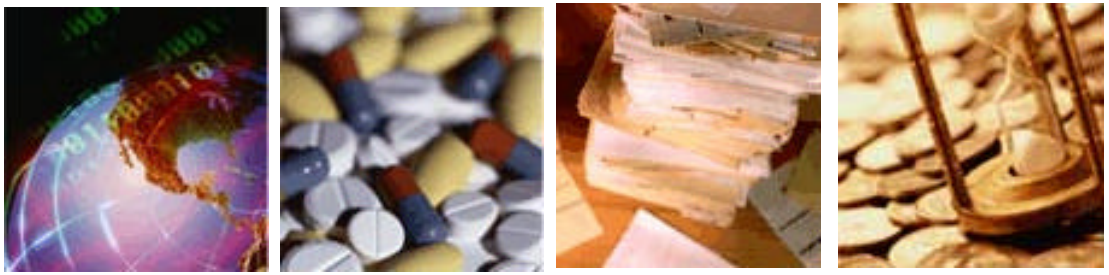


GxP Compliance for Computerized Systems

The Second Annual Pharmaceutical Industry Regulatory and Compliance Summit

David L. Stone
General Manager, Validation Services
Glemser Technologies
June 13, 2001

About Glemser Technologies Corporation

- Founded 1987 in Bethlehem, PA
- Professional staff of 35, most with degrees in Computer Science or related disciplines
- Recently opened a satellite office in Bernardsville, NJ
- Provided services to nearly all of the major pharmaceutical manufacturers

Our Mission

- Help regulated companies implement and validate global document management and e-commerce solutions.
- Attract and retain professionals who understand document management, e-commerce, software engineering, project management and regulatory requirements.
- Develop and maintain integrated methodologies designed to withstand rigorous regulatory audits.
- Provide consulting and services that assist our clients in achieving and maintaining regulatory compliance.

Service Offerings

Documentum

- General Implementation
- 4i Migration
- DCM Implementation
- Training & Support

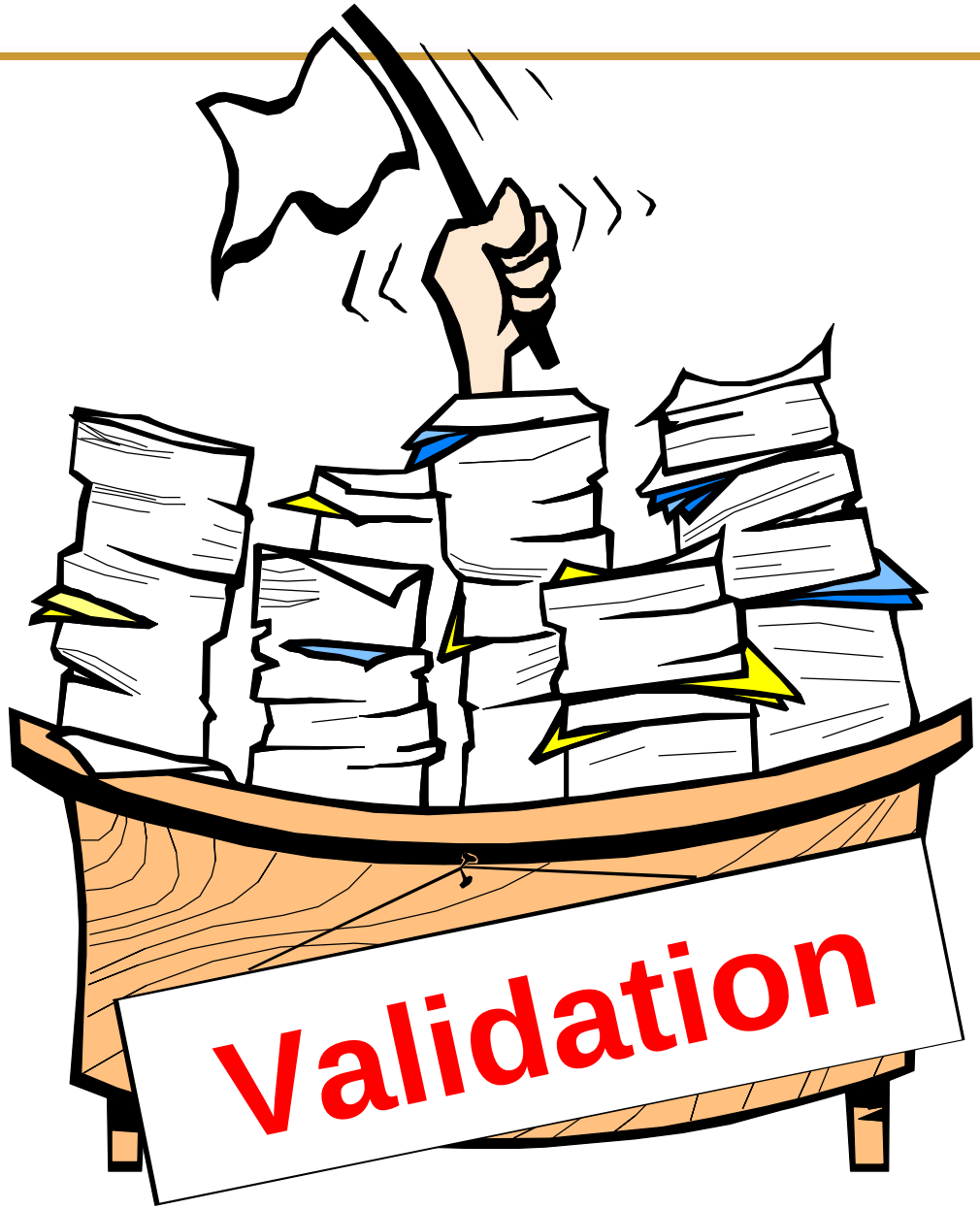
E-Commerce

- Strategic Web Analysis
- Web Application Dev.
- Web Design/Architecture

Validation

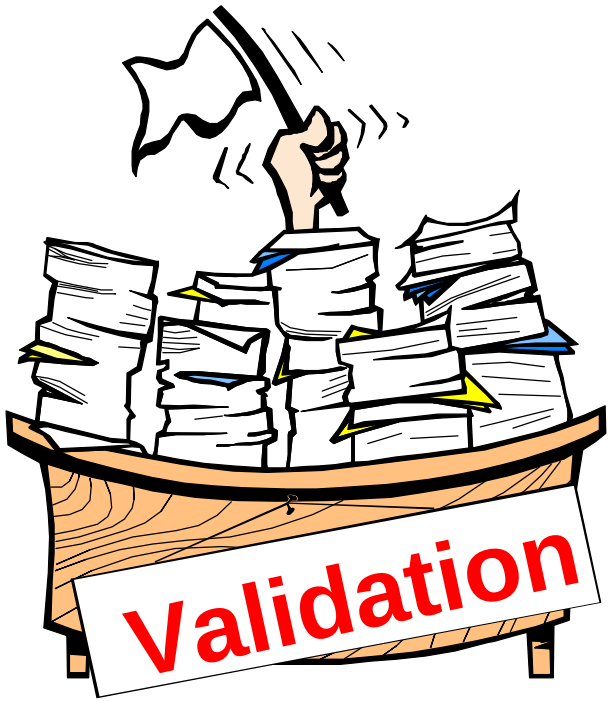
- Regulatory Consulting (incl: 21 CFR Part 11)
- Validation Strategies
- Turnkey Validation
- Validation Training/Support
- Qualification Execution
- SOP Development
- Change Control Systems
- Post Validation Audits
- Software Vendor Audits

It’s 2001 - Business as Usual



Everybody Has Problems

- Too much work
- Budget pressures
- Not enough staff
- No time to do training
- Projects out of control
- Non-compliant legacy systems
- The Part 11 blues



Is There a Way Out?

…could be

Some Suggestions

- Develop a “project friendly” validation policy
- Train for success
- Build a repeatable validation process
- Invest in accelerators
- Build a compliant infrastructure
- Qualify vendors *before* signing contracts
- It takes a team
- Measure twice, cut once

Project Friendly Validation Policy

Project Friendly Validation Policy

- **Coordinate Validation and Development Methodologies**
- **Make QA / Validation role clear from the beginning**
  - **Active participant (develop documents, execute testing)**
  - **Process Advisor (validation strategy, etc.)**
  - **Reviewer and Approver**
  - **(Perceived Obstacle)**

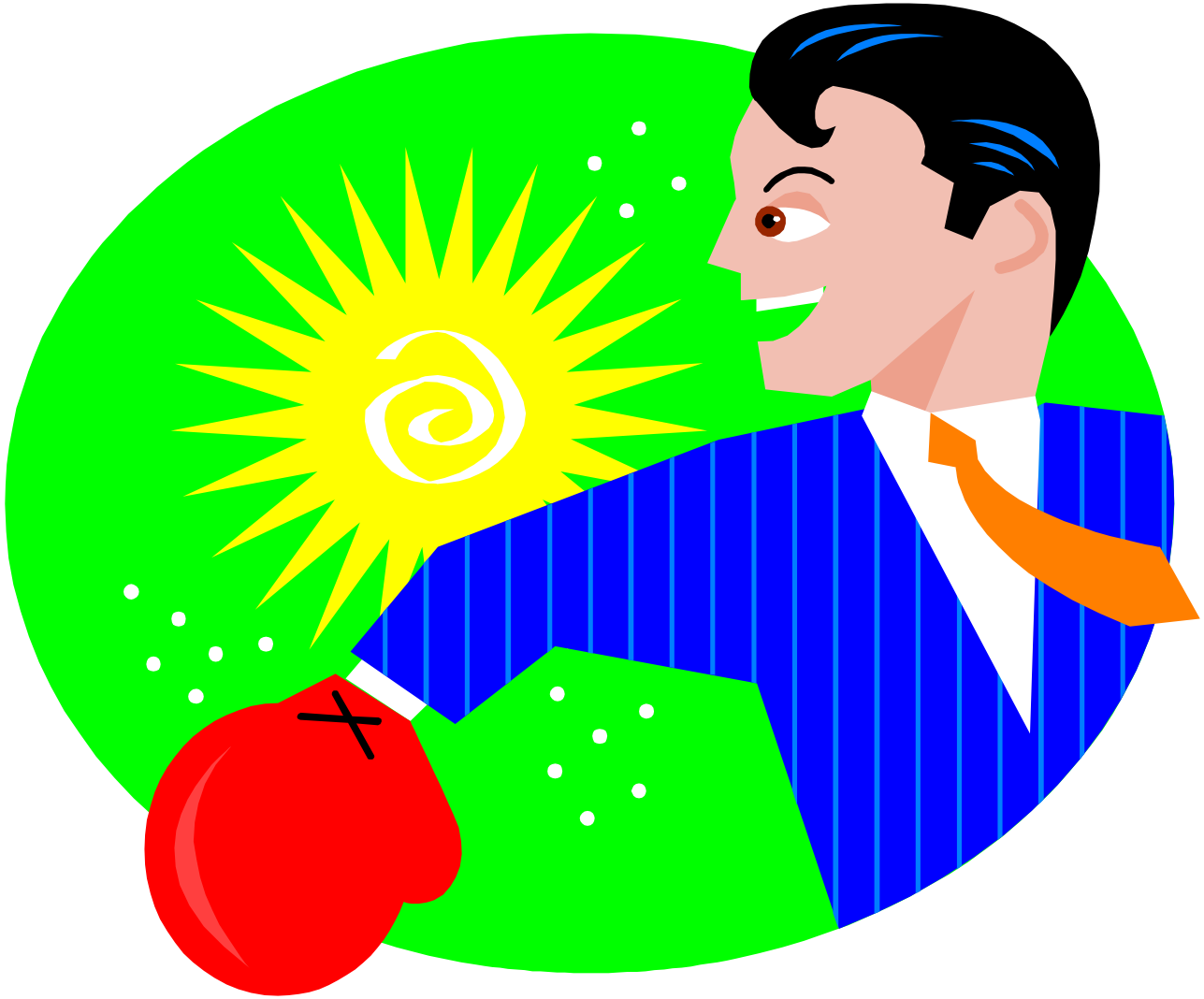
Project Friendly Validation Policy (cont'd)

- **Assign a liaison to major projects**
  - Guides and advises team on regulatory issues
  - Maintains awareness of validation status
  - Prevents "end-runs" and "work-arounds"
- **Define clear requirements and expectations for attaining production-status approval**
- **Partner**
  - An un-validated system isn't completed
  - An incomplete system isn't ever validated

Project Friendly Validation Policy (cont'd)

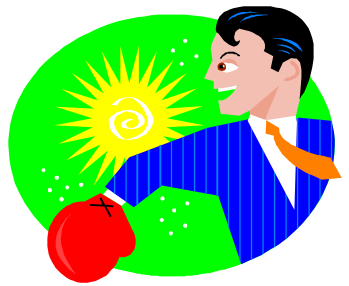
- Assure that emergency procedures exist that permit reasonable flexibility when dealing with unexpected situations
- Verify that emergency actions are appropriately documented after the fact

Train for Success



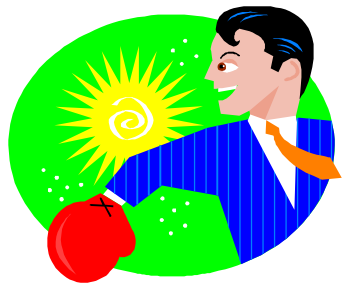
Train for Success

- **Conduct focused GxP training for your IT organizations**
  - **IT- specific FDA requirements and expectations**
  - **Security**
  - **Activity logs**
  - **Audit trails**
  - **Good testing practices**
  - **21 CFR Part 11**
  - **FDA inspections**
  - **Internal policies (blue ink / black ink)**



Train for Success (cont'd)

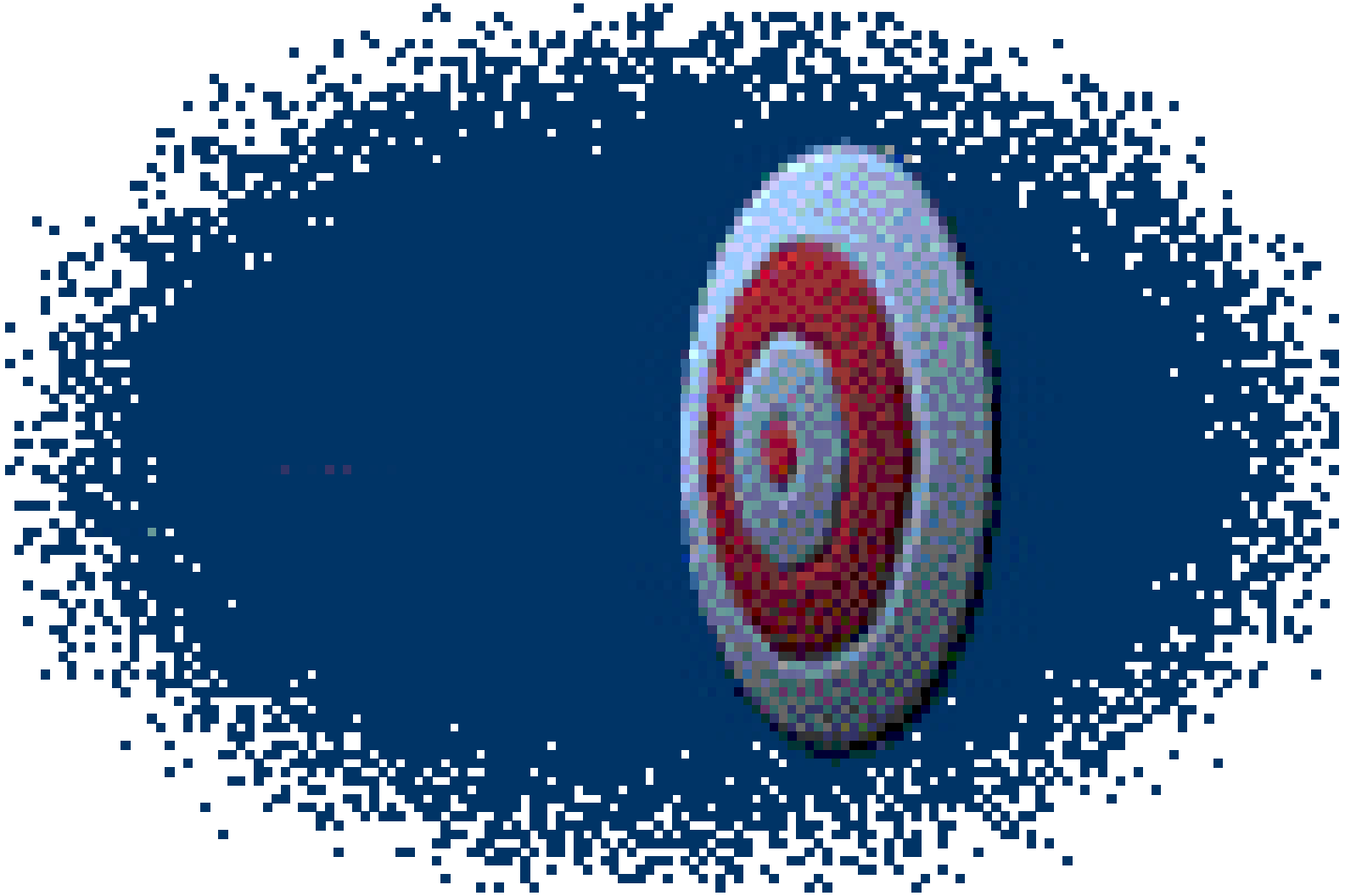
- **Training should include:**
  - Project Managers
  - Developers
  - Technical Support and Operations
  - System Security Analysts
  - Help Desk staff
- **Explain why developing systems for your company isn't the same as it is for a non-regulated organization**



Train for Success (cont'd)

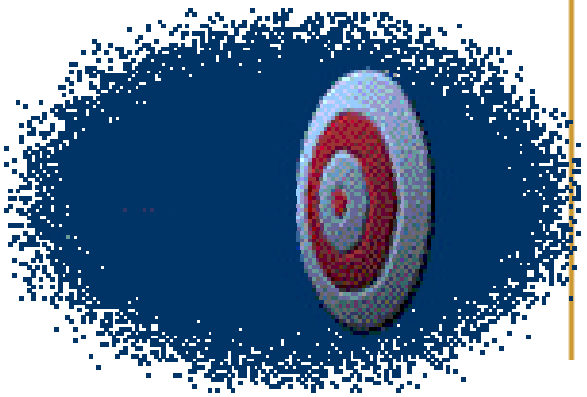
- **Discuss the consequences of non-compliance**
  - **483 examples**
  - **Warning Letters**
  - **Fines**
- **Conduct periodic new hire / refresher training**
- ***Tip: Try lunch-time briefings - IT staffers will show up for any meeting that promises food***

Repeatable Validation Process



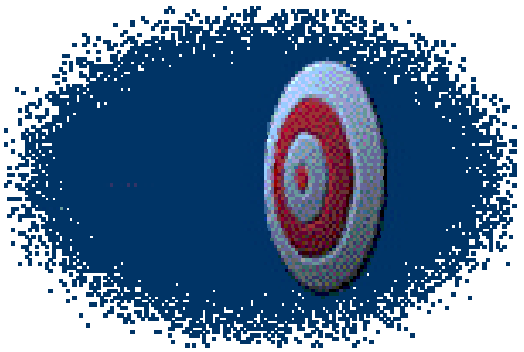
Repeatable Validation Process

- Provide templates for key documents
- One process may not fit all situations
  - Excel spreadsheet
  - Mid-range custom application
  - Large “configurable” Implementation (SAP)
- Make “real-world” examples available
  - Master Plans
  - Protocols
  - Test Scripts (annotated)
  - Reports

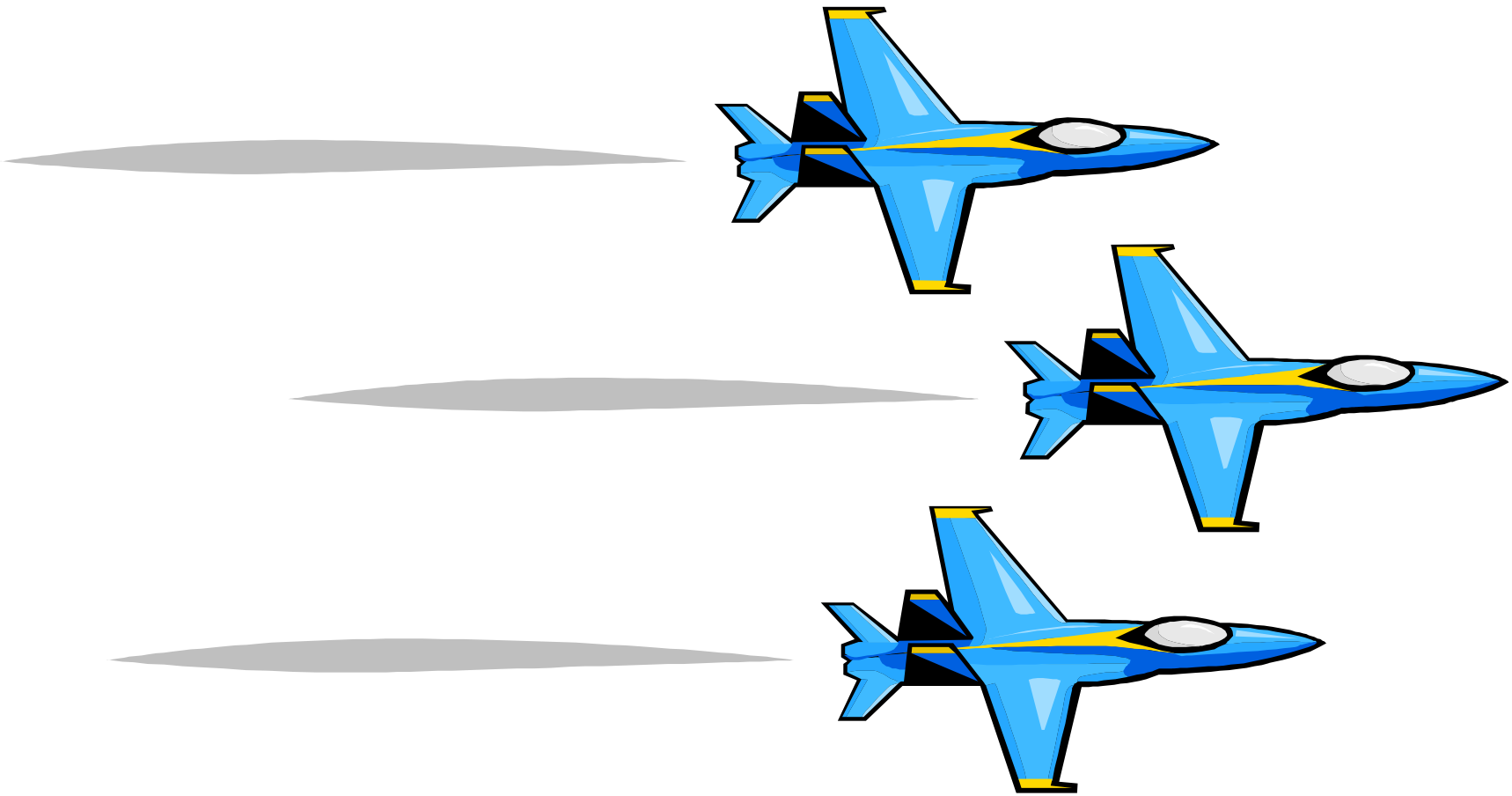


Repeatable Validation Process

- Monitor progress on a regular basis (liaison)
- Assure a consistent stream of information to the project team
- Adjust the validation process - when a change is warranted

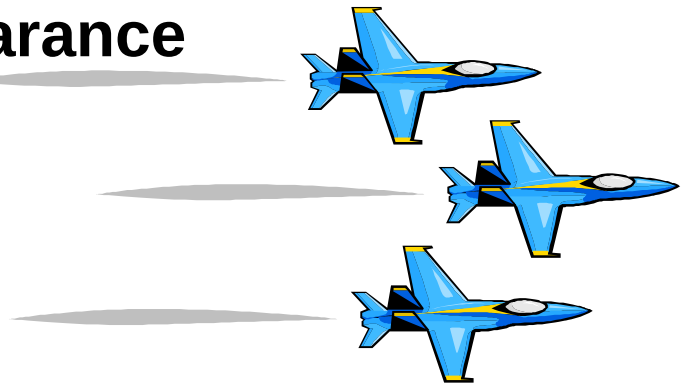


Invest in Accelerators



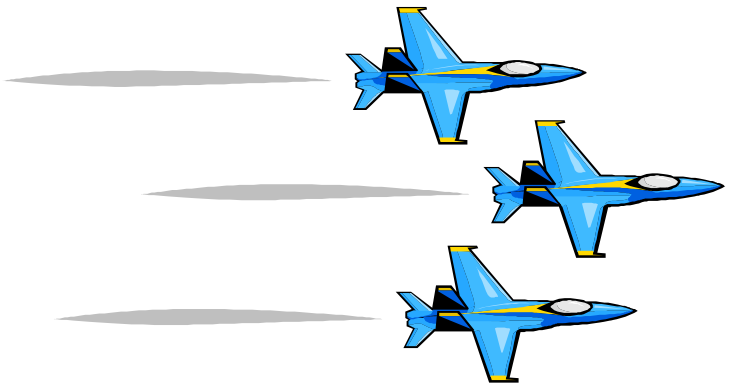
Invest in Accelerators

- **Automated testing tools**
  - Initial overhead
  - Long-term payback
- **Validation Support Systems**
  - Content Management
    - Workflow
    - E-signatures
    - Audit Trail
  - Test Deviation Tracking and Clearance
  - Change Control



Invest in Accelerators (cont'd)

- **Documented Compliance Methodology**
  - Should dovetail with Development Methodology
- **Subject Matter Experts**
  - Good testing practices
  - Part 11 compliance
  - System specific expertise (SAP, LIMS, etc)
- **Administrative Support**



Build a Compliant Infrastructure

Build a Compliant Infrastructure

- **Make compliance a consideration when developing the infrastructure for a new system.**
  - **Segregate validated systems**
  - **Maintain documentation**
    - **Device specifications**
    - **Environmental requirements**
    - **Model numbers**
  - **Develop and use formal checklists for loading operating systems and application software**
    - **Often available from HW and SW vendors**
  - **Physically identify validated hardware**

Build a Compliant Infrastructure

- **Make sure your operations staff and support vendors are aware of restrictions on "validated" hardware**
  - **No parts "swapping"**
  - **Change control procedures apply**
  - **Even emergency repairs must be documented**
  - **Upgrades should be planned in advance**
  - **Deviations should be reported**

Qualify Vendors *Before* Signing Contract

Qualify Vendors *Before* Signing Contracts

- **Considerations**
  - Is the developer stable and competent to deliver?
  - Are they familiar with the pharmaceutical industry?
    - Consider experience in other regulated industries (banking, securities, defense, etc.)
    - Specific orientation and training may be required
  - Are they familiar with specific GxP requirements that may apply to them?

Qualify Vendors *Before* Signing Contracts (cont'd)

- Do they have an infrastructure capable of delivering quality software and documentation?
  - Training
  - Change control
  - Version control
- Can they provide tools to aid in the validation process?
- How will they respond to requests for changes and unplanned failures?

Qualify Vendors *Before* Signing Contracts (cont'd)

- If not, you have some choices to make
  - Find another developer
  - Work with the developer to address their deficiencies
- Conduct periodic re-inspections to document progress

It Takes a Team

It takes a Team

- **The best way to achieve and maintain compliance is to make it an integral part of the core activity**
  - **Maintaining sterility**
  - **Appropriate storage of materials**
  - **Product label verification**
- **Validating computer systems shouldn't be any different.**
  - **Work with IT and outside developers**
  - **Provide guidance and training**
  - **Lead from the front**

Measure Twice, Cut Once

Implementation

- Conduct load testing well in advance
- Identify key users and provide additional training
- Saturate area with support staff
- Resist knee-jerk reactions

Implementation (cont'd)

- All changes through change control process (may be as emergency change – if warranted)
- Test all changes thoroughly
- Stabilize system before adding new functionality
- Monitor system security carefully

Ongoing support

- Change control
- Change control
- Change control
- And……
  - Maintain an up-to-date list of validated systems
  - Maintain documentation and test cases
  - Monitor access authorizations
  - Be aware of changes to desktop devices (replacement printers)
  - Plan ahead for routine upgrades

Validation is Forever

- A system is only validated until the first change. At that point the validated state begins to deteriorate unless aggressive change control is observed.
- To maintain the validated status of the system, every change must be noted, documented, and (most) tested to assure that no adverse impact is introduced.

Validation is Forever (cont'd)

- **Challenges to the validated state include:**
  - Hardware upgrades (servers, storage devices, desktop)
  - System software changes (server OS, database, desktop OS, GUI, etc.)
  - Application software modifications (upgrades, patches, new interfaces, bolt-ons, custom development, etc.)

System Retirement

- Retirement is the final phase in the SDLC
- Validated systems have special retirement issues
  - Data access must be maintained
    - Convert data to new system AND verify conversion
    - Maintain old system(s) in perpetuity (including hardware)
- Document retirement process and activities
- Issue a formal system retirement notice

21 CFR Part 11

It's later than you think…..

Part 11: When does it apply?

- Part 11 applies even if paper records are printed from the electronic records. (manufacturing records, laboratory data)
- Part 11 Applies to electronic records that do not include an electronic signature
- Part 11 applies to existing legacy systems, no grandfather clause!

Glemser TECHNOLOGIES

Part 11 – Industry Implications

- Expect increased enforcement activities
- Increased industry and user awareness
- More solutions provided by software and hardware suppliers
- Greater acceptance of electronic record keeping and signatures
- Expect further FDA Guidance

Broad Impact

- Application Systems
- Operating Systems
- Support Infrastructure
- Validation Process / Procedures
- Organizational Impact
  - IT
  - End-users
  - Human Resources
  - Regulatory and Quality
  - Legal

Part 11 will most likely have a greater impact on your infrastructure than did Y2K

Cultural Compliance

- Requires changes in corporate culture to acknowledge the importance of managing corporate information assets in accordance with GMPs
- Requires training programs that explain the WHAT and WHY surrounding these changes
- Requires consistent responses to activities that constitute a threat to compliance

User Compliance

- **Acknowledge responsibilities**
  - Acknowledge that their electronic signatures are equivalent to handwritten signatures
  - Understand and observe security requirements
- **Act responsibly**
  - Protect passwords and user IDs more carefully
  - Halt “sharing” of passwords and user IDs to expedite approvals
  - Report security anomalies and deviations

Glemser TECHNOLOGIES

Alternative

Warning Letter: Baxter Healthcare Corporation – August 11, 2000

We (FDA) further request details regarding steps your firm is taking to bring electronic GMP records into conformance with 21 CFR Part 11.

The inspection disclosed deficient controls in the laboratory record keeping system, which is used for maintaining chromatographs and audit trails.

The Real Reasons To Do It Right

- We develop, manufacturer and distribute products that are used by individuals who trust us to deliver safe and effective products.
- Our reputations are based on the confidence of our prescribing physicians and their patients.
- If our products fail to perform as expected, their lives are placed at risk.




SOPs

- **Corporate SOPs**
  - Change control
- **IT Department SOPs**
  - Security
  - Back-up and Recovery
- **System-level SOPs**
  - Access authorization
  - Database recovery
  - Application of patches
- **The FDA often evaluates SOPs with a critical eye!**