regulatory, Safety and Quality Assurance Systems**
- **August 15, 2013**

AstraZeneca



Dan Pink "Surprising Science of Motivation" www.ted.com/talks/dan_pink_on_motivation.html

How are customer requirements and value understood in software development today?



“Any effort that is not absolutely necessary for learning what customers want should be eliminated.” So how do we do that? By building what Eric Ries call a minimum viable product—or MVP.

So, what is the problem?

We do not develop validated/regulated systems in a modern, "lean" way

Computer systems validation is generally accepted to contribute 25% to the total project cost. [5]

Pressures on pharma and healthcare – do more with less

Easier problems are solved already?

- ☑ data entry/processing - OK
- ☒ bioinformatics, personalised healthcare, RWE, predictive modeling, etc - ??

Low satisfaction with IT departments, speed of delivery, usability and value of solutions

Traditional software development

"Waterfall methodology"

1. Business analyst works with users to create the user and functional requirements.
2. Solution architect creates the system design specifications and then hands off to the developers.
3. Developers (often offshore) perform build of the system.
4. The system build is handed off to the validation team.

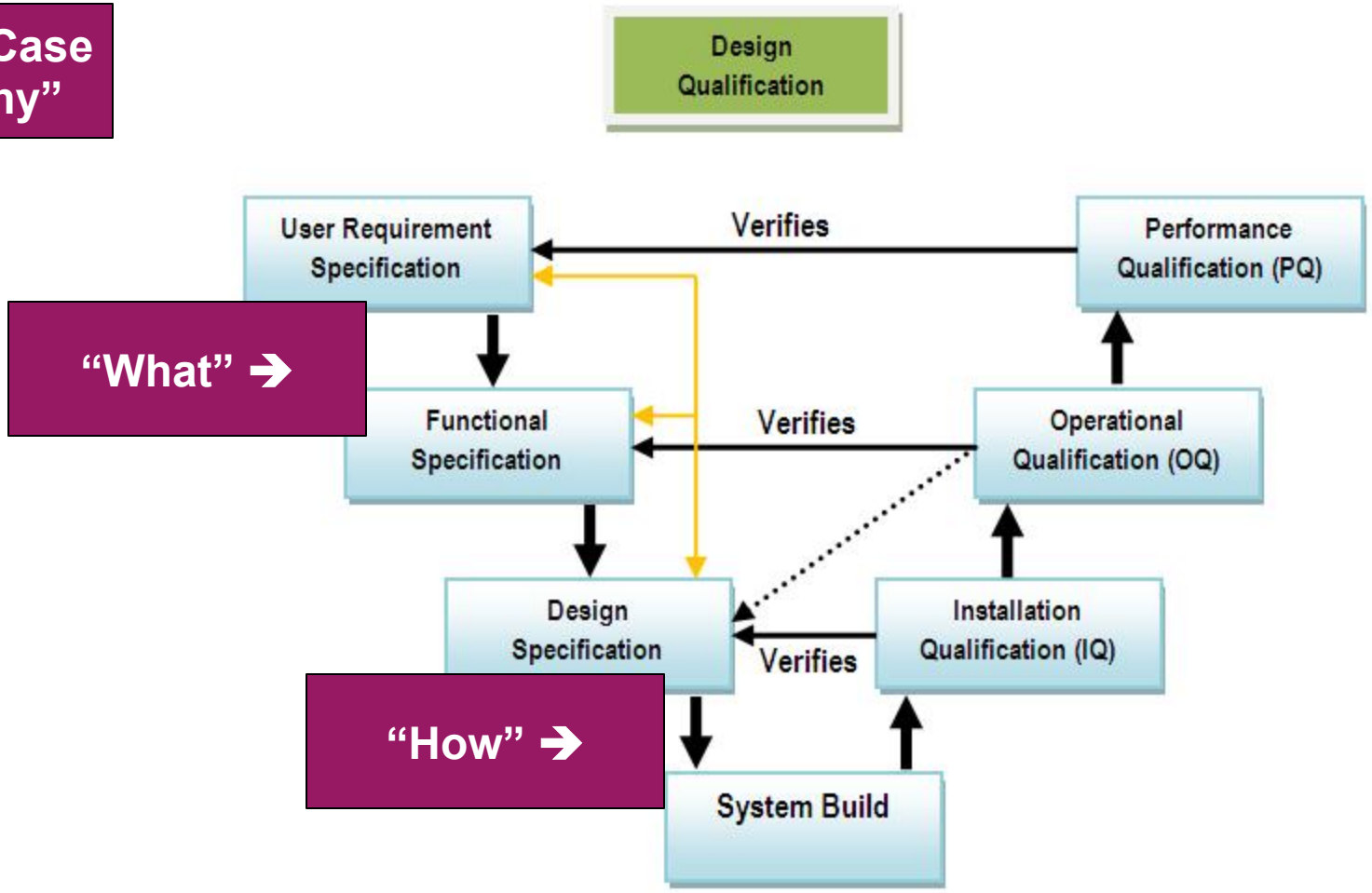
The waterfall process sequentially leverages isolated expertise (e.g. analyst to architect to developer to tester).

AGILE pairs end users and development resources to rapidly implement and test the system in smaller incremental phases called sprints.

…*Minimum Viable Products?*

The “V model” – GAMP 5 allows for flexibility

Business Case = the “Why”



Document Centric or Agile?

Old approach – keep CSV team in dark during requirements development and design

Or, Agile:

- **Individuals and interactions [are preferred] over processes and tools.**
- **Working software [is preferred] over comprehensive documentation.**
- **Customer collaboration [is preferred] over contract negotiation.**
- **Responding to change [is preferred] over following a plan.**

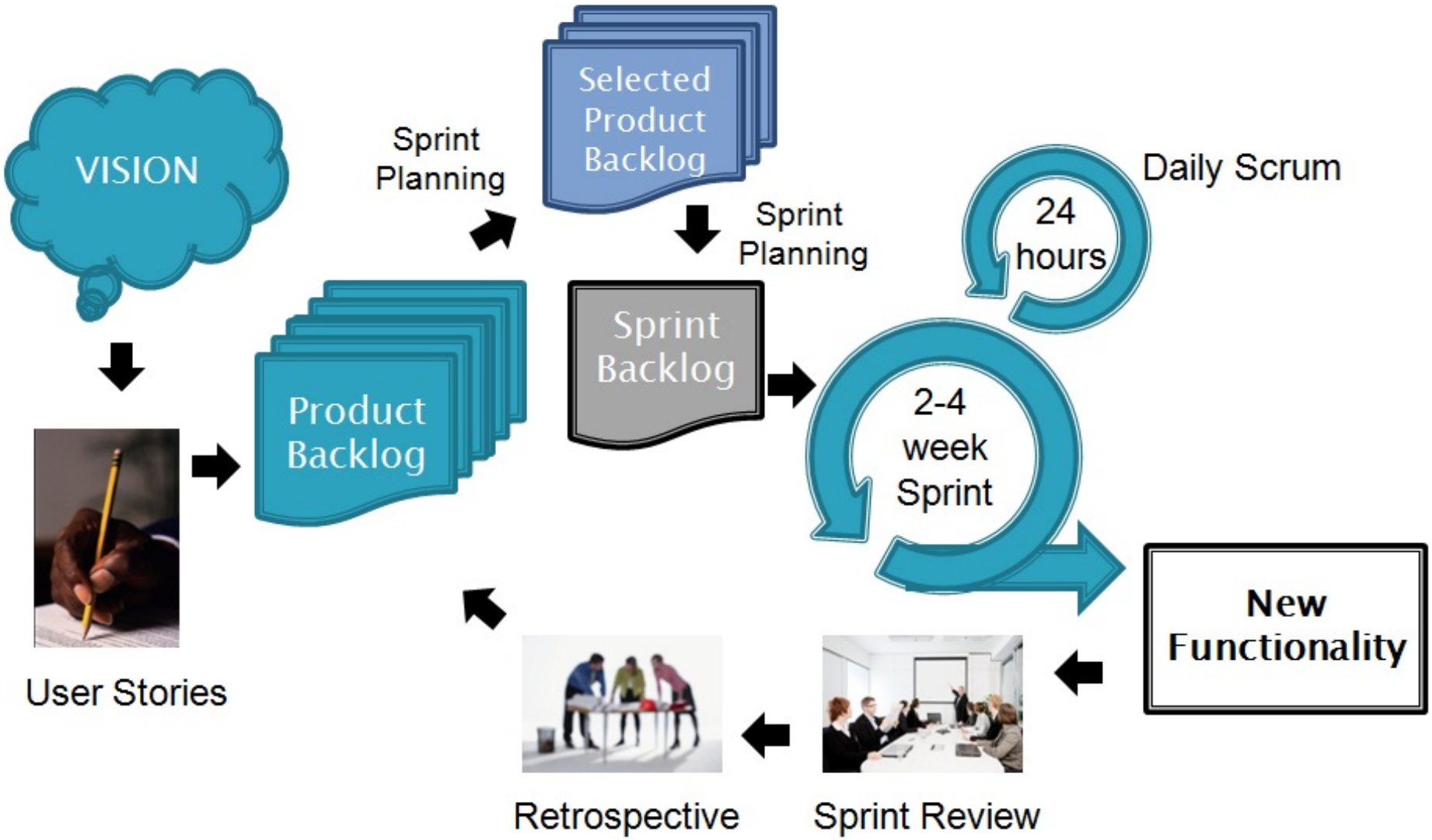
Other problems with waterfall

Lack of prioritization
-In waterfall, requirements have similar priorities
-In agile, priorities of tasks are reassigned with each sprint

False precision
-Danger of creating very detailed but outdated documentation

Inflexibility
- Project can be obsolete before it is implemented

SCRUM Overview



Reasons against using Scrum in regulated industry?

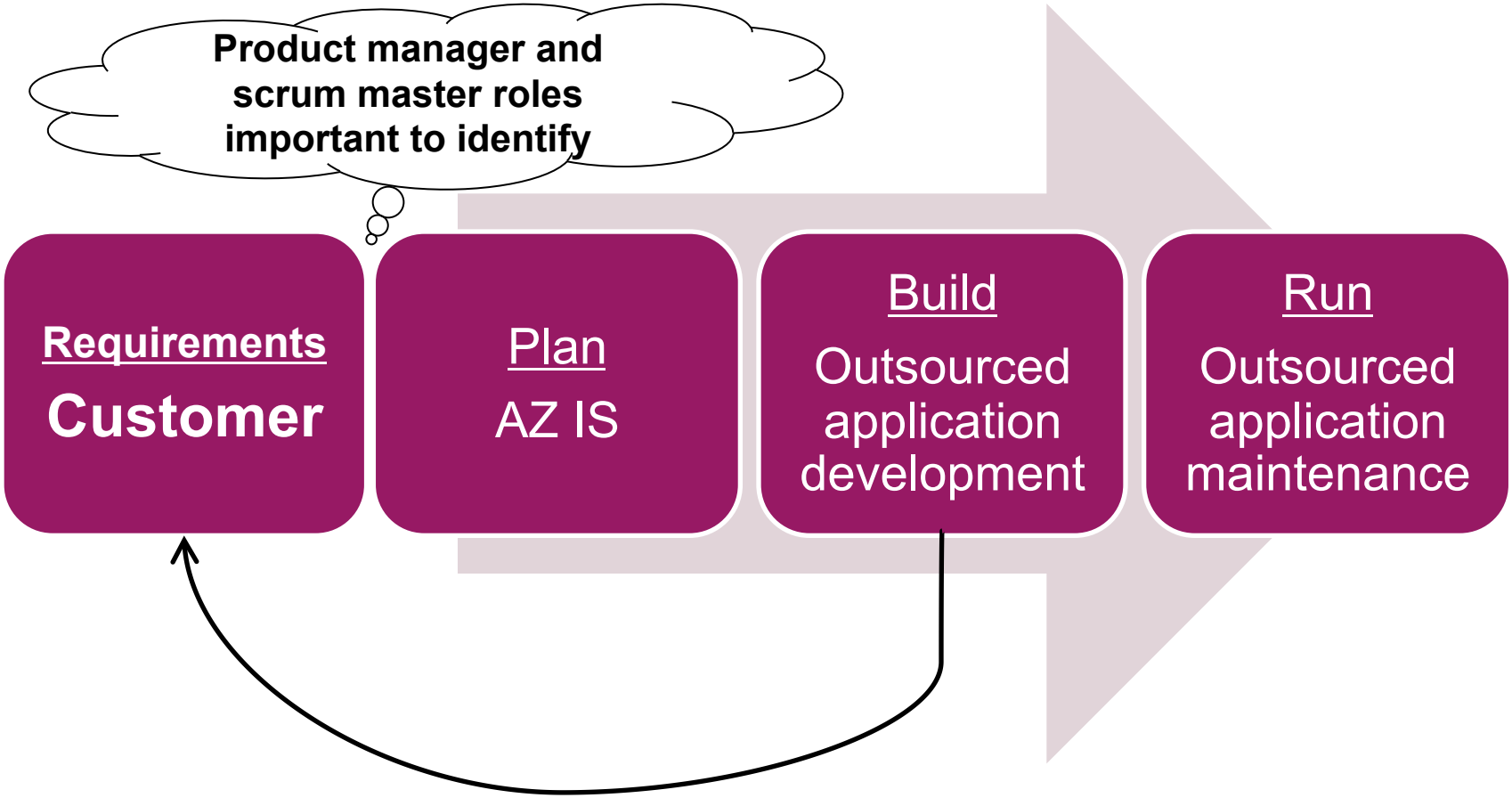
“V models are needed for validation!”
- user requirements do not need to be finalized before functional and technical specs are written

“Incomplete documentation!”
-In agile, a complete product has priority over complete documentation. This does not imply that no documentation is needed.

“Lack of testing documentation!”
-Because requirements can frequently change during scrum development, complete documentation of testing is a valid concern.
- When the product design has achieved stability, have special sprints to create formal test documentation.

Action (Feature)		FDA Guidance[3]		EMEA Guidance[4]
Procedural	A	Study Protocols. Each specific study protocol should identify each step at which a computerized system will be used to create, modify, maintain, archive, retrieve, or transmit source data.	6.4.9	The clinical trial protocol should contain the identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered source data.
Procedural	B	There should be sops and controls in place when using computerized systems to create, modify, maintain, or transmit electronic records, including when collecting source data at clinical trial sites.	5.5.3. b	Maintain sops for electronic systems.
Procedural	C	When original observations are entered directly into a computerized system, the electronic record is the source document. under 21 CFR 312.62, 511.1(b)[7] (ii) and 812.140, the clinical investigator must retain records required to be maintained under part 312,§511.1(b), and part 812, for a period specified in these regulations.	4.9.4	The investigator/institution should maintain the trial documents as required by the applicable regulatory requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
Technical (Authorization)	D1	Access must be limited to authorized operators (21 CFR 11.10)(d) that have an individual account. The user should always log out at the completion of data entry session or when leaving the workstation. Alternatively, an automatic log off may be appropriate.	5.5.3. d	Maintain a security system that prevents unauthorized access to the data.
Technical (Audit Trail)	D2	Keep track of all changes made to information in the electronic records that document activities related to the conduct of the trial (audit trails). Audit trails or other security methods used to capture electronic record activities should describe when, by whom, and the reason changes were made to the electronic record.	5.5.3. c	Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e., maintain an audit trail, data trail, edit trail).
Technical (Audit Trail)	D3	Ensure that the system's date and time are correct. The ability to change the date or time should be limited to authorized personnel.		
Technical (Authorization)	E	External safeguards to ensure that access to the computerized system and to the data are restricted to authorized personnel. Prevent the altering, browsing, querying, or reporting of data via external software applications that do not enter through the protective system software.	5.5.3. e	Maintain a list of the individuals who are authorized to make data changes.
Technical (Data Validation)	F1	Incorporate features into the computerized system to encourage consistent use of clinical terminology and to alert the user to data that are out of acceptable range.		
Technical (Attributability)	F2	The computerized system should be designed in such a way that retrieved data regarding each individual subject in a study is attributable to that subject.		
Procedural	F3	Documentation should identify what software and hardware will be used to create, modify, maintain, archive, retrieve, or transmit clinical data.	5.5.3. b	Maintain sops for electronic systems.
Technical (System Integrity)	F4	Sufficient backup and recovery procedures should be designed to protect against data loss.	5.5.3. f	Maintain adequate backup of the data.
Technical (System Integrity)	F5	Integrity of the data and the integrity of the protocols should be maintained when making changes to the computerized system, such as software upgrades, including security and performance patches, equipment, or component replacement.		
Procedural	G	Training should be provided to individuals in the specific operations with regard to computerized systems that they are to perform.		

Implementing agile/scrum has changed our fundamental IS model at AstraZeneca



Benefits seen from Agile development?

6 X reduction in project validation costs? [6]

- Waterfall: Validation is 25% of project costs
- Agile: Leading pharma now estimate validation cost to be 4%

AstraZeneca system development project comparison:

- 2009 project following traditional waterfall approach – 8mUSD and 3 years – benefits realized only at end of project.
- Project delivering in Q1 2014 – 1.3mUSD and 1.5 years – benefits realized earlier, delivered in releases during the project
- Both had similar complexity/size

Invest these savings into more value added innovation.

So how do we implement agile development for regulated systems?

- Develop an SOP that describes your particular agile methodology.
- Produce the same deliverables that waterfall would do: validation plan, requirement specification, system design, test scripts and final validation report.
- Requirements will still get frozen, but significantly further along in the process.
- Take time to explain agile methodologies to your regulatory and quality specialists – they may need to explain in an inspection!

Conclusion

The end goal of every methodology is the same: to produce a quality software product.

Agile methodologies accomplish this goal with greater flexibility and user input, often resulting in shorter development times, fewer defects, and greater user satisfaction with the end product.

By taking the time to understand the FDA's objectives and applying them to agile methodologies, you can develop better (and more innovative) software in a validated environment.

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