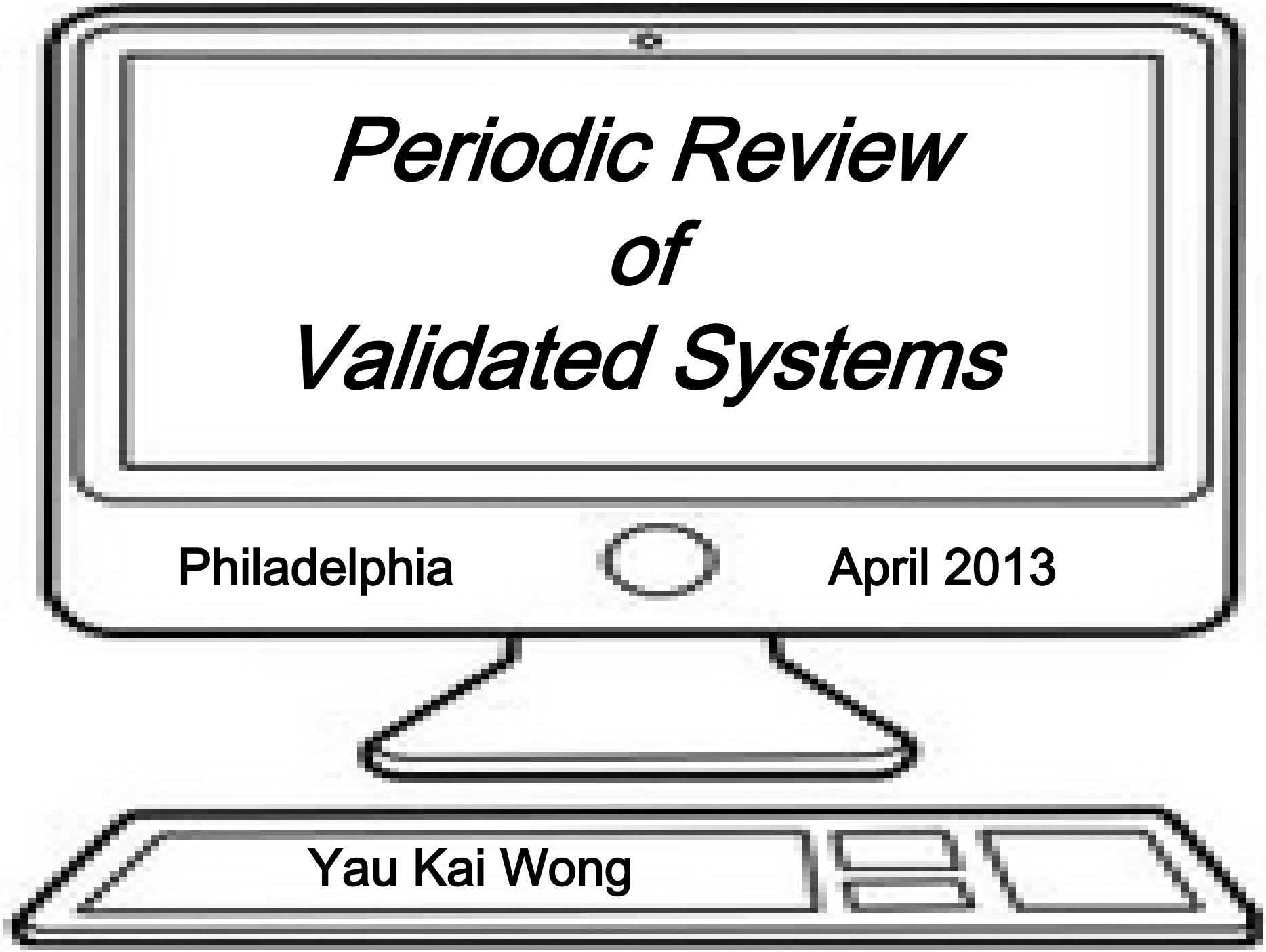
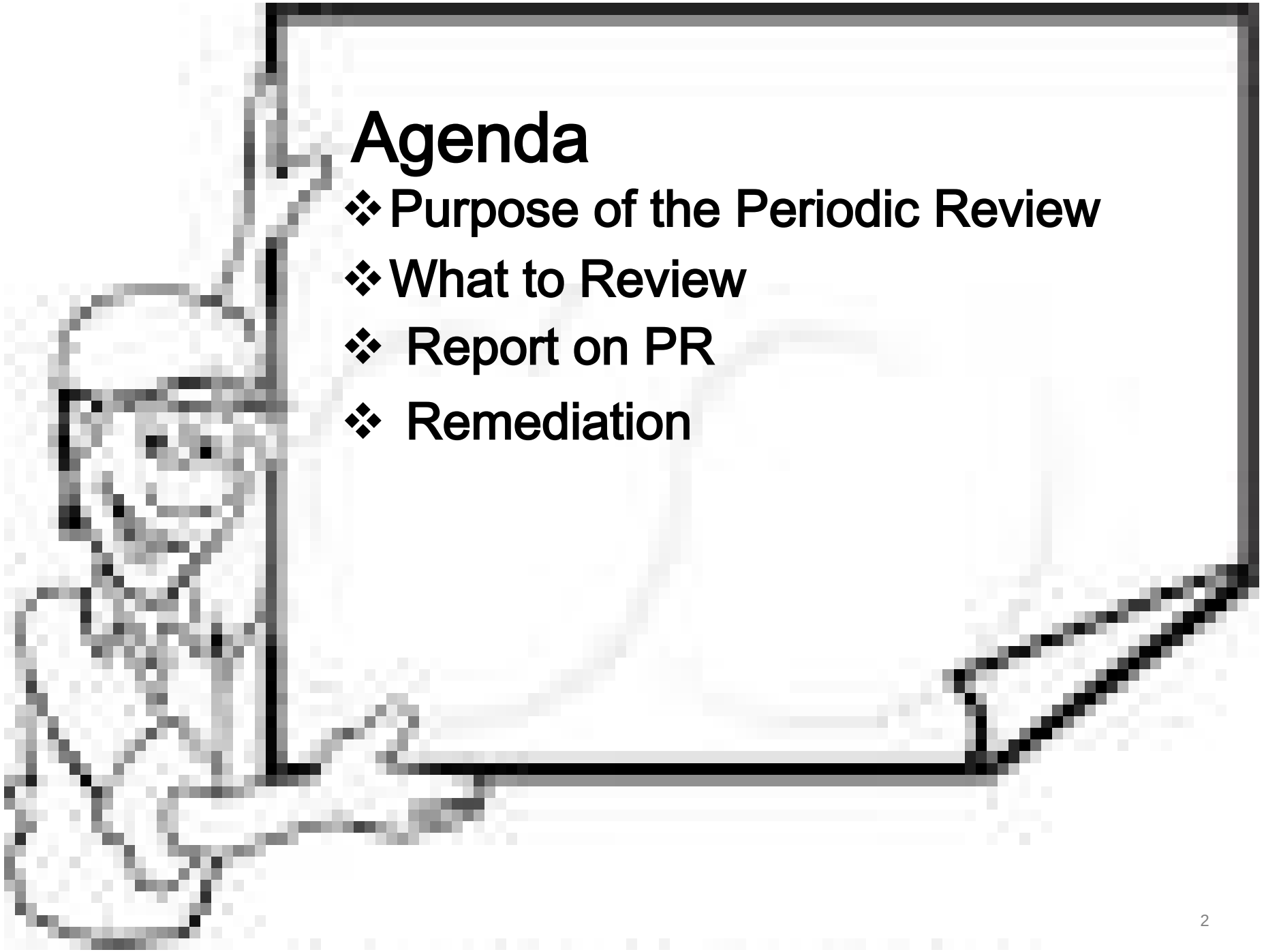

Periodic Review
of
Validated Systems
Philadelphia
April 2013
Yau Kai Wong



Agenda

- Purpose of the Periodic Review
- What to Review
- Report on PR
- Remediation

Regulatory requirement

Both the FDA and EU GMP's detail the requirement for demonstrating that a computer system remains in a validated state throughout its operating history.

- **FDA 21 CFR 211.68(b)**
  - *"Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system."*

Regulatory requirement

- EU Annex 15
  - *"Facilities, systems, equipment and processes, including cleaning, should be periodically evaluated to confirm that they remain valid. Where no significant changes have been made to the validated status, a review with evidence that facilities, systems, equipment and processes meet the prescribed requirements fulfills the need for revalidation."*

Purpose of the Periodic Review

- The purpose of the Periodic Review is to ensure that the system *remains* compliant with regulation, is *fit* for its intended use, and *satisfies* company policies & procedures.
- It may also fit with the companies Operation Excellence / *Continuous Improvement* program.

Objectives of Periodic Review

- To provide *independent* assurance to the process owner and senior management that controls are in place around the system being reviewed and are functioning correctly. The system is validated and *controls* are working adequately to maintain the validation status.

- To identify those controls that are not working and to help the process owner and senior management improve them and thus eliminate the identified weaknesses. The impact of a finding may be applicable to a single computerized laboratory system or all systems in a laboratory.

Benefits of Periodic Review

- Quality and the Business
- Improve the operation
- Maintain compliance
- Support the continuous improvement

Frequency of Periodic Review

- The frequency of performing Periodic Reviews should be dependent on the Complexity, Criticality, Novelty, and Operating History of the (computer) system.

- For example an automated control system (Category 4 / 5) the computer system periodic review should be performed more frequently than an off the shelf item.

Frequency of Periodic Review

- The periodic review of computer systems can be a considerable overhead for regulated companies. Low risk to patient safety and GMP requirements may not require a periodic review. The decision and rationale must be documented.

Frequency of Periodic Review

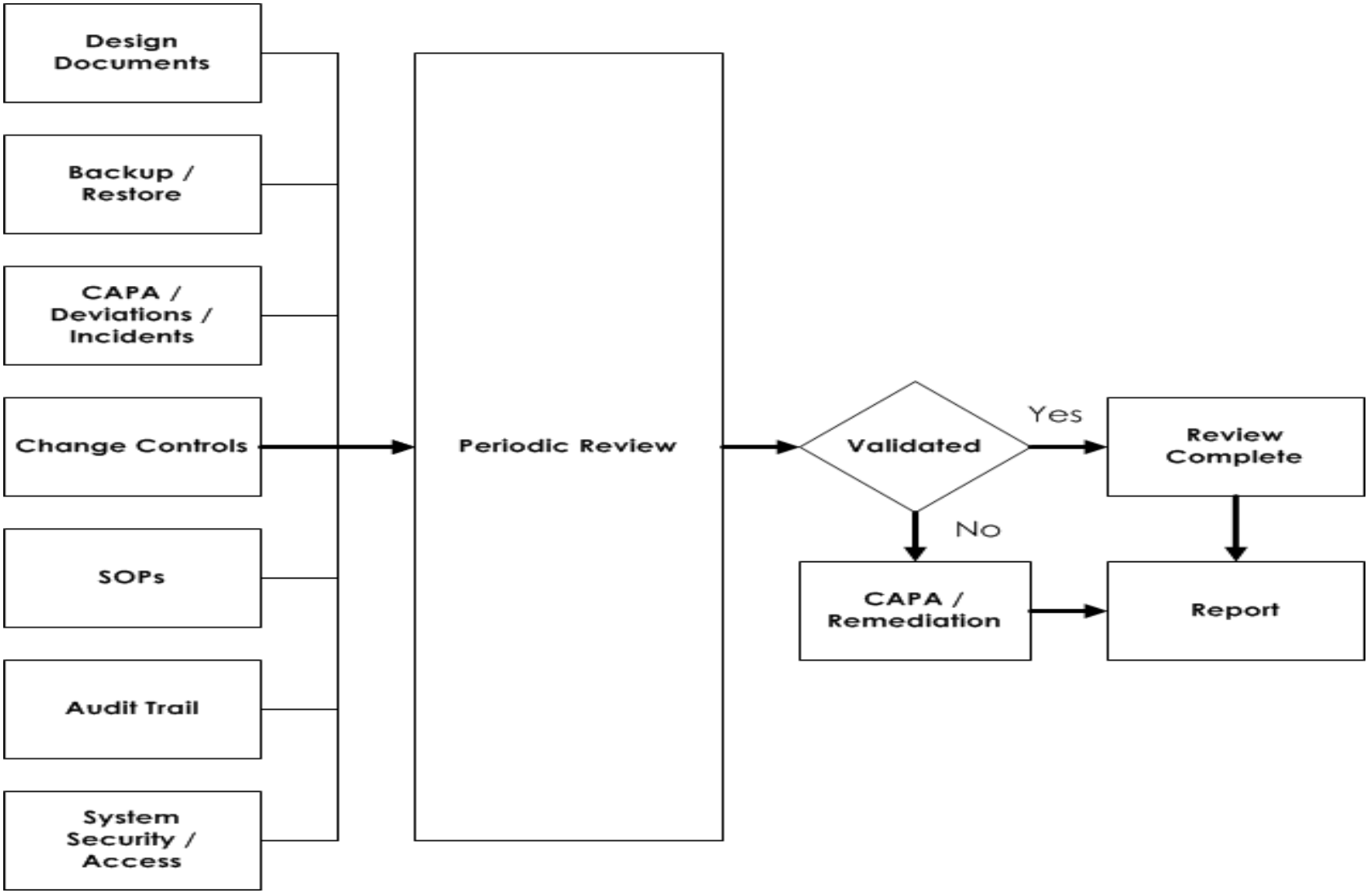
- **Once the operating history has been established and the system is stable (minimal incidents and changes) then the frequency can be reduced.**

- The frequency of review should be defined with a minimum and maximum time between reviews, for example a scale of 1 to 4 years can be set for the review period. Only new GAMP category 4 and 5 Computer Systems would have an annual review period. This would be extended as discussed above as the operating history demonstrated that the system operation is stable.

Frequency of Periodic Review

- Non configurable systems starting with a frequency of 2 years when first installed through to a maximum 4 years once a stable operating history is established.

Overview of the PR process



Who performs Periodic Review

- Process Owner – laboratory person who is responsible for the system
- System Owner – the person responsible for the availability and support of the system
- IT - system administrator or a member of the computer validation group
- Quality Assurance

Qualification of reviewer

- Knowledge of the GxP
- Experience working with computerized systems and knowing where (noncompliance) "bodies" can be buried and where bad practices can occur
- Understanding & knowledge of the current procedures used by the company
- Open and flexible approach, coupled with the understanding that there are many ways of being in control
- Good interpersonal skills coupled with a hide as thick as an elephant's

Planning for a periodic review

- Scheduling
- Recruit of personnel
- Coordination for system documentation retrieval
- Assign review tasks

Carry out periodic review

- **Static**
  - Sit in a room and read and evaluate system documentation or logs against procedures and polices
- **Dynamic**
  - Look at the system and see how the software and instrument operates, examine the IT support, and have discussions with users and IT staff

In reality, the periodic review is a mixture of the dynamic and static options

Performing the Review

Periodic review can be a labor and time intensive process .

Two methods which can be followed for establishing and maintaining the validated state.

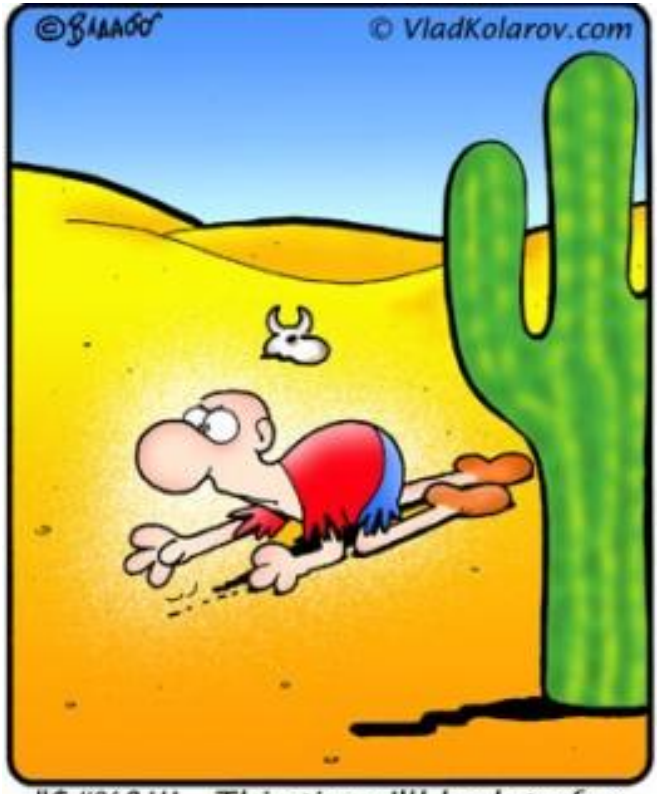
- Traditional periodic review
- Continual monitoring and trending

Performing the Review

- **Continual monitoring and trending**
  - Equipment history or validation equipment files
    - Change control records, deviations, incidents logs
    - Trending of the system
  - Risk assessments

What to review

- System ID # & location
- Validation status
- System *security* & access
- *Audit trail*
- Change control
- *Backup* and *restore* & *disaster recovery*
- Deviation
- CAPAs
- Trending



"$#%&!!!...This time I'll be late for Jay Leno for sure!!!"

Conducting the Periodic Review

- Prepare a checklist
- Obtain information from the person that you will interview and have discussions with during the PR
  - Ask open-ended questions
  - "state of MO" – "show me" to verify
- List of current company SOPs
- Review of the last system validation

Conducting the Periodic Review

- **Review of the last system validation**
  - Validation plan
  - Validation summary report
  - User requirement specifications
  - Current system configuration
  - Operational review

Documentation of the Periodic Review

- **Periodic Review Report**
  - Findings
  - recommendations

Actions for Periodic Review

- CAPAs
- Remediation
  - Re-validate
  - Patching
  - Upgrade / update software, documentation
- System decommissioning / retire

CSV FDA Warning Letter: Periodic Review

Observation

6. Your firm *failed to check* the accuracy of the input to and output from the computer or related systems of formulas or other records or data and establish the degree and *frequency* of input/output verifications [21 CFR § 211.68(b)].

For example, the performance qualification of your (b)(4) system software (Validation No. 4000-03-PQ-0002) failed to include verification of the expiration date calculations in the (b)(4) system. In addition, there is no established degree and frequency of performing the verification. Discrepancy reports have documented that product labeling with incorrect expiration dates have been created and issued for use.

Your response states that you opened Investigation T-139 and you provide a January 29, 2010 through February 26, 2010 completion timeline. You have not provided a response to correct this violation and establish a corrective action plan to assure that computer systems are properly qualified.