Managing FDA regulatory compliance with IBM Rational solutions

Executive summary

Today's healthcare, life sciences and medical device industries are faced with unpredictable market change, global competition, and constantly evolving regulatory mandates and guidelines. To remain viable and competitive, corporations must balance rapid innovation with compliance mandates that dictate safety and effectiveness. The necessity to innovate and evolve the business in order to leverage new technologies such as biologics, advanced drug treatments or software-enabled medical devices while maintaining compliance requires organizations to undergo significant business process and development life cycle transformations. Many in the industry have expressed concern that the processes dictated by the broad and evolving governmental regulations and guidelines (such as FDA, GMP, etc.) negatively impact time-to-market and increase development time.

The United States Food and Drug Administration (FDA) regulates over $1 trillion in products including, but not limited to:

- Pharmaceuticals for human and animal use.
- Biological and related products including vaccines, and biological therapeutics.
- Medical devices.
- Radiation emitting devices.

The FDA monitors the production, import, transport, storage and sale of these products in the United States. Compliance with FDA regulations is a market requirement. Failure to comply can be very costly, not only due to expensive violations or recalls, but also due to criminal penalties and loss of market share for those who don't comply with regulations.

Achieving development life cycle efficiencies and injecting more agile development practices while maintaining compliance to regulations such as those dictated by the FDA is often reported as a foremost concern. It is our view that given high-quality development and design control processes and sufficient tools to support and automate these processes, time to market can actually be *decreased*, while resulting in higher quality, and higher reliability products and services. This document gives a brief overview of the current challenges that the healthcare industry faces and discusses how IBM® Rational® solutions can help address these challenges.

The Rational solutions for systems and software engineering can assist with reaching FDA compliance goals through integration, collaboration, automation and reporting. The solutions support the creation and management of life-cycle work products necessary to fulfill FDA regulations and guidelines. The solutions provide a core set of best-in-class tools and processes for systems and software engineering teams, facilitating engineering collaboration with unprecedented high level of transparency of project progress, control of artifacts, traceability with audit trails, task management and change control.

Lastly, the Rational solutions address the FDA identified *lack of design controls as one of the major causes of device recalls* by:

- Maintaining design control specifications in a central, automated repository
- Providing design control specifications using customizable document templates
- Facilitating the design control process models, attributes and reports
- Maintaining up-to-date traceability matrices
- Facilitating change impact analysis and capturing design history
- Managing compliance

Smarter healthcare

Today's healthcare field is quickly evolving and increasingly becoming more networked and interconnected. Whether you are developing a cutting-edge medical device, researching new drug therapies or providing healthcare services, the common thread is an increasing reliance on interconnected information, networks, products, and complex systems.

To meet innovation goals and bring new products to market faster, companies must focus on optimizing the development processes supporting and automating these efforts. As today's healthcare providers, payers and consumers move towards electronic records management and smarter healthcare, this will mean that medical devices used to implement our care must not only communicate data to doctors, nurses and clinicians but may also transmit data for more accurate billing and more comprehensive patient data management. Medical devices are becoming more sophisticated and complex with the greater ability to give real-time statistics to clinicians in order to make better diagnosis and care decisions. Many devices today record and transmit patient and device data back to physicians and device manufacturers to aid in patient care, and to help influence development of new products and features in order to repurpose or modernize existing product lines. Devices are becoming more and more customized and offer variances that meet hospital, emergency response and field needs. Data is being continually analyzed to make diagnosis early and to predict outcomes.

In the life sciences field, drug trials and drug therapies are becoming customized with new research leading to new solutions, drugs and biological applications. Pressure to increase output from clinical research and development (R&D) is expanding as life sciences companies ward off market pressures from generic drugs.

Healthcare reform will potentially impel tens of millions of Americans who do not currently have healthcare insurance into the healthcare network, driving demand for access to treatments such as drugs, biologics and increasing medical device usage. The push towards electronic medical records and mandates such as the Health Insurance Portability and Accountability Act (HIPAA) and massive changes in electronic data interchange and International Classification of Diseases (ICD) codes will drive modernization of core healthcare applications and systems. The cost of reform and compliance will drive technology investments to modernize legacy systems and to develop new business models.

What is the common driver to delivering smarter healthcare such as sophisticated devices, drugs and biologics or modern health maintenance networks? Software. Software is increasingly becoming the key factor for injecting new features, functions, and providing protocols for networking and building system user interfaces. All these software-driven capabilities lead to what we call smarter healthcare—such as modern portal-based payer/provider/consumer networks, complex information data management systems, intelligent medical devices, and pioneering drug and biologics research and development. Software is the key to competitive advantage.

In the next few sections we will look at some of the regulatory and compliance demands on the healthcare industry and look at the corresponding challenges created by compliance driven development within the medical device, healthcare payers, healthcare service providers and life sciences industries and explore how Rational solutions help address these challenges.

Medical device and life sciences industry challenges

Medical device manufacturers must manage complex system requirements and provide quality development processes to manage portfolios of products. Medical device developers

must base product strategies on real data, classify risks and ensure proper mitigation of hazards while controlling software and systems development life cycles to ensure quality through rigorous testing. Ongoing studies of effective product development point to significant failure rates—failure to deliver on time with the right features and functionality. Success depends on the ability to deliver faster, increase productivity and ensure high quality while reducing costs in the development cycle. All of these challenges are compounded by the need to ensure adherence to regulations and mandates.

Listed below are just a few of the challenges medical device developers face along with some of the key factors that they must control to remain competitive and successful:

- **Corporate strategy and planning:** Percentage of sales due to new products or new systems released, return on market investment, strategic planning operating budget per revenue, return on total assets.
- **Product/Platform strategy:** Number of products per platform, amount of software per platform, cost for each new product or system, cost of modernization.
- **Functional innovation:** Improving time to market, increasing market share, achieving price premiums and return on investment for development.
- **Prototype development and testing:** Time from development to maturity, new product or system success rate, cost per engineering change, time and cost for conceptual mockups.
- **Risk and hazard mitigation:** Meet mandates for classification and management of risks and hazards (Failure Modes and Effects Analysis **[FMEA]**).
- **Legal and regulatory compliance:** FDA, number of notices of violations from regulatory agencies, dollar value of potential legal liabilities, patents, corrective and preventive actions (CAPA)

Life sciences companies face the need for increased operational efficiency and cost containment as payers worldwide actively push-back on new and existing drug pricing. New innovations are always necessary to retain market share: discovery research is an important area with considerably growing risk, compliance and change control requirements. There is a need for a reliable infrastructure for reducing the possibility and impact of clinical data security and compliance vulnerabilities. Increasingly, scientists who are testing new discoveries are using outdated and inefficient tools and techniques at the same time that research and development has become more expensive. The result is a slow and costly process. Drug manufactures must support collaborative environments, automate the change control process and more effectively capture and communicate data to encourage quicker development.

Listed below are just a few of the challenges life sciences companies face along with some of the key factors that they must control to remain competitive and successful:

- **Product portfolio management:** Make the right R&D investments, return on investment, strategic product planning, percentage of sales due to new products, impact of generics and competition on product lines.
- **Security:** Ensure security of data and reliable management of the infrastructure; reduce the possibility and impact of security vulnerabilities.
- **New scientific initiatives:** Targeted treatments and tailored medicine challenge traditional push oriented development model.
- **Operational excellence:** Maintain requirements for manufacturing execution process, meet product, regulatory and productivity requirements.
- **Legal and regulatory compliance:** CGMP, GAMP (Current Good Automated Manufacturing Practice).

- **Verification and validation (V&V):** Validate tools and processes used in development and manufacturing of products, verify processes.
- **Change control:** Manage change, impact analysis of change during development or manufacturing processes.
- **Cost pressures:** Control costs of infrastructure for commercial and clinical development.

Regulations impacting the medical device industry

The medical device industry is faced with ever increasing regulation and oversight of the design control process due to increased focus on device recalls and unintended consequences of improper use. In the FDA's own words, "Since 1984, FDA has identified lack of design controls as one of the major causes of device recalls. The intrinsic quality of devices, including their safety and effectiveness is established during the design phase"[1]

In response to device safety concerns the FDA created the Quality Systems Regulations (QSR CFR 21 part 820) to ensure that products meet requirements and specifications and that current good manufacturing practices are followed in the development of devices.

Some of the key parts of the QSR that are of concern to device development organizations are:

- Strict design control measures.
- Use of tools to improve the development process.
- Separate definition and traceability of user requirements to design input.
- Separation of validation (user and patient needs are met) from verification procedures and record keeping (specified requirements are met).
- Software validation requirements that apply to software used as components in medical devices, to software that is itself a medical device, and to software used in production of the device or in implementation of the device manufacturer's quality system.

The FDA regulation provides a framework but leaves it up to device developers to implement quality development procedures. It is the responsibility of manufacturers to establish requirements for each type or family of devices that will result in products that are safe and effective, and to establish methods and procedures to design, produce, and distribute devices that meet the quality system requirements. Lack of design controls is one of the major reasons for device recalls and violation notices resulting from FDA audits. Adherence to a development process that defines requirements, indentifies risk, manages change and facilitates and supports simulation and test well before implementation lowers development risk and costs and reduces time to market. Product expenditure skyrockets when deficiencies are discovered late in the development life cycle. Following a design control process that is repeatable, scalable, and automated can provide better project visibility and predictability, lowering overall costs, reducing product development time, and helps to navigate regulatory acceptance into the market.

However, developers often view compliance to these design control standards as overhead, interfering with their design work. The regulatory and quality populace is ultimately responsible for design control compliance, but they depend on hardware, software and mechanical designers and developers to do the actual work. Developers often respond to the regulatory professionals with "What do you want, a product or documentation?" However, medical device manufactures require confirmation that user needs are met by design inputs and that the design elements that are essential to the proper functioning of the device are identified, recorded, and tracked, in order to survive inspections and bring safe products to market. Companies must also establish reasonable design control processes and ensure that risk analysis is performed, changes to requirements and development artifacts are controlled and design history files are maintained. Management and proper

tracing of requirements from the original design and development phase through the verification and validation phase along with an accompanying risk management plan is crucial to remaining viable in the medical device market.

Automation of the capture, recording and traceability between these items not only cuts the time spent focused on regulatory compliance but can speed development time. Adherence to a process that identifies requirements *before* implementation and then controls and manages requirements and requirement change throughout the design process is more efficient and requires fewer design iterations. When the requirements are identified, progress metrics and projection of completion dates are more objective and quantitative. Even when new requirements are identified mid-design or mid-implementation, the impact on the overall schedule is more quantitatively predictable when the requirements are properly captured and dependencies between requirements are maintained. Clients are often skeptical that following such a process can reduce time to market, but in addition to the efficiencies noted above, a good design control process followed by change and design reviews supported by change management allows problems to be identified earlier in the process while they are smaller, simpler, faster, and cheaper to fix.

Regulations impacting the life sciences industries
The task of the FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) is to ensure drug products are safe and effective. CDER and CBER regulate new drug and biologic application development, perform quality testing, evaluate manufacturing processes and enforce post-market surveillance for safety and efficacy.

Some of the key parts of the regulations that are of concern to life sciences organizations comprise:

- Overseeing new drug development
- Review of drug and biologic product applications
- Managing safety, performance and promotion of marketed drugs
- Monitor drug quality and efficacy

While the FDA does not do any drug testing, the agency does review results of non-clinical and clinical studies submitted by a manufacturer and inspects the manufacturer of the products. The vast majority of time invested in drug development is in the pre-clinical research and the clinical studies phases. While less time is invested in FDA submission and review processes, process concerns, errors or problems in the research, data recording or execution systems can lead to very costly rework or missed market opportunities. Very few candidate compounds have the desired effect leading to drug products that can actually make it to market. Therefore, management, traceability and security of information related to drug development is of paramount concern, especially due to the ongoing involvement of the FDA regulators throughout the drug development and review process.

How Rational solutions can help
IBM Rational can help with implementing an effective design control process and a standard quality systems process supported by best-in-class tooling to allow an organization to develop a corporate standard process which will provide efficiencies of scale. Developers can know what to expect and can incorporate design control processes in line with FDA quality systems and Good Manufacturing Practice (GMP) guidelines. The Rational solutions for systems and software engineering supports collaborative tasks and linking of the life-cycle work products. Compliance can be made simpler with automated capture of design history, life cycle traceability and quality management processes required to manage compliance to regulations.

Demonstrating compliance means control and documentation of the typical development tasks such as requirements gathering, analysis, system design, detailed design, verification and validation, risk analysis, project management and reporting.

The IBM Rational software and systems delivery solutions offer visibility, control and automation. It is an open, proven, complete and modular solution comprising a comprehensive set of tools and best practices. IBM Rational solutions offer all the tools that teams need to successfully define requirements, model, build, test, and deploy products.

Without integrations across the systems delivery life cycle, systems and software teams are left to operate in silos. When silos form, product delivery effectiveness suffers. In order to deliver smarter products that respond to changing market needs, it is necessary to allow systems and software engineering teams to perform efficiently and to collaboratively manage all the life-cycle work products. The Rational solutions for systems and software engineering provide complete life-cycle management—an integrated and collaborative environment for requirements analysis; architecture management; and work, change and configuration management for teams of systems engineers. The Rational solutions include:

- **IBM Rational Focal Point™** software for product and portfolio management
- **IBM Rational DOORS®** software for requirements management, traceability, and impact analysis capabilities
- **IBM Rational Rhapsody®** software for systems architecture, design and modeling
- **IBM Rational Quality Manager** software for life cycle quality management from requirements, to build, to test cases and defects
- **IBM Rational Team Concert™** software for integrated version control, automated work flows, and build capabilities enabling real-time visibility and complete project collaboration.
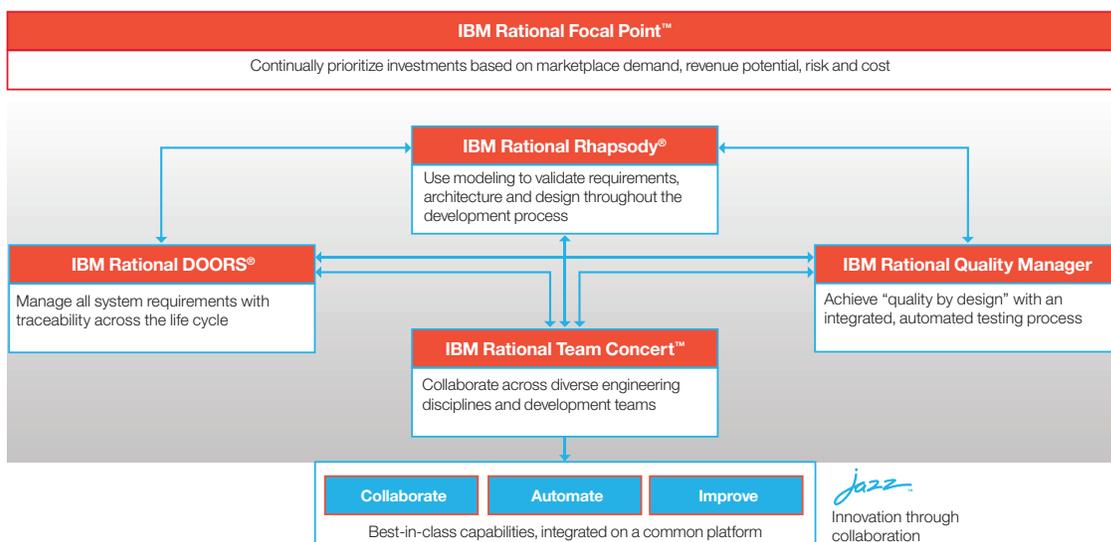
Figure 1: Rational solutions to help manage FDA regulatory compliance

Portfolio, product and project management

Solutions that help to align products and projects to business and stakeholder priorities to improve the predictability of product success. IBM Rational portfolio, product and project management solutions help companies understand the market needs and measure the business value, cost, and risk of proposed and/or delivered products. They help to align product investments with business objectives, improve predictability and product success, manage and optimize project execution, and measure team performance and project results. Rational Focal Point software fosters prioritization of investments based on revenue potential, risk, and cost. It can be leveraged to gather and use stakeholder input to prioritize products, applications, and projects. Prioritizing the right products and maintaining clear visibility into performance across the product life cycles can help companies define and meet product and solution strategies and more accurately track and predict returns on investments.

Requirements management and definition

Solutions that help to define and manage requirements to reduce rework, demonstrate compliance, and minimize costs and risks. Rational solutions can help address concerns related to product innovation such as improving time to market and achieving return on investments. Through requirements traceability, development teams can trace requirements to (and from) system requirements to test and risk analysis results facilitating more accurate business analysis and demonstration of compliance. In a recent industry study, organizations surveyed incurred a cost of as much as 60 percent on time and budget when they used poor requirements practices. Organizations with poor business analysis capabilities had three times as many project failures as successes.[2] When requirements are defined and managed properly, project overruns can be significantly reduced by lowering the number of inaccurate, incomplete, and omitted requirements.

Rational DOORS software is a leading requirements management solution that can help reduce costs, increase efficiency and improve quality by managing requirements collection, control, communication, collaboration and verification. The use of its integrated requirements design environment can help manage traceability of your compliance and regulatory needs throughout the design and implementation life cycle.

Rational DOORS software design control templates built against FDA design control inspectional techniques can jumpstart projects subject to FDA regulations. Rational DOORS software attributes can be used to properly classify and manage risks and hazards as required by the FDA. Rational DOORS software maintains requirement and specification records of the design process which can demonstrate how your design and development plans are met by verification and validation plans and how risks can be mitigated.

Using Rational DOORS software, traceability reports and matrices can be produced in a fraction of the time that it would take to produce them manually. Most importantly, Rational DOORS software maintains a full audit trail on all changes: what was and what is, user ID and date/time stamps of changes so that the design history file is created automatically as users go about their work of entering data and creating links. Electronic sign off is also available.

Integrated collaboration, change and configuration management

Integrated change and configuration control, and automated work flows enabling real-time cross-team communication and collaboration for rapid response to change. The solution is integrated on the IBM Jazz™ platform which is suited to global and distributed teams. The Jazz platform can help transform systems and software delivery by making it more collaborative, productive, and transparent. IBM Rational Team Concert software is the collaborative engine of the solution, coordinating the system engineering tasks and workflows; all governed by a customizable team
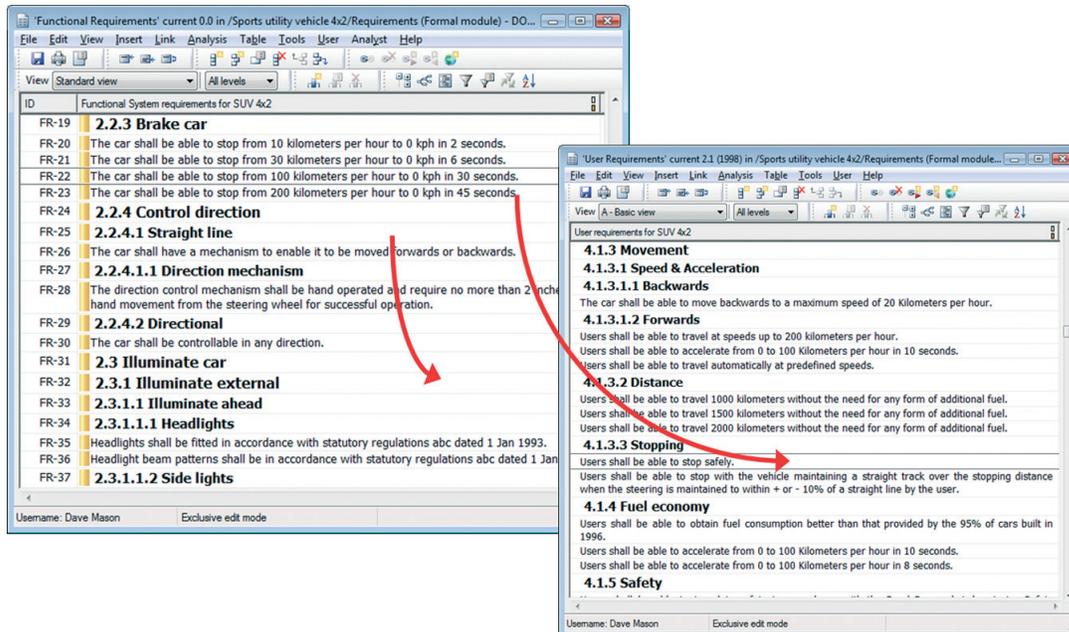
Figure 2: Demonstrate compliance by ensuring full traceability of requirements using Rational DOORS

workflow process. Requirements from Rational DOORS software can be linked to work items in the Rational Team Concert tool: this linkage helps developers or stakeholders review the requirements linked to a work item. The work item type may be a requirements change request, an implementation task, a defect, or other standard or custom work item type.

FDA regulation guidelines require identification of the major development tasks to be undertaken, deliverables for each task, and individual or organizational responsibilities (staff and resources) for completing each task. The Rational Team Concert tool integrates stakeholders, project leads, and systems engineers to facilitate compliance to FDA requirements for a quality design control process. It offers the collaborative task environment and automated change control process required by medical device developers and life sciences teams

to manage FDA quality systems regulations and design control change management guidelines. Project dashboards in the Rational Team Concert software can help further improve project tracking through transparency and reporting of team status and project health. Dashboards present live project and plan information in tabular or graphical form further facilitating the control over the development process while also providing flexibility and agility in team workflows. The team build component in Rational Team Concert software implements a standardized and controlled build process and provides build awareness, control, and traceability to the software engineering team and the software test team. Teams can also expect improved configuration management to control product content as required by the FDA controls for design documentation and artifacts.

"*The Rational tools help us enforce our processes and our procedures, so the developers can be writing code as efficiently as they can, the whole project team, starting with the requirements all the way through to the test results.*"

—Jim Ring, Tools and Methods Practitioner Principal, Blue Cross Blue Shield[3]

Design and development

Solutions that help model, design, and build resilient architectures for today's most innovative products, systems, software and systems of systems. Architectural decisions and design activities are supported by IBM Rational Rhapsody software. Rational Rhapsody software offers capabilities for modeling system and software requirements, as well as developing and delivering the software components. It provides an easy-to-use yet rigorous environment for the creation, management, and execution of both SysML and UML models.

Rational Rhapsody software is a visual development environment for systems engineers and software developers creating real-time or embedded systems and software. Rational Rhapsody software helps diverse teams collaborate to understand and elaborate requirements, and abstract complexity visually using industry standard languages. Rational Rhapsody software provides medical device engineers with a collaborative development environment with simulation for early requirements, architecture and behavioral validation, fostering better understanding of complex requirements and trade-off analysis of complex systems.

The intent of the FDA quality system requirements is that the product's conceptual description be elaborated, expanded, and transformed into a complete set of design input requirements which are written to an engineering level of detail. Rational Rhapsody software can facilitate meeting the intent of this regulation. FDA regulations require procedures for the formal review and documentation of the evolution of the design and identification of concerns and potential design issues. Rational Rhapsody software helps capture design evolution and its powerful simulation abilities support design reviews and help in the early identification and capture of potential design issues.

Quality management

Solutions that help teams advance productivity and quality across the entire life cycle. IBM Rational Quality Manager software provides a collaborative environment for test planning, construction, and execution, supporting continuous testing as well as test management of system validation and acceptance testing. IBM Rational Test Lab Manager software can help improve the efficiency of system test labs and help manage how test resources are requested and provided.

FDA regulations are very much focused on verification and validation (V&V). A defined and controlled process is required. V&V planning, reviews, methods and results all must be documented and linked to changes or corrective actions that result from testing. Rational Quality Manager software links test artifacts across the life cycle so that traceability to and from requirements, change requests, development tasks and development artifacts may all be traced. And Rational Quality Manager software also facilitates effective workflow control, tracking, and traceability features for test and verification. Using the Rational Quality Manager software dashboards (Figure 3), testers can review the systems quality metrics and project status, which may include tasks assigned in Rational Team Concert software, requirements defined in Rational DOORS software or software integration builds ready to be tested.

Figure 3: Effective test management using Rational Quality Manager, integrates test planning and execution with requirements

Summary

The Rational solutions for systems and software engineering can assist with reaching FDA compliance goals through integration, collaboration, automation and reporting. The solutions support the creation and management of life-cycle work products necessary to fulfill FDA regulations and guidelines. The solutions provide a core set of best-in-class tools and processes for systems and software engineering teams, facilitating engineering collaboration with unprecedented high level of transparency of project progress, control of artifacts, traceability with audit trails, task management and change control.

The Rational solutions address the FDA identified *lack of design controls as one of the major causes of device recalls* by:

- Maintaining design control specifications in a central, automated repository
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About the author

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Kim is a member of a specialized IBM Rational Industry Tiger Team for software and systems development focused on the healthcare, medical device, electronics and life sciences industries. Kim's expertise is in development life cycle management processes, tools and deployment. In her role as an Industry Solution Executive, Kim works closely with clients to build strategies to help tackle industry, regulatory and business challenges that are derived from establishing and modernizing quality software and systems development processes while maintaining compliance with various standards and regulations such as CMMI, HIPAA, ICD10, cGMP, FDA, European Medical Device Directives and Quality Systems Regulations. Over the last 15 years, Kim has participated directly on product development teams and in support of complex client implementations using IBM Rational/Telelogic solutions.

For more information

To learn more about the IBM Rational solutions for the healthcare and life sciences industries, contact your IBM representative or IBM Business Partner, or visit:
ibm.com/software/rational/solutions/healthcare/

Additionally, financing solutions from IBM Global Financing can enable effective cash management, protection from technology obsolescence, improved total cost of ownership and return on investment. Also, our Global Asset Recovery Services help address environmental concerns with new, more energy-efficient solutions. For more information on IBM Global Financing, visit: **ibm.com**/financing

[1] http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/ucm126252.htm

[2] http://www.batimes.com/articles/the-impact-of-business-requirements-on-the-success-of-technology-projects.html

[3] http://www-01.ibm.com/software/success/cssdb.nsf/cs/CCLE-82XVLA?OpenDocument&Site=corp&ref=crdb

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