



Guest Letter from Editor: Brace Yourself, an Interim Final AMP Rule in May?

By: Chris Cobourn, VP, Regulatory Affairs

The word on the street is that CMS may publish an Interim Final Average Manufacturer's Price (AMP) Rule in May, perhaps around Memorial Day.

A rule was expected, although we did not know when, and it was thought that it might follow the "normal" process of a proposed rule with a public comment period followed by a Final Rule.

So what is an Interim Final Rule? I am not a lawyer, but from what I understand, it is one that can take effect on a specified date (defined in the rule) and have the force of law. It can allow for public comments, but does not wait to consider the comments before taking effect. However, the agency may tweak the interim rule, as they deem appropriate, and may later issue a "final" rule that discusses these comments. The process for an Interim Final Rule is allowed for by the Administrative Procedures Act, where agencies can make an exception to the normal process of issuing a preliminary rule and seeking public comment.

The exception can be based upon "good cause," which generally consists of impracticability, public interest, or statutory deadlines. So, what date could an interim final rule take effect? I would guess the start of a quarter, which could be July or October. Let's hope for October.

CMS had to publish an AMP rule because the legislative language in the Patient Protection and Affordable Care Act (PPACA) was in conflict with the CMS 2007 Final AMP Rule. The PPACA redefined "Retail" to Retail Community Pharmacy (RCP), established language on

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wholesaler fees and added an Alternative 5i AMP. The regulatory language conflict led CMS to withdraw the AMP definition from the 2007 Final Rule, (<http://www.pharmacomplianceblog.com/blog/?p=3167>, <http://www.pharmacomplianceblog.com/blog/?p=2993>), and left a void of no regulatory language to define the specifics of the PPACA.

The big question is what the new AMP will be and how much it may reflect the perspective of the Retail industry. The industry brought CMS to court over the 2007 Final Rule, and was successful in getting a court injunction on certain reimbursement and publication provisions based upon the fact that they did not feel that AMP, as defined in the Final Rule, reflected the true price at retail. This mattered to Retail because AMP was going to be published and used for Federal Upper Limit (FUL). With the change to AMP being based upon RCP, the legislative language in the PPACA reflected much of the Retail industry's primary concerns. Subsequently, the injunction was dismissed, and the Retail industry sent a letter to CMS outlining what they thought AMP should be (<http://www.pharmacomplianceblog.com/blog/?p=2655>). So, the new AMP that may be defined in an Interim Final Rule will be used for Medicaid Rebates, and the weighted AMP will be published and used for FUL.

One thing we know, is that when a rule is put in place it will have a huge impact on the GP function for Pharmaceutical manufacturers.

The 2007 Final Rule and the 2010 October AMP change from the PPACA has taught us some important lessons on what the impact may be. You may want to start preparing your company for the impact, and start thinking of resources you may need to have available, whether internal (GP, IT, Finance), external GP consultants like CIS, system vendors or your external counsel.

- Policy and methodology review
- New AMP definition, including the RCP AMP and the Alternative 5i AMP
- Clarification on the question of a build up versus build down methodology, and data sources/

- approach in the event of a build up
- Clarification on Line Extensions
- Class of Trade impact
- Wholesaler Fees, inclusions and exclusions as Bona

Fide Service Fees

- Potential change on Authorized Generics products
- Systems Impact, system requirements
- Ability to restate Base AMP based upon the new AMP
- Updates to Policies and Procedures
- Financial Impact Modeling
- Question on timing, will the new AMP definition be retroactive to October 2010



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The Public Health Service (PHS) Extension Program

By: Kathy Castoro, Senior Manager

The enactment of the Veterans Health Care Act of 1992 resulted in the creation of the 340B Drug Pricing Program. This program provides eligible safety-net providers significant savings on outpatient drugs. Savings from this program can be used to reduce prescription drug prices to patients, increase the scope of services offered, serve more patients and offset losses. In short, savings from participation in this program are not regulated by the Office of Pharmacy Affairs.

The PHS extension program under the Affordable Care Act of March 23, 2010 consists of expansion of, and increase in access to the 340B Program. The new eligible entity types include Critical Access Hospitals, Rural Referral Centers, Sole Community Hospitals, and Free Standing Cancer Hospitals and Children's Hospitals (these were previously eligible under the Deficit Reduction Act (DRA) of 2005 and were also named within the Affordable Care Act).

Entities listed in the Affordable Care Act were offered rolling admissions and could applied starting August 2, 2010. Those eligible applications that were complete were enrolled into the 340B Program as they were received and were not subject to the quarterly cutoff. This rolling admission only applied to the entities listed in the Affordable Care Act. Regular enrollment on a quarterly basis began on October 1, 2010 and entities were not eligible to participate until January 1, 2011.

The 340B Prime Vendor Program (PVP) service is offered at no cost. Since the PVP brings value-added drug negotiation services listed below, I would think that the PVP program would grow accordingly.

- Discounts on over 3,500 covered drugs
- Discounts are on average 15% below the 340B ceiling price
- Represents over \$5 billion in purchase volume or over 10,000 participants

The PVP has multiple wholesale distributor agreements with most national and regional wholesalers. Enrollment in the PVP does not require the entity to change their distributor. They also offer favorable distribution costs and discounts on other pharmacy related products and services.

Additionally, on December 15, 2010 President Obama signed the Medicare and Medicaid Extenders Act of 2010 which removed children's hospitals from the orphan drug exclusion in section 340B(e) of the Public Health Service Act.



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In Defense of Pharma: Why and How We Should Perform Self-Audits of Our Government Programs

By: Chris Cobourn, Vice President of Regulatory Affairs

At CIS we have been performing Government Program (GP) audits for Pharmaceutical Manufacturers of all sizes and types for many years. We speak on the topic at most conferences, and have a certain passion for it. I think that most GP professionals know that it is important to perform audits. I also think that many still struggle to get their arms around how to audit, and how to communicate the importance of audits to key stakeholders within their organization.

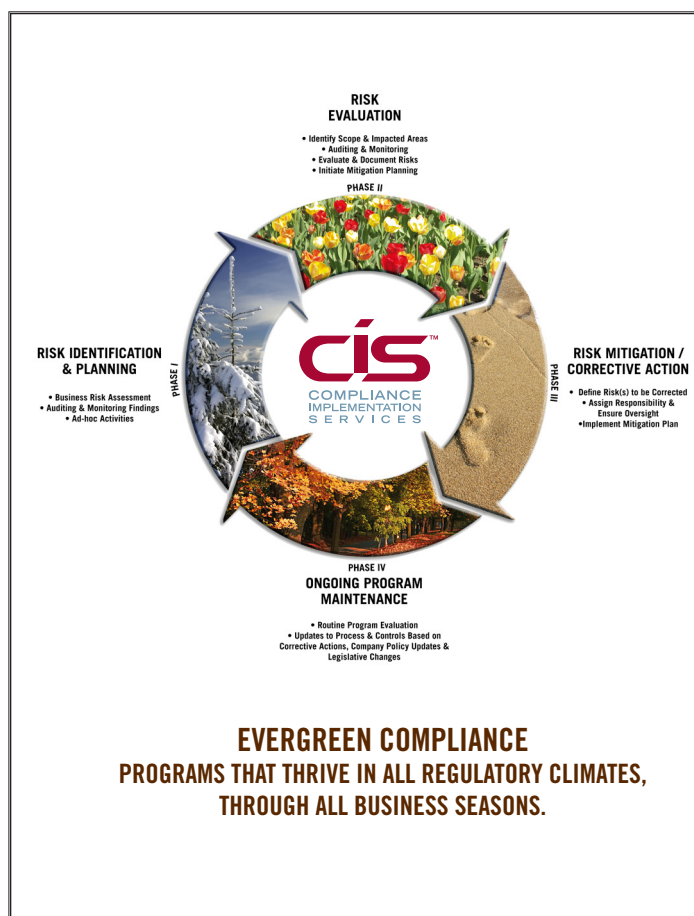
Having worked in this space for many years now, and being what we at CIS lovingly call a “GP Geek,” I know that my counterparts in industry are doing everything they can to understand what they have to do and to get it right. We all know how hard that is in today’s environment. Ongoing legislative initiatives and guidance continue to shake our world. In addition, there are no substantive regulations for Medicaid, Medicare ASP, or the PHS program.

With the audit activities, recovery statistics, and language coming from the states, one would think that Pharma could be trying to overcharge the government across these programs. That simply is not true. In defense of Pharma, and of my many GP Geek friends out there, we know that the vast majority of companies are doing what they can to understand the “rules” and get the calculations right.

So, where does an audit plan come in to the discussion? Without some level of self-assessment/audit, you lack the ability to demonstrate to the government that you’ve evaluated yourself, made sure you were in compliance with the programs and checked to see that your calculations were correct. Those of you who know me know that my mantra is to be able to tell a story of compliance. I believe in demonstrating that you take compliance seriously and have done your due

diligence to self evaluate your GP program, identify potential gaps or risks, and put a plan in place. I think this is key to looking a government auditor in the eye and demonstrating that you have the ability to tell your story and to show a practical and meaningful plan.

Being able to show that you are striving for compliance may be almost as important as being in compliance. The burden of proof will be upon you, the manufacturer.



Medicare Part D Coverage Gap Questions & Answers

By: Lisa C. McNair, Senior Manager

Yesterday, Compliance Implementation Services (CIS) conducted a webinar addressing questions pharmaceutical manufacturers and other interested parties had regarding the new Medicare Part D Coverage Gap Program as we approach the release of the first round of invoices.

CIS solicited questions from the pharmaceutical industry and contacted CMS and the TPA, Palmetto GBA to obtain guidance on addressing and answering these questions.

There are numerous questions still outstanding, as these questions are answered and guidance is provided we will continually update our blog. We are working towards another webinar in the near future on this subject, inviting several special guests.

Below, please find the submitted questions and their responses. In reviewing these questions, if you have additional questions, please feel free to submit them to me at lisamcnair@cis-partners.com.

APPEALS

Q: The draft letter sent out regarding the Appeals Process, how is that different from the Dispute Process?

A: CMS is implementing the appeals process in accordance with Section 1860D-14A(c)(1)(A)(vii) of the Affordable Care Act of 2010 and Section V of the Medicare Coverage Gap Discount Program Agreement. CMS is required to provide a way for pharmaceutical manufacturers to resolve disputes.

DISPUTES

Q: Can a manufacturer dispute a claim that was submitted as a paper claim from an in-network pharmacy?

A: Yes, if it fits one of the dispute codes provided. If the manufacturer believes that the claim

was processed as an electronic claim and as a paper claim they may dispute as a duplicate.

Q: How will the dispute process work and when will it be implemented?

A: The dispute process was outlined in the March 2nd webinar. The dispute process is in the process of being implemented. Manufacturers may dispute claims within the allotted time frame from the release of the data. Details are in the webinar slides which are located at <http://www.csscooperations.com/Internet/Cssc.nsf/docsCat/TPA%20Drug%20MFG~Webinar%20Information?OpenDocument&Start=1&Count=45&Expand=1>

INVOICES

Q: Do we need to provide any product or sales information for invoicing?

A: No, the products eligible for this program are based upon the information in the FDA database. It is the responsibility of all pharmaceutical manufacturers to ensure this information current and up-to-date.

Guidance has been released on this subject. Please refer to the “Medicare Coverage Gap Discount Program – Manufacturer Program Guidance” located on the CMS website at: http://www.cms.gov/PrescriptionDrugCovGenIn/05_Pharma.asp#TopOfPage.

Q: Is Palmetto on time to send invoices?

A: Yes. They are scheduled for release on April 30th.

Q: Please clarify that if an invoice is received and requires remediation by the TPA, the manufacturer would not be required to submit payment until a new invoice is submitted.

A: Pharmaceutical manufacturers may correct an invoice only when they have been invoiced for NDCs with labeler codes not covered under their Manufacturer Agreement. Manufacturers must complete and submit a “Manufacturer Invoice

the TPA will confirm the invoice correction and if correct, the manufacturer will not be responsible for paying those NDCs.

PAYMENT

Q: If a manufacturer is unable to set all plan sponsors up for payment, are there other options for payment for the first time?

A: Unfortunately, there is no other available option; EFT (electronic funds transfer) is the only way to submit payment. The EFT information was distributed on 14 March 2011 which should have provided enough time for set-up.

Q: Please clarify that the 15-digit character identifier has to be in the header transmitted with the payment. It cannot be provided any other ways such as an email or letter.

A: This is correct.

Q: Has the banking information for EFT payments been validated?

A: Yes.

Q: If one (1) payment fails to a plan sponsor, is the entire payment considered late?

A: No.

Q: What date is considered the paid date? Is it the date the EFT is sent to the bank or the process date?

A: The banking confirmation date is the date the of the file transfer to the payer's bank.

Q: We have not received our first invoice yet, working with TPA, does that impact our payment deadline?

A: The first invoice has not been released; it is scheduled for release at the end of next week. The payment is due thirty-eight (38) days from the release of the invoice.

Q: What is the process/rational behind making the invoice payment 1099 reportable?

A: Form 1099 is an informational return required for any business that pays a vendor or contractor

more than \$600 in a tax year. Included in the Patient Protection and Affordable Care Act was the provision that required all corporations to submit a 1099 for each qualifying payment relationship beginning in 2012.

It has been reported this week that Congress has repealed this legislation and the Bill is awaiting the President's signature.

Q: Are we to pay the Low Volume Discount (LVD) data displayed in the summary without having visibility of the detail?

A: Yes, the invoice must be paid in full each quarter. Once the Low Volume data is available, the amount will display as \$0 (zero) on the detail file; at that time, the manufacturer will have the ability to dispute the claim.

PLAN D SPONSORS

Q: How will manufacturers know when a plan sponsor is no longer participating in the program?

A: All Part D Sponsors are required to participate in the Coverage Gap Program, thus Sponsors will not be withdrawing from the program.

PROCESSES

Q: How will double-dipping be prevented?

A: CMS and the TPA have been processing Part D claims since 2006. The processing system used by CMS determines beneficiary eligibility, if the claim falls within the coverage gap, and if there is other health insurance. It is strongly believed by CMS and Palmetto GBA that data is scrubbed to eliminate double-dipping.

Q: 1099's have been addressed, what about W-9's; will manufacturers have to request from the plan sponsor directly or will Palmetto provide?

A: CMS has not decided on this process as of yet. Once a determination is made guidance will be released.

Q: Will there be opportunities to change/improve the process after the first round of invoices?

A: CMS and Palmetto GBA are always interested

in receiving feedback from pharmaceutical manufacturers. At anytime suggestions and comments can be submitted and are greatly appreciated.

Q: The manufacturer's labeler code is NOT listed or provided to CMS and the plan sponsor authorizes a prior authorization to obtain the drug, will the manufacturer even know they did not submit a labeler code listing or a signed agreement still be responsible for the discount amount?

A: In this situation when the Plan D Sponsor submits for a discount, CMS will deny based on the labeler code is not a Part D Coverage Gap participant.

Q: Will we have the ability to ask questions and get a rapid response once invoices are received?

A: Yes. It has been sincerely expressed that the TPA (Palmetto GBA) wants to ensure pharmaceutical manufacturers receive top notch service. Their contact information will be provided at the end of this webinar.

PRODUCTS

Q: What guidance is there for manufacturers who sell or divest a product during the benefit year?

A: This question seems to address those instances when a manufacturer sells or divests a product within a labeler code. CMS has made it clear that the labeler code discounts are processed in their entirety. Thus if a manufacturer sells one of its products, the selling manufacturer is still responsible for paying the discounts on that product since it still carries their labeler code.

CIS NOTE: Manufacturers may need to address this situation during the negotiation of the sale of a NDC.

Q: In the future, will CMS allow manufacturers to add individual NDCs for products purchased from other drug companies?

A: At this time, this is not under discussion.

Q: Is there any sense of how limited the claims may be for small companies with two (2) or four (4) products, perhaps some only pediatric?

A: Not at this time.

REPORTS

Q: How can we obtain product information on summary script information?

A: This information is contained in the Manufacturer Data Report.

Q: How will paper claims be identified in the data?

A: Paper claims will be identified as such in the PDE claim which is submitted to CMS by the plan sponsors.

Q: In the invoice report and payment confirmation report there is a field titled, "Submitting Contract Number," which field in the detail report corresponds to this field? Based upon the layout of the dispute and detail report, there is not a way to go back to identify the contract for the disputed claim.

A: The Manufacturer's Data Report does not list the contract number and a pharmaceutical manufacturer will not be able to tie a contract number to this report. With the information CMS is requesting on the Dispute Report, CMS will be able to take the information and tie it to the particular claim for the plan sponsor.

Q: What data validations, if any, are being done prior to transmitting to manufacturers?

A: CMS and the TPA have been processing Part D claims since 2006. The processing system used by CMS determines beneficiary eligibility, if the claim falls within the coverage gap, and if there is other health insurance.

Q: Will the falls we receive always have the same names?

A: Yes, please refer to the file layouts on the TPA website <http://www.csscooperations.com/Internet/Cssc.nsf/docsCat/TPA%20Drug%20MFG~File%20Layouts?open>

The List Gets Longer: CVS Pharmacy Becomes the Latest False Claims Act Settlement

By: Erika Scholl, Senior Associate

On Friday, April 15, 2011 it was announced that CVS Pharmacy Inc., which is the retail division of CVS Caremark Corporation, had agreed to a settlement with the United States and ten individual states in regards to a False Claims allegation. This settlement will cost CVS \$17.5 million, \$8 million of which will be paid to the United States government and \$9.5 million to the individual states . ¹According to the government, CVS allegedly “billed and was paid a higher amount by Medicaid than what the insured would have been obligated to pay if the claims [had] been submitted solely to a third-party insurer.” ² CVS, in response to the settlement, stated that they “did not intentionally overcharge any state Medicaid program,”³ and contended that they settled the matter due to the expense of litigation.

False Claims Act violations and subsequent settlements are nothing new. We continue to see an increased level of allegations brought by the government as a part of the Department of Justice and Office of Inspector Generals’ joint task force, Health Care Fraud Prevention and Enforcement Action Team (HEAT). HEAT exists to fight the abuse of the health care system and to prevent the “stealing of billions of dollars from the federal government, American taxpayers and some of our most vulnerable citizens.”⁴ In fighting these abuses, the HEAT partnership recovered nearly \$4 billion in 2010 which was a return of \$6.80 for every \$1 spent on funding. With this substantial return only continuing to rise there is no doubt that the scope of investigations will only increase instead of decrease.

Perhaps that is what is most interesting about the CVS investigation and subsequent settlement. Historically, the False Claims Act investigations have focused on areas like manufacturer misconduct. A

- 1 <http://www.justice.gov/opa/pr/2011/April/11-civ-485.html>
- 2 <http://online.wsj.com/article/BT-CO-20110415-711530.html>
- 3 <http://online.wsj.com/article/BT-CO-20110415-711530.html>
- 4 <http://www.stopmedicarefraud.gov/heatsuccess/index.html>

pharmacy being probed provides further evidence of the growth of investigations related to False Claims Act violations. This serves as a reminder to all of the wide scope that these investigations may take and further emphasizes the need to be cognizant of the way the government utilizes the False Claims Act.

Resources:

The United States Department of Justice: <http://www.justice.gov/opa/pr/2011/April/11-civ-485.html>

The Wall Street Journal: <http://online.wsj.com/article/BT-CO-20110415-711530.html>

HEAT Task Force: <http://www.stopmedicarefraud.gov/heatsuccess/index.html>

U.S. Department of Health & Human Services: <http://www.hhs.gov/secretary/about/speeches/sp20110217b.html>

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How Important Is a Label?

By: Yasmeen Muhammad, CIS Senior Consultant

Labels used on the packaging of drug products should include the product name, manufacturers name and address, an identification code, lot number, active and inactive ingredients, the quantity of product in the container, the dosage, usage instructions, storage conditions and an expiration date. When any part of the information on the label is incorrect or a label is placed on the wrong package, problems can arise.

The labeling of a drug product may not seem like an important aspect of the manufacturing process, but it is a major part of a company's overall quality system.

Labels and labeling errors such as labeling mix-ups and misbranding are among the top reasons for product recalls. Recently, two major pharmaceutical companies's recalled products due to labeling errors. One incident involved the recall of two products due to the possibility that incorrect labels were placed on the bottles by a third-party manufacturer. The other incident involved the recall of a product due to incorrect wording on their label. In both instances, the product reached the patient level and could have resulted in serious adverse side effects.

Labeling errors such as these indicate that there is a lack of control in the packaging and labeling system. The regulatory basis for the control of labeling falls under 21 CFR Subpart G and ICH Q7A Section IX. Some of the regulatory requirements that are in place for the control of this quality system are:

- Having written approved procedures that include details for examining labeling and packaging material as they are received
- Having written approved specifications for the approval or rejection of labeling and packaging material
- Having separate storage areas for labels and labeling materials of different products to prevent mix-ups
- Having specified personnel review and approve labeling

- Having a system for the examination of labeling and packaging materials to ensure suitability and correctness before use
- Having a process for the reconciliation of labels issued, used and returned
- Having a system for the destruction of returned, obsolete and out dated labels
- Inspecting the labeling and packaging areas to ensure all labeling and packaging previously used have been removed from the area
- Performing inspections of the finished product to ensure correct labeling
- Having all manually applied labels examined by one person and verified by a second person

Ensuring that your company is appropriately prepared to maintain compliance with regulation, while also being prepared to adjust as necessary to other potential legislative changes or updates to guidance is a challenge. However, there are some key steps that all manufacturers should consider in assessing the company's preparedness. The mini assessment below details five major tasks manufacturers should have in place currently to ensure ongoing compliance and reporting preparedness.



**PROVIDING COMPLIANCE SOLUTIONS
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Clinical QMS – Something Borrowed

By: Karen Brown, Senior Director

With the increased scrutiny of data integrity, global operations and vendor compliance, as well as a strong collaboration with foreign agencies, the FDA is taking a hard line on current GCP requirements, as well as adding changes to their regulatory lineup.

With these changes, clinical departments should start to look at current processes and systems and determine whether or not they offer a truly comprehensive quality management program. One approach to consider as sponsor companies organize their GCP compliance responsibilities is a clinical Quality Management System (QMS) and the best way to kick-start this program is to borrow from traditional manufacturing practices.

Already familiar to those with a manufacturing background, the term “quality management system” is defined and explained in recently published ICH Guideline Q10¹. While the Q10 document is based on Good Manufacturing Practice (GMP), concepts and language from the Q10 document are appearing with increasing frequency in FDA GCP inspection reports (Form 483s) and Warning Letters. In addition to Q10, you should consider GMP Guidelines Q9 on Quality Risk Management².

Leveraging GMP Q9 and Q10 Guidance will provide direction however there are challenges to adapting processes intended for manufacturing facilities to a clinical R&D environment. For instance, GMP-related timelines, systems and supply chain requirements will not easily translate into clinical policies, procedures, and tools such as CAPA systems, root cause analysis, KPIs and training.

If you are considering a clinical QMS, this multi-part series blog will provide step-by-step suggestions for developing a successful program, including assessing your current SOP management system, developing a right-sized QMS for your company, and implementing the changes across the organization. Look for the next blog that discusses key clinical R&D QMS elements.



1 International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals For Human Use, ICH Harmonised Tripartite Guideline, Pharmaceutical Quality System Q10, Current Step 4 Version, June 2008.

2 International Conference on Harmonisation, <http://www.ich.org/products/guidelines/quality/article/quality-guidelines.html>

Federal Supply Schedule – “State of Compliance”

By: Dave Rice, FSS Director

Do you struggle with Federal Supply Schedule (FSS) compliance? Are you confused about the rules governing FSS compliance? Do you feel that if you ask the same question to 5 different people, you get 5 different answers?

If you answered yes to any of these questions, then you are not alone! Very little is black and white in this area of compliance. Basic FSS contract compliance issues fall within the grey area, as there is no or little communication of the compliance requirements to guide manufacturers. The National Acquisition Center (NAC), Veterans Affairs (VA) Legal, and Office of Inspector General (OIG) may all have different interpretations of what is required by the same regulation. Not only do the different enforcement functions have differing interpretations, but each VA contracting officer may have a different understanding of the same rule. The inconsistent application of a particular rule by the multiple contracting officers that manufacturers are now forced to work with almost ensures non-compliance, at some level. The lack of guidance, inconsistent application of rules, and lack of communication of the “current period” thinking can, and does create confusion with manufacturers as to what is required. If the government agencies and individual contracting officers cannot agree on their compliance requirements, how can manufacturers ever expect to be compliant?

Companies are forced to function within a system that lays down literal rules which make compliance extremely difficult, turning nearly everyone into a rule violator. The ambiguity and incomprehensibility of many of the rules results in confusion not only to manufacturers but also to personnel that are responsible for enforcement. The government can literally pick and choose when, where and on whom to enforce its interpretation of its rules. This creates challenges in negotiating FSS contracts and complying with the terms and conditions of the contract,

which may result in significant financial liabilities if an OIG auditor has a different interpretation of a rule than that of the contracting officer, whom the manufacturer relied upon for guidance.

It is clear that there is an inherent risk of non-compliance and retrospective liabilities when doing business in this \$13.0 billion dollar FSS market. The rules are complex, indistinct, and are subject to the interpretation of the contracting officer, auditor, or other government employee with whom you may be dealing. Audit activity and/or legal challenges force clarification of some of the basic compliance issues. However, the lack of a centralized forum within the VA to communicate these outcomes internally or externally results in very little impact on the clarification of the rules for either the contracting officers or manufacturers (unless you are the manufacturer experiencing the audit).

To survive in this environment, manufacturers must know the compliance requirements as well as or better than the contracting officer and/or OIG auditor with whom you have interactions. Remember, there is no definitive guidance on many of the rules for the manufacturer, auditor, or contracting officer. Each operates under their own interpretation of the rule. There are many opportunities for manufacturers in this \$13 billion market, but it is critical that you inform your management team of the potential risks associated with doing business with the government. Typically, however, the reward is worth the risk.

In conclusion, do not be afraid to challenge your contracting officer if you believe that they are incorrectly interpreting the rules and regulations of the FSS contract. Further, you should attend conferences, industry meetings, and NAC Industry Day to learn the current thinking on different compliance issues. Work with consultants and lawyers specializing in FSS contracts to make sure you have a good understanding of the compliance requirements and can support your position legally.

Prescriptions for non-prescription drugs?

By: Lyndsay Giger, Senior Associate

People are now flooding doctor's offices to obtain prescriptions for everyday over the counter items such as aspirin and cold medicine because of provisions in the health care reform bill that, summed up, state that people who want a tax break to buy such items with what's known as flexible-spending accounts, they need to get a prescription first."

"Used by an estimated 35 million Americans, flexible-spending accounts enable participants to set aside a portion of their income on a pre-tax basis to pay for out-of-pocket medical costs that aren't covered by insurance. These costs include items like deductibles, co-payments for office visits, prescription drugs, vision and dental care and over-the-counter supplies. "

It wasn't until the bill took effect on January 1st that the repercussions of the changes were seen. Patients have begun to request prescriptions from their doctors for over-the-counter medications and supplies, resulting in an increase in doctor's and pharmacist's workloads as well as, adding to their risk of a malpractice lawsuit. Many doctors have started to impose prescription writing fees to try and discourage patients from requesting prescriptions for over-the-counter items.

"Though the new rules on over-the-counter drugs amount to a small part of the massive overhaul of the health-care system, the unintended side effects show how difficult it can be to predict how such game-changing legislation will play out in the real world."

Since the bill has taken effect, the House and the Senate have introduced legislation to repeal the new requirements around the flexible-spending account program in order to return it to the old requirements. Meanwhile, other councils are meeting with Congress in the hope of getting them to end the "use it or lose" policy that is currently imposed on flexible spending accounts. The use it or lose rule means that participants of flexible spending accounts have until

the end of the year to use all the money they set aside in their flexible spending accounts, otherwise they must forfeit their unused portion. So until a bill has been passed to change the new regulations surrounding the flexible spending account program, be prepared for the possibility of now having the added cost of a prescription writing fee tacked onto your doctor's visit.

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FDA and EMA to Initiate Pilot Program on Parallel Evaluation of Quality Data in New Drug Applications

By: Suma Kallurkar, Senior Manager

On March 16, the Food and Drug Administration (FDA) and European Medicines Agency (EMA) announced that they will be jointly running a pilot program to conduct parallel assessments of quality data termed Quality by Design (QbD) in new drug marketing applications that are filed with both agencies. The QbD approach is focused on pharmaceutical development and manufacturing processes with the aim of ensuring product quality. The International Conference on Harmonisation (ICH) defines QbD as the following (refer to ICH Harmonised Tripartite Guideline Q8 (R2), Pharmaceutical Development):

“A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management.”¹

ICH has developed guidelines on the implementation of QbD, but issues have arisen concerning differing interpretations of these guidelines by the US and Europe. The FDA and EMA pilot program has been developed with the aim of addressing these issues and establishing consistency in the implementation of QbD guidelines in the process of evaluating new drug marketing applications.

In the pilot program to begin on April 1, reviewers from the FDA and EMA will evaluate the Chemistry, Manufacturing and Control (CMC) components of New Drug Applications (NDAs) submitted to the FDA and Marketing Authorization Applications (MAAs) submitted to the EMA, respectively. The two agencies will conduct these assessments separately but in parallel, maintaining communication and consulting

with one another throughout the process. The goal is to establish consistent standards between the agencies in evaluation of QbD data and formulation of regulatory decisions. Participation will be voluntary and include companies that file concurrent applications with the FDA and EMA. The duration of the pilot program is 3 years and is scheduled to end on March 31, 2014. The program will include chemical entities only and not biologically-derived products.

This is one of several examples of the culture of collaboration that has developed between the FDA and EMA in recent years. In recent months, the FDA and EMA indefinitely extended their confidentiality agreements allowing the agencies to share information related to their respective regulatory and scientific processes. Such exchange of information will continue to be beneficial in harmonizing processes and regulatory requirements in both the Good Manufacturing Practice (GMP) and Good Clinical Practice (GCP) environments.

Sources:

ICH Harmonised Tripartite Guideline Q8 (R2), Pharmaceutical Development: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q8_R1/Step4/Q8_R2_Guideline.pdf

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Quality Management System – Defining Corrective and Preventive Action (CAPA) for Clinical Trials

By: Diane Dellaratta, CIS Senior Clinical Compliance Specialist

When developing a Quality Management System (QMS) within the biopharmaceutical industry for clinical trials, a key component of this system is an effective Corrective and Preventive Action (CAPA) program. CAPA requirements are not specifically stated in Good Clinical Practice (GCP) regulations, however, requirements for a QMS and a subsequent CAPA process in clinical trials are guided by ISO 9000 and ICH GCP 5.1.1.

There has been a recent shift in expectations for sponsors and clinical trial oversight. The regulatory agencies are now looking for a structured investigation of issues that are encountered during a clinical trial. Poor CAPA investigations continue to be among the top deficiencies issued to drug, biologic, and medical device companies resulting in warning letters to clinical investigators, institutional review boards, contract research organizations, and sponsors.

Quality in the clinical context addresses the benefits and risks of a medical product or procedure while assuring protection of human subjects, therefore, clinical CAPAs should focus on issues that compromise patient safety and/or data integrity. A systematic CAPA approach includes incident identification (routine non-compliance vs. serious non-compliance), investigation of incident causality, development of an action plan based on root cause analysis, action plan verification and validation, action plan implementation, effectiveness checks and closure. CAPA management programs may also include the analysis and tracking of any GCP compliance trends or issues to identify ongoing quality improvement initiatives across trials and and development projects.

Developing an effective CAPA program is in the industry's self interest to improve the quality of investigations as it has always been either a requirement or an expectation that the biopharmaceutical industry will perform thorough investigations and implement effective CAPA to ensure subject safety and data integrity during clinical trials.

