by REVORG

White Paper J-Pharma
SAP Business One

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1. INTRODUZIONE E ASPETTI GENERALI

1.1. Aspetti normativi

Il **sistema ERP SAP Business One di Revorg** può essere fornito in vari ambiti regolamentati (es. prodotti finiti farmaceutici, principi attivi, dispositivi medicali, ecc.), che sono soggetti a diverse normative e regolamenti.

Per l'utilizzo in questi ambiti in ambito **manufacturing** si ritiene necessaria e sufficiente la conformità al **21 CFR Part 11** (FDA) [9] e all'**Annex 11** (EU GMP) [2], integrata con i principi e requisiti definiti nelle recenti linee guida per la **Data Integrity** (e in particolare la Linea Guida PIC/S PI 041-1) [15].

I produttori di principi attivi farmaceutici (API) sono soggetti alla **norma ICH Q7** [4], recepita in Europa nella Parte II delle EU GMP, e in America dalla FDA come Q7A.
Questa norma contiene requisiti specifici per i sistemi computerizzati, in massima parte già inclusi nell'Annex 11 e nella Part 11.

Dove applicabile **la linea Guida GAMP** [11] e le relative Good Practice Guide sono utilizzate come approfondimento e riferimento per le buone pratiche nello sviluppo e nella convalida del software.

1.2. Descrizione del sistema

1.2.1. Architettura del sistema

La struttura del sistema può essere suddivisa in due componenti principali:

Modulo SAP Business One (SAP)

Il modulo ERP SAP Business One costituisce il fondamento operativo del sistema ERP e gestisce numerose funzionalità di base, prevalentemente destinate alla gestione del business (Amministrazione, Finanza, Controllo di Gestione, Contabilità, ecc.).

Entrambi i moduli sono configurati (Categoria software 4 secondo GAMP), poiché si tratta di prodotti standard sviluppati per il mercato che prevedono una mera configurazione delle funzioni standard già disponibili. Se necessario, Revorg può anche realizzare personalizzazioni specifiche per il cliente (ovvero sviluppo di nuove funzioni non esistenti nel software standard).

Modulo applicativo verticale J-Pharma (Revorg)

Il modulo add-on J-Pharma gestisce le funzionalità aggiuntive per la gestione dei processi produttivi (anagrafiche, distinte base, produzione, gestione qualitativa del lotto, audit trail, ecc.).
Questo modulo nasce dall'esperienza pluriennale di Revorg nel settore farmaceutico. Per facilitarne l'implementazione la soluzione SAP B1 di Revorg è pre-configurata per il settore farmaceutico, sulla base della consolidata esperienza di Revorg nel settore specifico. L'impostazione predefinita dei parametri di configurazione permette una significativa riduzione dei tempi e dei costi del progetto, e assicura al tempo stesso una maggiore qualità e una più agevole convalida.

1.2.2. Funzionalità del sistema

Una descrizione delle funzionalità del sistema è disponibile nella letteratura del prodotto realizzata da Revorg, come ad esempio la brochure illustrativa "Gestione della produzione e distribuzione nel Life Sciences". Le funzionalità principali del sistema sono riportate di seguito, raggruppate per area funzionale e classificate in base alla rilevanza GxP tipica di ciascuna funzione. È indicato anche il modulo prevalente che gestisce la funzionalità.

Legenda:
• = funzionalità soggetta a normativa GxP;
- = funzionalità non soggetta a normativa GxP, non previsto add-on J-Pharma di Revorg
x = funzionalità non presente su SAP B1
v = funzionalità presente su SAP B1
v+ = previsto add-on J-Pharma di Revorg

FUNZIONI	GxP	SAPB1	J-Pharma
Prodotti			
Approvazione modulare anagrafica prodotti (per tipologia e competenza)	•	x	v+
Interfaccia prodotti con sala pesata e laboratorio	•	x	v+
Assegnazione e calcolo automatico delle scadenze e data di fabbricazione di un lotto. Configurazione modulare sulla numerazione del lotto sia in acquisto che in produzione	•	x	v+
Gestione delle versioni (es. materiale stampato)	•	x	v+
Approvazione dei dati critici GMP	•	x	v+
Produzione			
Ricetta di produzione	•	x	v+
Ricette di produzione: gestione dei componenti alternativi	•	x	v+
Approvazione ricette e versioni	•	x	v+
Configurazione compensatore per articoli soggetti a titolo	•	x	v+
Definizione consumi ai quantitativi fissi (es. vetreria)	•	x	v+
Unità di misura di produzione	•	x	v+
Configurazione delle lavorazioni esterne e/o risorse	•	v	v+
Consultazione ricette down e drill up	•	x	v+
Configurazione regole per gestire differenti tipologie di produzione: lotti di convalida, lotti per ricerca e sviluppo, lotti standard o multipli	•	x	v+
Componenti: assegnazione automatica dei lotti idonei alla produzione	•	x	v+
Consuntivazione dei materiali e risorse utilizzate e dichiarazione scarti	•	v	v+
Versamento del semilavorato o del prodotto finito con lo stato qualitativo appropriato (quarantena o da rilasciare)	•	v	v+
Gestione della produzione in sequenza (treno)	•	x	v+
Lotti			
Gestione dello stato qualitativo del lotto: quarantena, approvato o respinto, rilasciato	•	x	v+
Gestione regole automatiche assegnazione lotti	•	x	v+
Gestione approvazione lotti (configurabile per laboratorio)	•	x	v+
Rilascio lotti	•	x	v+
Autorizzazione spedizione lotti	•	x	v+
Analisi lotti prodotti nel periodo	•	x	v+
Analisi per lotto delle modifiche GMP avvenute nel tempo (Audit Trail)	•	x	v+

FUNZIONI	GxP	SAPB1	J-Pharma
Lotti			
Configurazione alert interni o via mail su tutte le condizioni critiche dei lotti	•	v	v+
Gestione automatica di lotti scaduti e respinti	•	v	v+
Gestione della data di fabbricazione, shelf-life e scadenza	•	x	v+
Identificazione univoca del lotto e lotto fornitore	•	x	v+
Rintracciabilità dei lotti, drill down e drill up	•	x	v+
Rintracciabilità lotti per destinatario	•	v	-
Tracciabilità del farmaco	•	x	v+
Riconciliazione etichette dei prodotti/lotti	•	-	v+
Prelievi			
Impegno dei componenti in base al titolo	•	x	v+
Generazione automatica delle richieste di trasferimento per i materiali da prelevare	•	x	v+
Attribuzione lotti automatica con criterio FEFO	•	x	v+
Prelievi per ordine e piani di produzione	•	x	v+
Approvazioni e Rilascio			
Autorizzazioni per utente o gruppo utenti	•	x	v+
Autorizzazioni specifiche per tipologia prodotto (es. prodotti finiti con AIC, PZN, semilavorati, soluzioni etc.)	•	x	v+
Motivo della modifica	•	x	v+
Log delle approvazioni per lotto, con identificazione utente data e ora	•	x	v+
Magazzino			
Gestione delle ubicazioni, BarCode	•	v	v+
Movimentazione dei materiali di magazzino con dispositivi mobili	•	x	v+
Gestione del conto deposito	•	v	v+
Gestione del conto lavoro pieno o su fase	•	v	v+
Monitoraggio dei lotti in scadenza o scaduti	•	x	v+
Gestione dei materiali respinti	•	x	v+
Audit Trail			
Configurabile sui dati critici Gmp	•	x	v+
Configurazione report che identifica il dato modificato	•	x	v+
Consultazioni mirate per utente, data, prodotto, lotto etc.	•	x	v+
Firma elettronica	•	x	v+
Amministrazione e finanza			
Gestione prima nota e modelli di generazione scritture automatiche	-	v	-
Scritture provvisorie	-	v	-
Incassi e pagamenti	-	v	-
Flusso di cassa	-	v	-
Estratti conto e scadenzari	-	v	v+

FUNZIONI	GxP	SAPB1	J-Pharma
Amministrazione e finanza			
Riconciliazioni interne ed esterne	-	v	-
Creazione e controllo del budget	-	v	v+
Gestione valute estere	-	v	-
Bilanci e modelli finanziari	-	v	-
Intrastat	-	v	-
Contabilità analitica	-	v	-
Cespiti	-	v	-
Acquisti			
Pianificazione fabbisogni dei materiali su analisi delle scorte o su previsioni o impegni	-	v	-
Raccomandazioni (il sistema suggerisce che cosa acquistare)	-	v	-
Richieste di acquisto e controllo del budget (es. OPEX, CAPEX)	-	v	v+
Richieste d'offerta	-	v	-
Acquisti di beni, servizi e contratti	•	v	-
Associazione allegati per la documentazione interna e del fornitore (es. certificati)	•	v	-
Entrate da fornitore e Verifica ed etichettatura dei materiali entrati	•	v	v+
Gestione dello stato qualitativo dei lotti, "quarantena"	•	v	v+
Alert e monitoraggio delle forniture o dei materiali in consegna	-	v	v+
Gestione dei Fornitori/Produttori Qualificati	•	x	v+
Gestione dei resi e contestazioni	-	v	-
Configurazione modulare dei flussi approvativi su richieste, acquisti e resi	-	v	-
Import fatture elettroniche e controllo contabilizzazione fatture	-	v	v+
Analisi delle performance sulle attività di approvvigionamento e dei fornitori	-	v	-
Vendite			
Budget di vendita	-	v	v+
Ordini e contratti e listini di vendita	-	v	-
NSO ordini elettronici e DDT elettronici	-	x	v+
Gestione Shelf Life Cliente	-	x	v+
Gestione vincoli produttore-Cliente	•	x	v+
Gestione delle spedizioni e allestimento consegne	•	v	-
Fatturazione immediata o differita	-	v	-
Resi clienti	•	v	-
Configurazione modulare dei flussi approvativi su condizioni particolari di vendita e resi	-	v	-
Gestione delle provvigioni e matrice provvigionale modulare	-	x	v+

1.3. Stato dei fornitori

La realizzazione del sistema e la sua fornitura vedono coinvolti due attori principali:

- SAP SE (sviluppo del prodotto base e piattaforma ERP)
- Revorg (sviluppo add-on farmaceutico e fornitura dei sistemi)

SAP SE
(sviluppo del prodotto base e piattaforma ERP)

1.3.1. SAP

Il produttore del prodotto SAP Business One, elemento di base del sistema ERP, è SAP SE, azienda internazionale con sede principale in Germania e produttrice anche della soluzione SAP ECC (prodotto leader nel settore farmaceutico).

Lo sviluppo software del prodotto SAP B1 è governato da un Sistema Qualità certificato secondo la norma ISO 9001:2015, che riguarda anche il supporto e l'assistenza al prodotto.

La società è anche dotata di un sistema qualità certificato secondo la norma ISO 27001:2017 per quanto riguarda la sicurezza informatica.

Ai fini della convalida non è in generale necessaria una valutazione formale di tale fornitore perché il modulo base SAP B1 non contiene elementi particolarmente rilevanti dal punto di vista GxP.

Revorg
(sviluppo add-on farmaceutico e fornitura dei sistemi)

1.3.2. Revorg

Il modulo add-on J-Pharma, specifico per il settore Life Sciences, è sviluppato dalla società Revorg, ben nota nel settore farmaceutico, e produttore anche di un sistema ERP storico omonimo operante su piattaforma IBM AS400, installato e convalidato presso diverse aziende farmaceutiche.
La società Revorg ha un Sistema Qualità certificato secondo la norma ISO 9001:2015 riguardante le attività di Progettazione, produzione, commercializzazione e assistenza di software.

Più in dettaglio il Sistema Qualità copre i seguenti servizi:

- Sviluppo di nuovi prodotti software, incluso il modulo add-on J-Pharma per SAP B1.
- Fornitura di soluzioni ERP complete, inclusa l'attività di configurazione dei sistemi sulla base delle esigenze dei singoli clienti.
- Manutenzione dei prodotti software sviluppati internamente e assistenza ai clienti durante la vita operativa dei sistemi forniti.

Revorg è disponibile per verifiche di valutazione da parte di potenziali clienti e consulenti, sia on-site sia a distanza (es. questionari di postal audit). Inoltre ha preparato e reso disponibile un documento standard di autovalutazione.

2. APPENDICE

Di seguito è riportata la tabella di dettaglio per documentare la conformità del sistema ERP SAP B1.

Sono integrati i requisiti delle principali normative e linee guida applicabili al sistema quando utilizzato in ambiti regolamentati:
• EU GMP Annex 11 (Computerised Systems)
• FDA 21 CFR Part 11 (Electronic Records, Electronic Signatures
• PIC/S PI 041-1 (Data Integrity).

I requisiti sono soddisfatti attraverso controlli di natura tecnica (funzionalità del software) oppure di tipo procedurale (ad esempio Procedure Operative Standard). I controlli tecnici riguardano il software e quindi sono di responsabilità del fornitore, mentre quelli procedurali sono a carico dell'utente.

La tabella contiene i seguenti elementi:

1. **Riferimento alla normativa**
2. **Descrizione del requisito**
3. **Responsabilità.** S= Supplier, U = User
4. **Commenti e/o riferimenti** ad altre normative collegate, dove appropriato.
5. **Natura del controllo** (applicabilità al sistema).
   "Yes" oppure "No" specifica se il controllo è di natura tecnica e quindi applicabile al sistema.
   N/A indica che il controllo non è applicabile al sistema ERP.
6. **Descrizione del controllo**, se il requisito è applicabile al sistema, oppure raccomandazioni per l'azienda utilizzatrice se rilevante.

I requisiti sono raggruppati per area per una maggiore facilità di consultazione.

PART 11 AND OTHERS	Requirement	S, U	Other associated regulations and comments	Yes/ No	If yes, how, specifically, is the requirement satisfied using SAP B1? If no, what is the recommendation
Validation					
Part 11 11.10(a)	Is the system validated to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records?	S, U	Required by all regulations. This is a shared responsibility between the system supplier and the user organization. The user organization has ultimate responsibility for validation, but some tasks can only be done and must be delivered by the software supplier, e.g., documentation and testing activities during development.	Yes	SAP and Revorg have extensively verified the performance of the ERP system software using tests that evaluate accuracy, reliability and consistent performance. The user organization is required to validate their system according to regulatory expectations. The identification of GxP critical functions and data should be performed with a risk assessment during validation. Revorg can support the user organization during validation.
Annex 11	Is infrastructure qualified?	U		N/A	Qualification of infrastructures, such as servers and networks, is the responsibility of the user organization.
Accurate Copies and Secure Retention and Retrieval of Records					
Part 11 11.10(b)	Is the system capable of generating accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the FDA?	S		Yes	Copies of the records can be generated printed on paper or electronically as a PDF file.
Annex 11 8.1	Is it possible to obtain clear printed copies of electronically stored e-records?	S		Yes	Records are available printed on paper or electronically as a PDF file.
Part 11 11.10(c)	Does the system protect records to enable their accurate and ready retrieval throughout the records retention period?	S, U		Yes	All raw data, metadata, and result data generated by SAP B1 is stored in a protected location. Physical security (control of physical access to workstations and servers) is the responsibility of the user organization. It is the user organization's responsibility to develop a review by exception protocol based on a risk-based assessment of unplanned events, such as network connectivity loss which would initiate a failover mode.
Annex 11 17	Are data checked during the archiving period for accessibility, readability, and integrity?	U		N/A	It is the responsibility of the user organization to ensure that data are checked during archival for accessibility, readability, and integrity.
Annex 11 17	If relevant changes are made to the system (e.g., computer equipment or programs), is then the ability to retrieve the data ensured and tested?	S, U		Yes	The system is designed to read data from legacy versions of SAP B1. The user organization is responsible for ensuring readability of this data during their implementation and validation processes.
Annex 11 7.1	Are data secured by both physical and electronic means against damage?	S, U		Yes	All Raw data, Metadata, result data generated by the system is stored in a protected location. Physical security is the responsibility of the user organization.
PI 041-1 9.6	Are there controls implemented that allow the reconstruction of the electronic source / raw documentation for review of the activities?	S		Yes	All raw data and metadata (e.g. audit trail) is maintained in secure storage to allow reconstruction of activities as needed.

Accurate Copies and Secure Retention and Retrieval of Records					
Annex 11 7.1	Does the system allow performing regular backups of all relevant data?	S	Part 211, 68 b IC Q7, 5.48	Yes	Backing up data is the responsibility of the user organization. Detailed instructions are available for creating the appropriate scheduled automatic backups of all relevant files.
Annex 11 7.2	Is the integrity and accuracy of backed-up data and the ability to restore the data, checked, validated, and monitored periodically?	U	Part 211, 68 b	N/A	It is the responsibility of the user organization to ensure the integrity and accuracy of backed- up data, and to check, validate and monitor restored data periodically. Backup and restore systems and processes should be verified during validation. Backing up data is the responsibility of the user organization. Detailed instructions are available for creating the appropriate scheduled backup of all relevant files.
Authorized Access to Systems, Functions, and Data					
Part 11 11.10(d)	Is system access limited to authorized persons?	S, U	IC Q7, 5.43	Yes	Each user is identified by a unique ID and password combination. Entry of both is required to access the system.
	Is each user clearly identified, e.g., through his/her own user ID and Password?	S, U		Yes	Each user is identified by a unique ID and password combination. Entry of both is required to access the system.
Annex 11 12.3	Are there controls to maintain a cumulative record that indicates, for any point in time, the names of authorized personnel, their titles, and a description of their access privileges?	S, U	Creation, change, and cancellation of access authorizations should be recorded.	Yes	SAP B1 is able to authenticate users via either the Windows Domain or locally in the application itself. Access privileges are set in the application and any changes can be recorded in the activity log. Reports are available that show users' individual privileges.
Electronic Audit Trail					
Part 11 11.10(e)	Is there a secure, computer-generated, time-stamped audit trail to independently record the date and time of operator entries and actions that create, modify, or delete electronic records?	S		Yes	All user activities are recorded in secure, computer generated, time-stamped audit trails. Audit trails are created for all result data, methods, and sequences.
Annex 11 9	Does the audit trail record who has made which changes, when and why?	S		Yes	The audit trail includes the user ID, date and time of the change, and the before and after values together with the reason why the change was made. The reason is managed in data approval functions.
Annex 11 8.2	Can the system generate printouts indicating if any of the e-records have been changed since the original entry?	S	Required for records supporting batch release.	Yes	Audit trails for records can be printed. As a standard, there is a report on the batches tab where it is possible to compare the critical data modified from time zero to the last change of state or in the intermediate changes. This report is available only if the Audit trail is active.
"PI 041-1 9.6.1"	Is the audit trail function configured to be always on and can it not be switched off by system users?	S, U		Yes	"Audit trails should be properly configured and then validated. System is preconfigured for typical need in the pharma industry. Once audit trails are activated, they cannot be de-activated by any user."

Electronic Audit Trail					
"Annex 11 9"	Is audit trail available in a generally intelligible form for regular review?	S	PI 041-1, 9.6	Yes	"Audit trails are readily available in a configurable viewer."
	Can audit trail contents be configured such that only relevant activities are recorded for realistic and meaningful review of audit trail information?		Implicitly required by Annex 11 with many warning letters related to review of audit trail.	Yes	"SAP B1 (J-Pharma) allows the audit trail to be filtered prior to displaying its contents to address user preferences for reviewing the information.
Part 11 11.10(e)	Is previously recorded information left unchanged when records are changed?	S		Yes	Previous data value is maintained. Some data are managed with a version. During selection of results for further processing or reporting, the version of the result used can be chosen by the user.
Part 11 11.10(e)	Is audit trail documentation retained for a period at least as long as that required for the subject electronic record?	S		Yes	Audit trail information is stored within the electronic record and cannot be separated from it.
Part 11 11.10(e)	Is audit trail available for review and copying by the FDA?	S, U		Yes	Audit trails can be reviewed and printed.
"Annex 11 8.1"	Is it possible to obtain clear printed copies of electronically stored e-records (e.g., e-audit trail?)	S		Yes	Audit trails can be reviewed and printed.
Operational and Device Checks					
Part 11 11.10(f)	Are there operational system checks to enforce permitted sequencing of steps and events, if required?	S		N/A	It is the responsibility of the user organization to designate and enforce procedural controls.
Part 11 11.10(g)	Are there authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand?	S	Part 211, 68 b	N/A	The system supports configurable user roles that control system access at a detailed level. Access can segregated and defined such that certain users have certain specific types of access to certain specific types of data sets while having different access to other types of data sets.
Annex 11 12.4"	Is the system designed to record the identity of operators entering, changing, confirming or deleting data including date and time?	S		Yes	The identity of operators taking action in the system is recorded in the both the audit trail and activity log.
Part 11 11.10(h)	Does the system allow use of device checks to determine, as appropriate, the validity of the source of data input or operational instruction?	S		Yes	The system is designed to continually ensure a valid connection between the system and the computer workstation and/ or any external system connected through a data interface.
Part 11 11.10(i)	Is there documented evidence that persons who develop, maintain, or use electronic record/electronic signature systems have the education, training, and experience to perform their as-signed tasks?	U		N/A	It is the responsibility of the user organization to maintain documented evidence that the persons who develop, maintain, or use electronic record and electronic signature systems have the education, training, and experience needed to perform these tasks. SAP and Revorg software professionals involved in development of SAP B1 and J-Pharma have received training in relevant aspects of GxP, validation and data integrity.
Part 11 11.10(j)	"Is there a written policy that holds individuals accountable and responsible for actions initiated under their electronic signatures, in order to determine record and signature falsification? Have employees been trained on this procedure? (Implied requirement of Part 11 11.10(j))"	U		N/A	It is the responsibility of the user organization to establish a written policy (SOP) and training that holds staff responsible for the actions initiated under their electronic signatures.

Operational and Device Checks					
Part 11 11.10(k)	Are there appropriate controls over systems documentation including: 1. Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance? 2.Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.	U	ICH Q7, 5.48	N/A	It is the responsibility of the user organization to establish systems documentation. Revorg maintains development and testing documentation for SAP B1. Upon request, this documentation is available for user review.
Data Integrity, Date and Time Accuracy					
Annex 11 5	Do computerized systems that exchange data electronically with other systems include appropriate built-in checks for the correct and secure entry and processing of data?	S		N/A	SAP B1 can be interfaced and exchange data with other systems. Interfaces are related to project s and should be properly implemented and validated. Revorg can provide support for proper implementation and validation of system interfaces.
Annex 11 6	Is there an additional check on the accuracy of the data? This check may be done by a second operator or by validated electronic means.	S, U	ICH Q7, 5.45	Yes	Throughout the management of the software it is possible to configure a workflow for the approval of an object (whether it is a purchase request, customer / supplier order or return). On the batch data the approval activities are already preconfigured when the status changes.
PI 041-1 9.5.1	Are controls established to ensure that the system's date and time are correct?	S, U		Yes	Revorg recommends that the system be configured to reference a time server to ensure accuracy of the system date and time. This is configured in and controlled by the operating system.
	Can date or time only be changed by authorized personnel, and is such personnel notified if a system date or time discrepancy is detected?	S, U		N/A	SAP B1 is designed to synchronize with local Windows time. It is the user organization's responsibility to: • Limit access controls of Windows time settings to only authorized personnel. • Maintain procedural controls for setting and maintaining the accuracy of Windows time.
Controls for Open Systems (Only Applicable for Open Systems)					
Part 11 11.30	Are there procedures and controls designed to ensure the authenticity, integrity, and, as appropriate, the confidentiality of electronic records from the point of their creation to the point of their receipt?	S, U		N/A	SAP B1 is not intended to be deployed as "open" system as per 21 CFR Part 11.3(b) (9): it is normally configured as a "closed" system.
Part 11 11.30	Are there additional measures such as document encryption and use of appropriate digital signature standards to ensure, as necessary under the circumstances, record authenticity, integrity, and confidentiality?	S		N/A	SAP B1 is not intended to be deployed as "open" system as per 21 CFR Part 11.3(b) (9).
Electronic Signatures – Signature Manifestation and Signature/Record Linking					
Annex 11 14	When electronic signatures are used, do they have the same impact as hand- written signatures within the boundaries of the company? Are they permanently linked to their respective record? Do they include the time and date that they were applied?	S, U	ICH Q7.6.18	Yes	The user organization must establish the impact of electronic signatures. Signatures are permanently linked to their respective records. Signed electronic records includes the date and time the signature was executed.

Electronic Signatures – Signature Manifestation and Signature/Record Linking					
Part 11 11.50 (a)	Do signed electronic records contain information associated with the signing that clearly indicates all of the following: 1.The printed name of the signer? 2.The date and time when the signature was executed? and 3.The meaning (such as review, approval, responsibility, or authorship) associated with the signature?	S		Yes	Signed electronic records show the name of the signer, the date and time the signature was executed, and the meaning of the signature.
Part 11 11.50 (b)	Are the items identified in paragraphs (a)(1), (a)(2), and (a)(3) of this section subject to the same controls as for electronic records and are they included as part of any human readable form of the electronic record (such as electronic display or printout)?	S		Yes	All electronic signature components are displayed in a human readable form and may be printed.
Part 11 11.70	Are electronic signatures and handwritten signatures linked to their respective electronic records to ensure that the signatures cannot be excised, copied, or otherwise transferred to falsify an electronic record by ordinary means?	S		Yes	Handwritten signatures are not addressed by the system and must be managed by procedurally by the user organization. Electronic signatures are embedded in the electronic record and cannot be modified, overwritten or deleted.
Part 11 Preamble	Is there a user-specific automatic inactivity disconnect measure that would "de-log" the user if no entries or actions were taken within a fixed short timeframe?	S	Part 11 Preamble section 124	Yes	Automatic session locking enables the user organization to configure a time after which the user is automatically logged-out.
Electronic Signatures - General Requirements and Signature Components and Controls					
Part 11 11.100(a)	Is each electronic signature unique to one individual and not reused by, or reassigned to, anyone else?	S,U		Yes	The system will not allow duplicate user IDs. Each user has a unique login and thus a unique signature that cannot be used by an-other user.
Part 11 11.100(b)	Does the organization verify the identity of the individual before the organization establishes, assigns, certifies, or otherwise sanctions an individual's electronic signature, or any element of such electronic signature?	U		N/A	It is the responsibility of the user organization to verify the identify of staff before it establishes, assigns, certifies, or otherwise sanctions an individual's electronic signature, or any element of such electronic signature.
Part 11 11.100 (c)	Are persons using electronic signatures, prior to or at the time of such use, certified to the agency that the electronic signatures in their system, used on or after August 20, 1997, are intended to be the legally binding equivalent of traditional handwritten signatures? Do persons using electronic signatures, upon agency request provide additional certification or testimony that a specific electronic signature is the legally binding equivalent of the signer's handwritten signature?	U		N/A	It is the responsibility of the user organization to verify that staff using electronic signatures meet these requirements.
Part 11 11.200(a) (1)	Do electronic signatures that are not based upon biometrics employ at least two distinct identification components such as an identification code and password?	S,U		Yes	Both identification (user ID) and password are required to make an electronic signature.
Part 11 11.200(a) (1) (i)	When an individual executes a series of signings during a single, continuous period of controlled system access, is the first signing executed using all electronic signature components?	S		Yes	Both identification (user ID) and password are required to make all electronic signatures.

Electronic Signatures - General Requirements and Signature Components and Controls				
Part 11 11.200(a) (1) (i)	When an individual executes a series of signings during a single, continuous period of controlled system access, are subsequent signings executed using at least one electronic signature component that is only executable by, and designed to be used only by, the individual?	S	Yes	Both identification (user ID) and password are required to make all electronic signatures.
Part 11 11.200(a) (1) (ii)	When an individual executes one or more signings not performed during a single, continuous period of controlled system access, is each signing executed using all of the electronic signature components?	S	Yes	Both identification (user ID) and password are required to make all electronic signatures.
Part 11 11.200(a) (2)	Are controls in place to ensure that electronic signatures that are not based upon biometrics are used only by their genuine owners?	S	N/A	It is the user organization's responsibility to ensure that user names and passwords are known only by the assigned individuals and are traceable to individual users.
Part 11 11.200(a) (3)	Are the electronic signatures administered and executed to ensure that attempted use of an individual's electronic signature by anyone other than its genuine owner requires collaboration of two or more individuals?	S,U	Yes	Misuse of electronic signatures by anyone other than the owner would require intentional co-operation of a user and the System Administrator.
Part 11 11.200(b)	Are electronic signatures based upon biometrics designed to ensure that they cannot be used by anyone other than their genuine owners?	S	N/A	Biometric authentication is not supported in SAP B1.
Controls for Identification Codes and Passwords				
Part 11 11.300(a)	Are controls in place to maintain the uniqueness of each combined identification code and password, such that no two individuals have the same combination of identification code and password?	S, U	Yes	SAP B1 does not allow duplicate user IDs.
Part 11 11.300(b)	Are controls in place to ensure that identification code and password issuance are periodically checked, recalled, or revised (e.g., to cover such events as password aging)?	S, U	Yes	Password expiration is configurable via either the Windows Domain or locally in the application itself. The user organization should configure password expiration based on a documented risk assessment.
Part 11 11.300(c)	Are there procedures to electronically de-authorize lost, stolen, missing, or otherwise potentially compromise tokens, cards, and other devices that bear or generate identification code or password information, and to issue temporary or permanent replacements using suitable, rigorous controls?	U	N/A	It is the responsibility of the user organization to establish controls to test devices initially as well as periodically to ensure they function properly and have not been altered in an unauthorized manner.
Part 11 11.300(d)	Are there transaction safeguards in place to prevent unauthorized use of passwords and/or identification codes, and to detect and report in an immediate and urgent manner any attempts of their unauthorized use to the system security unit, and, as appropriate, to organizational management?	U	N/A	It is the responsibility of the user organization to establish these transaction safe-guards.

Controls for Identification Codes and Passwords					
Part 11 11.300(e)	Are there controls for initial and periodic testing of devices, such as tokens or cards that bear or generate identification code or password information to ensure that they function properly and have not been altered in an unauthorized manner?	U		N/A	It is the responsibility of the user organization to establish controls to test devices initially as well as periodically to ensure they function properly and have not been altered in an unauthorized manner.
System Development and Support					
Annex 11 4.5	Has the software or system been developed in accordance with an appropriate quality management system?	S,U	GAMP The user should require the supplier to provide documented evidence that software is developed within the framework of a quality management system (QMS).	Yes	SAP B1 is developed by SAP within their ISO 9001 Quality Management Standard. J-Pharma is developed by Revorg within the ISO 9001 Quality Management Standard and the plurennial experience in the pharmaceutical sector.
Annex 11 3.1	For outsourced activities, is there a written agreement between the contract giver and contract acceptor?	S,U	(e.g. development, configuration, validation and support)	Yes	A maintenance contract (SLA – Service Level Agreement) can be established between the user organization and Revorg.
Part 11 11.10(i)	Is personnel developing and supporting software trained?	S, U	The supplier must ensure its staff is trained, and the user should have assurance, e.g., through audits that SW developers are trained and that this training is documented.	Yes	All Revorg personnel are required to be trained.
System Security					
PI 041-1 9.5	Physical Security	U	Annex 11, 12.1	N/A	Physical security is a responsibility of the user organization.
	Logical security / user's roles, segregation of duties	S, U	Annex 11 §12 21 CFR Part 11, 11.10(d)	Yes	User's roles are defined and set-up during system configuration. It is a responsibility of the user organization to define user's roles in to ensure proper access to system function and segregation of duties, restricting access to critical functions, including configuration to authorized personnel. ERP user roles come preconfigured for typical users to simplify configuration and validation. User roles should be verified during validation and maintained with appropriate user's SOPs.
	"Network system security should include appropriate methods to detect and prevent potential threats to data, based on an assessment of data risk. Firewalls should be used to prevent unauthorized access, and their rules should be subject to periodic reviews. Appropriate virus-protection or intrusion prevention/ detection systems should be used to protect data and computerized systems from attempted attacks and malware."	U		N/A	Network security, including firewalls and the relevant rules, as well as virus protection, intrusion detection/protection are set-up and managed by the user organization. SAP and Revorg have tested the system in conjunction with industry standard anti-virus applications. However, it is the responsibility of the user organization to implement anti-virus software.

3. RIFERIMENTI

Normative e Linee Guida generali:

1.EU GMP: European Commission, The Rules Governing Medicinal Products in the European Union – Volume 4: Good Manufacturing Practices Medicinal Products for Human and Veterinary Use
2.EU GMP, Annex 11 "Computerised Systems" (Gen 2011)
3.EU GMP, Part III "Quality Risk Management" (ICH Q9, Nov 2005)
4.Guidance for Industry Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (Aug 2001)
5.EudraLex Volume 4, EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Annex 15: Qualification and Validation (Oct 2015).
6.PIC/S Guidance: Good Practices for Computerised System in Regulated GxP Environment, Document PI 011-3 (Sep 2007)
7.US FDA - Code of Federal Regulations, Title 21, part 210: Current Good Manufacturing Practice in Manufacturing, Processing, Packaging, or Holding of Drugs; General
8.US FDA - Code of Federal Regulations, Title 21, part 211: Current Good Manufacturing Practice for Finished Pharmaceuticals
9.US FDA - Code of Federal Regulations, Title 21, part 11 (21 CFR Part 11): Electronic Records; Electronic Signatures (Final Rule, 1997)
10.US FDA "Part 11 Scope and Application" (Aug. 2003)
11.GAMP (Good Automated Manufacturing Practice) – A Risk Based Approach to Compliant Computerized Systems v. 5 (Feb 2008)
12.GAMP Good Practice Guide: A Risk Based Approach to Compliant Electronic Records and Signatures (Feb 2005)
13.GAMP Good Practice Guide: Testing of GxP Systems (second edition, Dec 2012)

Normative e Linee Guida specifiche per la Data Integrity:

14.PIC/S Guidance: Good Practices For Data Management And Integrity In Regulated Gmp/Gdp Environments, Documents 041-1 (final, Jul 2021)
15.MHRA: Guideline "GMP Data Integrity Guidance and Definitions for Industry" (March 2018)
16.WHO: Guidance On Good Data And Record Management Practices (WHO technical report series; no. 996, Annex 5 - May 2016)
17.FDA: Data Integrity and Compliance With Drug CGMP - Questions and Answers - Guidance for Industry (final, Dec 2018)
18.EMA: Questions and answers: Good manufacturing practice (Aug 2016)
19.GAMP Guide: Records and Data Integrity (Apr 2017)
20.GAMP Good Practice Guide: Records and Data Integrity – Key Principles (Nov 2018)
21.GAMP Good Practice Guide: Records and Data Integrity – Manufacturing Records (May 2019)
22.GAMP Good Practice Guide: Records and Data Integrity – Data Integrity by Design (Oct 2020)

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