



## July 2009 Monthly Newsletter

### SPECIAL ANNOUNCEMENT

CIS and Cardinal Health's Specialty Pharmaceutical Services (SPS) are pleased to announce a joint collaboration that offers clients the "gold standard" in outsourced compliance activities.

SPS is a leading third-party logistics company for the healthcare industry, providing manufacturers with superior warehousing operations and logistics services, order management, chargeback/membership management, order-to-cash management, Quality Assurance and Regulatory compliance, information technology, returns processing and Account Management services.

By joining forces, CIS and SPS will offer clients who use both companies a practical, integrated and defensible process in compliance strategies, with auditable systems that are consistent, regardless of changes within the manufacturer's organization. The result is a confidence of compliance in every area managed by CIS and SPS, that allows manufacturers to focus on their core business activities, rather than the complexities of maintaining compliance.

If you would like more information on how the CIS -SPS partnership can benefit your company, please contact Katie Lapins via phone, 303.725.9075, or email, [katielapins@cis-partners.com](mailto:katielapins@cis-partners.com).

### FEATURED ARTICLES

#### **Ensuring Patient Safety in the Age of Outsourcing**

By: Jon Dellaquila, Senior Compliance Associate

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The pharmaceutical industry is an ever changing environment shaped by complex rules and regulations, and enforced by regulatory agencies. Faced with increasing pressure to improve compliance while decreasing costs in a struggling economy, the industry is embracing some of its most difficult challenges. One of the areas receiving increased scrutiny is clinical research. Patient

safety is at the top of any government watchdog's review list, and the regulations ensuring patient safety are under constant examination. Pharmaceutical companies harbor the same feelings with respect to patient safety, which is why significant resources and attention are required to conduct clinical trials. In the midst of increasing competition and regulatory scrutiny, pharmaceutical companies continue to seek ways to comply with regulations, while at the same time cutting costs. These factors have led to the unprecedented use of contract research organizations (CROs) to support clinical trial operations.

Early in the life of a clinical trial, a company is faced with the decision to determine whether trial activities should be conducted in-house, using its own staff and resources, or whether to use an external service provider such as a CRO. Several factors contribute to this decision, including current availability of staff, company resources, and the complexity of the trial. A recent survey conducted by the University of the Sciences in Philadelphia (USP) and TTC, llc (a drug development data company) indicated that 64% of all post Phase I studies use CROs for at least one aspect of their studies. Further examining these results revealed that of the 20 largest companies surveyed, 52% use CROs in post Phase I studies, while this number increases to 88% for smaller companies because of their limited resources.<sup>1</sup> Based on this information, it is evident that CROs play a critical role in the industry; and due to the escalating costs associated with Research and Development (R&D), there is an increasing potential for companies to outsource their clinical trial activities.

While outsourcing is a viable cost-cutting solution, it is not without risk. The transfer of activities in any process increases the potential for error, creating additional compliance concerns. As the number of outsourcing functions such as data management, site monitoring, and medical writing increase, the transition becomes more complex. It is similar to a puzzle. The degree of difficulty of a puzzle is directly related to the number of pieces it has. The same holds true for clinical trials. As the number of teams or companies involved increases, so do the associated compliance risks. When a pharmaceutical company decides to use a CRO to conduct one or all aspects of a clinical trial, there are many functions and tasks that require discussion and procedures to be worked out. However before negotiations begin, pharmaceutical companies are faced with the challenge of selecting a CRO. One of the first points to consider during the selection process is to determine the trial components that will be outsourced. Is it in the best interests of the company to outsource the entire trial?

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By: Meredith Taylor, Esq.  
Editor-In-Chief and PCX Product Manager

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Or does the company have some in-house staff available for support and only needs to outsource some trial activities such as monitoring or data management? This must be considered on a case-by-case basis, as each company understands the extent of outsourcing they are comfortable with. In addition, it is imperative to understand the expectations one has when evaluating a potential CRO, as all CROs are not created equal. Some CROs may have extensive experience in certain indications such as oncology or cardiovascular trials; or perhaps they have a reputation for having accomplished monitors or medical writers. It may be difficult for sponsor companies to come to a conclusion without having previously worked with a particular CRO. Therefore, the CRO selection process is critical.

A sound decision regarding CRO selection is essential to the overall success of a trial. Performing due diligence activities up front will often go a long way in running a successful trial. Once the pool of potential CROs is narrowed, a company should further investigate operations within the CRO. In an effort to gain a deeper level of understanding of the CRO, many companies conduct pre-contract assessments of CROs and external service providers to aid in the selection process, however; resource limitations and confidentiality issues could make this process challenging.

Still, however, using a third party to conduct these assessments may be a logical choice for a variety of reasons. Using a third party may take any bias out of the selection process, and consultation with individuals outside the company may provide functional or therapeutic area expertise that may not be present in the current organization. In order to ensure a thorough assessment is conducted, it is imperative to formulate a comprehensive list of questions that would allow one to gain insight into how the CRO operates. Some potential questions include:

- How many studies is the CRO working on?
- What previous experience does the CRO have building relationships between company teams and themselves?
- How experienced are the employees who will be involved in the trial?
- Who will be involved in the project, and how will the project execution plan be implemented?
- What is the issue escalation plan and how will issues be resolved?
- What is the CRO's familiarity with electronic data capture systems?
- Does the CRO have experience working with global studies?<sup>1,2</sup>

The assessment questions should be specific to the functions the CRO is being asked to perform, and it is not unreasonable to request sample documentation that has been prepared by the CRO. When making such a large investment, manufacturers must make every effort to ensure patient safety is maintained, compliance risks are minimized, and trials are successful.

The assessment questions should be specific to the functions the CRO is being asked to perform, and it is not unreasonable to request sample documentation that has been prepared by the CRO. When making such a large investment, manufacturers must make every effort to ensure patient safety is maintained, compliance risks are minimized, and trials are successful.

Choosing a CRO is only the beginning. Successful trials continue for years, so starting a CRO relationship off on the right foot, with a thorough selection process, will provide the framework for what one hopes is a collaborative and productive relationship. Again – it is only the beginning. Putting in the extra effort at the start tends to go a long way in the end; however, nothing is guaranteed. CRO selection is not a simple task and should not be treated as such. Getting the trial off to a strong start will help minimize issues as the trial progresses and monitors begin site assessments. As monitoring reports begin to pour in, other issues are bound to arise, such as quality of monitoring (another component vital to the success of the trial that deserves its own discussion). The role of the CRO will be pivotal to the trial, so pick wisely.

#### Sources

<sup>1</sup> Glass HE, Beaudry DP. Key Factors in CRO Selection. *App Clin Trials* (online). April 2008. Accessed on 22 Jun 2009.

<sup>2</sup> Schinzel S, Hundt F, Theobald K, Theis F, Buchmann A, Herbold M. CRO Precontract Audits. *Applied Clin Trials* (online). June 2009. Accessed on 22 Jun 2009.

## A Brief Dimer on DESI

By: Amy VanDeCar, Senior Compliance Manager

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What do you know about DESI codes? If you work with government pricing calculations or Medicaid rebates, you've probably heard the term. You probably know that the DESI code has something to do with whether a drug is eligible for Medicaid reimbursement. You may even know which code is associated with each of your company's products. But could you define a DESI code and explain what the classification means? Do you know the difference between a "DESI code" and a "DESI drug"?

A "DESI code" or "DESI indicator" is a value (2 through 6) assigned to drugs to indicate whether they are safe and effective. A "DESI drug" is a drug that lacks substantial evidence of effectiveness, including drugs that are identical, related, or similar (IRS) to DESI drugs. Most of the drugs your company sells probably have a DESI code of "2." Confusingly, a DESI code of "2" means that the drug is not a DESI drug. This means that your company's drug is eligible for federal Medicaid reimbursements. The full list of DESI codes is as follows:

2 = Safe and effective non-DESI drug

3 = Drug under review (no Notice of Opportunity for Hearing issued)

4 = Less Than Effective (LTE)/IRS drug for SOME indications

5 = LTE/IRS drug for ALL indications

6 = LTE/IRS drug withdrawn from the market [1]

States may opt to cover DESI drugs, but there is no federal reimbursement for these drugs.

Where did "DESI" come from?

In 1938, the Federal Food, Drug, and Cosmetic Act required manufacturers to demonstrate that new drugs were safe prior to marketing them in the United States. Between 1938 and 1962, drugs identical, related, or similar (IRS) to approved drugs were permitted to be marketed without independent approval. The Kefauver-Harris Amendment, passed in 1962, required manufacturers to show that new drugs not only were safe, but also that they were effective for each indication for which they were marketed. This new efficacy requirement was applied retroactively to all drugs – including approved drugs, IRS drugs, drugs "generally recognized as safe," and drugs the FDA indicated were not new drugs – that entered the market between 1938 and 1962. The evaluation process for determining whether a drug was effective for the marketed indications was called the Drug Efficacy Study Implementation (DESI) review. [2] The FDA contracted with the National Academy of Science/National Research Council to evaluate the effectiveness of more than 3,400 drugs approved between 1938 and 1962. [3] The results of this review were mixed. Approximately 60% of the drugs were effective for at least one of the marketed uses, but only 12% were effective for ALL of the marketed uses.[4]

DESI Indicator field definition:

1 <http://www.cms.hhs.gov/MedicaidDrugRebateProgram/downloads/proddata.pdf>

2 [http://en.wikipedia.org/wiki/Kefauver\\_Harris\\_Amendment](http://en.wikipedia.org/wiki/Kefauver_Harris_Amendment)

3 <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074382.htm>

4 [http://findarticles.com/p/articles/mi\\_m1370/is\\_v18/ai\\_3541522/](http://findarticles.com/p/articles/mi_m1370/is_v18/ai_3541522/)

## Is Alabama Setting a Trend?

By: Katie Lapins, Compliance Director

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One component of the Deficit Reduction Act (DRA) was that individual states were encouraged to implement their own False Claims Act (FCA) if one was not already in place. This would enable individual states to not only partake in any settlement between pharmaceutical manufacturers and the Office of the Inspector General (OIG), but would allow new lawsuits to be brought by the individual states.

It seems Alabama has identified FCA violations as an alternative revenue source in this new economic environment. In May, the Alabama Attorney General announced that it had reached settlements with six manufacturers for a total of \$89 million. These six companies are part of a larger pool of 70 manufacturers sued in 2005 for manipulating prices in the Medicaid Drug Rebate Program. However, the numbers in Alabama are actually even bigger. A previous settlement with 10 other companies totaled almost \$35 million, and trials for four additional companies have resulted in judgments totaling over \$352 million.

The total amount Alabama has either won or settled over the last four years is \$476 million. Spreading out the recoveries over the four years, this represents 6.3% of the 2008 actual expenditures by the Alabama State Government. This is not the end, either; there are three more lawsuits that were scheduled to begin at the end of June and dozens more that could result in settlements or court cases from the original 70 cases. There's the potential for a lot of money to be collected from our industry.

Now consider the current economic environment, and the fact that many states are facing budget a crisis... The opportunity to "find" an additional 6% is going to continue to grow under the current health care environment. Add in the proposed changes to health care, which may result in an expansion of services, and states will have even stronger motivation to look for additional funding.

California is a great example. Its financial woes have been well-publicized, with threats to "shut down the government" on July 28, 2009. The general fund is expected to have a shortfall of over \$24 billion, or approximately 24% of the projected 2009-10 budget. Although timing makes this type of "solution" impossible for California's current fiscal issues, it is reasonable to assume that long term budget strategies are being re-examined, and alternatives being implemented by other states are sure to be part of this evaluation.

### Sources

<http://finance.yahoo.com/news/Ala-settles-suits-with-6-drug-apf-15333302.html?v=3>

[http://www.lfo.state.al.us/pdfs/FY2010%20Spreadsheets/05.12.09\\_GF%20FY%202010%20PASSED%20LEGISLATURE%20FOR%20WEB.pdf](http://www.lfo.state.al.us/pdfs/FY2010%20Spreadsheets/05.12.09_GF%20FY%202010%20PASSED%20LEGISLATURE%20FOR%20WEB.pdf)

<http://www.kpbs.org/news/2009/jun/24/california-doomsday-state-could-run-out-cash/>

<http://www.ebudget.ca.gov/pdf/BudgetSummary/SummaryCharts.pdf>

## Health Care Reform: Taking a Position

By: Lauren Pellicciotti, Compliance Manager

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On June 9th, the Senate Committee on Health, Education, Labor, and Pensions released a proposed Bill relating to the Healthcare Reform Plan of 2009. The Bill, called the Affordable Health Choices Act, also known as the Kennedy Bill, identifies the specific requirements an individual American would need to follow in order to ensure cheaper healthcare options. The proposed Bill outlines the following options including, but not limited to: an employer mandate, income caps for eligibility, and age demographics. According to the Senate Committee, if the Bill is passed, those who refuse insurance would be penalized [1].

The recent elections have established Democratic majorities in both houses of Congress, and brought the issue of comprehensive health care reform to the forefront of next year's political agenda. Congress believes that Healthcare Reform will assist with improving the Country's current economic status. Washington and the Democrats on Capitol Hill are making many efforts to rally public support and awareness regarding our Country's Healthcare System.

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Blue Dogs, a conservative Democratic rights group, questions whether or not the Healthcare Reform should be a public option. According to Blue Dogs, setting conditions will protect the consumer choice and promote competition in the market place [2]. Blue Dogs has recently become more vocal over the newest Healthcare Reform pressures. Compared to the Democratic Party, Blue Dogs recommended an opinion that promotes fiscal conservatism and accountability on the latest Healthcare Reform. The Blue Dogs are fighting against a public option and have provided many provisions [3]. Representative Jim Cooper (D-TN), Blue Dog Health Care Task Force Vice Chairman, said “The conditions we’re laying out today ensure that Americans who like their current health insurance can keep it; that they will have access to their choice of quality, affordable health care plans; and that any public option exists on a level playing field. And of course, we strongly support President Obama’s commitment to keep health care reform deficit-neutral. [3]”

In the next few months, Americans should begin to educate themselves about what their options will be if the Bill is passed.

Sources

1 Senate Democrats Release Health Care Reform Proposal

<http://www.courant.com/health/hc-health-care-dodd-0610.artjun10.0,1489093.story>

2 Blue Dogs: Health Care Reform Must Protect Consumer Choice, Promote Competition in the Marketplace

<http://www.house.gov/melancon/BlueDogs/Press%20Releases/Blue%20Dogs%20-%20Health%20Care%20Reform%20Must%20Protect%20Consumer%20Choice.pdf>

3 Health Care Reform: Ensuring Choice in the Marketplace

<http://www.house.gov/melancon/BlueDogs/Press%20Releases/Health%20Care%20Reform%20-%20Ensuring%20Choice%20in%20the%20Marketplace.pdf>

## Letter from the Editor

### Paper Compliance Just Isn't Enough

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Dear Readers,

In order to have an effective Corporate Compliance Program, it is not sufficient to point to a binder full of Policies and Procedures on your Compliance Officer's desk. This is a common pitfall for many pharmaceutical companies that do not have a robust Corporate Compliance Program and do not have many resources to implement, monitor, and audit the documents. Without a process in place to monitor and audit employees' compliance with written Policies and Procedures, the documents are nothing more than words on a page, and they certainly do not constitute a Corporate Compliance Program.

Does this sound at all familiar? Imagine that PharmaCo is a small pharmaceutical company with 10 NDCs. The Compliance Officer is also the VP Finance, with no compliance staff to support him. The Compliance Officer, in an attempt to create an effective Compliance Program pursuant to OIG guidelines, decides that Sales and Marketing and Operational Compliance documents must be drafted. He studies the relevant laws, regulations, and guidance documents; conducts interviews and meets with key stakeholders; and begins to draft the documents. After a year of hard work and long hours, PharmaCo has plethora of Corporate Compliance documents! The Compliance Officer follows his new Document Control SOP, finalizes all of the documents, and ensures that they are signed. Over the course of the next few months, the Compliance Officer holds various training sessions for relevant employees, and all the employees sign off on the documents, pursuant to the new Training SOP. A few months pass, and there are some regulatory and company changes that require him to update his documents. He does this, and holds the appropriate training sessions. This pattern goes on for the next two years.

Seems like PharmaCo is in pretty good shape right? Not quite. PharmaCo failed to monitor and audit its employees' compliance with the terms of its Policies and Procedures. For all the Compliance Officer knows, the sales reps could be distributing sports tickets to doctors, the Marketing Department could be promoting the Grants Program, and employees could be forgetting to retain documents pursuant to the Document Retention Policy. Just having the documents and training the employees on them is not enough; there is no way to know if the employees are compliant without systematically monitoring and auditing their compliance.

Monitoring and auditing may seem synonymous, but I can assure you they are not. Your Company must conduct both on an annual basis in order to maintain an effective Corporate Compliance Program.

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### **Monitoring**

Monitoring is defined as ongoing, real-time checks and balances implemented and executed by a functional/operational group to ensure proactive evaluation, identification, and mitigation of risk.

Monitoring is typically performed by the Corporate Compliance Officer. It is his or her responsibility to determine whether employees are complying with established Policies and Procedures, and whether the documents should be revised. Typically, documents are scheduled for monitoring every quarter, but monitoring can also take place on an ad hoc basis when deemed necessary. The Compliance Officer will review those documents to ensure that they still make sense from a compliance standpoint; he may also seek assistance from the legal department. If he feels there is a need to revise a document, it should be put through the Document Control process. Assuming the document is sound, he will interview a few (not many and not randomly selected) employees, pull training records to ensure employees are being trained, review call notes or other documentation (not many and not randomly selected), etc to see if the employees are following the policies and procedures in those documents. If not, the document should be re-reviewed by the Compliance Officer and another member of senior management, and revised if necessary.

The training materials should also be reviewed and revised if necessary to ensure they are in line with the document. Then, training should be held again for relevant employees. This document should be monitored again at least one year later.

### **Auditing**

Auditing is defined as the routine evaluation of the effectiveness of controls and adherence to laws, regulations, and guidance documents as incorporated in Company Policies and Procedures. Audits should be performed by a party who possesses substantive expertise in the subject matter, but is not affiliated with the functional/operational group or task being audited.

Audits typically assume the legal sanctity of the Policies and Procedures, and test criteria is prepared to test compliance against the requirements in the documents.

The process of auditing compliance with the documents begins by selecting a sample size. This typically should be random, but some subjective decision making may be required. Next, a formal communication should go out to all employees in the sample, and to all audit sponsors, to announce the audit. A document request may also be distributed to the sample size. The employees in the sample size are then interviewed, and may be asked to perform a task. The auditors may then perform the same task, using the Policy and/or Procedure document as a guide, to ascertain if the same result is found. Testing criteria against the Policy and Procedure is typically developed and completed during a review of any documentation. A final Audit Report is prepared with a section for Management Responses. The key stakeholders have an opportunity to respond and remediate.

Here is a summary chart (courtesy of Clarissa Crain, CIS Compliance Director) to decipher between Monitoring and Auditing:

	<b>Monitor</b>	<b>Audit</b>
Who	Operational/Functional	Independent 3 <sup>rd</sup> Party
What	Checks and balances of day to day operations	Holistic and independent review and identification of risk with key controls
When	Ongoing	Based on Risk Evaluation / Business Assessment (at least annual)
Why	To ensure ongoing compliance and proactively identify potential risk	To ensure independent review and identification of process risks
How	Development, Documentation, and Implementation of monitors by Department	Use of Internal Audit, External 3rd Party, or other independent party

I cannot stress enough how important it is to systematically monitor and audit compliance with your Policies and Procedures. If the Government ever audits your compliance in this area, it will want to know whether your documents are actually implemented and whether employees are truly complying with them.

Best regards,  
Meredith Taylor, Esq.  
Editor-In-Chief