

Workshop

**"Data Integrity: reliability,
quality**

and competitiveness factors

of API manufacturers"

Università degli studi di Pavia

Paper, paperless and hybrid systems



Anna Tarzia, Senior GMP Inspector

10 Novembre 2017



Agenzia Italiana del Farmaco
AIFA

Dichiarazione di trasparenza/interessi*

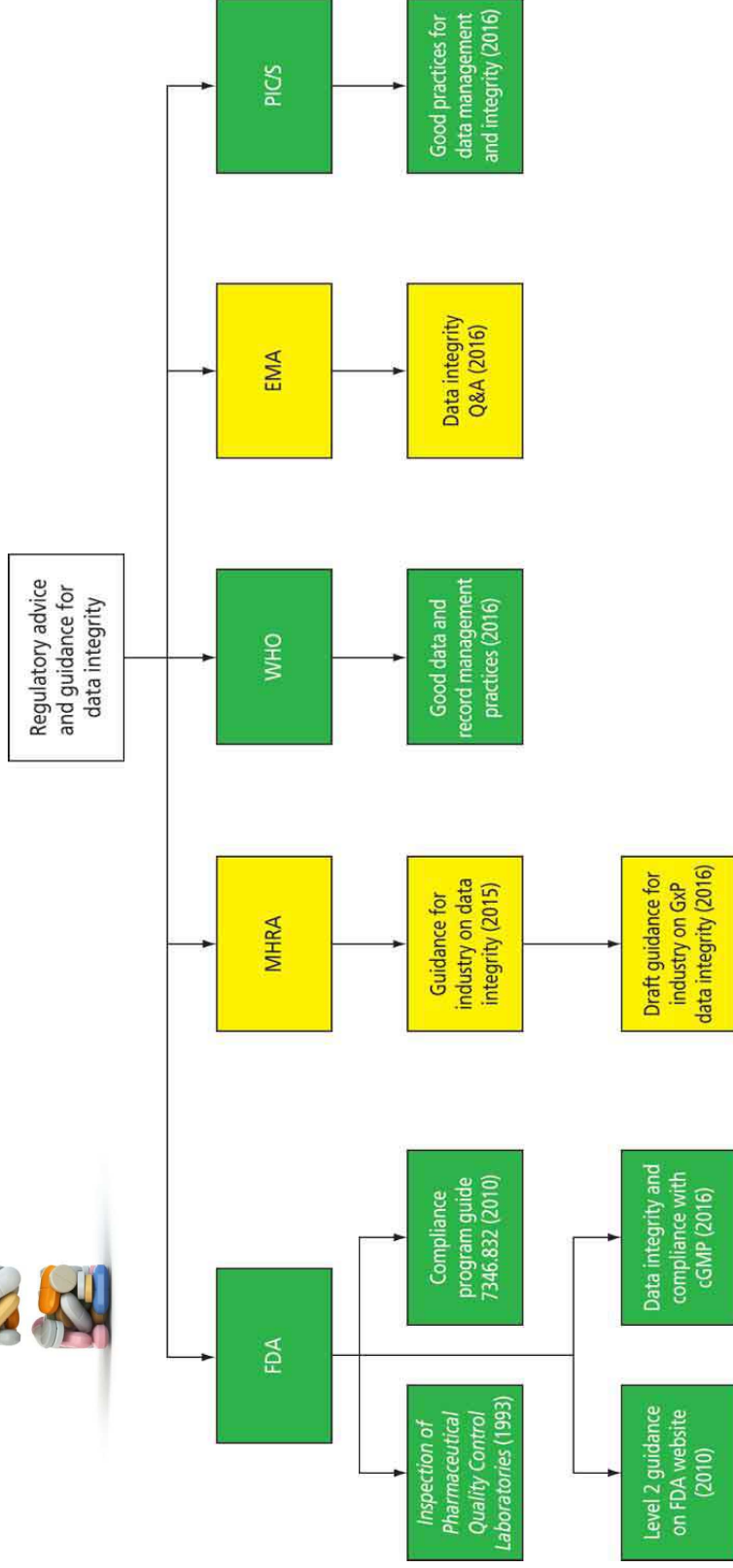
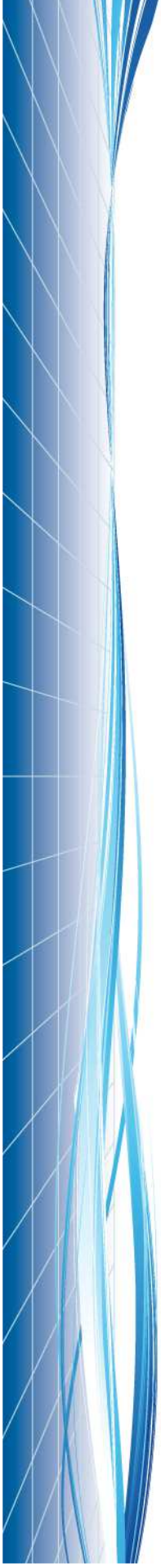
Le opinioni espresse in questa presentazione sono personali e non impegnano in alcun modo l'AIFA

| Interessi nell'industria farmaceutica | NO | Attualmente | Da 0 a 3 anni precedenti | oltre 3 anni precedenti |
|---|----|--------------------------|--------------------------|---------------------------------------|
| <i>INTERESSI DIRETTI:</i> | | | | |
| 1.1 Impiego per una società: Ruolo esecutivo in una società farmaceutica | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> obbligatorio |
| 1.2 Impiego per una società: Ruolo guida nello sviluppo di un prodotto farmaceutico | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> obbligatorio |
| 1.3 Impiego per una società: altre attività | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |
| 2. Consulenza per una società | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |
| 3. Consulente strategico per una società | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |
| 4. Interessi finanziari | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |
| 5. Titorità di un brevetto | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |
| <i>INTERESSI INDIRETTI:</i> | | | | |
| 6. Sperimentatore principale | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |
| 7. Sperimentatore | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |
| 8. Sovvenzioni o altri fondi finanziari | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |
| 9. Interessi Familiari | X | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> facoltativo |

* Anna Tarzia, secondo il regolamento sul Conflitto di Interessi approvato dal CdA AIFA in data 25.03.2015 e pubblicato sulla Gazzetta Ufficiale del 15.05.2015 in accordo con la policy EMA /626261/2014 sulla gestione del conflitto di interessi dei membri dei Comitati Scientifici e degli esperti.

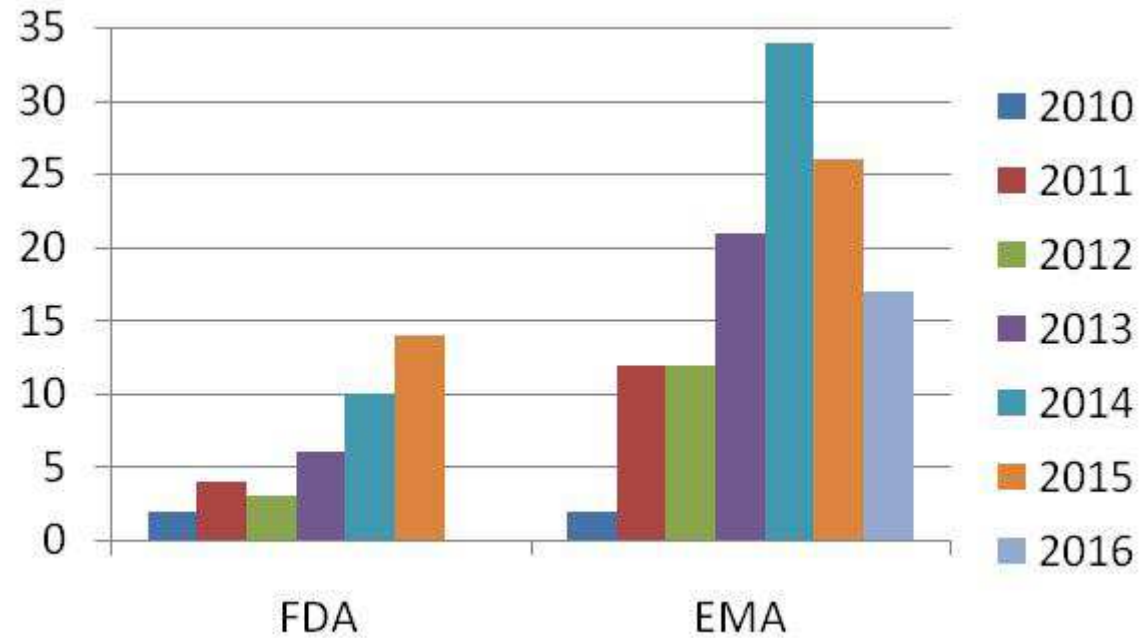
N.B. Per questo intervento non ricevo alcun compenso







Warning Letters and Non-Compliance inspection outcomes





Data Integrity

Attributable Data Original Contemporaneous
Legible Cloud Accurate

EU GMP Part II:

6.10 *All documents related to the manufacture of intermediates or APIs should be prepared, reviewed, approved and distributed according to written procedures. Such documents can be in paper or electronic form.*

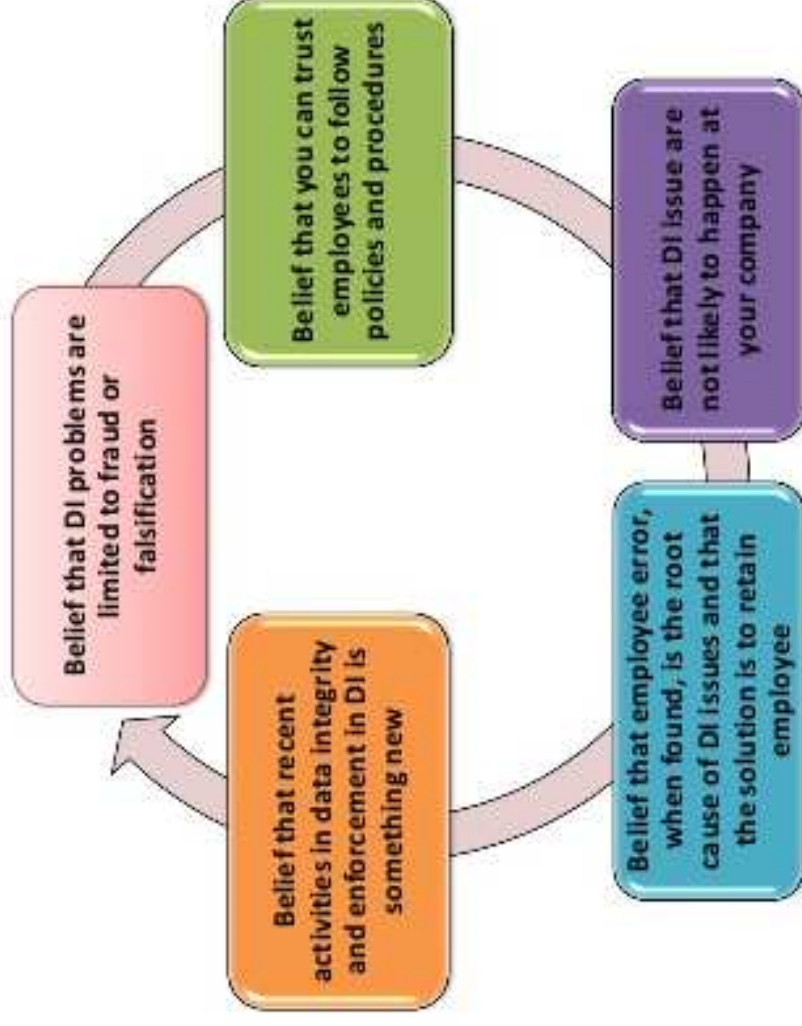




EU GMP Part II:
 6.10 All documents related to the manufacture of intermediates or APIs should be prepared, reviewed, approved and distributed according to written procedures. Such documents can be in paper or electronic form.



Misconceptions About Data Integrity



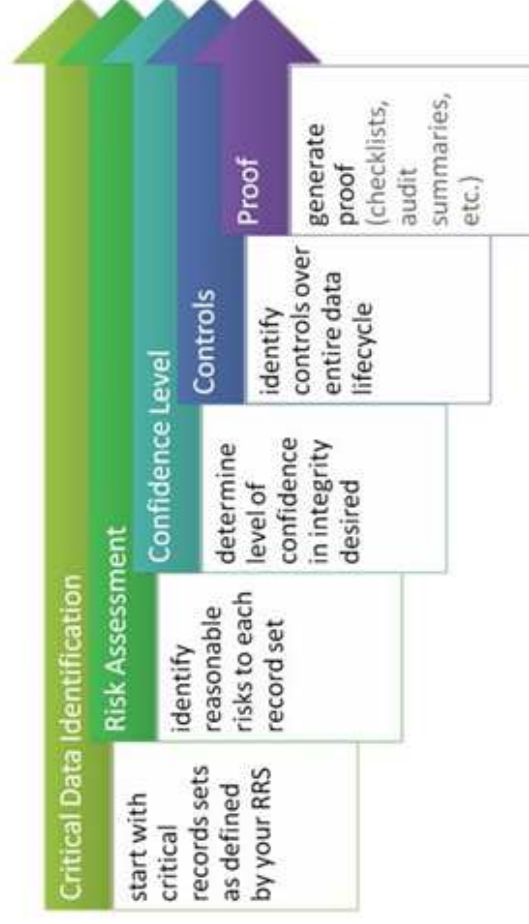
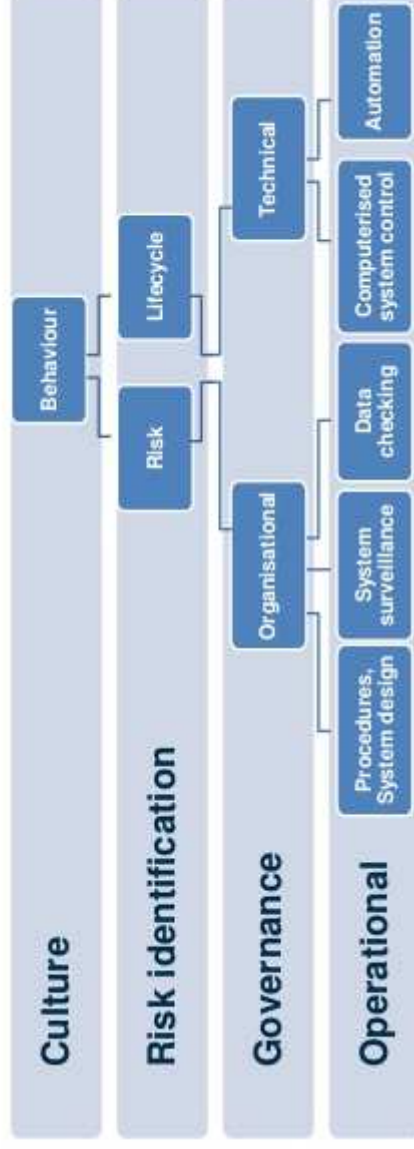
Risk

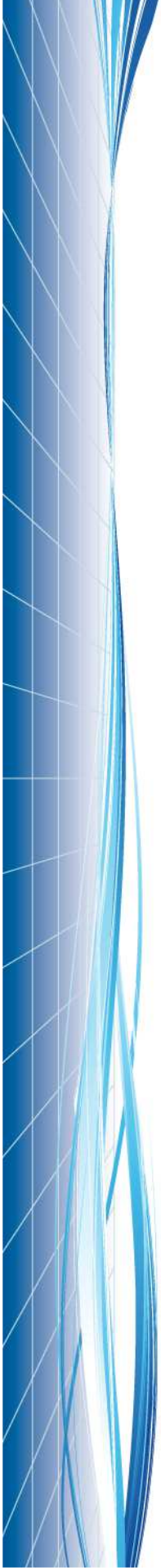


- Concerns: Consistency, Accuracy, Reliability
- Accidental Errors
 - Crashes, Concurrent Access, Logical Errors
 - Actions:
 - Integrity Constraints
 - Redundancy
- Malicious Errors
 - Not Totally Preventable
 - Actions:
 - Authorization, Authentication, Enforcement Policy
 - Concurrent Updates to Backup DBs
 - Dual Homing



Data integrity: Risk reducing strategies





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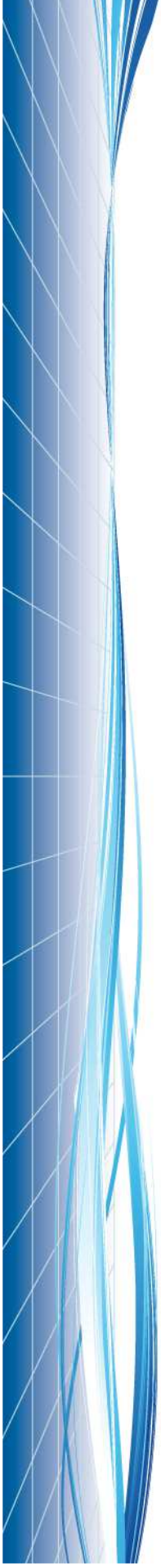


I can't believe...they sent the wrong form again.....



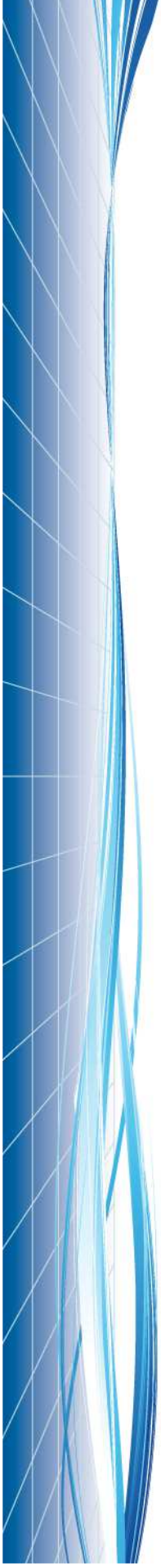
Agenzia Italiana del Farmaco

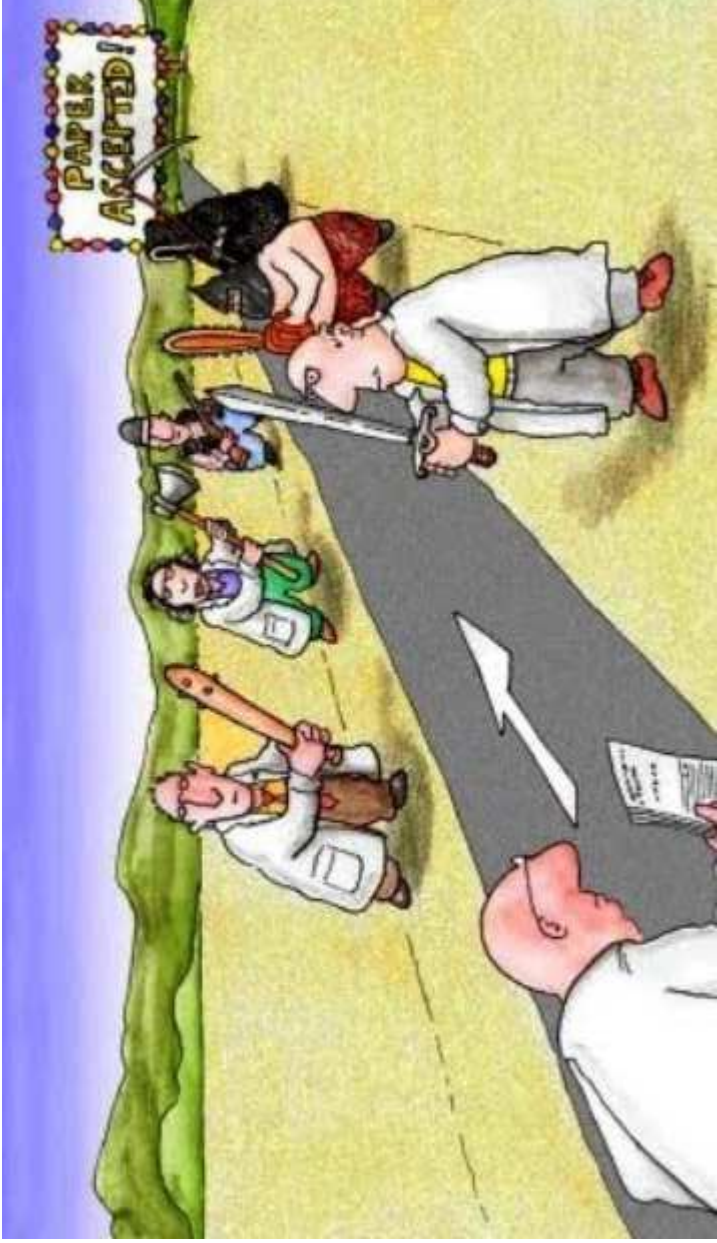
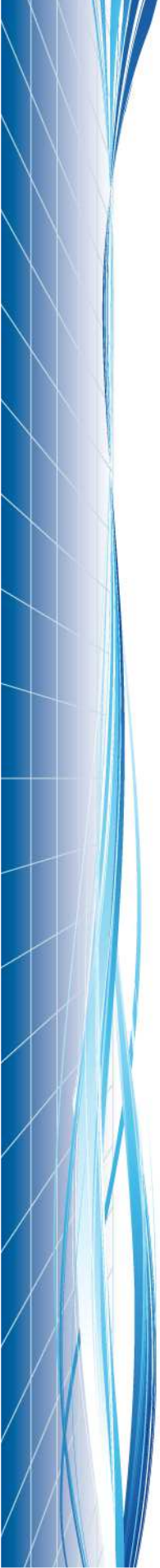
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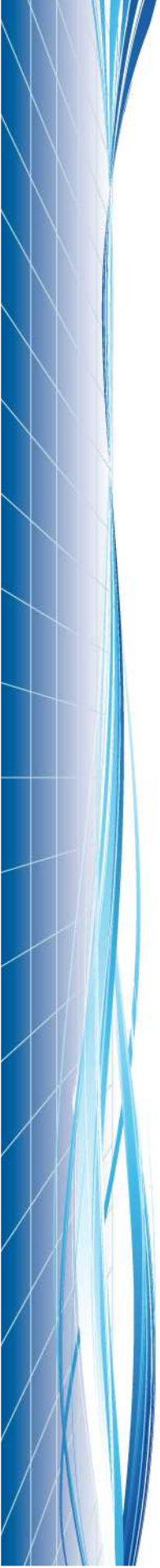
AIFA

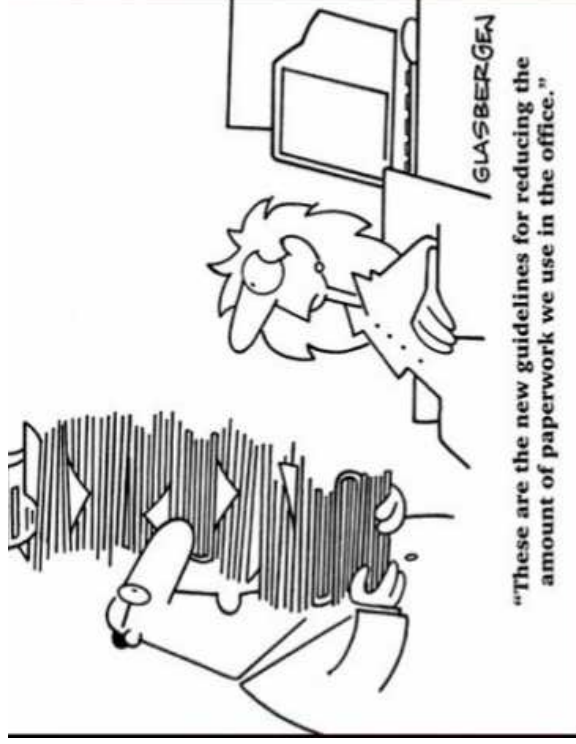
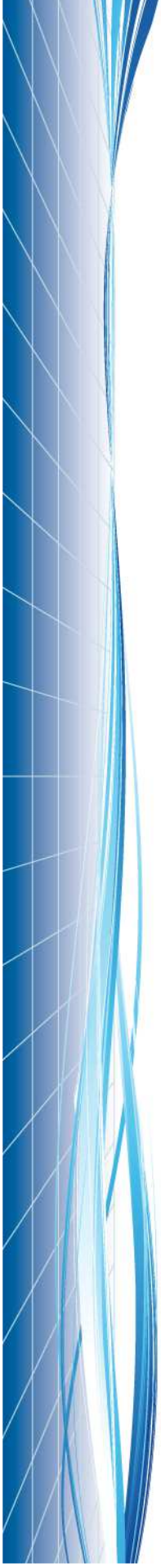




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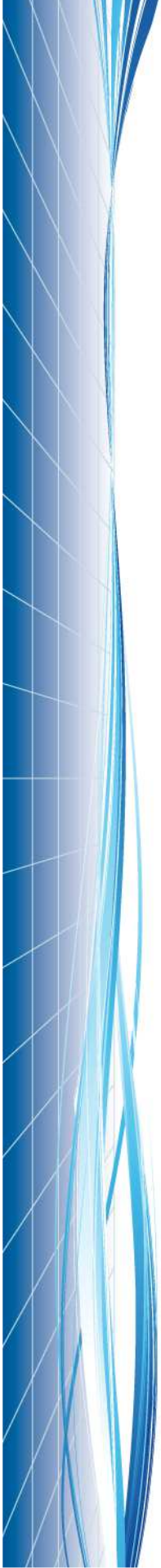
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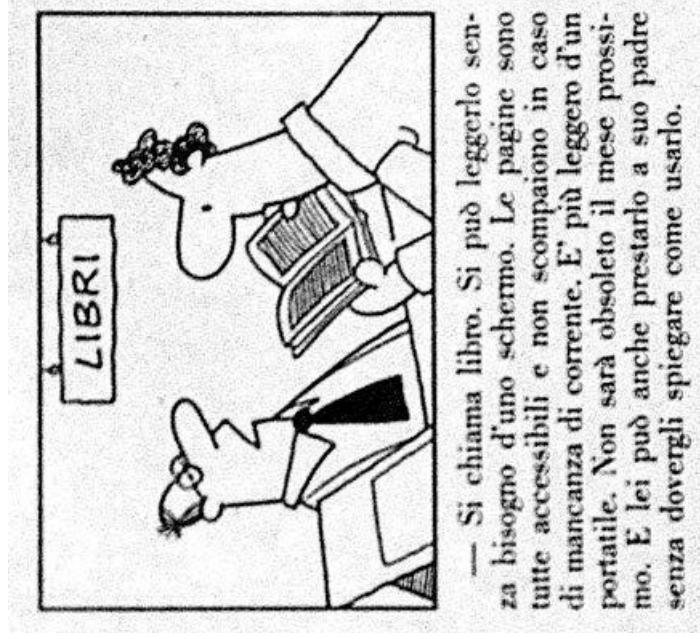
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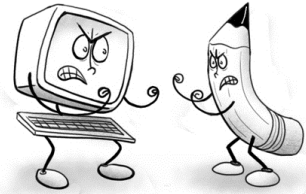


— Si chiama libro. Si può leggerlo senza bisogno d'uno schermo. Le pagine sono tutte accessibili e non scompaiono in caso di mancanza di corrente. E' più leggero d'un portatile. Non sarà obsoleto il mese prossimo. E lei può anche prestarlo a suo padre senza dovergli spiegare come usarlo.



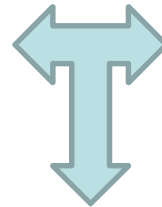
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Paper-based

E-based



Controlled docs:

- **Content**
- **identification**
- **traceability of the distributed / printed/withdrawn copies**

risk omission, loss, manipulation, falsification

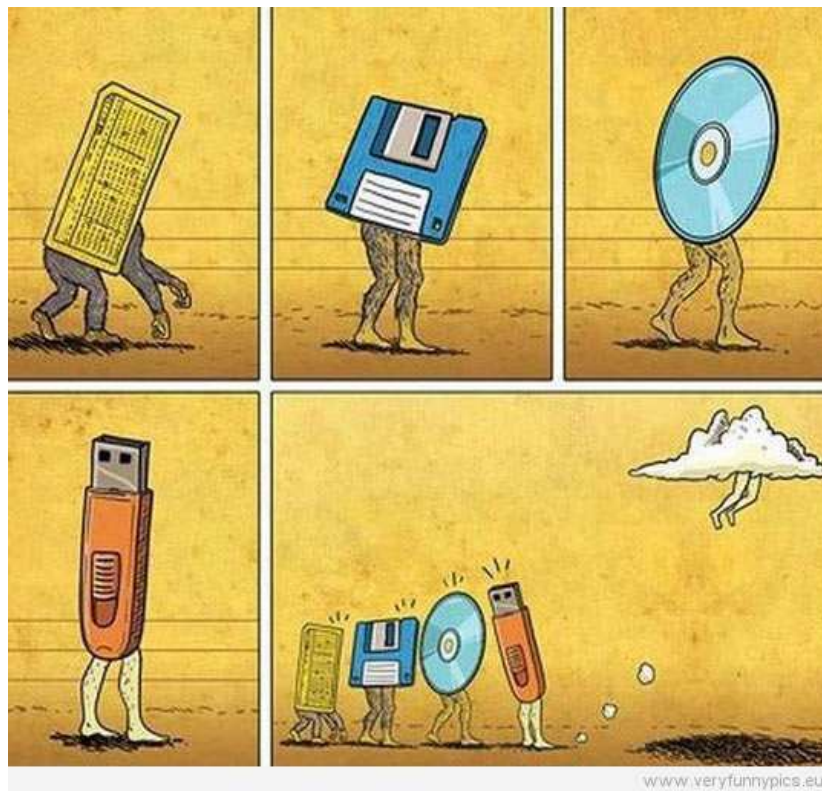
Storage:

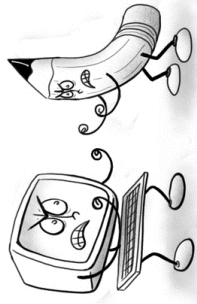
- **data security**
- **limited access**

Improper use , disaster, damage, loss and retrievability, retention time defined by regulations



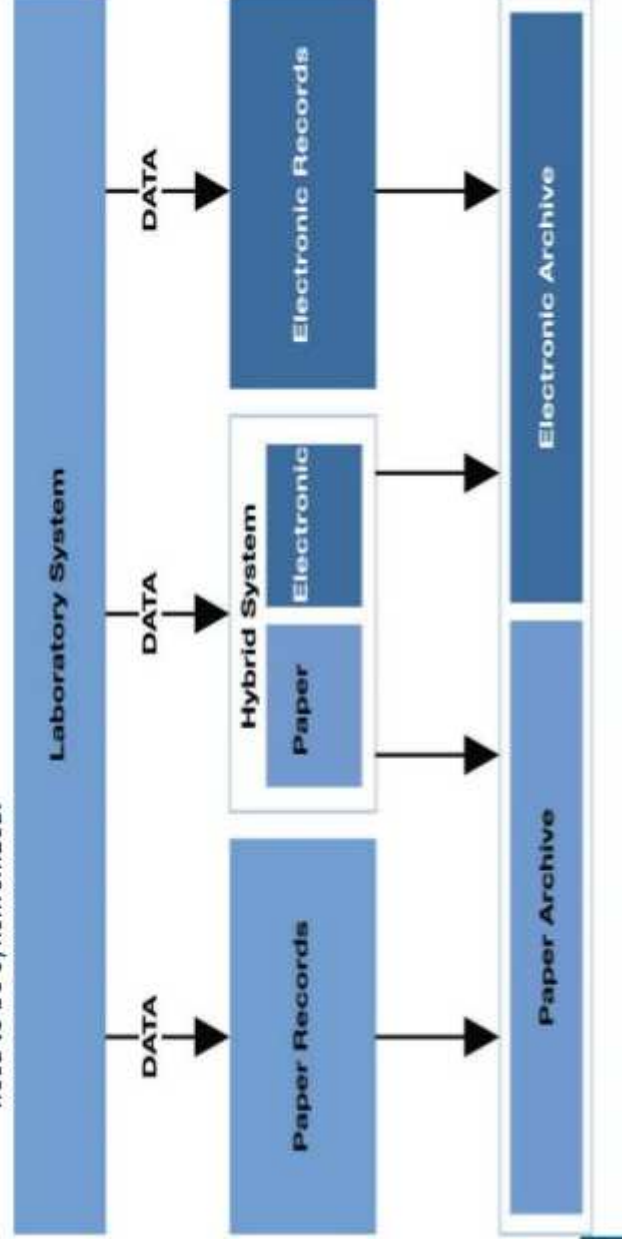
Data storage evolution

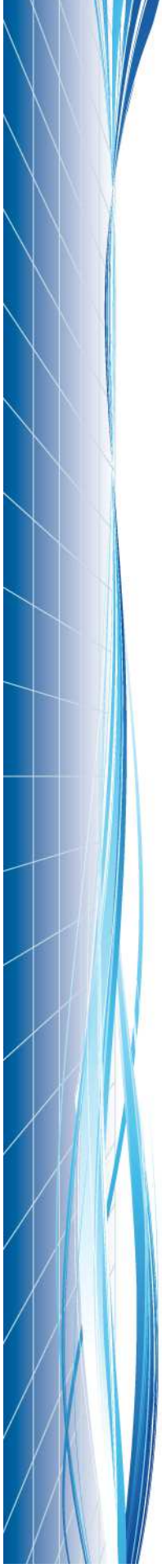




Data Integrity-Challenges

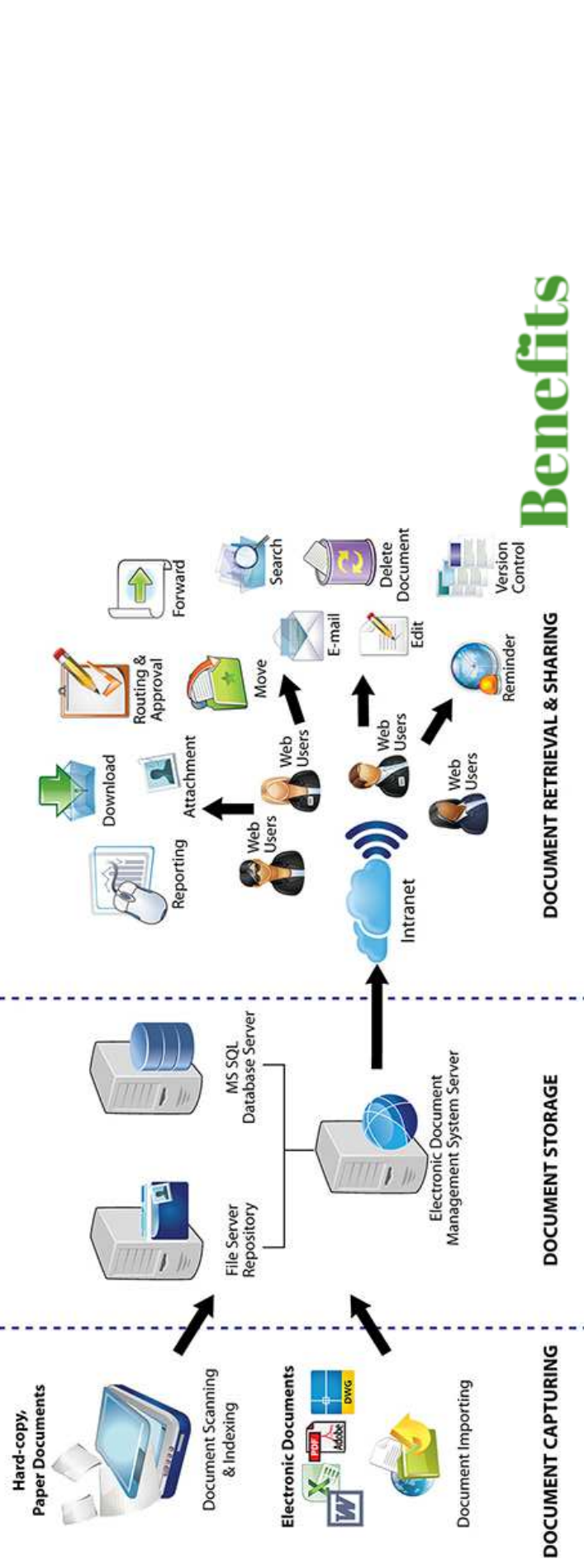
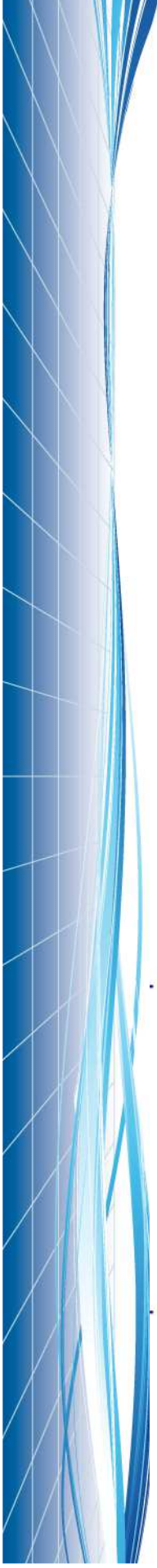
- Utilization of hybrid systems : If both are used, paper and electronic records need to be synchronized.





| | Paper-based system | | Electronic Document Management System (EDMS) | |
|---------------------------------------|---|--|--|---|
| | Method | Assessment | Method | Assessment |
| Collaboration | <ul style="list-style-type: none"> - Email review - Paper approval - Wet-ink signature | <ul style="list-style-type: none"> - Complex - Resource-intensive - Lengthy | <ul style="list-style-type: none"> - Centralized review, approval and signature in the EDMS | <ul style="list-style-type: none"> - Fast - Audit trail - Electronic Signature |
| Document Repository | <ul style="list-style-type: none"> - Physical storage | <ul style="list-style-type: none"> - Space requirements - Cabinet requirements - Limited access to documents - Complexity of classification and search | <ul style="list-style-type: none"> - Centralized electronic storage | <ul style="list-style-type: none"> - Safe tested storage - 100% accessibility - Ease of sorting and search by metadata - Access control rules are simple to implement |
| Taxonomy & Standardization | <ul style="list-style-type: none"> - Procedural controls - Centralized templates | <ul style="list-style-type: none"> - Manual process progress - Sporadic use of chosen model | <ul style="list-style-type: none"> - Procedural controls - Centralized templates | <ul style="list-style-type: none"> - Automatic process progress - Universal use of chosen model |
| Security & Permissions | <ul style="list-style-type: none"> - Physical controls (human intervention) - Procedural controls | <ul style="list-style-type: none"> - Low tech - Prone to human error - Complex processes | <ul style="list-style-type: none"> - Physical controls - Logical controls - Procedural controls | <ul style="list-style-type: none"> - Safer - Tighter permissions control - Harmonized |
| Technology Integration | <ul style="list-style-type: none"> - None | <ul style="list-style-type: none"> - Manual integration required - Prone to human error | <ul style="list-style-type: none"> - Possible integration between systems, including electronic regulatory submission tools | <ul style="list-style-type: none"> - Improved productivity - Safer |





Benefits

Standardized and efficient document workflow



Centrally and readily retrievable documentation

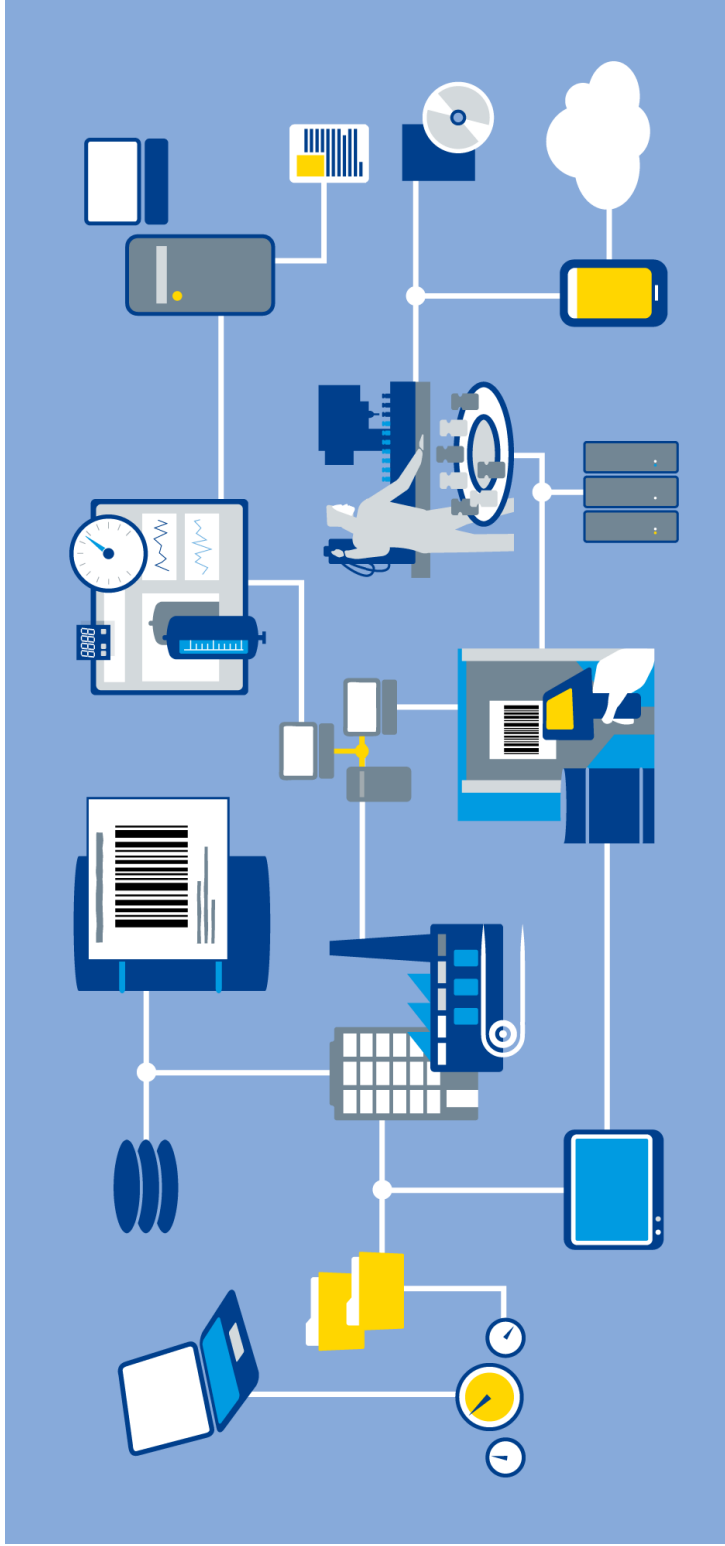
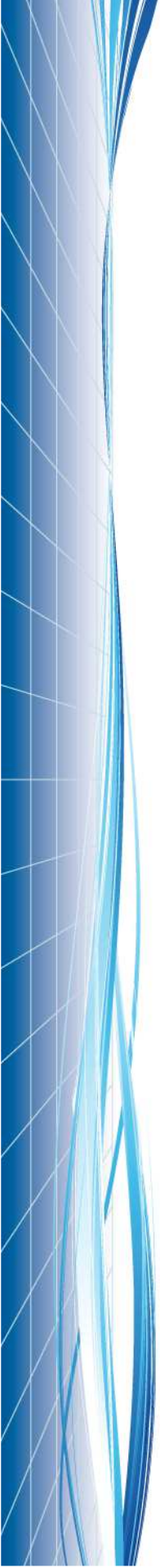
GMP compliant

Works on personal computers, laptops, tablets and smart phones.



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Automated systems in Industry

Various IT Systems in Pharmaceutical Industry

Computerized physician order entry (CPOE)

Enterprise Resource Planning (ERP)

Laboratory Information Management System (LIMS)

Sales Force Automation (SFA)

eBR (Electronic Batch Records)

Customer Relationship Management (CRM)

Clinical trial Management system (CTMS)

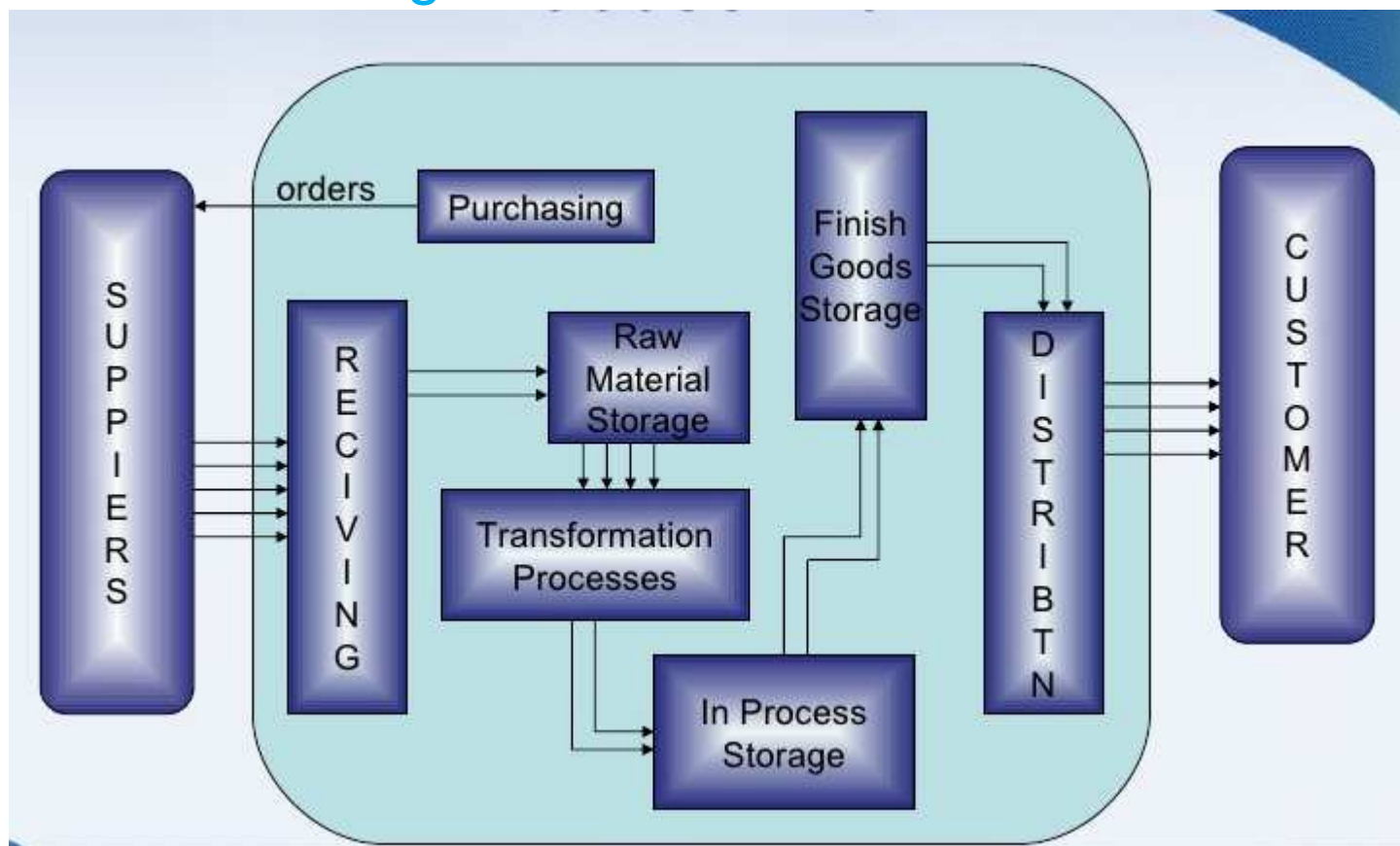
Corrective Action & Preventive Action (CAPA)

Distributed Control System (DCS)

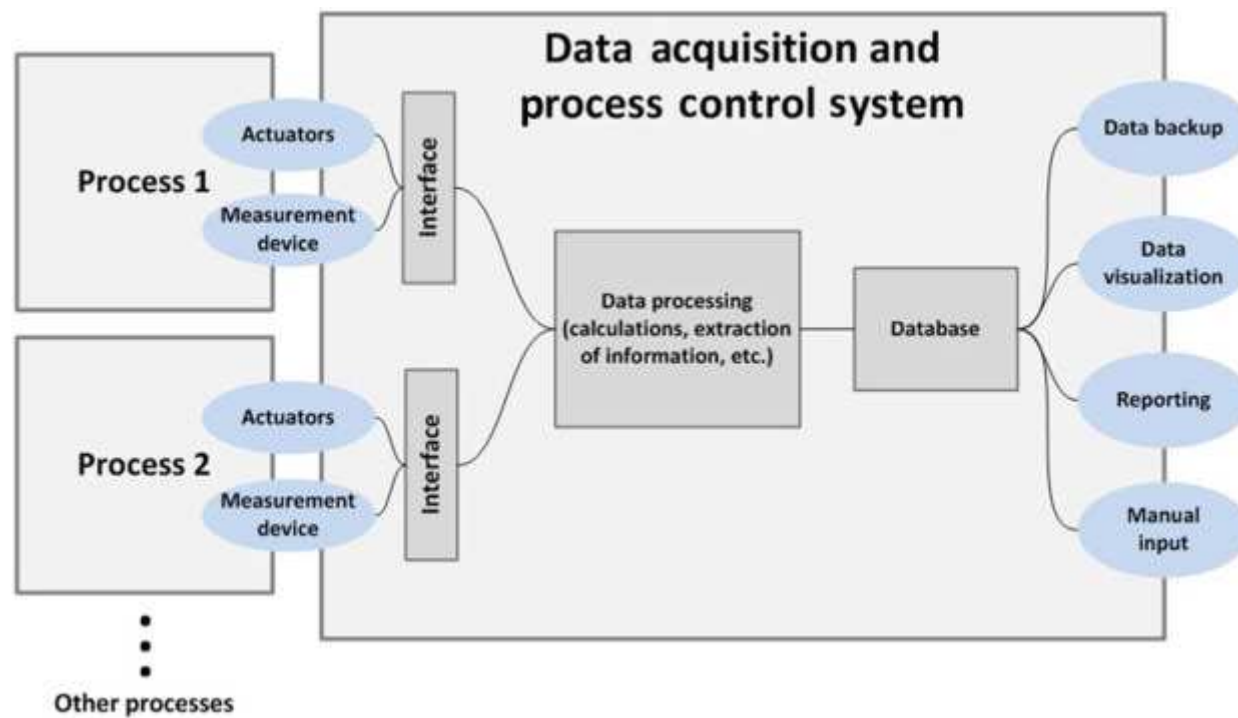
Computerized Maintenance Management System (CMMS)

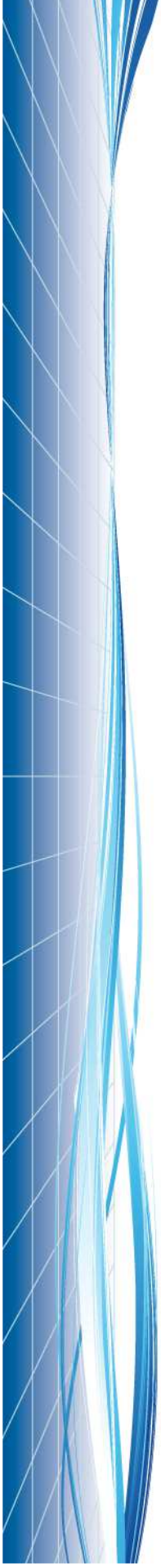


Material management

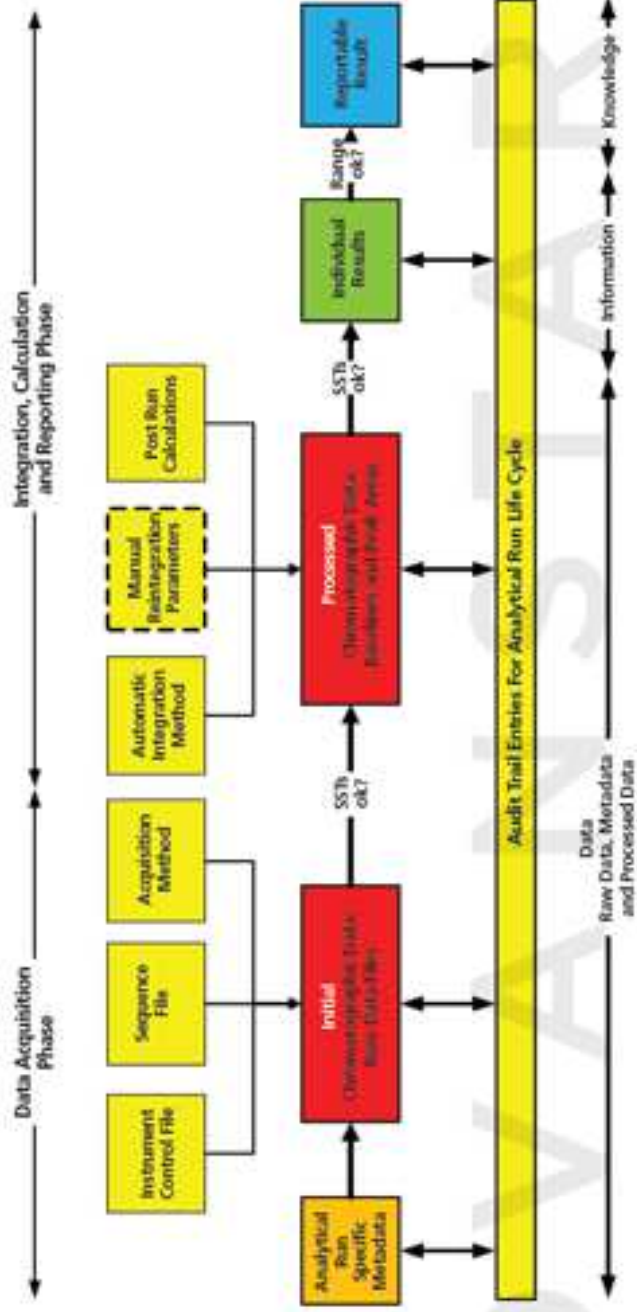


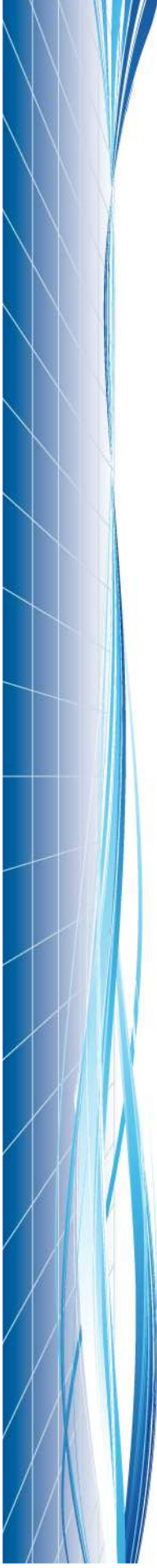
Production





Primary Analytical Record





Transaction History Records {Company 1}

Print... Export Patron Order Unpost Reverse Debits and Credits Analyze TS Transactions

Trans Date: from JUL 1 2000 12:00 AM to JUL 14 2013 11:59 PM

| Seq # ¹ | Trans Date ¹ | Type | Code | Transaction Desc | Description Of Entry | Ip Addr | User | First Name | Last Name |
|--------------------|-------------------------|-------|------|-----------------------------|--|---------------|------|------------|-----------|
| 917 | 2012/11/27 22:41:43.88 | Audit | ALO | User logged out | Logged out: User Master | 192.168.56... | UM | User | Master |
| 918 | 2012/11/27 22:45:24.01 | Audit | ALI | User logged in | Logged in: User Master | 192.168.56... | UM | User | Master |
| 920 | 2012/11/28 05:28:49.57 | Audit | ALO | User logged out | Logged out: User Master | 192.168.56... | UM | User | Master |
| 921 | 2012/11/28 05:28:51.29 | Audit | ALI | User logged in | Logged in: Listener Web Sales | 192.168.56... | WWW | Listener | Web Sal |
| 922 | 2012/11/28 06:57:40.25 | Audit | ALO | User logged out | Logged out: Listener Web Sales | 192.168.56... | UM | User | Web Sal |
| 923 | 2012/11/28 06:59:21.12 | Audit | ALI | User logged in | Logged in: User Master | 192.168.56... | UM | User | Master |
| 926 | 2012/11/28 20:25:21.87 | Audit | ALO | User logged out | Logged out: User Master | 192.168.56... | UM | User | Master |
| 927 | 2012/11/30 05:54:27.55 | Audit | ALI | User logged in | Logged in: User Master | 10.96.6.236 | UM | User | Master |
| 930 | 2012/12/04 06:47:59.57 | Audit | AC | Patron Card Viewed by Au... | Credit Card detail: Viewed card ending in 4242 | 192.168.0.92 | UM | Doug | Easterbi |
| 931 | 2012/12/04 06:48:18.31 | Audit | AC | Patron Card Viewed by Au... | Credit Card detail: Viewed card ending in 4242 | 192.168.0.92 | UM | Doug | Easterbi |
| 932 | 2012/12/04 06:48:24.45 | Audit | AC | Patron Card Viewed by Au... | Credit Card detail: Viewed card ending in 4242 | 192.168.0.92 | UM | Doug | Easterbi |
| 933 | 2012/12/04 06:48:29.96 | Audit | AC | Patron Card Viewed by Au... | Credit Card detail: Viewed card ending in 4242 | 192.168.0.92 | UM | Doug | Easterbi |
| 934 | 2012/12/04 14:12:38.03 | Audit | ALO | User logged out | Logged out: User Master | 192.168.0.92 | UM | User | Master |
| 935 | 2012/12/04 15:10:13.27 | Audit | ALI | User logged in | Logged in: User Master | 192.168.0.92 | UM | User | Master |
| 938 | 2012/12/04 22:52:05.16 | Audit | ALO | User logged out | Logged out: User Master | 192.168.0.92 | UM | User | Master |
| 939 | 2012/12/05 06:22:58.01 | Audit | ALI | User logged in | Logged in: User Master | 192.168.0.92 | UM | User | Master |
| 942 | 2012/12/05 09:42:42.79 | Audit | ALO | User logged out | Logged out: User Master | 192.168.0.92 | UM | User | Master |
| 943 | 2012/12/05 10:44:07.22 | Audit | ALI | User logged in | Logged in: User Master | 192.168.0.92 | UM | User | Master |
| 946 | 2012/12/05 15:59:53.58 | Audit | ALO | User logged out | Logged out: User Master | 192.168.0.92 | UM | User | Master |
| 947 | 2012/12/05 16:00:41.79 | Audit | ALI | User logged in | Logged in: User Master | 192.168.0.92 | UM | User | Master |
| 949 | 2012/12/05 16:20:14.43 | Audit | ALO | User logged out | Logged out: User Master | 192.168.0.92 | UM | User | Master |
| 950 | 2012/12/05 17:19:15.78 | Audit | ALI | User logged in | Logged in: User Master | -11001 | UM | User | Master |

1 of 1320





Audit Trail

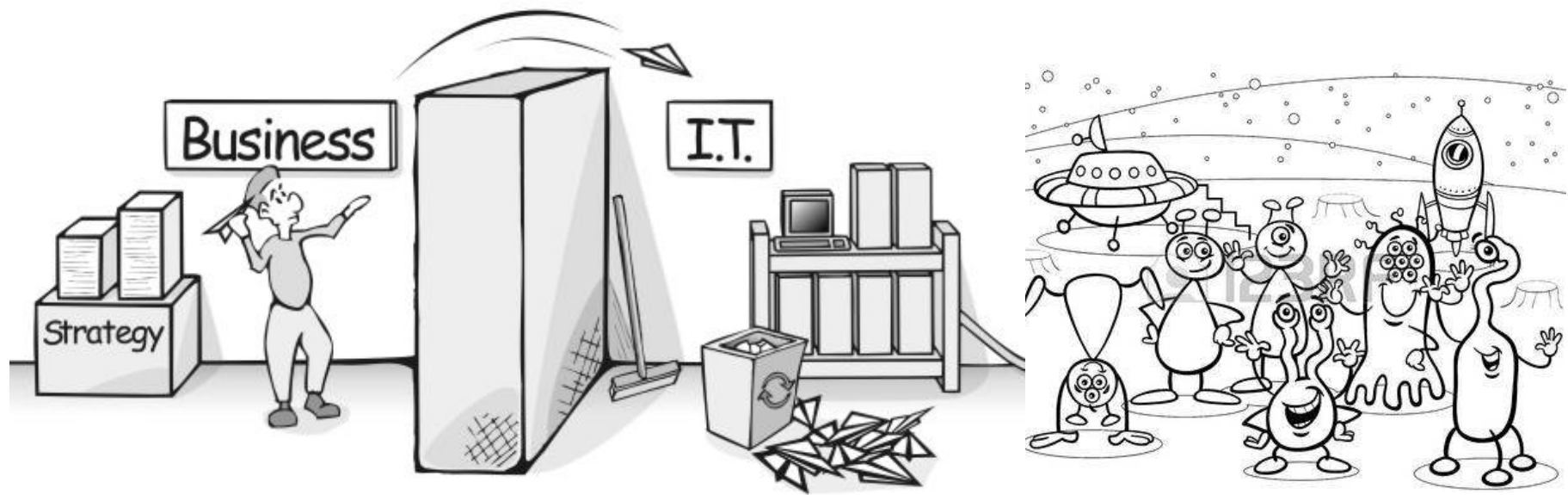
Audit Trail Calibration 1.1 - _001_008-0101.D (Number of entries: 13)

Find Manual entry +
 From 9/23/2015 To 9/28/2015 Filter

| State | User name | Date (GMT+00:00) ▼ | Description | Host name | Reviewed | Reason | Category |
|------------|--------------------------------|--------------------|--|------------------|-----------------|--------|--------------------|
| 2015/09/28 | admin | 9/28/2015 10:45 AM | Saved results. | WIN-30QABAHCQ... | | | Saving |
| | admin | 9/27/2015 7:49 AM | Saved results. | WIN-30QABAHCQ... | admin 9/28/2... | | Saving |
| | admin | 9/23/2015 11:42 AM | Saved results. | WIN-30QABAHCQ... | admin 9/28/2... | | Saving |
| | admin | 9/23/2015 11:29 AM | Saved results. | WIN-30QABAHCQ... | admin 9/28/2... | | Saving |
| | admin | 9/23/2015 11:18 AM | Saved results. | WIN-30QABAHCQ... | admin 9/28/2... | | Saving |
| 2015/09/28 | Reprocessing (3 entries) | | | | | | |
| State | User name | Date (GMT+00:00) ▼ | Description | Host name | Reviewed | Reason | Category |
| | admin | 9/28/2015 10:04 AM | Injection successfully reprocessed with option 'Clear c... | WIN-30QABAHCQ... | admin 9/28/2... | | Reprocessing |
| | admin | 9/23/2015 11:42 AM | Injection reprocessed with warmings using method '/d... | WIN-30QABAHCQ... | admin 9/28/2... | | Reprocessing |
| | admin | 9/23/2015 11:29 AM | Injection reprocessed with warmings using method '/d... | WIN-30QABAHCQ... | admin 9/28/2... | | Reprocessing |
| 2015/09/28 | Manual integration (2 entries) | | | | | | |
| State | User name | Date (GMT+00:00) ▼ | Description | Host name | Reviewed | Reason | Category |
| | admin | 9/28/2015 10:12 AM | Deleted peak from 9.543 min to 9.698 min on signal 'D... | WIN-30QABAHCQ... | admin 9/28/2... | | Manual integration |
| | admin | 9/26/2015 3:32 PM | Deleted peak from 9.543 min to 9.698 min on signal 'D... | WIN-30QABAHCQ... | admin 9/28/2... | | Manual integration |
| 2015/09/23 | Extraction (2 entries) | | | | | | |
| State | User name | Date (GMT+00:00) ▼ | Description | Host name | Reviewed | Reason | Category |
| | admin | 9/23/2015 11:15 AM | Extract background spectrum 'DAD1LUV Scan RT=4.312 M... | WIN-30QABAHCQ... | admin 9/28/2... | | Extraction |
| | admin | 9/23/2015 11:15 AM | Extract spectrum 'DAD1LUV Scan RT=9.996 Minutes'. | WIN-30QABAHCQ... | admin 9/28/2... | | Extraction |
| 2015/09/28 | Audit trail review (1 entries) | | | | | | |
| State | User name | Date (GMT+00:00) ▼ | Description | Host name | Reviewed | Reason | Category |
| | | | | | | | |



IT activities should be under QA control



Anche il giorno in cui.....



Lineeguida:leggi o.....

buonsenso [buon-sèn-sol] o
buon senso, s.m.(solo sing.)

Capacità naturale e istintiva
dell'individuo di valutare e distinguere
il logico dall'illogico, l'opportuno
dall'inopportuno, e di comportarsi
in modo giusto, saggio ed equilibrato,
in funzione dei risultati pratici
da conseguire.



Agenzia Italiana del Farmaco
AIFA



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AIFA

Dr. Anna Tarzia

GMP Inspector

Manufacturing Authorization Office
Inspections and Certification Dept.

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