Comparison of FDA's Part 11 and the EU's Annex 11

Introduction

The relationship between FDA's Part 11 (21 CFR Part 11) and the European Union's Annex 11 (EUDRALEX Rules Governing Medicinal Products in the European Union, Volume 4, Good Manufacturing Practice, Medicinal Products for Human and Veterinary Use) diverges in philosophy. Both documents cover the same topic, the use of computerized systems in regulated activities. However, the approach of Part 11 is to make clear there are requirements to be met in order to conform to regulations. The emphasis is on activities and reporting.

In contrast, the approach of Annex 11 is to make clear how to conform to its rules. Annex 11 is a detailed guide to the areas of compliance that need documentation. A significant difference is the approach to risk management. Annex 11 points to risk assessment as the start of compliance activities. Part 11 differentiates security for open and closed systems, with extra security measures for open systems but without reference to risk or criticality. The aggregate of these differences is represented visually with the point-to-point comparison matrix shown below.

Table 1: High Level Comparison of Annex 11 and Part 11

	Annex 11	Part 11
Scope/Principle	Computerized systems as part of GMP regulated activities. Application should be validated. IT infrastructure should be qualified.	Electronic records and electronic signatures as used for all FDA regulated activities.
Focus	Risk- based quality management of computerized systems.	Using electronic records and signatures in open and closed computer systems.
Objective	Using a computerized system should ensure the same product quality and quality assurance as manual systems with no increase in the overall risk.	Electronic records and signatures should be as trustworthy and reliable as paper records and handwritten signatures.

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Table 2: Cross-Reference from Annex 11 to Part 11

Annex 11 Section No.	Annex 11 Title	Part 11 Cross Reference (substantially equivalent)
	Principle	***11.2(b)- Implementation*** ***11.10(a)- Validation***
	General	
1	***Risk Management***	not covered
2	***Personnel***	***11.10(i)- Personnel***
3	***Suppliers and Service Providers***	not covered
3.1	***formal agreements***	not covered
3.2	***audit supplier***	not covered
3.3	***review documentation for COTS***	not covered
3.4	***supplier audit available on request***	not covered
	Project Phase	
4	***Validation***	***11.10(a)- Validation***
4.1	***cover life cycle***	not covered
4.2	***change control and deviations***	***11.10(k)- Documentation control***
4.3	***systems inventory***	not covered
4.4	***user requirement specifications***	not covered
4.5	***quality management system***	not covered
4.6	***process for customized systems***	not covered
4.7	***evidence of appropriate test methods***	not covered
4.8	***data transfer validation***	***11.10(h)- Device checks***
	Operational Phase	
5	***Data***	***11.10(f)- Operational system checks*** ***11.30- Controls for open systems***
6	***Accuracy Checks***	***11.10(f)- Operational system checks***
7	***Data Storage***	***11.10(c)- Protection of records***
7.1	***secured and accessible***	***11.10(d)Limiting system access*** ***11.10(e)-Secure Records*** ***11.10(g)-Authority checks***
7.2	***back-up***	not covered
8	***Printouts***	
8.1	***clear printed copies***	***11.10(b)- Generate accurate and complete copies***
8.2	***batch release/changed since original***	*not covered*

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9	***Audit Trails***	***11.10(e)- Electronic audit trail,*** ***11.10(k)(2)- Documentation control***
10	***Change and Configuration Management***	***11.10(d)- Limiting system access*** ***11.10(e)- Electronic audit trail***
11	***Periodic evaluation***	***11.300(b) and (e)- periodically checked*** ***11.10(k)- Documentation control***
12	***Security***	***11.10(c)- Protection of records***
12.1	***physical/logical***	***11.10(d)- Limiting system access*** ***11.10(g)- Authority checks*** ***11.200(a) and (b)biometrics*** ***11.300(a) Unique*** ***11.300(d)- prevent unauthorized use***
12.2	***criticality***	not covered
12.3	***Security-record events***	***11.300(b)and (c)-Controls for Identification Codes/Passwords***
12.4	***data management/operators entries***	***11.10(e)-Controls for Closed Systems***
13	***Incident Management***	not covered
14	***Electronic Signature***	***11.50-Signature manifestations***
14(a)	***same as hand-written***	***11.1(a) Scope*** ***11.3(b)(7) Definitions*** ***11.100(c) Certify equivalent to handwritten***
14(b)	***permanent link***	***11.70- Signature/record linking***
14(c)	***time and date***	***11.10(e)- Electronic audit trail***
15	***Batch release***	not covered
16	***Business Continuity***	not covered
17	***Archiving***	***11.10(c)- Protection of records for accurate retrieval***

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Table 3: Cross-Reference from Part 11 to Annex 11

Part 11 Section No.	Part 11 Title	Annex 11 Cross Reference (substantially equivalent)
	Subpart B--Electronic Records	
11.10	***Controls for closed systems***	
11.10(a)	***Validation***	***4-Validation***
11.10(b)	***Generate accurate and complete copies***	***8.1-Printouts***
11.10(c)	***Protection of records for accurate retrieval***	***17-Archiving, 12-Security 7-Data Storage***
11.10(d)	***Limiting system access to authorized individuals***	***7.1- secured and accessible 10- Change and Configuration Management 12.1-Security, physical/logical***
11.10(e)	***Record of operator entries (audit trail)***	***7.1- secured and accessible 9-Audit Trails 10-Change and Configuration Management 12.4- data management/operators entries 14(c)-Electronic Signature***
11.10(f)	***Operational system checks***	***5-Data, 6- Accuracy Checks***
11.10(g)	***Authority checks***	***7.1- secured and accessible 12.1-Security, physical/logical***
11.10(h)	***Device checks***	***4.8-Validation***
11.10(i)	***Personnel (who develop, users and maintain systems)***	***2-Personnel***
11.10(j)	***User accountability for actions initiated under e-signatures***	not covered
11.10(k)	***Documentation control***	***9-Audit Trails 4.2- change control and deviations 10-Change and Configuration Management 11- Periodic evaluation***
11.30	***Controls for open systems***	***Principle (all systems) 5. Data***

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Part 11 Section No.	Part 11 Title	Annex 11 Cross Reference (substantially equivalent)
11.50	***Signature manifestations***	***14-Electronic Signature***
11.70	***Signature/record linking***	***14(b)-Electronic Signature***
	Subpart C--Electronic Signatures	
11.100	***General requirements***	
11.100(a)	***Unique/not reused***	not covered
11.100(b)	***Verify identity***	not covered
11.100(c)	***Certify equivalent to handwritten***	***14(a) same as hand-written***
11.200	***Electronic signature components and controls.***	
11.200(a)	***not based on biometrics***	***12.1-Security, physical/logical***
11.200(b)	***based on biometrics***	***12.1-Security, physical/logical***
11.300(a)	***Unique***	***12.1-Security, physical/logical***
11.300(b)	***periodically checked***	***11. Periodic Evaluation*** ***12.3-Security- record events***
11.300(c)	***procedures to deauthorize***	***12.3-Security, record events***
11.300(d)	***prevent unauthorized use***	***12.1-Security***
11.300(e)	***proper function***	***11-Periodic evaluation***

Conclusions

Annex 11 for computerized systems impacts manufacturers who export to the EU and those who manufacture products in the EU. Close scrutiny of the parallel FDA and EU rules shows the authorities share a mutual intent to have safe, validated computer systems and qualified networks for drug and device manufacturing.

Limited areas of Part 11 are dissimilar to Annex 11; these, for the most part, are limited to the verification of identity and accountability of actions by authorized individuals, as well as to the reporting to authorities. Part 11 applies to e-submissions to the FDA. Annex 11 is different from Part 11 in that it takes a risk management approach to criticality and emphasises a systems approach to periodic evaluations. Annex 11 is 'how to' while Part 11 is 'thou shalt' in tone. Together they form a robust and usable guide for computer validation professionals leading their companies and clients to compliance.

About EduQuest

EduQuest is a global team of FDA compliance experts based near Washington, DC. Founded by former senior FDA officials, EduQuest provides practical auditing, validation and training services to bio-pharmaceutical and medical device companies worldwide.

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