

RCRI

More than a CRO

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Welcome from RCRI

On behalf of RCRI, I would like to welcome you to this first edition of our newsletter. We are excited to provide a forum for the communication of important developments in the medical device and in-vitro diagnostic industries. This newsletter will serve as a vehicle to deliver a broad range of information that is relevant to how you conduct your business. We will explore such topics as changes in regulatory law and practices, evolving domestic and international clinical study requirements, increasing data demands for justification of reimbursement, and novel approaches for compliance with Good Manufacturing Practices and Quality System Requirements. In delivering this information, we will go beyond the simple reporting of facts to provide interpretations that we hope will provide timely guidance as to how you can respond to these developments. Lastly, this newsletter will identify RCRI's resources that are available to provide more detailed information or assistance on any of the topics presented.—*Steve Norsted, President & Principal Advisor, RCRI, Inc*

HIPAA Update

Compliance with the Health Insurance Portability and Accountability Act (HIPAA) became effective April 14, 2003. Data collected during a current or new clinical study must comply with the new HIPAA regulations. New forms, entitled "Authorization for the Use and Disclosure of Health Information" are required for study subjects enrolled on or after April 14, 2003.

Areas of HIPAA that impact your business include:

- "Informed Consent Form" revision to include the "Authorization for the Use and Disclosure of Health Information"
- IRB approval of the revision
- Investigator agreements
- Investigational plans
- Contracts with research sites
- Contracts with vendors associated with data monitoring and collection
- Internal staff training on patient privacy collection
- Clinical study standard operating procedures
- International data collection privacy protection

RCRI would like to assist you with compliance to this major legislative initiative. We offer practical and affordable solutions, including drafting and reviewing study documents, staff training, SOP creation/revision, and database considerations.

Please contact your RCRI Project Manager or our HIPAA Compliance Advisor, Mary Kay Sobcinski, at (952)746-8080 x 257 for timely assistance with your HIPAA needs.



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Clock Ticking on IVD's

The European Union's In-Vitro Diagnostic (IVD) directive becomes mandatory this year and companies must have their CE marked goods stocked and ready by the deadline to be in compliance – yet many companies are not well prepared to meet that deadline. Given the sales opportunities available in the Euro marketplace, getting IVD products CE marked should be a “***pull out all the stops, do anything necessary***” situation for IVD companies. However, some companies are still scrambling while others are confused by what they need to do to be compliant.

If you haven't already done so, the time to start thinking about logistics, production schedules, customer expectations and compliance is **NOW!!!**

The Directive has a dramatic impact on many manufacturers that are active on the European market or are considering market entry. In the past, most IVDs could be sold in most European countries without any regulation to deal with. Now manufacturers have to integrate the new requirements into their regulatory strategy.

The Directive contains elements that can be expected in any regulatory system, such as vigilance, quality system requirements, notification and product approval, etc. However, the Directive also contains very specific elements that are rather new to IVD manufacturers that will have significant operational impact:

Conformity assessment

Essential requirements

Compliance with international or EU standards

Common Technical Specifications (CTS's)

Risk analysis

Technical documentation

Multilingual labeling

Appointment of an authorized representative (if the manufacturer is outside Europe)

Declaration of conformity

The European regulators have given the manufacturers the important responsibility to decide about conformity. The Directive explains what the manufacturer must do to assess conformity and to justify the decision to apply the CE mark. Technical documentation and risk analysis play a key role in this process. Compliance with all applicable Essential Requirements has to be demonstrated by the technical documentation that is to be established by the manufacturer.

Currently, many manufacturers underestimate the importance of risk analysis. However, they should understand that it is a key element in the philosophy of the IVD Directive. The manufacturer must identify the risks associated with the device and adopt solutions to eliminate risk, reduce risk or inform the user and patient of the residual risk – in that order of preference. Risk analysis is not an isolated regulatory exercise, but a major input and output in design control, manufacturing, labeling and post-marketing surveillance.

To integrate risk management in the daily operations is a major challenge for any manufacturer. Strategic decisions involve the choice of methodologies such as failure modes and effects analyses or fault tree analysis, how to embed risk management principles in various processes, and how to use risk management as a business tool and not merely consider it as a regulatory obligation.

Manufacturers will have to assess their labeling and make modifications if it does not meet the Directive. Translation into at least 10 languages is required for products to be sold in the countries that are currently covered by the IVD Directive. Equally important are the logistical implications of multilingual labeling. The manufacturer has to decide whether to include all languages with every device or to create products specifically for a country or a group of countries.

Manufacturers without a registered place of business in a European Member State must appoint an authorized representative. The latter is defined in the Directive as:

“...any natural or legal person established in the Community who, explicitly designated by the manufacturer, acts and may be addressed by the authorities and bodies in the Community instead of the manufacturer with regard to the latter's obligations under this Directive.”

The authorized representative will be contacted by the competent authorities in the case of incidents.

Make no mistake, the European IVD Directive will impact the manufacturer's operations and business. Even without covering all aspects of the IVD Directive, it demonstrates that important operational and business decisions have to be made and IVD companies will have to establish a strong regulatory strategy to cope with the consequences of the Directive in an efficient way. - ***for further information on the IVD Directive, please contact Carole Stamp, Principal Regulatory & Quality Advisor, RCRI Inc (952) 746-8080 x 234 or cstamp@rcri-inc.com***

**Compliance deadline is December 7th 2003 –
how efficient is your CE marketing plan?**

Auditing for Clinical Studies

With FDA now conducting inspections of clinical studies prior to completion, in some cases during the feasibility phase, it is never too soon to ensure your studies are on the right track. RCRI has a team of experienced clinical auditors to assist your company with any clinical auditing needs. Whether it's auditing of clinical study sites early in a trial to confirm adequate study management or at the end of a trial in preparation for a potential FDA inspection, RCRI will work with you to create and implement a customized audit plan. RCRI has expertise in conducting various types of clinical study site audits such as compliance assessments in preparation for an FDA inspection, evaluation of monitoring practices, and identification of issues at difficult sites. Additionally, RCRI has expertise in conducting sponsor audits of clinical standard operating procedures and processes related to areas such as data management, documentation, adverse event reporting, training, and test article tracking according to regulations and guidelines as well as conducting complete audits of Investigator files maintained in-house. RCRI will also assist in developing and implementing a correction action plan to address any findings from such audits - for further information please contact *Jill Cernohous, Project Director, Clinical Affairs (952) 746-8080 x 236 or jcernohous@rcri-inc.com*



21 CFR Part 11

What is 21 CFR Part 11?

[Title 21](#) of the Code of Federal Regulations (CFR) is the section of United States legal code that describes in detail the government regulations which govern the Food, Drug, Biologic and Device industries. [Part 11](#) is a specific section within 21CFR that outlines the requirements involved in the creation and maintenance of electronic records and the use of electronic signatures.

What is an Electronic Record?

An electronic record is defined as data stored in an electronic format that can be retrieved, viewed, or otherwise manipulated by some pre-defined identifying information (i.e. patient enrollment data, electronic copies of SOPs, Device LOT information, etc.). Electronic records can range in complexity from simple text files to extensive clinical databases used in clinical trials.

To what extent do you need to be compliant? Take the RCRI Part 11 quiz to discover more about the new regulations.

What is an Electronic Signature?

An electronic signature is an electronic mark or identifier that functions in a capacity identical to that of a handwritten signature. Electronic signatures are stored electronically as a part of an electronic record and must be unique to the individual for which it is assigned.

Is it true that the FDA recently made meeting Part 11 compliance easier?

When the original draft FDA guidance on Part 11 was released, it appeared that the extent to which systems had to be Part 11 compliant represented an immense undertaking. Companies under the jurisdiction of the FDA began spending extraordinary amounts of time and money to make every system which relied on an electronic record Part 11 compliant. In February 2003 the FDA recognized these difficulties, rescinded all previous draft guidance on Part 11, and released a new draft guidance document entitled [Guidance for Industry: Part 11, Electronic Records; Electronic Signatures – Scope and Application](#). This guidance acknowledged that previous guidelines were confusing and proposed a new approach which suggested that companies employ a risk-based analysis of their Part 11 governed systems. The FDA also clarified their definition of which systems must be Part 11 compliant, giving companies a much better understanding of which systems the FDA would examine.

Do I have to be Part 11 compliant?

RCRI recognizes that the first step to meeting compliance is to determine if you need to make your system Part 11 compliant in the first place. Your system may require compliance to the full extent of the regulation, it may not be governed by Part 11, or via a Risk Analysis, it may be determined that your system falls somewhere in-between. To help you decide to what extent your system is required to be compliant, RCRI has put together a short [quiz](#) on our website to guide you through some of the most basic premises of the guidance. This quiz is not meant to be all inclusive, but should give you a better understanding as to what extent you may be required to be compliant. To review Part 11 information, please visit the RCRI website at <http://www.rcri-inc.com> and click on the "21 CFR Part 11" button. For more information, please contact *Ryan Bolduan (952) 746-8080 x 238* or *Carole Stamp (952) 746-8080 x 234* or email info@rcri-inc.com

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Your comments, questions and general feedback are very important to us. Please address comments to us at the above location or send email to info@rcri-inc.com.

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