

Regulatory Compliance

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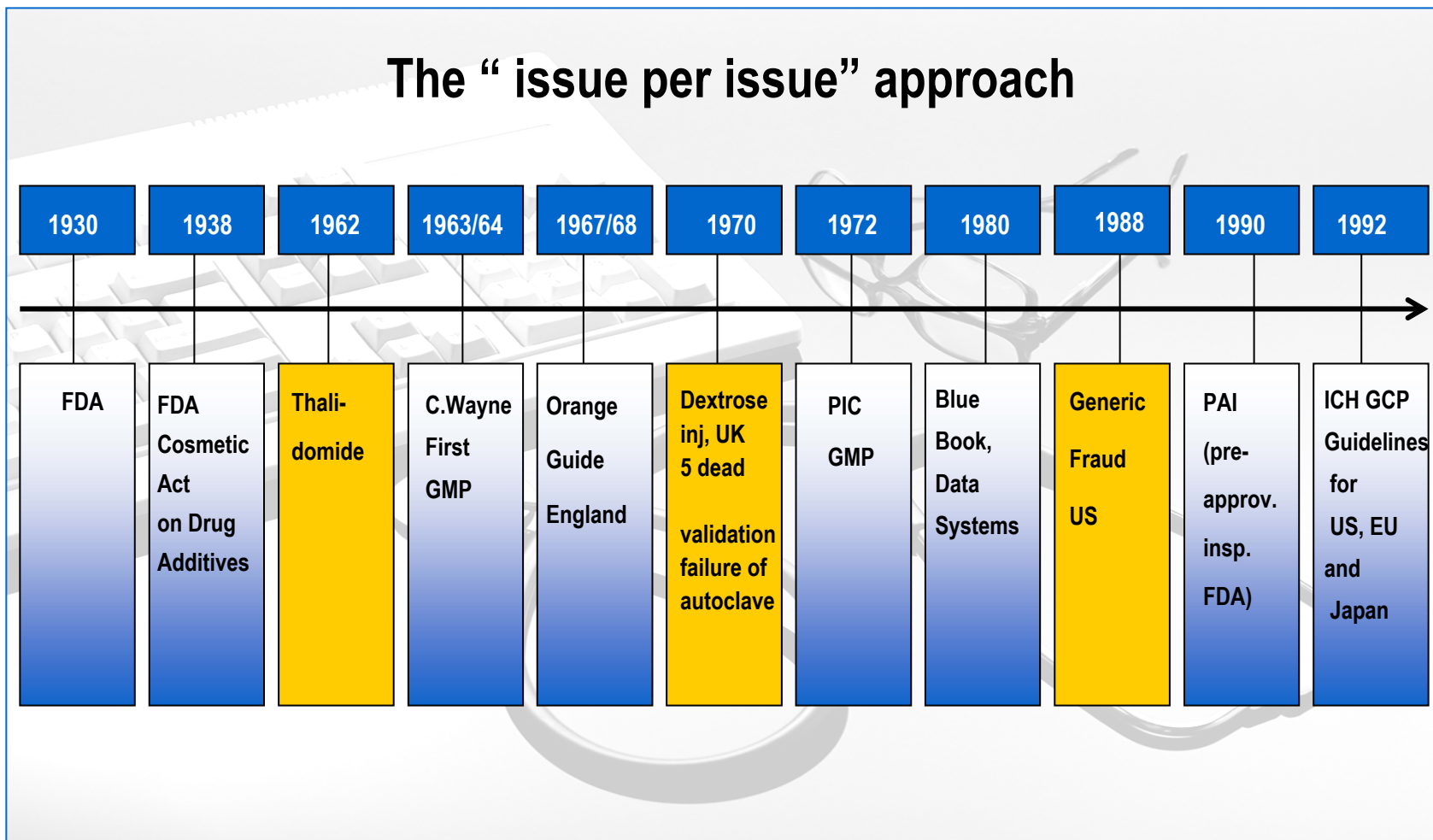


Why Compliance in Pharma?



Evolution in Regulation

The “issue per issue” approach



Regulations in Drug Development Process

	Pre Clinical Testing		Phase I	Phase II	Phase III		FDA	Approval
Years	3.5		1 - 2	2 - 4	4 - 6		1 - 5	Total = 12 - 17
Test Population	Laboratory and Animal Studies	FILE IND	20 to 100 Healthy Volunteers	100 – 300 Patient Volunteers	1,000 to 3,000 Patient Volunteers	FILE NDA		Post Marketing Safety Monitoring
Purpose	Assess Safety and Biological Activity		Determine Safety and Dosage	Evaluate Effectiveness. Look for Side Effects.	Verify Effectiveness, Monitor Adverse Reactions from Long-Term Use		Review Process	Large Scale Manufacturing ----- Distribution ----- Education
% of all new drugs that pass			70% of INDs	30% of INDs	27% of INDs		20% of INDs	

Regulatory Compliance to Ensure

- Pharmaceutical product **quality** is assured by
 - comprehensive development program
 - extensive manufacturing and environmental controls
 - rigorous validation procedures and requirements
- The high quality thus built into the final product is ensured through in-process controls and verified in a series of confirmatory tests before each manufactured batch is released to the market

Regulatory Agencies

- **FDA** : USA
- **MHRA** : UK
- **MHW** : Japan
- **EMA** : Europe
- **DCGI** : India
- **TGA** : Australia
- **SAMMDRA** : South Africa

* IFPMA, ICH, ICMR, PhRMA etc

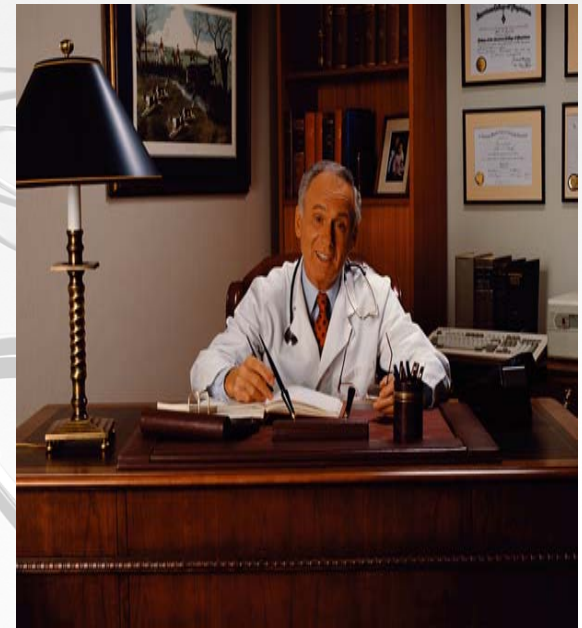
Applicable Guidelines used in Pharma

- Good Manufacturing Practice - EU Annex 11
- ICH Topic E6 - Guideline for Good Clinical Practice
- FDA Guidance - Computerized Systems Used in Clinical Trial
- **FDA CFR 21 Rule 11 - e-Records & e-Signatures**
- GLP Consensus Document - The Applications of the Principles of
GLP to Computerized Systems

Manufacturer

Each manufacturer which has a licence must have:

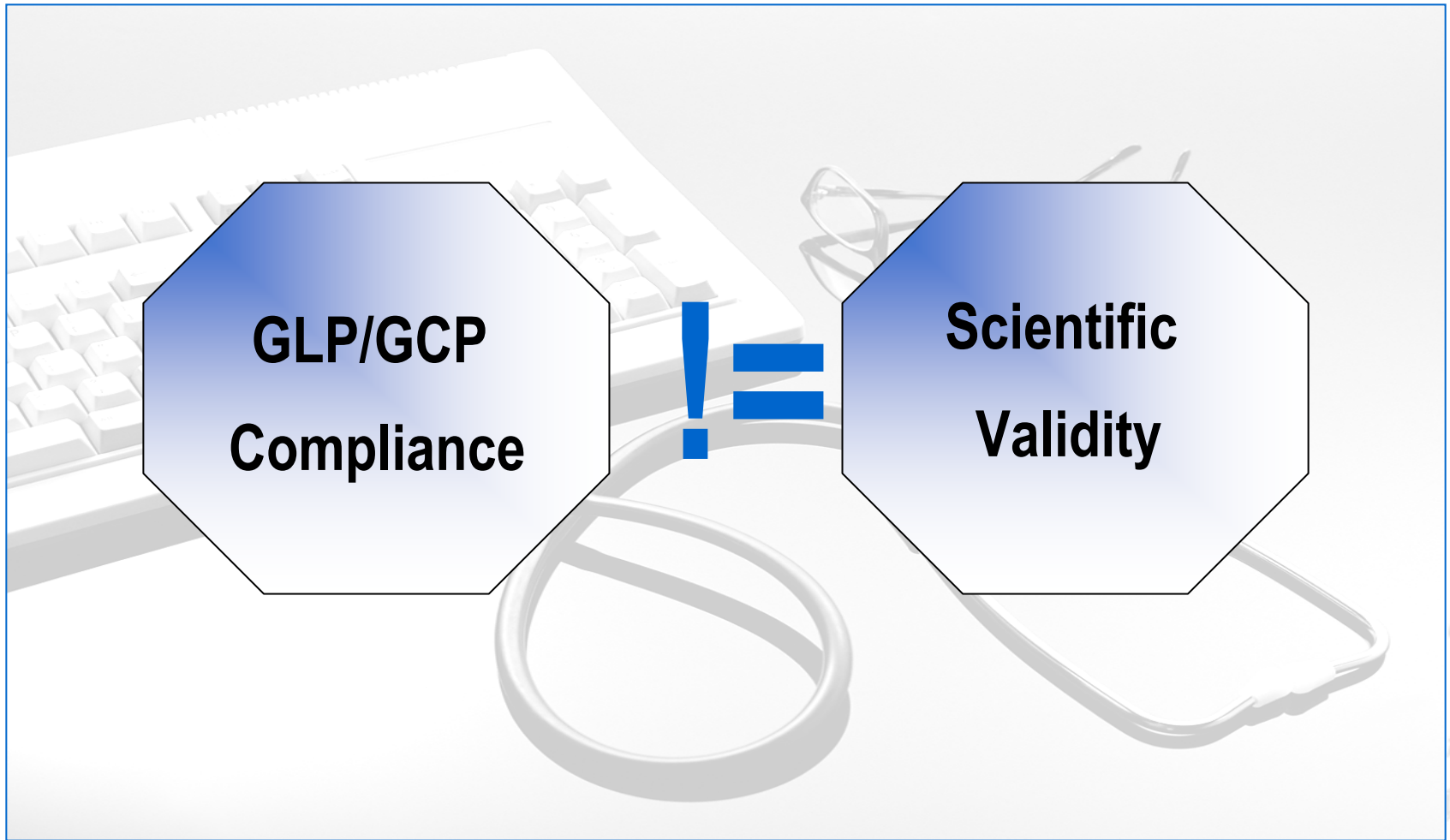
- Qualified person
- Premises and equipment in accordance with GMP requirements
- All operations in accordance with GMP independent QC unit
- Contracted activities in accordance with GMP



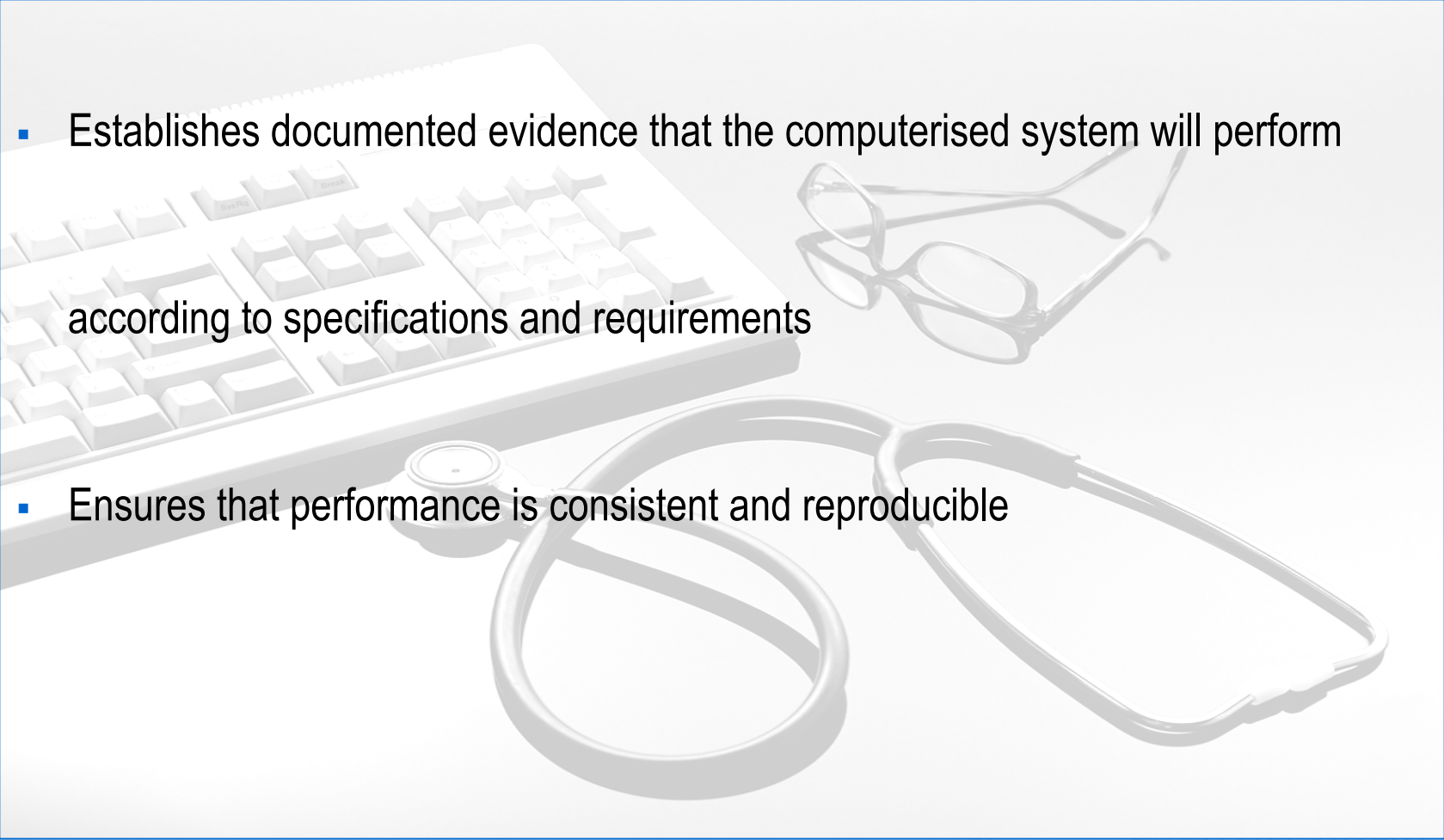
Qualified person

- The same requirements for QP as in directive 2001/83/EC
- QP can be pharmacist, chemist, biologist or medical doctor
- All subjects listed in article 49 paragraph 2 of directive must be covered by some kind of education (e.g. postgraduate courses)
- Special courses for QP's are running (for existing QP's to complete necessary knowledge and also for candidates for QP position)

It means.....



What does Compliance Ensure?

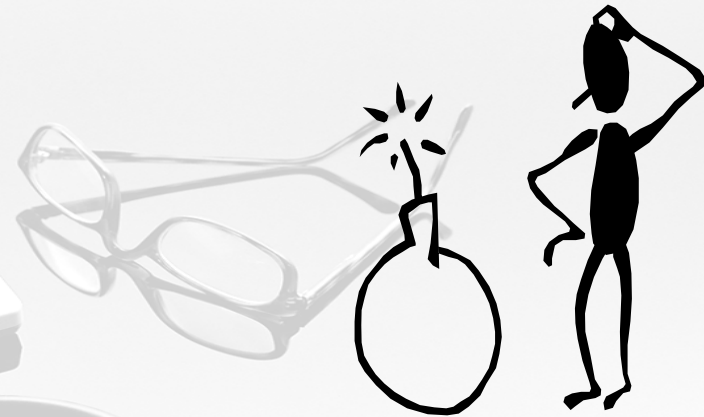
- 
- Establishes documented evidence that the computerised system will perform according to specifications and requirements
 - Ensures that performance is consistent and reproducible

Risk of NO ensured Compliance

Data can not be relied upon due to

- Risk of e-data corruption.
- Missing system control.
- Consequences of changes unknown
- No control over risk factors.
- Nothing can be based on the results
- Regulated data on system can be disqualified during any inspection
- Risk to the patient

System cannot pass regulatory inspection.



How to get started to ensure everything is in place!



**A validation effort must be planned based on a broad overview,
several things needs to be in place.**

**Think of it, as one would a clinical trial
or a development program.....**

[Market Fact Sheet.doc](#)

Way Forward : PhRMA

- High priority systems compliant within 5 years
- Medium and low risk systems to be addressed based on the availability of commercial software and a system's position in the overall lifecycle.
- Each company to generate a remediation plan to be available for inspectors and tracked during the course of inspection
- A record is a record only once it is final/has been signed, and subsequent changes are to be audit trailed
- Long term archiving should focus on the ability to restore records in a human readable format



Thank-You

