Data Integrity and Electronic Records Compliance with DoseControl®

GEX Doc# 100-282

1.0 PURPOSE

To provide detailed descriptions of the functional specifications for the GEX DoseControl Dosimetry System, related to data integrity and electronic records compliance.

2.0 BACKGROUND

The DoseControl System was born from a recognition of the need for accurate electronic record-keeping and data management of dosimetry measurements and metadata to be used in various quality management and operational aspects of commercial irradiation applications. The primary purposes of DoseControl are for users to have the ability to rely on DoseControl system data for validating processes, assessing product and process conformance, and providing data feedback for process control analysis.

The DoseControl System is intended to ensure compliance with U.S. FDA 21 CFR part 11, EudraLex Vol. 4 Annex 11, and FDA CGMP standards for data integrity and electronic records. The DoseControl design team researched, identified, and interpreted the requirements of these standards, and incorporated these elements into the system design and development. To date, aspects of U.S. FDA 21 CFR part 11 are the only ones to be formally validated.

GEX maintains a Quality Management System certified to ISO 9001:2015 and ISO 17025:2005 standards.

3.0 INTEGRITY OF USER ASSOCIATION WITH RECORDS

Access Control

DoseControl utilizes access controls to ensure that the system can accurately record the user that is working on the system, including authentication by corporate Windows® Active Directory (LDAP). All records of user associations are maintained, even after users are deleted from the Active Directory.

The application lock-out feature locks the application to the Login Screen after an administrator-designated set number of idle minutes.

User Roles and Permissions

- *System Administrator Role* – IT configuration and user management only.
- *Application Administrator Role* – Settings for all operational aspects, except the System Administrator items.
- *Technician Role* – Ability to create reports and measure dosimeters, performance verification, and generate system outputs.
- *Re-read Permission* - Users authorized to re-read dosimeters.
- *Sample Editing Permission* - Users that are authorized to edit the ID of a sample, or to execute soft-deletion of a sample ID and related measurement data from a report.
- *Edit Dosimeter Thickness Permission* - Users that are authorized to edit the thickness of a dosimeter sample.

4.0 INTEGRITY OF DATA - GENERAL

Date and Time Records

The database records the Date and Time according to UTC, to provide a consistent record, and to eliminate confusion due to user time zone differences.

Auto and Manual Saving
Configuration data and manually entered metadata are saved by user action ("save" button). The GxP data acquisition from instruments, including associated metadata and data resulting from calculations (including associated metadata), is auto-saved by the software.

Deletion of Records
Measurement records (data) and/or any related record metadata (and configuration data associated with the creation of such records) can never be deleted.

An administrator can delete configuration data without restriction only if the data is not used by DoseControl as part of a Dosimetry Report (i.e. in case of an error during initial entry of data or faulty configuration entry). An example is an unused dosimeter calibration; it can be deleted unless it is used in one or more reports.

System Data Archiving & Backup
System data is maintained in a single, relational, SQL database instance. DoseControl does not backup or archive automatically, and does not feature any in-application options to manually do so. The DC software requires the user to utilize the features of Microsoft SQL for backup and archiving activities.

5.0 INTEGRITY OF EVERY MEASUREMENT

Sample Identification
One of the key features of DoseControl is the unique identification of every measurement taken by the system. Measurements require a unique Sample ID (called "Dosimeter ID") so that all measurements can be individually identified in the database using application logic. The system does not allow duplicate ID's, and this feature is an element of the DoseControl system.

The DoseControl System has an optional barcode scanner for the Evolution 220 Spectrophotometer which is used to verify and record the Dosimeter ID with every measurement; this feature is available for B3 DoseStix dosimeter type only.

Note: Future plans are to incorporate a barcode scanner with the GENESYS 30 Spectrophotometer, and to introduce a barcode on a new version of the B3 WINdose dosimeter, which will give all B3 dosimeters the ability to be under the same level of control as the B3 DoseStix using this barcode scanning feature of the DoseControl System (see Future Development Plans section for more information).

Irradiation Pathway Identification

For users with more than one irradiator or irradiation "pathway", every measurement is associated with one specific pathway for traceability. Dosimeters from multiple pathways are not allowed within same report.

Dosimeter Batch Identification

Each measurement record associates with only one specific dosimeter batch. Dosimeters from multiple batches are not allowed within a single report. For B3 dosimeters, the software will associate the Batch ID from a dosimeter barcode with the Batch ID of the calibration being used. If the dosimeter is of a different batch, it is not allowed to be measured in the report.

Instrument Identification
With every measurement, DoseControl verifies that the serial number of the attached instrument does in fact match the serial number of the instrument from the Reader Configuration used in the dosimeter batch calibration currently loaded in the software. The integrity of the measurement process is maintained by

eliminating the possibility of an instrument mix-up, either intentionally or inadvertently, before or during a measurement session.

Spectrophotometer Wavelength Verification

Before acquiring the instrument response during a measurement, DoseControl verifies that the wavelength setting of the instrument matches the required setting from the dosimeter batch calibration. The user cannot change the instrument settings using the instrument buttons while connected to DoseControl when using the GENESYS 30 or Evolution 220 Spectrophotometers. Even though it is not possible for the user to change the setting using the soft keys on the instrument, even if this was a possibility, DoseControl would verify that there was not a match.

If the wavelength is found to not match, the software will guide the user through a workflow of re-setting to the proper wavelength and re-zeroing the instrument before that measurement can be acquired.

Modification of a Dosimeter

Dosimeter ID (sample ID) and related measurements can be removed from a report, or the ID can be modified only by users with the assigned permission to make these modifications. In each such instance, DoseControl requires the user to provide an explanation from the user, which is recorded in the Audit Trail.

DoseControl has the option to make such data locked from user modification.

6.0 INTEGRITY OF ALL RE-MEASUREMENTS

Sample Identification

The application uses a Revision Control System for recording any re-measurement of the same Sample ID (Dosimeter ID). Each measurement of the same Sample ID constitutes a new row in the SQL database with the respective version ID.

For re-measurement, the optional barcode for B3 DoseStix will verify the Sample ID before measurement acquisition.

Admin-Configurable Reread Policy

The Application Administrator can set policy to control re-measurement of samples to enforce any variation of the following policy aspects:

- Restrict the total number of re-measurements allowed of the same Sample ID.
- Require the use of a statistical evaluation of multiple measurements of the same sample.
- Uses the mean value accepted when measurement variation is less than the administrator-defined limit, with or without including the original measurement. Otherwise, the re-read is rejected if the variation of measurement is higher than the limit and the original measurement is retained as the measurement of record.
- Require a comment on every re-measurement.
- Require a different user to re-measure.
- Require only specific personal to re-measure based on user role assignment.

7.0 INTEGRITY OF THE MEASUREMENT SETS AND METADATA (DOSIMETRY REPORTS)

A set of measurements and associated metadata is referred to as a “Report” or “Dosimetry Report” in the DoseControl system. Each Report can be thought of as a “measurement session” or similar concept of group

of dosimeters measured for a specific purpose. DoseControl assigns a unique Report ID that is traceable to all related measurements and metadata within a given Report. All modification of metadata is allowed without comment (assumption of incorrect data – faulty entry), and this modification is recorded (gives the value before and after modification) in the Audit Trail.

Reports are also revision controlled. The user explicitly confirms the completion of a specific revision of a Report by "Processing" the report. If changes are necessary, the user then must explicitly "Version" that report. Data from any version can be assembled into a "Report Output" at any time; the user can produce an output of each version independently at the time of creation or anytime in the future.

8.0 IT CONFIGURATION DATA

IT configuration data is not considered to be GxP data and is not subject to the electronic data rules described herein. Changes to file pathways for saving, SQL connection strings, or peripheral connection information (such as COM port or Baud Rate information for a device) are modifiable without creating an Audit Trail event; this is because any modification is restricted to administrators and there is no direct data integrity risk with their modification; incorrect modification will only result in operational failures, such as inability to connect to the spectrophotometer.

9.0 AUDIT TRAIL

DoseControl's Audit Trail is compliant with FDA 21 CFR part 11 and Annex 11.

Audit Trail Details	Yes	No
Includes user login and failed access attempts?	☒	☐
Can the audit trail be turned off?	☐	☒
Are any users, roles, or permissions able to modify the Audit Trail?	☐	☒
All creation/modification/deletion of configurations and data (records) captured?	☒	☐
Each audit trail event captures: • Date and time?	☒	☐
• User responsible?	☒	☐
• Description of activity/event?	☒	☐
Modification/Deletion of existing GxP records captures, in addition: • New value/previous value?	☒	☐
• Reason for change or allows for comment?	☒	☐

10.0 INTEGRITY OF SYSTEM OUTPUTS

Outputs of the system are in three formats that can be official records: Electronic data, PDF, and MS Excel.

Electronic Data

An optional output is the electronic data directly from SQL tables. DoseControl features a standardized integration method which allows users to collect GxP Data (measurements and metadata) from a series of SQL tables, designed precisely for integration with other electronic systems. The DoseControl Licensing

Agreement forbids users to integrate with SQL tables used by the application logic. Instead, DoseControl has "Export Tables" that can be accessed by the user to retrieve the output data electronically. When electronic integration is utilized, the customer (owner of the data) is responsible for the integrity of the transfer and destination of the electronic data.

PDF

Both standard and customized layouts of PDF's can be output for any dosimetry report output. Backup of any PDF dosimetry report outputs are the responsibility of the end-user. The files are created and stored by the application in an admin-configurable local or network file location, and at that point are the responsibility of the end-user. The outputs can also be saved by the end-user to any local or network location using the Save feature of Adobe ® PDF applications or equivalent.

The PDF output was designed to manage batch conformance records. All other system report outputs (e.g. Instrument Performance Verification Report) are available strictly in this PDF format.

MS Excel

The MS Excel output option is intended for research, testing, and validation efforts in which the data is to be further analyzed by the user either in MS Excel or some other application.

A standard layout MS Excel Worksheet can be used to output any dosimetry report. MS Excel records may be exported in a format that is locked with a password. Locked or unlocked MS Excel templates are uploaded into DoseControl and maintained in the SQL database. When this output is used, the user saves the MS Excel file to any local or network location. Data security and backup of these records are the responsibility of the end-user.

11.0 SYSTEM DEVELOPMENT, VALIDATION, AND TESTING

DoseControl Software Code Verification

GEX utilizes a software development team, which requires a code review of each functional addition or change to the code by a different senior team member.

Unit and Integration Tests

The software development team employs a vast network of unit and integration tests to automatically check the logical and functional operations of the software each time a software 'build' is performed. This is an automated process and all tests must pass to successfully push a new build to the verification testing phase.

System Verification Testing

A process is employed to verify that each specific bit of development results in outputs that meet the functional requirements specification (FRS). First, the software development team uses its own devoted QA resources to test the software and hardware integration against the specifications. Then, a separate verification is performed using GEX QA resources. At this stage, major system interaction points are also tested if there are any expected influences of a change or additions to the existing system on a related function or aspect.

System Validation Testing

The total system of hardware and software, along with operating instructions, are validated for each public release to document that the system meets the User Requirements Specification and intended uses. System validation testing is managed by GEX Quality Assurance.

12.0 FUTURE DEVELOPMENT

As of the Release Date of this document, new development is underway to complete the following new features and changes of DoseControl:

- Completion of a user interface and querying functions for the dynamic searchable audit trail and to provide a method for audit trail data export directly from the user interface (PDF).
- Integration of a new imaging scanner, with 2D barcode scanning capabilities, to be employed for future sample identification purposes.

The following items are under consideration or in a stage of design:

- Addition of the capability to use an alternate, open-source, SQL database.
- Dosimeter batch count/tracking for inventory management of routine dosimeter stocks.
- Technician metrics report – number of measurements, re-reads, instrument zeroing, P.V. checks, etc.
- Integration of barcode scanner in the GENESYS 30 samples compartment.
- Daily P.V. Routine for the GENESYS 30 Spectrophotometer.
- Electronic Signature capabilities.

13.0 REVISION CONTROL HISTORY

DATE	CHANGE DESCRIPTION	REVISION
3/21/19	Initial release.	A

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