# BIcosmos Digital Solution BI Platform

## 21 CFR Part 11 and Annex 11 Assessment

BIcosmos

BI Platform a complete solution

## 1. INTRODUCTION

The purpose of this document is to outline the roles and responsibilities for compliance with the FDA's 21 CFR Part 11 and alignment with the European Union's Annex 11 as they apply to BIcosmos BI platform. The regulations require organizations to have administrative, procedural, and technical controls in place.

This document is to provide clarification and guidance for customers regarding the applicability of the 21 CFR Part 11 and EU Annex 11 requirements. Each section and sub-text of FDA 21 CFR Part 11 was evaluated for relevance to BIcosmos practices. Where applicable, a statement of compliance is provided. Customer responsibilities have been highlighted where applicable in achieving compliance.

## 2. HIGH-LEVEL COMPARISON OF EU ANNEX 11 AND FDA 21 CFR PART 11

| | 21 CFR PART 11 | Annex 11 |
|---|---|---|
| Scope/Principle | Electronic records and electronicsignatures as used for all FDA regulated activities. | Computerized systems as part ofGMP regulated activities.<br>Application should be validated.<br>IT infrastructure should be qualified. |
| Focus | Using electronic records and signatures in open and closedcomputer systems. | Risk- based quality management of computerized systems. |
| Objective | Electronic records and signaturesshould be as trustworthy and reliable as paper records and handwritten signatures. | Using a computerized system should ensure the same product quality and quality assurance as manual systems with no increase in the overall risk. |

## 3. CONTROL FOR CLOSED SYSTEM

| 21 CFR Part 11 | EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| **§11.10(a)** Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records. | **§4.1** Do validation documents and reports cover the relevant steps of the life cycle? | BI platform (out of the box processes) is validated with each release. If changes are made to the platform that do not impact their system, customers may choose to leverage BIcosmos validation package. validation before each release in accordance with their internal documented SOPs or processes.<br>CSV deliverables are reviewed and approved by the BIcosmos Quality Unit. | - | X | - |
| | | Platform offers a full audit trail where changes to quality records are logged. The audit trail includes user ID, old and new value, and time stamp. | X | - | - |
| | | Customers are responsible for validation of any changes that impact their Digital implementation, performing risk- based testing and validation before each release in accordance with their internal documented SOPs or processes inform of PQ or UAT | - | - | X |
| **§11.10(b)**The ability to generate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency. | **§8.1** It should be possible to obtain clear printed copies of electronically stored data. | BI platform provides the records in human readable form suitable for inspection, review, and copying by the agency. Configurable reports, print and exports permit review of records in pdf. | X | - | - |
| **§11.10(c)**Protection of records to enable their accurate and ready retrieval throughout the records retention period. | **§17** Is data archived? If data is archived, is it checked for accessibility, readability and integrity? When changes are made to the system, is the ability to retrieve archived data ensured and tested? | BI platform architecture ensures all records are retained and can be retrieved from the production environment throughout the record retention period. No separate archive storage is required. | X | - | - |
| | | Data retention / archived; the customer is responsible for managing archive in compliance with retention periods defined in applicable predicate rules. | - | - | X |
| **§11.10(d)**Limiting system access to authorized individuals. | **§ 12.1** Physical and/or logical controls should be in place to restrict access to computerised system to authorised persons. | BI platform limits system access to authorized individuals through the use of user ID and password combinations. Role-based security configurations control all access to system functions. | X | - | - |

| 21 CFR Part 11 | EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| | | Customers may configure the system to their security policies and define roles and privileges to align with their business requirements. Customer administrators are responsible for managing accounts and ensuring compliance with this section of the regulation. | - | - | X |
| **§11.10(e)**Use of secure, computer-generated, time- stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records.<br><br>Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying. | **§14.c** include the time and date that they were applied.<br><br>**§9 Audit trail** Consideration should be given, based on a risk assessment, to building into the system the creation of a record of all GMP-relevant changes and deletions | BI platform provides full audit trail for create and modify operations.<br><br>The BI platform audit trail records previous values. Audit trail entries and record data cannot be deleted. The audit trail information is available to system administrators for review, download | X | - | - |
| **§11.10(f)**Use of operational system checks to enforce permitted sequencing of steps and events, as appropriate. | **§5 Data;** Computerised systems exchanging data electronically with other systems should include appropriate built-in checks for the correct and secure entry and processing of data, in order to minimize the risks. | BI platform allows for configurable workflow management that "required" data is completed prior to allowing the user to proceed with the next process step; Customer can define the required sequence of steps and events and ensure the proper process which must be followed. | X | - | X |
| **§11.10(g)**Use of 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. | **§7.1** Data should be secured by both physical and electronic means against damage. Stored data should be checked for accessibility, readability and accuracy. Access to data should be ensured throughout the retention period.<br>**§12.1** Physical and/or logical controls should be in place to restrict access to computerized system to authorised persons | BI platform has controls to ensure that only authorized individuals can use the system by configurable security modeling. | X | - | - |
| | | Access and role application are under customer's control; customers have to review their policies and procedures and modify them accordingly to BI platform user roles and profiles are configured. | - | - | X |
| **§11.10(h)**Use of device (e.g., terminal) checks to determine, as appropriate, the validity of | | The validity of the source of data input or operational instructions is controlled through the | X | - | - |

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|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| the source of data input or operational instruction. | | authentication process and is systematically assured throughout the user session. | | | |
| **§11.10(i)**Determination that persons who develop, maintain, or use electronic record/electronic signature systems have the education, training, and experience to perform their assigned tasks. | **§2** There should be close cooperation between all relevant personnel such as Process Owner, System Owner, Qualified Persons and IT. | Within BIcosmos, employees are formally trained on policies, SOPs, and work instructions. These SOPs outline how relevant personnel work together to complete their tasks. Employees also receive on the job training appropriate to their responsibilities. | - | **X** | - |
| | | Customer's responsibility to demonstrate that their administrators and users have the education, training, and experience to perform their assigned tasks. | - | - | **X** |
| **§11.10(j)**The establishment of, and adherence to, written policies that hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification. | | We advise customers to have written policies compliance with this section of the regulation. | - | - | **X** |
| **§11.10(k)(1)** Use of appropriate controls over systems documentation including: 1-Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance. | | We advise customers to establish procedures covering the distribution of, access to, and use of documentation once the system is in use. | - | - | **X** |
| **§11.10(k) (2)** Use of appropriate controls over systems documentation including: 2- Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation | **§4.2** Validation documentation should include change control records (if applicable) and reports on any deviations observed during the validation process. | We advise customers to ensure adequate change control procedures for documentation related to their implemented solution. | - | - | **X** |

## 4. CONTROL FOR OPEN SYSTEM

| 21 CFR Part 11 | EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| **§11.30** Persons who use open systems to create, modify, maintain, or transmit electronic records shall employ 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. Such procedures and controls shall include those identified in 11.10, as appropriate, and 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. | **§4.1** | Not applicable as BI platform is a closed system. | - | - | - |

## 5. SIGNATURE MANIFESTATION

| 21 CFR Part 11 | EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| **§11.50(a)** Signed electronic records shall contain information associated with the signing that clearly indicates all of the following:<br>(1) The printed name of the signer;<br>(2) The date and time when the signature was executed; and<br>(3) The meaning (such as review, approval, responsibility, or authorship) associated with the signature. | **§4.1** | Signature manifestation within BI Platform includes (a) the printed name of the signer; (b) the date and time when the signature was executed; and (c) the meaning of the signature. The system enforces the consistent application of these components. | X | - | - |
| **§11.50(b)** The items identified in paragraphs (a)(1), (a)(2), and (a)(3) of this section shall be subject to the same controls as for electronic records and shall be included as part of any human readable form of the electronic record (such as electronic display or printout). | | The signature manifestation associated with signed records in BI platform is subject to the same controls as the individual record to which it is attached. When selected, the electronic signature is manifested within all human readable forms of the record (display and printout). | X | - | - |

## 6. SIGNATURE / RECORD LINKAGE

| 21 CFR Part 11 | EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| **§11.70** Electronic signatures and handwritten signatures executed to electronic records shall be 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. | **§14 (b)** be permanently linked to their respective record. | BI platform prevents all system users, including administrators cannot cut, copy, or otherwise transferring electronic signature through ordinary means. | X | - | - |

## 7. ELECTRONIC SIGNATURES – GENERAL REQUIREMENT

| 21 CFR Part 11 | EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| **§11.100(a)** Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else. | | BI platform ensures unique id and the id is associated to their e- Signature. Prohibiting new accounts with an existing user ID | X | - | - |
| | | We advise customers to have procedural control ensure accounts are never re- assigned to different users. | - | - | X |
| **§11.100(b)** Before an organization establishes, assigns, certifies, or otherwise sanctions an individual's electronic signature, or any element of such electronic signature, the organization shall verify the identity of the individual. | | It is the customer's responsibility to verify the identity of individuals assigned to an electronic record. Login to the system must occur by a named user before e-signature can be executed. | - | - | X |
| **§11.100(c)** Persons using electronic signatures shall, prior to or at the time of such use, certify 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. | **§14 (a)** have the same impact as hand-written signatures within the boundaries of the company | Customers must notify the FDA of their own intent to use electronic signatures in order to comply with this section of the regulation. | - | - | X |

## 8. ELECTRONIC SIGNATURE COMPONENTS AND CONTROLS

| 21 CFR Part 11 | EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| **§11.200 (a)** Electronic signatures that are not based upon biometrics shall:<br>(1) Employ at least two distinct identification components such as an identification code and password. | **§4.1** | All Signatures within BI platform consist of a User ID and Password. | **X** | - | - |
| **§11.200(a)(1)(i)** When an individual executes a series of signings during a single, continuous period of controlled system access, the first signing shall be executed using all electronic signature components; subsequent signings shall be executed using at least one electronic signature component that is only executable by, and designed to be used only by, the individual | | The password is required at each signing. When a user initially signs into BI platform the first signing, both a user name and password are required. | **X** | - | - |
| **§11.200(a)(1)(ii)** When an individual executes one or more signings not performed during a single, continuous period of controlled system access, each signing shall be executed using all of the electronic signature components. | | For non-continuous sessions, the user will be logged out of the application and be required to enter both the user name and password to log back into the system prior to performing additional electronic signatures. | **X** | - | - |
| **§11.200(a)(2)** Be used only by their genuine owners; | | We advise customers to have their policies and procedures to ensure full compliance with this section of the regulation. | - | - | **X** |
| **§11.200(a)(3)** Be 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. | | Customers need procedures that users do not disclose their electronic signature (e.g., password). | - | - | **X** |
| **§11.200(b)** Electronic signatures based upon biometrics shall be designed to ensure that they cannot be used by anyone other than their genuine owners**.** | | Currently biometric authentication are not applicable in BI Platform | - | - | - |

## 9. CONTROLS FOR IDENTIFICATION CODES/PASSWORDS.

| 21 CFR Part 11 | EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|---|
| | | | Product | Process | Customer |
| **§11.300(a)** Maintaining the uniqueness of each combined identification code and password, such that no two individuals have the same combination of identification code and password. | | BI platform ensures that user IDs cannot be duplicated or reused | X | - | - |
| **§11.300(b)** Ensuring that identification code and password issuances are periodically checked, recalled, or revised (e.g., to cover such events as password aging). | **§11** Periodic Review: Computerised systems should be periodically evaluated to confirm that they remain in a valid state and are compliant with GMP. | BI platform allows customers to set the password aging controls in accordance with their security policies | X | - | - |
| | | Customer responsible for defining and executing a periodic review of user access | - | - | X |
| **§11.300(c)** Following loss management procedures to electronically deauthorize lost, stolen, missing, or otherwise potentially compromised 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. | | BIcosmos product are not currently employ any devices to assist with authentication.<br>It is the responsibility of the customer to establish procedures for disabling tokens, cards, or other devices | - | - | X |
| **§11.300(d)** Use of transaction safeguards to prevent unauthorized use of passwords and/or identification codes, and to detect and report in an immediate and urgent manner any attempts at their unauthorized use to the system security unit, and, as appropriate, to organizational management. | | BI platform can be configured to notify the administrator when a set number of login attempts in a single instance were unsuccessful. | X | - | - |
| | | We advise customers to have their policies and procedures to ensure full compliance with this section of the regulation. | - | - | X |
| **§11.300(e)** 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. | | BIcosmos product are not currently employ any devices to assist with authentication.<br>It is the responsibility of the customer to establish procedures for managing tokens, cards, or other devices. | - | - | X |

## 10. EU ANNEX 11 CONTROL FOR WHICH THERE IS NO PART 11 EQUIVALENT

| EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|
| | | Product | Process | Customer |
| **§1** Risk management should be applied throughout the lifecycle of the computerised system taking into account patient safety, data integrity and product quality. As part of a risk management system, decisions on the extent of validation and data integrity controls should be based on a justified and documented risk assessment of the computerised system. | Customers are responsible for decisions regarding validation and data integrity controls. | - | - | X |
| **§3.1** When third parties (e.g. suppliers, service providers) are used e.g. to provide, install, configure, integrate, validate, maintain (e.g. via remote access), modify or retain a computerised system or related service or for data processing, formal agreements must exist between the manufacturer and any third parties, and these agreements should include clear statements of the responsibilities of the third party. IT-departments should be considered analogous. | BIcosmos provides the business proposal and maintains formal contracts with all third parties utilized for staff augmentation purposes. | - | X | - |
| | Customers are responsible for developing and executing agreements with third parties. | - | - | X |
| **§3.2** The competence and reliability of a supplier are key factors when selecting a product or service provider. The need for an audit should be based on a risk assessment. | Customers are responsible for auditing any third parties they utilize. | - | - | X |
| **§3.3** Documentation supplied with commercial off-the-shelf products should be reviewed by regulated users to check that user requirements are fulfilled. | Customers are responsible for reviewing and accepting the Sparta Systems validation package. | - | - | X |
| **§3.3** Quality system and audit information relating to suppliers or developers of software and implemented systems should be made available to inspectors on request. | BIcosmos can support for required need. | - | X | X |
| **§4.3** An up to date listing of all relevant systems and their GMP functionality (inventory) should be available.<br>For critical systems an up to date system description detailing the physical and logical arrangements, data flows and interfaces with other systems or processes, any hardware and software pre-requisites, and security measures should be available. | BIcosmos provides the Design document during the implantation. | - | X | - |
| | We advise customers to have their policies and procedures to ensure full compliance with this section of the regulation. | - | - | X |
| **§4.5** The regulated user should take all reasonable steps, to ensure that the system has been developed in accordance with an appropriate quality management system. The supplier should be assessed appropriately. | BIcosmos is ISO 9001:2015 certified. | - | X | - |
| **§4.6** For the validation of bespoke or customised computerised systems there should be a process in place that ensures the formal assessment and | BIcosmos provide an outbox solution and validation as a service.<br>It is the responsibility of the customer to ensure a formal assessment is completed is | - | X | X |

| EU Annex 11 | BIcosmos control | Applicability / Responsibility | | |
|---|---|---|---|---|
| | | Product | Process | Customer |
| reporting of quality and performance measures for all the life-cycle stages of the system. | they choose to customize BI platform. | | | |
| **§4.8** If data are transferred to another data format or system, validation should include checks that data are not altered in value and/or meaning during this migration process. | BIcosmos can only migrate the data provided by the customer. it's the responsibility of the customer to verify the and check the migrated data. | - | X | X |
| **§7.2** Regular back-ups of all relevant data should be done. Integrity and accuracy of backup data and the ability to restore the data should be checked during validation and monitored periodically. | BIcosmos can provide a backup procedure. it's the responsibility of the customer to backup and monitor the data using any backup tools.<br><br>We advise customers to have their policies and procedures to ensure full compliance with this section of the regulation. | - | X | X |
| **§8.2** For records supporting batch release it should be possible to generate printouts indicating if any of the data has been changed since the original entry. | BI Platform is not currently maintaining the batch records | - | - | - |
| **§13** All incidents, not only system failures and data errors, should be reported and assessed. The root cause of a critical incident should be identified and should form the basis of corrective and preventive actions. | BIcosmos address the incident; incidents are investigated, root cause analysis completed, and if applicable, a corrective action is identified. | - | X | - |
| | Customer is responsible to have a support plan with BIcosmos on completion of qualification for support | - | - | X |
| **§16** Business continuity for the availability of computerised systems supporting critical processes, provisions should be made to ensure continuity of support for those processes in the event of a system breakdown (e.g. a manual or alternative system). | Customer is responsible to have business continuity plan. BIcosmos can support the customer during the DR on support as service. | - | - | X |

| Version No | Description |
|---|---|
| 1.0 | Initial version release 2019 |