# BIOVIA QUALITY SYSTEM RESPONSES TO CUSTOMERS IN REGULATED INDUSTRIES

FAQ

## DOES BIOVIA HAVE A QUALITY SYSTEM?

Yes. A Quality Management System (QMS)is used at BIOVIA. Our business and development processes are designed around the Food and Drug Administration (FDA) requirements and guidelines for software development and validation, including those outlined in the Good Automated Manufacturing Practice (GAMP) guide published by the International Society for Pharmaceutical Engineering (ISPE). The QMS also incorporates key elements of ISO 9000 and the Institute of Electrical and Electronics Engineers (IEEE) standards for software engineering.

### Background

The BIOVIA Quality Management System (QMS) facilitates the objectives of our customers to reduce the cost, time and complexity of software validation. This Quality System ensures that we follow good software development practices, and that we create and release high quality products that enable our customers to meet regulatory requirements. Our business and development processes are designed around the Food and Drug Administration (FDA) requirements and guidelines for software development and validation, including those outlined in the Good Automated Manufacturing Practice (GAMP) guide published by the International Society for Pharmaceutical Engineering (ISPE). Customer feedback is incorporated into our quality system to ensure that our products meet or exceed customer expectations. The Quality Management System (QMS) at BIOVIA also incorporates key elements of ISO 9000 and the Institute of Electrical and Electronics Engineers (IEEE) standards for software engineering. The ISO 9000 standard from the International Standards Organization establishes a basis for the content of the quality system, and IEEE provides additional standards for processes, tools and documentation.

## WHAT IS THE IMPACT OF OUR RECENT MERGER & ACQUISITION (M&A) ACTIVITIES ON THE QUALITY SYSTEM FOR SOFTWARE DEVELOPMENT AT BIOVIA?

BIOVIA, with the combined companies through M&A, has been developing software for over 30 years backed by a Quality System for software development and testing, product release, product support and maintenance. Any changes to the Quality System related to or resulting from M&A activities are controlled and maintained through written procedures under change control.

## WHO IS THE CONTACT PERSON AT BIOVIA IF A CUSTOMER REQUESTS A SITE AUDIT AND WHERE WILL THE AUDIT BE CONDUCTED?

All site audits will be conducted at BIOVIA headquarters in San Diego, CA, regardless of where the product is developed. You can schedule an audit with your sales rep or directly with Michael Brown (Michael.Brown@3ds.com) Director Quality Compliance.

## DOES BIOVIA HAVE EXPERIENCE WITH CUSTOMERS GOVERNED BY THE FDA AND OTHER REGULATORY AGENCIES?

Yes. BIOVIA solutions are used by more than 2,000 companies as well as academic and government entities in the pharmaceutical, biotechnology, energy, chemicals, aerospace, consumer packaged goods and industrial products industries—including 10 of the top 10 pharmaceutical companies, 20 of the top 25 biotech companies, 7 of the top 10 chemical companies, 4 of the top 5 consumer packaged goods companies, 5 of the top 10 oil & gas companies, 5 of the top 5 aerospace companies and significant government agencies and academic institutions.

The BIOVIA R&D, Product Management, Customer Support and Professional Services teams are trained on 21 CFR Part 11 FDA and related regulations and their relevance to product feature development. They are also trained on implementing BIOVIA solutions in a compliant environment.

## WHAT SERVICES CAN BIOVIA PROVIDE?

BIOVIA provides Solution Consulting, Management Consulting, Training and Support services for BIOVIA products.

Go to http://accelrys.com/services/ for more information.

## DOES BIOVIA PROVIDE VALIDATION SERVICES? WHO IS THE CONTACT PERSON FOR THIS AT BIOVIA?

Yes. Please contact your sales rep to discuss a validation related Professional Services engagement.

## DOES BIOVIA PROVIDE A VALIDATION CERTIFICATION FOR BIOVIA PRODUCTS?

No. BIOVIA certifies products based on BIOVIA internal requirements and release criteria. BIOVIA products can only be certifiable in the customer environment per customer's validation SOPs and business requirements. As per the regulations FDA 21 CFR Part 11 and EU Annex 11, it is the customer's responsibility to validate per their requirements.

## DOES BIOVIA PROVIDE A VALIDATION PACKAGE FOR BIOVIA PRODUCTS?

Yes. Through a Professional Services engagement, an Installation Qualification (IQ) protocol can be provided with the site installation of the product. A Validation Collateral Package is also available for BIOVIA Workbook, which includes a Validation Collateral Plan, Validation Assessment, Functional Requirements, Operational Qualification (OQ), Executed script of the OQ and Validation Summary Report.

## DOES BIOVIA HAVE A WHITE PAPER OR DOCUMENTATION ON 21 CFR PART 11 FOR BIOVIA PRODUCTS?

Yes. BIOVIA Regulatory Checklists lists all FDA 21 CFR Part 11 requirements, as well as EU Annex 11 requirements, and identifies what technical control is satisfied by the BIOVIA products and what is the customer's responsibility for procedural controls to ensure the BIOVIA products are maintained in a 21 CFR Part 11 and validated environment.

## CAN BIOVIA PRODUCTS BE VALIDATED IN A 21 CFR PART 11 ENVIRONMENT?

BIOVIA products are built with technical features to enable compliance in a 21 CFR Part 11 and Annex 11 environment.

Regulatory Checklists for each BIOVIA product are available to identify what the technical features are built to satisfy the 21 CFR Part 11 and Annex 11 regulatory requirements.

### Background

FDA regulation 21 CFR Part 11 and other similar regulations such as EU Annex 11 describe a set of technical and procedural controls that are shared responsibilities between the customer and the software supplier. BIOVIA can provide guidance on what technical features are built into the BIOVIA product through the Regulatory Checklist (available for BIOVIA Workbook, BIOVIA LIMS, BIOVIA Discoverant). However, according to the regulations the ultimate responsibility is at the system owner to ensure technical and procedural controls are in place to enable their computerized system to be validated and compliant in a 21 CFR Part 11 environment based on the customer's validation Standard Operating Procedures (SOPs) and business requirements.

## WHO IS RESPONSIBLE FOR OVERSIGHT OF BIOVIA PRIVACY COMPLIANCE PROGRAM?

This is a distributed function within BIOVIA:

Employee Privacy is managed by HR, Data Privacy by IT, Data Retention by Legal

Customer Data is managed by the following governing documents:

BIOVIA employees through IT Security Policies

BIOVIA Professional Services and Pre-Sales through NDA and contractual agreements with customer

## WHO IS RESPONSIBLE FOR OVERSIGHT OF THE BIOVIA INFORMATION SECURITY PROGRAM?

BIOVIA VP of IT

## HOW CAN WE REQUEST TO COMPLETE A VENDOR ASSESSMENT OR QUESTIONNAIRE

Allow up to 30 days to have the assessment or questionnaire completed.  Send it to your sales rep or directly to Michael Brown ([Michael.Brown@3ds.com](mailto:Michael.Brown@3ds.com)) Director Quality Compliance.

## HOW CAN WE ENGAGE IN A FORMAL QUALITY AGREEMENT

The terms in a standard quality agreement are generally incorporated into or analogous to the Statement of Work (SOW), Project Plan, Quality Plan or Governance document, and are best suited under a BIOVIA Professional Services engagement and not in the standard agreement for the product.

### Background

The Quality Agreement is a formal agreement required by the following regulations (BIOVIA is not subjected to these regulations):

- Medical Device Regulations 21 CFR Part 820.50 Purchasing Controls

- European Union (EU) GMPs Chapter 7 (7.10 – 7.15 [Contracts])

- ICH Q7, 16.12: There should be a written and approved contract or formal agreement between a company and its contractors that defines in detail the GMP responsibilities, including the quality measures, of each party."

However, BIOVIA is subject to two federal regulations in a limited capacity with regard to the software products we provide: US FDA 21 CFR Part 11 and EU Annex 11 by building the product features (technical controls) in our products.  EU Annex 11, Section 3.1 calls out the need for a formal agreement: "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 computerized 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."

These agreements are generally incorporated into or analogous to the Statement of Work (SOW), Project Plan, Quality Plan or Governance document, and are best suited under a BIOVIA Professional Services engagement and not in the standard agreement for the product.

## WHO IS RESPONSIBLE FOR THE QUALITY OF THE PRODUCT AND WHO DO I CONTACT REGARDING TESTING OF BIOVIA PRODUCTS?

All BIOVIA Product Team members contribute to the quality of the product.  The Product Team consists of members representing the following functions: Development, Software Test (QA), Product Management (PM), Customer Support, Configuration Management/Release Engineering (CMRE) and Information Development (InfoDev).

The Software Test (QA) organization is the key stakeholder that provides independent assessment of product quality.

The Quality Management System (QMS) is the key stakeholder that oversees the compliance with the Quality System.

## HOW DOES BIOVIA ENSURE CUSTOMER REQUIREMENTS ARE BUILT INTO THE PRODUCT?

Product Management (PM) and Customer Support (CS) are the key stakeholders that act as the customer advocate in defining the requirement or ensuring customer issues are considered during product development.  PMs sign-off on product features after every two-week iteration to ensure the features are built and tested as expected.

## WHAT IS THE CORRELATION BETWEEN BIOVIA SOFTWARE DEVELOPMENT METHODOLOGY (AGILE) AND CUSTOMER VALIDATION EFFORTS?

A customer can verify if specific testing as per their business requirement has been performed per our standard, which can reduce the customer's testing scope for validation.

### Background

Customer may expect BIOVIA to follow the same validation practices as the regulated industry. As BIOVIA is not subject to federal or international regulations for drug or medical device development, there is no legal obligation for BIOVIA to follow a specific software development methodology, such as Agile engineering and project management practices. Any software vendor can use any software development methodology as long as the software vendor can demonstrate that the software is developed using a standard and that testing is traceable for a specific requirement (User Story). A customer can verify if specific testing as per their business requirement has been tested per our standard, which can reduce the customer's testing scope for validation.

## HOW CAN CUSTOMERS LEVERAGE BIOVIA TESTING TO REDUCE THEIR VALIDATION TESTING EFFORTS?

Depending on a customer's requirements and validation procedures, a customer can leverage BIOVIA testing as follows:

- Conduct a Site Audit
- Verify specific test cases on basic functionality and key 21 CFR Part 11 features
  - Verify processes and deliverables for standard core product
  - Purchase Validation Collateral Package through BIOVIA Professional Services
- Engage with BIOVIA Professional Services for Validation Services and product expertise to identify key areas for testing for configuration/customization of the product

## HOW DO YOU JUSTIFY RISK-BASED APPROACH IN DEVELOPMENT AND TESTING?

The landscape is changing, and while keeping GAMP 5 principles and Annex 11 in mind, these initiatives drive to help our customers reduce operational costs (such as validation) and for BIOVIA to deliver product releases in a predictable manner.

## HOW ARE BIOVIA AGILE DEVELOPMENT AND PROJECT MANAGEMENT PRACTICES SUPERIOR TO OTHER METHODS?

Agile has been shown by the software industry to have a superior track record of developing complex software that meets customer needs in a high quality and predictable manner when compared to waterfall. The basis for this improvement is the close customer collaboration that Agile encourages. BIOVIA has demonstrated predictability in meeting customer and scheduled commitments using agile.

An established QMS framework is in place to ensure consistent standards for development of User Stories (requirements) and Test Cases and execution of testing.

### Background

Product features and functionality can be produced within two-week iterations, where customers can provide immediate feedback during the development process.

Requirements, specifications and test cases are now managed, maintained and documented electronically, providing ease of traceability.

The mapping of product requirements to User Stories now defines product functionality from a user standpoint across all application layers, enabling BIOVIA to implement design and architectural considerations in accordance with customer requirements.

During the two-week iterative process, design specifications in the former waterfall model become obsolete and now map to the test case, which incorporates built-in agile engineering

practices of unit testing, test-driven development, pair programming and continuous integration for every checked-in code.

Test cases are accepted at the end of the two-week iteration, and are continuously run throughout the development process and final stabilization phases.

## AGILE METHODOLOGY IS BELIEVED TO LACK IN DESIGN DOCUMENTATION AS REQUIRED FOR VALIDATION OF A COMPUTERIZED SYSTEM IN GXP ENVIRONMENT, HOW DOES BIOVIA ACCOUNT FOR THIS?

Requirements and design specifications are captured in the form of User Stories and Test Cases, where feature teams (composed of Product Management, Software Test and Development) meet daily to flesh out the requirements and specifications until the product feature is completed within the two week iteration. The design is inherently built into the process as the requirements are further refined, expected test results are defined and verified, resulting in the final product feature, which all are accepted by Product Management.

Furthermore, BIOVIA has established an Architectural Board consisting of product architects from distributed BIOVIA product teams. High level designs are planned at the Architecture Board level, including feedback from customers, and are fed back into requirements in the form of User Stories.

## WHAT IS GAMP 5? WHY SHOULD IT BE IMPORTANT FOR OUR CUSTOMERS AND FOR BIOVIA?

Good Automated Manufacturing Practice (GAMP) guide published by the International Society for Pharmaceutical Engineering (ISPE) 1  is a set of guidelines and standards for the regulated industry and suppliers (including software suppliers like BIOVIA) driven by representatives from the FDA, MHRA and other regulated agencies and large pharma companies like Johnson and Johnson, Pfizer, Novartis, GSK and AstraZeneca.

With the emphasis of risk-based approach, European Regulation Annex 11 and initiatives of GAMP 5 is changing the way regulated companies are validating and maintaining their computerized systems. The key GAMP 5 initiatives are to:

- Promote business agility

- Reduce duplication of activities

- Leverage vendor activities

- Leverage software product technical features and vendor expertise

### Background

Customers must understand the limitations of what's out of the box, what's configurable and what will have to be customizable. GAMP 5 has provided software categories to help our users scale lifecycle activities and documentation required to validate and maintain their systems. Understanding GAMP 5 will enable BIOVIA to be the experts and provide guidance to our customers. See GAMP 5 category designations and target US regulation for each BIOVIA product in the following question.

- Avoid duplication of activities

- Leverage supplier activities

- Scale lifecycle activities and documentation according to risk, complexity and novelty

- Recognize that most software is now based on configurable packages

- Acknowledge that other development models than waterfall exist and are more appropriate

## HOW ARE BIOVIA PRODUCTS CATEGORIZED PER GAMP 5?

| Product | GAMP 5 Category* | Target U S Regulation+ |
|---|---|---|
| BIOVIA Cheminformatics Applications | Category 4 | R&D |
| BIOVIA Workbook | Category 3, 4 | R&D, GLP, GMP |
| BIOVIA LIMS | Category 4 | GMP |
| BIOVIA LES | Category 4 | GMP |
| BIOVIA Notebook | Category 3 | R&D, GLP |
| BIOVIA Discoverant | Category 3 | R&D, GMP |
| BIOVIA Request | Category 3 | R&D, GLP, GMP |
| BIOVIA Experiment | Category 4 | GLP, GMP |
| BIOVIA Discovery Studio | Category 3 | R&D |
| BIOVIA Materials Studio | Category 3 | R&D |
| BIOVIA Foundation | Category 3, 4, 5 | R&D, GCP, GLP, GMP |
| BIOVIA CISPro | Category 3 | OSHA, EPA |

\* Category 3: Commercial Off the Shelf (COTS); Category 4: Configurable; Category 5: Customizable
+ Also identifies the area of compliance in product development

### Background
The customer's validation SOPs would generally identify the level of testing required based on the GAMP Category designation for the product. Typically, a vendor site or postal audit is sufficient for a Category 3 product. If the vendor site audit is acceptable, this implies that the testing is adequate for the standard product and no additional testing is required during validation efforts. If the standard product is configured or customized, validation testing would generally be conducted against the requirements for specific configuration(s) or customization.

### The definitions for the GAMP 5 categorization are as follows:
**Category 1:** Operating Systems (no longer used by GAMP)

**Category 2:** Standard Instruments, Micro Controllers, Smart Instrumentation (Firmware) (no longer used by GAMP)

**Category 3:** Commercial off-the-Shelf (COTS) or Non-Configured Product

- Off-the-shelf product that does not require configuration to support business processes, or where the default configuration is used by the regulated company
- Supplier involvement is limited to the provision of documentation, training, support and maintenance
- Product developed and maintained by supplier in accordance with good practices (QMS)

**Category 4:** Configured Product

- Product requires configuration to support specific business processes
- Supplier involvement will typically include support with specification, configuration, verification and operation of the system
- Procedures to follow agreed between regulated company and supplier per plan
- Product developed and maintained by supplier in accordance with good practices (QMS)

**Category 5:** Custom Application

- Regulated company typically contracts supplier to develop application based on defined requirements; supplier involved during full project lifecycle of the system and provides support during operation
- Procedures to follow agreed between regulated company and supplier per plan

## GLOSSARY

### SOP
Standard Operating Procedure

### GAMP
Good Automated Manufacturing Practice

Both a technical sub-committee of International Society for Pharmaceutical Engineering (ISPE) and a set of guidelines for manufacturers and users of automated systems in the pharmaceutical industry.

### GxP
General term for Good Practice quality guidelines and regulations.  These guidelines are used to ensure a product is safe and meet its intended use manufactured in regulated industries including food, drugs, medical devices and cosmetics.  Documentation is critical tool for ensuring GxP adherence

### GCP
Good Clinical Practice

An international quality standard provided by International Conference on Harmonisation (ICH), an international body that defines standards, which governments transpose into regulations for clinical trials involving human subjects.  A similar guideline for clinical trials of medical devices is the international standard ISO 14155 that is valid in the European Union as a harmonized standard.  These standards for clinical trials are sometimes referred to as ICH-GCP or ISO-GCP.

FDA Regulations related to GCP and Clinical Trials

### GLP
Good Laboratory Practice

Set of principles that provides a framework within which laboratory studies are planned, performed, monitored, recorded, reported and archived.  These studies are undertaken to generate data by which the hazards and risks to users, consumers and third parties, including the environment, can be assessed for pharmaceuticals (only preclinical studies), agrochemicals, cosmetics, food additives, feed additives and contaminants, novel foods, biocides, detergents etc.... GLP helps assure regulatory authorities that the data submitted are a true reflection of the results obtained during the study and can therefore be relied upon when making risk/safety assessments.

FDA Regulation for GLP: 21 CFR Part 58

### GMP
Good Manufacturing Practice

Practices required in order to conform to guidelines laid down by agencies which control authorization and licensing for manufacture and sale of food, drug products, and active pharmaceutical products. These guidelines are laid down with the intention of providing minimum requirements that a pharmaceutical or a food product manufacturer must meet while manufacturing drugs or food products ,which then assures that the products manufactured/ produced are of high quality and do not pose any risk to the consumer or public. Good manufacturing practice guidelines provides guidance for manufacturing, testing, and quality assurance in order to ensure that drug product is safe for human consumption.  Basic concepts of all of these guidelines remain more or less similar to the ultimate goals of safeguarding the health of patient as well as producing good quality medicine, medical devices or active pharmaceutical products.

- [FDA: Good Manufacturing Practices](#)
- [Health Canada: Good Manufacturing Practices](#)
- [Pharmaceutical Inspection Cooperation Scheme: GMP Guides](#)
- [MHRA Good Manufacturing Guide](#)
- [Therapeutic Goods Association: Good Manufacturing Practices](#)
- [WHO: GMP Guidelines](#)
- [EU: GMP Guidelines](#)

**Part 11**

FDA Code of Federal Regulation [21 CFR Part 11](#) provides guidelines on electronic records and electronic signatures (ERES) to ensure electronic records are trustworthy, reliable and generally equivalent to paper records and handwritten signatures executed on paper.

**Annex 11**

European Commission (EudraLex) Volume 4 of "the set of rules governing medicinal products in the European Union" contains guidance for the interpretation of the principles and guidelines of good manufacturing practices for medicinal products for human and veterinary use. Annex 11 is an addendum to these guidelines specific for computerized systems used as part of a GMP regulated activity.

[Annex 11: Computerized Systems](#)

## FOOTNOTES

1. ISPE GAMP® 5: A Risk Based Approach to Compliant Computerized Systems, International Society for Pharmaceutical Engineering (ISPE), Fifth Edition, February 2008, www.ISPE.org.

2. Members of the ISPE GAMP® Leveraging Supplier Effort Special Interest Group, Effective Computerized System Compliance through Leveraging Supplier Effort, May/June 2013, Vol. 33, No. 3, [www.PharmaceuticalEngineering.org](#)

3. Members of ISEP GAMP D-A-C-H SIG ASDMM, Alternative Software Development Models and Methods in GxP Environments, January/February 2012, Vol.32, No. 1, [www.PharmaceuticalEngineering.org](#)

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Dassault Systèmes
175 Wyman Street
Waltham, Massachusetts
02451-1223
USA

**BIOVIA Corporate Americas**
BIOVIA
5005 Wateridge Vista Drive,
San Diego, CA
92121
USA

**BIOVIA Corporate Europe**
BIOVIA
334 Cambridge Science Park,
Cambridge CB4 0WN
England

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